Human Immunodeficiency Virus

A Medical Dictionary, Bibliography,
and Annotated Research Guide to
Internet References

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and Philip M. Parker, Ph.D., Editors

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FORWARD

In March 2001, the National Institutes of Health issued the following warning: "The number of Web sites offering health-related resources grows every day. Many sites provide valuable information, while others may have information that is unreliable or misleading."[1] Furthermore, because of the rapid increase in Internet-based information, many hours can be wasted searching, selecting, and printing. Since only the smallest fraction of information dealing with human immunodeficiency virus is indexed in search engines, such as **www.google.com** or others, a non-systematic approach to Internet research can be not only time consuming, but also incomplete. This book was created for medical professionals, students, and members of the general public who want to know as much as possible about human immunodeficiency virus, using the most advanced research tools available and spending the least amount of time doing so.

In addition to offering a structured and comprehensive bibliography, the pages that follow will tell you where and how to find reliable information covering virtually all topics related to human immunodeficiency virus, from the essentials to the most advanced areas of research. Public, academic, government, and peer-reviewed research studies are emphasized. Various abstracts are reproduced to give you some of the latest official information available to date on human immunodeficiency virus. Abundant guidance is given on how to obtain free-of-charge primary research results via the Internet. **While this book focuses on the field of medicine, when some sources provide access to non-medical information relating to human immunodeficiency virus, these are noted in the text.**

E-book and electronic versions of this book are fully interactive with each of the Internet sites mentioned (clicking on a hyperlink automatically opens your browser to the site indicated). If you are using the hard copy version of this book, you can access a cited Web site by typing the provided Web address directly into your Internet browser. You may find it useful to refer to synonyms or related terms when accessing these Internet databases. **NOTE:** At the time of publication, the Web addresses were functional. However, some links may fail due to URL address changes, which is a common occurrence on the Internet.

For readers unfamiliar with the Internet, detailed instructions are offered on how to access electronic resources. For readers unfamiliar with medical terminology, a comprehensive glossary is provided. For readers without access to Internet resources, a directory of medical libraries, that have or can locate references cited here, is given. We hope these resources will prove useful to the widest possible audience seeking information on human immunodeficiency virus.

The Editors

[1] From the NIH, National Cancer Institute (NCI): **http://www.cancer.gov/cancerinfo/ten-things-to-know**.

CHAPTER 1. STUDIES ON HUMAN IMMUNODEFICIENCY VIRUS

Overview

In this chapter, we will show you how to locate peer-reviewed references and studies on human immunodeficiency virus.

The Combined Health Information Database

The Combined Health Information Database summarizes studies across numerous federal agencies. To limit your investigation to research studies and human immunodeficiency virus, you will need to use the advanced search options. First, go to **http://chid.nih.gov/index.html**. From there, select the "Detailed Search" option (or go directly to that page with the following hyperlink: **http://chid.nih.gov/detail/detail.html**). The trick in extracting studies is found in the drop boxes at the bottom of the search page where "You may refine your search by." Select the dates and language you prefer, and the format option "Journal Article." At the top of the search form, select the number of records you would like to see (we recommend 100) and check the box to display "whole records." We recommend that you type "human immunodeficiency virus" (or synonyms) into the "For these words:" box. Consider using the option "anywhere in record" to make your search as broad as possible. If you want to limit the search to only a particular field, such as the title of the journal, then select this option in the "Search in these fields" drop box. The following is what you can expect from this type of search:

- **A Profile of Human Immunodeficiency Virus - Infected Adolescents Receiving Health Care Services at Selected Sites in the United States**

  Source: Journal of Adolescent Health; Vol. 19, No. 6, Dec. 1996.

  Contact: Elsevier Science Publishing Company, Society for Adolescent Medicine, Journal of Adolescent Health, 655 Avenue of the Americas, New York, NY, 10010, (212) 989-5800, http://www.elsevier.nl.

  Summary: This article describes a study conducted to determine the demographics and clinical profile of HIV-infected adolescents receiving care at selected sites in the United States. A survey was mailed to physicians in government-funded HIV research and care

programs requesting prevalence data on HIV-infected youth (10-21 years of age) receiving care. A total of 49 percent responded yielding information on 978 subjects. The predominant transmission modes were vertical, blood, and sexual. Three-quarters were of an ethnic or racial minority, and 50 percent were female. Examination of data from selected sites indicates three transmission-driven adolescent HIV epidemics with different characteristics. Minority youth are disproportionately represented. Many vertically infected infants are surviving into adolescence, and sexual activity is a significant transmission factor. HIV-infected youth appear to enter care with considerable immunosuppression. Clinical profiles and treatment patterns appear to differ by transmission mode. It is concluded that further study is needed on adolescent HIV disease progression and determinants of access to care and treatment.

- **Is There A Risk of Human Immunodeficiency Virus (HIV) Transmission in Dialysis Centres?**

  Source: International Journal of STD & AIDS; Vol. 6, No. 2, Mar/Apr 1995.

  Contact: Royal Society of Medicine Services Limited, 1 Wimpole St, London.

  Summary: This editorial considers the prevalence of HIV infection in dialysis units in the United Kingdom. Screening for HIV in dialysis centers is neither a universally adopted nor an accepted policy, often making detection difficult. The rate of seroconversion after patients develop end-stage renal disease and begin dialysis is unknown. Even though they conclude that transmission in the dialysis setting does not appear to be a cause for concern, the authors state that as there are no general recommendations to screen routinely, all dialysis center patients should be treated as if they are HIV positive, and procedures for environmental control, disinfection, and sterilization should be applied.

- **Longitudinal Study of Human Immunodeficiency Virus Transmission by Heterosexual Partners**

  Source: New England Journal of Medicine; Vol. 331, Aug. 1994, p. 341-346.

  Contact: CDC National Prevention Information Network, PO Box 6003, Rockville, MD, 20849-6003, (800) 458-5231, http://www.cdcnpin.org.

  Summary: A prospective study to examine the risk of heterosexual HIV transmission and efficacy of prevention measures is described in this report. This longitudinal study looks at 304 HIV-negative subjects, whose only known HIV risk is having a heterosexual, HIV-positive partner. Results show the risk of transmission appears related to the stage of the HIV infection in the index partner. In addition, genital infections, especially ulcerative, seem to facilitate transmission. Limiting factors to longitudinal studies are that many couples stop having sexual relations before the studies are complete and the ethical requirements for counseling must be considered. The author suggests examining the immunology and virology of partners who remain HIV-negative.

- **Nurse - Midwifery Management of Women With Human Immunodeficiency Virus Disease**

  Source: Journal of Nurse - Midwifery; Vol. 38, No. 2, March/Apr. 1993.

  Contact: Johns Hopkins University, School of Medicine, Division of Pediatric Infectious Diseases, Pediatric AIDS Clinical Trials Group, 600 N Wolfe St Blalock 1142, Baltimore,

MD, 21287, (410) 955-9728. American College of Nurses - Midwives, 818 Connecticut Ave NW Ste 900, Washington, DC, 20006, (202) 728-9860, http://www.midwife.org.

Summary: This article discusses nurse-midwifery management of care, both independent and collaborative, for women with HIV disease. Advantages in using nurse-midwives in the areas of access to care, partner notification, reproductive choice, and breastfeeding are described. Management concerns for HIV disease in pregnancy are reviewed including subjective diagnosis, perinatal transmission, and prenatal and postpartum care. In addition, guidelines for clinical care of AIDS are provided.

- **Antiretroviral Therapy and Medical Management of the Human Immunodeficiency Virus - Infected Child**

  Source: Pediatric Infectious Disease Journal; Vol. 12, No. 6.

  Contact: National Pediatric and Family HIV Resource Center, 30 Bergen St ADMC #4, Newark, NJ, 07107, (973) 972-0410, http://www.pedhivaids.org.

  Summary: This report summarizes results of a meeting on pediatric HIV consultants, and community representatives who met to develop guidelines for state-of-the-art antiretroviral therapy and other medical management of HIV-infected children. Among the topics covered are: 1) identification of "at risk" infants; 2) diagnosis of HIV infection; 3) institution of antiretroviral treatment (including CD4 lymphocyte counts and other clinical criteria); 4) choice of drug and regimen; 5) indications for alternative antiretroviral treatment; and 6) supportive treatment and prophylaxis.

- **Infection With the Human Immunodeficiency Virus in Prisoners: Meeting the Health Care Challenge**

  Source: American Journal of Medicine; Vol. 95, Dec. 1993.

  Contact: Brown University, Miriam Hospital, Fain Building Ste E, 164 Summit Ave 2Fl, Providence, RI, 02906, (401) 793-2500, http://www.brown.edu/departments/brunap/mirindx.htm.

  Summary: This article describes a low-cost program for health care of HIV-infected incarcerated persons, both in the correctional setting and after discharge. Incarcerated persons represent a substantial proportion of HIV-infected individuals in North America. A high proportion of inmates are injecting drug users (IDUs) who often have not received appropriate medical care. Health care of HIV-seropositive prisoners has been less than optimal to date. Among inmates at a Rhode Island correctional facility, 4 percent of the men and 12 percent of the women test seropositive. The key to this program is the linking of the expertise and services of the Rhode Island Departments of Health and Corrections with those of a major medical university. The HIV Management Team, consisting of an attending physician, an Infectious Diseases fellow, and a registered nurse who serves as an on-site coordinator, evaluates patients on intake to the correctional facility and at all subsequent encounters. The program has taken the burden of diagnosis and treatment of HIV-related disease from already overworked physicians working in correctional settings and placed it in the hands of consulting specialists and support staff. Eliminating many of the costly outside appointments has also reduced expenses. Replicating this program in other jurisdictions should be possible, according to the authors.

- **Prevalence of Syphilis, Hepatitis B Virus (HBV), and Human Immunodeficiency Virus (HIV) Infection in New Arrestees at the Lake County Jail, Crown Point, Indiana**

  Source: Journal of Prison & Jail Health; Vol. 12, no. 2, Winter 1993.

  Contact: Eli Lilly and Company, Eli Lilly Corporate Center, Indianapolis, IN, 46285, (317) 276-2000, http://www.lilly.com.

  Summary: This article reviews a study conducted to determine the prevalence in arrestees of syphilis, hepatitis B virus (HBV), and HIV infection by demographic and behavioral characteristics, and to evaluate the costs associated with universal screening for these sexually transmitted diseases compared with a theoretical targeted screening program. Three hundred and nineteen arrestees were screened for syphilis, HBV, and anonymously for HIV infection. The prevalence of syphilis was 2.5 percent; hepatitis B surface antigen prevalence was 1.6 percent; the prevalence of past or present HBV infection was 21.9 percent; and the prevalence of HIV infection was 1.6 percent. Targeted screening for sexually transmitted diseases was found to be more cost-effective.

- **Knowledge, Attitudes, and Practices of Obstetricians - Gynecologists Regarding the Prevention of Human Immunodeficiency Virus Infection**

  Source: Obstetrics & Gynecology; Vol. 81, No. 1.

  Contact: Georgetown University, School of Medicine, Department of Community and Family Medicine, 3750 Reservoir Rd NW, Kober-Cogan Rm 204, Washington, DC, 20007.

  Summary: This study was conducted to assess the knowledge, beliefs, attitudes, and practices regarding HIV of Washington, D.C., office-based obstetricians/gynecologists. Obstetricians/gynecologists who reported providing primary care were interviewed by telephone. The survey response was 62 percent. The percentages of obstetricians/gynecologists who reported assessing the HIV risk of new adolescent and adult patients were 67 and 40 percent. Seventy-two percent reported regularly counseling at risk patients to use condoms for vaginal intercourse, and 60 percent regularly counseled at risk patients to limit their number of sexual partners. Results indicate the percentage of obstetricians/gynecologists who assess and counsel patients about HIV risk is below the 75 percent goal for the year 2000 established by the United States Department of Health and Human Services. The results suggest a need to continue medical education for obstetricans/gynecologists to improve their knowledge and skills in HIV prevention.

- **Human Immunodeficiency Virus - Associated Periodontal Diseases: A Review**

  Source: Journal of Dental Hygiene; Vol. 67, No. 4, May-June 1993.

  Contact: University of Illinois Chicago, 840 S Wood St, Rm7 C/C778, Chicago, IL, 60612, (312) 996-1226.

  Summary: This journal article reviews the classification, etiology, pathogenesis, clinical features, and treatment of periodontal diseases which are associated with HIV infection. It focuses on the clinically distinctive types of periodontal diseases associated with HIV infection. Concentrating on HIV-associated gingivitis, HIV-associated periodontis, necrotizing stomatitis, and necrotizing ulcerative gingivitis, the author identifies diagnostic criteria, discusses prevalence, and examines the microbiology of HIV-related periodontal diseases.

- **Guidelines for Human Immunodeficiency Virus (HIV) - Infected Children and Their Foster Families**

  Source: Pediatrics; Vol. 89, No. 4.

  Contact: American Academy of Pediatrics, Department of Maternal Child and Adolescent Health, Committee on Pediatric AIDS, 141 NW Point Blvd, Elk Grove Village, IL, 60007-1098, (847) 434-4000, http://www.aap.org.

  Summary: This article presents guidelines formulated by the American Academy of Pediatrics regarding placement of HIV-infected children in adoptive or foster care homes and in child care settings. It briefly examines the following topics: diagnostic techniques to identify HIV infection in infants and children, transmission methods, dangers to immunodeficient children from infectious illnesses, and confidentiality and testing issues. The recommendations include the following: 1) HIV-positive children should not be restricted from foster care, adoptive placement, or child care settings, since the danger of transmission in a family or child care environment is negligible; 2) child care personnel need not be informed of a child's HIV status to protect the health of staff or other children; 3) universal precautions in the handling of blood and body fluids should be observed in all child care settings; 4) all preschool child care programs should routinely inform parents whenever a highly infectious illness occurs in any child; and 5) courts should adopt methods for rapid processing of court orders allowing HIV testing of infants and children whenever this would facilitate foster care or adoptive placement.

- **Micronutrients: Implications in Human Immunodeficiency Virus Disease**

  Source: Topics in Clinical Nutrition; Vol. 7, No. 3.

  Contact: Aspen Publishers, 200 Orchard Ridge Dr, Gaithersburg, MD, 20878, (301) 417-7500, http://www.aspenpub.com.

  Summary: This journal article analyzes the use of vitamins and minerals in the treatment of HIV disease. It says that some experts feel that evidence suggests that slightly excessive intakes of beta carotene, vitamins A and E, zinc, and selenium may be associated with an improvement in immune system function. The article says while some proponents of vitamin and mineral therapy suggest that nutrients taken in large quantities will help restore the immune system, the authors feel it is premature to make definitive statements. The article goes on to review deficiencies specific to HIV and to address toxicities associated with megadoses of nutrients. It first looks at nutrition and immunity, then analyzes specific micronutrient deficiencies, such as B vitamins and minerals, in HIV infection. The possibilities of megadose therapy are examined, looking at toxicities in substances such as Vitamin C, iron, zinc, and selenium.

- **Sexual Abuse of Human Immunodeficiency Virus - Positive Children: Outcomes for Perpetrators and Evaluation of Other Household Children**

  Source: American Journal of Diseases of Children; Vol. 146.

  Contact: Duke University, Medical Center, P O Box 3971, Durham, NC, 27710.

  Summary: This article presents the results from a study to determine: 1) the prevalence of sexual abuse among siblings and other children living with sexually abused HIV-positive children; and 2) if programs designed to restrain identified perpetrators from further acts of child sexual abuse were instituted. This study demonstrated that the majority of children who cohabited with HIV-positive, sexually abused children were themselves also sexually abused. Identified assailants were members of the extended

households. None of the identified assailants was tried for a criminal offense, restricted from unsupervised visits of the children or required to participate in offender therapy.

- **Human Immunodeficiency Virus Transmission by Child Sexual Abuse**

  Source: American Journal of Diseases of Children; Vol. 145.

  Contact: Duke University, Medical Center, P O Box 3971, Durham, NC, 27710.

  Summary: This study describes the results of the evaluation of sexually abused children, the circumstances surrounding the abusive experiences, the perpetrators, and the means by which the children had acquired HIV. Data from this study indicate that child sexual abuse was the proven mode of transmission in at least 4 percent of all the children in the study with HIV. The abused children lived in circumstances that put them at risk for sexual abuse and HIV infection (promiscuous adult sexual activity with multiple partners in the child's home; physical trauma; lack of barrier protection; genital mucosal lesions; and drug and alcohol use). Assailants abused children in spite of knowing themselves or the child to be HIV positive.

- **Human Immunodeficiency Virus [Acquired Human Immunodeficiency Syndrome (AIDS) Virus] in the Athletic Setting**

  Source: Pediatrics, Vol. 88, No. 3, September 1991.

  Contact: American Academy of Pediatrics, Department of Maternal Child and Adolescent Health, Committee on Pediatric AIDS, 141 NW Point Blvd, Elk Grove Village, IL, 60007-1098, (847) 434-4000, http://www.aap.org.

  Summary: This journal article offers recommendations from the American Academy of Pediatrics regarding HIV transmission in the athletic setting. After presenting background information on the possibility of infection during an athletic contest, it lists recommendations that include allowing athletes infected with HIV to participate in sports, respecting an athlete's right to confidentiality, and following universal precautions.

- **Human Immunodeficiency Virus Infection Among Homeless Men in a New York City Shelter**

  Source: Archives of Internal Medicine; Vol. 150, no. 10.

  Contact: Saint Vincents Catholic Medical Centers of New York, Saint Vincents Hospital Manhattan, Comprehensive HIV Center, 153 W 11th St, New York, NY, 10011, (212) 604-8321, http://www.svcmc.org/hiv/manhattan/staff.asp.

  Summary: This reprint of a journal article outlines the result of a study of Human immunodeficiency virus (HIV) infection among homeless men in a congregate shelter in New York, NY, associated with mycobacterium tuberculosis infection, where seroprevalence is relatively high. It concludes that seropositivity for HIV correlated significantly with intravenous drug use and active tuberculosis. Most cases of active tuberculosis were among homeless men with Acquired immunodeficiency syndrome (AIDS) or AIDS-related complex; and significant CD4 lymphocyte depletion was associated with active tuberculosis. Compliance rates with return for HIV antibody test results, medications, and follow-up visits were 70 percent, suggesting a significant degree of knowledge, awareness, and personal concern regarding HIV infection among homeless men; yet 28 percent of homeless injecting drug users (IDU's) continue active drug injection, despite HIV infection. Cohabitation in overcrowded congregate

dormitories creates a risk of airborne transmission of tuberculosis, which is a common reactivation infection in HIV-seropositive homeless men. Medically appropriate housing should be provided to such homeless persons, and expanded HIV antibody testing, counseling, and medical services on-site should be offered to residents of shelters.

Federally Funded Research on Human Immunodeficiency Virus

The U.S. Government supports a variety of research studies relating to human immunodeficiency virus. These studies are tracked by the Office of Extramural Research at the National Institutes of Health.[2] CRISP (Computerized Retrieval of Information on Scientific Projects) is a searchable database of federally funded biomedical research projects conducted at universities, hospitals, and other institutions.

Search the CRISP Web site at **http://crisp.cit.nih.gov/crisp/crisp_query.generate_screen**. You will have the option to perform targeted searches by various criteria, including geography, date, and topics related to human immunodeficiency virus.

For most of the studies, the agencies reporting into CRISP provide summaries or abstracts. As opposed to clinical trial research using patients, many federally funded studies use animals or simulated models to explore human immunodeficiency virus. The following is typical of the type of information found when searching the CRISP database for human immunodeficiency virus:

- **Project Title: ACTG 383:SUBJECTS W/ HEPATITIS C VIRUS & HUMAN IMMUNODEFICIENCY VIRUS**

  Principal Investigator & Institution: Friedman, Harvey; University of Pennsylvania 3451 Walnut Street Philadelphia, PA 19104

  Timing: Fiscal Year 2001

  Summary: This abstract is not available.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: ADJUVANT DNA VACCINES FOR SYSTEMATIC THERAPY OF AIDS**

  Principal Investigator & Institution: Fuller, Deborah H.; Powderject Vaccines, Inc. 585 Science Dr Madison, WI 53711

  Timing: Fiscal Year 2001; Project Start 30-SEP-2001; Project End 29-SEP-2002

  Summary: Highly active antiretroviral therapy (HAART) suppresses HIV viral replication and restores immune function in HIV-infected individuals but HIV-1 can still persist in circulating, resulting CD4+ T cells. Immunotherapeutic strategies capable of targeting or eliminating the reservoir of HIV-1 infected, quiescent T cells represent an attractive possibility for control or eradication of AIDS. In particular vaccine stimulation of HIV-specific T cell responses during T cell recovery and reduced viral burden induced by anti-virals could result in reduction or elimination of residual virus and infected cells. Our recent studies demonstrate that particle-mediated DNA vaccination

[2] Healthcare projects are funded by the National Institutes of Health (NIH), Substance Abuse and Mental Health Services (SAMHSA), Health Resources and Services Administration (HRSA), Food and Drug Administration (FDA), Centers for Disease Control and Prevention (CDCP), Agency for Healthcare Research and Quality (AHRQ), and Office of Assistant Secretary of Health (OASH).

to the skin can induce CTL and protective immune responses against a highly pathogenic, heterologous SIV challenge in the macaque model for AIDS. These results suggest that DNA vaccination may be an effective strategy for therapy of HIV. We will evaluate the enterotoxins Vibrio cholerae Cholera toxin (CT) and E. coli heat-labile enterotoxin (LT) in the form of DNA as novel Th1 adjuvants for DNA vaccines. Our goal is to optimize DNA vaccine induction of peripheral blood CTL and T helper cell responses. We will test the potential for adjuvanted skin-administered DNA vaccines to induce or boost SIV-specific T cell therapy. These studies are designed to demonstrate feasibility of the approach and support development of skin administered DNA vaccines for therapy against HIV disease, including initiation of human clinical trials. Our specific aims are: 1) Test the hypothesis that co-delivery of SIV DNA vaccines with plasmids expressing bacterial enterotoxin adjuvants to the skin enhances antigen-specific CTL and Th cell responses in monkeys. 2) Measure the efficacy of DNA vaccination to the skin in combination with anti-retrovirals for therapy of SIV infection in rhesus macaques. 3) Develop therapeutic HIV DNA vaccine vectors for clinical trials and test immunogenicity in the murine model. 4) Test the immunogenicity of therapeutic HIV DNA vaccine vectors in asymptomatic HIV-1 infected human volunteers receiving HAART.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: ADULT AIDS CLINICAL TRIALS GROUP**

  Principal Investigator & Institution: Saag, Michael S.; Professor of Medicine; Medicine; University of Alabama at Birmingham Uab Station Birmingham, AL 35294

  Timing: Fiscal Year 2001; Project Start 01-APR-1992; Project End 31-DEC-2004

  Summary: (adapted from the application's abstract): This is a competitive renewal of the UAB ACTU, established in 1992 at the UAB AIDS Outpatient (1917) Clinic, and is submitted in conjunction with the ACTG Group application led by Robert T. Schooley, M.D. (Principal Investigator). The UAB ACTU has developed and implemented clinical trials that link therapeutics and pathogenesis, a priority of the ACTG recompetition. With the last competitive renewal, investigators from Emory University were added to the UAB ACTU site through the establishment of a subunit at the Ponce de Leon Clinic in Atlanta. Since that time, investigators from the UAB/Emory ACTU have continued to assume leadership positions within the ACTG and have played a role in the establishment and performance of the Group's Scientific Agenda. The UAB/Emory ACTU has the primary foci: (1) establish collaborative studies within the ACTG that focus on the clinical significance and therapeutic implications of recent insights into **human immunodeficiency virus** (HIV) viral- and immuno- pathogenesis; (2) further develop improved therapeutic approaches in the treatment of cytomegalovirus, mycobacterial, human papillomavirus, herpes- related viruses, mycoplasma, and fungal disease, areas where UAB/Emory investigators have made contributions and have expertise; (3) continue to improve access of women and minorities to ACTG-related clinical trials through the 1917 Women's Clinic and the Women's Clinic at the Ponce de Leon Center and through targeted outreach programs to HIV-infected African Americans; and (4) continue to contribute to the overall mission and Scientific Agenda of the ACTG through active participation in Group activities and provision of leadership within key administrative committees.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: ADULT AIDS CLINICAL TRIALS UNIT**

  Principal Investigator & Institution: Fass, Robert J.; Internal Medicine; Ohio State University 1800 Cannon Dr, Rm 1210 Columbus, OH 43210

  Timing: Fiscal Year 2001; Project Start 30-SEP-1987; Project End 31-DEC-2004

  Summary: (adapted from the application's abstract): The Ohio State University AIDS Clinical Trials Unit (ACTU) proposes to collaborate with the Adult ACTG Coordinating and Research Operations Center (CORC) that has identified Robert T. Schooley, M.D., from the University of Colorado as Group Leader. The Ohio State University ACTU proposes to participate in the discovery and development of therapies to improve the quality and duration of life of **Human Immunodeficiency Virus** (HIV)-infected individuals. The proposed cadre of investigators are from multiple disciplines including infections diseases, virology, immunology, nursing, oncology, neurology, gynecology and clinical pharmacology. They have conducted single- and multi-center HIV/AIDS clinical trials and have established multi-disciplinary collaborations to participate in the AACTG scientific agenda. There are nursing, pharmacy, social work, data management and outreach personnel proposed to: recruit and screen potential patients including women and minorities; implement clinical research protocols; perform protocol required assessments; dispense investigational agents and appropriately document clinical events; and meet all data reporting requirements. There are certified laboratory facilities proposed to conduct or obtain virologic, immunologic and pharmacologic assays in support of AACTG clinical trials with appropriate internal quality controls. There are clinical facilities proposed, including a dedicated Infectious Diseases inpatient service, a full-time outpatient clinic with an ACTU pharmacy and a General Clinical Research Center to execute protocols and provide clinical care in an integrated fashion.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: ADULT AIDS CLINICAL TRIALS UNIT**

  Principal Investigator & Institution: Jacobson, Jeffrey M.; Clinical Trials Unit; Mount Sinai School of Medicine of Nyu of New York University New York, NY 10029

  Timing: Fiscal Year 2001; Project Start 30-JUN-1986; Project End 31-DEC-2001

  Summary: The Mount Sinai/Beth Israel Adult AIDS Clinical Trials Unit (ACTU) is applying for competitive renewal of its multi-hospital consortium, a member of the AIDS Clinical Trials Group (ACTG) program since 1987. Our unit has demonstrated leadership in its ability to generate protocols and contribute to a multidisciplinary scientific agenda, to recruit a diverse patient population with HIV infection, coordinate data and specimen collection, perform virologic and immunologic evaluations as well as pharmacokinetic studies, collect and report high quality clinical and laboratory data, and collaborate with NIAID and other institutions involved in adult and pediatric trials. This unit has enrolled more than 1,000 patients on over 60 different protocols, and has consistently been among the leaders in enrollment of women, minorities, and intravenous drug users. Based on data in the ACTG nationwide database as of 12/16/94, our unit was first in enrollment of patients with a history of IV drug use, second in the number of Hispanics, third in total number of women enrolled, and fourth in the number of Blacks enrolled of all ACTUs across the country. We were first in each of these categories in New York State, except women. By integrating and coordinating access to clinical trials with access to clinical care, despite a decrease in our total budget request, we propose: (1) to accrue and retain a minimum of 75 new patients per year in diverse multicenter trials of new treatments for **human immunodeficiency virus** type 1 (HIV-1) infection and the associated opportunistic infections and malignancies. The

studies will be conducted at hospitals which serve some of the highest AIDS prevalence areas in the country and can offer access to trials to large numbers of HIV-infected persons from groups which have been traditionally underrepresented in AIDS trials. By capitalizing on the investigative strengths of our multidisciplinary research team, recruited from within and outside our institutions, we also propose: (2) to contribute to the design and conduct of trials that will explore the pathogenesis of HIV-1 infection and further the research agendas of the ACTG Scientific Committees.

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- **Project Title: AIDS CLINICAL TRIALS UNIT**

  Principal Investigator & Institution: Mitsuyasu, Ronald T.; Director; Medicine; University of California Los Angeles 10920 Wilshire Blvd., Suite 1200 Los Angeles, CA 90024

  Timing: Fiscal Year 2001; Project Start 30-JUN-1986; Project End 31-DEC-2004

  Summary: (adapted from the application's abstract): The ACTU has been an active participant in clinical trials for the treatment of **human immunodeficiency virus** (HIV) and related diseases of the ACTG since 1986. Metropolitan Los Angeles is culturally diverse and its residents are significantly affected by the AIDS epidemic. The UCLA ACTU, located on the west side of Los Angeles, with its subunits in various areas of greater Los Angeles is applying for competitive renewal as part of the ACTG under the group leadership of Robert T. Schooley, M.D. The goal of the UCLA ACTU is to fully participate in the scientific and operational activities of the Group. This would include involvement in the Group scientific and administrative leadership via participation in ACTG research agenda committees, working groups and protocol teams, accruing patients to studies, and providing laboratory expertise in specific areas in which this ACTU has expertise such as immunology. Both the UCLA main site and the Harbor-UCLA subunit will enroll patients in high priority Phase I, II and III clinical trials of antiretroviral drugs, immune-based therapies and treatments for opportunistic infections, neurologic disorders and complications of HIV treatment. Patients also will be enrolled and maintained in the longitudinal assessment study (ALLRT protocol) to help answer important questions about the pathogenesis and clinical management of HIV, as well as in other studies designed to address the specific aims of the ACTG. Administrative oversight, specimen storage and shipping, performance of protocol mandated laboratory assays, data quality assurance, maintenance of a CAB and outreach activities to stimulate greater participation of women and racial/ethnic minorities in ACTG clinical trials will be the responsibility of the UCLA main site.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: AIDS DEMENTIA COMPLEX AND NEUROPHYSIOLOGY**

  Principal Investigator & Institution: Benos, Dale J.; Professor & Chair; Physiology and Biophysics; University of Alabama at Birmingham Uab Station Birmingham, AL 35294

  Timing: Fiscal Year 2001; Project Start 01-SEP-1993; Project End 31-JUL-2004

  Summary: Central nervous system (CNS) involvement often occurs in individuals infected with **human immunodeficiency virus** type-1 (HIV-1). The most common clinical syndrome characterized by cognitive, motor, and behavioral disturbances is the acquired immunodeficiency syndrome (AIDS) dementia complex (ADC) or HIV-associated dementia (HAD), and is unique to HIV-1 infection. Although anti-retroviral agents (RT and protease inhibitors) are being used in HIV-infected individuals, it is not yet clear how these agents will affect HAD or if these drugs can even penetrate the

brain. Thus, a major problem facing HAD patients is the that drugs used to combat systemic viral infection may not influence the CNS, a potential reservoir for virus. Because the physiological status of the brain in AIDS patients cannot be readily sampled, there is a critical need for the development of non-invasive techniques to detect and monitor the extent of HIV- associated cognitive/motor disorders. In this application, we intend to translate basic science findings obtained in the previous grant period to the human, and perform clinical cognitive studies on HIV-infected patients. We will develop non- invasive methodologies, based on 31P nuclear magnetic resonance (NMR) spectroscopy, eventually to investigate how pharmacological and/or immunological manipulations can affect the pathological and psychomotor abnormalities in humans infected with HIV-1. We will also correlate such brain metabolic changes with the degree of dementia in HAD patients. This will be accomplished through he neuropsychological assessment of participants. Thus, a sophisticated array of experimental approaches will be used to define molecular mechanisms underlying the pathophysiology of HAD, which ultimately will be critical for the development and assessment of new therapeutic strategies. There is one specific aim: 1) to test the hypothesis that cerebrospinal fluid (CSF) viral load, CD4+ cells, and/or cytokine content correlates with increases in pH in various regions of the brain, specifically the basal ganglia and cerebellum. In addition, neuropsychological testing will be performed on all subjects enrolled in this study in an effort to a) assess subject neurocognitive/motor status and b) to link the clinical developmental stage of dementia with CSF viral load and brain pH.

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- **Project Title: AIDS INTERNATIONAL TRAINING AND RESEARCH PROGRAM**

  Principal Investigator & Institution: Johnson, Warren D.; Chief and Professor; Medicine; Weill Medical College of Cornell Univ New York, NY 10021

  Timing: Fiscal Year 2001; Project Start 21-SEP-1998; Project End 31-MAY-2003

  Summary: The objective of this proposal is to build on previous successful collaborations between (Cornell) researchers from Weill Medical College of Cornell University (formerly known as Cornell University Medical College), the Haitian Study Group on Kaposi's Sarcoma and Opportunistic Infections (GHESKIO), the Haitian Red Cross, and the Haitian Ministry of Health to develop a national blood safety program for Haiti, which may serve as a model for blood safety programs in other developing countries. Studies by Cornell-GHESKIO researchers in 1983, during the early stages of the HIV epidemic in Haiti, demonstrated that 40% of the HIV infected women in Port-au-Prince had received a blood transfusion. Cornell-GHESKIO researchers identified a for-profit blood bank as a source of many of these transfusions. Based upon this information, the Haitian Ministry of Health closed the for-profit blood bank in 1986, and placed the Haitian Red Cross in charge of blood safety in Haiti. In 1988, with the assistance of a Fogarty training grant, Cornell-GHESKIO researchers trained the administration and technical staff of the Haitian Red Cross in blood safety testing. The Haitian Red Cross, with on-going technical advice from Cornell-GHESKIO researchers, continues to monitor blood safety in Port-au-Prince. The current proposal aims to solidify the training of the Haitian Red Cross in Port-au-Prince and to expand their activities to rural Haiti where 70% of the population lives. The highest priority will be given to the training of personnel directly involved in blood banking operations (laboratory technicians, counselors and data entry staff), as well as physicians who are most likely to use blood products (obstetricians and surgeons). In addition, the general public will be educated and encouraged to give regular blood donations and to avoid

paid donors. The current proposal also aims to address several areas of research of importance for blood safety in Haiti: 1) determine the prevalence rate and risk factors for infection with blood borne pathogens among blood donors in urban and rural Haiti including HIV-1, HIV-2, HTLV-1, HCV, HBV, syphilis, and malaria; 2) determine the prevalence and risk factors among blood donors of HIV-infected individuals in the "window period", the time between HIV infection and development of HIV antibodies detectable by standard ELISA assays.

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- **Project Title: AN ADJUVANTED THERAPEUTIC DNA VACCINE FOR AIDS**

  Principal Investigator & Institution: Haynes, Joel R.; Powderject Vaccines, Inc. 585 Science Dr Madison, WI 53711

  Timing: Fiscal Year 2003; Project Start 01-JUL-2003; Project End 31-DEC-2006

  Summary: (provided by applicant): The program project application of PowderJect Vaccines, Inc. (PJV) and the University of Pittsburgh entails the evaluation of a therapeutic DNA vaccine regimen for **human immunodeficiency virus** (HIV) infection using the simian immunodeficiency virus (SIV) model in rhesus macaques. The therapeutic DNA vaccine to be evaluated is a single, CMV promoter-based DNA vaccine vector encoding the gag, RT, and nef products of the 17e Fr clone of SIVmac239. This vaccine will be delivered using the clinically-proven particle-mediated (gene gun) delivery device that has been shown to elicit Th1 humoral and cellular responses in man and monkeys. The design of the SIV DNA vaccine vector is intended to closely mimic a clinical HIV-1 DNA vaccine vector that is on a clinical track for human evaluation via the joint clinical development efforts of GlaxoSmithKline (GSK) and PJV. Therefore, the activities described in this application are an integral part of the GSK/PJV clinical co-development efforts for prophylactic and therapeutic AIDS vaccines and will serve three important functions to promote clinical success. First, these activities will provide non-human primate model validation of the immunogenicity and therapeutic vaccine potential of GSK's clinical DNA vaccine vector strategy in the highly relevant SIV/rhesus monkey model. Our recent DNA vaccine trials in the rhesus model using earlier vectors have proven our ability to induce significant prophylactic and therapeutic effects via particle-mediated DNA vaccine technology, in addition, these activities will allow for the evaluation of an exciting new DNA vaccine adjuvant vector encoding the heat-labile enterotoxin of E. coli. This adjuvant vector has been proven safe in an extensive nonhuman primate safety trial and dramatically augments Th1 cellular immune responses to a variety of model antigens in mice and monkeys. Finally, activities described in this application will provide important mechanistic data regarding the induction of systemic and mucosal immunity and virus load containment following therapeutic DNA vaccination (with and without adjuvant) in the rhesus SIV model. Specifically, the proposed therapeutic DNA vaccine trials will allow for determination of the importance of the strength and quality of systemic cellular responses, the role of mucosal immunity and importance of gut viral reservoirs, and the importance of DC / T cell interactions in therapeutic DNA vaccine efficacy.

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- **Project Title: ANALYSIS OF INTERACTION BETWEEN DC AND HIV VIRIONS**

  Principal Investigator & Institution: Wu, Xiaoyun; Assistant Professor; Medicine; University of Alabama at Birmingham Uab Station Birmingham, AL 35294

  Timing: Fiscal Year 2002; Project Start 01-JUN-2002; Project End 31-MAY-2004

Summary: Human immunodeficiency virus type 1 (HIV-1) infection continues to spread globally and predominantly by heterosexual contact. In order for HIV to be transmitted through sexual intercourse (heterosexual and homosexual) the virus must cross the epithelial barrier of the mucosa. Rational prophylactic strategies for controlling HIV transmission rely upon a detailed cellular and molecular understanding of the initial interactions that occur between the virus and host after sexual exposure. While advances have been made to identify the kinds of cell that are first infected, very little progress has been made to delineate and understand the earliest interaction(s) of HIV-1 virions with the mucosal surface. On uninjured mucosal membranes, the first cells encountered are CD4-negative epithelial cells. Studies of mucosal transmission (vaginal) in a non-human primate model demonstrated that the first cells infected (expressing viral RNA 18 hrs after infection) are Langerhans' cells, which are located within the mucosa, beneath the epithelial cells. Although evidence continues to accumulate that suggests other cellular molecules mediate attachment of virions to the surface of CD4-negative cells there remains a great void in our understanding of the molecular and cellular events that proceed infection of Langerhans' cells. This is due in great measure to the lack of experimental methods with sufficient sensitivity and specificity to directly analyze the interactions of HIV-1 virions with the mucosa. Our previous finding clearly demonstrated the ability to directly visualize infectious HIV-1 virions that have been labeled with GFP. We have also demonstrated that GFP+ virions can be quantitatively visualized on both cell and mucosal surfaces. Thus, we propose to conduct a detailed and dynamic analysis of HIV-1 mucosal transmission. The research proposed in this grant address questions regarding the molecular determinants (viral and cellular) of initial virus attachment, penetration of virus into or across the mucosa and virus-host cell infection. Our central hypothesis is that luminal epithelial cells play an important role in the earliest events of HIV-1 mucosal transmission. It follows that this work has significant clinical implications for providing the experimental basis to proceed rationally with new strategies for inhibiting HIV-1 transmission. To test our central hypothesis we propose: (1) To define the nature of the interaction between HIV-1 and primary epithelial cells - at the level of virus binding, entry and infection; (2) To define the host-cell and virus-associated molecular determinants which mediate the physical interaction between HIV-1 virions and primary epithelial cells; (3) To define the nature of the interaction between HIV-1 virions and epithelial cells using an organ culture system and human and monkey mucosal tissues (vaginal and intestinal) and (4) To analyze the earliest events of HIV-1 mucosal transmission in animal models.

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- **Project Title: ANTIBODIES TO HPV CAPSID PROTEINS AS IMMUNITY CORRELATES**

  Principal Investigator & Institution: Viscidi, Raphael P.; Associate Professor; Pediatrics; Johns Hopkins University 3400 N Charles St Baltimore, MD 21218

  Timing: Fiscal Year 2001; Project Start 01-AUG-1998; Project End 31-JUL-2003

  Summary: (Adapted from the Investigator's Abstract): One gap in our understanding of the biology of HPV infection is that it is not known if infection with an HPV type confers immunity to subsequent reinfection with the same type. The availability of sensitive and specific serological assays using virus-like particles (VLPs) composed of HPV capsid proteins now makes it possible to address this issue. Studies to determine whether anti-capsid protein antibodies will prevent infection in human populations would have relevance for efforts to develop VLP-based vaccines and may provide an estimate of the level of anti-capsid antibody that a vaccine would have to induce in order to be

protective. We recently obtained permission to test serum specimens from women enrolled in three large prospective studies of the natural history of HPV infection; the CDC sponsored HERS, the NIH sponsored WIHS, and the NCI sponsored Guanacaste Project in Costa Rica. The former two studies include HIV positive and HIV negative women. Because HIV infected individuals may be a prime target population for an HPV vaccine, it is important to know if the relationship of pre-existing anti-HPV antibodies to the risk of subsequent HPV infection for these women is the same or different from that for HIV negative women. Recruitment sera from women enrolled in three studies will be tested by ELISA for antibodies to VLPs of HPV-16, -31, -18, -45, -6, and -11. The antibody status at recruitment will be related to incident HPV infection and/or disease over a follow-up period of 4-7 years. The following are the questions to be addressed in this proposal: (1) Are serum antibodies to VLPs of a particular HPV type associated with a decreased frequency of incident infection with that HPV type? (2) Are serum antibodies to an HPV type associated with a decreased frequency of incident infection with genetically closely related types? (3) What is the minimum level of VLP antibodies that confers full protection? (4) Are serum antibodies to VLPs associated with reinfections characterized by a lower viral load, shorter duration of viral shedding and/or lower risk of cytological abnormalities than that of incident infections in antibody negative women? (5) Are serum antibodies to HPV VLPs in HIV seropositive women, as compared to HIV seronegative women, associated with the same or a higher frequency of incident HPV infection and/or disease? (6) In HIV seropositive women, is the extent of immunodeficiency, as measured by CD4+ cell counts, inversely correlated with the degree of protection provided by pre-existing anti-VLP antibodies?

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- **Project Title: ANTI-HIV-1 ACTIVITY OF MANNAN-BINDING LECTIN**

  Principal Investigator & Institution: Spear, Gregory T.; Professor; Rush-Presbyterian-St Lukes Medical Ctr Chicago, IL 60612

  Timing: Fiscal Year 2001; Project Start 01-AUG-2000; Project End 31-JUL-2004

  Summary: (Adapted from Abstract) Mannan-binding lectin (MBL) is an effector molecule of the innate immune system found in human serum that binds to carbohydrate and mediates recognition and killing of pathogens. Although the **human immunodeficiency virus** (HIV) would appear to be a good target of MBL due the unusually high level of high mannose glycosylation of gpl20, this has not been well studied. Our research - group found that MBL binds to a wide range of HIV isolates including primary isolates. Thus, MBL has several highly desirable features of an anti-HIV effector molecule; 1) it binds to a wide range of virus isolates; 2) binding of MBL to HIV is likely via the unusual cluster of high mannose microgram levels. These features of MBL suggest it mediates anti-viral activity in vivo and inforrnation gained about its interaction with HIV will lead to a better understanding of both the role of innate immunity during HIV infection and the importance of carbohydrate structures on HIV. The overall goals of this study are to determine the mechanism of interaction between MBL and HIV and to determine methods to enhance the anti-HIV activity of MBL. These goals will be accomplished by the following specific aims: Deterrnine the type and location of carbobydrates responsible for high-level binding of HIV- 1 to MBL. 2. Investigate factors that affect the interaction between HIV and MBL. 3. Utilize inhibitors of glycosylation to enhance biological effects of MBL. Exarnine the interaction of MBL with anti-viral antibodies in mediating anti-viral effects. Deterrnine the interaction of HIV-1 with MBL in vivo.

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- **Project Title: ANTIMICROBIALS AGAINST HSV AND HIV-1 INFECTION**

  Principal Investigator & Institution: Herold, Betsy Clement.; Chief, Division of Pediatric Infectious; Children's Hospital Med Ctr (Cincinnati) 3333 Burnet Ave Cincinnati, OH 45229

  Timing: Fiscal Year 2001

  Summary: The goal of this program is to develop safe and effective topical antimicrobial agents for intravaginal use that will block sexual and perinatal transmission of viral and bacterial pathogens. Focusing on human primary cell cultures, Project 1 will evaluate candidate compounds that block **human immunodeficiency virus** type 1 (HIV-1) and herpes simplex virus types 1 and 2 (HSV-1 and HSV- 2) infection. Although cell tropism for HSV and HIV is quite different and both viruses bind unique receptors and co-receptors during the processes of attachment and penetration, both interact with a common cell surface component, heparan sulfate (HS) glycosaminoglycans (GAGs). Similarly, the bacterial STD pathogens, Chlamydia trachomatis and N. gonorrhoeae, which are the focus of studies in Project 2, interact with HS GAGs during bacterial invasion. The binding of microbes to cell surface HS can be competitively blocked by sulfated polysaccharides (SPS). We have successfully identified several SPS or sulfated polymers that inhibit HSV and HIV-1 infection and exhibit little or no cytotoxicity. In further studies, we will more extensively evaluate this class of compounds. This will involve defining the HS sequence required for HSV invasion of cells of the human female genital tract as this receptor is the target for this class of candidate antimicrobials. We will also evaluate novel classes of candidate antimicrobials which may block other steps in viral pathogenesis. Because compounds cannot be optimally evaluated using cell lines, which are transformed and differ markedly from in vivo conditions, we have established primary cell culture systems for evaluation of candidate compounds. Using these model culture systems, we propose to further evaluate SPS and related compounds, identify new compounds, and determine how these agents inhibit viral pathogens. Knowledge gained about the mechanism of antiviral activity will facilitate the selection of rational combinations of compounds with enhanced potency or limited toxicities. Taken together, results of these studies should lead to identification of promising novel agents for topical formulation for intravaginal use to prevent STDs.

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- **Project Title: ASSESSMENT OF CD8 SUPPRESSION OF HIV/SIV TO VACCINES**

  Principal Investigator & Institution: Gupta, Phalguni; Professor; Infectious Diseases and Microbiology; University of Pittsburgh at Pittsburgh 350 Thackeray Hall Pittsburgh, PA 15260

  Timing: Fiscal Year 2001; Project Start 15-SEP-2000; Project End 31-AUG-2003

  Summary: (Adapted from Applicant's Abstract) Although an effective vaccine must elicit high levels of broad HIV-1 specific neutralizing antibodies, CTLs and helper T cell response, none of these immune parameters has been shown to control virus replication and prevent the development of disease in a consistent manner. Therefore, it is necessary to search for other immune markers that may be correlated with protection. Recently, some studies have shown that protection in SIV vaccinated monkeys are correlated with CD8+ cell suppressive activity against SIV, but not with CTL or virus neutralizing antibody. The hypothesis is that CD8 suppressive activity is correlated with protection against challenge virus. The overall objective of this project is to develop a high throughput CD8 suppression assay with fresh and frozen cells, and to determine whether the level of this antiviral activity is increased following immunization in

humans and correlated with protection against challenge virus in the SIV/Macaque model. Specific aims of the project are 1) to develop a high through put quantitative CD8 suppression assay for HIV-1 and SIV. The present assay format will be miniaturized such that it would require small numbers of cells and be performed rapidly in fresh and frozen cells. 2) To determine whether CD8 suppression of SIV, like that of HIV-1, is dependent on phenotypic properties of SIV. 3) To evaluate longitudinally the level of CD8 suppressive activity against the immunizing strain of HIV-1 and CCR5 tropic HIV-1 in vaccinated humans enrolled in the AVEG studies. 4) To evaluate longitudinally the level of CD8 suppressive activity against the immunizing and challenge strain of SIV in vaccinated monkeys and to determine whether its level is correlated with protection in the NCVDG study. The information generated from this project will be extremely useful in determining the utility of the suppressive activity in evaluating efficacy of a vaccine.

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- **Project Title: BLOOD BRAIN BARRIER DYSFUNCTION--AIDS NEUROLOGIC DISEASE**

  Principal Investigator & Institution: Nelson, Jay A.; Director & Professor; Molecular Microbiol and Immun; Oregon Health & Science University Portland, OR 972393098

  Timing: Fiscal Year 2001; Project Start 01-APR-1994; Project End 28-FEB-2003

  Summary: (Adapted from applicant's abstract): The long term goal of this project is to understand the mechanism of human immunodeficiency (HIV)-induced central nervous system (CNS) disease in AIDS. AIDS dementia complex (ADC) is an important neurological syndrome occurring in approximately 10-25 percent of HIV-infected individuals. Even with the success of anti-HIV triple drug therapy in eradicating virus from the circulatory system, recent evidence has indicated that the brain is still a major reservoir of virus. Although ADC has been the subject of intense study by many groups, the cause(s) of the syndrome are unknown. The overall aim of this project is to characterize the role of HIV infection of human brain capillary endothelial (BMVEC) cells in the pathogenesis of AIDS dementia. MVEC are naturally infected by HIV in vivo in both the brain and bone marrow of humans as well as SIV-infected macaques. The investigators hypothesize that HIV infection of BMVEC contributes to AIDS neuropathogenesis by acting as a reservoir of viral amplification which facilitates transfer of virus into the brain parenchyma. In addition, viral infection of BMVEC may perturb formation of tight junctions (TJ) in the BBB with neurotoxic consequences. Over the past funding period, the investigators have identified the HIV gp120 sequences which mediate HIV entry into BMVEC as well as the cellular adhesion molecules which are upregulated and may alter the trafficking of peripheral blood mononuclear cells into the brain parenchyma. They have also obtained preliminary evidence that HIV inhibits the formation of TJ which are essential for BBB function. Finally, they have established an in vitro BBB (DIV BBB) which demonstrates the same functional and physiological characteristics of the BBB in vivo such as high electrical resistance and selective transport of ions from the luminal to the abluminal compartment. In the current proposal, they plan to extend these observations to understand mechanisms of HIV neuroinvasion and pathogenesis. In the first specific aim, they will identify mechanisms which mediate intracellular trafficking of virus to the basolateral surface which may determine the ability of the virus to cross the BBB. In these experiments, they will introduce into the cytoplasmic tail of gp 41, which has been implicated in the trafficking of glycoprotein to the basolateral surface, to test in polarized BMVEC. In the second specific aim, they will identify the HIV gene(s) that dramatically inhibit the formation of

TJ utilizing viral vectors expressing individual and combinations of viral genes. In the last specific aim, they will utilize the DIV BBB to examine the ability of HIV to perturb barrier function, including: decrease in electrical resistance, permeability to sucrose and stereospecific uptake of amino acids. This model will also be used to examine the ability of trafficking mutants to cross the DIV BBB as well as the effect of HIV genes which inhibit TJ formation. The successful completion of this project will identify mechanisms of HIV entry into the brain parenchyma as well as viral perturbation of BBB. Experiments proposed in this project aim to establish the usefulness of the DIV BBB as a model for analyzing the function of this organ during disease processes.

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- **Project Title: CD8+ T CELL CYTOKINE PRODUCTION IN HIV-1 INFECTION**

  Principal Investigator & Institution: Goepfert, Paul A.; Assistant Professor of Medicine and Micr; Medicine; University of Alabama at Birmingham Uab Station Birmingham, AL 35294

  Timing: Fiscal Year 2001; Project Start 20-SEP-2001; Project End 19-SEP-2002

  Summary: (provided by applicant) Cytotoxic T lymphocyte responses play a major role in the control of **human immunodeficiency virus** type 1 (HIV-1) infections; however, most HIV-1-infected patients eventually are unable to efficiently control viral replication and succumb to their disease. The reasons for this eventual failure of virologic control are not well understood. One possibility is that the constant antigen stimulation in the context of a weak CD4-helper response as seen in chronic HIV infection leads to a loss of CD8+ T cell lytic activity by donal deletion or anergy. The first specific aim hypothesizes that within the same individual, distinct populations of HIV-1 specific CD8+ T cells are maintained which vary in their functional characteristics. If our hypothesis were correct, then we would expect to detect virus specific CD8+ T cells that fail to produce interferon-g (IFN-g). To experimentally address this hypothesis, we will comprehensively analyze peripheral blood mononuclear cells (PBMC) from HIV-1 infected subjects using tetramer and intracellular and secretory cytokine staining. The second SA hypothesizes that functional differences seen in HIV-1 specific CD8+ T cells are an important factor in determining disease progression. If our hypothesis were correct, then we would predict that the clearance of HIV-1 infected cells, plasma viral load, and the development of cytotoxic T lymphocyte (CTL) escape mutations correlates with virus specific CD8+ T cell functional heterogeneity. We will test this hypothesis by comparing the functional heterogeneity of virus specific CD8+ I cells with markers of HIV-1 disease progression and epitope specific CTL escape mutations to determine a correlation. Our final SA hypothesizes that HIV-1 specific CD8+ T cells require CD4 help and the level of required help varies depending on the amount of MHC bound peptide. If this hypothesis were correct, then we would predict that low levels of cell surface peptide concentrations correlate with poorly functioning CD8+ T cells specific for that epitope. We Will test this hypothesis by comparing HIV-1 specific MHC peptide concentrations on the surface of CD4+ T cells with the function of HIV-1 specific CD8+ I cells ex vivo to demonstrate that CD8+ T cells activated with relatively low concentrations of antigen require greater CD4 help for optimal function. We will also incubate PBMC or CD8+ I cells with CD4 helper cytokines in order to change the functional phenotype, thereby supporting the notion that CD4 helper responses augment virus specific CD8+ T cells. Findings from this study could lead to better therapeutic options for patients infected with HIV-1 and allow for prolonged discontinuation of antiretroviral treatment.

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- **Project Title: CELL MEDIATED IMMUNITY TO HCV IN HIV+ PERSONS**

  Principal Investigator & Institution: Kim, Arthur Y.; Massachusetts General Hospital 55 Fruit St Boston, MA 02114

  Timing: Fiscal Year 2003; Project Start 01-APR-2003; Project End 29-FEB-2008

  Summary: (provided by applicant): Hepatitis C virus (HCV) infection has emerged as a major cause of morbidity and mortality in persons living with **human immunodeficiency virus** (HIV-1). Growing data from studies early in the course of HCV suggests that the cellular immune response is a crucial determinant of the eventual outcome; however, the role of the HCV-specific immune response in HIV-1 infected individuals is not clear. The recent development of sensitive techniques allows comprehensive and detailed assessment of this immune response, and the candidate has begun systematic application of these methods in co-infected patients. This proposal aims to characterize the HCV-specific cellular immune response in co-infected individuals. After determining the breadth, magnitude, and epitope specificity of these responses within this cohort, they will be compared to control subjects who are not infected with HIV. Moreover, these responses will be followed longitudinally to determine their dynamics before and after antiviral therapies, and in particular to find correlates of immune reconstitution. Finally, the lymphocytes specific against HCV will be characterized using tetramer-based methods. These studies will lend important insight into the pathogenesis of HCV, especially in regards to this clinically important group of patients. They will additionally contribute to our understanding of vaccine designs and potential immune-based therapies. The candidate is currently enrolled in his third year of clinical and research fellowship training in Infectious Diseases at the Massachusetts General Hospital, and seeks further training in both bench and clinical research skills that will allow him to develop into an independent clinical investigator. These skills will be essential to allow translation of this research into novel immunotherapies. This plan will be implemented under the supervision of Dr. Bruce Walker, and will involve bench research, data analysis, and didactic learning.

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- **Project Title: CELLULAR AND MOLECULAR BASIS OF HIV BASED THROMBOCYTOPEN**

  Principal Investigator & Institution: Ratajczak, Mariusz Z.; Research Assistant Professor; Medicine; University of Louisville University of Louisville Louisville, KY 40292

  Timing: Fiscal Year 2001; Project Start 30-SEP-1998; Project End 31-AUG-2003

  Summary: (Adapted from applicant's abstract) Autoimmune mechanisms are known to play a role in the thrombocytopenia observed in individuals infected with the **human immunodeficiency virus** (HIV) who suffer from the Acquired Immune Deficiency Syndrome (AIDS). However, immunologic mechanisms alone are unlikely to account for all aspects of the pathogenesis of thrombocytopenia seen in AIDS. Among these other mechanisms are possible direct effects of the HIV, or its associated proteins, on the development of megakaryopoietic progenitors in the bone marrow, or the ability of these cells to carry out thrombopoiesis, the process of platelet production. It is also possible that these effects may be brought about indirectly by effects of the virus, or viral proteins, on marrow stromal and accessory cells supportive of megakaryocytopoiesis. To investigate these issues, The applicants propose the following four specific aims: I. Determine the effect of HIV infection on megakaryopoiesis and platelet formation. They will infect human megakaryocytic cells at various stages of development with HIV-1 and HIV-2 viruses and examine the ability of these cells to

differentiate into mature megakaryocytes and form platelets. If these processes are impaired, they will determine the mechanism(s) involved. II. Characterize the chemokine receptors on megakaryocytes and the influence of their corresponding ligands on megakaryopoiesis. They will characterize the chemokine receptors displayed on uninfected and infected megakaryocytes, and study the influence of these receptor-ligand pairs on the developmental biology of these cells. These studies will shed light on the function of these chemokines during megakaryocytopoiesis and thrombopoiesis. III. Investigate the role of HIV proteins and HIV-induced cytokines on thrombocytopenia. They will evaluate the influence of viral proteins and inflammatory cytokines elaborated during infection by accessory cells on the developmental biology of megakaryopoietic precursors and mature cells. IV. Develop strategies for preventing HIV-induced thrombocytopenia. Inhibitory mutants of chemokines have already been developed and shown to prevent HIV infection. Based on findings in the first 3 specific aims, they plan to test blocking chemokines and monoclonal antibodies, and blocking of various cytokines on megakaryopoiesis both ex vivo and in NOD/SCID (non obese diabetic/severe combined immunodeficiency) mice/human hematopoietic chimeras. In toto, the studies proposed in this grant will increase the knowledge about pathogenesis of AIDS associated thrombocytopenia and may lead to development of new strategies for its treatment of prevention. (End of Abstract)

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- **Project Title: CELLULAR IMMUNE RESPONSES TO SUBUNIT IMMUNODEFICIENCY VIRUS VACCINES**

  Principal Investigator & Institution: Greenberg, Philip D.; Professor of Medicine; University of Washington Seattle, WA 98195

  Timing: Fiscal Year 2001

  Summary: Advances in the development of a vaccine for HIV have been substantial. New vaccine vectors to deliver viral immunogens have been designed, vaccine preparations with enhanced immunogenicity have been produced based on a better understanding of the mechanisms of in vivo processing of antigens, new non-human primate models for HIV infection have been developed, and protective immunity in vaccinated non-human primates has been demonstrated under defined challenge conditions. Although many immunologic effector mechanisms with activity against HIV have been identified, the nature of the host immune responses necessary and sufficient for mediating protection have not been precisely defined. Characterizing such protective responses is essential to provide direction and establish immunologic goals for candidate vaccines. Studies are proposed in this project to continue our efforts to evaluate the role of specific components of vaccine-induced CD4+ and CD8+ T cell responses in protective immunity, determine the immunologic and virologic reasons why potentially protective T cell responses successfully or unsuccessfully resolve a viral challenge, and examine methods to improve the efficiency of T cell activation during vaccination. The studies will be performed in a non-human primate model with SHIV, a chimeric virus comprised of elements of HIV-1 and SIV, as the challenge virus. The specific aims are to: 1. evaluate the function, specificity, magnitude, and durability of T cell responses elicited by candidate vaccines; 2. correlate the T cell responses elicited by vaccines with the outcome of challenge with SHIV; 3. analyze the immunologic basis for failure of protection in vaccinated hosts; 4. evaluate the importance of CD4+ and CD8+ T cell subsets in protection by using adoptive T cell transfer to selectively enhance individual responses; and 5. examine new strategies designed to augment T cell responses elicited by candidate vaccines.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: CHARACTERIZAT OF NOVEL SIMIAN IMMUNODEFICIENCY VIRUS (SIV) FROM L=HOEST MONKEYS**

  Principal Investigator & Institution: Hirsch, Vanessa M.; Oregon Health & Science University Portland, OR 972393098

  Timing: Fiscal Year 2001

  Summary: The human immunodeficiency viruses, type 1 and 2 (HIV-1 and HIV-2), appear to have originated by cross-species transmission of simian immunodeficiency virus (SIV) from asymptomatically infected African primates. Of the viruses characterized to date, only those originating from sooty mangabeys (SIVsm) efficiently infect human primary lymphocytes, consistent with the appearance of the genetically-related HIV-2 in humans. Further study of the lentiviruses infecting nonhuman primates is important because it may provide insight into the origins and evolution of HIV in humans. In this study, we characterized a novel SIV isolate from an East African monkey of the Cercopithecus genus, l=hoest monkey (C. l=hoesti), which we designated SIVlhoest. This SIV isolate efficiently infected both human and macaque lymphocytes and resulted in persistent infection of macaques characterized by high primary virus load and a progressive decline in circulating CD4 lymphocytes consistent with progression to AIDS. Phylogenetic analyses showed that SIVlhoest is genetically distinct from other previously characterized primate lentiviruses but clusters in the same lineage as SIV from mandrills (SIVmnd), a West African primate species. The phylogenetic relationship between these SIV isolates suggests that SIVmnd origi nated by cross-species transmission from a West African relative of the l=hoest monkey. This observation lends support to the hypothesis that the primate lentiviruses originated and co-evolved within monkeys of the Cercopithecus genus. Regarded in this light, documentation of SIV in other primates such as mandrills, baboons, mangabeys and humans, may actually be the result of relatively recent cross-species transmission. FUNDING NIAID Intramural Program PUBLICATIONS None

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: CHARACTERIZATION OF HIV-1 GAG-LYSRS INTERACTIONS**

  Principal Investigator & Institution: Kennedy, Robert; Chemistry; University of Minnesota Twin Cities 200 Oak Street Se Minneapolis, MN 554552070

  Timing: Fiscal Year 2003; Project Start 11-AUG-2003; Project End 10-AUG-2005

  Summary: (provided by applicant): **Human immunodeficiency virus** type 1 (HIV-1) is a retrovirus that is the causative agent of human acquired immunodeficiency syndrome (AIDS). In retroviruses tRNA molecules are recruited as primers to initiate reverse transcription. In the case of HIV-1 a specific host cell tRNA, human tRNALys3, serves as the initiation primer. All three human tRNALys isoacceptors are selectively packaged into the HIV-1 virion. It has recently been shown that the tRNALys binding protein, human lysyl-tRNA synthetase (LysRS) is also packaged into HIV-1 virions and into viral-like particles formed from the HIV Gag protein alone. These data and recent pull-down assays support an interaction between human LysRS and Gag in vivo and in vitro. This proposal will explore this hypothesis further by quantitatively measuring and mapping the interaction in vitro. The goals will be accomplished by employing isothermal titration calorimetry (ITC), fluorescence polarization (FP), and protein footprinting techniques. Information gained from the proposed research will provide

valuable insights into the molecular interaction between LysRS and Gag. Additionally, this information may be useful in the design of new therapeutic agents against AIDS.

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- **Project Title: CHARACTERIZATION OF MOLECULARLY CLONED SIMIAN HUMAN IMMUNODEFICIENCY VIRUSES**

  Principal Investigator & Institution: Karlsson, Gunilla B.; Oregon Health & Science University Portland, OR 972393098

  Timing: Fiscal Year 2001

  Summary: The study of simian immunodeficiency virus (SIV) infection in Asian macaques has provided numerous insights into the pathogenesis of AIDS in **human immunodeficiency virus** type 1 (HIV-1)-infected humans. The divergence of the envelope glycoproteins of SIVmac and HIV-1, however, limit the utility of the SIVmac model for studying HIV-1 envelope glycoprotein determinants of pathogenicity, and for testing vaccine strategies directed against the HIV-1 envelope glycoproteins. In vivo passage of a chimeric simian-human immunodeficiency virus (SHIV-89.6) expressing HIV-1 tat, rev, vpu and env genes generated pathogenic virus (SHIV-89.6P) inducing rapid CD4+ lymphocyte depletion and AIDS-like illness in rhesus monkeys (J Virol 70:6922-6928, 1996). Virus generated from some proviral clones of SHIV-89.6P caused a rapid and profound decline of CD4+ lymphocytes in a high percentage of inoculated macaques. Nucleotide changes potentially responsible for increased virulence of SH IV-89.6P were limited to the env, tat or long terminal repeat sequences, with most of the observed changes in env. Nucleotide changes in env altered 12 amino acids in the gp120 and gp41 exterior domains, and a 140 bp deletion in env resulted in the substitution of the carboxyl terminus of the SIVmac gp41 glycoprotein for that of the HIV-1 gp41 glycoprotein. Both the level of viremia and the structure of the HIV-1 envelope glycoprotein ectodomains individually contributed to the efficiency with which CD4+ T lymphocytes were depleted. The envelope glycoproteins of recombinant SHIVs that efficiently caused loss of CD4+ T lymphocytes exhibited increased chemokine receptor binding and membrane-fusing capacity compared with those of less pathogenic viruses. These studies identify the HIV-1 envelope glycoprotein ectodomains as determinants of CD4+ T lymphocyte loss in vivo and provide a foundation for studying pathogenic mechanisms. FUNDING Collaboration with Dr. Letvin, Harvard University PUBLICATIONS Karlsson GB, Halloran M, Schenten D, Lee J, Racz P, Tenner-Racz K, Manola J, Gelman R, Etemad-Moghadam B, Desjardins E, Wyatt R, Gerard NP, Marcon L, Margolin D, Fanton J, Axthelm MK, Letvin NL, Sodroski J. The envelope glycoprotein ectodomains determine the efficiency of CD4+ T lymphocyte depletion in simian-human immunodeficiency virus-infected macaques. J Exp Med 188(6):1159-1171, 1998.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: CHEMOKINE DYNAMICS IN THE HIV-1/SIV INFECTED LUNG**

  Principal Investigator & Institution: Kirschner, Denise E.; Associate Professor; Microbiology and Immunology; University of Michigan at Ann Arbor 3003 South State, Room 1040 Ann Arbor, MI 481091274

  Timing: Fiscal Year 2002; Project Start 30-SEP-2002; Project End 31-JUL-2007

  Summary: (provided by applicant): The lung is an extremely large interface between the host and its environment, and this is especially problematic for HIV-1 infected individuals. We propose to comprehensively define the chemotactic environment in the lung during health and infection. To this end, we will develop a virtual model of the

immunological events ocurring in the lungs during HIV-1 infection in humans. This will allow for integration of the plethora of information on chemokine and cytokine modulation, cellular influx, and other relevant immunological factors. We will build the model based on data reported from human studies together with those we generate in a SIV/cynomolgous macaque nonhuman primate (NHP) model for HIV-1 infection and disease progression. Using methods to define cellular populations and protein and gene expression patterns within the lungs of SIV infected macaques, we will determine both local and systemic immunological mediators that are most important during nonpathologic and pathologic states, and the timing and modulation of their expression levels. This will in turn inform the model providing important mechanistic and kinetic data. Utilizing these two experimental systems will elucidate the dynamics of the immune responses within the lung, whether directed against the virus or other pathogens. The local dynamics include the complex networks of cells, cytokines, chemokines, virus, and other pathogens within interstitium and bronchoalveolar lavage fluid (BALF). Our specific aims are to use data from models of both nonhuman primate and virtual human models to: (1)Determine the homeostatic and modulated chemokine expression patterns during SIV infection in the lung, draining lymph node and blood. (2) Predict chemokine and cellular dynamics during homeostasis and HIV-1 infection in the lung, draining lymph nodes, lymph tissue and blood. (3) Identify associations between altered chemokine patterns and local cytokine production, cellular populations, virus, and opportunistic infections on the chemotactic environment in the lung during SIV/HIV-1 infection. Through this work, we will also explore the respective compositions of BAL fluid and lung interstitium and determine which is more predictive of a favorable disease outcome. Utilizing this unique approach of pairing computer and NHP models, the interaction of multiple factors that control the chemokine environment will be defined. Key parameters governing these interactions will be identified. The ability to synthesize the data generated by the experiments in the modelsallows for an understanding of the dynamics within lung in both NHP and humans during SIV/HIV-1 infection as more than the sum of its parts and will provide information useful in the generation of additional therapeutic intervention strategies. (End of Abstract)

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- **Project Title: CHEMOKINE RECEPTOR INTERVENTION USING GENE THERAPY AND ANIMAL MODELS--HIV+**

  Principal Investigator & Institution: Littman, Daniel; University of Michigan at Ann Arbor 3003 South State, Room 1040 Ann Arbor, MI 481091274

  Timing: Fiscal Year 2001

  Summary: Infection of human cells with HIV requires a receptor complex consisting of CD4 and one of several chemokine receptors. Early after strains to date have been show to be specific for the chemokine receptors CCR5 and/or CXCR4. Early after acquisition and during the asymptomatic phase, most viruses are tropic for CCR5, while late in the disease many viruses are specific for CXCR4 or both of these receptors. Individuals with a homozygous null mutation in the CCR5 gene are relatively resistant to infection with HIV, and their immune systems appear normal. Strategies aimed at interfering with the ability of CCR5 to function as an HIV receptor are hence likely to result in a significant decrease in viral load without impairing the immune system, The effects of blocking CXCR4 function in vivo are not yet known, but blocking HIV usage of this receptor may be particularly important for reversing or delaying the onset of immunodeficiency. Interference with HIV interactions with chemokine receptors can potentially be achieved

with compounds that specifically bind to CCR5 and CXCR4 and block their ability to serve as viral receptors. Alternatively, blocking expression of CCR5 or CXCR4 by lymphocytes, monocytes, and macrophages may also be an effective means of interfering with infection. We propose to develop approaches to interfere with the expression of these molecules in vivo. Modified chemokines, particularly MIP-1beta, Rantes, and SDF-1, will be designed so that they are retained in the endoplasmic reticulum and thus block cell surface expression of the chemokine receptors. The effectiveness of these molecules will be tested in transgenic mice that express human CCR5 and CXCR4, both by introduction of the molecules as transgenes and by retroviral vector transduction. In additional collaborative studies, these approaches will be compared to ribozyme-directed inhibition of CCR5 expression. The role of CXCR4 in mice will be determined by gene targeting and particular attention will be devoted to effects on T helper cells and macrophages, the principal targets of HIV infection. In collaboration with Project 3, retroviral vectors designed to express the modified chemokines in macrophages and T helper cells will be used to transduce these genes into bone marrow cells of the CCR5/CXCR4 transgenic mice, and the effect on expression of both mouse and transgenic human receptors will be assessed. The immune functions of these animals will be studied in collaborations with the Immunology Core. Successful inhibition of expression of human CCR5 and CXCR4 in these transgenic mice, in the absence of significant effects on immune responses, all allow us to apply this technique to patients infected with strains of HIV-1 of known receptor phenotype.

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- **Project Title: CHEMOKINE RECEPTORS AND HIV AND SIV INFECTION**

  Principal Investigator & Institution: Doms, Robert W.; Professor and Chair; Pathology and Lab Medicine; University of Pennsylvania 3451 Walnut Street Philadelphia, PA 19104

  Timing: Fiscal Year 2001; Project Start 01-JAN-1997; Project End 31-DEC-2001

  Summary: The envelope protein (env) of HIV-1 plays two critical roles in the initial stages of virus infection: it binds virus to the cell surface by a high affinity interaction with CD4, and undergoes a conformational change that leads to fusion between the viral envelope and a cellular membrane. While env-CD4 interactions have been well characterized, the mechanisms controlling the subsequent membrane fusion reaction are poorly understood. It is clear, for example, that binding to CD4 alone does not lead to membrane fusion. CD4 expressed in nonhuman cells is not sufficient for virus infection due to a block in entry, and different HIV-1, HIV-2, and SIV strains can exhibit marked cellular tropism: while some virus strains preferentially infect T-cells, others infect macrophages and some infect both of these CD4-positive cell types. These and other findings have shown that in addition to CD4 one or more cell-specific co-factors are required for HIV-1 entry. While a number of molecules have been proposed to serve as HIV-1 co-factors, none have proven to be required for either virus infection or syncytia formation. Very recently, a seven transmembrane domain protein has been found to serve as a co-factor for T-cell tropic HIV-1 strains. The molecule, termed Fusin, is related to the chemokine receptor families. The investigator has found that introduction of both Fusin and human CD4 into many different nonhuman cell lines renders them permissive for T-tropic env mediated cell-cell fusion and for virus infection. Furthermore, preliminary studies showed that env-CD4 complexes interact directly with Fusin, whereas env alone binds weakly. The data suggest that Fusin also serves as a alternate receptor in models of CD4-independent infection by HIV-2. Identification of

this and related molecules represents an exciting opportunity to study virus tropism and entry at the molecular level.The proposal has 4 specific aims 1) Characterize the role Fusin plays in the entry and fusion activity of different HIV-1 strains; 2) Examine the extent to which chemokine receptors and related molecules can serve as co-factors for T- and M-tropic HIV-1 strains as well as for HIV-2 and for SIV; 3) Explore the interactions between env, CD4, and Fusin or related molecules; identify the regions in env that participate in these interactions; and investigate whether these interactions lead to conformational changes in env that may lead to membrane fusion; and 4) Extend preliminary observations that a variant of HIV-2, which has the ability to infect a number of CD4 negative human cells, can utilize Fusin as an alternate receptor.

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- **Project Title: CLINICAL TRIALS**

  Principal Investigator & Institution: Lennox, Jeffrey; Emory University 1784 North Decatur Road Atlanta, GA 30322

  Timing: Fiscal Year 2001; Project Start 01-SEP-2001; Project End 31-AUG-2006

  Summary: (from applicant's abstract): Immunization strategies using DNA priming and recombinant Modified Vaccinia Ankara (MVA) boosters have proved to raise broad and high titer T-cell responses in preclinical models. The goals of this IPCAVD are to evaluate the ability of DNA/MVA vaccines for **human immunodeficiency virus** to generate vaccines for cross-clade immune responses. This project will provide data on whether worldwide vaccination can be accomplished with a single DNA/MVA immunogen, or whether a mixture of DNA/MVA immunogens will be required. This project includes: assay development diagnostic and immune assay standardization, and Phase 1 human trials. The specific aims are: 1. Develop and optimize T-cell assays to measure HIV specific immune responses in HIV-1 DNA/MVA vaccines to be quantitative, sensitive, high throughput, field adaptable and capable of measuring the breadth of responses to subtype A/G and B vaccines. 2. To test the validity of molecular diagnostic techniques for detecting HIV in patients with Clade B and Clade A infection, and to optimize detection of HIV infection for vaccinees who may have low level viral replication due to strong cytotoxic T-cell responses. 3. To test HIV clade B and IbNG-like AG vaccines, singly and in combination, with an MVA boost for their ability to generate high levels of intra-clade and cross-clade ELISPOT responses. Specific Aim 1 & 2 will involve participants in both the United States and in the Ivory Coast (through our CDC collaboration). For Specific Aim 3, three Phase 1-vaccine protocols will test the safety and immunogenicity of single, mixed and formulated DNA/MVA vaccines. Each of these will be preceded by protocols establishing the safety of the proposed MVA boosters, and of a formulation designed to increase the efficiency of DNA priming. The goals of these trials are to provide seminal data regarding the need for clade specific vaccines, and to establish the foundation for further Phase II/III testing of DNA/MVA vaccines

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- **Project Title: CNAA & B3005:3TC & ZDV & 1592U89 & 3TC & ZDV & IDV IN HIV 1 INFECTED**

  Principal Investigator & Institution: Hyslop, Newton E.; Tulane University of Louisiana New Orleans, LA 70118

  Timing: Fiscal Year 2001

Summary: Infection with the **human immunodeficiency virus** (HIV) is characterized by a progressive decline in immune function, usually over a period of years. For most HIV-1 infected individuals, this decline will eventually result in the development of opportunistic infections (OIs) and/or malignancies associated with the acquired immunodeficiency syndrome (AIDS). Although a long-term AIDS-free survival period may be seen, the majority of individuals will eventually develop AIDS and die as a result of their disease. Currently, treatment for HIV-1 infection consists of antiretroviral chemotherapeutic drugs and the management of the OIs and malignancies associated with AIDS. This is a phase III, randomized double-blind, parallel group, international multicenter study, designed to evaluate the antiviral effect and durability of response (as measured by HIV-1 RNA) and safety of 3TC/ZDV/1592U89 as compared to 3TC/ZDV/IDV. Patients will be evaluated for antiretroviral activity, safety, and tolerance of the treatment regimen.

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- **Project Title: CNS METABOLIC CORRELATES OF HIV DEMENTIA BY MRS IMAGING**

  Principal Investigator & Institution: Pomper, Martin G.; Associate Professor; Radiology; Johns Hopkins University 3400 N Charles St Baltimore, MD 21218

  Timing: Fiscal Year 2001; Project Start 28-SEP-1999; Project End 31-MAY-2003

  Summary: The **human immunodeficiency virus** type 1 (HIV) gains access to the central nervous system (CNS) early in the course of infection. Nevertheless, dementia due to HIV (HIV-D), seen in about 15 percent of HIV+ individuals, is a relatively late manifestation of the illness occurring usually in the context of a severely immunocompromised state and a high viral load. Once HIV has transgressed the blood-brain barrier (BBB), the potential exists for unchecked replication within the brain, even after peripheral viral levels have been reduced to undetectable levels by highly active antiretroviral therapy (HAART). Therapeutic failures with HAART occur in about 50 percent of patients and new cases of HIV dementia are still developing. It is unclear as to what extent dementia arises due to reseeding of the brain late in the disease or to what extent subcortical or neocortical structures contribute to dementia. Are there markers that could be measured noninvasively that reflect changes in CNS viral load and the attendant brain injury? Is there a marker that could be assessed easily that reflects a developing resistance to HAART? Can the temporal course of regional brain injury be mapped in the brain, noninvasively? Magnetic resonance spectroscopy (MRS) is a noninvasive tool with easy reproducibility that measures brain metabolites, reflecting CNS function. We intend to address these questions in humans using MRS and MRS imaging (MRSI), proposing that brain metabolite concentrations may serve as surrogate markers of CNS HIV activity. Concurrent assessment of CNS immune activation, BBB integrity and viral load through measurement of appropriate CSF and peripheral markers would further enhance understanding of viral CNS activity in vivo, and the ability for that activity to continue to engender dementia even during HAART. The broad objectives of the proposed research are to determine a) how the level of HIV-related CNS activity, as measured by MRS and MRSI, can be correlated to neurological status and b) whether brain metabolite levels reflect the adequacy of therapy at keeping HIV in check in the CNS.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: COMBINATION IMMUNIZATION AS AN APPROACH TO AIDS VACCINES**

  Principal Investigator & Institution: Hu, Shiu-Lok; Professor; National Primate Research Ctr; University of Washington Seattle, WA 98195

  Timing: Fiscal Year 2001; Project Start 01-MAR-1988; Project End 31-DEC-2002

  Summary: This proposal builds upon the strengths of two successful NCVDG awards to the University of Washington since 1987. The overall objective of this program is to develop and evaluate combination immunization strategies that are broadly protective against blood-borne and mucosal infection by primary isolates of HIV-1. The central hypothesis of this program is two-fold: (1) protection against HIV infection is immune-mediated, and (2) protection can be achieved by combination immunization with recombinant vaccines. These hypotheses are supported by work accomplished in the present NCVDG demonstrating that a combination immunization regimen with recombinant live vector priming followed by recombinant protein immunogen boosting protected macaques against intravenous and intrarectal infection by pathogenic uncloned virus, SIVmne. We recently extended these observations to include protection against SHIV IIIB in macaques. The goal of this proposal is to develop novel combination immunization strategies that will result in protection against primary isolates of HIV-1 in relevant non-human primate models. The Specific Aims are: (1) To refine a combination immunization approach with proven efficacy in the SIVmne and Shiv IIIB models and to determine the immune mechanisms and the limits of protection against SHIV with envelope from primary isolates of HIV-1 (Project/HU); (2) To generate broadly protective immune responses by "quasispecies" vaccination, using a combination of DNA and recombinant immunogen immunization strategies (Project 2/Haigwood); (3) To examine combination systemic and/or mucosal immunization approaches to elicit immunity against mucosal infection (Project 3/Bosch); and (4) To examine the role of T-cell immunity in protection as well as combination vaccination strategies designed to augment T-cell responses (Project 4/Greenberg). These efforts will be supported by three scientific Cores to develop chimeric Shiv representing the diversity of primary HIV-1 isolates (Core B/Mullins), to develop and maintain non-human primate resources (Core A/Anderson) as well as virological/serological techniques (Core C/ Agy) necessary for the preclinical evaluation of candidate HIV-1 vaccines. Results from this program project will contribute directly to current and future clinical development of AIDS vaccines and enhance our basic understanding of the protective immunity against primate lentiviruses.

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- **Project Title: COMBINATORIAL & RATIONAL DESIGN APTAMERS TARGETING HIV**

  Principal Investigator & Institution: Gorenstein, David G.; Director of Nmr; Human Biol Chem and Genetics; University of Texas Medical Br Galveston 301 University Blvd Galveston, TX 77555

  Timing: Fiscal Year 2001; Project Start 01-NOV-1988; Project End 31-JAN-2005

  Summary: Novel combinatorial and structure-based design methods will be used to develop phosphorothioate and phosphorodithioate DNA decoys or aptamers as targeted therapeutics towards the **human immunodeficiency virus** (HIV). Development of these anti-AIDS agents will be facilitated by nuclear magnetic resonance (NMR) spectroscopy and computational biochemistry of both agent and protein agent complexes. We will specifically synthesize thioated backbone aptamer oligonucleotide

analogues targeted to HIV-1 reverse transcriptase (RT) and nucleocapsid (NCp7) and the human transcription factor NF-kappaB. We have recently developed a novel combinatorial selection scheme for phosphorothioate hybrid backbone aptamers targeting the nuclear factor for human IL6 (NF-IL6), a transcription factor involved in the induction of acute-phase responsive and cytokine gene promoters in response to inflammation. Using a random combinatorial selection approach and dNTP(alpha)S s in PCR amplification, we have selected specific thio-substituted agents which have the highest specificity in binding (nM range) to NF-IL6. This is currently being extended to NF-kappaB and will also be applied to NCp7 and RT. A split synthesis scheme will be developed for combinatorial selection of dithiophosphate aptamers for these proteins. Since phosphorothioate and phosphorodithioate substituted oligonucleotides show reduced nuclease activity, these combinatorial thiophosphate-selection experiments can offer wide application for rapid identification of new therapeutic agents. This technology will allow us to develop separate aptamers targeting in principle any one of the 15 possible combinations of 5 homo- and heterodimers of the 5 different forms of NF-kappaB/Rel. NF-kappaB/Rel transcription factors, are key mediators of the immune and acute phase responses, apoptosis, cell proliferation and differentiation, and are key transactivators acting on the LTR of HIV-1. They thus represent potential therapeutic targets for control of HIV-1 proliferation. NMR will be used to define the three-dimensional structure of monothio- and dithiophosphate modified oligonucleotide agents and aptamer NCp7 complexes. We will also assess the in vivo activity of the aptamers in tissue culture testing to arrest HIV-1 proliferation and gene expression as well as to activate HIV gene expression to identify hidden reservoirs of infection. Finally, we will explore the feasibility of utilizing these highly selective thioaptamers for recognition of protein-protein interactions using a new DNA/protein chip technology for genetic analysis at the level of functional protein expression.

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- **Project Title: COMPARTMENTALIZATION OF HIV WITHIN THE GENITAL TRACT**

  Principal Investigator & Institution: Smith, David M.; Medicine; University of California San Diego 9500 Gilman Dr, Dept. 0934 La Jolla, CA 92093

  Timing: Fiscal Year 2003; Project Start 01-JUL-2003; Project End 30-APR-2008

  Summary: (provided by applicant): Career Development Aim: To develop into an independent, productive academician conducting translational research in the field of HIV pathogenesis. Career Development Methods: An individualized, mentored curriculum of peer and faculty interactions, formal didactics, and study development are proposed. Scientific Background: 15,000 people in the world will become infected with **human immunodeficiency virus** (HIV) today. Most of these infections will occur through sexual contact, and yet HIV within genital secretions is not as well characterized as that found in the blood. Genital tract compartmentalization has profound consequences on the development of drug resistance and the selection of HIV quasispecies for transmission. Research Aim: To characterize the genital tract as a separate compartment than from the blood secondary to different host cell selection immunologic responses and pharmacologic penetration. Research Methods: Male genital secretions are a complex mixture of secretions and cells. The amount of HIV within male genital secretions is highly variable. Sequestration of HIV within the genital tract will be explored by studying the role of the prostate, which is known to sequester both bacterial and fungal pathogens and is a source of seminal fluid. This will be investigated by examining the effect of prostate massage, which increases the amount of

prostatic fluid in genital secretions, on the amount of cell-free and cell associated virus. Longitudinally collected paired samples of genital secretions and blood from subjects enrolled in the UCSD Acute and Early HIV Cohort will be examined. From these samples HIV RNA will be extracted and examined with clonal and consensus sequencing and length polymorphism detection of the HIV env and gag coding regions. Comparing the genetic diversity of HIV between the genital tract and blood and subsequent divergence will give a better idea of the type of compartmentalization that is occurring and what kind of virus is ultimately being transmitted. Using these same samples the appearance and disappearance of drug resistance will be tracked. This may shed light on the mechanism of drug resistance development and why so many new infections are occurring with drug resistant HIV. Significance: These studies are important to characterize the compartmentalization of HIV in the genital tract, and to understand factors affecting the transmission of HIV and treatment approaches to minimize drug resistance.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: COOPERATIVE HUMORAL & CELLULAR IMMUNITY AGAINST HIV/SIV**

  Principal Investigator & Institution: Burton, Dennis R.; Professor; Scripps Research Institute 10550 N Torrey Pines Rd La Jolla, CA 920371000

  Timing: Fiscal Year 2002; Project Start 15-MAY-2002; Project End 30-APR-2006

  Summary: (provided by applicant): It is not known whether, to what degree or under what circumstances, cellular and humoral immunity can act cooperatively in clearing or controlling HIV-1 infection. In a vaccine context, the major hurdle has been the inability of candidate vaccines to consistently elicit significant neutralizing antibody titers in contrast to their ability to elicit strong T cell responses. Similarly in established infection, where neutralizing antibody titers are usually very low, we do not know the extent to which cellular and humoral responses may act, or be induced to act, in concert to control infection. Here we propose to investigate the ability of combined cellular and humoral immunity to protect against HIV infection by providing, prior to viral challenge, a cellular response through vaccination and neutralizing antibodies by passive administration. We refer to this approach as "active T cell/passive antibody." We propose to evaluate the approach in SIVmac239 challenge of macaques using vaccination protocols already established to elicit vigorous T cell responses to SIV proteins and using an antibody CD4-IgG2 molecule that we have shown is highly effective in neutralizing this generally resistant virus. SIVmac239 is chosen as one of the most appropriate models of HIV-1 infection. CD4-IgG2 is chosen because it behaves in key respects as a conventional monoclonal antibody but has particularly potent activity against SIVmac239. We also propose to further our understanding of the impact of antibodies on ongoing infection in the context of a cellular response in the SIV and SHIV/macaque models by passively transferring neutralizing antibodies to infected animals. The specific aims are: 1. To evaluate the activity of antibody CD4-IgG2 against SIVmac239 in macaques in protection against mucosal challenge and in an ongoing infection. To evaluate the effects of having specific T cells and neutralizing antibody (CD4-IgG2) present together in macaques prior to challenge with SIVmac239. The neutralizing antibody levels will be chosen to be below those giving sterile protection as determined in Aim 1 and will correspond more to those that cold be achieved through vaccination. 3. To evaluate the effects of anti-HIV-1 neutralizing monoclonal antibodies, singly or as a cocktail, and CD4-IgG2 against an ongoing SHIV162P infection in

macaques. This will provide us with the first opportunity to look at the effects of potent human mAbs on established infection in the presence of functional T cells.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: CORE--BSL-3 AND GMP LABORATORY**

  Principal Investigator & Institution: King, Steven; Investigator; University of Michigan at Ann Arbor 3003 South State, Room 1040 Ann Arbor, MI 481091274

  Timing: Fiscal Year 2001

  Summary: This Biosafety Level 3 (BSL-3)/GMP core facility will be responsible for providing laboratory support for gene therapy research designed to limit HIV infection. Three laboratories combine to form the BSL-3/GMP core facility and provide a unique environment in which to pursue both preclinical and clinical gene therapy research. The three laboratories that make up the core facility include the Biological Containment Laboratory, the Vector Core Laboratory, and the Human Applications Laboratory. The Biological Containment Laboratory contains two BSL-3 suites. One suite is a dedicated laboratory for preclinical experiments using infectious human pathogens. This laboratory will be used to test the effect of gene therapy vectors on HIV infection in preclinical studies. The second BSL-3 suite is a specialized facility designed to received and transduced patient cells with vectors prepared by the Human Applications Laboratory. The second BSL-3 suite will also be used during the course of clinical trials to perform molecular assays with patient samples to determine the efficacy of the gene therapy. The Vector Core Laboratory will construct, prepare, and characterize large amounts of both viral and non-viral vectors for use in preclinical gene transfer experiments. The Vector Core Laboratory also operates in collaboration with the University of Michigan site of the National Gene Vector Laboratory (NGVL) that will provide non-viral DNA vectors produced under GMP conditions for use in clinical research studies. The third facility is the Human Applications Laboratory, a newly designed facility that is dedicated to culture of both human cells and viral vectors for use in human gene therapy trials. This laboratory will provide a clean and controlled environment for optimal GMP conditions that are required to prepare viral vectors for gene transfer into cells that will be reinfused into patients. The combination of the three laboratories that comprise the BSL-3/GMP facility results in unique pooling of knowledge, expertise, and resources to enhance the ability to develop gene therapy strategies at the laboratory bench and to translate this research into clinical trials using gene therapy in HIV infected patients.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: CORE--CELL, TISSUE AND ANIMAL FACILITY**

  Principal Investigator & Institution: Gendelman, Howard E.; Director; University of Rochester Orpa - Rc Box 270140 Rochester, NY 14627

  Timing: Fiscal Year 2001; Project Start 30-SEP-2001; Project End 31-AUG-2005

  Summary: (Provided by applicant): The purpose of this core is to assist in the design of adjunctive therapeutic strategies for treatment and/or prevention of neurologic disease following **human immunodeficiency virus** type-one (HIV-1) infection. In this regard, purified human monocyte-derived macrophages (MDM) and MDM conditioned media (MCM) will be supplied, following HIV-1 infection and/or immune activation, to all investigators on request, within the Rochester Cooperative NeuroAIDS Drug Discovery Group (RCNDDG). In addition, promising anti-inflammatory and/or neuroprotective drugs, developed in laboratory assays or proposed, will be tested for therapeutic

efficacy in a severe combined immune deficiency (SCID) mouse model of HIV-1 encephalitis (HIVE). Brain tissue and/or sera will be made available for measuring drug levels and pathology in the HIVE mice. Such works will support translational (bench to bedside) research efforts and directly effect the performance of subsequent clinical trials. The works, in toto, are based on the concept that HIV-1 associated dementia (HAD) is, in part, a reversible metabolic encephalopathy caused by defective immunity of virus-infected mononuclear phagocytes [(MP), microglia, perivascular and parenchymal macrophages]. These MPs serve both as reservoirs for productive HIV-1 infection and principal sources of neurotoxic activities within the central nervous system (CNS). The development of ways to inhibit toxic inflammatory activities in brain may serve to both ameliorate and prevent complications of persistent viral replication in brain serving as critical adjunctive therapies to ongoing potent anti-retroviral regimens, the principal goals of the RCNDDG.

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- **Project Title: CORECEPTORS AND VIRAL TROPISM IN HIV-1 NEUROPATHOGENESIS**

  Principal Investigator & Institution: Goldsmith, Mark A.; Associate Professor of Medicine; J. David Gladstone Institutes 365 Vermont St San Francisco, CA 94103

  Timing: Fiscal Year 2001; Project Start 25-SEP-1999; Project End 31-MAY-2002

  Summary: Human immunodeficiency virus (HIV) penetrates the brain early in the course of disease, and frequently causes dementia and other neurologic manifestations. The mechanism(s) underlying the neuropathologic effects of HIV infection are poorly understood. Prominent infection has been documented in microglia and macrophages, and less widespread infection of astrocytes, endothelial cell lines and even neurons has also been noted. Pathogenesis is likely to involve both direct cytopathic effects on target cells and indirect pathways driven by secreted cellular factors that alter neuronal viability. Elucidation of the mechanisms of infection for each cell type is a key step toward uncovering these pathogenic pathways as a foundation for informing new therapies to retard neurologic manifestations. The principal determinant of cellular tropism is the variable envelope glycoprotein gp120, which typically engages CD4 and particular chemokine receptors (coreceptors) expressed on cell surfaces. Relatively little is known about the distinct infection properties of viruses that infect the brain or about the specific routes of cellular infection by these viruses. A working hypothesis of neuropathogenesis is that gp120 determinants of specific strains of HIV promote entry into the CNS and infection of select grain cells through the use of CD4 in conjunction with a restricted subset of coreceptors. We have recently found that functional viral receptor complexes can also be formed using components expressed on separate cell surfaces, and this type of trans-receptor pathway may permit infection of CD4-negative brain cells types such as astrocytes that are vital to maintaining the microenvironment within the brain. This proposal seeks to test select aspects of this general hypothesis through the functional characterization of a novel and large set of gp120 clones derived from primary HIV-1 strains isolated from brain specimens from a cohort of AIDS patients with dementia. These studies will first define the receptor properties of these envelopes in order to delineate their routes of cellular infection. We will then evaluate the properties of these envelopes with regard to selective tropism in brain cell cultures, including a previously- described, three-dimensional heteroaggregate brain culture system. Finally, we will determine the pathobiologic consequences of infection in these cultures, including direct and indirect pathways of toxicity. Collectively these integrated studies will provide essential new information about the role of envelope glycoproteins

in directing HIV variants toward specific brain cell types, and the ensuing pathologic events that may contribute to impairment in neurologic function.

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- **Project Title: CORE--MOLECULAR BIOLOGY FACILITY**

  Principal Investigator & Institution: Hofmann-Lehmann, Regina; Dana-Farber Cancer Institute 44 Binney St Boston, MA 02115

  Timing: Fiscal Year 2001

  Summary: Development of prophylactic strategies to prevent infection of HIV-1 requires a suitable virus/animal model Chimeric simian-human immunodeficiency viruses (SHIVs) have been shown to productively infect non-human primates and to induce AIDS-like disease in infected animals. To test prophylactic strategies against HIV-1 clade C in vivo (Projects 2 and 3), the construction of a chimeric SHIV that expresses and HIV-1 clade C envelope from a primary patient isolate as essential. DNA-based vaccines, with their ability to express antigens in vivo, represent a new approach to protect against AIDS virus infections. DNA vaccines are able to raise humoral and cell-mediated immune responses against HIV. Thus, we propose to construct a recombinant DNA vaccine expressing HIV-1 clade C env, and to test its ability in vivo to raise a protective immune response (Project 3). Other retrovirusal infections (SRV/D, STLV-I) can confound experiments with SHIV. Core B will screen all experimental animals (Projects 2 and 3) for these viruses. Plasma viral RNA load is a key parameter in disease progression of lentiviral infection. We have developed a very sensitive real-time RT-PCR in our laboratory that will be used to monitor viral plasma kinetics in experimental animals (Projects 2 and 3). In addition, DNA pro-viral loads will be quantified by DNA PCR in experimental animals. The overall goal of Core B is to provide molecular biology expertise and support for projects 2 and 3: (1) Generation of chimeric SHIV containing env of a recently transmitted pediatric HIV-1 clade C isolate (SHIVenvC) (2) Generation of plasmids expressing codon-optimized HIV-1 clade C env and SIV gag-pol (3) Monitoring of experimental animals for other retrovirus infections (4) Monitoring of viral kinetics of SHIVenvC

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- **Project Title: CORE--SIMIAN AND RODENT IMMUNOLOGY FACILITY**

  Principal Investigator & Institution: Frelinger, Jeffrey A.; Kenan Professor and Chair; University of North Carolina Chapel Hill Office of Sponsored Research Chapel Hill, NC 27599

  Timing: Fiscal Year 2001

  Summary: The neutralizing antibody component of this core imrnunology laboratory will provide support for all three projects of this program. Specifically, we will assess the magnitude, breadth and duration of neutralizing antibodies against homologous and heterologous strains of SIV, HIV-1 and simian-human immunodeficiency virus (SHIV). Assays will be performed in either human CD4+ T cell lines or peripheral blood mononuclear cells (PBMC) as appropriate, and will include a T cell line adapted (TCLA) variant and multiple primary isolates of HIV- l. These assessments will permit a detailed evaluation of neutralizing antibodies generated by modified recombinant VRP vaccine vectors and modified forms of Env as described in Projects I and 2, respectively. They will also be designed to evaluate neutralizing antibodies as a correlate of immunity against experimental SIV challenge in macaques as specified in Project 3. Cellular immune responses elicited in Projects I, 2 and 3, will be assessed in the cellular

immunology component of the core. CTL will be measured as will cytokine synthesis using intracellular assays. Further, tetramer staining will used and specific tetramers produced for particular animals.

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- **Project Title: CORE--VIRAL PATHOGENESIS**

  Principal Investigator & Institution: Kornbluth, Richard S.; Professor; University of California San Diego 9500 Gilman Dr, Dept. 0934 La Jolla, CA 92093

  Timing: Fiscal Year 2001

  Summary: The Viral Pathogenesis Core serves as a centralized source for isolates and assays related to HIV-1, HIV-2, and SIV. In addition, the Core acts as an interface between users and the laboratories of UCSD CFAR members specializing in the herpes virus affecting HIV-infected individuals (CMV, HSV, and HHV-8). Four basic types of services are provided: (1) As a viral resource, the Core provides aliquots from a wide collection of characterized and titered viral strains of HIV-1, HIV-2, and SIV. (2) As a cell resource, the Core provides virus susceptible cells, including cell lines, isolated CD4+ T cells and macrophages. (3) As a virus characterization resource, the Core provides testing for cell tropisms, syncytium-inducing (SI) versus non-SI, co-receptor usage, cytopathic versus non-cytopathic, replication kinetics, drug susceptibilities, and other properties of HIV. (4) As a screening service, the Core provides the initial testing for investigational therapeutics (antiviral compounds, gene therapies, antibody neutralization, etc.). These resources make it easier for both novices and experienced investigators to pursue their virological research ideas. Without the Core, each investigator would need to set up and validate the different methods and assays required for their work, which could take months. Also, many of the Core's users have no BL3 training or experience themselves, and thus would need to expend months of effort on gaining the permission needed to work with these viruses. While the Core is not meant to replace a full scale research program set up by an investigator as one of the major projects, it is ideal for conducting pilot experiments and the screening of compounds for antiviral activity.

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- **Project Title: DEK EFFECTS ON GROWTH OF HEMATOPOIETIC CELLS**

  Principal Investigator & Institution: Grosveld, Gerard C.; Member & Chairman; St. Jude Children's Research Hospital Memphis, TN 381052794

  Timing: Fiscal Year 2001; Project Start 15-DEC-1997; Project End 30-NOV-2002

  Summary: (Adapted from investigator's abstract) The gene encoding the sequence specific DNA binding protein DEK is the target of t(6:9) found in human acute nonlymphocytic leukemia, and is associated with a poor clinical prognosis. This translocation creates a chimeric nuclear protein that contains almost the entire DEK protein fused to the C-terminal two thirds of the nucleoporin CAN. DEK binds to a sequence in the long terminal repeat (LTR) of **human immunodeficiency virus** type 2 and is essential for mitogen-induced transcription of the viral LTR in T cells and myeloid cells. CAN, part of the nuclear pore complex, is involved in nucleocytoplasmic transport. To investigate the normal function of DEK and the leukemogenic potential of DEK-CAN, the investigators generated DEK-deficient mice and DEC-CAN expressing mice by homologous recombination. Preliminary results show that Dek -/- mice exhibit an enhanced immune response upon viral infection and have elevated numbers of myeloid progenitors, suggesting a regulatory role for DEK in cell proliferation. DEK-

CAN-expressing mice do not spontaneously develop leukemia, indicating that additional mutations are needed to cause malignancy. The investigators hypothesize that DEK-CAN acts as an altered transcription factor that interferes with the expression of DEK target genes, resulting in abnormal hematopoietic responses and eventually leukemia. In this project, the investigators will define the transcription properties of DEK and assess how these properties are affected by DEK s fusion to CAN. This will also involve phenotypic complementation analysis of DEK-deficient mice with mutant DEK genes, to determine which domains of DEK are essential for its function in vivo, and whether DEK-CAN can rescue the loss of DEK. In addition, the investigators will identify DEK and DEK-CAN target genes by using cDNA RDA. The in vivo leukemogenic potential of DEK-CAN will be determined by testing its ability to accelerate leukemogenesis in mice predisposed to develop leukemia. The investigators state that these studies will provide valuable insights into the normal functions of DEK and generate important information on how DEK-CAN contributes to leukemogenesis.

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- **Project Title: DELIVERY OF MOLECULAR THERAPEUTICS TO SKIN**

  Principal Investigator & Institution: Khavari, Paul A.; Associate Professor; Stanford University Stanford, CA 94305

  Timing: Fiscal Year 2002; Project Start 27-SEP-2002; Project End 30-JUN-2003

  Summary: (provided by applicant): During the prior funding cycle, the goal of establishing capabilities for the genetic correction of several human genodermatoses was achieved by this group using model systems. As this advance is extended toward human trials, however, the complicated, costly and traumatic features of ex vivo gene transfer are increasingly evident. New approaches to introduce molecular therapies directly into intact skin that do not require tissue harvesting, growth in culture and regrafting represent the next level of needed advances. To address this, plans are proposed to develop the capability for direct delivery of genetic and protein therapeutics to skin using human tissue models of epidermolysis bullosa (EB) and epidermal cancer as prototypes of inherited and acquired human skin disease. First, because they still offer the most efficient means of gene transfer, we will develop capabilities for direct viral vector gene transfer to human skin. To do this, they will use the feline immunodeficiency (FIV) and **human immunodeficiency virus** (I HV) based lentiviral vectors as well as adeno associated virus (AAV) because they represent complementary approaches to achieve durable genomic integration directly into human skin tissue. Second, due to its attractive safety, cost and stability, the capability for non-viral vector gene transfer to skin will be developed. In doing this, they will attempt to address the two major problems plaguing this approach, namely transience of plasmid retention and low efficiency of gene transfer. To increase persistence, they will use new non-viral transposase and integrase-based methods of plasmid genomic integration. To boost efficiency, they will link DNA elements to newly characterized protein transduction sequences (PTS). Finally, because of its complementary strengths to genetic therapies and its more direct translation to conventional therapeutics, the capability for direct polypeptide delivery to human skin will be developed. Using PTS they have recently shown capable of traversing the cutaneous barrier and entering all cells within human skin, they plan to develop the capability to deliver both small peptides and larger proteins in corrective models of human epidermal neoplasia and EB. At the end of the proposed funding period, they hope to have developed capabilities to deliver new molecular therapeutics directly to skin tissue and to have established their potential utility using models of inherited and neoplastic skin disease.

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- **Project Title: DETERMINATION OF RETROVIRUS MUTATION RATES**

  Principal Investigator & Institution: Dougherty, Joseph P.; Associate Professor; Molecular Genetics & Microbiol; Univ of Med/Dent Nj-R W Johnson Med Sch Robert Wood Johnson Medical Sch Piscataway, NJ 08854

  Timing: Fiscal Year 2001; Project Start 15-JUN-1989; Project End 31-DEC-2003

  Summary: (Adapted from investigator's abstract) This application concentrates upon determining the rates and spectra of mutation arising during a single cycle of HIV and MLV vector viral replication.One objective is to develop HIV-based packaging cells needed to carry out HIV mutation rate studies. Once such HIV-based packaging cells are available, they will be utilized for HIV forward mutation rate (loss-of- function) analysis. One of the genes to be employed as a reporter is the lacZa gene. The studies to be done with MLV are an extension of already described work indicating that MLV vectors can undergo genetic rearrangement at a particularly high rate, including a high rate of transduction of sequences from infected cells. Experiments are proposed to extend MLV mutation rate analysis to a number of genes to address the sequence-dependence of mutational events.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: DETERMINATION OF TRIAPINE ANTIVIRAL ACTIVITY**

  Principal Investigator & Institution: Belcourt, Michael F.; Vion Pharmaceuticals, Inc. 4 Science Pk New Haven, CT 06511

  Timing: Fiscal Year 2003; Project Start 15-SEP-2003; Project End 14-MAR-2004

  Summary: (provided by applicant): Triapine (3-aminopyridine-2-carboxaldehyde thiosemicarbazone is a novel ribonucleotide reductase inhibitor with antineoplastic activity that is 1000 times more potent than hydroxyurea as an inhibitor of ribonucleotide reductase with activity against cell lines resistant to hydroxyurea and gemcitabine. Hydroxyurea, widely used in the treatment of human malignancies, potentiates the antiviral activities of various nucleoside analogues against **human immunodeficiency virus** (HIV-1) and herpes simplex virus-1 and -2 (HSV-1 and -2). The preclinical data suggests that Triapine is superior to hydroxyurea as a cancer chemotherapeutic and thus warrants investigation as an adjuvant to antiviral therapies. This application proposes to investigate the potential of Triapine as an adjuvant to existing antiviral therapies by a) determining the levels of the dNTP pools in host cell lines following exposure to concentrations of Triapine, in combination with nucleoside analogues, yielding antiviral activity; b) measuring the effect of Triapine on nucleoside kinase enzymes to assess their impact on the recovery of specific dNTP pools and on the degree of phosphorylation of the nucleoside analogues; and c) assessing the toxicity and antiviral activity of Triapine combined with various nucleoside analogues (selected based on the impact of Triapine on specific dNTP pools) against HIV-1, HSV-1 and -2, and Hepatitis B virus.

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- **Project Title: DEVELOPMENT OF GENE TRANSFER APPROACHES FOR NEUROAIDS**

  Principal Investigator & Institution: Lu, Yuanan; None; University of Hawaii at Manoa 2500 Campus Rd Honolulu, HI 96822

Timing: Fiscal Year 2002; Project Start 01-SEP-2002; Project End 31-JUL-2007

Summary: (provided by applicant): **Human immunodeficiency virus** (HIV) is a primary disorder of the central nervous system (CNS) that affects about 20% of individuals infected with HIV. Treatment for HIVD are limited, in part because many antiretroviral drugs fail to penetrate the blood-brain barrier (BBB); novel approaches are therefore needed. One such approach may be to target cells that normally traffic across the BBB-such as blood monocytes. The hypothesis of this proposal is that it may be possible to genetically modify bolld monocytes and to use them as a "Trojan horse" delivery system, to effect gene transfer into the CNS, for treatment of neuroAIDS. This project will be conducted as an integrated, coordinated collaboration between investigators at the University of Hawaii and the University of Rochester. The applicant component of this project will focus on the testing and comparative analysis of different virus vectors for their potential ability to transduce blood monocytes; vectors will also be evaluated with respect to their efforts on monocyte transmigration across the blood-brain barrier. Experiments will also be conducted to determine (1) whether monocytes transduced with a defective interfering lentivirus vector (DLV) are less permissive for replication of infectious HIV-1, and (2) whether the DLV can be mobilized, amplified and spread to untransduced bystander cells by infectious HIV-1. The collaborator component of this application will focus on analyzing whether vector-transduced monocytes release soluble neurotoxic factors associated with cellular activation. In addition, the collaborator with construct a virus vector encoding a soluble neuroprotective factor, and will determine if monocytes transduced with this vector are capable of promoting the survival of bystander neurons exposed to well-defined candidate HIV- neurotoxins. The entire project comprises a tightly integrated whole, and will allow for the complementary expertise of the investigators to be applied in a maximally productive and mutually beneficial way. The collaboration will also provide ample opportunitites for the PI, and his students and fellows, to obtain training in neuroscience and a wide range of related techniques. Overall, the work is expected to result in significant insight into new approaches for treatment of neuroAIDS and other neurologic diseases.

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- **Project Title: DEVELOPMENT OF TRANSGENIC RAT MODELS FOR HIV-1 INFECTION**

  Principal Investigator & Institution: Reid, William C.; None; University of Md Biotechnology Institute Baltimore, MD 212023101

  Timing: Fiscal Year 2001; Project Start 01-APR-2000; Project End 31-MAR-2005

  Summary: (adapted from the application s abstract): The **human immunodeficiency virus** type 1 (HIV-1) is a human retrovirus that causes AIDS. The exact pathogenic roles of HIV-1 in AIDS, however, are not well understood. Possible roles include apoptosis and dysregulation of cytokine expression, mediated by the viral transactivator, Tat, and synctium formation, bystander killing, and cell cycle dysregulation, mediated by binding of the envelope glycoprotein gp120 to CD4 or to one of several co-receptors, which are the chemokine receptors CCR5 and CXCR4. Most studies have focused on cell-virus interactions in cell culture. These systems, however, lack the complexity of interactions that occur in infected people. Animal model systems are needed; unfortunately, only primates are readily infected with human immunodeficiency viruses, and only chimpanzees can be infected with HIV-1. Mice trangenic for human CD4 (jCD4) are not highly susceptible to infection. Blocks to HIV-1 infection of mice include a lack of functional receptors and co-receptors and an inability to support Rev function in relevant cell types. HIV-1 has been established as a transgene in mice to

circumvent problems of viral entry, but the transgene is not expressed well in peripheral blood mononuclear cells (PBMC) (in contrast to PBMC in infected humans), and the lack of functional interactions between envelope proteins and murine cell surface receptors precludes induction of pathogenic effects due to envelope-receptor binding. Rat CXCR4 has been reported to support infection of hCD4+ rat cells with some syncytium inducing (SI) strains of HIV-1. The investigators have established rats transgenic for a SI HIV-1 provirus lacking gag and pol genes. Envelope gp 120 is expressed on PBMC and in serum of transgenic rats. This application focuses on characterizing HIV-1 gene expression and pathology in the HIV-1 gene expression and pathology in the HIV-1 Tat-inducible promoter will also be established and their susceptibility to exogenous HIV-1 infection analyzed. The hCD4+ rat will be transplanted with bone marrow or peripheral blood mononuclear cells from the HIV-1 trangenic rat to provide envelope protein and elicit antibodies and CTLs against HIV-1. This may provide clues as to what role the host immune system plays in HIV-1 pathogenesis.

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- **Project Title: DISPLAY OF HIV-1 EPITOPES ON PLANT VIRUS PARTICLES**

  Principal Investigator & Institution: Palmer, Kenneth E.; Large Scale Biology Corporation 3333 Vaca Valley Pky, Ste 1000 Vacaville, CA 95688

  Timing: Fiscal Year 2003; Project Start 15-SEP-2003; Project End 31-AUG-2005

  Summary: (provided by applicant): The **human immunodeficiency virus** type 1 (HIV-1) pandemic now eclipses all other known epidemics in terms of its impact on human morbidity and mortality, as well as the global economy. The need for an efficacous and cost effective vaccine is urgent, but has proven to be an enormous scientific challenge. Ideally, an HIV-1 vaccine will induce sterilizing immunity against infection with a broad range of virus variants. There have been some notable advances in development of vaccine regiments that are able to generate significant levels of protection against development of AIDS in non-human primate models. These vaccines allow animals to control viral challenge by strong priming of virus-specific cytotoxic T cells, but this cannot prevent infection and mechanisms to induce neutralizing antibodies remains a vital goal. Recombinant virus-like particles show great promise for development of potent immunogens that are able to induce high levels of antibody production. Large Scale Biology Corporation has developed a virus-like particle antigen display system based on rod-shaped plant viruses. Linear epitopes that represent the binding site of HIV-1 neutralizing antibodies, and HIV-1 surface glycoprotein loop structures will be displayed in ordered, repetitive, quasicrystalline arrays on the surface of rod-shaped tobacco mosaic virus and potexviruses, and are expected to induce high levels of peptide-specific antibodies. Methods to enhance the expression and purification of recombinant viruses displaying HIV-1 peptides will be employed. The recombinant viruses will be characterized by biophysical, chemical and immunological methods. Recombinant viruses that appear promising will be used to immunize guinea pigs, and guinea pig sera will be used to assay for HIV-1 neutralizing activity in vitro. Demonstration of neutralizing activity will justify future work on development of plant virus peptide display systems for HIV-1 subunit vaccines. This system is very easy to scale up, and allows production of extremely cheap, effective vaccines.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: DOMAIN-SPECIFIC SEROLOGY FOR SIV/SHIV VACCINE EVALUATION**

  Principal Investigator & Institution: Montelaro, Ronald C.; Professor; Molecular Genetics & Biochem; University of Pittsburgh at Pittsburgh 350 Thackeray Hall Pittsburgh, PA 15260

  Timing: Fiscal Year 2001; Project Start 30-SEP-2000; Project End 31-JUL-2005

  Summary: We recently described novel serological assays that revealed for the first time a complex and lengthy maturation of envelope-specific antibody responses to HIV-1 and animal lentivirus (SIV, SHIV, EIAV, FIV) infections, Using these novel serological parameters to characterize antibody responses elicited by a diverse panel of experiments SIV)and EIAV) vaccines , we further demonstrated a close association between protective efficacy and the extent of immune maturation achieved by a particular vaccine. Based on this model of immature/non-protective and mature/protective antibody responses, we hypothesize that a more detailed definition of the maturation of envelope-specific antibody responses to experimental SIV and SHIV vaccines can provide fundamental new insights into the nature of protective immunity and provide new parameters that can be used as predictive immune correlates of experimental vaccine SIV and HIV-1 envelope proteins, i.e., "domain- specific serology", can provide a higher resolution definition of the antibody responses to vaccines compared to the use of complete envelope protein antigens in serological assays. Therefore, we propose the following specific aims to develop and evaluate domain-specific serology in the SIV and SHIV monkey vaccine models: (1) To map and characterize conformationally dependent epitopes of SIV envelope proteins using complementary techniques of HIV-1/ SIV chimeric antigens and antibody protected proteolysis. (2) To develop deep novel domain-specific serological assays to characterize the maturation of antibody responses to attenuated SIV vaccines and its association with the development of protective immunity, (3) To evaluate domain-specific serology as a correlate of SIV vaccine efficacy in experimental trials of subunit, DNA, live attenuated and vector expression-based vaccine trials. (4) To develop domain-specific serological assays to map HIV-1 envelope antigenic determinants, to characterize the maturation of antibody responses to SHIV infection, and to identify immune correlates of SHIV vaccine efficacy. It is anticipated that the information gained from the proposed domain- specific serological studies in the SIV and SHIV vaccine models will provide importance guidance for the design of human AIDS vaccine strategies and validate the new serological methods as potential correlates of HIV-1 vaccine efficacy in human clinical trials.

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- **Project Title: DRUG ABUSE, DEPRESSION AND RESPONSES TO HIV COUNSELING**

  Principal Investigator & Institution: Marmor, Michael; Environmental Medicine; New York University School of Medicine 550 1St Ave New York, NY 10016

  Timing: Fiscal Year 2002; Project Start 01-APR-2002; Project End 31-MAR-2005

  Summary: (provided by applicant) The long-term objective of this research is to reduce the incidence of infection with **human immunodeficiency virus** type 1 (HIV) in industrialized countries by developing methods to identify and treat high-risk individuals whose response to HIV testing and counseling is hindered by psychopathology. The project's specific aims are (1) to describe the distribution of psychopathologies among persons undergoing HIV testing and counseling, and (2) to test the hypotheses that high-risk, HIV-seronegative persons with mild-to-moderate

depression will be more likely to adopt protective behavior changes when provided with pharmacotherapy for their depression than when treated with placebo. The study design to achieve specific aim 2 will be a randomized, double-blinded clinical trial of bupropion hydrochloride versus placebo administered for a total of 7 months. The study population will be initially high-risk, HIV-seronegative men who have sex with men (MSM). Individuals who are ineligible or decline entry into the clinical trial will be entered into an observational study. The primary outcome measure of the clinical trial will be self-reported numbers of partners in unprotected receptive anal intercourse. Secondary outcomes will be substances used and frequency of substance use by self-report and toxicology; (c) new infections with sexually transmitted infections including gonorrhea, syphilis, Kaposi's sarcoma-associated herpesvirus, and hepatitis C virus (HCV) and HIV; and (d) measures of psychological factors that have been shown to be, or are thought to be, associated with HIV incidence rates, including measures of self-efficacy, self-esteem, stage of change, and depression. Enrollment data from the observational study will be combined with enrollment data from the clinical trial to provide a description of the distribution of psychopathologies and substance abuse among high-risk MSM. Longitudinal data form the observational study will be used to assess the associations of psychopathologies, substances used and frequency of substance use with adverse outcomes.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: DUAL SUBTYPE QUASISPECIES ENVELOPE SHIV VACCINES**

  Principal Investigator & Institution: Haigwood, Nancy L.; Director; University of Washington Seattle, WA 98195

  Timing: Fiscal Year 2003; Project Start 01-JAN-2003; Project End 31-DEC-2007

  Summary: The overall goal of this project is to explore the mechanisms that are involved in the development of neutralizing antibodies and protective immunity during vaccination and during the immediate post-challenge time frame. This knowledge will be used to design improved vaccine strategies to offer protection from infection, not only protection from disease. These experiments will be performed in the SHIV(SF162P) model of moderate pathogenesis in the pigtailed macaque (M. nemestrina). Virus neutralizing antibodies can be elicited by some limited number of vaccination strategies, but these have been typically low in quality and quantity. In the course of this project, we plan to develop immunogens that can elicit broad cellular immunity and broad, cross-clade protective humoral immunity. Naturally occurring HIV Envelope variants (quasispecies Envelope variants) will be used in combination with the other structural and regulatory genes encoded by SHIV in vaccine challenge experiments in macaques. Vaccines will be delivered by recombinant vaccinia virus, DNA, and recombinant oligomeric gp140 proteins. There are four aims: AIM 1. Develop quasispecies vaccines based on the viral variants arising in the course of SHIV(SF162P) infection of M. mulatta and M. nemestrina and HIV subtype A infection of human patients from Kenya (Project 1). Choose subjects that developed broadly reactive neutralizing antibodies. Select variants that represent Envelopes present during the development of the quasispecies and that are neutralized by sera from SHIV-infected macaques, human HIV + sera, and human mAbs that neutralize primary HIV-1 isolates. AIM 2. Examine the rote of quasispecies Envelopes derived from SHIV(SF162P) in eliciting broadly neutralizing antibodies. By presenting combined and individual quasispecies variant Envelopes to the immune system during vaccination, determine which pattern of exposure to the variants elicits qualitatively different responses compared with the exposure to a single Envelope protein. Choose the optimal vaccination strategy that offers the best protection

from infection or disease following SHIV(SF162P) challenge. AIM 3. Compare subtype A Envelope quasispecies vaccines and subtype B subtype quasispecies vaccines for the ability to provide same-clade and cross-clade protection from a SHIV-A challenge. Measure correlates of protection from infection and disease.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: DYNORPHIN AND GLIAL CELL IMMUNOMODULATION**

  Principal Investigator & Institution: Peterson, Phillip K.; Professor and Director; Minneapolis Medical Research Fdn, Inc. 600 Hfa Bldg Minneapolis, MN 55404

  Timing: Fiscal Year 2001; Project Start 01-JUL-1995; Project End 31-MAR-2004

  Summary: Endogenous opioid peptides have been postulated to modulate the neuropathogenesis of **human immunodeficiency virus** (HIV)-1, the etiologic agent of acquired immunodeficiency syndrome (AIDS) dementia. The principal hypothesis of the work proposed in this grant renewal application is that kappa opioids have a neuroprotective role in HIV-l-induced brain disease by suppressing HIV-1 expression and by reducing viral-induced neuronal injury. In the past several years, we have found that kappa opioid receptor (KOR) ligands inhibit HIV-1 expression in acutely infected human microglial cell cultures. In preliminary studies, KOR ligands also appear to suppress viral expression in cultures of human monocytes, the precursor cells of microglia. Although the mechanism of this antiviral effect has not yet been elucidated, kappa opioids are proposed to trigger a cascade of cellular events resulting in reduced viral expression by one or more of the following mechanisms: 1) inhibition of viral entry into target cells, 2) reduced activation of nuclear factor-kappaB, a cellular transcription factor required for the activation of the HIV-1 replication, 3) suppression of HIV-1 promoter activity, or 4) potentiation of the production of antiviral beta-chemokines by opioid-treated cells. Also, the anti-viral effects of U5O,488 will be tested using primary HIV-1 isolates (Specific Aim l). In addition to their antiviral activity, KOR ligands will be evaluated for their neuroprotective activity against HIV-1-induced toxicity using the HIV-l SF162 strain and primary isolates. The protective mechanism of KOR ligands is postulated to involve either l) an indirect mechanism by inhibiting microglial cell- and monocyte- induced production of neurotoxins (i.e., quinolinate, Tat, or cytokines [interleukin-1beta and tumor necrosis factor-alpha] or 2) a direct mechanism protecting neurons against toxicity induced by these toxins (Specific Aim 2). The findings from these studies will potentially provide insights into mechanisms associated with antiviral and neuroprotective effects of kappa opioids and hopefully will lead to development of new therapeutic approaches for AIDS dementia.

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- **Project Title: E1-DELETED ADENOVIRAL VECTORS FOR ORAL IMMUNIZATION**

  Principal Investigator & Institution: Ertl, Hillegund C.; Wistar Institute Philadelphia, PA 191044268

  Timing: Fiscal Year 2003; Project Start 10-JUL-2003; Project End 31-MAY-2005

  Summary: (provided by applicant): The aim of this application is to test novel E1 - deleted adenoviral recombinants expressing antigens of HIV-l for induction of mucosal and systemic transgene product-specific CD8+ T cell responses upon application to the oral cavity. Our long-term goal is to develop an optimized oral vaccination protocol in a pre-clinical mouse model for eventual use in a non-human primate model and then in humans. We will use the E1-deleted adenoviral (Ad) recombinant of the recently

vectored simian serotype 6 (AdC6) either alone or in a heterologous prime boost regimen with the AdC68 recombinant which is also of simian origin or the well characterized Ad vector of the human serotype 5 (AdHu5). For the initial proof of principle studies we will use vectors expressing a truncated form of gag of HIV-l clade B. Results will then be extended to vectors expressing a codon-humanized polypeptide of gag/pol/nef in conjunction with vectors expressing a codon-humanized envelope protein (env) of HIV-1 clade B. In aim 1 we will determine the frequencies of transgene product-specific interferon (IFN)-gamma producing CD8+ T ceils that are induced in local and distant lymphoid tissue upon a single oral immunization with an Ad vector. Frequencies in different tissues will be determined during the effector and memory phase of the immune response. In aim 2, we will test for the induction of CD8+ T cell responses following oral prime boost regimens with homologous or heterologous Ad vaccine carriers. In aim 3, we will compare biological functions of CD8+ T cells induced by oral immunization to those induced by systemic vaccination emphasizing their lytic activity, cytokine production profile and epitope recognition repertoire. In aim 4, we will determine the tropism of the simian and human Ad recombinants upon oral application emphasizing localization of and cytokine production by transduced antigen presenting cells (APCs).

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- **Project Title: EFFECT OF ALCOHOL ON SHIV NEUROINVASION**

  Principal Investigator & Institution: Stephens, Edward Brice.; Associate Professor; Microbiology, Molecular Genetics, and Immunology; University of Kansas Medical Center Msn 1039 Kansas City, KS 66160

  Timing: Fiscal Year 2002; Project Start 30-SEP-2002; Project End 31-JUL-2005

  Summary: (provided by applicant): Approximately 20% of humans infected with **human immunodeficiency virus** type 1 (HIV-1) develop a neurological disease known as HIV-associated cognitive/motor complex or AIDS dementia complex. It is known that chronic use of ethanol can lead to an immunocompromised state that results in increased susceptibility to bacterial and viral pathogens. A significant number of HIV-1 positive individuals drink moderate to excessive amounts of alcohol. Detailed studies directly assessing the role of alcohol on HIV-1 neuroinvasion and neuropathogenesis have not been performed in a relevant animal model system. The investigator's laboratory has derived a variant of simian-human immunodeficiency virus (SHIV500LNV) that following inoculation into pig-tailed macaques, results in high virus burdens, depletion of the CD4+ subset of T cells, and a neuropathology (perivascular cuffing, microglial nodules) in 50% of the macaques that is similar to that seen in HIV-1 infected humans. In the proposed studies, the investigators propose to use the neuropathogenic SHIV/macaque model to determine if alcohol can directly affect the early events of neuroinvasion as well as the incidence of SHIV-induce encephalitis. Sixteen macaques will be placed on a self-administered ethanol diet to model moderate drinking and sixteen macaques on lacking ethanol for 9 months. At this point, sixteen macaques (eight on the ethanol diet and eight on the ethanol free diet) will be inoculated with SHIV500LNV, maintained on their ethanol diet and sacrificed at 2 weeks to determine if self-administered ethanol will result in increased neuroinvasion during the primary phase of infection, which is a period of unrestricted virus replication and when the host has not yet developed an effective immune response against the virus. In the second group of sixteen macaques (again eight on the ethanol diet and eight on the ethanol-free diet), the virus will be inoculated and macaques followed until moribund to determine if an ethanol diet will result in an increased incidence of neurological disease.

The results of these studies should provide direct evidence on the effect of ethanol on primate lentivirus neuroinvasion and neuropathogenesis.

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- **Project Title: EFFECTS OF NUCLEOSIDE ANALOGS ON HIV-1 INFECTION OF BRAI**

  Principal Investigator & Institution: Nath, Avindra; Professor; Neurology; University of Kentucky 109 Kinkead Hall Lexington, KY 40506

  Timing: Fiscal Year 2001; Project Start 01-AUG-1999; Project End 31-AUG-2002

  Summary: It has been recognized since the beginning of the AIDS epidemic that the brain may be an important reservoir for the **human immunodeficiency virus** (HIV). Drug development for treatment of HIV infection has progressed to the remarkable pace of two to three drugs being introduced in the clinic every year. However, we currently know very little about their ability to cross the blood brain and brain-cerebrospinal fluid barriers and almost nothing about their ability to enter susceptible cells in the brain, form active metabolites within these cells, or their ability to incorporate into HIV DNA and inhibit its replication. In this proposal we will examine each of six clinically used antiretroviral nucleoside analogs targeted against the reverse transcriptase enzyme and determine their ability to enter human glial cells, to form active metabolites, and to control HIV infection in these cells.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: EFFECTS OF PROGESTERONE & ESTROGEN ON SIV VAGINAL TRANSMISSION: MENOPAUSE**

  Principal Investigator & Institution: Marx, Preston A.; Professor; Tulane University of Louisiana New Orleans, LA 70118

  Timing: Fiscal Year 2001

  Summary: The objective is to search for mechanisms by which the female hormones, progesterone and estrogen, influence vaginal transmission and pathogenesis of Simian Immunodeficiency Virus (SIV) in rhesus macaques. Progesterone?s known effects on female physiology are numerous. They include thinning of vaginal epithelium and immune suppression. In a recent study, progesterone was shown to increase SIV vaginal transmission. Thinning the vaginal barrier to SIV infection is a potential cause of this increase, but immune suppression, possible increases in target cells in vaginal tissues or direct effects on in vivo SIV replication need study. Moreover, an important inference from the progesterone study was that estrogen, an antagonist of progesterone, may actually protect against SIV vaginal transmission. Two specific aims are proposed to identify and characterize the action of progesterone, estrogen and the anovulatory state in vaginal transmission and pathogenesis of SIV. Aim 1. To individually test the effects of progesterone and estrogen on SIV vaginal transmission and their effects on SIV pathogenesis and the SIV immune response. Aim 2. To test progesterone and estrogen on in vivo pathogenesis independent of vaginal mucosal changes through intravenous infection of hormone treated- macaques. In both aims, each hormone will be examined independently by testing virus load, clinical outcome and immune responses in ovariectomized macaques with and without progesterone and estrogen implants. Ovariectomy is a standard technique for individual in vivo study of the sex hormones. Natural states of elevated hormones or their absence as in menopause, bear on vaginal physiology and may therefore, influence vaginal transmission of **human immunodeficiency virus** (HIV). Moreover, drugs based on these hormones are used in

female contraceptives. Because human epidemiologic studies are difficult to design and control, an understanding of hormones gained in the SIV model may help to elucidate the effects of these natural and drug-based co-factors on HIV vaginal transmission. FUNDING NIH (1R01 AI41952) PUBLICATIONS Sodora, D.L., A. Gettie, C.J. Miller and P.A. Marx. Vaginal transmission of SIV assessing infectivity and hormonal influences in macaques inoculated with cell-free and cell-associated viral stocks. AIDS Research and Human Retroviruses, 13:S1-S5.

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- **Project Title: EPIDEMIOLOGY OF ANAL HIV-1 INFECTION**

  Principal Investigator & Institution: Kiviat, Nancy B.; Director of Pathology; Medicine; University of Washington Seattle, WA 98195

  Timing: Fiscal Year 2000; Project Start 05-FEB-1992; Project End 31-DEC-2003

  Summary: We are in the fourth and final year of a study of the relationship between **human immunodeficiency virus** (HIV), and types of human papillomavirus (HPV), immunosuppression, and risk of development of high grade anal squamous intraepithelial lesions (HGASIL), the anal cancer precursor lesion most closely related to invasive anal cancer (R01CA55488, Nancy Kiviat PI). Our major findings included: a) development of high grade anal squamous intraepithelial lesions (HGASIL) is associated with HIV seropositivity, with HIV seropositive men with CD4 count below 500/mul at greatest risk; b) among both HIV seropositive and HIV seronegative men, development of HGASIL associated with high levels of HPV types 16/18; (c) development of HGASIL is associated with low risk HPV type HPV in addition to HPV 16/18 among HIV seropositive, but not among seronegative men; and d) HIV seronegative were much more likely to regress from HGASIL to normal than were HIV seropositive men. We now propose a survey of questions focused on further exploring the relationship between HIV and HPV. We will: 1) test the hypothesis that the development of ASIL is associated with the presence and amount of HIV; 2) determine whether there is support of the hypothesis that the effect of anal HIV on anal HPV is (a) the result of local HIV induced immunosuppression (b) direct effect of HIV on HPV; and 3) initiate studies examining the characteristics, pathogenesis and clinical consequences of anal HIV variants: by cross sectional analysis of first visit samples. In summary, we propose a survey of questions that are likely to contribute significantly to our understanding of both general HIV pathogenesis and the development of HPV-related pathology among HIV-seropositive men.

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- **Project Title: EPIDEMIOLOGY OF HIV-1/HIV-2 DUAL INFECTION**

  Principal Investigator & Institution: Gottlieb, Geoffrey S.; Medicine; University of Washington Seattle, WA 98195

  Timing: Fiscal Year 2001; Project Start 01-JUL-2001; Project End 30-JUN-2006

  Summary: (provided by applicant): This application, entitled Molecular Epidemiology and Viral Evolution in HIV-2 and HIV-1/HIV-2 Dually Infected Individuals in Senegal, for a K08 Mentored Clinical Scientist Development Award, will help enable Dr. Geoffrey S. Gottlieb, under the sponsorship of Dr. James I. Mullins and collaborators at the University of Washington School of Medicine and the University of Dakar, Senegal, to acquire the skills necessary to continue to pursue the immediate goals of this research plan as well as to continue his path toward an innovative and productive independent academic research career as a physician-scientist. A global understanding of the

diversity and evolution of Human Immunodeficiency Viruses (HIVs) will be important to developing prophylactic vaccines and understanding the pathogenesis of AIDS. Although structurally and genetically similar, HIV-1 and HIV-2, behave quite differently, both at the level of the individual patient and as agents of the global epidemic. The reasons for this are not clear. Evidence suggests that patients dually infected with both HIV-1 and HIV-2 have greater control of their viral burden. Our longitudinally followed cohort of Senegalese individuals whom are infected with HIV-1, HIV-2 or both viruses provides a unique opportunity to study the molecular epidemiology and evolutionary dynamics of AIDS in West Africa and to correlate them with virologic, immune and clinical outcomes. This application will examine the following hypotheses: 1) If intra-patient, HIV-2 viral diversity and divergence will be attenuated compared to that seen in HIV-1 and if the rate of HIV evolution, as measured by viral divergence and diversity, will be slower in dually infected individuals. Whether emergence of CXCR4 HIV-1 variants will be delayed in dually infected individuals and whether these events correlate with immune status, viral load and clinical outcomes; 2) That cross-reactive immune responses and viral interference between HIV-1 and HIV-2 selects for infection with unique HIV-1 subtypes in dually infected individuals; and 3) If recombinant HIV-1/HIV-2 viruses can emerge in dually infected individuals and if they do, whether they alter the natural history of HIV infection in these people.

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- **Project Title: EPIDEMIOLOGY OF ORAL HIV 1 & 2 INFECTION IN HIGH RISK WO**

  Principal Investigator & Institution: Critchlow, Cathy W.; Associate Professor; Epidemiology; University of Washington Seattle, WA 98195

  Timing: Fiscal Year 2001; Project Start 30-SEP-1999; Project End 31-AUG-2004

  Summary: (Adapted from Applicant's Abstract) Transmission of HIV via oral-genital contact has now been convincingly documented. Risk of HIV transmission during unprotected oral-genital sex appears to be low compared to that encountered during unprotected vaginal sex. However, the true risk of oral HIV transmission has been difficult to assess as relatively few individuals engage exclusively in oral sexual contact. Attempting to estimate this risk using HIV seroconversion as an endpoint would be prohibitively expensive and present ethical problems. Other approaches are needed to assess aspects of oral HIV transmission. Development of HIV education and risk reduction programs related to oral HIV transmission are currently important since recent data suggest that in some high risk groups, attempts to decrease high risk behaviors (such as unprotected anal or vaginal sex) have made unprotected oral sex exceedingly common, perhaps increasing the proportion of HIV infections in these populations attributable to orogenital sexual contact. Development of educational programs concerning risk of oral HIV transmission is urgently needed in Africa where the majority of HIV infections have occurred, and where commercial sex workers (CSWs) have been integral to the spread of HIV-1 and HIV-2. Little is known about the frequency and determinants of fellation and its relationship to risk of HIV infection. However, a survey the investigators undertook during the emergence of the HIV-1 epidemic in Senegal revealed that most CSMs frequently engaged in both vaginal sex and fellatio. Some CSWs in Senegal have enrolled in HIV testing and counseling programs and it is possible that such programs have stressed fellatio in lieu of vaginal sex. The investigators are proposing a study among CSWs in Senegal to examine the role of fellatio in the spread of HIV-1 and HIV-2. Specifically, they propose to (1) describe the frequency and determinants of the practice of fellatio among CSWs, and among CSWs

who have not been previously tested for HIV or been enrolled in HIV risk reduction programs, to determine the associations between HIV serologic status and fellatio and other sexual practices, (2) provide insights into risk of transmission of HIV from infected CSWs to uninfected male partners during fellatio by describing the determinants of the frequency and quantity with which HIV is shed into oral secretions, and (3) undertake a small pilot study to attempt to decrease the frequency and level of HIV in oral secretions by using low cost topical treatments for lesions known to be associated with inflammation.

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- **Project Title: ESTABLISHMENT OF HIV INFECTION IN COTTON RATS**

  Principal Investigator & Institution: Blanco, Jorge C.; Virion Systems, Inc. 9610 Medical Center Dr, Ste 100 Rockville, MD 20850

  Timing: Fiscal Year 2003; Project Start 01-MAY-2003; Project End 30-APR-2004

  Summary: (provided by applicant): The development of a small animal model to study **human immunodeficiency virus** type-1 (HIV-1) infection would significantly facilitate studies on disease pathogenesis, as well as vaccine and anti-viral drug development and testing. However, HIV-1 replication is subjected to a number of species-specific restrictions at the level of cellular entry and/or post-entry. To date, no satisfactory small animal model for HIV-1 infection has been identified. The cotton rat has been a superb model for human infectious diseases. This animal is susceptible to an extraordinary spectrum of human pathogens, particularly viruses. Inspired by these observations, it has been cloned and characterized a battery of more than 20 cotton rat genes of immunological and inflammatory importance, and reagents for their detection has been developed. **Human immunodeficiency virus** (HIV-1) was shown to infect two species of cotton rats, Sigmodon hispidus and S. fulviventer and infectious virus was transmitted from animal to animal by blood. In new studies it was found that cotton rat cells (primary macrophages and a cotton rat osteosarcoma cell line) after transfection with a plasmid containing the backbone genome of HIV-1 support levels of HIV transcription analogous to those observed in human monocytes, indicating the absence of transcription blockage. Additionally, cotton rat cells became permissive to a HIV-1 pseudotyped infection when they transiently co-expressed human CD4 and CCR5 or CXCR4 chemokine receptors. The overall goal of this proposal is to generate a small animal model for HIV-1 infection by generating transgenic cotton rats expressing HIV-1 co-receptors. An HIV-1-permissive cotton rat could be widely used by the research community. At the completion of the exploratory experiments proposed for phase I of this SBIR, we will know the potential of the cotton rat as a transgenic model for HIV-1 studies, and whether is worth the time and expense to develop transgenic animals in a phase II study.

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- **Project Title: EVALUATION OF THE HIV-1 SUBTYPE C ISOLATES FROM INDIA**

  Principal Investigator & Institution: Ahmad, Nafees; Microbiology and Immunology; University of Arizona P O Box 3308 Tucson, AZ 857223308

  Timing: Fiscal Year 2001; Project Start 01-SEP-2000; Project End 31-JUL-2003

  Summary: An effective vaccine against **human immunodeficiency virus** type 1 (HIV-1) infection must incorporate features necessary to neutralize variant viral subtypes present in different parts of the world. South Asia, particularly India, is currently recording the steepest increases in new HIV-1 infections. The predominant strains

infecting patients in India, as also parts of Africa, is subtype C. It has been estimated that subtype C infections account for about 50 percent of global HIV-1 infections. Yet, little is known about the biological properties of these viruses. Better characterization of HIV-1 has important implications for the development of prevention strategies because it should be targeted at the properties of viruses involved in transmission, pathogenicity and disease progression. We hypothesize that there are specific properties of HIV-1, including the functional domains in the env gp120 that are critical determinants of transmission and pathogenesis of infection. In this AIDS-FIRCA grant, it is proposed to study the biological properties of HIV-1, including replication efficiency cellular tropism, co-receptor usage, cytopathic effects, and genotypic and phenotypic properties involved in mother-to-child transmission of subtype HIV-1 C isolates obtained from patients in India. This will be accomplished by: (1) constructing proviral chimeras and recombinant viruses containing eng gp120 from HIV-1 subtype C in the background of an HIV-1 subtype B infectious molecular clone, pNL4-3, and (2) using the recombinant viruses so generated to infect T-lymphocyte lines and primary cells (primary blood lymphocytes and monocytes/macrophages), and reporter cell lines containing CD4 and various co-receptors. The ability of recombinant viruses to infect cell lines and primary cells of different lineages, their ability to induce syncytia, and a comparison to well characterized HIV-1 isolates will help understand the biological properties of HIV-1 subtype C viruses mediated by env gp120. An analysis of mother-infant pairs will provide information on properties conducive to perinatal transmission and test the hypothesis proposed by the P.I. about transmission of minor variants in a non-B subtype background. The information obtained may be useful in designing vaccination strategies againts HIV-1 subtype C and in developing intervention strategies to limit its perinatal transmission.

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- **Project Title: EVOLUTION AND PROPERTIES OF HIV/SIV STRAINS IN CAMEROON**

  Principal Investigator & Institution: Nyambi, Phillipe N.; Pathology; New York University School of Medicine 550 1St Ave New York, NY 10016

  Timing: Fiscal Year 2001; Project Start 01-APR-2000; Project End 31-MAR-2004

  Summary: The genetic relatedness of SIVcpz and HIV-1 supports the hypothesis of cross-species transmission and suggests that the three main groups of HIV-1 (M, O, and N), all found in Cameroon, are a result of separate introductions into humans. The Cameroon population is genetically diverse, with more than 250 ethnic groups living in isolated villages. Because cross-species transmissions may occur in distinct pockets of genetic diversity in Cameroon, recently introduced SIV/HIV-1 strains could be evolving separately in small and remote communities before spreading and further evolving in urban centers where the human genetic environment consists of a composite from various groups and locales. Furthermore, because the divergence of the subtypes may have originally occurred or may be occurring in a few ethnic groups where human genetic diversity is limited by cultural and geographic factors, the divergence of SIV/HIV-1 strains within each ethnic group may also be limited, resulting in relatively restricted immunologic and biologic characteristics. Studies are urgently needed at this point in time to understand the evolution of SIV/HIV in distinct local communities because new roads are linking these communities and thus increasing interaction. In addition, infection with multiple HIV groups or subtypes, or with recombinant viruses, has been documented in urban areas of Cameroon, yet little is known of the evolution of these viruses. Because information about viruses which have evolved little from their

SIV ancestors is lacking, as is information about viruses from multiple and recombinant HIV infections, we propose the following work: AIM l: To identify the distribution of HIV-1 variants circulating in different human ethnic groups, risk groups, and geographic locales in Cameroon and to study whether specific strains of HIV-1 exist exclusively or preferentially within any of these study populations. AIM 2: To study the antigenic and biologic characteristics of the HIV-1 strains found in AIM 1 and determine how their characteristics correlate with the different ethnic groups, risk groups, and geographic locales in which they are found. AIM 3: To monitor the viral evolution and disease progression in patients infected with multiple HIV-1 groups/subtypes, recombinants and "pure subtypes": AIM 4: To compare the rates and nature of mutations of viruses (as a measure of viral evolution) from persons infected with inter-subtype recombinants and "pure subtypes" and to correlate these changes with the host's humoral immune response. AIM 5: To identify the distribution of SIVcpz-like infections among non-human primate pets in the different geographic locales of Cameroon.

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- **Project Title: FELINE IMMUNODEFICIENCY VECTOR SYSTEM**

  Principal Investigator & Institution: Looney, David J.; University of California San Diego 9500 Gilman Dr, Dept. 0934 La Jolla, CA 92093

  Timing: Fiscal Year 2001

  Summary: Non-primate lentiviral vectors offer potentially safer and more convenient gene transfer to human cells than vectors based upon HIV-1. While the primate lentiviruses are derived from lethal human pathogens, there is no evidence that humans can be infected by FIV. Mobilization of HIV vectors in HIV infected individuals, while a possible advantage, raises the concern of transfer of vector to unintended targets, including germ cells. Recently, our studies showed that the only restriction to productive infection of human cells by feline immunodeficiency virus (FIV) is the inactivity of the FIV promoter. The use of a heterologous promoter allows production of FIV-based vectors in human cells (avoiding the risk of contamination by endogenous retroviruses present in non-human cells, while retaining the desirable lenti-retroviral capacity to transduce non-dividing, terminally differentiated cells such as neurons and monocyte-macrophage. However, the relative efficiency of FIV- and HIV-based vector systems for transduction and expression remains to be determined. FIV packaging systems which minimize recombination by use of separate constructs have yet to be developed. The antiviral activity of FIV vectors expressing ribozymes has not been examined, and the mobilization of FIV vectors by HIV or SIV infection has not been studied. The major goals of this project are: [1] To compare transduction efficiency of analogous FIV and HIV based vectors, and the extent to which these vectors are mobilized by HIV or SIV infection in vitro, [2] To develop safe and efficient packaging cell lines for production of high-titer FIV vectors, [3] To compare the efficiency of HIV and HIV expressing anti- HIV or SIV ribozymes to confer antiviral resistance, and [4] To examine the ability of FIV vectors to transduce primate hematopoietic stem cells capable of repopulation in macaque models, in collaboration with Project III. This project should provide valuable information needed to make a rational choice of FIV or HIV vectors for clinical applications such as gene therapy for HIV infection.

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- **Project Title: FETAL IMMUNOPROPHYLAXIS AGAINST A PRIMATE LENTIVIRUS**

  Principal Investigator & Institution: Ruprecht, Ruth M.; Professor of Medicine; Dana-Farber Cancer Institute 44 Binney St Boston, MA 02115

  Timing: Fiscal Year 2001; Project Start 01-DEC-1997; Project End 31-DEC-2002

  Summary: Our long-range goal is to develop immunoprophylaxis against maternal HIV-1 transmission by active and passive vaccination. Here, we propose to study passive immunoprophylaxis with combinations of human neutralizing monoclonal antibodies (mAbs) directed against different HIV-1 Env epitopes in rhesus macaque models that mimic intrapartum and in utero infection. We will challenge with SHIV-89.6P, a chimeric virus that contains tat, rev, vpu and env of a primary HIV-1 isolate, 89.6, in a simian immunodeficiency virus backbone. The Specific Aims are to: 1. Determine whether human mAbs that neutralize primary HIV-1 strains inhibit SHIV-89.6P synergistically when used in combination. 2. Perform pharmacokinetic studies with the most potent mAb combination in pregnant macaque dams and in their offspring. Neutralizing mAbs levels will be measured in maternal blood, amniotic fluid, cord blood and in neonatal mucosal secretions after passive therapy of pregnant macaque dams and newborns. 3. Test whether the most potent triple combination of neutralizing mAbs can protect neonatal macaques against intravenous (i.v.) SHIV-89.6P challenge. We will enroll 3 groups of 4 pregnant dams and their offspring. Group 1 animals will not be treated. Group 2 offspring will receive the mAb combination prenatally (by passive therapy of the pregnant dams) as well as after birth; and group 3 offspring will be given mAbs only postnatally. All 12 neonates will be challenged i.v. on day 1 of life with 10 50 percent animal infectious doses (AID50-i.v.) of SHIV-89.6P. 4. Test whether the most potent combination of human neutralizing mAbs can protect neonatal macaques against mucosal SHIV-89.6P challenge. A similar experimental design will be employed as described for Specific Aim #3. Neonates will be challenged orally (po) at birth with cell-free SHIV-89.6P (10 AID50-po). 5. Test whether the most potent combination of human neutralizing mAbs can protect macaque fetuses against intra-amniotic fluid challenge with SHIV-89.6P during the late 3rd trimester. Passive immunoprophylaxis will be given at weekly intervals during gestation; control dams will be left untreated. Cell-free virus will be instilled into the amniotic fluid under ultrasound guidance. The proposed experiments are highly significant because they allow a direct evaluation of human neutralizing mAbs directed against primary HIV-1 strains in primates. Data generated from this work can be translated into human clinical trials aimed at preventing maternal HIV-1 transmission.

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- **Project Title: FETAL STEM CELL GENE THERAPY**

  Principal Investigator & Institution: Muench, Marcus O.; Surgery; University of California San Francisco 500 Parnassus Ave San Francisco, CA 94122

  Timing: Fiscal Year 2001; Project Start 01-SEP-2001; Project End 31-AUG-2004

  Summary: (adapted from the application) A growing number of hematological diseases can be diagnosed before birth. In some cases, early treatment may benefit the health and survival of the fetus. Either in utero stem cell transplantation (IUT) or fetal gene therapy may treat diseases such as the hemaglobinopathies. This application aims to determine the best method for the introduction of genes into fetal hematopoietic stem cells (HSCs). Fetal HSCs are more proliferative than their adult counterparts and are, therefore, hypothesized to be more susceptible to transduction by retroviral vectors based on

murine leukemia virus or **human immunodeficiency virus.** IUT offers another means of curing a number of hematological diseases by generating a state of hematopoietic chimerism. However, in the absence of any advantage for the donor HSCs, the levels of chimerism that can be achieved by IUT are low. This limits the use of this therapy to very few diseases. Our aim is to extend the use of IUT to the treatment of diseases, such as thalassemia and sickle cell anemia, by engineering HSCs to have a proliferative advantage over normal HSCs. This application will test if introduction of the erythropoietin receptor (EpoR) into HSCs will render these altered cells responsive to erythropoietin (EPO). This will in turn result in the altered HSCs and their progeny having a proliferative advantage over normal progenitors. Truncated forms of EpoR (tEpoR) will also be tested. These tEpoR, having deletions in the negative regulatory region of their cytoplasmic domains, deliver stronger proliferative signals than EpoR. The effects of introducing the EpoR genes on the proliferation and differentiation of HSCs and their progenitor progeny will be determined using various in vitro culture systems. It is hypothesized that ectopic expression of either EpoR or tEpoR will confer the ability of HSCs and early progenitors to proliferate in response to EPO with minimal effect on the differentiation program of these cells. To test if ectopic EpoR or tEpoR expression on HSCs can make these cells more competitive than their normal counterparts, modified HSCs will be tested against control HSCs in a mouse model of human hematopoiesis. The ability of HSCs expressing ectopic EpoR to engraft bone marrow after no or only minimal cytoablation will also be tested. These in vivo experiments will further determine if making HSCs responsive to EPO will have any detrimental effect on the long‑term reconstituting‑ and multilineage‑ potential of HSCs. A positive outcome from the proposed studies would aid in developing treatments for hemoglobinopathies based on generating hematopoietic allochimerism.

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- **Project Title: FITNESS OF ENFUVIRTIDE-(T-20)-RESISTANT HIV-1**

  Principal Investigator & Institution: Kuritzkes, Daniel R.; Director of Aids Research; Brigham and Women's Hospital 75 Francis Street Boston, MA 02115

  Timing: Fiscal Year 2003; Project Start 01-JUL-2003; Project End 31-DEC-2006

  Summary: (provided by applicant): Mutations in **human immunodeficiency virus** type 1 (HIV-1) that confer drug resistance may also impair replication capacity of the virus. Reduced replication capacity of multi-drug resistant viruses may explain, in part, the persistent immunologic benefits of protease inhibitor-containing regimens in the setting of virologic failure. Plasma virus titers remain significantly below the viral set point due to the combined effects of the residual activity of the failing regimen and the reduced replication capacity compared to wild-type. Removal of selective pressure by treatment interruption leads to re-emergence of the fitter wild-type virus that is associated with a rise in virus load and fall in CD4 cell count. Enfuvirtide (T-20) is a novel HIV- 1 entry inhibitor with potent activity in vitro and in vivo. This 36-amino acid peptide blocks HIV-1 entry by binding to the first heptad repeat (HR-1) of the gp41 ectodomain, thereby preventing formation of a hairpin loop that is essential for virus-cell fusion. Mutations at several positions in HR-1 confer resistance to T-20. Although resistance to T-20 can develop quickly, data from clinical studies suggest that T-20 remains at least partially active despite emergence of T-20-resistant virus. Preliminary data show that these viruses are less fit than wild-type in growth competition assays in the absence of drug using a novel recombinant marker virus assay developed in our laboratory. We therefore propose a series of experiments to characterize further the effects of T-20

resistance mutations on HIV-1 fitness, kinetics of HIV-1 entry, and virulence. Specific aims of these experiments are: 1) To compare fitness of T-20 -resistant viruses in presence and absence of drug; 2) To test the hypothesis that fitness loss associated with T-20 resistance is significantly correlated with persistent antiviral activity of T-20; and 3) To test the hypothesis that fitness differences associated with T-20 resistance mutations are due to differences in the rate of virus-cell fusion. Results of these studies will provide a deeper understanding of the molecular, virologic, and clinical consequences ofT-20 resistance, and may help guide the use of T-20 in salvage therapy.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: GENETIC AND BIOLOGICAL VARIABILITY IN MATERNAL INFANT STRAINS OF HIV-1**

  Principal Investigator & Institution: Goodenow, Maureen M.; Professor; University of Florida Gainesville, FL 32611

  Timing: Fiscal Year 2001

  Summary: The purpose of this study is to examine the **human immunodeficiency virus** (HIV-1) that causes AIDS.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: GENITAL HIV-1 COMPARTMENT IN HETEROSEXUAL TRANSMISSION**

  Principal Investigator & Institution: Yamamura, Yasuhiro; Professor; Ponce School of Medicine G.P.O. Box 7004 Ponce, PR 00731

  Timing: Fiscal Year 2001; Project Start 30-SEP-1986; Project End 31-MAY-2005

  Description (provided by applicant): Incidence of acquired immunodeficiency syndrome (AIDS) has markedly declined in the USA through implementation of the development of highly active antiretroviral therapy (HAART). However, the proportion of females who were newly infected by **human immunodeficiency virus** type 1 (HIV-1) through heterosexual contacts is rapidly increasing. Indeed, one in three new cases of HIV-1 infection in the USA now occur in females. HAART may significantly reduce but does not eliminate the risk of heterosexual transmission. HIV-1 infection is also highly compartmentalized within the body. In order to effectively prevent heterosexual HIV-1 transmission, it is important to understand; (a) Which compartment(s) are heterosexually (male-female or female-male) transmitted HIV-1 derived from? (b) How readily does HIV-1 migrate from one compartment to the others? Based on existing (albeit rather scant) data, we hypothesize; (i) that HIV-1 in the blood and the genital tracts of infected individuals form separate compartments, each of which is "well insulated but not closed" and maintains a relatively "autonomous" viral dynamics, and also (ii) that HIV-1 heterosexual transmission are mediated by cell-free (M-tropic) genital viruses. We propose to examine our hypotheses through investigation of the cell-free and the cell-associated HIV-1 populations of the blood and the male/female genital tracts. Specifically, we will address the following questions: (1) What are the genetic distances (a) within "cell-free" and "cell-associated" HIV-1 population of the blood and the genital compartments, respectively; and (b) between each of the four populations? (2) Do the viral replication dynamics of HlV-1 compartment(s) differ from one to the others? (3) Do all compartments similarly respond to antiretroviral therapy (ART)? And are the patterns of drug resistance mutations identical in all the compartments? And finally, (4) From which HIV-1 compartment(s) is a heterosexually transmitted virus derived? The proposed study will clearly elucidate which HIV-1 compartment(s) is

directly associated with heterosexual transmission, and how each HIV-1 compartment responds to an antiretroviral therapy. Efficacy of HAART to reduce HIV1 sexual transmission risk may need to be evaluated for its ability to reduce the genital, rather than the plasma, HIV-1 compartments.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: GULF SOUTH RETROVIRAL COINFECTION CLINIC**

  Principal Investigator & Institution: Beilke, Mark A.; Associate Professor; Tulane University of Louisiana New Orleans, LA 70118

  Timing: Fiscal Year 2001; Project Start 01-DEC-2000; Project End 30-NOV-2001

  Summary: The health effects of coinfection with **human immunodeficiency virus** and human T lymphotropic virus types I or II are unknown, and conflicting data exist as to whether coinfection enhances progression to AIDS. This is an important question, since approximately 5% of HIV infected patients may be coinfected. The investigator will seek to study the clinical and immunologic responses and viral load during HIV and HTLV I/II viral coinfection. Specific laboratory studies will include both quantitative culture methods and quantitative RNA and in situ PCR. The effects of coinfection on immune phenotypes will be compared with HIV infected patients without HTLV I/II coinfection.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: HCV GENOMIC VARIABILITY IN HIV INFECTED HEMOPHILIACS**

  Principal Investigator & Institution: Sherman, Kenneth E.; Associate Professor; Internal Medicine; University of Cincinnati 2624 Clifton Ave Cincinnati, OH 45221

  Timing: Fiscal Year 2001; Project Start 01-JUN-2001; Project End 31-MAY-2005

  Summary: Hemophiliacs with symptomatic disease are multiply exposed to blood products including factor concentrates to correct the Internet clotting factor deficiencies. Prior to routine use of heat inactivation and screening of donor blood for specific viral pathogens, hemophilia patients were routinely exposed to, and infected with, viruses such as hepatitis B (HBV), hepatitis C (HCV) and **human immunodeficiency virus** (HIV). Cohort studies in hemophiliacs suggest several clinically and scientifically important findings that warrant further detailed investigation including; a) Liver disease progression may be altered in hemophiliacs infected with HCV with more rapid progression to liver failure and death; b) The source of infection from large pools of concentrate that were potentially infected by multiple discreet donors leads to a high risks of mixed infection represented by both genotype and quasi species heterogeneity; c) The HIV coinfected hemophiliacs may have different clinical outcomes and an altered immune response may facilitate our understanding of the underlying process of mutant virus selection, and the associated clinical outcomes. The overall goals of this proposal include the study and characterization of the genomic RNA of HCV in infected hemophilic patients with and without confection with HIV. In the retrospective Phase 1, we utilize the NCI Multi center Hemophiliac Cohort Study serum bank database to study the relationship between progression to decompensated liver disease and quasi species variability in the viral envelope hyper variable and core domain. Heteroduplex analysis will be used to rapidly screen samples from index patients and matched controls using samples longitudinally collected over a 10 year or longer period of time. Peptides will be produced from unique quasi species and these peptides will be evaluated for their function as CTL epitomes. Phase 2 involves the initiation and performance of a clinical intervention trial designed to determine variable kinetic response rates to PEG-interferon+ribavirin between hemophiliacs with HCV alone vs

HCV/HIV coinfected subjects. Quasi species populations will be modified/cloned, sequencing will be performed to generate families of closely related core peptides that will be studied for their ability to bind and stimulate an immune response. Treatment nonresponders will be followed in a prospective cohort study for up to 3 additional years so that the evolution of the virus, and its associated immune response in this group can be evaluated.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: HCV, HIV AND OPIOIDS: CELLULAR INTERACTIONS**

  Principal Investigator & Institution: Ho, Wenzhe; Professor; Children's Hospital of Philadelphia 34Th St and Civic Ctr Blvd Philadelphia, PA 19104

  Timing: Fiscal Year 2002; Project Start 27-SEP-2002; Project End 31-JUL-2005

  Summary: (provided by applicant): This is a R21 application in response to RFA-DA-02-008. Injection drug users (IDUs) are the single largest risk group for hepatitis C virus (HCV) infection and the co-infections with **human immunodeficiency virus** (HIV) and HCV are frequently found in IDUs. These two pathogens are also likely to be responsible for the highest infectious disease morbidity and mortality rates among IDUs. The general aim of this study is to determine the role of opioids (e.g., morphine) in the immunopathogenesis of HCV disease in the presence or absence of HIV infection. We hypothesize that opioids, through their receptors on human hepatocytes and immune cells, modulates HCV infection and replication. We will use both in vitro and in vivo models to directly address the question whether opioids have the ability to enhance HCV infection and replication. We seek to understand how HCV and HIV modify each other's replication in both in vitro and in vivo systems. We propose four specific aims: 1) We will determine whether opioids such as morphine enhances HCV infection of and replication in primary human hepatocytes, hepatoma cell lines (HepG2, Huh-7) and T cell lines (MT-2 and MT-2C); 2) We will determine whether opioids have the ability to induce HCV RNA expression in HCV replicon containing human hepatoma cell lines (Huh.5 and Huh.8). We will also examine whether HCV has ability to infect chronically HIV infected human T and monocytic cell lines (ACH-2, J 1.1 and U 1); 3) We will determine whether the removal of CD8+ T cells from PBMCs, and opioids, when added to CD8+ T cell-depleted PBMC isolated from HCV and/or HIV-infected subjects, induce HCV replication. In addition, we will examine whether HIV induces HCV replication in PBMCs isolated from HCV/HIV coinfected subjects; 4) We will determine plasma and PBMC HCV RNA levels in HCV and/or HIV-infected subjects attending methadone program. We will directly measure the levels of HCV RNA in plasma and PBMC using our newly developed real time RT-PCR assay. The investigation of the impact of opioids on HCV infection and its interaction with HIV will contribute to our basic understanding of host defense processes and the role of drug abuse in HCV and/or HIV infection of human liver and immune cells, ultimately further the design and development of improved treatment for drug-abusing patients infected with HCV and/or HIV.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: HEPATITIS C VIRUS COINFECTION IN HIV-1 INFECTED SUBJECTS**

  Principal Investigator & Institution: Rakela, Jorge L.; Chair; Mayo Clinic Arizona Sc Johnson Research Medical Building Scottsdale, AZ 85259

  Timing: Fiscal Year 2001; Project Start 30-SEP-2000; Project End 31-AUG-2003

Summary: (Applicant's Abstract) Hepatitis C virus (HCV) coinfection is common in **human immunodeficiency virus** type I (HIV-1) infected subjects. Epidemiological data suggest that in HIV-1 and HCV coinfected patients, HCV infection is more severe and progression to AIDS is more rapid. Furthermore, HIV infection was reported to facilitate mother-to-infant transmission of HCV and also HCV infection was reported to facilitate mother-to-infant transmission of HIV. Our overall hypothesis is that HCV replicates in lymphoid cells and that this phenomenon is responsible for the observed interactions between HIV-1 and HCV infections. Using strand-specific assays, we have demonstrated the presence of HCV RNA negative strand, which is a viral replicative intermediary, in multiple extrahepatic sites, but particularly common in lymphoid tissue. This infection was mainly localized in monocyte/macrophage cells. Moreover, we found that viral sequences at extrahepatic replication sites commonly differ from circulating and liver-derived sequences. Our proposal aims to further characterize extrahepatic HCV replication among HIV-1-infected subjects. Furthermore, we will analyze the presence of HCV replication in peripheral blood mononuclear cells (PBMCs) and cervical lavage cells in a large group of HIV-1-positive mothers and we will correlate these data with transmission of HCV and HIV-1 into children. To determine whether macrophage-derived HCV strains are responsible for viral transmission into children, we will analyze viral quasispecies composition in serum and PBMCs from mothers and children and in cervical lavage cells from mothers. We will also determine whether HCV infection of antigen presenting cells affects their function. Accordingly, we will culture dendritic cells from HCV-infected and uninfected individuals and compare them in functional assays in vitro. In summary, our studies will further characterize extrahepatic replication of HCV in HIV-1 infected subjects and will elucidate its role in mother-to-infant transmission of these two viruses.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: HIV 1 TATS PROMOTION OF KAPOSIS SARCOMA**

  Principal Investigator & Institution: Samaniego, Felipe C.; Assistant Professor; Clinical Cancer Prevention; University of Texas Md Anderson Can Ctr Cancer Center Houston, TX 77030

  Timing: Fiscal Year 2001; Project Start 01-AUG-1999; Project End 31-AUG-2003

  Summary: (Applicant's Description): The Principal Investigator plans to develop his intellectual and analytical skills to become a successfully funded independent investigator. A program of didactic and laboratory training in virology and mentoring by senior investigators with expertise in virology and immunology will be used. The long term goal of the PI is to establish himself as a nationally recognized investigator in Human herpesvirus 8 [HHV8]-Kaposi's sarcoma biology. The presence of either **human immunodeficiency virus** (HIV-1) or HHV8 alone is not associated with a high frequency of Kaposi's sarcoma. Their combined presence, however, leads to frequent development of KS. The applicants' hypothesis is that the high frequency and aggressiveness of KS in HIV-I- infected individuals is due to a direct effect of HIV-I Tat on cells or HHV8. Preliminary studies show Tat signals through binding to cell surface integrin receptors through its RGD integrin binding motif in a manner that mimics the integrin ligands, fibronectin and vitronectin. The investigators will test for activation of focal adhesion kinase (FAK) and involvement of the integrin-FAK- Ras-MAP kinase signaling pathway by blockade at steps along the integrin pathway and the use of dominant negative mutants of ras. Further studies will employ single exon Tat, which is still competent for trans-activation of the HIV-1 promoter, but lacks the RGD motif, versus full length Tat. Initial studies have shown that Tat activates HHV8 replication in

vitro. Tat transgenic mice will be used for studies on whether Tat also promotes HHV8 replication in vivo. The elucidation of the effects of Tat on integrin- dependent cell signaling, and HHV8 replication will provide insights into HIV- 1 pathogenesis in KS and could lead to the identification of sites for intervention in the commonest cancer seen in HIV-1 infected people.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: HIV AND PLASMACYTOID DENDRITIC CELLS IN THE THYMUS**

  Principal Investigator & Institution: Uittenbogaart, Christel H.; Professor; Pediatrics; University of California Los Angeles 10920 Wilshire Blvd., Suite 1200 Los Angeles, CA 90024

  Timing: Fiscal Year 2002; Project Start 01-MAY-2002; Project End 30-APR-2004

  Summary: (provided by applicant): Plasmacytoid dendritic cells (pDC) or natural interferon type I producing cells play an important role in linking innate and acquired immunity. pDC express high levels of interleukin 3 (IL-3) receptor (CD123) and are present in cord and peripheral blood, T cell areas of the lymph nodes and in the thymus and have the capacity to produce high levels of IFN-a in response to viruses and other stimuli. A depletion of peripheral blood pDC in patients with AIDS and a decrease in IFN-a production with disease progression have been found. Since our preliminary data show that pDC in the thymus are targets for HIV infection and express X4 HIV-1, our general objective is to gain an understanding of the role of pDC in virus spread and immunodeficiency in HIV infection. The present proposal represents a unique collaborative approach to elucidate the effects of HIV infection on pDC development and function, to define the role of pDC in normal T cell development and to determine the mechanisms of interactions of HIV with pDC and thymocytes. We will use our established methods as well as novel approaches and unique reagents to answer the questions presented by the specific aims. Our specific aims are intended to test the hypothesis that HIV infection disturbs the development of pDC and their function thereby affecting normal T cell maturation and immune responses to HIV. The aims are: 1) To investigate the effects of primary HIV isolates on development and function of pDC in the thymus; 2) To define the function of pDC in development of T cells in the thymus; 3) To determine the mechanisms of the interactions of HIV with pDC and developing T cells. The following is an outline of our experimental strategy. We will address how X4 and R5 HIV infection of the thymus affect development of pDC from tagged CD34' cells injected into the HIV-infected SCID-hu mouse and exposure of CD34' cells developing in vitro to HIV or HIV (Env) proteins. Levels of HIV coreceptor expression at different stages of maturation of pDC will be tested by Quantitative FACS analysis. Since pDC produce IFN-a after exposure to HIV we will investigate whether IFN-a influences pDC viability and function and whether IFN-a inhibits human T cell development as observed in the mouse. The role of pDC in negative selection will be evaluated in human and murine fetal thymic organ culture. To determine the mechanism of interaction of HIV on pDC, unique HIV molecular cloned and primary isolates will be used. The binding capacity of HIV virions to thymic pDC as compared to myeloid derived DC will be assessed by novel tetrameric Env constructs. The study of pDC in HIV infection of the thymus provides an opportunity to improve our understanding of HIV induced immunodeficiency.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: HIV DIPSTICK FOR RESORUCE-LIMITED BLOOD BANKS**

  Principal Investigator & Institution: Lee, Helen H.; Diagnostics for the Real World, Ltd 50 Mounds Rd, Unit 512 San Mateo, CA 94402

  Timing: Fiscal Year 2002; Project Start 16-SEP-2002; Project End 31-AUG-2003

  Summary: (provided by applicant): According to WHO statistics on blood safety, 80 percent of the world's population has access to 20 percent of the world's safe blood supply. However, more than 20 percent (13,000,000 units) of the world blood supply is not tested for the three major transfusion-transmissible infections: HIV, HBV and HCV. Transfusion of unsafe blood accounts for 80,000-160,000 HIV infections each year. The problem is especially severe in resource-poor countries where the availability of safe blood clearly needs to be increased, If inexpensive, rapid, improved dipsticks with sensitivity comparable to EIA were developed for blood screening, it would greatly improve the safety of the blood supply in developing countries.The overall aim of the project is to develop an HIV dipstick assay with high sensitivity, designated as the reflex diagnostic. The test can be used in developed countries under circumstances where an immediate result is required. For the developing countries, we propose that this test be integrated into a triplex test (HBV, HIV & HCV) and used as the initial step of pre-donation screening in high prevalence countries. The associated second step is to use the HIV reflex diagnostic test in order to identify the agent responsible for the positive Triplex test result.The specific aims of Phase I are to clone and express the HIV-1 trans-membrane glycoprotein (gp4l), HIV-1 integrase (p-32) and HIV-2 trans-membrane glycoprotein (gp36). We intend to screen and select immuno-reactive clones and produce the reagents in milligram quantities for test development.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: HIV DISEASE RESEARCH AGENDA**

  Principal Investigator & Institution: Sacks, Henry S.; Director; Mount Sinai School of Medicine of Cuny New York, NY 10029

  Timing: Fiscal Year 2001

  Summary: Hepatitis B virus (HBV) and **human immunodeficiency virus** (HIV) infection share similar epidemiologic features; moreover both viruses require reverse transcription for replication. During studies to examine the possible role played by HBV in the development of AIDS, two extrachromosomal 3.2kb DNAs hybridizing to HBV DNA were cloned from the peripheral blood mononuclear cell (PBMC) DNAs of HIV infected patients. One of the clones appears to be typical HBV DNA; however the other clone hybridized to both HBV and HIV DNA probes. A major objective of this proposal is to survey the various populations of HIV-infected patients in our medical school complex, especially those patients in the various ACTU protocols, for the presence of HBV-related sequences in PBMCs. We want to determine whether correlations exist between the presence of HBV-related DNA with stage of the HIV infection; the numbers of CD4+ cells; the clinical course of the HIV infection; the presence of neurologic disease; the presence of various opportunistic infections; the presence of various neoplasias; the response to the various therapies, including those of the ACTG protocols; and the isolation of HIV strains resistant to the various therapeutic agents such as AZT, ddC and ddI. Experiments will be performed to determine whether the HBV-related DNA is cell associated or found in the supernatants of the PBMC cultures of HIV-infected patients, in the free state or in particulate forms. PBMCs containing the HBV-related DNA will be examined for the location of the DNA, whether cytoplasmic or intranuclear; the expression of HBV antigens; and the expression of HBV and HIV-HBV homologous

transcripts. The cellular subtype that harbors the HBV-recombinant DNA, whether T4, T8 or non-T cell will be determined. Experiments will be performed to examine the effect of HIV on the replication of HBV DNA in PBMCs and H9 cells. The major questions to be addressed by these studies are: 1) can data be garnered to implicate HBV as a cofactor in the progression of HIV infection to AIDS; 2) does the presence of HBV DNA in the PBMCs affect the clinical course of HIV infection including the response to treatment; 3) does treatment of HIV infection with nucleoside analogues affect the presence of HBV DNA in the PBMCs; 4) does HIV facilitate the replication of HBV DNA in mononuclear cells; and 5) what are the correlates of the presence of apparent HIV-HBV recombinant DNA molecules in PBMCs of HIV-infected patients and what are some of the molecular characteristics of the replication of this apparent recombinant molecule in PBMCs and H9 cells?

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- **Project Title: HIV ENV & MACROPHAGE CHEMOKINE RECEPTOR IONIC SIGNALING**

  Principal Investigator & Institution: Freedman, Bruce D.; Assistant Professor; Animal Biology; University of Pennsylvania 3451 Walnut Street Philadelphia, PA 19104

  Timing: Fiscal Year 2001; Project Start 01-JUN-2001; Project End 31-MAY-2005

  Summary: The chemokine receptors CCR5 & CXCR4 serve as co-receptors for HIV-1 entry. Since their normal function is to transduce signals in response to chemokines, HIV-1 gp12O could also activate intracellular signals, with consequences for pathogenesis by modifying viral entry, post-entry steps or cell functions apart from infection. Ca+2 elevations or protein phosphorylation responses to gp12O through CCR5 or CXCR4 have been reported in lymphoid cells in some but not all studies. While co-receptor signaling domains are dispensable for entry in transfected cell lines, recent studies suggest that signaling may affect entry or post-entry infection steps in some primary cells. Macrophages express CD4, CCR5 & CXCR4, and are important targets of HIV-1 in vivo but gpl2O/chemokine receptor signaling has not been addressed in them. Indeed, relatively little is known in general about mechanisms of chemokine receptor signaling in primary macrophages. In preliminary studies, we have found that gp12O initiates intracellular signals in primary human macrophages through CCR5 & CXCR4, activates K+, Cr, & non-selective cation channels, and elevates intracellular Ca +. R5 and X5 gp12O elicited qualitatively similar but quantitatively different responses and, unexpectedly, the patterns of ion channel signaling elicited by gp120 differed from those elicited by the receptors' natural chemokine ligands. Our hypothesis is that HIV-1 Env initiates intracellular signals in macrophages through the co-receptors that lead to critical alterations in cellular function, virus entry, and/or post-entry steps of infection. To better understand the mechanisms of chemokine receptor signaling & ion channel activation in macrophages by gp120 (as well as chemokines), and consequences of gp120-mediated signals for macrophage function & infection, we will (a) Define the ionic signaling pathways activated in primary macrophages by gp 120 using primary & prototype HIV- 1 & SIV strains and strains that differ in ability to utilize macrophage chemokine receptors, and chemokines; (b) Identify the mechanisms of chemokine receptor ionic signaling in macrophages by defining CCR5 & CXCR4 coupling to K+, Cl- & non-selective cation channels, role of CD4 co-engagement, source & coupling for Ca2 elevations, and structural elements in CCR5 involved; (c) Determine the role of Env signaling in entry, infection & replication in macrophages, including the formation & significance of gp12O-induced capping as well as post-entry events, and; (d) Determine

the effects of gp120 signaling on macrophage function such as aberrant secretion of mediators, phagocytosis, and killing.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: HIV EVOLUTION IN WOMEN**

  Principal Investigator & Institution: Grant, Robert M.; Assistant Investigator; J. David Gladstone Institutes 365 Vermont St San Francisco, CA 94103

  Timing: Fiscal Year 2001; Project Start 23-APR-2001; Project End 31-MAR-2006

  Summary: (Abstract Provided by Applicant) **Human Immunodeficiency Virus** Types 1 and 2 (HIV) are estimated to have infected 33.4 million persons by the end of 1998 and Acquired Immune Deficiency Syndrome (AIDS) has become the leading cause of death worldwide. Although recently developed antiretroviral therapy can decrease mortality due to HIV infection, these therapies are limited by the development of drug resistant HIV, which can be sexually transmitted to previously uninfected persons. The virulence of drug resistant HIV-1 in individual humans and human populations remains unclear. The capacity of drug resistant HIV-l to cause immunological injury within individual humans and transmission between humans will determine the long-term clinical and epidemiological outcomes of currently available therapy, which is associated with relatively high rates of drug resistance. The capacity of drug resistant HIV-1 to be transmitted is partly determined by the penetration of these viruses into genital secretions from which transmission may occur. The studies proposed here aim to understand the frequency that drug resistant HIV-1 appears in the genital secretions of women under treatment with combination therapy. Phylogenetic analysis of multiple viral sequences from envelope, reverse transcriptase, and protease reading frames will be used to assess the extent of viral compartmentalization and exchange between blood-associated virus populations and virus populations contributing to genital secretions. This analysis will be performed at different stages of treatment, including subjects who are not treated, subjects who experience early virological failure of therapy, and subjects who have been viremic on therapy for extended periods of time. Decreased penetration of drug resistant HIV-1 into genital secretions could be due to decreased tropism for macrophages, which are infected in the female genital tract and appear to be important for establishing infection in new human hosts. Preliminary reports indicate that drug resistant HIV-1 may have decreased capacity to replicate cell lines measured in single-cycle assays and in thymus tissue cultured as explants or after implantation into SCID mice. The studies proposed here will confirm our own preliminary observations suggesting that protease inhibitor resistant HIV-1 also has decreased tropism for macrophages and will develop cell culture models that will be used for studies to elucidate the mechanism of decreased tropism. Decreased tropism for macrophages of drug resistant HIV-1, if confirmed, could account for prolonged clinical benefit after virological failure in treated persons and would provide a basis for decreased transmissibility between hosts. This information is essential for predicting clinical and epidemiological outcomes of therapy and for development of novel therapy.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: HIV IMMUNE REACTIVITY 'IN VIVO' AND 'IN VITRO'**

  Principal Investigator & Institution: Smith, Kendall A.; Professor of Medicine/Chief; Medicine; Weill Medical College of Cornell Univ New York, NY 10021

  Timing: Fiscal Year 2002; Project Start 15-MAR-2002; Project End 28-FEB-2007

Summary: ((provided by applicant) The goals of this research project are to determine the extent of antiviral immunity to **Human Immunodeficiency Virus** (HIV) in vivo, and to quantify this immunity by new in vitro immunological assays.Specific Aim 1 is to use the viral and lymphocyte dynamics that occur after a short-term (12 weeks) interruption of antiviral therapy, termed a Diagnostic Treatment Interruption (DTI), to analyze the efficacy of immune-based therapies (IBT) for chronic infection by HIV. Two IBTs will be tested, therapeutic immunization with an HIV vaccine (canarypox, ALVAC, vCP1452), and daily low dose interleukin 2 (IL2) adjuvant therapy, in a 2 step, 2x2 factorial, randomized, controlled, phase II clinical trial of 92 subjects. IBTs will be administered to 4 distinct groups during 12 weeks of Step I, while during the 12 succeeding weeks of Step II, the extent of in vivo antiviral immune reactivity will be detrmined by the plateau "trough" plasma HIV concentration, determined between weeks 8-1 2 after the DTI. Additional objectives are to determine whether viral relapse is prevented by any of the IBTs, as well as the duration of IBT control of viremia. Specific Aim 2 is to use a short-term activation of peripheral blood mononuclear cells with mixtures of 15-20 amino acid peptides from each of the HIV gene products to determine the frequency of both CD4+ and CD8+ T lymphocytes capable of responding by expressing cell surface activation markers, and by producing cytokines (IL2, interferon-gamma, tumor necrosis factor-alpha) detectable by flow cytometry. The absolute concentratoins of HIV antigen-specific Cytokine Producing Lymphocyte precursors (CPLp) in each of the 4 IBT groups will be quantified before, and during both Steps I L II of the immunotherapy trial. The function of HIV-specific cells will be determine by quantifying the numbers of CPLp. Selected subjects will also be studied to relate the viral genotype with in vitro immune responsiveness. The aim is to test the hypothesis that IBTs will add therapeutic benefit to standard antiviral therapy, and that this can be quantified in vivo and in vitro. Thus, this project is designed to determine the capacity of IBTs to control HIV, and to develop laboratory assays that are predictive of effective HIV immunty.

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- **Project Title: HIV INFECTION/COCAINE EFFECT ON CARDIOVASCULAR PATHOLOGY**

  Principal Investigator & Institution: Ansari, Aftab A.; Professor; Pathology; Emory University 1784 North Decatur Road Atlanta, GA 30322

  Timing: Fiscal Year 2001; Project Start 01-JUL-1999; Project End 30-JUN-2004

  Summary: The etiology of HIV-related cardiovascular disease (CVD) specially in patients with a history of cocaine use is most likely multifactorial. This is highlighted by the finding that there is an increase in the incidence of CVD in individuals with a history of cocaine abuse who are not HIV-1 infected and a similar increase in CVD in HIV-1 infected individuals who have no history of drug use. In addition, marked vascular lesions have been documented in SIV infected juvenile rhesus macaques who have no history of drug use. Thus, the effects of cocaine and HIV-1 infection leading to CVD may operate by separate but overlapping pathways, synergistically accelerating the disease process. It is our working hypothesis that insult to the vascular endothelium is one of the factor that contributes to CVD in HIV-1 infection which is further exacerbated by the use of drugs such as cocaine. Our lab has been studying the biology of lymphoid-endothelial cell interaction in both humans and non-human primates (NHP) in a variety of settings including responses to viral infections. During this process we have acquired unique sets of reagents, tools, techniques, knowledge, experience and important preliminary data which we submit will aid in defining some of the mechanisms of pathogenesis of HIV and cocaine induced cardiac disease. Specifically, we propose to a)

determine if HIV/SIV infected lymphoid cells show increased adherence to human and NHP microvascular endothelial cells (MVEC), respectively in the presence/absence of cocaine/catecholamines using both a static and dynamic culture system b) to define the effect of HIV/SIV infected lymphoid cells in the presence and absence of cocaine/catecholamine on the expression of select cell adhesion/costimulatory molecule (CAM/CSM's), cytokines and chemokines by human and NHP MVEC c) determine if the effect on CAM/CSM's, cytokines and chemokines requires a disease inducing lentivirus isolate d) determine if HIV infected lymphoid cells in the presence/absence of cocaine/catecholamine induces the breakdown of latency in latent CMV infected autologous aortic endothelial cells e) determine if co-culture of MVEC and autologous smooth muscle cells (SMC's) in the presence of cocaine/catecholamine alone, HIV/SIV infected autologous cells alone or in combination leads to SMC proliferation and remodeling and, f) determine whether interaction of HIV-1/SIV infected cells alone and/or in the presence of cocaine/catecholamine leads to the synthesis of metalloproteinases. We reason that such studies may provide unique insights on the relationship between the effects of cocaine and HIV infection in the pathogenesis of cardiovascular disease.

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- **Project Title: HIV NC PROTEIN MEDIATED INITIATION COMPLEX FORMATION**

  Principal Investigator & Institution: Lee, Nick; Chemistry; University of Minnesota Twin Cities 200 Oak Street Se Minneapolis, MN 554552070

  Timing: Fiscal Year 2002; Project Start 28-JAN-2002

  Summary: (Provided by the applicant): **Human immunodeficiency virus** type 1 (HIV-1) is a retrovirus that is the causative agent of human acquired immunodeficiency syndrome (AIDS). In retroviruses, tRNA molecules are recruited as primers to initiate reverse transcription. In the case of HIV-1, a specific host cell tRNA, human tRNA LyS'3, serves as the replication primer. The 3' 18 nucleotides of this tRNA are unwound and annealed to the primer binding site (PBS) in a process that is facilitated by the HIV nucleocapsid protein (NC). Previous studies primarily using heat-annealed complexes, have suggested that a specific ruination complex forms between the tRNA primer and the genome that involves extensive interactions outside the PBS region. This proposal will explore this hypothesis further using NC-annealed complexes. RNA structural changes that occur upon HIV-1 NC binding to the HIV-1 genome and to the tRNA-genome initiation complex will be elucidated. We will also probe the functional significance of the interactions outside the PBS that are formed upon tRNA-Lys,3 annealing by HIV- 1 NC. The goals will be accomplished by employing nucleotide analog interference mapping (NAIM) experiments, metal ion cleavage assays, fluorescence resonance energy transfer (FRET) studies, and crosslinking experiments. Information gained from the proposed research will provide valuable insights into the molecular interactions that contribute to the specificity of NC-tRNA primer and NC-tRNA primer-HIV genome interactions. Additionally, this information may be useful in the design of new therapeutic agents against AIDS and retroviral-derived cancers.

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- **Project Title: HIV NEUTRALIZATION IN VITRO & IN SHIV INFECTED MACAQUES**

  Principal Investigator & Institution: Moore, John P.; Tulane University of Louisiana New Orleans, LA 70118

Timing: Fiscal Year 2001

Summary: Our goal in this proposal is to assess the effect on HIV-1 replication in vitro, and on SHIV replication in vitro and in vivo, of combinations of agents proven by us in published studies to have broad and potent neutralizing activity against primary HIV-1 isolates, when used as single agents. The agents we plan to use are the human MAbs IgG1b12, 2G12 and 2F5 and the CD4-IgG2 molecule, which has many of the properties of a human MAb. We believe that broad, potent neutralization of primary isolates in vitro is of paramount importance in determining the suitability of MAbs for human clinical trials. Triple combinations of the above agents have outstanding HIV-1 neutralizing activity under cell culture conditions. We wish to test whether this in vitro effect correlates with in vivo reductions in viral load in SHIV-infected macaques, or predicts protection from SHIV infection. An emphasis of this proposal will be the use of HIV-1 and SHIV strains from genetic subtypes other than B, to facilitate the development of immunotherapy for the developing worlds. All four of the above agents have proven capacities to neutralize primary isolates from multiple HIV-1 genetic subtypes, including African and Asian strains. The information accruing from the proposed studies might assist in the identification of suitable immunotherapeutic strategies for the treatment of HIV-1 infection, or the prevention of HIV-1 transmission from infected mothers to their children, as well as providing information on the effects of neutralizing antibodies on the dynamics of HIV-1 production and clearance in vivo. FUNDING NIH (HL-97-002) PUBLICATIONS Trkola, A., T. Ketas, V.N. KewalRamani, F. Endorf, J.M. Binley, H. Katinger, J. Robinson, D.R. Littman and J.P. Moore. Neutralization sensitivity of **human immunodeficiency virus** type 1 primary isolates to antibodies and CD4-based reagents is independent of co-receptor usage. Journal of Virology, 72:1876-1885, 1998. Montefiori, D.C., R.G. Collman, T.R. Fouts, J.Y. Zhou, M. Bilska, J.A. Hoxie, J.P. Moore and D.P. Bolognesi. Evidence that antibody-mediated neutralization of **human immunodeficiency virus** type 1 by sera from infected individuals is independent of coreceptor usage. Journal of Virology, 72:1886-1893, 1998. Fouts, T.R., A. Trkola, M.S. Fung and J.P. Moore. Interactions of polyclonal and monoclonal anti-glycoprotein 120 antibodies with oligomeric glycoprotein 120-glyoprotein 41 complexes of a primary HIV type 1 isolate Relationship to neutralization. AIDS Research and Human Retroviruses, 14:591-598, 1998. Sullivan, N., Y. Sun, Q. Sattentau, M. Thali, D. Wu, G. Denisova, J. Gershoni, J. Robinson, J.P. Moore and J. Sodroski. CD4-induced conformational changes in the **human immunodeficiency virus** type 1 gp120 glycoprotein Consequences for virus entry and neutralization. Journal of Virology, 72:4694-4703, 1998. Burton, D.R. and J.P. Moore. Why do we not have an HIV vaccine and how can we make one? Nature Medicine, 4:495-498, 1998.

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- **Project Title: HIV SUPPRESSION BY BETA-DEFENSINS**

  Principal Investigator & Institution: Garzino-Demo, Alfredo Garzino.; None; University of Md Biotechnology Institute Baltimore, MD 212023101

  Timing: Fiscal Year 2003; Project Start 15-JUL-2003; Project End 31-MAY-2005

  Summary: (provided by applicant): beta-Defensins are small (3-5Kd in size) secreted proteins that are components of innate immunity; some are constitutively expressed, such as human beta-defensin (HBD)-1, while others, like hBD2 and -3, are inducible by cytokines or other immune response stimuli. beta-defensins are secreted preeminently by epithelial cells, and by neutrophil cells, although their secretion has been observed also in T and NK cells, and initially they were described as antimicrobial proteins; recent research has indicated that they also act as chemoattractants. Their expression is

elevated in the epithelia of the mouth, tongue, digestive apparatus, and also in airways, mammary gland, liver and other organs. In particular, beta-defensins are present in saliva, and the concentration of these proteins can be very high in the oral cavity, with measured local concentration as high as 100mu g/ml, in a 100mu m-thick layer in the tongue. Therefore, it appears that beta-defensins, as important component of the innate imniunity, control the occurrence of infections in the oral cavity. The antimicrobial activity of beta-defensins is due to their ability to permeabilize bacterial membranes. Taken together, this information indicates that beta-defensins could provide a form of innate immunity against oral HIV infection that might be exploited for anti-HIV prophylaxis. In agreement, our preliminary data show that select beta-defensins, especially hBD2, inhibit R5 HIV infection in a dose dependent manner, at doses that are compatible with or below those measured in the oral cavity. In addition, our studies show that hBD2 treatment directly on the virus lowers HIV infection. This antiviral activity is reminiscent of the recently reported HIV suppressive properties of alpha defensins. However, only beta-defensins are naturally present in the oral cavity at HIV-suppressive concentrations. Therefore, our central hypothesis is that beta-defensins mediate and antiretroviral mechanism, based on inhibition of viral entry, in the oral cavity that is capable of preventing oral HIV transmission. Accordingly, we propose to a) characterize which HIV- 1 phenotypes are suppressed by hBD2. These experiments will define the broad suppressive effects of hBD2 and whether its mechanism of suppression functions in vivo b) determine the effects of hBD2 on events in the HIV-1 life cycle. In this aim we will examine and compare the effects of hBD2 on HIV entry/fusion and on intracellular steps of viral replication. The elucidation of the event(s) in HIV infection and expression that are affected by hBD2 will allow for a thorough study of its mechanism of action and for structure-function studies, thus proving basis for novel antiviral therapeutic and preventive strategies. Finally, these studies will constitute a contribution towards the understanding of the role of innate immunity in the oral cavity.

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- **Project Title: HIV TAT ASSOCIATED KINASE**

  Principal Investigator & Institution: Rice, Andrew P.; Professor; Molecular Virology & Microbiol; Baylor College of Medicine 1 Baylor Plaza Houston, TX 77030

  Timing: Fiscal Year 2001; Project Start 15-SEP-1995; Project End 31-AUG-2003

  Summary: The Tat protein of the **human immunodeficiency virus** acts to stimulate transcription of the integrated proviral genome and also affects T-cell activation and apoptosis during infection. Because of this pivotal role during infection, it is generally believed that inhibition of Tat function will be of therapeutic benefit to HIV-infected individuals. To rationally develop specific Tat inhibitors, it will be necessary to identify cellular factors that mediate Tat function and to gain an understanding of the role of these factors in normal physiology and in HIV infection. Recent work by several laboratories has demonstrate that a cellular protein kinase, named TAK (Tat associated kinase), mediates Tat function. TAK is composed of more than one subunit and it is closely related to a transcriptional elongation factor termed pTEFb that was first identified in Drosophila melanogaster nuclear extracts. The catalytic subunit of TAK is a kinase called PITALRE, a member of the cyclin-dependent family of protein kinases (CDKs). Prior to its identification as a component of TAK, no specific function had been ascribed to PITALRE. TAK probably mediates Tat transcriptional activation by phosphorylating the carboxy terminal domain (CTD) of RNA polymerase II in a manner that stimulates transcriptional elongation. Additionally, TAK was found recently to be

induced in activated primary human CD4+ T-cells and in promonocytic cell lines induced to differentiate to macrophages, suggesting that TAK may normally have an important function in the host cells of HIV infection. It is proposed to continue studies on regulation of TAK function and mechanisms of transcriptional activation by TAK. It is also proposed to extend studies of TAK into a new and important area by investigation TAK's normal role in T-cells and macrophages, the two major host cells of **human immunodeficiency virus** infection. The completion of the proposed research should provide insight into Tat and TAK and will be important background for future development of therapeutic strategies directed against Tat function.

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- **Project Title: HIV: GENDER AND SEX HORMONE EFFECTS ON T CELL KINETICS**

  Principal Investigator & Institution: Hellerstein, Marc K.; Professor of Medicine; J. David Gladstone Institutes 365 Vermont St San Francisco, CA 94103

  Timing: Fiscal Year 2001; Project Start 23-APR-2001; Project End 31-MAR-2006

  Summary: (Abstract Provided by Applicant) Gender differences have been documented for many aspects of immune function and are likely mediated by the major reproductive hormones (androgens, estrogens and progesterone). Gender differences in the natural history of human immunodeficiency virus-type 1 (HIV-l) infection have also been described. In particular, a different relationship between HIV-1 viral load (VL) and progression of disease has been reported for women as compared to men. The in vivo effects of gender or reproductive hormones on proliferation and survival of T cells, including thymic production of T cells, in the setting of HIV- 1 infection have not been directly tested, however. The objectives of our proposed studies are to compare the natural history of T cell turnover in men and women with early HIV-1 disease and to establish the consequences of sex steroids on T cell turnover, including thymopoiesis, in HIV-l infection. These studies are now possible in humans because of the recent development of stable isotope-mass spectrometric techniques for directly measuring the kinetics of purified T cell subpopulations in vivo. Three clinical studies will be performed. Study #1 will compare the natural history of CD4+ and CD8+ T cell kinetics in untreated, CD4-matched men and women with early HIV-l infection (CD4 counts 500-750 cells/uL; n~l5 per group). T cell kinetics will be measured by two complementary techniques ([6,6-2H2] glucose incorporation and die-away curves, to characterize memory/effector-phenotype T cell dynamics; long term 2H2O incorporation, to characterize kinetics of naive-phenotype T cells) at baseline then every 12-18 months over a 3-4 year follow-up. Correlation between VL, CD4 count, thymic mass (by CT scan), excision circles, and blood measurements (cytokines, hormones) will be compared in men and women. Our hypothesis is that chances in T cell kinetics will track with CD4 count in both genders, but at a lower VL in women. Study #2 will compare the effects of puberty in HIV-1 infected pre-adolescent boys and girls (n=8 per group). The outpatient 2H2O approach will be used to measure T cell dynamics. Other parameters will be correlated as in study #1. The central hypothesis is that the rise in sex steroids will suppress thymopoiesis in both genders. perhaps greater affecting boys. Study #3 will compare the effects of reproductive hormone replacement therapy in hypogonadal adult men and women with HIV-1 infection (n=8 per group). The 2H2O method for measuring T cell dynamics will be used. with other measurements as in Studies I and 2. The hypothesis is that sex steroids will reduce production of naive-phenotype T cells in both men and women, with perhaps a greater effect in men. In summary, we propose to determine directly, in vivo, whether sex steroids alter T cell

kinetics (particularly thymopoiesis) in HIV-1 infected humans. and whether T cell turnover tracks better with CD4 count than VL in women, compared to men.

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- **Project Title: HIV1 + IDU'S--ENDOCRINE CONSEQUENCES & MEDICAL OUTCOMES**

  Principal Investigator & Institution: Kumar, Mahendra; Professor & Director; Psychiatry and Behavioral Scis; University of Miami Box 016159 Miami, FL 33101

  Timing: Fiscal Year 2001; Project Start 01-MAY-2001; Project End 30-APR-2006

  Summary: (provided by applicant) This application proposes to investigate the mediating role of endocrine consequences on the occurrence of mental health outcomes that take place among HIV-1+ IDUs. Injecting drug use (IDU) is one of the major risk factors for contracting human-immunodeficiency virus, type-i, (HIV-1) infection. abnormalities in various endocrine systems develop in IDUs and HIV-1+IDUs and may be associated with number of mental health outcomes. Our earlier reports show that the ACTH and cortisol responses to a cold pressor challenge are attenuated in HIV-1 + individuals and, thus, support the proposed hypothesis. An array of outcomes including, anxiety, depression, and perceived psychological distress and difficulty adapting to stressors occurs in HIV-1 + IDUs. Since HIV is present in the brain soon after infection and esides in very high concentrations in the hippocampus, it is proposed that different endocrine systems are likely to be adversely impacted centrally in HIV-1 infection. It is important to understand the mechanisms involved in the development of neuroendocrine abnormalities - central or peripheral - in order to intervene n mental health-related problems. This five-year proposal investigates the responses of the thyroid and gonads to trophic hormones, hyroid releasing hormone (TRH), and luteinizing hormone-releasing hormone (LHRH), as well as adrenal Aictivity in response to a low-dose ACTH challenge. This investigation will be carried out using a crossectional three-group design (HIV-i+ lDUs, N+1OO, HIV-1- IDUs, N=100, and HIV-1- non-IDUs, N=100) with the total N = 300, X 3 ethnicitlies (African-Americans, Hispanics, Caucasians) X 2 genders (Women and Men). Only those HIV seropostiive subjects who do not have AIDS-defining symptoms and are not being treated with triple-drug therapy will be enrolled since the effect of triple-drug therapy on the endocrine system is unknown at this time. It is proposed to investigate whether the endocrine responses nediate mental health outcomes (i.e., depression, anxiety, and perceived psychological distress). These data will be useful in designing suitable interventions.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: HIV-1 AND HIV-2 INFECTION OF NON-DIVIDING CELLS**

  Principal Investigator & Institution: Malim, Michael H.; Associate Professor; Microbiology; University of Pennsylvania 3451 Walnut Street Philadelphia, PA 19104

  Timing: Fiscal Year 2001; Project Start 01-MAR-2000; Project End 28-FEB-2004

  Summary: The human immunodeficiency viruses type-1 (HIV-1) and type-2 (HIV-2) are able to infect both dividing and non-dividing (post-mitotic) cells productively. Interestingly, the capacity to replicate in non-dividing cells is a feature of the HIVs that is not shared by oncogenic retroviruses such as murine leukemia virus (MLV). This fundamental difference between the life cycles of these viruses is attributable to the ability of HIV post-entry nucleoprotein complexes (referred to as pre-integration complexes, PICs) to be specifically imported into the nucleus through nuclear pore

complexes (NPCs) during interphase. By analogy with cellular nuclear import pathways, not only must specific signals reside within HIV-1 and HIV-2 PICs that target them to the nuclear interior, but cellular factors (proteins) must also be responsible for mediating the import process. in terms of nuclear localization sequences (NLSs) that are present in PICs, we hypothesize that the major signal for HIV-1 resides within integrase (IN) and that the accessory protein Vpr may serve to enhance the efficiency of import further by directly tethering PICs to the NPC. in contrast, the HIV-2 accessory protein Vpx appears to play a major role in PIC import, whereas the possible contribution of IN remains unexplored. The principal goals of this proposed research are, therefore, to expand on these ideas and to investigate the viral and cellular determinants of HIV- 1 and HIV-2 PIC nuclear import - these planned experiments are organized into three complementary areas. One, the NLS of HIV- 1 IN that we have mapped to residues 161 to 173 will be characterized, and the consequences of its disruption for virus infection and replication defined. Two, the NLSs of HIV- 1 Vpr and HIV-2 Vpx, which both appear to mediate import via a novel mechanism(s), will be characterized using site-directed mutagenesis and the construction of chimeric proteins; also, the effects of HIV-2 Vpx NLS disruption on infection will be analyzed. Three, a combination of assorted functional, biochemical and cDNA library screening strategies will be used to identify and study host cell proteins important for the nuclear import of HIV-1 and HIV-2 PICs. importantly, HIV infections of non-dividing cells such as macrophages are critical for the establishment of pathogenic infections in infected persons. Thus, an improved understanding of the viral and cellular factors that govern such infections should provide new insights into HIV pathogenesis and, potentially, suggest new approaches or targets for the treatment of HIV infections and AIDS.

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- **Project Title: HIV-1 GP120-INDUCED ENDOTHELIAL CELL DYSFUNCTION**

  Principal Investigator & Institution: Kanmogne, Georgette; Pathology; University of Oklahoma Hlth Sciences Ctr Health Sciences Center Oklahoma City, OK 73126

  Timing: Fiscal Year 2003; Project Start 01-APR-2003; Project End 31-MAR-2008

  Summary: (provided by applicant): The **human immunodeficiency virus** (HIV) invades the brain in the early stages of infection For patients in the advanced stage of infection, dysfunction of the central nervous system (CNS) is a common cause of morbidity and often leads to progressive dementia, cerebral atrophy and death. Evidence suggest that HIV and /or HIV-associated proteins are critical to the pathogenesis of the HIV-associated dementia (HAD)complex .To elucidate the pathogenesis of HAD, it is important to understand by what mechanisms HIV invades the brain. Breakdown of the blood-brain barrier is commonly seen in patients with HAD, despite the lack of productive HIV-infection of the brain endothelium. The HIV-1 envelope protein gp120 is present in the brain of patients with HIV encephalitis, and is neurotoxic Recent evidence from our laboratory, and by others, suggests a direct effect of gp120 on the brain endothelium. It is our hypothesis that gp120 directly causes blood-brain barrier dysfunction and plays a major role in viral invasion of the brain To test this hypothesis, we plan the following aims. Aim 1: To test the hypothesis that HIV-1 gp120 proteins are toxic to human brain microvascular endothelial cells and directly induce a disruption and/or damage of the blood-brain barrier we will measure endothelial cell permeability and apoptosis. Aim 2 To test the hypothesis that exposure of gp120 proteins to human brain microvascular endothelial cells result in the loss of tight junction proteins we will assess the expression of occludin, claudia-5 and zonula occludens-1 using western blotting and immunofluorescence. Aim 3: To determine if chemokine receptors are

involved in gp120-induced blood-brain barrier disruption and/or damage Aim 4: To determine the signal transduction pathways involved in gp120-induced blood-brain barrier dysfunction. Data from these experiments will help determine the role that gp120 plays in the breach of blood-brain barrier integrity and HIV invasion of the brain, and will suggest therapeutic approaches to preventing gp120-mediated dysfunction of the brain endothelium during HIV infection.

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- **Project Title: HIV-1/HIV-2 EPITOPE PROJECT, THE GAMBIA, WEST AFRICA**

  Principal Investigator & Institution: De Groot, Anne S.; None; Brown University Providence, RI 02912

  Timing: Fiscal Year 2001; Project Start 01-SEP-1998; Project End 28-FEB-2002

  Summary: (adapted from the Abstract): In this application, the Principal Investigator outlines an effort to identify "protective" HIV-2 cytotoxic T-cell (CTL) epitopes that are recognized by individuals of Gambian, or sub-Saharan African, genetic backgrounds. The spread of HIV-1 into sub-Saharan countries where HIV-2 was previously endemic has resulted in the exposure of HIV-2 infected individuals to HIV-1. As some HIV2-infected individuals appear to be resistant to HIV-1 infection, some have proposed that recognition of cross-reactive CTL epitopes may contribute to protection from HIV-1. The elucidation of the roles CTL epitopes and genetic background (HLA) play in the resistance to HIV-1 infection in the presence of HIV-2 infection may contribute to our understanding of HIV immunopathogenesis. Advances in the development of computer-driven algorithms that prospectively identify putative MHC-binding regions/CTL epitopes, such as the TB/HIV research laboratory's EpiMatrix, will facilitate the comparison of immunologically relevant regions of HIV-2 sequences to HIV-1 sequences. The Investigator and her associates have demonstrated that EpiMatrix efficiently and accurately identifies MHC-binding regions from HIV protein sequences. She proposes now to apply the algorithm to the sequences of HIV-2 and HIV-1 strains that are common in West Africa, selecting putative MHC-binding regions that are conserved between these strains. The specific aims of this project are to (1) identify conserved HIV-2/HIV-1 CTL epitopes and (2) test whether these putative epitopes are recognized by HIV-2 infected individuals. The long-term goal is to evaluate the relation between the recognition of the CTL epitopes and presence of HIV-2/HIV-1 co-infection. Modeling and MHC-binding studies will be performed in Providence, Rhode Island (United States) with the participation of MRC personnel. Selected peptides will then be tested in CTL assays using CTL lines and clones derived from HIV-2 infected individuals. The CTL assays will be performed at the Medical Research Council Laboratories in Fajara, The Gambia, West Africa, as a collaboration between TB/HIV Research lab personnel and MRC Laboratories personnel.

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- **Project Title: HIV-2 CELLULAR IMMUNITY CROSS-REACTIVE WITH HIV-1**

  Principal Investigator & Institution: Kanki, Phyllis J.; Professor; Immunology/Infections Diseases; Harvard University (Sch of Public Hlth) Public Health Campus Boston, MA 02460

  Timing: Fiscal Year 2001; Project Start 30-SEP-1999; Project End 31-AUG-2004

  Summary: The development of a safe and effective HIV vaccine is reliant on our ability to identify and understand correlates of HIV-1 immunity and protection. The identification of such correlates has been hampered by relatively rare instances of

natural immunity that have withstood the challenge of viral exposure. Over the past 13 years, we have established an international collaborative research effort to study the biology of HIV-2 infection and its interaction with HIV-1 in Senegal, West Africa. Not only is HIV-2 infection less readily transmitted by heterosexual and perinatal routes, but progression to AIDS is substantially slower compared to HIV-1. Thus, we hypothesized that a related yet attenuated virus infection might provide protection from the more virulent HIV-1 virus. In 1995, we described studies of HIV-2 infected women that demonstrated such protection and, to date, >60% protection continues in this cohort with 13+ years of observation. The mechanisms for the postulated protective effect in HIV-2 infection remains unclear, although host cellular immune responses may play an important role. Comprehensive studies of the immune responses elicited in HIV-2 infection are still lacking and could support the protective role of cellular immune response against HIV-1 infection. In addition, the evaluation of CTL and T helper responses in HIV-2 infection will offer crucial information in understanding the immunopathogenesis of HIV. We will take advantage of our unique cohort population of women at high risk for both HIV-1 and HIV-2 in order to identify those women that have been superinfected and those HIV-2 infected women that possess determinants suggestive of HIV-1 exposure, i.e., the protected individuals. Comparison of the cellular immune responses in these two groups of women will include: (a) evaluating the spectrum of CTL responses in HIV-2 infection and determining the level of cross-reactivity with HIV-1; (b) fine mapping of the immunogenic HIV-2 CTL epitopes; (c) assessing these CTLs in a functional inhibition assay and (d) studying the HIV-2 T helper function and determining if these proliferative responses are cross-reactive with HIV-1. Not only will these studies provide new information on the breadth and cross-reactivity of the HIV-2 cellular immune responses, but we also hope to correlate such responses with HIV-1 protection in vivo.

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- **Project Title: HIV-SPECIFIC CD8+ T CELLS--FREQUENCIES AND PHENOTYPES**

  Principal Investigator & Institution: Altman, John D.; Assistant Professor; Microbiology and Immunology; Emory University 1784 North Decatur Road Atlanta, GA 30322

  Timing: Fiscal Year 2001; Project Start 01-JAN-1998; Project End 31-DEC-2002

  Summary: (Taken from applicant's abstract) Following infection with **human immunodeficiency virus** type 1 (HIV-1), a quasi-steady state is achieved where viral replication appears to be balanced by the immune response and by death (and replacement) of target cell populations. Highly active antiretroviral therapy (HAART) effectively perturbs the steady state by reducing viral loads and unmasks the dynamic characteristics of the CD4+ T cell population; the effects of HAART on HIV-specific CD8+ T cell responses have not been characterized. Direct staining techniques, using soluble tetramers of human leukocyte antigen (HLA) class I complexes with peptides from HIV, allow rapid enumeration of HIV-specific CD8+ T cells and qualitative analyses of many of their phenotypic and functional properties. Preliminary studies of a small number of patients (prior to HAART) reveal frequencies of antigen specific cells often exceeding 1.5% of CD8+ cells, yet in most cases, these cells do not appear to be activated, an unexpected finding given the chronic exposure to antigen. In several cases, antigen-specific cells appear to die following in vitro stimulation with antigenic peptides. The investigator will extend these studies to monitor frequencies and phenotypes of HIV-specific CD8+ T cells as a function of time before and following the initiation of HAART, and to include greater numbers of patients. The prevalence and cause of resting phenotypes will be investigated through phenotypic analysis of cell

surface markers, staining of molecules directly responsible for effector function, and analysis of potential negative regulation due to changes in signaling molecule expression or T cell antagonism. Antigen availability will be analyzed by sequencing viral epitopes to monitor CTL escape. The functional potential of the antigen-specific populations will be determined by staining of cultures stimulated with antigenic peptides in vitro for short periods of time. These experiments will reveal the fraction of the populations that proliferate, develop effector function, or are primed to die upon contact with antigen. Finally, the repertoire of the antigen-specific populations as a function of time following viral load reduction will be monitored over time by T cell receptor spectratyping analysis of magnetically sorted antigen specific cells.

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- **Project Title: HOST CELL FACTORS AND AIDS PATHOGENESIS**

  Principal Investigator & Institution: Alkhatib, Ghalib; Assistant Professor; Microbiology and Immunology; Indiana Univ-Purdue Univ at Indianapolis 620 Union Drive, Room 618 Indianapolis, IN 462025167

  Timing: Fiscal Year 2002; Project Start 15-MAY-2002; Project End 30-APR-2007

  Summary: Human immunodeficiency virus type 1 (HIV-1) requires CD4 and a coreceptor for entry, into susceptible host cells. The chemokine receptors CXCR4 and CCR5 are the major coreceptors used by T cell line-tropic (X4) and macrophage-tropic (R5) HIV-1 isolates. A naturally occurring frame-shift mutation caused by a 32 base pair deletion (delta32) in the human CCR5 gene resulted in a truncated protein that does not function as a coreceptor. Relative to the general population, CCR5delta32 homozygotes (-/-) are rarely found among HIV-1 infected individuals. In addition, HIV-1 infected CCR5delta32 heterozygotes (+/-) progress more slowly to AIDS than individuals lacking this allele indicating that even one delta32 allele confers some resistance. We have found that expression of full-length delta32 protein in human cell lines or normal human peripheral blood mononuclear cells (PBMCs) can specifically downmodulate endogenous CXCR4 and inhibit X4 infection. We have demonstrated efficient co-localization of delta32 and either CXCR4 or CCR5. Truncation of the delta32 C-terminus resulted in the loss of CXCR4 downmodulation activity. Furthermore, we showed that PBMCs from several (-/-) individuals express lower CXCR4 levels in comparison to wild-type CCR5 (+/+) PBMCs. We hypothesize that one mechanism of resistance to HIV-1 is caused by the unique activity of the delta32 protein. Using delta32-specific antibodies, we have shown that native delta32 protein was expressed in (-/-) PBMCs isolated from exposed/uninfected [1]but was absent in an infected (-/-) individuals [2], indicating a critical role for the delta32 protein in resistance to HIV-1 infection. The overall purpose of this proposal is to determine the mechanism(s) that underlies the observed more broad protective effect by the naturally occurring delta32 protein. The following specific aims are based on preliminary data generated in my laboratory: 1. Analyze how delta32 impairs functional expression of CCR5 and CXCR4. 2. Analyze the mechanism of failure of delta32 protective effect in an infected delta32 homozygous individual. 3. Determine the structural determinants involved in delta32 activity.

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- **Project Title: HUMAN ANTITAT INTRABODY GENE THERAPY AGAINST SHIV**

  Principal Investigator & Institution: Marasco, Wayne A.; Dana-Farber Cancer Institute 44 Binney St Boston, MA 02115

  Timing: Fiscal Year 2001; Project Start 01-JUN-1999; Project End 31-MAY-2004

Summary: Gene therapy for the treatment of HIV-1 infection and AIDS represents an attractive addition to conventional pharmacologic therapies due to the limited success of even highly active anti- retroviral therapies (HAART) and because genetic alteration of the host cell could potentially confer permanent suppression of viral replication after infection. Pre-clinical evaluation of new anti-HIV-1 gene therapies in an animal model is required to address many of current limitations of gene therapy including the duration of in vivo survival of transduced cells, loss of detectable anti-viral transgene expression and rapid clearing of transduced cells due to immune responses against the marker gene. Chimeric primate lentiviruses (SHIVs) composed of SIV and HIV genes have proven useful in the analysis of the role of discrete HIV genes in viral pathogenesis in macaque monkeys. Non-pathogenic SHIVs establish chronic infection and pathogenic SHIVs cause high levels of viremia, rapid and profound CD4+ T cell depletion and AIDS. Thus, the SHIV-macaque model offers a unique and important experimental system, to evaluate the effects of anti-viral genes without anti-viral Rx, to control input virus, to evaluate for development of resistance and to analyze for immune responses against the anti-viral gene products. We have characterized a human anti-tat intracellular single-chain antibody, termed sFvhutat2 "intrabody" with potent anti-HIV-1/SHIV activity in vitro and we now propose to test this gene therapy strategy in the SHIV-macaque model. In this proposal, we will optimize conditions for CD4+-enriched macaque T cell activation, transduction (with MuLV vectors either empty (control) or encoding sFvhutat2), phenotypic selection (via human NGFR) and ex vivo expansion and will complete in vitro challenge experiments to choose an isogeneic pair of non-pathogenic and pathogenic SHIVs that can be used for in vivo gene therapy studies. Both a pre-SHIV infection model and post-SHIV infection model are proposed using both non-pathogenic and pathogenic SHIVs in both models. For both models, we infuse equal numbers of both empty vector transduced or sFvhutat2 transduced CD4+-enriched T cells into 4 macaques (gene therapy arm) and mock transduced CD4+-enriched T cells into 4 macaques (control arm). The primary goal of these studies is to determine if there is increased survival of sFvhutat2 verses vector transduced cells. The secondary goal of these studies is to determine if in vivo resistance to sFvhutat2 develops. These studies will establish a valuable new primate model for the testing of anti-HIV-1 gene therapies. In addition, the results from these studies will substantially advance our understanding of how to apply and improve this promising technology for the treatment of HIV-1 infection and AIDS.

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- **Project Title: HUMAN EXPLANT CULTURES AND A MOUSE TO EVALUATE SAMMA**

  Principal Investigator & Institution: Cara, Andrea; Mount Sinai School of Medicine of Nyu of New York University New York, NY 10029

  Timing: Fiscal Year 2001; Project Start 26-SEP-2001; Project End 31-JUL-2005

  Description (provided by applicant): Approximately 90% of new **human immunodeficiency virus** (HIV) infections are acquired through sexual contact. The development of safe, effective, and affordable topical microbicides for vaginal or rectal use could play a critical role in reducing HIV transmission rates worldwide. Clinical, epidemiological and molecular studies strongly support the role of herpes simplex virus (HSV) as a major cofactor for the transmission of HIV. Genital ulcers lead to breaks in the epithelial barrier and HSV induces the expression of pro-inflammatory cytokines that are known to enhance HIV replication. The goal of the proposed studies is to characterize the effects of sodium dimandelic acid ether (SAMMA) and its leading

derivatives on HIV and HSV infection utilizing relevant biologic culture systems. SAMMA has excellent anti-mV and anti-HSV activity, while exhibiting no cytotoxicity in cell culture. While cell cultures may provide important information for the evaluation of microbicides, they may not adequately simulate events that occur in vivo. Human explant cultures (endocervical, ectocerivcal, vaginal and rectal), biologic fluids (cervicovaginal secretions and semen) and a mouse genital herpes model will be used in this Project to assess anatomic, physiologic, and immunologic factors that might impact on the activity of this novel class of compounds. Building on the in vitro cell culture data of Projects I, II and IV, the applicant will study the most active derivatives/isomers of SAMMA using biologic culture systems. In Aim 1, the most active derivatives will be evaluated for efficacy against HIV-1 infection of primary macrophages using human genital tract fluids and mucosal explant cultures. In Aim 2, mucosal explant cultures and a mouse model will be used to determine the efficacy of SAMMA to block HSV infection of epithelial cells. Inflammatory cells and cytokines will be measured to study the effects of SAMMA on the innate immune system (Aims 1,2 and 3). The interrelationship between HIV and HSV and the efficacy of SAMMA to inhibit dual infection will be studied in Aim 3. Efficacy and safety data in relevant biologic culture systems may provide compelling support for advancing SAMMA or one of its derivatives to clinical trials.

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- **Project Title: HUMAN HERPESVIRUS 8 INFECTION IN ZIMBABWE**

  Principal Investigator & Institution: Campbell, Thomas B.; Medicine; University of Colorado Hlth Sciences Ctr P.O. Box 6508, Grants and Contracts Aurora, CO 800450508

  Timing: Fiscal Year 2001; Project Start 30-SEP-1999; Project End 31-AUG-2003

  Summary: (Adapted from applicant's abstract):Kaposi's sarcoma is the most common cancer in persons with the acquired immunodeficiency syndrome (AIDS) worldwide, and is the most prevalent cancer in all persons living in Zimbabwe. The occurrence of KS in persons with, and without AIDS has been linked to infection with the recently discovered human herpesvirus 8 (HHV-8; also called Kaposi's sarcoma-associated virus or KSHV). Available data strongly suggest that HHV-8 is the causative agent of Kaposi's sarcoma and that coinfection with **human immunodeficiency virus** type 1 (HIV-1) and HHV8 greatly increases the risk of developing Kaposi's sarcoma. Thus, the present epidemic of Kaposi's sarcoma in Zimbabwe is likely the result of a high risk of concomitant infection with both HHV8 and HIV-1 in Zimbabweans. To date, the prevalence of HHV8 in Zimbabweans has not been defined and the relationship between HHV8 replication, HIV-1 related immunodeficiency and Kaposi's sarcoma pathogenesis is unknown. Even though Kaposi's sarcoma is epidemic in Zimbabwe, Zimbabwean investigators have limited experience with the techniques used to diagnose and monitor HHV8 infection and detailed studies on HHV8 epidemiology and pathogenesis in Zimbabwe have not been conducted. The purpose of the present proposal is to develop a strong collaboration between American and Zimbabwean investigators for studies on HHV8 infection and Kaposi's sarcoma. These studies will define the prevalence of HHV8 infection in Zimbabwe and to determine the relationship between HHV8 gene expression and Kaposi's sarcoma disease status in Zimbabweans with Kaposi's sarcoma. In addition to providing important information on the epidemiology and pathogenesis of HHV8 infection, it is expected that these initial studies will provide the basis for future investigations on the role of HHV8 in Kaposi's sarcoma.

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- **Project Title: HUMAN IMMUNODEFICIENCY VIRUS AND CYTOMEGALOVIRUS VIRAL BURDEN**

  Principal Investigator & Institution: Frank, Michael; Indiana Univ-Purdue Univ at Indianapolis 620 Union Drive, Room 618 Indianapolis, IN 462025167

  Timing: Fiscal Year 2001

  Summary: This abstract is not available.

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- **Project Title: HUMAN IMMUNODEFICIENCY VIRUS PROTEINASE**

  Principal Investigator & Institution: Dunn, Ben M.; Distinguished Professor; Biochem and Molecular Biology; University of Florida Gainesville, FL 32611

  Timing: Fiscal Year 2001; Project Start 01-JUL-1989; Project End 30-JUN-2005

  Summary: (Provided by applicant): Antiretroviral therapy with a combination of RT and PR inhibitors has had a profound effect upon the management of HIV-1 infection. However, under drug pressure, the virus is able to evolve into forms that are resistant to the available drug regimens. Thus, drug resistance has become the most significant challenge to AIDS therapy. We have been studying a pediatric population undergoing a clinical trial with protease inhibitors in combination with RT inhibitors. We have discovered that evolution of the protease sequence is accompanied by evolution of the sequence of the cleavage sites within Gag/Pol, thus affecting the efficiency of processing. Furthermore, the evolution of protease is accompanied by alterations in cleavage specificity. We hypothesize that the Gag/Pol cleavage sites and PR form a functional unit in which sequence evolution may be co- dependent. In our renewal period, we will exploit these discoveries to gain additional understanding of the mechanisms of Gag/Pol processing. To this end, we will pursue the following specific aims: Specific Aim I will analyze natural Gag/Pol alleles for processing phenotype in a bacterial expression developed in the current period of support. We will also map the determinants by preparation of chimeric gag/pol constructs and analyze replication of recombinant virus with natural or chimeric gag/pol regions. Specific Aim 2 will study the growth of recombinant virus in the presence of anti-protease drugs in culture. In addition, new protease alleles will be subcloned and expressed for analysis by studies of substrate specificity using a combinatorial library of substrates, and by analysis of the binding of inhibitors. Specific Aim 3 will study the effects of changes in the sequence of Gag processing sites on the efficiency of processing. We will prepare peptides representing products of Gag/Pol processing and test their ability to inhibit the enzyme. We will also conduct structural analyses of fusions of Gag/Pol proteins with an inactive form of HIV PR in order to determine the role of structural organization in the processing events.

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- **Project Title: IDENTIFICATION OF HOST FACTOR(S) INVOLVED IN HIV RELEASE**

  Principal Investigator & Institution: Sutton, Richard; Assistant Professor; Molecular Virology & Microbiol; Baylor College of Medicine 1 Baylor Plaza Houston, TX 77030

  Timing: Fiscal Year 2003; Project Start 01-JUL-2003; Project End 30-JUN-2005

  Summary: (provided by applicant): By the end of this year, the World Health Organization has estimated that approximately 0.7% of the world's population will be seropositive for **human immunodeficiency virus** (HIV). Most of these individuals live

in the developing world and do not have access to highly active anti-retroviral therapy (HAART). A safe and efficacious vaccine may be a decade away. Most therapy is directed towards inhibition of viral reverse transcriptase or protease. Although over the last two decades much has been learned regarding the replicative cycle of HIV and the cellular factors involved, there are still gaps in our knowledge that could represent future therapeutic targets. For example, in the mouse entry and post-entry blocks to HIV replication have been circumvented by expressing human CD4, a chemokine co-receptor, and cyclin T1. These mouse cells, however, are still not fully permissive for HIV replication, perhaps due to a defect in Gag processing. Mouse-human cell fusions produce infectious virus, suggesting that mouse cells lack one or more factors required for HIV replication. This proposal seeks by genetic means to identify novel host cellular factors that may facilitate HIV release, using poorly permissive rodent cells as a model. In the first aim, a genetic screen will be used to identify such a missing factor(s). A cDNA library expression vector has been developed based upon HIV which is of high titer and has a selectable marker. This will be introduced into mouse cells expressing cyclin T1 (cycT1). Infectious virus will be recovered by providing trans functions, titered, and used to re-transduce na'fve mouse.cycT1 cells. This cycle will then be repeated in the hopes of amplifying and enriching for cDNAs that facilitate HIV replication in the mouse. In the second aim, a conventional plasmid-based cDNA library will be introduced into mouse cells (already expressing cycT1 and transduced with an HIV vector encoding both luciferase and a selectable marker). Cells will be divided into pools, and infectious virus recovered from each pool by methods similar to aim 1. Cell clones supporting the highest degree of HIV release will be isolated by sib selection. For both this and the preceding aim, cDNAs from individual clones will be recovered by PCR, characterized by DNA sequencing, and re-introduced into mouse cells to determine if the mouse cells are then rendered fully permissive for HIV replication. In the third aim, the Stanford panel of radiation hybrid (RH) cell lines will be individually transduced with a replication-defective HIV vector encoding cycT1 and a marker. Infectious virus will be recovered from each RH by methods similar to aim 1. The most promising RHs will be tested for their ability to rescue HIV Gag processing and support wild-type M-tropic HIV replication similar to the first two aims. This RH panel should allow functional genetic mapping to less than 1 Mb. From this aim it is hoped that a reasonable approximation of the number (and chromosomal location) of missing host factors will be obtained and this will be correlated with the results from the first two aims. Time permitting, candidate genes from the region of greatest interest will be tested for their ability to mediate HIV release from mouse cells. At the completion of these studies it is hoped that a better understanding of the host factors involved in HIV release will be achieved.

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- **Project Title: IMAGINH CANCER VIRUSES WITH TAT TRANSDUCIBLE PEPTIDES**

  Principal Investigator & Institution: Ratner, Lee; Professor; Washington University Lindell and Skinker Blvd St. Louis, MO 63130

  Timing: Fiscal Year 2002; Project Start 31-MAY-2002; Project End 31-MAR-2007

  Summary: (provided by applicant): Imaging cancer viruses in vivo will provide new tools for studies of pathogenesis, potential tools for prognosis, as well as new ways to evaluate efficacy of therapeutic agents. We will evaluate two infectious agents that are closely associated with human malignancies. **Human immunodeficiency virus** type 1 (HIV-1), although probably not a direct cause of malignancies, is associated with a very

high incidence of lymphomas and Kaposi's sarcomas as a result of interactions with herpesvirus infections. The methodology utilized in this proposal was first evaluated in HIV infected cells. Human T-cell leukemia virus type 1 (HTLV-1) is a cause of lymphoma in humans, as well as a neurological disorder known as HTLV-1 associated myelopathy (HAM), with which we have extensive molecular biology and animal models experience. The methodology developed for imaging will take advantage of a novel protein transduction system allowing efficient delivery of a wide range of proteins into all cell types that have been examined in tissue culture or in vivo, based on a peptide derived from the HIV-1 Tat protein. Recombinant fusion proteins are purified as polyhistidine-tagged proteins denatured in urea. Specific cleavage sites for HIV-1 or HTLV-1 proteases are inserted between the Tat sequence and the imaging compound to allow selective retention in infected cells. The specific aims are to 1) develop chelation peptides or imaging proteins fused to the Tat permeation sequence and specific protease cleavage sites to detect HIV-1 and HTLV, 2) examine targeting of specific chelation peptides or imaging proteins to infected cells in tissue culture, and 3) examine targeting of specific chelation peptides or imaging proteins to infected cells in animal model systems. This project seeks to combine highly experienced investigators at Washington University with complementary skills to explore the use of novel molecular imaging techniques to study viral pathogenesis. These techniques will be critical to addressing issues of virus load and tissue targeting that are primary determinants of pathogenicity.

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- **Project Title: IMMUNIZATION BY RAAV-MEDIATED ANTIBODY GENE TRANSFER**

  Principal Investigator & Institution: Clark, Reed; Immunization in Raav; Children's Hospital (Columbus) 700 Children's Dr Columbus, OH 43205

  Timing: Fiscal Year 2003; Project Start 01-JUL-2003; Project End 30-JUN-2008

  Summary: Neutralizing antibodies are critical for vaccine-induced protection of many viral diseases. They act in most cases by blunting the initial infection, which is then resolved by cytotoxic T cells. In fact, several lines of evidence argue that both arms of the adaptive immune response are indeed required to resolve experimental retroviral infections (and most likely HIV infection). However, it has been extraordinarily difficult to elicit antibodies that neutralize primary field isolates of HIV-1. Thus, if one considers such antibodies to be an important defense against HIV-1 infection and disease, there remains a significant gap in the design of current HIV-1 vaccine candidates. Therefore, we have developed an alternative strategy to generate serum antibodies that neutralize primary isolates of HIV-1. This novel approach exploits the existence of several potent broadly neutralizing human monoclonal antibodies against HIV-1 and the unique gene-delivery properties of recombinant adeno-associated virus (rAAV) vectors, rAAV vectors have been shown to transduce muscle with high efficiency and direct the long-term expression of a variety of transgenes. Because of the flexibility of this system, light and heavy chain antibody genes can be incorporated into a single rAAV vector, and the antibody-expressing vector can then be used to transduce muscle in vivo. This, in turn, leads to sustained expression and secretion of biologically active antibody molecules from transduced myofibers. We have shown that the human monoclonal antibody IgG1b12 can be expressed in exactly this fashion, with significant levels of HIV neutralizing activity present in sera of mice for over 6 months after a single intramuscular administration of the vector. In Project 4, we will further refine and optimize this novel strategy by developing rAAV antibody vectors based on rAAV-1 and rAAV-5, with the hopes of increasing IgG production 10-100 fold. We will also

investigate ways to enhance the specific activity of the antibody genes themselves by testing alternative antibody constructions (Fab or single-chain) that retain neutralizing activity, but may be more efficiently secreted than the full-length IgG molecule from skeletal myocytes. Lastly, the efficacy of this vaccine approach will be determined using a SHIV challenge model of HIV-1 infection.

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- **Project Title: IMMUNODEFICIENCY VIRUS CHIMERAE & GENETIC DETERMINANTS OF SPECIES SUSCEPTIBILITY**

  Principal Investigator & Institution: Axthelm, Michael K.; Oregon Health & Science University Portland, OR 972393098

  Timing: Fiscal Year 2001

  Summary: The study of simian immunodeficiency virus (SIV) infection in macaques has provided numerous insights into the pathogenesis of AIDS in **human immunodeficiency virus** type 1 (HIV-1) -infected humans. However, gene structure and, consequently, some regulatory and structural features of the HIV-1 and HIV-2/SIV families are constitutively different. SIV/HIV-1 envelope chimeras (SHIV) mitigate some of the concerns about differences in immune responses and tropism directed by envelope proteins but the gag and regulatory genes in the SIV backbone compromise their usefulness for addressing mechanisms of pathogenesis and anti-viral strategies unique to HIV-1 gag and regulatory genes. Several laboratories have constructed chimeric SHIVS on the SIVmac backbone that are infectious for NHPs. In these constructs, SIV genes other than the envelope gene, i.e., LTR, gag, pol, vif, vpx, vpr, tat, rev and nef genes, appear to influence SHIV replicative potential in NHPs, but they are not yet well understood. Since the nef genes of HIV-1 and SIV play an important role in viral infectivity and pathogenicity, we generated HSIV nef chimerae. The nef gene of cloned HIV-1pNL4-3 was precisely exchanged with that of SIVmac239 to generate the nef gene, chimeric HSIV. The nef genes of HIV-1 and SIV overlap with their 3'LTR U3 regions and two different nef chimerae, NF-1 and NF-2, were constructed. The HSIV NF-1 chimera HIV-1 was constructed by replacing all the HIV-1 nef coding regions, including the 3'LTR U3 with the corresponding SIVmac239 regions. Therefore, NF-1 contains a full-length SIV nef coding region and a hybrid 3'LTR. To construct the NF-2 chimera, only the HIV-1 nef unique region not overlapping with the U3 of the 3'LTR (from nef amino acid #1 through #96) was exchanged with the nef unique region of SIVmac239. Therefore, the NF-2 chimera encodes a hybrid nef protein between HIV-1 and SIV (N-terminus encodes SIV nef and the C-terminus encodes HIV-1 nef) and retains the wild-type HIV-1 3'LTR. Both the NF-1 and NF-2 chimerics are fully infectious for human T cell lines, and their replicative potential in human T cell lines was indistinguishable from wild-type HIV-1pNL4-3. The replicative potential of the nef chimeric viruses in PBL from humans and several macaque PBMC will be further examined in culture. If the nef chimerics exhibit a significant replicative potential in macaque PBMC in culture, experimental macaque studies and serial passage will be initiated to evaluate in vivo infectivity and pathogenicity. FUNDING NIH RR-00163 (Project 7) PUBLICATIONS None

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: IMPROVED SAFETY OF A THERAPEUTIC VACCINE**

  Principal Investigator & Institution: Xu, Jianqing; Senior Research Associate; Res Inst for Gen & Human Therapy

Timing: Fiscal Year 2003; Project Start 01-JUL-2003; Project End 30-JUN-2007

Summary: Our non-human primate studies have shown that a therapeutic vaccine, named DermaVir, could induce control of SIV and be beneficial for the survival of late-stage SIV-infected monkeys. In order to test the vaccine in human clinical trials, an HIV counterpart is needed, and the proper DNA component of DermaVir has to be constructed. However, the current construct, containing one genetic inactivation in the integrase region of the HIV genome, may not be safe enough to proceed to clinical use. This project proposes to improve the safety of the construct by introducing additional genetic modifications while retaining the efficacy of gene expression and immunogenicity. The project will have three aims: Specific Aim 1. Improve the safety of the HIV construct by a) removing the flanking human genome sequences, b) truncating the 3' LTR to block reverse transcription and integration of virus and/or c) replacing the gag sequence with a transdominant gag to eliminate viral release and inhibit incoming virus replication, thereby minimizing chances for recombination. Specific Aim 2. Screen the constructs in vitro to determine which construct contains the most safety modifications yet retains the expression efficacy and immunogenicity, to be used in pre-clinical and clinical studies (Project 4). Specific Aim 3. Construct the SIV counterpart of the HIV construct selected from Specific Aim 2 for evaluation in non-human primate studies (Project 3).

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- **Project Title: IMPROVING THE CNS DELIVERY OF ANTI-RETROVIRAL COMPOUNDS**

  Principal Investigator & Institution: Elmquist, William F.; Associate Professor; Pharmaceutics; University of Minnesota Twin Cities 200 Oak Street Se Minneapolis, MN 554552070

  Timing: Fiscal Year 2002; Project Start 01-APR-2002; Project End 31-MAR-2008

  Summary: (provided by applicant): **Human immunodeficiency virus** (HIV-1) renders the host susceptible to a variety of serious central nervous system (CNS) diseases such as AIDS dementia complex and HIV-1 encephalopathy. The use of highly active antiretroviral therapy (HAART), including protease inhibitors, has been effective in slowing the spread of the virus, however, drug resistant tissue reservoirs, such as the brain, remain. Treatment of HIV-1 in the brain has been hampered by the fact that nucleoside drugs do not penetrate the blood-brain barrier (BBB) well and newer treatments, i.e., protease inhibitors, also have very limited delivery to the brain. One component of the BBB that limits delivery of HAART into the CNS is the membrane-bound drug efflux pumps, such as p-glycoprotein (P-gp) and multidrug resistance-associated proteins (MRPs). Recently, it has been shown that both nucleosides and protease inhibitors are substrates for efflux transporters. The long-term objective of this research is to develop better therapeutic strategies to enhance the targeted delivery of antiretroviral drugs to the CNS by using novel drug delivery systems, such as polymeric carriers (Pluronics). Our hypothesis is that novel drug delivery systems will enhance the brain distribution and CNS targeting of HAART and therefore improve efficacy. The specific aims to test this hypothesis are: 1) examine the effect of Pluronics on the interactions of various antiretrovirals with isolated P-gp membranes using photoaffinity labeling and P-gp ATPase assay, 2) study the effects of Pluronics on the transport properties of antiretroviral drugs in the in vitro BBB and efficacy in infected target cells, i.e., monocytes/macrophages, and 3) determine the effect of this novel drug delivery technology on the brain distribution of antiretrovirals in vivo characterizing the efficacy of the most promising formulations in an HIV-infected SCID mouse model of HIV-

encephalopathy. The current proposal examines the CNS targeting of HAART in both in vitro and in vivo models of the blood-brain barrier, and the efficacy of that targeted drug delivery. New approaches to improve brain penetration of anti-HIV drugs will be valuable in the treatment of HIV-encephalopathy and in eradicating the virus from potential sanctuary sites.

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- **Project Title: IN VITRO AND IN VIVO FUNCTION OF HIV AND SIV NEF GENES**

  Principal Investigator & Institution: Luciw, Paul A.; Professor; Ctr for Comparative Medicine; University of California Davis Sponsored Programs, 118 Everson Hall Davis, CA 95616

  Timing: Fiscal Year 2001; Project Start 01-AUG-1995; Project End 31-JUL-2003

  Summary: Human immunodeficiency virus types 1 and 2 (HIV-1 and HIV-2) and the simian immunodeficiency virus (SIV) encode a gene, designated nef (negative effector), that is dispensable for viral replication in vitro (i.e., in tissue culture cells). However, genetic analysis of SIVmac mutants in rhesus macaques has demonstrated that the nef gene is important for maintaining high virus load and for pathogenesis (Kestler et al. 1991). Although numerous studies have been directed at determining the function of the HIV and SIV nef gene in vitro, a critical gap remains in the knowledge of the role of this gene in viral replication and pathogenesis. The goal of this proposal is to elucidate the function of the nef gene both in vitro and in vivo (i.e., a non-human primate model). Recent investigations have revealed that HIV-1 and SIV Nef associates with cellular factors, one of which has protein kinase activity. Accordingly, an important objective within this proposal is to identify these cellular factors and thereby elucidate the mechanisms of HIV and SIV Nef in both human and simian cells. Because SIV is genetically related to HIV and because SIV infection of macaques produces a fatal AIDS-like disease, this highly manipulatable animal model will be utilized to test the in vivo significance of the in vitro studies on nef protein function. HYPOTHESIS The hypothesis is that cellular factors, including a protein kinase, associated with HIV/SIV Nef are critical for Nef function in viral persistence and pathogenesis. SPECIFIC AIM 1: Functional properties of Nef proteins from novel and unique HIV-1 and SIV isolates will be analyzed in vitro. SPECIFIC AIM 2: The mechanism of Nef will be elucidated in in vitro systems; emphasis is directed at characterizing the host cell kinase that associates with this viral protein. SPECIFIC AIM 3: SIVmac mutants in functional domains of Nef will be constructed, characterized in vitro, and analyzed in vivo (i.e., by infection of rhesus macaques) to relate the results of the biochemical analysis of Nef to viral persistence and pathogenesis. SPECIFIC AIM 4: SIV/HIV-1 chimeras (i.e., SHIV) will be constructed by substituting the SIV nef gene with an HIV-1 nef gene, and these chimeric viruses will be tested in rhesus macaques to directly address the function of HIV-1 Nef in vivo. SIGNIFICANCE; The proposed research integrates studies on the function of the nef genes of HIV-1 and SIV. Results of biochemical studies on Nef function of both viruses will be related to in vivo findings in SIV- and SHIV-infected rhesus macaques. A major emphasis of the proposed research is to identify cellular factors which mediate Nef function; accordingly, this knowledge may provide a basis for developing and testing novel anti-viral therapies aimed at inhibiting Nef function and thereby preventing disease progression.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: IN VITRO ANTI-HIV1 CAP ACTIVITY**

  Principal Investigator & Institution: Jiang, Shibo; Associate Member; New York Blood Center 310 E 67Th St New York, NY 10021

  Timing: Fiscal Year 2001; Project Start 26-SEP-2001; Project End 31-JUL-2005

  Description (provided by applicant): Sexual transmission is the major mode of **human immunodeficiency virus** type 1 (HIV-1) infection worldwide. There is an urgent need to develop safe, topically applied microbicides that can efficiently reduce sexually transmitted infection by HIV-1. The applicant?s previous studies demonstrate that cellulose acetate phthalate (CAP), an inactive pharmaceutical excipient commonly used for the coating of enteric tablets and capsules has potent inhibitory activity against infection by HIV-1, herpesviruses (HSV), simian immunodeficiency virus (SlV), and several non-viral sexually transmitted disease (STD) pathogens, including N. gonorrhea, C. trachomatis, T vaginalis, and Haemophilus ducreyi, but has no effect on Lactobacilli, essential components of the normal vaginal flora. CAP has no significant in vitro and in vivo toxicity and has proven to be safe for human use. In addition, it is inexpensive. Thus, the applicant believes that CAP is an ideal candidate for rapid development as a microbicide applicable to prevention of sexual transmission of HIV-1 in both developing and developed countries. So far, the anti-HIV-l activity of CAP and its formulations have been evaluated using laboratory-adapted HIV-1 isolates. In order to bring CAP towards clinical application, it is critical to determine whether CAP (a) is also effective in blocking the infection of different target cells by distinct primary HIV-1 isolates, including cell-free and cell-associated viruses, and (b) inactivates the infectivity of these isolates. The specific aims of this Project are: 1) to evaluate the inhibitory activity of CAP on in vitro infection by primary HIV-1 strains with distinct genotypes and phenotypes; 2) to assess the virucidal activity of CAP and its formulations against primary HIV-1 isolates; 3) to determine the effect of CAP on in vitro cell-to-cell transmission of HIV-1; 4) to evaluate the efficacy and bio-compatibility of CAP in human genital and rectal tissue models of HIV-1 transmission; 5) to study the mechanism of action of CAP against infection by primary HIV-1 isolates. The goal of the proposed research is the rigorous and comprehensive pre-clinical evaluation of CAP and its formulations in order to expedite its transfer into human clinical trials.

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- **Project Title: IN VIVO ANTIVIRAL & INFLAMMATORY EFFECTS OF MICROBICIDES**

  Principal Investigator & Institution: Keller, Marla J.; Mount Sinai School of Medicine of Nyu of New York University New York, NY 10029

  Timing: Fiscal Year 2002; Project Start 01-APR-2002; Project End 31-MAR-2007

  Description (provided by applicant): The development of safe an effective topical microbicides for vaginal and rectal use could play a critical role in reducing **human immunodeficiency virus** (HIV) transmission rates worldwide. PRO 2000, a naphthalene sulfonic acid, is active against a wide range of HIV isolates in vitro, and also inhibits herpes simplex virus (HSV), a major cofactor in HIV transmission. A combination of PRO 2000 with a second microbicide that targets a different step in the HIV life cycle might have distinct advantages over either drug alone, including enhanced efficacy, reduced mucosal inflammation, and possibly, an expanded spectrum of activity against HIV and other sexually transmitted pathogens. The focus of this Program, therefore, is to identify optimal combinations that act additively or synergistically with PRO 2000 and provide even greater protection. A valuable lesson learned from the nonoxynol-9

(N-9) trials is that the use of topical microbicides may alter innate immune responses of the female genital tract at a mucosal level and enhance sexual transmission of HIV. It is clear that early pilot in vivo studies are needed prior to the initiation of large-scale clinical trials. Although monitoring for cervicovaginal lesions has been a routine part of clinical safety microbicide trials, little is known about potential subtle changes in the cervicovaginal mucosal barrier, including induction of mucosal inflammation. In Project 3, three pilot human clinical studies will be conducted to examine the effects of PRO 2000 on mucosal immunity and on genital tract HIV. In Specific Aim 1, the effects of PRO 2000 on mediators of inflammation will be evaluated. Healthy participants will apply PRO 2000 or placebo gel intravaginally daily for fourteen days and cell populations and cytokines associated with inflammation will be measured. Microbicides may be used by women knowingly or unknowingly infected with HIV. Therefore, a pilot clinical study will be conducted in Specific Aim 2 to assess the effect of PRO 2000 on infectious HIV-1 recovered from cervicovaginal lavage fluid. The impact of repeated application of PRO 2000 on HIV-infected women will be assessed in Specific Aim 3. HIV-infected women will apply PRO 2000 gel or a matched placebo daily for fourteen consecutive days and cell populations and cytokines associated with vaginal inflammation will be measured. The effect of PRO 2000 on genital tract viral RNA and DNA will also be determined. The impact on cell-associated HIV nucleic acid will be assessed using a laboratory-developed PCR-based assay for circular viral DNA, a surrogate marker for local de novo replication. This work will lay the groundwork for future clinical trials with combination microbicides identified in Projects 1 and 2.

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- **Project Title: IN VIVO MODELS FOR HUMAN GENITAL TISSUES AND SEXUALLY TRANSMITTED DISEASES**

  Principal Investigator & Institution: Howett, Mary K.; Professor; Pennsylvania State Univ Hershey Med Ctr 500 University Dr Hershey, PA 17033

  Timing: Fiscal Year 2001

  Summary: Vaccines do not exist for most STDs, and because vaccine development and implementation is costly and time-consuming, officials of the World Health Organization and the National Institutes of Health have recognized that on practical approach to control and prevention of STDs is development of topical microbicides which would be affordable, stable at ambient temperature and could be used discreetly by women. Vaginal microbicides are products for vaginal administration that can be used to prevent **human immunodeficiency virus** (HIV) infection and/or infections by other STDs. During the three years since this Program Project was initiated, great success has been achieved in establishing tubular, vaginal, human epithelial xenografts and susceptibility of these grafts to representative STDs [HPV and herpes simplex virus type 2 (HSV-2)] has been demonstrated. Uninfected grafts recapitulate the histological and cytochemical features of normal human vagina while infected grafts produce a profile of pathologic features and virus macromolecular synthesis identical to those in patient lesions. Xenografts have also been successfully used to demonstrate microbicidal prevention of HPV infection (by microbicides from the alkyl sulfate chemical family and by the microbicide C31G) as well as HSV-2 infection (by C1G). In the next phase of the grant, we will expand use of this model. Our Specific Aims will be to: (1) Continue characterization of human xenografts at the tissue and cellular level by: (a) Optimizing growth parameters for the grafts, including comparison of growth in nude mice, severe combined immunodeficient (SCID) mice, and SCID mice reconstituted with human lymphoreticular cells; (b) Characterizing the profile of xenografts in a progesterone-

dominant (as opposed to an estrogen-dominant) state; (b) Determining the repertoire of non-epithelial cells, specifically lymphoreticular cells, in the xenografts: (2) Complete the characterizing of the toxicity and efficacy of alkyl sulfate microbicides in the human vaginal xenograft system: (3) Determine the minimal inhibitory concentrations of non-formulated and formulated alkyl sulfates in inactivating or interdicting establishing grafts from human, fetal anal epithelium, in which efficacy of microbicides and infections of this target tissue might be studied.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: INFECTION OF MICROGLIAL CELLS BY HIV-1**

  Principal Investigator & Institution: Gendelman, h; St. Luke's-Roosevelt Inst for Hlth Scis Health Sciences New York, NY 10019

  Timing: Fiscal Year 2001

  Summary: The **human immunodeficiency virus** associated dementia complex (ADC) follows progressive viral infection and immunosuppression in a significant proportion of infected individuals. The mechanisms for disease, in measure, revolve around viral infection and immune activation of brain mononuclear phagocytes (macrophages and microglia). Studies from our laboratory support distinctive role for each cell type in disease. This component of the program project grant will investigate indirect mechanisms of HIV neuropathogenesis utilizing age-matched human microglia and blood-derived monocytes to examine the neurotoxic responses elicited following immune activation and HIV-1 infection. The mechanisms for viral entry, the chemotactic factors that underlie monocyte penetration into brain and the elucidation of the biological and molecular events in which mononuclear phagocytes induce neural injury will be explored. The hypothesis being tested is that functional differences exist between the two phagocytic cell types and that microglial cells are a principle participant in HIV-1 associated neuropathological injury. The laboratory has now gained significant expertise together with other project responses, it utilizing molecular and biochemical approaches for identifying HIV-induced neurotoxins and in developing small animal model systems for ADC. Such experimental systems will be utilized in determining the precise role played by mononuclear phagocytes in ADC.

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- **Project Title: INFLUENZA HA IN SHIV VLPS FOR MUCOSAL VACCINATION**

  Principal Investigator & Institution: Yao, Qizhi W.; Surgery; Baylor College of Medicine 1 Baylor Plaza Houston, TX 77030

  Timing: Fiscal Year 2003; Project Start 01-AUG-2003; Project End 31-MAY-2007

  Summary: (provided by applicant): Recently, we have successfully produced simian-human immunodeficiency virus-like particles (SHIV VLPs) which contain SIV Gag and HIV Env by using a baculovirus expression system. Furthermore, we have incorporated the influenza virus surface glycoprotein, hemagglutinin (HA), into SHIV VLPs. Taking advantage of HA having a high affinity to bind to the mucosa of the upper respiratory track, our central hypothesis is that use of SHIV VLPs containing influenza HA as a mucosal vaccine will enhance both systemic and mucosal immune responses against HIV infection. The major focus of this project is to investigate the efficiency and mechanisms of the built-in adjuvanticity of HA in SHIV VLPs for intranasal immunization in a mouse model. Specifically, we propose: 1). To determine the role of incorporation with influenza HA in SHIV VLPs as a mucosal vaccine in enhancement of immune responses against HIV. Proposed experiments will investigate: a) whether the

built-in adjuvanticity of influenza HA in SHIV VLPs as a mucosal vaccine is more potent than soluble influenza HA in enhancement of both systemic and mucosal immunity; and b). whether the receptor binding or membrane fusion activity of influenza HA affects its adjuvanticity for SHIV VLPs. 2). To determine the role of incorporation with influenza HA in SHIV VLPs in dendritic cell (DC) binding, activation, cytokine production, and antigen presentation. We propose to investigate: a). whether HA/SHIV VLPs have an increased ability to DC binding, internalization, and subcellular localization; b). whether HA/SHIV VLPs have an increased effect on DC activation, and cytokine production; c). whether HA/SHIV VLP-activated DCs increase naive T cell proliferation; and d). whether HA/SHIV VLPs increase the efficiency of antigen cross-presentation of DCs to CD8+ T cells and what are the associated intracellular pathways. 3). To determine the role of incorporation with influenza HA in SHIV VLPs in specific B cell binding, activation, and antibody production without CD4+ T cell help. Experiments are designed to investigate: a). whether HA/SHIV VLPs increase their ability to bind to naive B cells; b). whether HA/SHIV VLPs have an increased effect on naive B cell proliferation; c). whether HA/SHIV VLP-activated DCs have an increased ability to adhere to naive B cells; d). whether HA/SHIV VLP-activated DCs increase naive B cell proliferation; and e). whether B cell activation and differentiation and cytotoxic CD8+ formation occur in nasal-associated lymphoid tissue (NALT), an inductive site after intranasal immunization with HA/SHIV VLPs in CD4+ T-cell-deficient mice. This project represents a novel approach to develop an effective and safe HIV vaccine. Understanding the cellular and molecular mechanisms of HA/SHIV VLP-enhanced immune responses in mice is critical for the future design and testing of a successful HIV vaccine in non-human primate models and in human trials.

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- **Project Title: INHIBITION OF HIV GENE TRANSCRIPTION BY SMALL MOLECULES**

  Principal Investigator & Institution: Gottesfeld, Joel M.; Associate Member; Scripps Research Institute 10550 N Torrey Pines Rd La Jolla, CA 920371000

  Timing: Fiscal Year 2001; Project Start 01-FEB-1998; Project End 31-JAN-2005

  Summary: This is a continuation application for a program aimed at development of new drugs for the treatment of human acquired immunodeficiency syndrome by interference with HIV-1 RNA transcription. Our studies have focused on the pyrrole-imidazole polyamides, developed in the laboratory of the Co-PI, Dr. Peter Dervan at Caltech. These molecules can be designed and synthesized to target a wide range of DNA sequences with subnanomolar affinities, comparable to the affinities of cellular transcription factors for their DNA targets. During the previous years of support, we have developed polyamide ligands to target the binding sites for the host cell regulatory proteins involved in HIV-l RNA transcription. Studies in the laboratory of Dr. J. Gottesfeld at the Scripps Research Institute have shown that these molecules inhibit specific transcription factor-DNA interactions on the HIV-1 promoter and enhancer and are potent inhibitors of HIV-1 transcription in vitro. Importantly, through a collaborative effort with Dr. D. Mosier at Scripps, we have shown that these polyamides are effective inhibitors of HIV-1 replication in human peripheral blood lymphocytes. We now propose to optimize our DNA targets within the HIV-1 enhancer and promoter elements and to validate the hypothesis that inhibition of virus replication is a direct consequence of inhibition of protein-DNA interactions on the integrated HIV-1 proviral DNA. We will determine whether polyamides can access their target sequences in the context of cellular chromatin and we will examine the genome-wide effects of

polyamide treatment using DNA array technology. Given our success in inhibition of virus replication in cell culture, we propose collaborative preclinical studies with the Mosier laboratory to determine the effectiveness of polyamides in the human PBL-SCID mouse model.

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- **Project Title: INNOVATIVE HIV DIAGNOSIS AND MONITORING**

  Principal Investigator & Institution: Vardas, Eftythi; Univ of Witwaterstrand Johannesburg,

  Timing: Fiscal Year 2002; Project Start 01-JUN-2002; Project End 31-MAY-2007

  Summary: An important implication of the estimated 1,600 new HIV infections occurring per day in South Africa are the rising costs and increasingly complicated logistics associated with existing laboratory methodologies for the surveillance, diagnosis and monitoring of HIV and associated infections. Importantly, the arrival of free or affordable antiretroviral medications in South Africa is imminent, but the ability to affordably diagnose and monitor HIV infection in the laboratory remains an obstacle to national implementation of antiretrovirals. While there is a need to identify more feasible technologies for the monitoring of disease, these must be shown to be equivalent to the existing developed world standards in effectiveness. The Innovative HIV/AIDS Diagnostic and Monitoring project is divided into four sections; natural history, molecular epidemiology, genetics and innovative surveillance, diagnostic and monitoring assays. The aim is to develop innovative, rapid and inexpensive systems for epidemiological surveillance (disease, molecular and community) and individual diagnostic HIV and opportunistic infections testing and monitoring. This project encompasses field assessment and implementation of simple and easy to use surveillance tests and sample collection methodologies to expand existing infection and disease surveillance and molecular epidemiological systems and thus allow for the accumulation of essential baseline **human immunodeficiency virus** (HIV) virological and South African population genetic information. The largescale use of innovative sample collection methods for HIV surveillance such as dried blood spots and oral fluid or whole blood rapid HIV tests has not yet been done in South Africa. Furthermore, this project will develop and validate affordable alternative testing systems (CD4 counts, viral loads, heat denatured and imrnune-complexed p24, immune monitoring, resistance testing) that can be used as accurate alternatives to existing but more expensive diagnostic and monitoring tests. If implemented these novel sample-collecting techniques will decrease the potential risks of exposure to bio-hazardous material of health care staff and patients and could ensure a more feasible HIV laboratory service. The human subjects enrolled in the other projects will benefit directly from the diagnostic and monitoring information generated by the laboratory projects described here.

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- **Project Title: INTERACTION OF CELLULAR HOST FACTORS WITH HIV VIF**

  Principal Investigator & Institution: Sheehy, Ann M.; Microbiology; University of Pennsylvania 3451 Walnut Street Philadelphia, PA 19104

  Timing: Fiscal Year 2001; Project Start 01-JUN-2001

  Summary: 33.5 million people worldwide are infected with HIV and new lines of investigation are required to develop novel anti-viral therapies. In addition to the retroviral gag, pol and env genes, the HIV genome includes six auxiliary genes. Vif is an

accessory protein that enhances infectivity of HIV virions, although its specific function remains undefined. It is dispensable for the HIV replication in many T cell lines (permissive lines), but absolutely required for the establishment of infection in a subset of T cell lines (nonpermissive cells) and PBLs, the in vivo targets of HIV infection. Vif expression has also been linked to the cell species restriction of HIV-1 replication. SIVAGM does not replicate in human cells, but co-expression of human Vif restores replicative ability. To delineate protein motifs important for Vif function, chimeric proteins, from a functional HIV-1vif gene and a SIVAGM vif gene will be made. These proteins will be examined in a transcomplementation assay for their ability to complement Vif function in the deltavif HIV- 1 infection of a nonpermissive T cell line. Selective adaptation of an SIVAGM will also be used to identify amino acids important to Vif function. It has also been suggested that Vif functions to overcome an innate anti-viral host cell activity present in nonpermissive cell lines and PBLs. Therefore, the second aim of this proposal is to characterize this novel anti-viral activity using subtractive techniques designed to identify differences between permissive and nonpermissive T cell lines. Identification of host cell factors that mediate Vif function promises to lend insight not only into zoonosis, but also into the interplay between host cell and viral proteins and may lead to the development of novel anti-HIV therapeutics.

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- **Project Title: INTERFERON ALPHA AND HIV PATHOGENESIS**

  Principal Investigator & Institution: Fitzgerald-Bocarsly, Patricia; Associate Professor; Pathology and Lab Medicine; Univ of Med/Dent Nj Newark Newark, NJ 07103

  Timing: Fiscal Year 2001; Project Start 15-JUN-1991; Project End 31-MAY-2003

  Summary: The Acquired Immune Deficiency Syndrome (AIDS) results from infection with the **human immunodeficiency virus** (HIV-1). AIDS is characterized by profound and/or neoplasms in the infected individual. In addition to deficiencies in T mononuclear cells from AIDS patients to make interferon- alpha in response to herpes simplex virus type-1 infected fibroblasts has been observed. This deficiency was strongly correlated with the presence of OI in the patients studied and was also predictive of OI in the follow- up period for those not yet meeting the AIDS case definition. The cells responsible for IFN-alpha production were found to be light density HLA-DR positive cells and shared the phenotype of peripheral blood dendritic cells. In the present application, studies will be undertaken to positively identify the IFN-alpha producing cells, determine the interaction of HIV with this population and determine the mechanism of deficient IFN-alpha production in patients with AIDS and OI. Because the DR-positive cells represent only a small fraction of the mononuclear cells, density gradient techniques and sequential depletions with monoclonal antibodies will be utilized for enrichment. Frequency of IFN-producing cells will be monitored by immunoplaque assay and IFN-gene expression in activated cells will be measured by S1 mapping. Immunocytochemical and immuno-gold techniques for electron microscopy using antibodies to IFN will allow for direct detection of morphology of IFN-alpha producing cells. Enriched IFN-alpha producing cells will be used to determine the effect of HIV on these populations. Whether HIV replicates in and/or kills these cells will be determined and the effect of HIV on functional assays will be investigated. Finally, an evaluation of the mechanism of deficiency of IFN-alpha production in AIDS patients will be undertaken. IFN-alpha producing cells from AIDS patients will be evaluated using techniques developed in this application and functional studies involving co-culture to look for possible suppressor cells or factors will be performed. Together, the

proposed experiments involving both basic biology and patient studies should provide important information regarding an important mechanism of AIDS pathogenesis.

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- **Project Title: INTERNATIONAL TRAINING GRANT IN EPIDEMIOLOGY RELATED TO**

  Principal Investigator & Institution: Detels, Roger; Professor; Epidemiology; University of California Los Angeles 10920 Wilshire Blvd., Suite 1200 Los Angeles, CA 90024

  Timing: Fiscal Year 2001; Project Start 30-SEP-1998; Project End 31-MAY-2003

  Summary: Although China passed a comprehensive Blood Donation Law in 1997 following the discovery of high rates of **human immunodeficiency virus** (HIV) in blood and plasma donors, infection of donors continues. Rates of HIV as high as 6% and of hepatitis C virus (HCV) as high as 23% still occur, especially in the rural area hospitals. Thus, it is clear that HIV and HCV are being transmitted to recipients of contaminated blood units. Most county hospitals have neither the funds nor the technical skills to test every unit of blood that is collected for the most likely blood pathogens. This, therefore, is a proposal to measure the prevalence of HIV, HBV and HCV among blood donors in two county hospitals in each of two provinces in which transmission of HIV to blood recipients has been reported and to evaluate alternative strategies to protect the blood supply. Eight hundred donors, as well as 80 donors who were traced from 800 infected recipients, will be tested concurrently and analyzed for both the prevalence of infected donors and for correlates of infection. In addition, a survey of usual blood practices will be conducted among physicians at the county hospitals to estimate the prevalence of unnecessary use of blood. Following the survey a workshop will be conducted with representatives of the hospitals, the director of the Southern California Region of the American Red Cross Services, and representatives of the local and provincial anti-epidemic stations and departments of health and the Ministry of Health to discuss strategies to reduce the unnecessary use of blood using the results of the prior survey. The outcome of the workshop will be development of guidelines for the use of blood in county hospitals. A second survey will be conducted among the county level hospitals to identify the current and potential sources of blood and potential constraints to alternative strategies for protecting the blood supply at the county hospital level. Following the survey a second workshop will be held for 30 health professionals concerned with the safety of the blood supply at the local, provincial, and national levels to identify the most acceptable and feasible alternative strategy to protect the blood. This strategy will then be evaluated in a pilot study in county hospitals adopting and not adopting the alternative strategy. Results of the surveys and workshops and the pilot study will be disseminated to the county hospitals, local and provincial health administrators, and the Ministry of Health.

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- **Project Title: KAPOSIS SARCOMA AND HUMAN HERPESVIRUS IN AFRICA**

  Principal Investigator & Institution: Wood, Charles E.; Director and Professor; School of Biological Sciences; University of Nebraska Lincoln 14Th and R Sts Lincoln, NE 68588

  Timing: Fiscal Year 2001; Project Start 01-JUL-1998; Project End 30-APR-2003

  Summary: (adapted from the Abstract): Kaposi's sarcoma (KS) is a soft tissue tumor most commonly found in individuals with immunodeficiency, including the acquired immunodeficiency syndrome (AIDS). Recent studies have identified a new human herpesvirus, Kaposi's sarcoma-associated herpesvirus (KSHV)--or human herpesvirus-8

(HHV-8)--found in almost all KS tissues and body cavity-based lymphomas. This virus may play an important role in the transformation and development of KS. One of the many pertinent questions regarding this virus is its route of transmission. The Principal Investigator and his associates have initiated a collaboration with the University of Zambia Medical School to study the etiology of KS. Zambia has a very high incidence of HIV infection in women and children; moreover, KS constitutes about 20-25 of the malignancies seen in Zambian infants and children. These rates provide a unique opportunity to explore the possible vertical transmission route of HHV-8 and whether HHV-8 infection leads to KS development in children. The researchers have already found that Zambian children and infants with KS carry HHV-8 sequences and that many normal and HIV1-infected pregnant Zambian women are also infected by HHV-8. The Investigator proposes to expand on these initial observations to a large group of Zambian pregnant women to determine whether vertical transmission of HHV-8 occurs. He hypothesizes that HHV-8 can be transmitted vertically and that immune suppression, HIV-1, and other opportunistic infections increase the probability of transmission. His immediate experimental approach is to use serological tests, solution-based PCR, and in situ PCR to determine whether vertical transmission can occur, the cell types that harbor the virus, whether immune suppression, opportunistic infections, and high HHV-8 viral load correlated with vertical transmission. His long-term objective is to understand the roles played by HHV-8 in KS.

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- **Project Title: LATENT AND REACTIVATION TUBERCULOSIS**

  Principal Investigator & Institution: Flynn, Joanne L.; Associate Professor; Molecular Genetics & Biochem; University of Pittsburgh at Pittsburgh 350 Thackeray Hall Pittsburgh, PA 15260

  Timing: Fiscal Year 2003; Project Start 19-SEP-2003; Project End 31-AUG-2008

  Summary: (provided by applicant): Tuberculosis is a major killer of **Human Immunodeficiency Virus** (HIV)+ persons worldwide. Compared to the 10% lifetime risk of a PPD+ person developing tuberculosis, an HIV+PPD+ person has a 10% annual risk of this disease. The interaction between HIV and Mycobacterium tuberculosis is not well-understood. By necessity, many of the studies to date have been performed in vitro or in a natural infection human setting, due to lack of an appropriate animal model. The non-human primate model can be used to address this interaction using Simian (human) Immunodeficiency Virus (SIV/SHIV) and M. tuberculosis co-infections. Specifically, in this application we will address the serious problem of latent tuberculosis and mechanisms by which reactivation of latent tuberculosis can occur. Many people infected with HIV are already latently infected with M. tuberculosis, and reactivation can occur at any level of immunocompromise. Using a cynomolgus macaque model of low-dose M. tuberculosis infection recently developed in our laboratory, we will explore latent and reactivation tuberculosis. Our non-human primate model appears to mimic human latent tuberculosis. We will examine and compare reactivation of latent tuberculosis in the macaque model using three different immunocompromising strategies. The reactivation triggers we have chosen are CD4 T cell depletion by antibody, SHIV co-infection, and TNF-a neutralization. By comparing the effects of each strategy on latent tuberculosis, in terms of clinical, immunologic and pathologic parameters, we can gain an understanding of latent tuberculosis, and this knowledge will be useful in devising strategies to prevent reactivation. We will also learn about the mechanisms by which HIV leads to reactivation, by comparing each of our three

models. These studies are the first to study reactivation in an immunologically tractable animal model that is similar to human latent tuberculosis.

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- **Project Title: LENTIVIRAL MODULATION OF GENE EXPRESSION IN TARGET CELLS**

  Principal Investigator & Institution: Aldovini, Anna; Assistant Professor; Children's Hospital (Boston) Boston, MA 021155737

  Timing: Fiscal Year 2003; Project Start 01-APR-2003; Project End 31-MAR-2005

  Summary: (provided by applicant): HIV-I, HIV-2 and SIV infect primate cells that express the CD4 receptor and a coreceptor that varies among different viral stains. Among the different target cells infected are three cell types that are important components of the immune system: immature dendritic cells, macrophages, and CD4+ T cells. The initial infection leads to a chronic, non-pathogenic, systemic infection in the naturally infected primates (Chimpanzees, Sooty Mangabeys and African green monkeys), but it progresses to the clinical manifestations of AIDS in humans and in Rhesus macaques infected in captivity. The molecular basis of the different outcomes in the different species is not understood. Because interactions with different host cell environments may contribute to the different outcomes, it is important to understand how primate and human immune cells respond to HIV/SIV. Recent studies have shown that the gene expression programs of dendritic cells and macrophages are modified by pathogen exposure and that these modifications can provide important clues to pathogenesis. We have shown that dendritic cell reprogramming by HIV can create conditions that favor virus spread, and that the effect is mediated by the HIV transactivator Tat. We propose to use newly developed experimental and computational technologies to investigate how the gene expression programs of specific cell types from different species are affected by HIV and SIV infection. To accomplish this, the specific aims of the proposal are 1) To monitor gene expression in dendritic cells, macrophages and T cells from both humans and chimpanzees after infection with HIV and after intracellular expression of Tat, and to identify genes that are differentially regulated in the two species. 2) To monitor gene expression in uninfected human and chimpanzee T cells after their exposure to the supernatant of donor-matched HIV-infected primary cells and to identify genes that are differentially regulated in the two species. The information obtained from these studies should allow us to discover how HIV perturbs host cell gene expression programs, may identify differences in perturbations that contribute to different disease outcomes, and may suggest new strategies for pathogen control.

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- **Project Title: LENTIVIRAL VECTORS FOR POSITION-INDEPENDENT EXPRESSION**

  Principal Investigator & Institution: Hawley, Robert G.; Head; American National Red Cross Rockville, MD 20855

  Timing: Fiscal Year 2001; Project Start 15-JUN-2001; Project End 30-MAY-2005

  Summary: (Investigator's abstract) Gene therapy using hematopoietic stem cells (HSCs) as the target cell population has great potential to improve treatment of a wide range of inherited and acquired blood diseases. Replication-defective retroviruses have been the vehicles of choice for gene delivery and expression in HSCs because of their ability to stably integrate into the genome of target cells. For more than a decade, our laboratory

has been designing and optimizing retroviral vectors for gene transfer studies of HSC biology. In particular, our MSCV (murine stem cell virus) retroviral vector has proven to be highly efficient at delivering functional genes to the murine hematopoietic system. For this reason, the MSCV platform was chosen for use in two HSC gene therapy trials currently underway in the United States. To date, however, the outcomes of most clinical trials with retroviral vectors have been disappointing. This is believed to be due in part to low surface density of the amphotropic envelope receptor and the fact that retroviral vectors such as MSCV, which are derived from oncoretroviruses, can only integrate into cells undergoing mitosis. Thus it has been proposed that pantropic vectors developed from the lentivirus, **human immunodeficiency virus** (HJV), which can readily transfer genes into various types of stationary cells, may be more suitable for gene delivery to HSCs, which reside almost exclusively in the G0/G1 phase of the cell cycle. Even if efficient lentivirus-based gene transfer in HSCs is achieved, accumulated data indicate that in vivo transgene expression is frequently subject to transcriptional silencing and position effects. We propose therefore to develop next-generation HIV-based lentiviral vectors expressly for human HSC gene transfer applications. Our hypothesis is that utilization of transcriptional regulatory elements permissive for expression in HSCs in conjunction with chromatin insulator sequences and scaffold/matrix attachment regions will lead to maintenance of high-level transgene expression in HSCs and their differentiated progeny. To this end, the performance of next-generation lentiviral vectors utilizing the MSCV long terminal repeat as an internal promoter and harboring the chicken b-globin 5' constitutive hypersensitive site (5' HS4) insulator and/or the human interferon-b scaffold attachment region (IFN-SAR) will be assessed in human hematopoietic repopulating cells using a surrogate non-obese diabetic/severe combined immunodeficient (NOD/SCID) xenograft assay and in a murine hemophilia A model.

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- **Project Title: LYMPH NODE TARGETING AND IMMUNOGENICITY**

  Principal Investigator & Institution: Johnston, Robert E.; University of North Carolina Chapel Hill Office of Sponsored Research Chapel Hill, NC 27599

  Timing: Fiscal Year 2001

  Summary: Vaccine vectors based on Venezuelan equine encephalitis virus (VEE) offer a number of advantages for immunization against **human immunodeficiency virus** (HIV). These include a high margin of safety, high antigen expression levels, up to l mg per 107 cells in culture or 20% of total cell protein, and induction of balanced humoral and cellular immune responses that show protection against disease in a simian immunodeficiency virus (SIV)/macaque challenge model. In addition, the VEE replicon particles (VRP) naturally target to and express in lymphoid tissues, an optimal site for induction of an immune response, and they demonstrate sustained efficacy of priming and booster immunization over multiple simultaneous or sequential inoculations of the same individual. These latter two characteristics clearly distinguish VRP from other viral vector systems. In this project, we propose to determine l) the genetic and immunological basis for the lymph node targeting phenotype of VRP and 2) the ability of VRP to immunize in the face of pre-existing anti-VEE immunity. These properties will be correlated with the level and character of the immune response induced to vectored HIV genes. Not only will the results of these experiments contribute significantly to the design of a VRP-based HIV vaccine candidate, but they also will provide fundamental information regarding 1) the role of lymph node and/or dendritic cell (DC) targeting in induction of an immune response, 2) the initial stages of viral infection in an immune

host, and 3) the interactive effects of expression level, duration of expression, and cell targeting on immunogenicity of HIV proteins expressed from viral vectors.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: MACROPHAGE ANTIGEN PROCESSING OF HIV SUBTYPES**

  Principal Investigator & Institution: Knox, Kenneth S.; Medicine; Indiana Univ-Purdue Univ at Indianapolis 620 Union Drive, Room 618 Indianapolis, IN 462025167

  Timing: Fiscal Year 2001; Project Start 01-APR-2001; Project End 31-MAR-2006

  Summary: (Adapted from applicant?s abstract) CD8+, MHC-1 restricted cytotoxic T lymphocytes (CTL) are responsible for controlling viremia associated with **human immunodeficiency virus** (HIV) infection. CTL activity is directed against epitopes from lymphocytotropic (T-tropic) and monocytotropic (M-tropic) strains. T-tropic HIV strains do not cause a productive infection in human monocytes and macrophages. However, we have shown that macrophages exposed to T-tropic or M-tropic HIV are equally able to induce a primary CTL response, indicating that processing of viral antigens is occurring after exposure to both strains. Thus we hypothesize that macrophages can support both entry and processing of T-tropic HIV and subsequently elicit MHC class I-restricted cytotoxic T lymphocyte responses to specific viral epitopes in the absence of a productive infection. We will test this hypothesis by examining each of the steps involved in antigen processing using an in vitro fixed cell model of HIV infection. The following specific aims will be tested: 1) To determine the significance of various entry mechanisms by T-tropic and M-tropic HIV into alveolar macrophages and monocyte derived macrophages on subsequent CTL responses, 2) To determine whether MHC class I-restricted HIV epitopes are generated in the cytoplasmic compartment by proteasomes or in endosomes, 3) To determine if HIV peptide-MHC class I coupling requires synthesis of new MHC class I molecules or can occur with preexisting molecules via a regurgitant type pathway, 4) To determine specific epitopes recognized by CTL primed in vitro, and 5) To determine if specific HIV epitopes require transporter associated with antigen processing (TAP)-dependent MHC class I processing. Understanding these pathways may provide insight to novel therapies aimed at enhancing HIV antigen presentation and the subsequent cellular immune response in HIV. The candidate is currently a pulmonary fellow in the Department of Medicine at Indiana University. At the proposed start-up time the candidate will be a Lecturer on the faculty in the Pulmonary and Critical Care Division with 75 percent protected time allocated for research. To date the candidate has trained in the laboratory of Dr. Homer Twigg, acquiring basic immunologic knowledge and laboratory skills. This proposal is a logical mechanistic extension of this work designed to allow the candidate to develop a basic understanding of antigen processing pathways. Importantly, in this proposal the candidate will develop new research skills by working in the laboratories of Dr. Homer Twigg (CTL cloning, CTL generation and assays), Dr. Janice Blum (intracellular antigen processing pathways, transfection techniques using TAP-deficient cells), Dr. Randy Brukiewicz (working with vaccinia virus and constructs to study specific CTL epitopes), and Dr. Douglas Perry (liposome biology, phagocytic pathways). Each of these investigators have the expertise and resources (money and laboratory space) necessary to ensure successful completion of the training program. By acquiring the knowledge and skills outlined in this proposal, the candidate hopes to fulfill his career goal of becoming a full-time, funded researcher in an academic pulmonary division.

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- **Project Title: MALE GENITAL TRACT RESERVOIRS AND VIRAL SHEDDING**

  Principal Investigator & Institution: Krieger, John N.; Professor of Urology; Urology; University of Washington Seattle, WA 98195

  Timing: Fiscal Year 2001; Project Start 15-SEP-2000; Project End 30-JUN-2005

  Summary: (Adapted from the Applicant's Abstract): Little is known about factors that determine seminal shedding of **human immunodeficiency virus** type 1 (HIV), human cytomegalovirus (CMV), and human herpes virus type 8 (HHV-8). Our long-term goals are to delineate the anatomic sites and factors determining viral shedding, to develop strategies to lower the viral burden in semen, and, consequently, to reduce sexual transmission. Specific Aim 1: To determine the anatomic sites of viral infection and replication in the male genital tract. We will test the hypotheses that the prostate gland and urethra are critical viral reservoirs and that these sites remain reservoirs in HIV-infected men receiving highly active anti-retroviral therapy (HAART) by localizing and quantifying viral RNA and DNA in systematic prostate biopsies, urethral secretions, expressed prostatic secretions, and ejaculated semen. These data will increase our understanding of the biology of sexual transmission and the potential of therapy to reduce genital trac viral reservoirs in the male. Specific Aim 2. To examine mechanisms of viral-viral interaction that facilitate seminal virus shedding. We will test the hypothesis that expression of one genital virus can up-regulate expression and shedding of other genital tract viruses by investigating the effects of anti-CMV therapy on HIV, HHV-8, or CMV burden, including CMV-induced expression of chemokines and chemokine receptors in HIV-permissive cells that may activate latent infection or up-regulate low levels of HIV gene expression. These studies are important because coinfection with multiple genital viruses is common. Thus, controlling one genital tract virus may limit viral-viral interactions, reduce the viral burden in semen, and decrease the sexual transmission of other viruses.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: MECHANISM OF NEF ACTION IN HIV 1 INFECTION**

  Principal Investigator & Institution: Aiken, Christopher R.; Associate Professor; Microbiology and Immunology; Vanderbilt University 3319 West End Ave. Nashville, TN 372036917

  Timing: Fiscal Year 2001; Project Start 01-JUN-1997; Project End 31-DEC-2005

  Summary: The **Human Immunodeficiency Virus** Type 1 (HIV-1), the major causative agent of Acquired Immune Deficiency Syndrome (AIDS), encodes the accessory protein Nef. Nef plays a crucial role in primate lentivirus replication and pathogenesis. Nef also enhances HIV-1 infectivity in single-cycle infection assays and accelerates HIV-1 replication in vitro. The focus of this application is to elucidate the molecular mechanism by which Nef enhances HIV-1 infection. Based on our two key discoveries that Nef is associated with the HIV-1 core and that targeting HIV-1 infection to an endocytic entry pathway relieves the requirement for Nef, a mechanistic model is proposed in which Nef facilitates the intracellular transport of the viral genome. In this model, Nef tethers the incoming viral nucleoprotein complex to the endocytic machinery via simultaneous interactions with the viral core and with cellular adaptor proteins, resulting in routing of the incoming core to an intracellular compartment permissive for reverse transcription. Three specific predictions of this model will be tested. First, the hypothesis that Nef is active in the virion will be tested using two novel technologies for delivery of proteins into virions. The second hypothesis, that interaction of Nef with the core is required for infectivity enhancement, will be tested through

identification of the target of Nef binding and genetic analysis of the interaction. The third hypothesis, that interaction of Nef with cellular adaptor proteins is required for efficient HIV-1 infection, will be tested through mutational analysis of Nef binding to cellular adaptor proteins and assays of HIV-1 infection. Finally, the relationship between the effect of Nef in single cycle infection assays and in continuous replication assays will be determined by analyzing the kinetics of wild type and Nef-defective HIV-1 replication in T cell cultures inoculated with either HIV-1 particles or with known numbers of infected cells. These experiments will reveal novel functional targets of Nef in HIV-1 infection, will contribute to our mechanistic understanding of Nef function, and will define the relative requirements for Nef in cell-free virus infection vs. cell-to-cell transmission. These studies should therefore facilitate the development of a biochemical assay for rapid identification of specific inhibitors of Nef as potential antiviral drugs.

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- **Project Title: MECHANISMS OF T CELL APOPTOSIS DURING HIV1 INFECTION**

  Principal Investigator & Institution: Gandhi, Rajesh T.; Massachusetts General Hospital 55 Fruit St Boston, MA 02114

  Timing: Fiscal Year 2001; Project Start 01-SEP-1997; Project End 31-AUG-2003

  Summary: This application presents a research program to study the role and mechanisms of apoptosis of T lymphocytes in human immunodeficiency virus-I (HIV-1)infection. Programmed cell death T lymphocytes has been strongly implicated in the pathogenesis of T cell depletion in the acquired immunodeficiency syndrome (AIDS), but how HIV-I induces apoptosis and which cellular mechanisms are involved are still not known. This research program addresses these issues by using a novel retroviral system in which the gene for a cell surface reporter protein, placental alkaline phosphatase (PLAP), is inserted into a replication competent l molecular clone, which permits analysis of infected cells by indirect immunofluorescence and flow cytometry. In addition, a technique for rapidly producing high-titer retroviral stocks allows for infection of a high percentage of cells in culture with recombinant HIV-PLAP. This method also makes it possible to analyze expression of components of the cellular apoptotic machinery in the setting of acute Hw-l infection. Using these techniques, the following specific aims will be addressed: First, does HIV- l predominantly induce apoptosis of infected cells (direct cytopathicity), uninfected cells (indirect killing) or both? Second, which cellular pathways are important in HIV induced apoptosis of T lymphocytes and does viral infection differentially affect the apoptotic machinery in infected versus uninfected cells? Our growing knowledge of the molecular mechanisms of programmed cell death ofT lymph0cytes will be particularly relevant to this issue. Third, which HIV genes are involved in inducing apoptosis? And finally, are there differences between primary viral isolates from patients in different stages of HIV-l infection on induction of apoptosis? This study of apoptosis ofT lymphocytes during HIV-1 infection should shed light on the immunopathogenesis of AIDS as-well as the role of programmed cell death in regulation of the human immune response.

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- **Project Title: MECHANISTIC ANALYSIS OF HIV RT**

  Principal Investigator & Institution: Johnson, Kenneth; Rutgers the St Univ of Nj New Brunswick Asb Iii New Brunswick, NJ 08901

  Timing: Fiscal Year 2001

Summary: There is no text on file for this abstract.

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- **Project Title: MEMORY AND EFFECTOR CTL RESPONSES TO VIRUS INFECTIONS**

  Principal Investigator & Institution: Casazza, Joseph P.; Assistant Professor of Patholgoy; Internal Medicine; University of Texas Sw Med Ctr/Dallas Dallas, TX 753909105

  Timing: Fiscal Year 2001; Project Start 30-SEP-1999; Project End 31-AUG-2003

  Summary: CD4+ T cell responses are thought to critical for the long term maintenance of effective host defense against chronic viral infections. Although animal models have been instrumental in delineating the general mechanisms underlying immunologic memory, detailed understanding of the development; functional heterogeneity, and homeostasis of antigen (Ag)-specific CD4+ memory cells in the human has not been accomplished. In this proposal, we will characterize fresh (e.g. non-cloned), viral pathogen-specific -- CMV, varicella zoster virus (VZV), and HIV - human CD4+ T cells with respect to the clonal complexity of their TCR (including characterization of dominant clonotypes), and their cytokine synthesis capabilities and activation threshold heterogeneity at the single cell and clonotype level. We bring to this effort novel technologies -- including 1) multiparameter flow cytometric analysis of Ag-specific CD4+ memory populations by detection of intracellular cytokine(s), CD40L and CD69 after short term activation with Ag, 2) characterization of clonotypic complexity and dominant clonotypes by PCR analysis of T cell receptor CDR3 regions on FACS-sorted Ag-specific CD4+ T cells, 3) quantification of clonotype +, Ag-specific, CD4+ T cells by QC-PCR, and 4) simultaneous analysis of TCR-Vbeta CDR3 and cytokine gene expression by single cell PCR -- that will enable us to functionally define and precisely quantify individual clonotypes among pathogen-specific human T cells, and follow the fate of these clonotypes with time, with exposure to Ag, or under conditions of T cell regeneration. Using these approaches we will investigate 1) mechanisms responsible for clonotypic dominance among CMV-, VZV-, and HIV-specific CD4+ memory T cells, 2) the extent and pattern of intra- and inter-clonal functional heterogeneity (cytokine synthesis and activation threshold) among these cells, 3) the degree of clonotypic expansion during the naive to memory transition, 4) pathways of differentiation within the memory subset (including the question of whether there is a true memory to naive "reversion"), and 5) the effect of time, Ag (re-exposure or elimination), progressive HIV immunodeficiency, and T cell regenerative mechanisms (after autologous stem cell transplantation and viral suppression in HIV disease) on the frequency and function of these viral-specific clonotypes. We are particularly interested in understanding the biology of HIV-specific CD4+ memory T cells, including the mechanisms responsible for their decline after long term viral suppression with effective antiretroviral therapy.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: METHAMPHETAMINE AND HIV PROTEIN-INDUCED NEUROTOXICITY**

  Principal Investigator & Institution: Maragos, William F.; Neurology; University of Kentucky 109 Kinkead Hall Lexington, KY 40506

  Timing: Fiscal Year 2001; Project Start 15-FEB-2001; Project End 31-DEC-2005

  Summary: Several lines of evidence indicate that the basal ganglia are highly susceptible to infection with the **human immunodeficiency virus** (HIV). However, the pathogenesis

of basal ganglia dysfunction is not well understood. Patients with HIV infection often abuse drugs such as methamphetamine, a drug that is well known to also cause long-term structural and functional changes to the basal ganglia. There is now mounting evidence that "virotoxins" (viral products released from infected cells) and methamphetamine share a common mechanism, which leads to neuronal damage. Two such products are the HIV proteins gp120 and Tat. In this proposal, we will examine the degree of synergy between these virotoxins and methamphetamine by determining the severity of damage they cause to the dopaminergic system in vivo and to human cortical neurons in vitro. To identify common mechanisms that lead to neuronal dysfunction and ultimately, to cell death, we will also examine two pathophysiological processes that contribute independently to virotoxin and MA toxicity, namely reactive oxygen species and the cytokine TNF-alpha. In studying these two processes, we will 2) measure production of compounds of interest (e.g. reactive oxygen species and TNF-alpha) and determine the efficacy of a variety of inhibitors on neurotoxicity. To accomplish these goals, we will assess the effects of intrastriatal injections of virotoxins in animals treated with methamphetamine and in vitro in human cortical neurons where cell types can be manipulated.

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- **Project Title: MICROGLIA AND THE NEUROPATHOGENESIS OF HIV DISEASE**

  Principal Investigator & Institution: Greene, Warner C.; Director; J. David Gladstone Institutes 365 Vermont St San Francisco, CA 94103

  Timing: Fiscal Year 2003; Project Start 01-APR-2002; Project End 31-MAR-2007

  Summary: (provided by applicant): **Human immunodeficiency virus** type 1 (HIV-1) penetrates the brain early in the course of disease, and frequently causes dementia and other neurologic manifestations in adults and children. Prominent viral infection has been documented in microglia and macrophages within brain parenchyma, and less widespread infection of astrocytes, endothelial cells and even neurons has also been noted. Pathogenesis is likely to involve both direct cytopathic effects on target cells via infection and indirect pathways driven by secreted cellular factors that alter neuronal viability andor excitability. Existing animal models, including rhesus macaques and a xenotransplant system, have provided important insights into these processes. A new rodent model would likely be a valuable additional tool for testing the contributions of specific pathways to pathogenesis, particularly if it can be manipulated genetically to vary selected host parameters. We have conducted extensive analyses of cells derived from several rodents, and have obtained evidence that rat cells have no insurmountable, species-specific blocks to the HIV-1 replication cycle. These experiments, using both rat-derived cell lines and primary cell cultures, have revealed relatively high levels of early and late HIV-1 gene expression as well as the production of infectious virions. Based on these findings, we have invested extensively in the development of a transgenic rat system for HIV-1 pathogenesis studies. Human molecules that are known entry cofactors for HIV-including human CD4, CCR5 and CXCR4-were expressed in rats via transgenesis. Substantial preliminary evidence has been obtained indicating that these transgenes are expressed in monocyte/macrophages, CD4 T-cells, and microglia. We have also found that these receptor/coreceptors are sufficient to permit productive infection of primary monocyte/macrophages and microglia by HIV-1. The present proposal seeks to use these novel transgenic animal lines to: (A) measure the effects of infection by HIV-1 on several biologic parameters relating to brain structure and function in vivo (Aim 1); (B) test the hypothesis that HIV-1 gp120 itself is a pathogenic factor acting through CD4 and a coreceptor (Aim 2); and (C) examine the trafficking of

HIV-1-infected cells from the periphery into the CNS (Aim 3). This work should both define the utility of this new experimental system for studying neuropathogenesis and provide new information about the pathologic events that may contribute to impairment of neurologic function in HIV disease.

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- **Project Title: MINIPROTEIN MIMETICS**

  Principal Investigator & Institution: Chaiken, Irwin M.; Research Professor of Medicine; University of Pennsylvania 3451 Walnut Street Philadelphia, PA 19104

  Timing: Fiscal Year 2001

  Summary: The central objective of this Project is to use miniprotein mimetic together with the emerging structure of the gp120/CD4 complex to design antagonists of the interaction of human cells with HIV-1, the **human immunodeficiency virus** responsible for AIDS. T-cell docking and entry by HIV-1, a major route of cell infection in AIDS, is driven by specific recognition of the T-cell surface protein CD4 by the HIV envelope protein gp120. The crystallographic structure of CD4 is known, and that of its complex with gp120 is close at hand. Structural components in both protein partners have been identified which are proposed to play key roles in CD4-gp120 recognition. The advancing high resolution structural understanding of the protein participants in virus-cell recognition together with the advancing technology of mimetics design now make it possible to combine structure determination, modeling and miniprotein engineering to obtain an advanced mechanistic understanding of the structural basis of CD4-gp120 interaction and to design new antagonists for AIDS. The specific aims of this Project are: (1) obtain miniprotein constructions by transplanting CD4 and gp120 binding site components into conformationally constrained miniprotein presentation scaffolds by chemical and recombinant DNA methods and establish their CD4/gp120 antagonist activities; (2) construct phage displayed libraries of CD4- and gp120-mimetic miniproteins and use these to identify novel CD4 and gp120 binding antagonists as well as to examine the key structural elements needed for CD4/gp120 antagonist design; (3) determine the high resolution structures of key miniprotein constructs complexed with CD4 or gp120 and use the binding interface structures in these complexes to refine the topological map of key structural elements in CD4- gp120 recognition. Overall, this project will yield miniprotein mimetic constructions for both an immunorecognition receptor (CD4) and a retroviral envelope glycoprotein (gp120);and advanced mechanistic definition of key structural elements for CD4-gp120 interaction; and structural lead information for small molecule antagonist design. Long term, the mimetics strategies derived will be useful to determine mechanism of, and design antagonists for other protein-protein interactions important in AIDS, such as the gp41-gp120 and chemokine receptor interactions, that also are associated with human cell - HIV-1 docking and viral entry.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: MODELING RNA-BASED HIV GENE THERAPEUTICS IN SCID-HU MICE**

  Principal Investigator & Institution: Akkina, Ramesh K.; Professor; Colorado State University Fort Collins, CO 80523

  Timing: Fiscal Year 2002; Project Start 01-JAN-2002; Project End 31-DEC-2006

  Summary: (provided by applicant): Animal models are critical for the preclinical evaluation of gene therapeutic strategies. The SCID-hu mouse, harboring a normally

functioning human thymus, sustains thymopoiesis for as long as one year and is susceptible to HIV infection. We and others have developed this system further for exogenous stem cell transfer. Purified CD34+ hematopoletic progenitor cells when gene transduced with retroviral vectors and introduced into thymic grafts, develop into normal human T lymphocytes. We have also recently demonstrated that vector delivered anti-HIV gene therapeutic constructs such as ribozymes were retained and expressed in these cells as they mature. The combination of virus-induced cell depletion and gene transduced CD34+ cell reconstitution taking place in a relatively short time, provides us with a unique experimental system in which to address many critical issues relevant for the success of gene therapy approaches. Furthermore, at present, the SCID-hu system is the only in vivo system to accurately evaluate the thymopoietic potential and HIV resistance of vector transduced hematopoietic progenitor cells. Several new exciting developments occurred recently in the areas of stem cell biology, lentiviral gene transfer vectors, ribozyme targeting, and RNA-based therapeutics and, therefore, the stage is currently set to achieve success. In the present proposal, we would like to exploit these new technologies and build upon our recent progress. Experiments outlined here (Project 2) are interactive and complimentary to the objectives of accompanying interactive R01 proposal (Project 1) by J. Rossi entitled "Combinatorial use of anti-HIV RNA-based therapeutics." The specific objectives of our proposal are: l) Determine the effect of retrovirally transduced pol III promoter driven nucleolar, nuclear and cytoplasmtargeted anti-HIV nbozymes TAR and RBE decoys, either individually or in combination, on the lineage specific differentiation of CD34+ cells into macrophages in vitro and into thymocytes in vivo in the SCID-hu thy/liv grafts and investigate the mechanism of action of RNA-based therapeutics in differentiated cells. 2) Determine the in vivo protective effects of different anti-HIV-1 RNAs, individually and in combination, in SCID-hu mice thy/liv grafts after HIV-1 challenge. 3) Determine the ability of new generation SIV-based lentiviral vectors to transduce various hematopoietic precursor cells that include CD34+ cells and the newly described primitive hematopoietic cells, namely CD34+ and KDR+ precursor cells, as well as side population (SP) cells. 4) Determine the engraftment and thymopoietic potential of lentivirally transduced primitive hematopoietic precursor cells i.e., a) CD34+ and KDR+ cells, b) SP cells in the SCID-hu mouse thymic microenvironment.

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- **Project Title: MOLECULAR ADJUVANTS FOR MALT BASED IMMUNITY TO SIV/HIV**

  Principal Investigator & Institution: Mcghee, Jerry R.; Professor; Microbiology; University of Alabama at Birmingham Uab Station Birmingham, AL 35294

  Timing: Fiscal Year 2001; Project Start 15-MAR-1998; Project End 28-FEB-2003

  Summary: This proposal will explore cellular and molecular mechanisms to induce mucosal and systemic immune responses specific for SIV and HIV through the nasal-associated lymphoreticular tissue (NALT). They will employ non-toxic cholera-toxin mutants as adjuvants in combination with SIV gp130 or HIV gp160 delivered intranasally as a means to understand the induction pathways in both mice and humans. In a separate proposal, they aim to conduct similar studies SIV/macaque model. In Aim 1, the applicant will characterize murine NALT and associated mucosal tissues after nasal immunization with SIV gp130 (or HIV gp160) with mCT and develop an in vitro human NALT system to assess mCT-induced antigen uptake. In Aim 2, signal transduction pathways of NALT antigen-specific CD4+ T cells will be analyzed following nasal immunization. In Aim 3, they will develop and characterize chimeric

mCTs which can mimic induction of antigen-specific Th1 or Th2 type responses following nasal immunization. In Aim 4, they will assess the effects of mCTs on antigen-presenting cells from human tonsils and adenoids for potentiation of Th1-or Th2-type responses. In Aim 5, they will determine the safety and immunogenicity of a combined gp160 and mCT nasal vaccine in humans in a phase I vaccine trial.

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- **Project Title: MOLECULAR MECHANISM OF TAT INDUCED ANGIOGENESIS**

  Principal Investigator & Institution: Morris, Cindy A.; Microbiology and Immunology; Tulane University of Louisiana New Orleans, LA 70118

  Timing: Fiscal Year 2001; Project Start 15-SEP-1998; Project End 30-AUG-2003

  Summary: (Adapted from the applicant's description) **Human immunodeficiency virus** type-1 (HIV-1)Tat is a potent transcriptional transactivator of both viral and cellular gene expression that possesses angiogenic properties. Tat cooperates with basic fibroblast growth factor(bFGF) in increasing the development of angiogenic lesions of Kaposi's sarcoma (KS) in HIV-1 infected individuals. Preliminary data suggest that this effect of Tat is triggered in vivo by inflammatory cytokines (IC)present in KS, including interleukin-1 beta (IL-1 beta), tumor necrosis factor-alpha (TNF-alpha) and gamma-interferon (gamma-IFN). Although both bFGF and vascular endothelial growth factor (VEGF) are expressed by KS cells in vivo and in vitro and IC upregulate the expression of both of these angiogenic factors, Tat exerts its angiogenic effects only with bFGF. The angiogenic process is complex, involving vascular endothelial cell growth, adhesion, migration, invasion and differentiation. To dissect the mechanism(s) for Tat-mediated angiogenic effects during each of these steps, in vitro and in vivo assays in which Tat, Tat mutants and Tat peptides are active have been developed. The central hypothesis of this proposal is that specific functional domains of Tat modulate proliferative, migratory and/or morphogenic effects on primary vascular endothelial cells during angiogenesis through a bFGF-mediated pathway. Toward this end, preliminary studies suggest that the ability of Tat to promote angiogenesis in synergy with bFGF is mediated, in part, by the selective interaction of the RGD domain of Tat with specific integrins (alpha5 beta1 and alphav Beta3) that are induced by bFGF. Through this interaction, the RGD domain of Tat promotes the locomotion and adhesion of KS and cytokine-activated primary vascular endothelial cells. In addition, the basic region of Tat retrieves extracellular bound bFGF into a soluble form that mediates cellular growth induced by Tat. Thus, Tat, a key regulatory protein of HIV-1 that can be released extracellularly from HIV-1-infected cells, upregulates angiogenesis, in part, by mimicking the functions of extracellular matrix proteins. The angiogenic effects of intracellular Tat are not known and determining this is a major focus of this proposal. The aims of the studies proposed herein are to determine whether (1) the transcriptional activating function of Tat, along with the RGD and basic region domains of Tat, plays a role during angiogenesis, (2) an endothelial cell-derived cyclin-dependent kinase, TAK/pTEF-b, activity that is essential for Tat transactivation, is induced through activation of primary human vascular endothelial cells by inflammatory cytokines or angiogenic factors that mediate Tat-enhanced angiogenesis and (3) Tat transactivates Bcl-2 gene expression in vascular endothelial cells stimulated to undergo angiogenesis, an effect that may involve the cellular Tat cofactor, TAK/pTEF-b.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: MOLECULAR RECOGNITION OF HIV1 PRIMER TRNA LYS**

  Principal Investigator & Institution: Musier-Forsyth, Karin M.; Associate Professor; Chemistry; University of Minnesota Twin Cities 200 Oak Street Se Minneapolis, MN 554552070

  Timing: Fiscal Year 2001; Project Start 01-JAN-1999; Project End 30-JUN-2002

  Summary: Human immunodeficiency virus type 1 (HIV-1) is a retrovirus that is the causative agent of AIDS. Human tRNALys,3, is selected as the natural primer for HIV-1 reverse transcriptase (RT). Prior to reverse transcription, the 18 nucleotides at the 3' end of this tRNA are annealed to a complementary sequence on the viral genome called the primer binding site (PBS). Although specific molecular interactions occur between the tRNALys,3 primer and various HIV components, the details of these interactions are not understood at the molecular level. Moreover, the complexes formed by human tRNALys,3, RT, and other HIV components such as the HIV-1 nucleocapsid protein (NC) and the RNA genome are attractive targets for new therapeutic agents. Therefore, we propose: 1. To elucidate the molecular interactions responsible for initiation of tRNA-primed DNA synthesis from complementary and non-complementary PBS sequences, (a) Specifically designed chimeric tRNALys,3 variants containing tRNAPro-specific domains, as well as HIV-RNA templates containing altered PBSs will be prepared and tested in in vitro primer/template annealing and reverse transcription assays. (b) Primer tRNAs containing randomized anticodon- and D-stem-loop sequences will be generated and employed in in vitro selection (SELEX) experiments. This study will delineate specific primer tRNA nucleotide bases that are critical for the initiation process. (c) Deoxy-phosphorothioate modification interference experiments will be carried out to identify backbone 2'-hydroxyl groups and phosphate oxygens that are crucial to tRNA primer annealing and extension. For (a)-(c) the results of assays using complementary versus non-complementary PBSs and heat-annealed versus NC-annealed primer/template complexes will be compared. 2. To probe the mechanism of primer tRNALys,3 unwinding and RNA-RNA annealing by HIV-1 NC, (a) Nuclease digestion experiments will be used to probe NC-induced conformational changes in tRNALys,3. (b) Fluorescence resonance energy transfer (FRET) measurements using steady-state and time-resolved techniques will be carried out to investigate NC unwinding of tRNALys,3 in the absence and presence of template. The formation of NC-annealed versus heat-annealed primer/template binary complexes will also be compared. (c) Stopped-flow fluorescence techniques will be used to investigate the kinetic mechanism of NC unwinding and annealing of tRNALys,3.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: MOLECULAR THERAPEUTICS FOR HIV1 INDUCED CNS DYSFUNCTION**

  Principal Investigator & Institution: Pomerantz, Roger J.; Chief, Infectious Diseases Division; Medicine; Thomas Jefferson University Office of Research Administration Philadelphia, PA 191075587

  Timing: Fiscal Year 2001; Project Start 15-MAY-1998; Project End 28-FEB-2003

  Summary: (Applicant's Abstract): **Human immunodeficiency virus** type 1 (HIV-1) infection can lead to severe central nervous system (CNS) dysfunctions. A syndrome consisting of cognitive and motor function abnormalities entitled the acquired immunodeficiency syndrome (AIDS) dementia complex (ADC) may occur in a significant portion of individuals infected with HIV-1. The pathogenesis of ADC remains enigmatic and molecular mechanisms leading to neuronal and glial cell damage

and death may involve toxic effects from viral proteins and proinflammatory cytokines. Recently, these laboratories have developed an in vitro blood-brain barrier (BBB) system with which to model HIV-1 CNS therapeutics. In the first specific aim of this proposal, they will use this newly developed in vitro BBB system, which contains human CNS microvascular endothelial cells (MVEC), human fetal astrocytes, neuronal elements, and microglia/macrophages, to study molecular therapeutics to inhibit HIV-1 infection in the CNS. Both RNA- and protein-based approaches will be utilized to inhibit HIV-1 expression in isolated CNS-based cell-types and in the in vitro BBB system. In addition, molecular therapeutics will also be modeled in macaque CNS cell-types, utilizing molecular moieties which inhibit simian immunodeficiency virus (SIV). As such, it is hoped that these initial studies will be useful in the design of animal models to explore molecular therapeutics for lentiviral infection of the CNS in vivo. In the second specific aim, pharmacological therapeutics will be utilized in these in vitro model systems to inhibit HIV-1 infection in CNS-based cells. There has been significant progress in treating HIV-1 infection, utilizing combination therapeutics which inhibit the reverse transcriptase (RT) and the protease of HIV-1. Nevertheless, the CNS may be a critical "sanctuary site" in the treatment of individuals with these combination modalities. As such, experiments will be performed to analyze a variety of combination therapeutics for their viral inhibitory properties and potential for crossing the BBB during therapy. Relevant protease and RT inhibitors will be utilized in these studies. As such, these specific aims hope to yield critical data in the design of therapeutics to alter HIV-1 infection in CNS-based cells, and potentially for ADC in HIV-1-infected-individuals.

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- **Project Title: MULTICENTER AIDS COHORT STUDY**

  Principal Investigator & Institution: Phair, John P.; Chief; Howard Brown Health Center 4025 N Sheridan Rd Chicago, IL 60613

  Timing: Fiscal Year 2001; Project Start 01-APR-1993; Project End 31-MAR-2004

  Summary: The Multicenter AIDS Cohort Study (MACS) is a prospective epidemiologic investigation of the natural history of infection due to the **human immunodeficiency virus,** type-1 (HIV-1) in homosexual/bisexual men. The MACS was initially funded in 1983 and the original cohort has entered the tenth year of follow-up. African-Americans were recruited into the study during the period 1987 to 1991 to increase the participation of this population . Specific aims of the investigation include; continued study, at semiannual visits, of all infected and selected seronegative participants, definition of varying patterns of clinical, including neurologic outcomes, and immunologic progression of HIV-1 infection, investigation of virologic and immunologic determinants of rapid versus "non-progression" in collaboration with the separately funded MACS Pathogenesis Research Laboratory and maintenance of epidemiologic and statistical expertise necessary for data management and analysis in collaboration with the Center for Analysis and Management of Data from the MACS (CAMACS) located at the Johns Hopkins School of Hygiene and Public Health. In addition, the incidence and prevalence of HIV-1 malignancies in the Chicago Cohort will be determined. If funding from the National Cancer Institute is continued, this will include an autopsy program. Finally health services utilization by the cohort will be evaluated if funding from the Agency for Health Care Policy and Research is continued. The primary methods of achieving the specific aims outlined above are to maintain participation of the cohort, assess the clinical status of participants by periodic interviews, physical examinations and neuropsychologic evaluations. Participants who have advanced HIV-1 infection, symptomatic or immunologic suppression, will be

followed at three month intervals. Immunologic status will be assessed by T-cell phenotyping at six (or three) month intervals. Appropriate specimens are obtained at each visit for storage in the local and national repositories to enable study of the pathogenesis of HIV-1 infection.

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- **Project Title: MURINE MODEL SYSTEM FOR HIV PATHOGENESIS**

  Principal Investigator & Institution: Littman, Dan R.; Professor; Skirball Institute; New York University School of Medicine 550 1St Ave New York, NY 10016

  Timing: Fiscal Year 2001; Project Start 01-DEC-1992; Project End 30-NOV-2003

  Summary: Our understanding of the mechanism of pathogenesis induced by HIV remains limited by the difficulty of conducting mechanistic studies in humans. Availability of a small animal model system that faithfully reproduces the viral pathogenic effects and the host anti-viral immune response observed in humans would significantly advance our understanding of HIV pathogenesis and would facilitate development of new approaches to block viral replication and to elicit neutralizing immune responses. Until recently, infection of murine cells with HIV has not been achievable because of a species-specific block at the level of viral entry. This restriction has been overcome with the discovery of chemokine receptor family members that function with CD4 as receptors for HIV and SIV. We have prepared mice that express human CD4 and human CCR5 or CXCR4 in T cells and macrophages, and have shown that their T cells can be infected with viruses pseudotyped with HIV and SIV envelope glycoproteins. However, other species-specific restrictions at several stages of the retroviral replication cycle currently limit the utility of this murine model. One of these restrictions, at the level of Tat transcriptional transactivation, can now at least be partially overcome, by expressing the human cyclin T gene in murine cells. We propose to introduce the human cyclin T gene into the germ line of mice that already express the human receptors for HIV and determine if this further facilitates viral replication in mice (Specific Aim 1). We will also develop approaches for infecting the genetically modified mice and for propagating HIV and/or SIV in vivo (Specific Aim 2). These approaches will emphasize the likely critical role of dendritic cells in potentiation of T cell infection both in vitro and in vivo. Expression cloning approaches, some of which we have already developed, will be used to identify new human genes that are involved in the HIV replication cycle and whose introduction into mice may further improve the model (Specific Aim 3). These aims constitute only the first steps towards building a useful mouse model, and are unlikely to provide a pathogenesis model in the short term. However, in vitro studies have suggested that the interaction of HIV envelope glycoprotein with the receptor complex consisting of CD4 and chemokine receptor results in signal transduction and impaired T cell function or even cell death. We will, therefore, determine if soluble gp120 or cell surface-bound gp120/gp41 influence T cell development and function in mice that express the human viral receptor complex (Specific Aim 4). This analysis may provide important insight into the mechanism of immunodeficiency, and will thus guide future studies using this animal model system.

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- **Project Title: MYCOBACTERIAL DISEASES IN AIDS**

  Principal Investigator & Institution: Ellner, Jerrold J.; Professor and Executive Vice President; Medicine; Univ of Med/Dent Nj Newark Newark, NJ 07103

  Timing: Fiscal Year 2001; Project Start 30-SEP-1987; Project End 31-MAY-2004

Summary: Mycobacterium avium is the most frequent cause of disseminated bacterial infection in patients infected with **human immunodeficiency virus** (HIV) and is associated with morbidity and shortened survival. It is not clear why M. avium infection is more common in HIV-infected persons than in other groups of immunocompromised individuals and reaches such high levels in tissues (10 9- 10/g). The regulation of the growth of M. avium within mononuclear phagoytes and the infected host is the subject of AI25799. Colonial morphotype is a reliable determinant of the potential for intracellular replication. Smooth, flat-transparent (SmT) isolates are phagocytosed less well, but undergo more intracellular replication than smooth domed-opaque (SmD) colonies, and differ in their capacity to induce expression of interleukin-1, and tumor necrosis factor, but not IL-6. Cytokines have bidirectional effects on the intracellular growth of M. avium; and IL-1 alpha and IL-6 also promote extracellular growth. Purified gp120 protein of HIV also appears to modulate phagocytosis and intracellular growth of M. avium, and multinucleated giant cell formation by monocytes. These observations suggest that differential induction of cytokines by M. avium colonial morphotypes, possibly as modulated by HIV- products, determines the growth characteristics of M. avium in the mononuclear phagocyte, and in the tissues of patients infected with HIV. Testing of this hypothesis and initial exploration of its potential relevance in the HIV-infected host will require in vivo and in vitro studies in healthy and HIV-infected persons. Accordingly, the Specific Aims to test this hypothesis are: (1) To explore whether the growth- enhancing properties of IL-1 and IL-6 for M. avium are associated with binding to receptors on the organisms, and account for intracellular growth characteristics; and whether these cytokines promote M. avium growth in the monocytes and tissues of HIV-infected persons. (2) To examine the potential role of glycopeptidolipids and lipoarabinomannans of M. avium in the differential induction of cytokines by SmT and SmD strains; and the effects of these organisms and their constituents on the intracellular pathways of cytokine expression within the mononuclear phagocyte. (3) To determine the basis for the interference by HIV gp120 with the phagocytosis and intracellular growth inhibition of M. avium by human monocytes and with multinucleated giant cell formation, in terms of modulation of cell surface receptors, cytokine expression, and effector function. These studies should provide novel insights into the pathogenesis of and potential therapeutic approaches to M. avium in HIV-infected subjects, and the means by which viral products and induction of host cytokines contribute to successful parasitism.

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- **Project Title: MYCOBACTERIUM TUBERCULOSIS & ACTIVATION OF HIV1 IN LUNG**

  Principal Investigator & Institution: Ghassemi, Mahmood; Medicine; University of Illinois at Chicago 1737 West Polk Street Chicago, IL 60612

  Timing: Fiscal Year 2001; Project Start 01-JUL-1998; Project End 30-JUN-2003

  Summary: (Adapted from the Applicant's Abstract): Several pieces of evidence suggest a strong association between **human immunodeficiency virus** (HIV) infection and M. tuberculosis (Mtb). In particular, data from the investigator and that of others suggest that co-infection of cells with mycobacteria and HIV results in increased HIV replication. The purpose of this proposal is to investigate the impact of Mtb on HIV activation in alveolar macrophages (AM), lymphocytes, and human pulmonary arteriolar endothelial cell (HPAE), and to elucidate the underlying mechanisms. The following specific aim are designed to investigate the hypothesis that Mtb infection enhances HIV replication in lung. Aim 1: To explore the effect of Mtb on HIV replication in AM and HPAE,

including cells from normal donors infected with either/both pathogens in vitro as well as cells from HIV and Mtb infected donors. AIM 2: To study the effect of Mtb on lymphocyte activation and HIV replication. AIM 3: To measure the induction of cytokines and their role in Mtb-mediated HIV enhancement. AIM 4: To determine whether HIV transcription is modulated by Mtb and whether Mtb induces cellular transcription factors such as Nfkb which may affect HIV replication. AIM 5: To examine the role of cell-cell contact between HIV and Mtb infected AM, HPAE and lymphocytes; in particular they will examine the role of ICAM-1 in this process.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: NATURAL HISTORY OF HIV INFECTION IN INJECTION DRUG USERS**

  Principal Investigator & Institution: Vlahov, David H.; Director; Epidemiology; Johns Hopkins University 3400 N Charles St Baltimore, MD 21218

  Timing: Fiscal Year 2001; Project Start 01-APR-1987; Project End 28-FEB-2002

  Summary: (Applicant's Abstract) We propose to continue our prospective study of HIV infection among injection drug users (IDUs) to characterize the rate of progression to immuno-suppression, AIDS, and death. Our earlier studies have examined the role of gender, age, clinical symptoms, immune activation markers, coinfections (e.g. HTLV-11), and frequency of injection drug use on the rate of developing endpoints (e.g., rapid CD4 loss, AIDS, death). We have also studied patterns of health care utilization. Here, we continue these objectives and add new foci for study including effects of type of drug used (opiates/cocaine), genetic markers (HLA haplotypes), wasting, other coinfections, and use of antiretrovirals on HIV progression. Continued follow-up is necessary to more fully describe the course of HIV infection, to permit identification of long term survivors with HIV for pathogenesis studies, to monitor temporal trends in the HIV epidemic (including the measuring of the effect of antiretroviral medications), and to increase the number of endpoints to permit focussed hypothesis testing (e.g., to identify risk factors for individual opportunistic AIDS diseases). The study population consists of 667 HIV seropositive and 209 seronegatives, of whom 330 and 140 remain alive and actively followed as of 6/95; 249 HIV seroconverters have been added between 1988-1995 (from DA05911) of whom 192 remain alive and active as of 6/95. The attendance rate at each 6 month visit exceed 90%. All participants undergo semiannual visits which include detailed behavioral interviews, medical histories, physical and gynecological examinations, and venipuncture (for laboratory assays, including T-cell subset studies, and storage of specimens in biological repository). Prospective data are summarized using survival and longitudinal data analysis; logistic regression is used to analyze nested case-control studies. We have formalized collaborations with a cohort of homosexual men in Baltimore (that are being followed with nearly identical protocols), as well as IDU cohorts in New York, Amsterdam and Italy to conduct parallel and, if appropriate, pooled analyses.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: NEF FUNCTION**

  Principal Investigator & Institution: Garcia-Martinez, J Victor.; Professor; Internal Medicine; University of Texas Sw Med Ctr/Dallas Dallas, TX 753909105

  Timing: Fiscal Year 2001; Project Start 01-MAR-1999; Project End 28-FEB-2003

  Summary: Individuals infected with the **human immunodeficiency virus** (HIV) develop a degenerative disease of the immune and central nervous systems that is

accompanied by a broad spectrum of opportunistic infections. How HIV causes these degeneration is unknown. Studies with SIV indicate that nef plays an important role in vivo for the maintenance of high virus load and the development of AIDS. These observations make nef a good target for drug development against AIDS. Our previous and current efforts have been to study the molecular basis of Nef function. We have developed a system tO study the molecular basis of Nef-induced cell surface CD4 downregulation and determined that the cytoplasmic tail of CD4 is required for its downmodulation by Nef. We have also shown that pathogenic isolates of Nef from both HIV-1 and SIV suppress CD4 expression. To determine if this conserved function of Nef is important in HIV pathogenesis we will correlate Nef function with disease progression and virus replication in vivo. This will be accomplished by a functional analysis of nef genes isolated from patients at different stages of disease and by comparing the ability of viruses containing wild type or mutant nef alleles which do not downmodulate CD4 expression to replicate in vivo. We also propose to determine possible therapeutic targets to inhibit Nef function by a) determining the mechanism of Nef action and b) identifying posttranslational modifications essential for Nef function. Our long term goal is to use our understanding of Nef function to develop inhibitors which by interfering with Nef could block progression to AIDS in HIV infected individuals.

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- **Project Title: NEUROLOGIC AIDS RESEARCH CONSORTIUM**

  Principal Investigator & Institution: Clifford, David B.; Professor and Head; Neurology; Washington University Lindell and Skinker Blvd St. Louis, MO 63130

  Timing: Fiscal Year 2001; Project Start 01-DEC-1993; Project End 31-JUL-2003

  Summary: We will establish the "Neurologic AIDS Research Consortium" (NARC) which will be a major contributor to neurologic projects in the AIDS Clinical Trial Group (ACTG). NARC will be dedicated to clinical investigation of **human immunodeficiency virus** (HIV) associated neurologic disease. The consortium initially will consist of sixteen units, established at ACTG sites combining neurologic leadership in the area of clinical AIDS research, access to subjects with HIV-related neurologic disease, and leadership within the local AIDS Clinical Trial Unit supportive of neurologic projects. This grant will supplement the resources of the ACTG system to achieve maximal productivity in the area of neurologic investigation. We will provide a network of support by supplying a base grant to establish coordination of the local neurologic effort and effective communication s and travel funds to effect a collaborative relationship in this group. The base grant will be supplemented on a per capita funding basis for successful study of subjects in clinical trials. The per capita funding will supplemental local ACTU support for extraordinary costs of neurologic studies and for professional time required to manage the study. We will coordinate our efforts through the leadership of NARC which will be located at Washington University in St. Louis. Statistical and data analysis for our studies will be carried out through the ACTG system, with supplemental support to the Harvard School of Public Health through this grant. The initial projects to be undertaken in the grant include: (1) Completion of the Phase I/II study of nimodipine as an adjunction to antiretroviral therapy in the treatment of HIV motor/cognitive disorder, (2) A study of the natural history of neurologic disease in advanced HIV patients identified by CD4 counts ,<50, with particular emphasis on neuropsychometric performance as a measure of disease progression, (3) A double-blind controlled study of amitriptyline and mexiletine in the treatment of HIV associated painful peripheral neuropathy, (4) A controlled clinical trial

testing the efficacy of cytosine arabinoside for treatment of progressive multifocal leukoencephalopathy, and (5) a trial of combination chemotherapy and radiation therapy for treatment of HIV associated primary central nervous system lymphoma. It is anticipated that these studies will be followed by subsequent studies to further develop therapy related to these problems. The group also anticipates participation cytomegalovirus induced neurologic disease. Plans for future study and use of resources will be guided by the ACTG Neurology Scientific Committee with review by appropriate ACTG Scientific Committees and by the ACTG Executive Committee.

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- **Project Title: NEUROPHARMACOLOGY OF HIV DEMENTIA**

  Principal Investigator & Institution: Limoges, Jenae; Internal Medicine; University of Nebraska Medical Center Omaha, NE 681987835

  Timing: Fiscal Year 2001; Project Start 01-MAY-1998; Project End 28-FEB-2003

  Summary: (Applicant's Abstract): Despite recent advances in antiretroviral therapies, the effect of **human immunodeficiency virus** type one (HIV-1) on the central nervous system remains a significant cause of morbidity in affected humans. The pathogenesis of the cognitive dysfunction associated with brain disease likely revolves around productive HIV infection of brain macrophages/microglia leading to the secretion of an inflammatory cascade for neurodegreneration. The hypothesis proposed in this application is that virus-infected immunologically competent brain macrophages and microglia play central but distinctive roles in HIV-1 neuropathogenesis. This mentored clinical scientist application is designed for 5 years of support for career development from a physician to a fully competent independent scientist in academic medicine. The goal of the program is to learn the necessary technical and didactic skills to perform hypothesis-driven research. Knowledge in molecular genetics, biochemistry, immunology, neurobiology, and medical ethics through specific laboratory rotations and coursework will be initiated at both the University of Nebraska Medical Center and at Creighton University. Research activities will take place within an integrated program at the Center for Neurovirology and Neurodegenerative Disorders. Mentored research will evolve from closely supervised works into fully independent research activities. The analysis of the molecular mechanisms of HIV-1 encephalitis will involve developmental laboratory and animal model systems, drug testing and combined research activities in neuroimmunology, virology, molecular genetics and pathology. This, taken together with coursework, broad university, clinical and center support aims to permit a research experience of the highest order for grasping the principals necessary for sustained success in academic biomedical research.

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- **Project Title: NEUROTROPISM AND MICROGLIAL INVASION**

  Principal Investigator & Institution: Gonzalez-Scarano, Francisco A.; Professor and Chairman; University of Pennsylvania 3451 Walnut Street Philadelphia, PA 19104

  Timing: Fiscal Year 2001

  Summary: Microglia are critical to the primary complications of the **human immunodeficiency virus** (HIV-1) in the central nervous system (CNS), since they are the most commonly infected cell and their infection represents the majority of the viral load in the CNS. This proposal will center on the biology of HIV-1 in microglial in order to develop a better understanding of the role of the virus in the development of this complication, and to identify potential, CNS-specific, treatment strategies in

collaboration with the other components of this program. In the first specific aim we will continue our studies on microglial- tropism of HIV-1 isolates using primary isolates from adults and children, and an isolate adapted to microglia bu sequential passage. We will first use a PCR-based assay to analyze the sequential steps of HIV-1 infection in microglia. For those isolates (like the microglia-adapted HIV-1/BORI- 15) which demonstrate a rapid entry phenotype, we will molecularly clones the envelopes, and define the mechanism of enhanced cellular penetration using molecular and biochemical (binding) assays. Where tropism for microglial cells is related to post-entry steps, other portions of the provirus, or the entire proviral genome, will be cloned. We will then determine whether isolates that do not replace to high levels in microglia can nevertheless establish a chronic infection. These isolates will then be used in a SCID-hu model in another Project. In the second specific aim we will determine whether the envelope proteins, and specifically gp120 from isolates with HIV encephalopathy can mediate changes in intracellular free Ca2+ concentrations in monocyte-derived macrophages (MDM), microglia, and other neural cells. Those gp120s that induce intracellular signals will be tested for their ability to mediate apoptosis. In the third specific aim we will determine whether microglial infection by certain HIV isolates results in increased production of chemokines, which could be responsible for increased cellular trafficking into the CNS, and potential amplification of a chronic infection. The result from these experiments will strengthen knowledge about the interactions between HIV-1 and microglial cells.

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- **Project Title: NMR OF HIV REVERSE TRANSCRIPTASE PRIMERS**

  Principal Investigator & Institution: Davis, Darrell R.; Professor; Medicinal Chemistry; University of Utah 200 S University St Salt Lake City, UT 84112

  Timing: Fiscal Year 2001; Project Start 01-AUG-1996; Project End 31-MAR-2005

  Summary: (Provided by the applicant): RNA hairpin oligonucleotides will be synthesized which contain the three modified nucleosides found in the anticodon domain of human tRNA LYS3, the primer for HIV reverse transcriptase. The solution structures of these RNA hairpins will be determined using NMR spectroscopy. The high-resolution structures will be used to understand how the modified nucleosides rncm5s2U, ms2t6A, and pseudouridine provide structural stability to the anticodon domain of tRNA and why this is important for proper function of tRNALYS3 as the reverse transcriptase primer. Binding studies between the modified RNA hairpins and HIV reverse transcriptase will be done to elucidate how modification affects reverse transcriptase recognition. NMR spectroscopy will be used to localize the divalent metal ion binding sites in E.coli and human tRNALYS3. Paramagnetic manganese relaxation studies and NOE measurements of cobalt hexanimine complexed with the tRNA hairpins will be used as analogs of the magnesium ions that we have shown bind specifically to the modified RNAs. The solution structure of the RNA complex formed between tRNA and the A-rich loop of HIV genomic RNA will be determined using heteronuclear multidimensional NMR. The fully modified anticodon domain of human tRNA will be used to form the RNA-RNA complexes in order to understand how the natural modifications contribute to structural stabilization and to provide a structural target for therapeutic development. NMR spectroscopy will be used to study the solution structure of the entire tRNA isoacceptor from E.coli in its fully modified form. These structural studies will elucidate the nature of the folded core of tRNALYS and the structural basis for reverse transcriptase recognition elements in the D stem and loop of tRNALYS

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- **Project Title: NONHUMAN PRIMATE MODELS FOR HIV VACCINE EVALUATION**

  Principal Investigator & Institution: Fultz, Patricia N.; Professor of Microbiology; University of Alabama at Birmingham Uab Station Birmingham, AL 35294

  Timing: Fiscal Year 2001

  Summary: A major goal of biomedical research is development of a vaccine that will lower significantly the rate of new infections of human immunodeficiency viruses (HIV), not only in this country, but worldwide. While positive results have come from both non-human primate and human Phase I and II trials, there have been obvious failures in both cases, emphasizing the need for novel vaccine strategies. Based on the hypothesis that the most effective vaccine against HIV infection and disease will be one that elicits not only mucosal and systemic but also humoral and cell-mediated immune responses that are broadly cross-reactive, two animal models will be used to test novel vaccines and assess cross-reactive immunity against HIV-1 strains from the same or different clades. First, the SHIV-macaque model will be used to characterize systemic and mucosal immune responses elicited by chimeric SIV/HIV virus-like particles and poliovirus replicons or naked DNA vaccines expressing SIV and HIV antigens. Furthermore, attempts will be made to enhance these responses by co-administering genes encoding various cytokines with candidate vaccines. Immune responses to be evaluated include inductions of antibodies in blood and mucosal secretions, neutralizing antibody activity, proliferative responses to immunogens, and cytotoxic T lymphocyte activity. Efficacy will be assessed by challenging immunized macaques either intravenously or vaginally with pathogenic SHIV-89.6P; these animals will then be monitored for evidence of infection. Second, chimpanzees infected with HIV-1 strains from clades B, D, or E will be exposed to unrelated strains, and both qualitative and quantitative changes in ongoing humoral and cellular immune responses will be determined. Whether super-infection occurs will be evaluated by PCR amplification of proviral DNA, heteroduplex assays, and DNA sequence analysis. In addition, disease course in naive chimpanzees inoculated by intravenous, cervical or rectal routes with a pathogenetic HIV-1 will be characterized and compared to that in HIV-1 infected chimpanzees which might become super-infected after inoculation with this strain. These studies will provide information on the feasibility of using poliovirus replicons and DNA vaccines to elicit protective immune responses, whether specific cytokines can enhance or alter the types of immunity elicited, and whether exposure of chimpanzees to multiple HIV-1 strains succeeds in broadening cross-reactivity such that infection or disease is prevented.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: NOVEL CONTRACEPTIVES WITH ANTI-HIV ACTIVITY**

  Principal Investigator & Institution: D'cruz, Osmond J.; Parker Hughes Institute 2699 Patton Rd St. Paul, MN 55113

  Timing: Fiscal Year 2001; Project Start 15-DEC-1998; Project End 30-NOV-2001

  Summary: (Adapted from Applicant's Abstract) **Human immunodeficiency virus** (HIV), the causative agent of AIDS is the fastest growing cause of death in women of reproductive age. Heterosexual transmission accounts for >80% of all HIV infections world- wide, and constitutes a growing proportion of new HIV infections in the United States. The currently used topical vaginal microbicide, nonoxynol-9 (N-9)-a detergent-

based virucidal spermicide in addition to its high contraceptive failure rates also causes mucosal erosion and local inflammation which might increase the risk of HIV transmission. Therefore, new, effective, safe, and female-controlled vaginal microbicides are urgently needed to curb vaginal transmission of HIV infection. With an attempt to identify a microbicide contraceptive potentially capable of preventing sexual transmission of HIV as well as providing fertility control, a series of bromo-methoxy substituted novel derivatives of the anti-HIV drug, azidothymidine (AZT; zidovudine), were synthesized and examined for dual anti-HIV activity and spermicidal activity. Two lead compounds, WHI-05 and WHI-07, exhibited potent anti- HIV as well as spermicidal activity. Results of in vivo spermicidal efficacy and lack of local toxicity in the mouse model indicated that SHI-05 and WHI-07 would be attractive candidates as dual function vaginal microbicides. The applicants are now proposing preclinical studies to further evaluate the clinical potential of these dual- function AZT derivatives. The specific aims are: (i) to evaluate the in vivo contraceptive activity of WHI-05 and WHI-07 in rabbits; (ii) to evaluate the ability of WHI-05 and WHI-07 to prevent transmucosal and perinatal transmission of feline immunodeficiency virus in cats as the natural host model; (iii) to evaluate the ability of WHI-05 and WHI-07 to prevent transmucosal transmission of HIV-1 in chimpanzees as a surrogate host model; and (iv) to perform in vivo developmental, reproductive toxicology, and carcinogenesis studies of WHI-05 and WHI-07 in rodent models. The development of dual function vaginal microbicides to curb HIV transmission and prevent fertility will be a significant step forward to protect sexually active women from vaginal HIV transmission. The preclinical data on in vivo efficacies of WHI-05 and WHI-07 will be essential to further explore the utility of these novel drugs for clinical studies in human patients.

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- **Project Title: NOVEL VECTOR DESIGN TO EXPRESS MULTIPLE ANTIGENS**

  Principal Investigator & Institution: Ayyavoo, Velpandi; Assistant Professor; Infectious Diseases and Microbiology; University of Pittsburgh at Pittsburgh 350 Thackeray Hall Pittsburgh, PA 15260

  Timing: Fiscal Year 2001; Project Start 15-AUG-2000; Project End 31-JUL-2003

  Summary: (Adapted from Applicant's Abstract) Development of a safe, effective and affordable vaccine for HIV-1 is potentially the most efficient means of controlling HIV-1 infection worldwide. However, the genetic and biological variability of HIV-1 represents significant obstacles for vaccine development. Recent evidence indicates that CTLs may play a role in clearing viremia during primary infection and maintaining a disease-free state in HIV-1-infected patients. Thus, efforts to develop an HIV vaccine should focus on eliciting a broad cross-reactive CTL response as one major component. One promising approach to generating an effective CTL response in vivo is through the use of DNA vaccination. Current efforts using HIV-1 env and gag/pol DNA constructs as immunogens suggest that additional vaccine components are needed to confer broad protection. Therefore, a putative HIV-1 vaccine might benefit by inclusion of additional immunogenic targets. In addition to the structural and enzymatic proteins, HIV-1 also contains regulatory and accessory genes. These genes are highly conserved in vivo and may provide additional targets for CTL responses. We hypothesize that such targets could induce a broad virus-specific CTL response that could help to limit viral escape and confer protection against viral challenge. To use the accessory genes as part of a multicomponent vaccine, we have engineered a novel construct that expresses HIV-1 accessory genes vif, vpu, and nef under the control of a single promoter. To test the "proof of concept" we propose the following aims: (1) We will immunize human HLA-

A2 transgenic mouse and evaluate the cellular immune responses using HIV-1 infected human targets; (2) we will use a non-human primate model to test the ability of this vaccine construct to confer protection either alone or in combination with env and gag/pol vaccine constructs. We hypothesize that cell-mediated responses induced by the accessory genes may include broader recognition of divergent HIV-1 clades and should be useful in both prophylactic as well as therapeutic vaccination schemes against HIV-1.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: NOVEL VIRAL VECTORS FOR AIDS VACCINES**

  Principal Investigator & Institution: Johnson, Philip R.; President; Therion Biologics Corporation 76 Rogers St Cambridge, MA 02142

  Timing: Fiscal Year 2001

  Summary: The long term goal of the proposed research is to develop a safe, efficacious, and practical vaccine against the human immunodeficiency viruses (HIV-1 and HIV-2). Although attenuated viruses (e.g., SIVdeltanef) are the currently accepted "gold standard" in protection experiments in the SIV macaque model of AIDS, concerns about the ultimate safety of such vaccines will probably inhibit their widespread acceptance and use. These concerns have prompter us to consider a vaccine approach that exploits the unusual genetic and biologic features of adeno-associated virus (AAV), a non-pathogenic parvovirus. AAV infection in humans is common, entirely asymptomatic, and not associated with disease. In the research proposed herein, we will characterize a novel approach to genetic immunization that exploits recombinant AAV (rAAV) vectors to deliver SIV and HIV genes. In preliminary work, we have made important breakthroughs in packaging methodology that rAAV a pragmatic DNA delivery system. In addition, we have demonstrated that rAAV carrying the SIV gp160 gene can engender a strong antibody response in vaccinated mice. Thus, we are now poised to move forwards with large-scale immunogenicity and challenge trials in the SIV/SHIV model in macaques. In related work, we propose to use rAAV vectors to perform "reverse immunization". The rationale for this approach is simple. From the work of Burton and others, we known that antibodies which broadly neutralize primary HIV-1 isolate are rare in infected humans, and difficult to elicit by immunization. Thus, it might make sense to deliver pre-selected antibody gene(s) as a form of passive or "reverse" immunization. For this purpose, rAAV will be used to deliver genes representing broadly neutralizing antibodies against HIV-1 (like b12). The hope is that high levels of potent and robust antibodies will be delivered to the circulation and will prevent HIV infection in vaccines.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: NUCLEAR LOCALIZATION OF HIV-1 PREINTEGRATION COMPLEXES**

  Principal Investigator & Institution: Engelman, Alan N.; Associate Professor; Dana-Farber Cancer Institute 44 Binney St Boston, MA 02115

  Timing: Fiscal Year 2003; Project Start 15-JAN-2003; Project End 31-DEC-2006

  Summary: (provided by applicant): The long-term goal of this proposal is to identify the mechanism of **human immunodeficiency virus** type 1 (HIV-1) preintegration complex (PIC) nuclear localization in infected cells. Previous work identified amino acid residues in the viral matrix, integrase and Vpr proteins that functioned in nuclear localization specifically in nondividing cells, and more recent findings identified novel nuclear

localization signals in the central DNA flap made by reverse transcription and integrase residues Val-165 and Arg-166 that functioned in both dividing and nondividing cells. However the Preliminary Studies described in this proposal refute the roles of these novel sequences in nuclear translocation. Viruses carrying mutations in the central DNA flap replicated under a variety of conditions. Although defective flap function was identified in primary T-cells, there was no evidence for a nuclear import defect. Although integrase mutants V165A and R166A were acutely defective, these viruses were primarily integrase-defective, not import defective. It was determined that the integrase mutants fell into a category of previously-described pleiotropically defective mutants, leading to the hypothesis that defective nuclear import is a phenotype common to a variety of defective integrase mutants, and that these mutants are primarily defective for intracellular trafficking as compared to nuclear membrane translocation. Thus, pleiotropic import-defective integrase mutants will be used to determine intracellular steps essential for HIV-1 replication complexes to reach the chromosomal targets of integration. Residues involved in specific nuclear import of HIV-1 PICs will be identified following extensive mutagenesis screens. Host cell factors essential for intracellular trafficking to chromosomes and PIC translocation through intact membranes will be identified using protein-protein interaction assays. The results will determine host protein-HIV-1 interactions essential for PIC nuclear import and intracellular trafficking, which should define targets for the development of novel antiviral drugs against essential steps in the HIV-1 life cycle.

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- **Project Title: OPTIMIZED HIV -SPECIFIC CTL ANTIGENS FOR VACCINE DESIGN**

  Principal Investigator & Institution: Blondelle, Sylvie E.; Associate Member; Torrey Pines Institute/Molecular Studies Molecular Studies San Diego, CA 92121

  Timing: Fiscal Year 2001; Project Start 01-JUL-2001; Project End 30-JUN-2003

  Summary: (Adapted from Applicant's Abstract) Despite the great advances in antiviral therapy for **human immunodeficiency virus** (HIV) infection, a successful global intervention for prevention and treatment of HIV infection will require an effective vaccine. Since the induction of cytotoxic T-lymphocyte (CTL) responses is now believed to be an important component in an effective HIV-1 vaccine, our approach to develop an HIV vaccine is based on the stimulation of CD8+ CTL response more efficiently than the natural infection. This will be accomplished by using mixture-based synthetic combinatorial libraries (SCLs) to identify optimized peptide ligands that would be effective as immunogens in stimulating T-cell mediated immune responses against HIV infection. The mixture-based SCL approach allows the rapid identification of highly active compounds from large pools of individual compounds. In particular, when generated in a positional scanning (PS) format, the key amino acid(s) of the active peptide sequence(s) can be determined directly from the initial screening of the library. CTLs recognize processed viral peptides generally 8 to 11 amino acids in length, which are presented as a molecular complex with MHC class I and Beta2-microglobulin. PS-SCLs of nonapeptides and decapeptides (having a carboxylic acid or carboxamide C-terminus, and an acetylated or non-acetylated N-terminal amino group) will therefore be used for the proposed studies. Each mixture will be screened for their ability to stimulate cytokine production and/or cytolytic activity by CTL clones having specificity for immunodominant epitopes of the Gag, reverse transcriptase, and Nef proteins. Following the deconvolution processes to identify epitope mimics from the libraries, the CTL reactivities to the identified agonists will be determined, and their immunogenicity

will be assessed by performing in vitro stimulation experiments. Thus, the immunologic reactivity of cells pulsed with peptides to the immunizing native peptide and/or identified mimics will be measured by cytokine release or chromium release assays. Furthermore, the cross-recognition of the most potent identified peptides will be investigated using a cohort of HLA-A2-positive patients. Although not yet applied to HIV research, the success of the PS-SCL approach has been reported for the identification of peptides being several order of magnitude more effective than native peptide ligands to stimulate clonotypic populations of autoreactive CD4+, and tumor-specific or alloreactive CD8+ T-cells.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: ORAL EPITHELIAL CELLS: INNATE IMMUNE "GATEKEEPER" OF HIV**

  Principal Investigator & Institution: Herzberg, Mark C.; Professor; Oral Sciences; University of Minnesota Twin Cities 200 Oak Street Se Minneapolis, MN 554552070

  Timing: Fiscal Year 2003; Project Start 01-AUG-2003; Project End 31-MAY-2007

  Summary: (provided by applicant): The oral mucosa is directly challenged with **Human Immunodeficiency Virus** (HIV) by exposure of infants to HIV-carrying vaginal fluids at birth and to breast milk postnatally, and with passive oral sex among men. Exposures commonly include both X4 and R5 HIV, yet R5 viruses account for most primary systemic infections. When exposed to HIV and Porphyromas gingivalis cysteine proteases, we hypothesize that oral keratinocytes up-regulate expression of innate immune molecules, including alpha- and beta-defensins and other associated genes, to enhance HIV R5 transcytosis and intracellular resistance to HIV infection. To test this hypothesis, we will: 1. show that expression of CXCR4 and CCR5 by oral keratinocytes contribute to coreceptor-specific transcytosis of X4 and R5 HIV isolates; 2. determine if exposure to HIV regulates expression of the innate immune molecules calprotectin and alpha- and beta-defensins directly or in association with PAR signaling mediated by specific P. gingivalis protease mutants; 3. identify and profile oral keratinocyte innate immune-associated gene expression patterns, including known plausible HIV co-receptors and other innate immune molecules, which are regulated by HIV in the presence and absence of P. gingivalis proteases; and 4 show how innate immune molecules modulate transcytosis, translocation by paracellular routes, and anti-HIV resistance in oral keratinocytes in vitro. This project will show that oral keratinocytes express innate immune molecules to resist intracellular infection by X4 and R5 HIV. In the presence of cysteine proteases, innate immune molecules and genes required for transcytosis of R5 HIV expression will be up-regulated, increasing intracellular anit-HIV resistance and facilitating transfer R5 HIV-1 to initiate systemic infection. Innate immune factor-related genes may prove to be novel targets to prevent mucosal HIV.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: ORAL IMMUNE RESPONSES IN HUMAN AND SIMIAN HERPESVIRUS INFECTION**

  Principal Investigator & Institution: Scadden, David T.; Director, Experimental Hematology; Primate Research Center Farm Way and Airport Rd Pullman, WA 99163

  Timing: Fiscal Year 2001; Project Start 15-SEP-2001; Project End 30-JUN-2006

  Summary: Oral immune response to viral infections have not been well- characterized despite the potential importance as an early line of defense. In particular, herpesviruses implicated in HIV related opportunistic malignancies and HIV itself have potential oral

mucosal modes of transmission and yet oral immunity against them remains unexplored. This proposal seeks to characterize oral mucosal immune responses in humans to KSHV, EBV and HIV comparing them to the more well defined immune responses against these viruses in the blood. In addition, we will user a non-human primate model of EBV infection to perform detailed analysis to perform detailed analysis of oral mucosal immunity at distinct sites and time points in rhesus macaques exposed to the rhesus lymphocryptovirus (LCV), a herpesvirus that is closely related to EBV. These experiments will compare immunocompetent animals with those immunodeficient through SIV infection. The specific goals of this project are to: 1. establish the targets of the anti-KSHV specific CTL response in KSHV infected individuals, leading to the further characterization of minimal CTL epitopes derived from KSHV. Using similar methods we will identify CTL responses to rhesus LCV, the similar herpesvirus homolog of EBV in rhesus macaques. 2. Compare the magnitude and target specificity of CTL responses to rhesus LCV and SIV in the oral cavity and peripheral blood of SIV naive and SIV-infected rhesus macaques, 3. Define human CTL responses to HIV, EBV and KSHV infection in the oral cavity compared with blood. We will correlate the magnitude, specificity and kinetics of these responses with 1) disease progression and 2) anti-retroviral treatment. The results from these studies will guide the development of vaccination strategies to induce mucosal immunity in the oral cavity against important pathogens in HIV disease.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: PATHOGENESIS OF HEPATIC INJURY WITH HCV/HIV COINFECTION**

  Principal Investigator & Institution: Groopman, Jerome E.; Chief; Beth Israel Deaconess Medical Center St 1005 Boston, MA 02215

  Timing: Fiscal Year 2001; Project Start 30-SEP-2001; Project End 31-AUG-2006

  Summary: (provided by applicant) The primary objective of this proposal is to examine how the hepatitis C virus (HCV) and the **human immunodeficiency virus** (HIV) envelope proteins may act collaboratively to trigger signaling events that contribute to hepatocyte inflammation and apoptosis. Coinfection with HIV and HCV confers a poor prognosis, with progressive hepatic dysfunction that often results in cirrhosis and death. Both intravenous drug users and hemophiliacs have a high incidence of coinfection and face this grim outcome. Why do coinfected hosts have such high rates of progressive liver disease? The pathogenesis of HCV-related hepatitis is believed to be due, in part, to immune-mediated inflammation as well as the effects of direct infection of hepatocytes. Our preliminary data suggest a novel third potential mechanism for hepatic inflammation and apoptosis. We observed in both HepG2 cells and primary hepatocytes that treatment with the HCV envelope protein E2, in conjunction with HIV gpl20, induced the inflammatory chemokine interleukin-8 (IL-8) and triggered apoptosis. These functional outcomes occurred at nanomolar concentrations of E2 and gp 120 that correspond to the Kd's for the cognate ligands binding to their respective receptors, CDS1 and CXCR4, and were associated with activation of specific signaling molecules, including the Src family Lyn kinase, RAFTK/Pyk2, Erkl/2 and p38 MAP kinases, and Fas-ligand. These data indicate that proinflammatory and apoptotic events may occur due to dual exposure to HCV and HIV envelope proteins via an "innocent bystander" mechanism. This proposal seeks to characterize the molecular mechanisms of IL-8 induction and the program of apoptosis caused by HCV E2 and HIV gpl20. A focused experimental approach is presented to delineate signaling events that originate at specific cell surface receptors, are transduced through intermediate signaling molecules,

and converge on transcriptional activators of the MAP kinase family. Elucidating how these HCV and HIV envelope proteins may interact with hepatocytes could not only further our understanding of the pathogenesis of disease in coinfected hosts but also lead to targeted therapeutic strategies to improve the currently poor prognosis of such individuals.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: PATHOGENESIS OF HIV ASSOC THROMBOTIC MICROANGIOPATHY**

  Principal Investigator & Institution: Alpers, Charles E.; Professor; Pathology; University of Washington Seattle, WA 98195

  Timing: Fiscal Year 2001; Project Start 08-JUL-1999; Project End 30-JUN-2004

  Summary: Thrombotic microangiopathy is probably the most common form of microvascular injury in patients infected with **human immunodeficiency virus** (HIV). Virtually nothing is known about the pathogenesis of this disorder, although it is likely endothelial cell injury, perhaps occurring as a direct result of viral infection, is a critical early event. The goal of the proposed studies is to utilize a relevant animal model for this thrombotic microangiopathy to delineate the role of chemokine receptor expression and viral infection of parenchymal tissues in the pathogenesis of this disease process. Preliminary studies have shown that a proportion of macaques, when experimentally infected with HIV2, will develop thrombotic microangiopathy that is morphologically similar, if not identical, to human HIV-associated thrombotic microangiopathy. We will define the chronology of this disease process in infected macaques by means of clinical monitoring of serum and urine for evidence of organ dysfunction, immunological abnormalities including those involving lymphocyte subsets, and serologic evidence of infection. Morphologic correlation will be established by periodic biopsy and by necropsy studies of relevant affected organs including heart, lung, brain, and gut. Specialized studies of the tissues obtained will include immunohistochemical and in situ hybridization probes for the presence of virus and/or viral proteins, and synthesis of expression of multiple chemokine receptors within these organs and, most specifically, at sites of microvascular injury. The HIV-2 infected primate model provides a unique opportunity to study the pathogenesis of this microvascular disease process. In one specific aim, in vitro studies using cultured aortic and microvascular endothelial cells are proposed to further dissect the central mediators of endothelial injury that lead to a pro- thrombotic state. Finally, we propose to utilize the insights gained from these studies of non-human primate and in vitro systems to studies of relevant human biopsy tissue, in order to assess the relevance of chemokine receptor expression and viral infectivity on the development of microvascular injury in humans infected with HIV. These studies, in aggregate, will substantially enhance our understanding of the role of parenchymal expression of chemokine receptors in the pathogenesis of HIV-associated thrombotic microangiopathy, and offer possible strategies for therapeutic interventions that may ameliorate this disease process.

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- **Project Title: PATHOGENESIS OF HIV INDUCED IMMUNODEFICIENCY**

  Principal Investigator & Institution: Haase, Ashley T.; Regents' Professor and Head; Microbiology; University of Minnesota Twin Cities 200 Oak Street Se Minneapolis, MN 554552070

  Timing: Fiscal Year 2001; Project Start 01-MAR-1999; Project End 29-FEB-2004

Summary: This proposal is directed to the molecular pathogenesis of infection by the **human immunodeficiency virus** (HIV) and in particular to the basis for its cardinal manifestation, the acquired immuno deficiency syndrome (AIDS). We describe longitudinal analyses of lymph node and bone marrow by in situ hybridization and cognate single cells methods to define the number and type of cells which harbor HIV, and the extent of virus gene expression vis-a-vis viral and regulatory genes and stage of disease. We think this analysis will provide support for a war of attrition hypothesis which accounts for the profound loss of T helper lymphocytes despite the relatively low frequency of cells in which viral RNA can be demonstrated. We also will look for a mutant virulent virus in the later stages of disease. If one is found we will characterize the genome of the virus for comparisons with earlier isolates with the aim of identifying viral genes with a critical role in pathogenesis.

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- **Project Title: PHAGE DISPLAY TECHNOLOGY IN AIDS VACCINE DESIGN**

  Principal Investigator & Institution: Baba, Timothy W.; New England Medical Center Hospitals 750 Washington St Boston, MA 021111533

  Timing: Fiscal Year 2002; Project Start 01-JUN-2002; Project End 31-MAY-2004

  Summary: (Provided by Applicant) A vaccine is needed to limit the worldwide spread of HIV-1 infection. Traditional approaches have not yielded a safe, effective vaccine. Exposure of rhesus monkeys to chimeric simian/human immunodeficiency viruses (SHIVs) is used to develop prophylactic strategies and to dissect the immune correlates that protect against virus exposure. Combinations of human anti-HIV-1 monoclonal antibodies (mAbs) neutralize SHIVs in a synergistic fashion, thereby requiring less antibody to achieve better neutralization. Recently, the P.I. passively administered the triple combination of human mAbs F105, 2G12, and 2F5 to rhesus monkeys prior to either mucosal or intravenous (i.v.) SHIV-vpu+ challenge. Each mAb-treated neonatal and adult monkey was completely protected from infection, providing evidence that antibodies reactive with these three epitopes can prevent systemic immunodeficiency virus infection following either mucosal or i.v. exposure. However, sera from HIV-infected individuals contain low or non-detectable levels of antibodies to the F105, 2G12 and 2F5-defined epitopes, demonstrating that these important, protective, native antigenic determinants are not immunodominant. Further, although mAb 2F5 interacts with a continuous, linear HIV-1 gp41 peptide sequence, protective human mAbs F105 and 2G12 recognize complex, discontinuous, conformationally dependent antigens which are unsuitable for use as vaccines. To overcome these obstacles, the P.I. proposes to: 1. Construct and immunoselect random peptide phage-displayed libraries for peptide mimics or "mimotopes" that bind to protective human anti-HIV-1 mAbs. 2. Immunize mice with phage particles displaying "mimotope" peptides and evaluate antisera for the ability to neutralize SHIV-vpu+ and HIV-1 strains in tissue culture. Flow cytometry will be used to detect virus-infected cells. Future studies will allow the P.I. to determine whether these mimetic epitopes protect SCID-hu reconstituted mice and non-human primates from immunodeficiency virus challenge.

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- **Project Title: PHASE I/II STUDY OF A VRP VACCINE**

  Principal Investigator & Institution: Eron, Joseph J.; Associate Professor; University of North Carolina Chapel Hill Office of Sponsored Research Chapel Hill, NC 27599

  Timing: Fiscal Year 2002; Project Start 30-SEP-2002; Project End 29-SEP-2006

Summary: (provided by applicant): This project is a therapeutic immunization trial in HIV -1 infected patients, successfully treated with highly active antiretroviral therapy, using the Venezuelan equine encephalitis virus (VEE) vaccine vectors expressing modified HIV gag and pol genes and full length gp160 env construct developed in Project 4. This vector, in the form of VEE replicon particles (VRP), has been used safely and successfully for immunization and protection against a variety of infectious agents, including attenuation of simian immunodeficiency virus replication in rhesus macaques. The rationale for this proposed therapeutic immunization trial is that a small minority of HIV infected subjects are able to successfully control HIV replication in the absence of antiretroviral therapy, and that this control is based on preserved HIV -specific immune responses. In addition, Rosenberg et al., demonstrated that in persons treated during acute infection HIV-specific immune responses could be augmented by serial interruption of antiretroviral therapy resulting in at least transient control of HIV replication in a substantially higher proportion of patients than would be expected from natural history studies. This evidence strongly suggests that HIV specific immune responses can be responsible for significant control of HIV replication in the absence of therapy. We hypothesize that a strongly immunogenic HIV vaccine based on the VEE vectors will be safe in individuals successfully treated during acute and chronic infection and will stimulate and/or augment broad HIV specific humoral and cellular immune responses. If such responses suppressed HIV replication in the absence of HAART, HIV disease progression could be delayed or prevented with sparing of antiretroviral therapy with its attendant cost, toxicity and risk of resistance development. Alternatively, augmentation of HIV specific immunity might enhance the durability of antiviral regimens, conferring significant clinical benefit. The specific aims of the proposed clinical trial are to I) Evaluate the safety and immunogenicity of three doses of the VEE replicon particle (VRP) vaccine vector containing modified HIV gag and pol genes and full length gp160 env gene in individuals with chronic HIV -1 infection on successful highly active antiretroviral therapy. 2) Evaluate the safety and immunogenicity of the VRP HIV vaccine in individuals who received antiretroviral therapy during acute HIV-1 infection. 3) Evaluate control of HIV-1 replication following supervised treatment interruption (STI) in subjects who received antiretroviral therapy during acute HIV -1 infection.

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- **Project Title: PREDICTING LIVER DISEASE IN HIV-HCV-INFECTED WOMEN**

  Principal Investigator & Institution: Taylor, Jill; Wadsworth Center Empire State Plaza Albany, NY 12237

  Timing: Fiscal Year 2002; Project Start 27-SEP-2002; Project End 31-AUG-2004

  Summary: (provided by applicant): The purpose of this retrospective pilot study is to identify adaptive mutations that are selected in nonstructural coding regions of the hepatitis C virus (HCV) genome. The dominant virus population that was present in women co-infected with **Human Immunodeficiency virus** (HIV) and HCV, when clinical signs of progressive liver disease were apparent, will be analyzed. The long-term goal is to understand the viral genomic characteristics of HCV that result in enhanced viral replication, and lead, in conjunction with host immunity and environmental factors, to liver damage. The central hypothesis is that efficient replication of specific HCV variants with enhanced growth properties contributes to liver damage. It is postulated that the enhancement of viral replication is due to the selection of adaptive mutations in the nonstructural coding regions of the genome. This viral population can then become dominant over time in a hepatic environment in which control of viral

replication has been weakened by HIV-induced immunosuppression, alcohol and substance abuse. To test this hypothesis we will sequence the NS3/NS4A and NS5B nonstructural coding regions of the HCV genome in virus from HIV-HCV co-infected women with and without clinical signs of progressive liver disease. The rationale for the proposed research is that once specific mutations are identified as markers of advanced disease, a prognostic assay can be developed to identify patients at higher risk of progression. The study population is 100 HlV-HCV co-infected women, with the additional risk factors of alcohol and substance abuse, enrolled in the Women's Interagency HIV Study (WIHS) at SUNY Downstate in Brooklyn, NY. The experienced investigators collaborating on this proposal represent the cross-disciplinary fields of molecular virology, HIV-HCV primary care and clinical research, and biostatistics. The WIHS cohort at SUNY Downstate has been selected, not only because of the availability of robust demographic and clinical information and stored plasma samples collected since 1994, but also because of the potential for expansion to include the entire WIHS cohort of >2,000 women. HIV-HCV co-infected individuals have been specifically chosen because of the mounting evidence that HIV infection exacerbates HCV disease. Liver failure has become a leading cause of death in the HIV-HCV co-infected population, emphasizing the urgent public health need for earlier treatment intervention.

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- **Project Title: PRIMATE LENTIVIRUS BASED THERAPY VECTORS**

  Principal Investigator & Institution: Chen, Irvin Sy.; Professor; Microbiology and Immunology; University of California Los Angeles 10920 Wilshire Blvd., Suite 1200 Los Angeles, CA 90024

  Timing: Fiscal Year 2001; Project Start 01-APR-1997; Project End 30-NOV-2005

  Summary: In this application our overall hypothesis is that HIV-1 vectors can be developed that are both safe and effective for delivery of genes to protect cells from HIV-1 infection. The use of gene therapy in humans requires, first, a better understanding of the parameters necessary for efficient transduction, transplant, marking and gene expression. Second, we must utilize this information to model gene therapy for specific human diseases in this case, H IV-1 disease. The primary advantage of HIV-1 based vectors is that they are derived from a virus which has evolved to efficiently infect human cells. However, this property is also the basis of the major reservation regarding the safety of these vectors. Since we believe there are many advantages to the use of lentiviral vectors, particularly in the context of HIV-1 disease, it is critical that if lentiviral vectors are to move forward into the human clinical arena, that their substantial theoretical advantages be documented in primate model systems. We propose to utilize the SCID-hu model for human CD34+ T-progenitor cell transplant and the rhesus macaque CD34+ cell autologous transplant system. As outlined in our Preliminary Studies, we successfully developed protocols to exploit these model systems to better understand the properties of HIV-1 vectors. We also developed a novel inducible HIV-1 vector (DAt1 ru) which itself inhibits HIV-1 replication in the absence of other anti-HIV-1 genes. We propose to understand the mechanism of action of this vector and then test this vector using the two primate model systems described above. The specific aims are: 1) Determine the mechanism by which the inducible HIV-1 based vector inhibits HIV-1 replication. 2) Develop further understanding of the requirements for efficient HIV-1 vector transduction, transplantation, multi-lineage marking, gene expression, and immune response. 3) Based upon the results of Aims 1 and 2, test the

effectiveness of the best anti-HIV gene therapeutic vectors to inhibit HIV-1 1/SIV replication in in vivo model systems of SCID-hu mice and rhesus macaque.

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- **Project Title: PRIME/BOOST VACCINE USING ALVAC 1452 W/ RECOMBINANT GP160 IN HIV INFECTION**

  Principal Investigator & Institution: Ho, David; Rockefeller University New York, NY 100216399

  Timing: Fiscal Year 2001

  Summary: HIV infection is characterized by high levels of virus replication at all stages of infection. Virus replication causes increased levels of CD4 cell destruction and turnover, and when unchecked, immunodeficiency, AIDS and death. This model of pathogenesis has prompted a dramatic change in the treatment paradigm which has evolved from late intervention in symptomatic individuals to a "hit early, hit hard" strategy. Therapies, though highly effective in many, are costly, complex, and require meticulous compliance and even in the best of circumstances, are difficult to maintain over the long term. We have enrolled HIV-infected individuals in a variety of clinical trials investigating the antiviral activity and immunologic effect of intensive antiretroviral regimens. Our patients include those newly infected; presenting for treatment within 90 days of infection, as well as chronically infected individuals. The response to therapy has been generally favorable, with nearly all subjects experiencing prolonged suppression of active virus replication and near complete disappearance of cells harboring detectable HIV in peripheral blood and tissue. This clinical trial aims to select subjects from our ongoing clinical trials with minimal detectable HIV-1. We plan to boost HIV-1 specific immune responses through vaccination in subjects with minimal viremia. Subjects will be given a prime/boost vaccine regimen using a canary pox construct expressing multiple HIV antigens including env, gag, pol, and nef as a prime and a soluble env protein as a boost. The induction of HIV-specific responses will be measured.

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- **Project Title: PROCESS ENGINEERING HIV-BASED RECOMBINANT MVA VACCINE**

  Principal Investigator & Institution: Berg, Jack R.; Geovax, Inc. Atlanta, GA 30306

  Timing: Fiscal Year 2002; Project Start 30-SEP-2002; Project End 31-MAR-2003

  Summary: (provided by applicant): Development of process optimization for production of the recombinant modified vaccinia Ankara (rMVA) virus booster component of a novel multiprotein-expressing DNA/rMVA HIV vaccine candidate is proposed. In preclinical trials in macaques, DNA priming and rMVA boosting with Gag-Pol-Env-expressing immunogen for a chimera of simian and human immunodeficiency viruses (SHIV) has successfully controlled a highly pathogenic SHIV-89.6p challenge administered by the mucosal route at 7 months after the last immunization (Science 292:69). Clade B Gag-Pol-Env DNAs and rMVAs have been constructed in the laboratories of Dr. Harriet Robinson (Emory) and Dr. Bernard Moss (NIAID). These will be entering phase I trials sponsored by the NIAID HIV Vaccine Trials Network in early 2002. A major problem in preparing reagents for phase I trials was GMP production of the rMVA. Given the success of the multiprotein DNA/rMVA vaccine in preclinical models, the Emory Vaccine Center and Emory University helped start GeoVax, Inc., a company whose initial goal is the translation of the DNA/rMVA

HIV-1 vaccine for human use. The overall goal of this proposal is to undertake the process engineering for GMP production of future lots of rMVA such that the vaccine used in phase III trials will have been produced under conditions that will support cost effective production of a licensed vaccine. The clade B Gag-Pol-Env rMVA grows well under standard laboratory conditions to titers as high as lxl0E10 pfu per 850 cm2 roller bottle. During GMP production for phase I trials, the best titers achieved were about 3x10E9 pfu per 850 cm2 roller bottle. The primary goal of this proposal is to achieve scale-up conditions that produce titers of at least lxl0E10 pfu and hopefully lxl0E11 pfu of rMVA per 850 cm2 roller bottle equivalent. The rMVA grows best on primary chick embryo fibroblast cells (CEF). Development of conditions for efficient large-scale production will use a novel scale-up methodology for CEF growth and virus production coupled with a logical design for growth optimization. CEF-derived vaccines have a long history for human use with a number of products approved and millions of doses administered. Our goal is to increase rMVA titers to lxl0E10 - lxl0E11 per 850 cm2 roller bottle equivalent to provide a safe and cost effective product to meet the global need for an HIV-1 vaccine.

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- **Project Title: QUANTITATIVE METHOD FOR MODELING HIV INFECTION DYNAMICS**

  Principal Investigator & Institution: Self, Steven G.; Professor; Fred Hutchinson Cancer Research Center Box 19024, 1100 Fairview Ave N Seattle, WA 98109

  Timing: Fiscal Year 2001; Project Start 15-SEP-1998; Project End 31-AUG-2002

  Summary: (adapted from the Abstract): The dynamic nature of interactions between the **human immunodeficiency virus** (HIV) and the human immune system is complex and remains poorly understood in spite of recent important findings about the kinetics of viral and T-cell replication and clearance and the identification of cell-surface-corecptors for HIV entry. Developing accurate descriptions and a deeper understanding of the interactions between HIV and the immune system during the acute and early stages of HIV infection is critical to the evaluation of new, promising therapeutic regimens. Mathematical models, in the form of system of deterministic or stochastic rate equations, provide the most natural and convenient framework for formal descriptions of interactions between HIV and various compartments of the human immune system. Various simplified biological models for these interactions have been translated into such mathematical models and published by numerous research groups. Most of these models are focused on descriptions of the long-term course rather than the acute/early stage of HIV infection. No serious and systematic study has been made of the mathematical and probabilistic properties of these models. Typically, these models have been fit to data from few, select patients using statistical models, and methods that give virtually no serious attention to assessing sources of variability across patients. Finally, no careful and comprehensive comparative study has been made of these models with respect to their ability to describe accurately systematic patterns in longitudinally-collected virolgical and immunological data and to predict clinical outcomes. This Principal Investigator proposes to perform a systematic assessment of mathematical models for interactions between HIV and the human immune system with a particular emphasis on the utility of these models for describing acute and early stage of HIV infection. He and his colleagues will refine the formulation of these mathematical models and derive from them statistical models in which important sources of variation in observable analogs of model variables are acknowledged. They will develop and implement formal statistical methods to fit these models to data from clinical studies of

acute/early HIV infection and perfrom a data-based comparative study of models. Through existing and ongoing collaborations with clinical researchers, they will use the models and methods to address specific scientific questions that are posed in the context of clinical studies.

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- **Project Title: REGULATION OF HIV-1 CORECEPTORS**

  Principal Investigator & Institution: Bodduluri, Haribabu; Pathology and Lab Medicine; University of Louisville University of Louisville Louisville, KY 40292

  Timing: Fiscal Year 2001; Project Start 01-JAN-2000; Project End 31-DEC-2002

  Summary: The chemokines are a family of structurally related peptides that interact through cell surface G-protein coupled receptors in leukocytes to mediate diverse biological and biochemical activities such as adhesion, directed migration and activation. They play a major role in the pathophysiology of many inflammatory disorders. Chemokine receptors CCR5 or CXCR4 were identified as essential co-receptors for the entry of **human immunodeficiency virus** HIV-1 into CD4 positive cells. While CCR5 is the target for the entry of primary viruses CXCR4 may be important in the progression to AIDS from asymptomatic infection. The overall objective of the parent proposal is to delineate the pathways of CXCR4 signaling, desensitization and internalization using the RBL-2H3 cells stably co-expressing epitope-tagged native or mutated CXCR4 along with human CD4. In this AIDS-FIRCA, Dr. Sozzani proposes to utilize many reagents (epitope-tagged, green fluorescent protein tagged native and mutated CXCR4 DNAs and transfected RBL cell lines) developed for the parent proposal to determine the role of MAPKs on cPLA2 activation by the ligand SDF-1 and the relevance of this pathway to leukocyte chemotaxis using both pharmacological and biochemical approach. The ability of the HIV-1 envelope glycoproteins (gp120) to induce second messenger formation in CXCR4-expressing RBL-2H3 will be investigated. Activation of MAPKs, and cPLA2 will be evaluated and correlated with the ability of gp120 proteins to induce cell migration. The parent laboratory is utilizing and HIV-1 infection permissive human astroglioma cell line, U87, transfected with human CD4 and native or mutated CXCR4 to determine the role of the signaling evens and internalization in HiV-1 infection. The studies on cPLA2 and MAPKs in RBLs will provide a basis for extension of the same to human cell lines in the parent laboratory and to determine the role of these pathways in HIV-1 infection.

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- **Project Title: REGULATION OF HIV2 TRANSCRIPTION AND REPLICATION**

  Principal Investigator & Institution: Markovitz, David M.; Internal Medicine; University of Michigan at Ann Arbor 3003 South State, Room 1040 Ann Arbor, MI 481091274

  Timing: Fiscal Year 2001; Project Start 01-SEP-1994; Project End 30-JUN-2003

  Summary: The replication of the human immunodeficiency viruses types 1 and 2 (HIV-1 and HIV-2) can be markedly suppressed in many patients, but the current therapies have not eradicated infection. Thus, an understanding of how HIV interacts with T cells and monocytes in cellular reservoirs is of biological and clinical importance. HIV-2 causes AIDS, but generally after a much longer asymptomatic period than follows infection with HIV-1. Therefore, an understanding of the biological differences and similarities between HIV-2 and HIV-1 is of clinical importance. To understand the viral and host factors which affect disease progression, our laboratory has analyzed the interaction between cellular factors and the HIV-2 transcriptional promoter. We have

identified five cis-acting HIV-2 enhancer elements which respond specifically to cellular stimulation and have focused on the peri-ets (pets) site, not found in HIV-1, which we have shown to be important to the replication of HIV-2 in cell lines and which binds at least two important cellular proteins in vitro: GLI-2/THP, a member of the GLI protooncogene family and DEK, previously associated with leukemia and juvenile rheumatoid arthritis, which we have shown to be a site-specific DNA-binding protein which mediates signal transduction through the pets site. DEK has little similarity to other known proteins and thus would appear to be a novel type of DNA binding protein. GLI-2/THP, while binding to the pets site in vitro, activates HIV-2 and HIV-1 gene expression through a pets- independent mechanism and synergizes with both Tat-1 and Tat-2. We now propose to further study the role of the pets site, GLI-2/THP and DEK in regulating HIV-2 (and HIV-1) transcription and replication. The mechanism of action and the biological importance of the GLI-2/THP-Tat interaction and the regulatory pathway by which DEK modulates HIV-2 gene expression will be examined. Further studies will address the role of the pets site and adjacent enhancer elements in HIV-2 replication in specific cell types. Also, an HIV-2 infectious clone in which the pets site has been mutated will be used to look for other genetic mutations which compensate for the mutated pets site and affect replication. These studies should cast light on how cellular proteins contribute to the regulation of HIV-2 and HIV-1 transcription and replication and suggest novel therapeutic interventions for both viruses.

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- **Project Title: RETROVIRUS AND LENTIVIRUS FOR STEM CELL TRANSDUCTION**

  Principal Investigator & Institution: Kohn, Donald; City of Hope National Medical Center Duarte, CA 91010

  Timing: Fiscal Year 2001

  Summary: As the field of gene therapy has developed, applications to treatment of infectious diseases, such as HIV-1 infection, have been explored. The hematopoietic stem cells (HSC) contained in either bone marrow or the umbilical cord blood from newborns represent a logical target cell for gene therapy of AIDS. HSC produce the full spectrum of cells involved in AIDS pathogenesis: T lymphocytes, monocytes, macrophages, dendritic cells, and microglial (17,18). HSC are long-lived, producing new progeny cells for the life of the recipient after transplant. Therefore, insertion of a gene capable of conferring resistance to HIV-1 into hematopoietic stem cells could result in that gene being present in the mature T lymphocytes and other HIV-1-susceptible cells which are produced. Recent incremental improvements in Moloney murine leukemia virus (MLV) retroviral-mediated gene transfer into human hematopoietic stem cells (HSC) have been achieved (e.g. 10%, up from the previous ceiling of 0.1- 1.0%). However, even higher levels of gene transduction of stem cells are likely to be needed for applications to AIDS. Lentiviral vectors hold the promise of producing increased transduction of HSC, due to their ability to transduce quiescent cells. For anti-HIV-1 genes, the requisite expression parameters will vary, based on specific aspects of the anti- HIV-1 gene product (e.g. active as RNA or translated into protein). To improve methodologies for gene therapy of HIV-1 using hematopoietic stem cells, this project (#1) will be highly interactive with the other Projects and Cores. We will work with Dr. Yee to evaluate the efficacy of novel lentiviral vectors for gene delivery to primitive human hematopoietic progenitor and stem cells. We will work with Dr. Rossi to evaluate gene expression and HIV-1 inhibition by novel expression cassettes for anti-

HIV-1 genes. We will also continue to translate the findings form these basic projects into clinical trials, both with preclinical studies as well as with performing the stem cell transductions for clinical trials. These studies will contribute to fundamental advances in the techniques for gene delivery and expression and to their evaluation in subjects with HIV-1 infection.

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- **Project Title: RNA DIRECTED SILENCING OF HIV AND SIV RECEPTORS**

  Principal Investigator & Institution: Murray, Michael F.; Brigham and Women's Hospital 75 Francis Street Boston, MA 02115

  Timing: Fiscal Year 2003; Project Start 01-AUG-2003; Project End 30-APR-2008

  Summary: (provided by applicant): My long-term career goal is to study scientific questions related to human genetic susceptibility to infection as a laboratory based clinician scientist. My current fellowship training, which has added Genetics to my previous training in Infectious Diseases, was specifically pursued in order to allow me to study mechanisms of host susceptibility to infection. This current research proposal seeks to study inhibition of HIV and SIV in hematopoietic cells by altering the expression of cellular receptors, an approach that is in line with my long-term interests in altering host susceptibility to infection. This K08 application is designed to take advantage of the expertise within three different local laboratories. If funded, this award will allow me to continue to work primarily in the laboratory of Phillip A. Sharp at MIT and to begin a transition in the second half of this award to an independent research position at Brigham and Women's Hospital. RNA interference (RNAi) is a mechanism of gene silencing that has been used to study gene function in vitro, and is believed to have therapeutic potential in human diseases. RNAi occurs in cells via complex endogenous machinery that recognizes double stranded RNA, cleaves it into small fragments (19-21 nucleotides), and then uses those fragments as guides to specifically degrade RNA species displaying complementary sequence. The small fragments, called short interfering RNA (siRNA), can be introduced directly into mammalian cells to enter this pathway at the post-cleavage level to induce the specific degradation of intracellular RNA. We have used the RNAi pathway in cultured human cells to block HIV entry via specific down regulation of CD4, CXCR4, and CCR5. While transfection of siRNA oligonucleotides has been used in these proof-of-principle experiments, new methods of delivery are now being employed. RNAi-inducing RNA hairpins (hpRNA) can be delivered to mammalian cells by retroviral transduction. This proposal seeks to investigate whether hematopoietic stem cells (HSC) from human peripheral blood and from rhesus macaque bone marrow can be transduced with retroviral vectors that will continue to deliver hpRNA following differentiation. The central hypothesis underlying this work is that retroviral-mediated delivery of hpRNA to HSCs will result in a sustained protection of derived cells from either HIV or SIV as a result of RNAi induced down-regulation of cell surface receptors.

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- **Project Title: ROLE OF CYCLOPHILIN A IN THE HIV-1 LIFE CYCLE**

  Principal Investigator & Institution: Gallay, Philippe A.; Assistant Professor; Scripps Research Institute 10550 N Torrey Pines Rd La Jolla, CA 920371000

  Timing: Fiscal Year 2001; Project Start 15-FEB-2001; Project End 31-JAN-2004

  Summary: Host cyclophilin A (CypA) is essential for the replication of the **human immunodeficiency virus** type 1 (HIV- I) and thus represents an attractive target for the

elaboration of new anti-viral therapeutic agents to combat AIDS pathogenesis. Despite intense interest in the involvement of CypA in HIV- I replication, its precise role in the virus life cycle has yet to be elucidated. Our recent work suggests that CypA is exposed at the viral surface and is necessary for the initial step in HIV- I infection - the virus attachment to target cells. We demonstrated that CypA-deficient viruses do not replicate because they fail to attach to target cells. We showed that CypA is exposed at the viral membrane and mediates HIV- I attachment. We identified heparan suiphates (HS) as the exclusive cellular binding partner for CypA. Furthermore, we found that CypA binds directly to heparan via a domain rich in basic residues similar to known heparin-binding motifs. Finally, we showed that this interaction between exposed CypA and cell surface heparans represents the initial step of HIV- I attachment and is a necessary precursor to gp12O-binding to CD4. Our objective is to further understand the precise mechanistic role of CypA in the HIV-l life cycle in order to develop novel anti-HIV-l therapies. We propose to pursue the following aims: 1) to identify and characterize cell surface heparan sulfate proteoglycans necessary for CypA-mediated HIV- I attachment to target cells; 2) to define the events that control both the release of CypA from Gag and its relocation to the viral surface; and 3) to determine the direct participation of exposed CypA and/or other virus-associated proteins in HIV- I attachment.

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- **Project Title: ROLE OF HOST-ENCODED MOLECULES ON HIV VIRIONS**

  Principal Investigator & Institution: Corbeil, Jacques; Associate Professor; Veterans Medical Research Fdn/San Diego Foundation of San Diego San Diego, CA 92161

  Timing: Fiscal Year 2001; Project Start 01-MAR-2001; Project End 28-FEB-2002

  Summary: This proposal is aimed at elucidating the role and contribution of host-derived cell surface components acquired by HIV-1 progeny virions in HIV infection and pathogenesis. A better understanding of the infection process may assist in vaccine development and therapy as well as providing further insights into the virus replicative cycle. Most enveloped viruses, including the **human immunodeficiency virus** type-1 (HIV-1), are extruded from the infected cell by budding through cell membranes. The insertion of host cell membrane molecules into the viral particle is likely to occur as the emerging virus is released with part of the host membrane itself. The putative functional role(s) of cellular molecules incorporated into progeny virions requires elucidation as these host-encoded proteins may affect the viral replicative cycle, contribute to transmission and to the overall pathogenesis of the disease. The first part of this proposal is focused on the analysis and identification of signal transduction pathways and host gene expression profiles relevant to the process of infection. These will be gathered following infection of different primary human cell subsets with isogenic progeny viruses bearing on their surfaces specific host-derived molecules (Specific Aim 1). This is a complex phenotype modulated by numerous genes which therefore requires the global approach of high-density microarray. The second part of this research project is centered on the putative modulatory effect(s) the virally embedded host proteins may have on the HIV-1 viral cycle and to assess the effect of virally-embedded host molecules on HIV-1 LTR-driven transcription and virus production (Specifics Aims 2 and 3).

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: SAFETY AND EFFICACY OF CAP IN VIVO**

  Principal Investigator & Institution: Cheng-Mayer, Cecilia C.; Associate Professor of Microbiology; New York Blood Center 310 E 67Th St New York, NY 10021

Timing: Fiscal Year 2001; Project Start 26-SEP-2001; Project End 31-JUL-2005

Description (provided by applicant): Cellulose acetate pthalate (CAP) possesses many of the desirable features of a topical microbicide for prevention of HIV-1 infections in humans, foremost of which is its anti-viral activity in vitro. However, the less than complete protection conferred by a CAP topical cream against vaginal transmission of the simian immunodeficiency virus (SIV) in rhesus macaques raises certain important issues that need to be addressed as part of its development. The applicant hypothesizes that distribution and/or epithelial changes induced by CAP affect its efficacy. Furthermore, structural as well as functional differences in the envelope glycoproteins of HIV and SIV may limit the translation of the finding in the SIV/macaque model to that of the human setting. For these reasons, the applicant proposes to conduct detailed irritation and distribution studies of CAP in rhesus macaques and to assess the protective effect conferred by CAP against vaginal challenge with pathogenic SHIVs. SHIVs are simian/human chimeric viruses in which the env, tat and rev genes of the pathogenic SIVmac239 strain were replaced with their corresponding HIV counterparts. SHIVs that carry the envelopes of CXCR4 (X4) and CCR5 (R5) HIV-1 viruses have been developed and shown to cause disease in naive animals when inoculated intravenously or mucosally. Thus, infection of macaques with X4 and R5 SHIVs provides a range of pathogenesis, cellular involvement and coreceptor usages that parallel HIV infection and disease in humans, and is probably one of the best models available to assess the protective effect of CAP. Three specific aims are proposed. (1) Assess the safety of CAP cream in vivo. Colposcopy as well as measurement of pro-inflammatory chemokines and cytokines will be performed to assess the effect of CAP cream on the vaginal epithelium of rhesus macaques. (2) Assess CAP distribution in vivo by colposcopy and magnetic resonance imaging. (3) Evaluate the protective effect of CAP against challenge with pathogenic X4 and R5 SHIVs. Results from the proposed studies should establish the safety as well as efficacy of CAP in vivo.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: SFV GENE DELIVERY TO INHIBIT HIV AND SIV INTEGRASE**

  Principal Investigator & Institution: Strayer, David S.; Professor; Pathology, Anat/Cell Biology; Thomas Jefferson University Office of Research Administration Philadelphia, PA 191075587

  Timing: Fiscal Year 2001; Project Start 15-SEP-1997; Project End 31-JUL-2006

  Summary: HIV-1 integrase (IN) is an uncommon target for experimental inhibition of HIV-1 infection. We propose to study protection from HIV-1 in vitro and in vivo using recombinant SV40-based vectors (rSV40) to deliver single chain Fv antibodies (SFv) against IN. We have found that rSV40 delivery of the anti- IN SFv, Aw, effectively blocks both IN activity and HIV-1 infection, in vitro in unselected human T cells, and in vivo in SCID-hu mice bearing human thymic implants. With Dr. Harris Goldstein, who has used his SCID-hu mouse model system to study HIV-1 infection, we will test single agent and combination genetic therapy using Aw and a second, complementary anti-IN SFv, SFv number 4. SV(Aw) + SV(IN4) inhibition of HIV-1 infection will be analyzed in vitro and in vivo. This proposal is based on this hypothesis: Combinations of anti-IN SFv delivered by rSV40 vectors to mature and pro-genitor cells will protect susceptible cells from HIV-1 in vitro and in vivo. To test this hypothesis, we propose 5 Specific Aims. We will test anti-HIV-1 protection by both anti- IN SFv, delivered by rSV40 vectors, and compare levels and duration of protection from HIV-1 achieved with these vectors in unselected cells to those achieved with retroviral vectors delivering the same transgenes to selected cells. Additive protection should be possible using SV(Aw) and

SV(IN4) in combination, and this will be examined. Single and multiple rSV40-transduction of human hematopoietic progenitor cells and protection of their mature, HIV-1-susceptible progeny will be examined in vivo in SCID-hu mice. Gene delivery to human thymic implants in SCID-hu mice will be used to confirm in vivo protection from HIV-1 infection afforded by this approach and to measure the levels of inhibition of HIV-1 that can be achieved by both rSV40 transduction and HIV-1 challenge in vivo. Effects of transduction on T cell development and physiology will be tested. We will prepare for testing anti-IN genetic therapy of immunosuppressive lentivirus in nonhuman primates by developing and testing in vitro a hybrid SIV-based virus containing HIV-1 IN. Finally, we propose quantitative studies to define the frequency and characteristics of the integration of rSV40 DNA into the host chromosomes. SV40-based gene delivery is highly efficient in transducing HIV-1-susceptible cells and their progenitors. Thus, it has great promise, particularly when combined with intracellular SFv, in inhibiting HIV-1 infection. Studies proposed here will help determine the potential efficacy and implications of this approach to intracellular immunization in the treatment of HIV-1 infection.

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- **Project Title: SMALL ANIMAL MODELS FOR MICROBICIDE TESTING**

  Principal Investigator & Institution: Phillips, David M.; Population Council 1 Dag Hammarskjold Plaza New York, NY 10017

  Timing: Fiscal Year 2001

  Summary: The overall goal of this project is to develop a vaginal dosage formulation that is an effective contraceptive which simultaneously protects against the sexual transmission of **human immunodeficiency virus** (HIV) and Chlamydia. Ideally, this would be achieved in a single active agent, but its attainment with a compatible combination of agents may prove more realistic. Candidate materials to be tested include compounds known to interfere with sperm function and compounds considered likely to interfere with the mechanisms of transmission of HIV. Four types of in vitro tests will be carried out: (1) Cytotoxicity which will include different assays under various conditions. (2) Spermatozoa: The P.I.'s research during the last 25 years has concentrated primarily on studies of sperm structure and function. The assays of sperm will concentrate on identifying agents which interfere with function including sperm metabolism, motility, and penetration of cervical mucus as well as agents which agglutinate spermatozoa. (3) HIV: This laboratory has been instrumental in elucidating the mechanisms of sexual transmission of HIV and developing in vitro methods to assay agents which inhibit sexual transmission of HIV. Assays will include a fluorescence-based cytotoxicity and cell-cell adherence assays, and an ELISA which detects the ability of agents to interfere with transmission of HIV from HIV-infected lymphocytes to epithelial cells derived from the human cervix. (4) Chlamydia: Screening for anti-Chlamydial activity will involve blocking infection of cells derived from the human cervix. We are developing a novel technique for Chlamydial testing. This method, which will employ a highly sensitive fluorescence cytotoxicity assay and uses a cell line derived from the human cervix, should be much more rapid, quantitative, and appropriate than the existing assays. Based on information in the literature and on our preliminary findings, the following five lead compounds have been selected for testing: (1) chlorhexidine, (2) propranolol, (3) 4'-acetamidophenyl-4-guanidinobenzoate, (4) diethyldithiocarbamate, and (5) dextran sulfate. Animal studies will include inhibition of Chlamydia trachomatis infection in mice, a system which the P.I. has worked with previously. In addition, fertility and vaginal irritability studies will be carried out in

rabbits. For studies of simian immunodeficiency virus (SIV) transmission we will contract Dr. Christopher J. Miller, at the California Primate Research Center, who will test inhibition of cell-free and cell-associated SIV transmission in rhesus monkeys. Within the five-year funding period we expect to have prepared one or more agents for clinical tests of effectiveness in humans. In formulating materials for such tests, particular cognizance will be taken of the necessity of protecting the entire vaginal surface in order to prevent transmission of HIV. Attention will also be directed to the desirability of effectiveness for at least 24 h. Preparation for testing effectiveness in humans will include assessment of vaginal irritation, preliminary assessment of carcinogenic potential by means of mutagenicity assays, and tests for teratogenic potential and toxicity in animal models.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: SMALL MOLECULE MIMETICS**

  Principal Investigator & Institution: Huffman, William; University of Pennsylvania 3451 Walnut Street Philadelphia, PA 19104

  Timing: Fiscal Year 2001

  Summary: The central objective of this research is to use the structure of the gp120/CD4 complex and structure-based mimetics to design antagonists of the interaction of human cells with HIV-1, the **human immunodeficiency virus** responsible for AIDS. T-cell docking and entry by HIV-1, a major route of cell infiltration and resultant infecting in AIDS, is driven by specific recognition of the T-cell surface protein CD4 with the HIV envelope protein gp120. The crystallographic structure of CD4 is known, and that of its complex with gp120 is close at hand. Structural components in both protein partners have been identified which are proposed to play key roles in CD4-gp120 recognition. The advancing high resolution structural understanding of the protein participants in virus-cell recognition together with the advancing technology of mimetics design now make it possible to combine structure determination, modeling, miniprotein engineering and organic synthesis to design new antagonists for AIDS. Other components of this research program aim to utilize the high resolution X-ray crystal structure of the CD4/gp120 complex in concert with previous crystallographic and mutational analyses (a) to identify the binding sites in the CD4-gp120 interface by computational modeling and (b) transplant CD4 and gp120 binding site components such as form loops and helices into conformationally constrained miniprotein constructions to obtain miniprotein mimetics and use these to define the minimum structure that contains a sufficient number of binding sites from the parent protein that maintains a comparable interaction. The specific aims of this proposal are to (1) utilize key structural elements as determined from modeling of the high resolution structure, and subsequently miniprotein mimetics to design small molecule CD4 and/or gp120 antagonist; (2) identify novel inhibitors of gp120/CD4 to augment the rational design efforts of Specific Aim 1, by screening the SB compound bank and by synthesizing constrained peptide and semipeptide helix, gamma-turn and beta- turn mimetic libraries. Overall, this project will yield miniprotein and organic synthetic technologies for protein mimetics construction. GRANTP01GM565509001 The interaction of HIV-1 with its primary receptor, CD4, is critical for viral entry into the target cell. The conserved nature of the CD4 binding site on the HIV-1 gp120 envelope glycoprotein makes this interaction an attractive target for intervention. The goal of this Program is to identify clinically useful compounds that can inhibit the gp120-CD4 interaction, taking advantage of very recent advances in understanding the molecular details of gp120-CD4 binding. Numerous candidate antiviralmolecules directed against the gp120 CD4 interaction will be

generated by all three projects in this Program. The goal of this Scientific Core is to understand the interaction of these CAMs with humanimmunodeficiency virus (HIV-1) and its components or with host cellmolecules (CD4 and chemokine receptors) important for HIV-1 entry. The specific aim of this Scientific Core are: 1) To establish high-throughput screen assays to identify inhibitors of gp120-CD4 binding; 2) To establish secondary binding and specificity assays to define molecules that are selective inhibitors of gp120-CD4 binding and to identify the molecular targets compounds; 3) To evaluate the ability of candidate antiviral molecules to inhibit HIV-1 entry and cell-cell fusion; and 4) To elevate the ability of HIV-1 to become resistant to selected antiviral molecules.

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- **Project Title: SPECIES SPECIFIC CYCLIN T1 RECOGNITION BY TAT AND TAR**

  Principal Investigator & Institution: Edgcomb, Stephen P.; Scripps Research Institute 10550 N Torrey Pines Rd La Jolla, CA 920371000

  Timing: Fiscal Year 2002; Project Start 01-FEB-2003

  Summary: (provided by applicant): Human (HIV) and bovine (BIV) immunodeficiency viruses exploit host cyclin T1 proteins to enhance viral transcription using interactions between cyclin T1, viral Tat proteins, and the TAR RNA hairpins located on viral transcripts. The two viruses have evolved distinct mechanisms for cyclin T1 recognition; however, these differences are not well understood in molecular detail. Biochemical and biophysical experiments will be used to characterize the domains of cyclin T1 that contain both the canonical cyclin fold and the binding region for the Tat:TAR complex. This includes purification of the human and bovine cyclin domains and assessment of protein folding by both spectroscopic assays, and proteolytic mapping. Additionally, individual contributions of cyclin, Tat, and TAR molecules to the formation of the protein-RNA complexes will be assayed through a series of titration experiments and proteolytic mapping. Finally, optimizing the conditions to generate correctly folded complexes will facilitate attempts at growing crystals of the complexes. The molecular details uncovered by these studies are expected to provide new information about transcription control mechanisms and may aid in the search for new therapies to treat viral disease and cyclin related cancers.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: SPECIFICITY STUDIES OF HIV AND HTLV PROTEASES**

  Principal Investigator & Institution: Weber, Irene T.; Professor; Biology; Georgia State University University Plaza Atlanta, GA 30303

  Timing: Fiscal Year 2001; Project Start 01-JUL-1999; Project End 30-JUN-2002

  Summary: (Adapted from the Applicant's Abstract) The proposal's short-term aim is to eludicate the molecular basis for the action of resistant variants of **Human Immunodeficiency Virus** 1 (HIV-1) protease by comparing the structures and activities of selected mutants of HIV-1 and Rous sarcoma virus proteases. The specificity studies proposed will be: 1) to cover a broader set of oligopeptide substrates in order to more fully characterize the inhibitor-resistant HIV-1 protease mutants; and 2) promote new studies on the molecular basis for the specificity of the related human T-cell leukemia virus type 1 (HTLV-1) protease. The long-term aim is to predict new protease inhibitors and therapeutic strategies to overcome the problem of drug-resistance.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: STRUCTURAL ANALYSIS OF HIV1 ENVELOPE GLYCOPROTEINS**

  Principal Investigator & Institution: Sodroski, Joseph G.; Professor; Dana-Farber Cancer Institute 44 Binney St Boston, MA 02115

  Timing: Fiscal Year 2001; Project Start 15-DEC-1996; Project End 30-NOV-2001

  Summary: (Adapted from applicant's abstract) Human immunodeficiency viruses, HIV-1 and HIV-2, are the etiologic agents of acquired immunodeficiency syndrome (AIDS) in humans. The HIV-1 and HIV-2 envelope glycoproteins, gp120 and gp41, are critical for the entry of these viruses into the target cell, mediating virus binding to the CD4 receptor and membrane fusion. The envelope glycoproteins are the major targets for neutralizing antibodies and are likely to represent an important component in HIV-1 and/or HIV-2 vaccines. The overall goal of this proposal is to achieve an atomic level of understanding of the structural biology associated with the envelope glycoproteins of the human immunodeficiency viruses and the related simian immunodeficiency viruses. The strategy that will be employed to achieve this goal is based upon approaches that have yielded X-ray quality crystals of a complex containing an HIV-1 gp120 fragment bound to soluble fragments of CD4 and a neutralizing antibody. The structure of this complex will be determined and analyzed in Specific Aim 1. In Specific Aim 2, an attempt will be made to determine comparable structures for gp120 fragments derived from primary HIV-1 isolates in different clades. Specific Aims 3 and 4 are directed at obtaining useful crystals of HIV-1 gp120 fragments containing the complete gp41-interactive region and soluble gp120-gp41 oligomers, respectively. An attempt will be made to extend these studies to the HIV-2/SIV envelope glycoproteins in Specific Aim 5.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: STUDIES ON DC-SIGN INTERACTIONS WITH HIV AND SIV**

  Principal Investigator & Institution: Lee, Benhur; Assistant Professor; Microbiology and Immunology; University of California Los Angeles 10920 Wilshire Blvd., Suite 1200 Los Angeles, CA 90024

  Timing: Fiscal Year 2002; Project Start 01-AUG-2002; Project End 31-JUL-2007

  Summary: (provided by applicant):Human immunodeficiency virus type 1 (HIV-I) envelope (Env), responsible for both receptor binding and membrane fusion, consists of a gpl20 surface subunit noncovalently associated with a gp41 membrane bound subunit. It is the gpl20 subunit that binds and interacts with CD4 and a coreceptor prior to entrance of the virus into a cell. In addition to the primary receptor and coreceptor required for viral entry, viral attachment molecules have been described which could modulate the efficiency of the viral entry process. The recent discovery of a calcium-dependent (C-type) lectin, DC-SIGN, which binds to monomeric HIV Env gpl20 with a greater affinity than CD4, prompted us to re-examine the nature of this viral attachment process and its contribution to the process of viral entry. It has been hypothesized that a crucial step in the establishment of primary HIV infection is the transfer of virus from dendritic cells (DCs) in the submucosa to permissive T-cells in secondary lymphoid organs. The relatively specific expression of DC-SIGN on DCs, and its proposed role as a conduit for this transfer of HIV underscores the need to understand further the biology of this process. Indeed, DC-SIGN may have additional functions that have been heretofore unrecognized. For example, we have found that DC-SIGN expression in cis, that is, on permissive cells that express CD4 and coreceptor, markedly enhanced the efficiency of viral entry. Thus, DC-SIGN expression in-cis allows viral entry via vanishing levels of co-receptor or via use of alternate co-receptors that are otherwise

used very inefficiently. In addition, it has also been reported that mRNA coding for putative soluble isoforms of DC-SIGN can be found in primary tissues. It is the driving hypothesis of this proposal that DC-SlGN can efficiently facilitate H1V/SIV infection in-trans and in-cis. The overall goal of this proposal is to gain a better understanding of DC-SIGN's biology and function and lay the foundation to better evaluate its putative role in viral transmission and pathogenesis in vivo. Understanding the structural basis for DC-SIGN/ gpl20 interaction will also inform efforts to design novel immunogens that might elicit antibodies that neutralize DC-SIGN/gpl20 binding. In this proposal, we will pursue three Specific Aims to (1) Examine the nature of enhanced viral entry and viral transfer when DC-SIGN is expressed in cis and in trans, respectively, (2) Determine the structural and mechanistic underpinnings of DC-SlGN/ HIV gpl20 interactions, and (3) Study the biology of DC-SIGN in vivo using two models for studying HIV pathogenesis in the gut mucosa and thymus, respectively.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: SV40 VECTORS FOR STEM CELL GENE THERAPY IN MACAQUES**

  Principal Investigator & Institution: Johnson, R. Paul.; Associate Professor of Medicine; Thomas Jefferson University Office of Research Administration Philadelphia, PA 191075587

  Timing: Fiscal Year 2001; Project Start 01-SEP-2001; Project End 31-AUG-2002

  Summary: Genetic modification of hematopoietic stem cells (HSC) offers the potential of reconstituting immune function in HIV-infected individuals with a lifelong source of hematopoietic cells resistant to HIV infection. However, retroviral vectors based on Moloney murine leukemia virus (MLV) have proved to be relatively inefficient in transducing primate HSC, in large part due to the inability of these vectors to transduce quiescent different hematopoietic cells, including hematopoietic stem cells. However, demonstrating of the efficacy and safety of these vectors for human clinical trials will require in vivo studies in non-human primates. Recent collaborative work between our laboratory and Dr. Strayer's laboratory has demonstrated quite efficient transgene in progeny T cells derived from transduced CD34+ cells. The overall objective of this project is to examine the ability of SV40-based vectors encoding a variety of different genes that inhibit SIV and SHIV replication to transduce rhesus macaque HSC and to protect hematopoietic progeny from SIV infection both in vitro and in vivo. Specific aims include: 1) To examine the efficacy of SV40-based vectors in delivering in inhibitory genes to rhesus hematopoietic cells in vivo; and 3) To examine the ability of SV40-based vectors to inhibit SV/SHIV replication in vivo in rhesus macaques. These studies should provide valuable information. regarding the safety and efficacy of SV40 vectors for stem cell gene therapy for AIDS.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: SYNAPTIC TRANSMISSION OF HIV-1-ASSOCIATED DEMENTIA**

  Principal Investigator & Institution: Anderson, Eric R.; Pathology and Microbiology; University of Nebraska Medical Center Omaha, NE 681987835

  Timing: Fiscal Year 2003; Project Start 01-SEP-2003; Project End 31-AUG-2004

  Summary: (provided by applicant): The biochemical basis for cognitive decline in **human immunodeficiency virus** type one (HIV-1)-associated dementia (HAD) is a selective and sometimes reversible neuronal impairment caused, in measure, by brain mononuclear phagocyte (MP) infection and immune activation. The mechanism(s) for how HIV-1-infected brain MP alter neural physiological processes (e.g., modulation of

synaptic transmission and plasticity) and lead to neural dysfunction during HAD is the focus of this proposal. Electrophysiological, pharmacological, immunological, and molecular techniques will be directed toward 3 specific aims including: (1) the determination of the relative contribution of viral (HIV-1ADA) and cellular (MP-derived) secretory factors to affect neural physiology; (2) the identification of neural receptor subtypes [e.g., N-methyl-D-aspartate] as a common mechanism for MP neurotoxicity; (3) the mechanisms for alterations in cellular and synaptic function will be sought in an animal model of HIV-1-encephalitis. These works, in toto, serve to cross-validate one another by providing both laboratory and animal model study neurophysiological paradigms for disease. Overall, these studies would provide a greater insight into the role(s) that MP-secreted factors play in HAD and the mechanisms underlying lentiviral neuropathogenesis. Moreover, such investigations could allow new opportunities for new drug interventions in a disease that remains a critical source of morbidity and mortality in the infected host.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: THE EMERGENCE OF HIV GENETIC DIVERSITY IN CAMEROON**

  Principal Investigator & Institution: Wolfe, Nathan D.; International Health; Johns Hopkins University 3400 N Charles St Baltimore, MD 21218

  Timing: Fiscal Year 2001; Project Start 30-SEP-1999; Project End 31-AUG-2002

  Summary: Human immunodeficiency virus (HIV) now causes more global mortality than any other single infectious agent and is the primary cause of death in Africa. Diagnostic assays and vaccines are central tools for addressing this problem. The effectiveness of these tools, however, may be limited by the genetic diversity of HIV. The forces that generate and maintain this diversity are incompletely understood. The proposed research investigates a potentially crucial natural mechanism for the introduction of novel HIV genetic diversity into the human population. We hypothesize that HIV genetic diversity emerges not only through the cross-species transmission of entire simian immunodeficiency virus (SIV) genomes, but also through the emergence of individual genes or genomic segments during recombination events between nonhuman lentiviruses and the fully human-adapted virus, HIV-1. While human hunters of nonhuman primates are at the front line of this interface, they have never, to our knowledge been systematically examined. This proposal includes four interrelated aims. First, we will assess the prevalence of HIV and HIV-related lentiviruses among hunters in Cameroon, using whole viral ELISAs and the Western Blot. Second, we will characterize positive isolates through the polymerase chain reaction (PCR) and heteroduplex mobility assay (HMA) at three independent genomic regions, which will reveal the broad phylogenetic relationships of these three regions of the HIV genome. Third, we will examine the detailed genetic mosaic structure of selected isolates in order to assess the genomic sites of recombination, using full-length genomic sequencing and phylogenetic analysis. Fourth, in the process of completing aims one through three, we will develop reagents from Cameroonian HIV isolates and adapt and field test an HMA appropriate for continued HIV surveillance in Cameroon. The proposed research will provide significant career development of the primary investigator through directed mentorship in the epidemiology, ecology, and molecular evolution of HIV and related viruses.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: THERAPEUTIC IMMUNIZATION IN NON-HUMAN PRIMATES**

  Principal Investigator & Institution: Lewis, Mark G.; Acting Director; Res Inst for Gen & Human Therapy

  Timing: Fiscal Year 2003; Project Start 01-JUL-2003; Project End 30-JUN-2007

  Summary: We have demonstrated that highly active antiretroviral therapy based structured treatment interruptions (STI-HAART) can boost SIV-specific immune responses, thereby reducing the viral rebound rate and inducing immune control of SIV in acutely SIV251-infected macaques. However, during chronic infection, characterized by impaired immune functions, STI-HAART does not induce immune control. To reconstitute virus-specific immunity we have developed a novel topical therapeutic DNA vaccine, called DermaVir. Application of DermaVir to the surface of the skin of mice and macaques resulted in transduction of Langerhans cells, migration of these cells into lymph nodes, gene expression by genetically-modified dendritic cells, and induction of vigorous, virus-specific T cell-mediated immune responses. In chronically SIV251-infected macaques and in macaques with late-stage disease, i.e. AIDS, DermaVir, in combination with STI-HAART, reduced viral rebound to a rate comparable to that observed during STI-HAART alone during primary infection. These unexpected and exciting initial results warrant further investigation of the effects of DermaVir on immune control of HIV. We propose to evaluate various aspects of this novel therapeutic modality in the same SIV251-infected macaque model to create the basis for moving to the clinical stage of development. This project will run a comparative study to evaluate the importance of a two major factors that may increase both efficacy and safety of therapeutic immunization: type of promoter (LTR or CMV), and the use of an adjuvant, such as IL-2. Additionally, we propose to study the virus-specific humoral and cellular immune responses to DermaVir during the proposed primate trials in order to establish immune correlates of virus control. Specific Aim 1. Comparative analysis of the DNA promoter and potential adjuvants during DermaVir therapeutic immunization in non-human primates. To run a comparative study of the type of promoter (LTR or CMV) and the effects of an adjuvant (IL-2) on therapeutic immunization in a non-human primate model. Specific Aim 2. Study of immune correlates of viral control during therapeutic immunization. To determine whether the immune response elicited by DermaVir is responsible for the control of viremia, and to elucidate the nature of such a response.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: THETA-DEFENSINS: NOVEL HIV-1 UPTAKE INHIBITORS**

  Principal Investigator & Institution: Lehrer, Robert I.; Professor; Medicine; University of California Los Angeles 10920 Wilshire Blvd., Suite 1200 Los Angeles, CA 90024

  Timing: Fiscal Year 2003; Project Start 01-SEP-2003; Project End 31-AUG-2004

  Summary: Our broad objectives are: to ascertain the role of innate immunity in protecting against HIV-infection and disease progression; to explore the antiviral properties of primate theta-defensins and determine their mechanism of activity, and identify promising 0-defensin peptides for future therapeutic development. Theta-defensins are circular octadecapeptides. They are formed in vivo by the post-translational splicing of two nonapeptides, each derived from a truncated, alpha-defensin-like propeptide that is encoded by a DEFT gene. Some 7.5 to 10 million years ago, the DEFT genes of a hominid ancestor of Homo sapiens acquired a premature stop codon in Exon 2, which encodes the signal sequence. Consequently, although human cells still express theta-defensin mRNA, they no longer produce theta-defensin peptides.

We synthesized three theta-defensin peptides (retrocyclins- 1, -2 and-3) that human ceils could have produced if their DEFT genes had not been silenced. Retrocyclin-2 was remarkably effective in protecting CD4-positive cells from infection by both T and Mtropic strains of HIV-1. Its wide protective spectrum encompassed the clade B isolates that cause most infections in our country and the Clade C isolates that predominate in southern Africa and India. Our preliminary data revealed that retrocyelins are lectins, and that they bind gp 120, CD4 and galactosylceramide with high affinity. The specific aims of this proposal are: a). To synthesize novel theta-defensins, including peptides based on DEFT gene sequences in non-human primates, b). To test theta-defensins and selected alpha- defensins (including human HN 1-3), against laboratory-adapted and wild-type strains of HIV-1, HIV-2, and SIV; c) To identify the sugars and oligosaccharides recognized by primate theta- and alpha-defensins and correlate this with their antiretroviral properties, and d) To determine which human lymphocytes express 0-defensin mRNA, and if arninoglycosides enable human cells to produce 0-defensin peptides. Health relatedness: 0- defensins constitute a novel class of HIV-uptake inhibitors with excellent potential for future therapeutic development. The proposed research will allow experienced investigators based at UCLA, The Yerkes Primate Center at Emory University and the CDC to build the required foundation for this development.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: THYMIC FUNCTION IN ADULTS WITH HIV1 DISEASE**

  Principal Investigator & Institution: Mccune, Joseph M.; Senior Investigator, Professor and Assoc; J. David Gladstone Institutes 365 Vermont St San Francisco, CA 94103

  Timing: Fiscal Year 2001; Project Start 01-MAR-1999; Project End 28-FEB-2003

  Summary: The thymus is the major organ of T cell production and is generally believed to be nonfunctional in adults. Even if present, it is destroyed by HIV-1 infection while, at the same time, T cells are destroyed in the peripheral lymphoid system. Given the absence of de novo T cell production and a pathologic acceleration of T cell destruction, the immune system collapses and immunodeficiency ensues. The experiments of this R01 address the hypothesis that the thymus may be more active in adults with HIV-1 disease than previously assumed. This hypothesis is based on the preliminary observation that abundant thymic tissue is detectable in a surprisingly large fraction (47/99) of HIV-1-seropositive adults, aged 20-59. Independent of age, radiographic demonstration of thymic tissue was significantly associated with both a higher CD4+ T cell count and a higher percentage and absolute number of circulating naive (CD45RA+CD62L+) CD4+ T cells. The prevalence of an abundant thymus was especially high in younger HIV-1-seropositive adults (less than or = 39 years) with CD4 counts in the range of 300-500 cells/mu1 and in older subjects (greater than 40 years) regardless of CD4 count (p=0.03). These studies suggest that the thymus is functional in many adults with HIV-1 disease, and raise the specific hypothesis that thymic function in the adult might be induced as a consequence of HIV-1- mediated peripheral T cell depletion. To test this hypothesis, the following specific aims are proposed: 1. To determine whether the thymus is functional in HIV-1-seropositive adults. 2. To determine whether suppression of viral replication is associated with enhanced thymic function in HIV-1-seropositive adults. 3. To determine whether peripheral feedback may upregulate thymopoiesis in HIV-1 -seropositive adults. The experiments of this R01 are linked scientifically and administratively (through an "Interactive Research Project Grant") with an R01 submitted by Dr. Marc Hellerstein, entitled "T cell kinetics and sources: effects of HIV and therapy." This interactive project will address the general

hypothesis that T cell dynamics in HIV-1 disease, and hence - the ability to regenerate a functional immune system -- are critically dependent upon the presence or absence of thymic tissue. A "shared resource" will be required to address this hypothesis, including a fluorescence activated cell sorter maintained under Biosafety Level 3 precautions in Dr. McCune's lab and a mass spectrometer maintained in Dr. Hellerstein's lab.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: THYMIC IMPACT ON HIV-1 IMMUNE RESPONSE**

  Principal Investigator & Institution: Harris, Jeffrey M.; J. David Gladstone Institutes 365 Vermont St San Francisco, CA 94103

  Timing: Fiscal Year 2001; Project Start 01-JUL-2001; Project End 31-OCT-2001

  Summary: (provided by applicant): Some individuals treated during acute HIV-1 infection with antiretroviral therapy now appear to be able to immunologically suppress HIV-1 replication for at least six months following discontinuation of therapy. Similar scenarios have not yet been well documented for people treated at a later stage of the infection, though HIV-specific CD8+ and CD4+ T cell responses are sometimes detectable. The desired effect of an immune response to HIV-1 is complicated by the fact that CD4+ T cells themselves are infected and may be further depleted by the immune response. Although CD4+ counts often recover after antiretroviral therapy, this recovery is largely due to redistribution and expansion of remaining memory cell clones. De novo T cell development, required for the generation of a widely diverse T cell repertoire, requires the thymus, which typically involutes after puberty. However, we have evidence showing that rebound of thymic mass and increased de novo T cell production can occur in some HIV-1-infected adults. The hypothesis of this application is that chronically HIV-1-infected individuals who have suppressed viral replication on HAART and who have increased thymic output compared to age-matched seronegative controls will generate and maintain HIV-1-specific immune responses that can control viremia during controlled interruptions of antiretroviral therapy. To test this hypothesis the following specific aims are proposed: 1) to prospectively assess the degree of thymic output in chronically infected people undergoing scheduled interruptions of antiretroviral therapy and to stratify these patients into two groups having either high or low thymic output compared to age-matched seronegative controls; 2) to phenotypically and functionally characterize HIV-1-specific T cell responses during scheduled treatment interruptions (STI) in the two subject groups stratified by thymic output; and 3) to measure the ability of HIV-1-specific T cell responses generated during STI in the two subject groups stratified by thymic output, to control the replication of autologous virus, as demonstrated not only in vivo by the pattern of rebound viremia, but also in vitro, by indirect and direct methods. The award candidate is a pediatric immunologist at the University of California, San Francisco, doing postdoctoral research on human thymic function in J.M. McCune's laboratory at the Gladstone Institutes. He intends to become an independent academic investigator and to continue to conduct patient-oriented research in the area of immunodeficiency disorders.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: TRANSCRIPTION ACTIVATION BY HIV, TAT, HTLV TAX & HBV PX**

  Principal Investigator & Institution: Green, Michael R.; Professor; Molecular Medicine; Univ of Massachusetts Med Sch Worcester Office of Research Funding Worcester, MA 01655

Timing: Fiscal Year 2001; Project Start 01-SEP-1990; Project End 31-AUG-2005

Summary: (from investigator's abstract): This is a competitive renewal application. The previous grant was for studying how the trancriptional regulatory proteins of three pathogenic viruses activate transcription, specifically, the Tat protein of **human immunodeficiency virus** type 1 (HIV-1), the Tax protein of human T-cell leukemia virus type 1 (HTLV-1), and the pX protein of hepatitis B virus (HBV). In this application, the applicant seeks to understand in greater detail the mechanism of action of these viral regulatory proteins and their role in viral replication and human disease. The rationale for the proposal relies heavily on two relatively new technologies. First, the chromatin immunoprecipitation (ChIP) assay, which allows for the detection of specific proteins that are physically associated with DNA in living cells. Second, the genome-wide expression analysis using high density DNA microarrays, which enables the analysis of transcription profiles of a large array of human genes. The specific aims are: (1) To understand in greater detail how HIV-1 Tat stimulates transcription in vitro and in vivo. The investigator has identified a Tat cofactor, Tat-SF1, and has shown that it is a general transcription elongation factor. A second elongation factor has been implicated, AIEF, and remains to be identified. Tat-SF1 and AIEF and the mechanisms of Tat activation in vivo will be investigated further. (2) To study how HTLV-1 Tax and HBV pX regulates DNA binding of cellular bZIP proteins. The investigator has shown that Tax and pX dramatically increase the DNA binding activity and alter the target selectivity of a wide variety of cellular proteins that possess a basic region-leucine zipper (bZIP) DNA binding domain, through promotion of dimerization. Experiments are proposed to undersstand the basis of altered DNA binding specificity, the cellular proteins involved, and details of the DNA-protein interactions. (3) To analyze how HTLV-1 Tax and HBV pX activate transcription in vivo and transform cells. To test the prediction of different models of how these proteins activate transcription, to identify cellular proteins involved in the activation, and to identify cellular genes activated that may contribute to disease. (4) To understand the mechanism of BEF action. The investigator has identified a nuclear protein BEF (for bZIP-enhancing factor) which is required for bZIP prtoein functions, work synergistically with Tax and pX. However, BEF works by a different mechanism, as a molecular chaperone. Experiments are proposed to further study the mechanism of BEF action.

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- **Project Title: TRANSDUCTION OF ANTI-HIV RNA INTO BLOOD STEM CELLS WITH LENTIVIRAL VECTOR**

  Principal Investigator & Institution: Lee, Jiing-Kuan; City of Hope National Medical Center Duarte, CA 91010

  Timing: Fiscal Year 2001

  Summary: Gene therapy approach has been adopted to treat HIV infection. A potentially attractive class of anti-HIV-1 genes is ribozymes, which have been targeted to specific sites of HIV-1-RNA. Ribozymes are RNA sequences, which have an ability not only to bind to but also to cleave RNA. The City of Hope has been involved in a clinical trial in which a tandem pair of anti-tat and anti-tat/rev ribozymes have been transduced into autologous CD34+ cells by a vector derived from Moloney murine leukemia virus (MoMLV) and reinfused into the patients. In contrast to vectors derived from MLA, lentiviral vectors derived from **human immunodeficiency virus** (HV) or feline could be due to the ability of lentiviruses to infect quiescent or terminal differentiated cells whereas MLV fails to infect. In our preliminary studies, we have produced high- titer HIV and FIV vectors from transfected 293T cells. We have shown

that these two vectors are able to transduce cultured quiescent fibroblasts and slow growing cells much more efficiently than a MLV vector. We now propose to use lentiviral vectors to deliver anti-HIV ribozyme genes into human CD34+ cells. We will (1) compare the transduction efficiency of human CD34+ cells with the HIV, FIV and MLV vectors; (2) compare different promoters in lentiviral vectors for efficient gene expression in CD34+ cells; (3) test the efficacy of ribozymes delivered by the lentiviral vectors; (4) establish stable human packaging cell lines for lentiviral vectors.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: TREATMENT MODELS FOR PRIMARY AND CHRONIC HIV INFECTION**

  Principal Investigator & Institution: Walensky, Rochelle P.; Massachusetts General Hospital 55 Fruit St Boston, MA 02114

  Timing: Fiscal Year 2001; Project Start 01-MAY-2001; Project End 30-APR-2006

  Summary: (provided by the applicant): Primary **Human Immunodeficiency Virus** (HIV) infection is the period of high-level viremia associated with initial acquisition of HIV, which is followed by chronic HIV infection. Clinical studies exploring the optimal management of patients with both primary and chronic HIV infection generally report short-term surrogate markers such as CD4 cell count or HIV plasma RNA rather than clinical outcomes. Disease simulation models are particularly useful for incorporating clinical trial results to assist in making long-term management decisions. A major strength of decision modeling in HIV is the ability to include up-to-date data on treatment efficacy into models to estimate outcomes such as life expectancy, quality of life, and costs of care. Using a detailed simulation model of HIV infection, the Cost-Effectiveness of Preventing AIDS Complications (CEPAC) group has focused on late-stage HIV clinical management. Using the CEPAC model as the basis for this research, this proposal will accomplish four specific aims: 1) to incorporate data on primary HIV infection and viral replicative fitness into the CEPAC model. 2) To project the impact of early highly active antiretroviral therapy for primary HIV infection on life expectancy, quality of life and costs of care using both a pilot simulation model and the CEPAC model. 3) To estimate at what prevalence of primary HIV infection it would be beneficial to screen episodic-care patients, who present with a viral syndrome, for primary HIV infection using an HIV plasma RNA test. 4) To assess the impact of changes in antiretroviral-induced diminished HIV replicative capacity on optimal treatment strategies for chronic infection. This work will provide insight into the ideal antiretroviral management of both primary and chronic HIV infection, a major goal of the Office of AIDS Research. A diverse team of mentors with expertise in infectious disease, clinical epidemiology, and disease modeling will provide Dr. Rochelle Walensky with a firm basis for career development as an independent, patient-oriented clinical researcher at the interface of these critical areas.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: UNCOVENTIONAL VECTORS FOR CODON-OPTIMIZED HIV ANTIGENS**

  Principal Investigator & Institution: Gambotto, Andrea; Assistant Professor; Surgery; University of Pittsburgh at Pittsburgh 350 Thackeray Hall Pittsburgh, PA 15260

  Timing: Fiscal Year 2002; Project Start 15-SEP-2002; Project End 31-AUG-2004

  Summary: (provided by applicant): In order to develop a vaccination strategy for stimulating the immune response against **Human Immunodeficiency Virus** (HIV), we

propose to construct adenoviral vectors based on serotypes 26, 33 and 35 encoding immunogenic proteins involved in HIV infection. We and other groups have demonstrated previously in murine and non human primate models that direct vaccination with recombinant adenovirus (rAd) type 5 encoding a variety of target antigens elicits strong specific immune responses against the transgene products (see Appendix 1-4). Currently, a major limitation to rAd immunization strategies in humans is the preexistence of neutralizing antibodies directed against the most prevalent strains of the virus. A second hurdle towards the development of an effective anti-HIV DNA vaccine has been the poor expression level of HIV-encoded proteins in transduced eukaryotic cells. Interestingly, however, preliminary studies conducted in Asian and North American populations have revealed that less than 10% of tested individuals have neutralizing antibodies against adenovirus serotypes 26, 33 or 35. Moreover, we and others have been able to optimize the codon of SIV and HIV antigenic sequences, resulting in high level expression in eukaryotic cells. Hence, we hypothesize that the current technical limitations of using adenovirus type 5-based live vaccine vectors may be overcome by implementing constructs based on "unconventional" recombinant adenoviral subtypes that integrate codon-optimized HIV antigen cDNAs. We also speculate that these studies should lead to more effective vaccination strategies designed to treat acquired immunodeficency disorders.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: VIRAL LOAD AND IMMUNE ACTIVATION MARKERS**

  Principal Investigator & Institution: Mcarthur, Justin C.; Professor of Neurology; Children's Memorial Hospital (Chicago) Chicago, IL 606143394

  Timing: Fiscal Year 2001

  Summary: AIDS is associated with a marked cognitive and motor dysfunction, termed HIV-associated dementia, in up to 20% of individuals. The introduction of potent combination antiretroviral therapy has reduced deaths from AIDS, and improved immunodeficiency in many. However, the impact of these therapies on neurological disease has only been studied to a limited extent; and the incidence and progression of dementia among injection drug users remains uncertain. Less severe cognitive impairment, termed minor HIV-associated cognitive/motor disorder has been less extensively studied and its prognosis and progression remain undefined. The progression of HIV-associated dementia can be variable, and some patients have rapid progression after diagnosis of dementia. The determinants of this variability remain unknown, but if defined, might be modified to affect disease progression. The relationship between HIV-1 viral load in the peripheral compartment and the brain has not been explored with currently available sensitive assays of viral load. A number of critical questions relating to viral load remain unanswered. First, does increasing systemic viral burden in the later stages of HIV infection "drive" the development of neurologic disease. Second, is the amount of virus in the CSF reflective of virus production in the brain, or in the periphery?, and does it changes with antiretroviral therapy?. Finally, how is CNS immune activation, which is a critical component of CNS pathophysiology, related to blood and CSF viral load. We plan a systematic evaluation of virological and immunological markers in CSF in patients with HIV-associated cognitive/motor dysfunction to determine their utility as predictive markers for neurological disease progression. We have the following aims: 1) to determine the prognostic significance of CSF levels of HIV-1 RNA copy number for neurologic progression in a cohort of HIV-seropositive individuals; 2) to determine the dynamics of changes in HIV-1 RNA levels in plasma and CSF after initiation of combination

antiretroviral therapy; 3) to determine the relationship between HIV RNA copy number in brain, plasma, and CSF and markers of immune activation. IF CSF HIV load measurement is validated as a predictive marker of neurological progression, individuals at high risk for neurological deterioration could be selected for aggressive neurologically-directed therapies.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: VIRAL LOAD IN CELLULAR SUBCOMPARTMENTS FOLLOWING HAART**

  Principal Investigator & Institution: Asmuth, David M.; Internal Medicine; University of Texas Medical Br Galveston 301 University Blvd Galveston, TX 77555

  Timing: Fiscal Year 2001; Project Start 30-SEP-1999; Project End 02-JUN-2002

  Summary: Combination therapy with new agents against the **human immunodeficiency virus** (HIV) has dramatically slowed the progression to AIDS and death. These treatments are capable of reducing virus in the peripheral blood to below the levels of detection. However, reservoirs of viral replication persist, largely in lymph node tissue, that potentially reignite HIV replication. This project examines serial samples from excisional cervical lymph node tissue and peripheral blood in patients before and during highly active therapy. It will establish a mechanism for obtaining samples from several compartments simultaneously and reproducibly. The combination of state-of-the-art flow cytometry and cell sorting, isothermal Nucleic Acid Sequence Based Assay (NASBA) HIV quantitation, and a non-radioisotope in situ hybridization technique will be used to measure cellular subtype (lymphocyte versus monocyte/macrophage) HIV viral load in these samples. Patterns of changes in cellular subcompartments across time and between the compartments will be examined in an attempt to understand treatment failure and to provide new insights into the design of more effective treatment strategies. Patients who fall into the unique category of response - coined Discordant Responders (the 15 - 20 percent of patients who experience a rise in both viral load and CD4 count in response to therapy yet appear to reap the same clinical benefits as patients with the expected virologic response), will also be studied in order to determine pathophysiologic parameters of response to therapy that go beyond absorption, adherence, and phenotypic/genotypic resistance patterns as explanations for virologic response. This project will investigate the role of viral tropism and the specific activity of treatment regimens in specific lymphoid cell subtypes, including terminally differentiated versus dividing cells. A further characterization of the subset of infected cells represents the future direction of this project, namely analysis of cell cycle by cyclins A, B and D, and will provide unique insights in how specific treatment regimens might affect total viral load. However, the paramount goal of this research career award is to provide the PI with didactic training overlapping a closely supervised period of clinical investigation leading to establishment of the PI as a viable independent researcher.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: VIRAL/CELLULAR DYNAMICS IN SHIV INFECTED LYMPHOID TISSUE**

  Principal Investigator & Institution: Bucy, R. Pat.; Professor; Pathology; University of Alabama at Birmingham Uab Station Birmingham, AL 35294

  Timing: Fiscal Year 2001; Project Start 01-JUN-1999; Project End 31-MAY-2004

Summary: The overall goal of this application is to determine the quantitative characteristics of in vivo SHIV replication in the Rhesus Macaque, as a model of human HIV-1 infection. Since viral replication occurs in lymphoid tissue, which is extremely difficult to obtain in a clinical setting, the focus is on detailed analysis of viral and cellular dynamics in multiple lymphoid tissues obtained at necropsy from infected non-human primates. The first hypothesis is that different lymphoid tissues (lymph nodes, spleen, and intestine) have unique quantitative patterns of SHIV replication. We will determine the quantitative contribution of viral replication in these compartments to the total body load of virus, as reflected with the plasma SHIV RNA. The second hypothesis is that the lineage of cells that support SHIV replication is distinctive, with infected macrophages (Mphi) supporting chronic infection that generates a higher frequency of infected T cells in the local histologic microenvironment. The third hypothesis is that a population of latently infected T cells exists in SHIV infection and contributes to persistent viral replication in animals treated with antiretroviral drugs. Each of these hypotheses will be critically examined in SHIV infected animals in three distinct stages of infection: 1) steady state infection, 2) acute infection, and 3) the response to a powerful antiretroviral agent PMPA. The approach is to perform a multiparameter analysis of in vivo viral and cellular dynamics in multiple tissue compartments. Specimens of blood, spleen, thymus, all available lymph nodes, multiple portions of gut, bone marrow, lung, liver, and brain will be examined by a standard set of quantitative analyses.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: WOMEN AND INFANT TRANSMISSION STUDY**

  Principal Investigator & Institution: Landesman, Sheldon H.; Professor; Medicine; Suny Downstate Medical Center 450 Clarkson Ave New York, NY 11203

  Timing: Fiscal Year 2001; Project Start 30-SEP-1997; Project End 31-AUG-2006

  Summary: (provided by applicant): The SUNY/HSCB site proposes to recruit approximately 50 pregnant HIV infected women per year into the WITS. Our site has a track record going back fifteen years of identifying, recruiting and retaining such a population into longitudinal studies. Four senior researchers, Drs. Landesman, Handelsman, Minkoff and Hittelman, who together have 60 years of experience in HIV cohort studies, direct our program. Our site, invited into the WITS in 1991, has averaged 46 new study entrants per year. Enrolled women who deliver have a retention rate of 92% at 6 months and 87% at the one-year time point, which is the time they would complete the study in the WITS4 protocol. Of children old enough, 97% continued on study long enough to determine their HIV status. Of these children, 94% of those eligible continue through 1 year and 94 % of these children continue through 2 years. Averaging 922 visits per year, we have missed only 11 percent of study visits and have submitted 99 % of expected forms. Our site has an extensive array of 21 integrated research and service programs which serve the needs of over 2,000 HIV infected patients. The extensive linkages within the community and with other hospitals allow us to easily recruit from the 275 to 300 HIV infected pregnant women giving birth in Brooklyn each year. The SUNY/HSCB site has arranged for all virology/immunology work to be performed at Dr. Jane Pitt?s laboratory at the Columbia Presbyterian WITS site. Dr. Pitt?s laboratory has an outstanding record in performing WITS required assays and is ACTG certified. Scientifically, Drs. Landesman, Handelsman, Minkoff and Hittelman are widely published in the field of perinatal HIV disease. Dr. Landesman was the first author on the 1996 WITS paper "Obstetrical factors and the transmission of **Human Immunodeficiency virus** type 1 from mother to Child". Dr. Minkoff is the premier

obstetrician in the country for women with HIV disease. Both Drs. Handelsman and Minkoff served on the New York State AIDS Institute Committee on Perinatal Transmission. Dr. Handelsman served as a special advisor to the US Food and Drug Administration in the area of perinatal transmission.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

E-Journals: PubMed Central[3]

PubMed Central (PMC) is a digital archive of life sciences journal literature developed and managed by the National Center for Biotechnology Information (NCBI) at the U.S. National Library of Medicine (NLM).[4] Access to this growing archive of e-journals is free and unrestricted.[5] To search, go to **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Pmc**, and type "human immunodeficiency virus" (or synonyms) into the search box. This search gives you access to full-text articles. The following is a sample of items found for human immunodeficiency virus in the PubMed Central database:

- **2'5'-Bis-O-(tert-Butyldimethylsilyl)-3'-Spiro-5''-(4''-Amino- 1'',2''-Oxathiole-2'',2''-Dioxide)Pyrimidine (TSAO) Nucleoside Analogues: Highly Selective Inhibitors of Human Immunodeficiency Virus Type 1 that are Targeted at the Viral Reverse Transcriptase.** by Balzarini J, Perez-Perez M, San-Felix A, Schols D, Perno C, Vandamme A, Camarasa M, Clercq ED. 1992 May 15;
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- **4[prime prime or minute]-Ethynyl Nucleoside Analogs: Potent Inhibitors of Multidrug-Resistant Human Immunodeficiency Virus Variants In Vitro.** by Kodama EI, Kohgo S, Kitano K, Machida H, Gatanaga H, Shigeta S, Matsuoka M, Ohrui H, Mitsuya H. 2001 May;
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- **A Bipartite Membrane-Binding Signal in the Human Immunodeficiency Virus Type 1 Matrix Protein Is Required for the Proteolytic Processing of Gag Precursors in a Cell Type-Dependent Manner.** by Lee YM, Tian CJ, Yu XF. 1998 Nov;
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[3] Adapted from the National Library of Medicine: **http://www.pubmedcentral.nih.gov/about/intro.html**.

[4] With PubMed Central, NCBI is taking the lead in preservation and maintenance of open access to electronic literature, just as NLM has done for decades with printed biomedical literature. PubMed Central aims to become a world-class library of the digital age.

[5] The value of PubMed Central, in addition to its role as an archive, lies in the availability of data from diverse sources stored in a common format in a single repository. Many journals already have online publishing operations, and there is a growing tendency to publish material online only, to the exclusion of print.

- **A Conformation-Specific Monoclonal Antibody Reacting with Fusion-Active gp41 from the Human Immunodeficiency Virus Type 1 Envelope Glycoprotein.** by Jiang S, Lin K, Lu M. 1998 Dec;
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- **A Family of Insertion Mutations between Codons 67 and 70 of Human Immunodeficiency Virus Type 1 Reverse Transcriptase Confer Multinucleoside Analog Resistance.** by Larder BA, Bloor S, Kemp SD, Hertogs K, Desmet RL, Miller V, Sturmer M, Staszewski S, Ren J, Stammers DK, Stuart DI, Pauwels R. 1999 Aug;
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- **A Global Neutralization Resistance Phenotype of Human Immunodeficiency Virus Type 1 Is Determined by Distinct Mechanisms Mediating Enhanced Infectivity and Conformational Change of the Envelope Complex.** by Park EJ, Gorny MK, Zolla-Pazner S, Quinnan GV Jr. 2000 May 1;
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- **A Group of V3 Sequences from Human Immunodeficiency Virus Type 1 Subtype E Non-Syncytium-Inducing, CCR5-Using Variants Are Resistant to Positive Selection Pressure.** by Shiino T, Kato K, Kodaka N, Miyakuni T, Takebe Y, Sato H. 2000 Feb 1;
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- **A Novel Human Immunodeficiency Virus Type 1 Reverse Transcriptase Mutational Pattern Confers Phenotypic Lamivudine Resistance in the Absence of Mutation 184V.** by Hertogs K, Bloor S, De Vroey V, van den Eynde C, Dehertogh P, van Cauwenberge A, Sturmer M, Alcorn T, Wegner S, van Houtte M, Miller V, Larder BA. 2000 Mar;
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- **A Pathogenic Threshold of Virus Load Defined in Simian Immunodeficiency Virus- or Simian-Human Immunodeficiency Virus-Infected Macaques.** by Ten Haaft P, Verstrepen B, Uberla K, Rosenwirth B, Heeney J. 1998 Dec; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=external&artid=110614
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- **A decontamination and sterilization protocol employed during reuse of cardiac electrophysiology catheters inactivates human immunodeficiency virus.**
  Author(s): Druce JD, Russell JS, Birch CJ, Yates LA, Harper RW, Smolich JJ.
  Source: Infection Control and Hospital Epidemiology : the Official Journal of the Society of Hospital Epidemiologists of America. 2003 March; 24(3): 184-90.
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  Author(s): Geffin R, Hutto C, Andrew C, Scott GB.
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  Author(s): Ostrowski SR, Gerstoft J, Pedersen BK, Ullum H.
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  Author(s): Hoffman NG, Seillier-Moiseiwitsch F, Ahn J, Walker JM, Swanstrom R.
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  Author(s): Des Jarlais DC, Diaz T, Perlis T, Vlahov D, Maslow C, Latka M, Rockwell R, Edwards V, Friedman SR, Monterroso E, Williams I, Garfein RS.
  Source: American Journal of Epidemiology. 2003 March 1; 157(5): 467-71.
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- **Variable prediction of antiretroviral treatment outcome by different systems for interpreting genotypic human immunodeficiency virus type 1 drug resistance.**
  Author(s): De Luca A, Cingolani A, Di Giambenedetto S, Trotta MP, Baldini F, Rizzo MG, Bertoli A, Liuzzi G, Narciso P, Murri R, Ammassari A, Perno CF, Antinori A.
  Source: The Journal of Infectious Diseases. 2003 June 15; 187(12): 1934-43. Epub 2003 May 22.
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  Author(s): Carrasco DA, Trizna Z, Colome-Grimmer M, Tyring SK.
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  Author(s): Fagan WA, Collins PC, Pulitzer DR.
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  Author(s): Chakraborty R, Rees G, Bourboulia D, Cross AM, Dixon JR, D'Agostino A, Musoke R, Boshoff C, Rowland-Jones SL, Klenerman P.
  Source: Clinical Infectious Diseases : an Official Publication of the Infectious Diseases Society of America. 2003 April 1; 36(7): 922-4. Epub 2003 March 19.
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  Author(s): Martinez-Picado J, Frost SD, Izquierdo N, Morales-Lopetegi K, Marfil S, Puig T, Cabrera C, Clotet B, Ruiz L.
  Source: Journal of Virology. 2002 December; 76(23): 12344-8.
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- **Virion-bound ICAM-1 and activated LFA-1: a combination of factors conferring resistance to neutralization by sera from human immunodeficiency virus type 1-infected individuals independently of the disease status and phase.**
  Author(s): Losier M, Fortin JF, Cantin R, Bergeron MG, Tremblay MJ.
  Source: Clinical Immunology (Orlando, Fla.). 2003 August; 108(2): 111-8.
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  Author(s): Carr A.
  Source: Jama : the Journal of the American Medical Association. 2002 November 20; 288(19): 2405-6; Author Reply 2406.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12435249&dopt=Abstract

- **Virtual inhibitory quotient predicts response to ritonavir boosting of indinavir-based therapy in human immunodeficiency virus-infected patients with ongoing viremia.**
  Author(s): Shulman N, Zolopa A, Havlir D, Hsu A, Renz C, Boller S, Jiang P, Rode R, Gallant J, Race E, Kempf DJ, Sun E.
  Source: Antimicrobial Agents and Chemotherapy. 2002 December; 46(12): 3907-16.
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- **Virus load and cytolitic responses in human immunodeficiency virus infection: what is cause and what is effect.**
  Author(s): Benito JM, Lopez M, Soriano V.
  Source: The Journal of Infectious Diseases. 2003 September 1; 188(5): 794-5; Author Reply 795-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12934198&dopt=Abstract

- **Virus load during primary Human Immunodeficiency Virus (HIV) type 1 infection is related to the severity of acute HIV illness in Kenyan women.**
  Author(s): Lavreys L, Baeten JM, Overbaugh J, Panteleeff DD, Chohan BH, Richardson BA, Mandaliya K, Ndinya-Achola JO, Kreiss JK.
  Source: Clinical Infectious Diseases : an Official Publication of the Infectious Diseases Society of America. 2002 July 1; 35(1): 77-81. Epub 2002 June 03.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12060878&dopt=Abstract

- **Virus population homogenization following acute human immunodeficiency virus type 1 infection.**
  Author(s): Learn GH, Muthui D, Brodie SJ, Zhu T, Diem K, Mullins JI, Corey L.
  Source: Journal of Virology. 2002 December; 76(23): 11953-9.
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- **Visceral leishmaniasis caused by Leishmania (Viannia) braziliensis in a patient infected with human immunodeficiency virus.**
  Author(s): Silva ES, Pacheco RS, Gontijo CM, Carvalho IR, Brazil RP.
  Source: Revista Do Instituto De Medicina Tropical De Sao Paulo. 2002 May-June; 44(3): 145-9.
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- **Vitamin A supplementation and human immunodeficiency virus type 1 shedding in women: results of a randomized clinical trial.**
  Author(s): Baeten JM, McClelland RS, Overbaugh J, Richardson BA, Emery S, Lavreys L, Mandaliya K, Bankson DD, Ndinya-Achola JO, Bwayo JJ, Kreiss JK.
  Source: The Journal of Infectious Diseases. 2002 April 15; 185(8): 1187-91. Epub 2002 March 22.
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- **Weight loss and wasting in patients infected with human immunodeficiency virus.**
  Author(s): Grinspoon S, Mulligan K; Department of Health and Human Services Working Group on the Prevention and Treatment of Wasting and Weight Loss.
  Source: Clinical Infectious Diseases : an Official Publication of the Infectious Diseases Society of America. 2003 April 1; 36(Suppl 2): S69-78.
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- **What constitutes efficacy for a human immunodeficiency virus vaccine that ameliorates viremia: issues involving surrogate end points in phase 3 trials.**
  Author(s): Gilbert PB, DeGruttola VG, Hudgens MG, Self SG, Hammer SM, Corey L.
  Source: The Journal of Infectious Diseases. 2003 July 15; 188(2): 179-93. Epub 2003 Jul 01.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12854072&dopt=Abstract

- **Whole-blood agglutination assay for on-site detection of human immunodeficiency virus infection.**
  Author(s): Gupta A, Chaudhary VK.
  Source: Journal of Clinical Microbiology. 2003 July; 41(7): 2814-21.
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- **Wild-type levels of nuclear localization and human immunodeficiency virus type 1 replication in the absence of the central DNA flap.**
  Author(s): Limon A, Nakajima N, Lu R, Ghory HZ, Engelman A.
  Source: Journal of Virology. 2002 December; 76(23): 12078-86.
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- **Xanthomas and hyperlipidemia in a human immunodeficiency virus-infected child receivng highly active antiretroviral therapy.**
  Author(s): Babl FE, Regan AM, Pelton SI.
  Source: The Pediatric Infectious Disease Journal. 2002 March; 21(3): 259-60.
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- **Yeast-derived human immunodeficiency virus type 1 p55(gag) virus-like particles activate dendritic cells (DCs) and induce perforin expression in Gag-specific CD8(+) T cells by cross-presentation of DCs.**
  Author(s): Tsunetsugu-Yokota Y, Morikawa Y, Isogai M, Kawana-Tachikawa A, Odawara T, Nakamura T, Grassi F, Autran B, Iwamoto A.
  Source: Journal of Virology. 2003 October; 77(19): 10250-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12970409&dopt=Abstract

- **Zidovudine and perinatal human immunodeficiency virus type 1 transmission: a population-based approach.**
  Author(s): Harris NS, Thompson SJ, Ball R, Hussey J, Sy F.
  Source: Pediatrics. 2002 April; 109(4): E60.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11927733&dopt=Abstract

CHAPTER 2. NUTRITION AND HUMAN IMMUNODEFICIENCY VIRUS

Overview

In this chapter, we will show you how to find studies dedicated specifically to nutrition and human immunodeficiency virus.

Finding Nutrition Studies on Human Immunodeficiency Virus

The National Institutes of Health's Office of Dietary Supplements (ODS) offers a searchable bibliographic database called the IBIDS (International Bibliographic Information on Dietary Supplements; National Institutes of Health, Building 31, Room 1B29, 31 Center Drive, MSC 2086, Bethesda, Maryland 20892-2086, Tel: 301-435-2920, Fax: 301-480-1845, E-mail: ods@nih.gov). The IBIDS contains over 460,000 scientific citations and summaries about dietary supplements and nutrition as well as references to published international, scientific literature on dietary supplements such as vitamins, minerals, and botanicals.[7] The IBIDS includes references and citations to both human and animal research studies.

As a service of the ODS, access to the IBIDS database is available free of charge at the following Web address: **http://ods.od.nih.gov/databases/ibids.html**. After entering the search area, you have three choices: (1) IBIDS Consumer Database, (2) Full IBIDS Database, or (3) Peer Reviewed Citations Only.

Now that you have selected a database, click on the "Advanced" tab. An advanced search allows you to retrieve up to 100 fully explained references in a comprehensive format. Type "human immunodeficiency virus" (or synonyms) into the search box, and click "Go." To narrow the search, you can also select the "Title" field.

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[7] Adapted from **http://ods.od.nih.gov**. IBIDS is produced by the Office of Dietary Supplements (ODS) at the National Institutes of Health to assist the public, healthcare providers, educators, and researchers in locating credible, scientific information on dietary supplements. IBIDS was developed and will be maintained through an interagency partnership with the Food and Nutrition Information Center of the National Agricultural Library, U.S. Department of Agriculture.

The following is a typical result when searching for recently indexed consumer information on human immunodeficiency virus:

- **Cellular antioxidant status and human immunodeficiency virus replication.**
  Source: Baker, D.H. Nutr-Rev. New York, N.Y. : Springer-Verlag New York Inc. January 1992. volume 50 (1) page 15-18. 0029-6643
- **Interactions between nutrition and infection with human immunodeficiency virus.**
  Author(s): Department of Community Health, Tufts University School of Medicine, Boston, MA 02111.
  Source: Gorbach, S L Knox, T A Roubenoff, R Nutr-Revolume 1993 August; 51(8): 226-34 0029-6643

The following information is typical of that found when using the "Full IBIDS Database" to search for "human immunodeficiency virus" (or a synonym):

- **2001 USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus.**
  Source: Infect-Dis-Obstet-Gynecol. 2002; 10(1): 3-64 1064-7449
- **A cyclic dodecapeptide-multiple-antigen peptide conjugate from the undecapeptidyl arch (from Arg(168) to Cys(178)) of extracellular loop 2 in CCR5 as a novel human immunodeficiency virus type 1 vaccine.**
  Author(s): Department of Biochemistry, Faculty of Pharmaceutical Sciences, Kumamoto University, Kumamoto 862-0973, Japan.
  Source: Misumi, S Nakajima, R Takamune, N Shoji, S J-Virol. 2001 December; 75(23): 11614-20 0022-538X
- **A human immunodeficiency virus type 1 pol gene-derived sequence (cPPT/CTS) increases the efficiency of transduction of human nondividing monocytes and T lymphocytes by lentiviral vectors.**
  Author(s): Istituto di Ricerche Farmacologiche Mario Negri, 20157 Milan, Italy.
  Source: Manganini, M Serafini, M Bambacioni, F Casati, C Erba, E Follenzi, A Naldini, L Bernasconi, S Gaipa, G Rambaldi, A Biondi, A Golay, J Introna, M Hum-Gene-Ther. 2002 October 10; 13(15): 1793-807 1043-0342
- **A novel short peptide is a specific inhibitor of the human immunodeficiency virus type 1 integrase.**
  Author(s): IFR 66, Pathologies Infectieuses: Aspects Biologiques et Therapeutiques, Bordeaux, France. vaea.desoultrait@reger.u-bordeaux2.fr
  Source: de Soultrait, Vaea Richard Caumont, Anne Parissi, Vincent Morellet, Nelly Ventura, Michel Lenoir, Christine Litvak, Simon Fournier, Michel Roques, Bernard J-Mol-Biol. 2002 April 19; 318(1): 45-58 0022-2836
- **A soluble factor(s) secreted from CD8(+) T lymphocytes inhibits human immunodeficiency virus type 1 replication through STAT1 activation.**
  Author(s): Weill Medical College of Cornell University, Department of Medicine, Mount Sinai School of Medicine, Public Health Research Institute, New York, New York 10021, USA.
  Source: Chang, Theresa Li Yun Mosoian, Arevik Pine, Richard Klotman, Mary E Moore, John P J-Virol. 2002 January; 76(2): 569-81 0022-538X
- **Activation of human immunodeficiency virus transcription in T cells revisited: NF-kappaB p65 stimulates transcriptional elongation.**
  Author(s): Medical Research Council Laboratory of Molecular Biology, Cambridge CB2 2QH, United Kingdom.

Source: West, M J Lowe, A D Karn, J J-Virol. 2001 September; 75(18): 8524-37 0022-538X

- **Antiviral activity of Rwandan medicinal plants against human immunodeficiency virus type-1 (HIV-1).**
  Author(s): Faculty of Pharmaceutical Sciences, University of Antwerp, Belgium.
  Source: Cos, P Hermans, N De, B T Apers, S Sindambiwe, J B Witvrouw, M De, C E Vanden, B D Pieters, L Vlietinck, A J Phytomedicine. 2002 January; 9(1): 62-8 0944-7113

- **Ascalin, a new anti-fungal peptide with human immunodeficiency virus type 1 reverse transcriptase-inhibiting activity from shallot bulbs.**
  Author(s): Department of Microbiology, College of Biological Science, China Agricultural University, Beijing, China.
  Source: Wang, H X Ng, T B Peptides. 2002 June; 23(6): 1025-9 0196-9781

- **Calcineurin-dependent mitochondrial disturbances in calcium-induced apoptosis of human immunodeficiency virus gp160-expressing CD4+ cells.**
  Author(s): Department of Virology, Medical Institute of Bioregulation, Kyushu University, Fukuoka 812-8582, Japan.
  Source: Sasaki, Masafumi Miyazaki, Kozo Koga, Yasuhiro Kimura, Genki Nomoto, Kikuo Yoshida, Hiroki J-Virol. 2002 January; 76(1): 416-20 0022-538X

- **Ciliochoroidal effusion and pulmonary hypertension in a patient with human immunodeficiency virus infection.**
  Author(s): W.K. Kellogg Eye Center, Department of Ophthalmology and Visual Sciences, University of Michigan School of Medicine, Ann Arbor, MI 48105, USA.
  Source: Dawson, D G Johnson, M W Retina. 2001; 21(6): 672-4 0275-004X

- **Cobalamin deficiency in patients infected with the human immunodeficiency virus.**
  Author(s): Department of Hematology, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain.
  Source: Remacha, A F Cadafalch, J Semin-Hematol. 1999 January; 36(1): 75-87 0037-1963

- **Conserved functional organization of the human immunodeficiency virus type 1 and visna virus Rev proteins.**
  Source: Tiley, L.S. Malim, M.H. Cullen, B.R. J-Virol. Washington, D.C. : American Society for Microbiology. July 1991. volume 65 (7) page 3877-3881. 0022-538X

- **Critical chemical features in trans-acting-responsive RNA are required for interaction with human immunodeficiency virus type 1 Tat protein.**
  Author(s): Allelix Biopharmaceuticals Inc., Mississauga, Ontario, Canada.
  Source: Sumner Smith, M Roy, S Barnett, R Reid, L S Kuperman, R Delling, U Sonenberg, N J-Virol. 1991 October; 65(10): 5196-202 0022-538X

- **Effects of prostratin on T-cell activation and human immunodeficiency virus latency.**
  Author(s): Department of Medicine, UCLA School of Medicine, and UCLA AIDS Institute, 90095-1678, USA.
  Source: Korin, Yael D Brooks, David G Brown, Stephen Korotzer, Andrew Zack, Jerome A J-Virol. 2002 August; 76(16): 8118-23 0022-538X

- **Elevated levels of tumor necrosis factor alpha (TNF-alpha) in human immunodeficiency virus type 1-transgenic mice: prevention of death by antibody to TNF-alpha.**
  Author(s): Experimental Medicine Section, Oral Infection and Immunity Branch, National Institute of Dental and Craniofacial Research, National Institutes of Health, Bethesda, Maryland 20892, USA.
  Source: De, S K Devadas, K Notkins, A L J-Virol. 2002 November; 76(22): 11710-4 0022-538X

- **Evaluation of natural products as inhibitors of human immunodeficiency virus (HIV) reverse transcriptase.**
  Source: Tan, G.T. Pezzuto, J.M. Kinghorn, A.D. Plant-Med. Stuttgart, W. Ger. : Georg Thieme Verlag. December 1990. volume 56 (6) page 504. 0032-0943
- **Examination of lectins, polysaccharopeptide, polysaccharide, alkaloid, coumarin and trypsin inhibitors for inhibitory activity against human immunodeficiency virus reverse transcriptase and glycohydrolases.**
  Source: Wang, H.X. Ng, T.B. Planta-med. Stuttgart : Georg Thieme Verlag,. October 2001. volume 67 (7) page 669-672. 0032-0943
- **Fine mapping of the interaction of neutralizing and nonneutralizing monoclonal antibodies with the CD4 binding site of human immunodeficiency virus type 1 gp120.**
  Author(s): Department of Immunology, The Scripps Research Institute, La Jolla, California 92037, USA.
  Source: Pantophlet, R Ollmann Saphire, E Poignard, P Parren, P W Wilson, I A Burton, D R J-Virol. 2003 January; 77(1): 642-58 0022-538X
- **Human immunodeficiency virus type 1 uses lipid raft-colocalized CD4 and chemokine receptors for productive entry into CD4(+) T cells.**
  Author(s): Oncology Center, The Johns Hopkins University School of Medicine, Baltimore, Maryland 21231, USA. wpopik@jhmi.edu
  Source: Popik, WaldeMarch Alce, Timothy M Au, Wei Chun J-Virol. 2002 May; 76(10): 4709-22 0022-538X
- **Identification of lentivirus Tat functional domains through generation of equine infectious anemia virus/human immunodeficiency virus type 1 tat gene chimeras.**
  Source: Carroll, R. Martarano, L. Derse, D. J-Virol. Washington, D.C. : American Society for Microbiology. July 1991. volume 65 (7) page 3460-3467. 0022-538X
- **In vivo emergence of drug-resistant mutations at less than 50 HIV-1 RNA copies/mL that are maintained at viral rebound in longitudinal plasma samples from human immunodeficiency virus type-1-infected patients on highly active antiretroviral therapy.**
  Author(s): Department of Laboratory Medicine, University of California San Francisco, Clinical Laboratories at San Francisco General Hospital, San Francisco, California, USA. elbeik@itsa.ucsf.edu
  Source: Elbeik, T Hoo, B S Campodonico, M E Dileanis, J Fay, F F Bortolozzi, R L Benetti, M S Fay, O H Marlowe, N Petrauskene, O Chernoff, D Smith, L Ng, V L J-Hum-Virol. 2001 Nov-December; 4(6): 317-28 1090-9508
- **Independent segregation of human immunodeficiency virus type 1 Gag protein complexes and lipid rafts.**
  Author(s): Departments of Pediatrics, Microbiology, and Immunology, Vanderbilt University School of Medicine, Nashville, Tennessee 37232-2581, USA.
  Source: Ding, L Derdowski, A Wang, J J Spearman, P J-Virol. 2003 February; 77(3): 1916-26 0022-538X
- **Indinavir-induced cholelithiasis in a patient infected with human immunodeficiency virus.**
  Author(s): Unite de Maladies Infectieuses, Centre Hospitalier Universitaire Cote-de-Nacre, 14033 Caen, France. verdon-r@chu-caen.fr
  Source: Verdon, Renaud Daudon, Michel Albessard, Francoise Brefort, Jean Louis Bazin, Claude Clin-Infect-Dis. 2002 September 1; 35(5): e57-9 1537-6591

- **Inhibition of cytopathic effect of human immunodeficiency virus type-1 by various phorbol derivatives.**
  Author(s): Institute of Natural Medicine, Toyama Medical and Pharmaceutical University, Sugitani, Japan.
  Source: El Mekkawy, S Meselhy, M R Abdel Hafez, A A Nakamura, N Hattori, M Kawahata, T Otake, T Chem-Pharm-Bull-(Tokyo). 2002 April; 50(4): 523-9 0009-2363
- **Inhibitory effects of triterpene-azidothymidine conjugates on proliferation of human immunodeficiency virus type 1 and its protease.**
  Author(s): Institute of Natural Medicine, Toyama Medical and Pharmaceutical University, Sugitani, Japan.
  Source: Ma, C M Nakamura, N Hattori, M Kawahata, T Otake, T Chem-Pharm-Bull-(Tokyo). 2002 June; 50(6): 877-80 0009-2363
- **Iron supplementation during human immunodeficiency virus infection: a double-edged sword?**
  Author(s): Department of Ophthalmology, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA.
  Source: Clark, T D Semba, R D Med-Hypotheses. 2001 October; 57(4): 476-9 0306-9877
- **National Cancer Institute intramural research on human immunodeficiency virus inhibitory and antitumor plant natural products.**
  Source: Cardellina, J.H. II. Gustafson, K.R. Beutler, J.A. McKee, T.C. Hallock, Y.F. Fuller, R.W. Boyd, M.R. ACS-symp-ser. Washington, D.C. : American Chemical Society, 1974-. 1993. (534) page 218-227. 0097-6156
- **Natural killer-like T-cell lymphoma of the parotid in a patient infected with human immunodeficiency virus.**
  Author(s): Department of Pathology, University of Florida College of Medicine, Gainesville, USA. cornf1@dca.net
  Source: Cornfield, Dennis B Papiez, Joseph S Lynch, James T Rimsza, Lisa M Arch-Pathol-Lab-Med. 2002 June; 126(6): 738-41 0003-9985
- **Nevirapine or lamivudine plus stavudine and indinavir: examples of 2-class versus 3-class regimens for the treatment of human immunodeficiency virus type 1.**
  Author(s): Service de Maladies Infectieuses et Tropicales, Hopital Bichat-Claude Bernard, Paris, France. odile.launay@avc.ap-hop-paris.fr
  Source: Launay, O Gerard, L Morand Joubert, L Flandre, P Guiramand Hugon, S Joly, V Peytavin, G Certain, A Levy, C Rivet, S Jacomet, C Aboulker, J P Yeni, P Clin-Infect-Dis. 2002 November 1; 35(9): 1096-105 1537-6591
- **Nuclear transport of human immunodeficiency virus type 1, visna virus, and equine infectious anemia virus rev proteins: identification of a family of transferable nuclear export signals.**
  Source: Meyer, B.E. Meinkoth, J.L. Malim, M.H. J-virol. Washington, D.C. : American Society for Microbiology. April 1996. volume 70 (4) page 2350-2359. 0022-538X
- **Positionally independent and exchangeable late budding functions of the Rous sarcoma virus and human immunodeficiency virus Gag proteins.**
  Source: Parent, L.J. Bennett, R.P. Craven, R.C. Nelle, T.D. Krishna, N.K. Bowzard, J.B. Wilson, C.B. Puffer, B.A. Montelaro, R.C. Wills, J.W. J-virol. Washington, D.C. : American Society for Microbiology. Sept 1995. volume 69 (9) page 5455-5460. 0022-538X

- **Protein phosphatase 2A enhances activation of human immunodeficiency virus type 1 by phorbol myristate acetate.**
  Author(s): Cellular and Molecular Biology Program. Division of Infectious Diseases, Department of Internal Medicine, University of Michigan Medical Center, Ann Arbor, Michigan 48109-0640, USA.
  Source: Faulkner, N E Lane, B R Bock, P J Markovitz, D M J-Virol. 2003 February; 77(3): 2276-81 0022-538X

- **Reduction of abdominal obesity in lipodystrophy associated with human immunodeficiency virus infection by means of diet and exercise: case report and proof of principle.**
  Author(s): Department of Community Health, Tufts University School of Medicine, and Jean Mayer US Department of Agriculture Human Nutrition Research Center, Boston, Massachusetts 02111 , USA. roubenoff@hnrc.tufts.edu
  Source: Roubenoff, Ronenn Schmitz, Heather Bairos, Lynn Layne, Jennifer Potts, Emily Cloutier, Gregory J Denry, Fabien Clin-Infect-Dis. 2002 February 1; 34(3): 390-3 1537-6591

- **Results of 2 years of treatment with protease-inhibitor--containing antiretroviral therapy in dutch children infected with human immunodeficiency virus type 1.**
  Author(s): Department of Pediatrics, Sophia Children's Hospital, 3015 GJ Rotterdam, The Netherlands.
  Source: van Rossum, A M Geelen, S P Hartwig, N G Wolfs, T F Weemaes, C M Scherpbier, H J van Lochem, E G Hop, W C Schutten, M Osterhaus, A D Burger, D M de Groot, R Clin-Infect-Dis. 2002 April 1; 34(7): 1008-16 1537-6591

- **Role of cholesterol in human immunodeficiency virus type 1 envelope protein-mediated fusion with host cells.**
  Author(s): Laboratory of Experimental and Computational Biology, Center for Cancer Research, National Cancer Institute-Frederick, National Institutes of Health, Frederick, Maryland 21702, USA.
  Source: Viard, M Parolini, I Sargiacomo, M Fecchi, K Ramoni, C Ablan, S Ruscetti, F W Wang, J M Blumenthal, R J-Virol. 2002 November; 76(22): 11584-95 0022-538X

- **Screening of South American plants against human immunodeficiency virus: preliminary fractionation of aqueous extract from Baccharis trinervis.**
  Author(s): Departamento de Farmacologia, Facultad de Farmacia, Universidad Complutense, Madrid, Spain.
  Source: Sanchez Palomino, S Abad, M J Bedoya, L M Garcia, J Gonzales, E Chiriboga, X Bermejo, P Alcami, J Biol-Pharm-Bull. 2002 September; 25(9): 1147-50 0918-6158

- **Shoots of rosemary and sage cultured in vitro as possible sources of carnosic acid, a reported inhibitor of the human immunodeficiency virus protease.**
  Source: Caruso, J.L. Winget, G.D. McGinnis, J. Jayasimhulu, K. Phytochemicals and health proceedings, tenth annual Penn State Symposium in Plant Physiology, May 18-20, 1995 / Penn State Symposium in Plant Physiology. Rockville, Md. : American Society of Plant Physiologists, c1995.. page 290-291. ISBN: 0943088321

- **Soybean saponin and isoflavonoids: structure and antiviral activity against human immunodeficiency virus in vitro.**
  Source: Okubo, K. Kudou, S. Uchida, T. Yoshiki, Y. Yoshikoshi, M. Tonomura, M. ACS-symp-ser. Washington, D.C. : American Chemical Society, 1974-. 1994. (546) page 330-339. 0097-6156

- **Structure of human immunodeficiency virus type 1 Vpr(34-51) peptide in micelle containing aqueous solution.**
  Author(s): Lehrstuhl fur Biopolymere, Universitat Bayreuth, Germany.
  Source: Engler, Andrea Stangler, Thomas Willbold, Dieter Eur-J-Biochem. 2002 July; 269(13): 3264-9 0014-2956

- **Subcellular localization of avian sarcoma virus and human immunodeficiency virus type 1 integrases.**
  Source: Kukolj, G. Jones, K.S. Skalka, A. J-virol. Washington, D.C. : American Society for Microbiology. January 1997. volume 71 (1) page 843-847. 0022-538X

- **Synergistic activation of human immunodeficiency virus type 1 promoter activity by NF-kappaB and inhibitors of deacetylases: potential perspectives for the development of therapeutic strategies.**
  Author(s): Laboratoire de Virologie Moleculaire, Service de Chimie Biologique, Institut de Biologie et de Medecine Moleculaires, Universite Libre de Bruxelles, 6041 Gosselies, Belgium.
  Source: Quivy, V Adam, E Collette, Y Demonte, D Chariot, A Vanhulle, C Berkhout, B Castellano, R de Launoit, Y Burny, A Piette, J Bours, V Van Lint, C J-Virol. 2002 November; 76(21): 11091-103 0022-538X

- **Tea polyphenols as a novel class of inhibitors for human immunodeficiency virus reverse transcriptase.**
  Source: Nakane, H. Hara, Y. Ono, K. ACS-symp-ser. Washington, D.C. : American Chemical Society, 1974-. 1994. (547) page 56-64. 0097-6156

- **The highly conserved C-terminal dileucine motif in the cytosolic domain of the human immunodeficiency virus type 1 envelope glycoprotein is critical for its association with the AP-1 clathrin adaptor [correction of adapter].**
  Author(s): Institute of Microbiology, University of Lausanne, CH-1011 Lausanne, Switzerland.
  Source: Wyss, S Berlioz Torrent, C Boge, M Blot, G Honing, S Benarous, R Thali, M J-Virol. 2001 March; 75(6): 2982-92 0022-538X

- **The late-domain-containing protein p6 is the predominant phosphoprotein of human immunodeficiency virus type 1 particles.**
  Author(s): Abteilung Virologie, Universitatsklinikum Heidelberg, D-69120 Heidelberg, Germany. Barbara.Mueller@med.uni-heidelberg.de
  Source: Muller, Barbara Patschinsky, Tilo Krausslich, Hans Georg J-Virol. 2002 February; 76(3): 1015-24 0022-538X

- **Translational effects of peptide antagonists of Tat protein of human immunodeficiency virus type 1.**
  Author(s): UMDNJ-Robert Wood Johnson Medical School, Department of Molecular Genetics and Microbiology, Piscataway, NJ 08854-5635, USA.
  Source: Choudhury, I Wang, J Stein, S Rabson, A Leibowitz, M J J-Gen-Virol. 1999 March; 80 (Pt 3)777-82 0022-1317

- **Two human immunodeficiency virus vaccinal lipopeptides follow different cross-presentation pathways in human dendritic cells.**
  Author(s): Departement d'Immunologie, Unite INSERM 567, UMR CNRS 8104, IFR 116, Institut Cochin, Paris, France.
  Source: Andrieu, M Desoutter, J F Loing, E Gaston, J Hanau, D Guillet, J G Hosmalin, A J-Virol. 2003 January; 77(2): 1564-70 0022-538X

Federal Resources on Nutrition

In addition to the IBIDS, the United States Department of Health and Human Services (HHS) and the United States Department of Agriculture (USDA) provide many sources of information on general nutrition and health. Recommended resources include:

- healthfinder®, HHS's gateway to health information, including diet and nutrition: **http://www.healthfinder.gov/scripts/SearchContext.asp?topic=238&page=0**
- The United States Department of Agriculture's Web site dedicated to nutrition information: **www.nutrition.gov**
- The Food and Drug Administration's Web site for federal food safety information: **www.foodsafety.gov**
- The National Action Plan on Overweight and Obesity sponsored by the United States Surgeon General: **http://www.surgeongeneral.gov/topics/obesity/**
- The Center for Food Safety and Applied Nutrition has an Internet site sponsored by the Food and Drug Administration and the Department of Health and Human Services: **http://vm.cfsan.fda.gov/**
- Center for Nutrition Policy and Promotion sponsored by the United States Department of Agriculture: **http://www.usda.gov/cnpp/**
- Food and Nutrition Information Center, National Agricultural Library sponsored by the United States Department of Agriculture: **http://www.nal.usda.gov/fnic/**
- Food and Nutrition Service sponsored by the United States Department of Agriculture: **http://www.fns.usda.gov/fns/**

Additional Web Resources

A number of additional Web sites offer encyclopedic information covering food and nutrition. The following is a representative sample:

- AOL: **http://search.aol.com/cat.adp?id=174&layer=&from=subcats**
- Family Village: **http://www.familyvillage.wisc.edu/med_nutrition.html**
- Google: **http://directory.google.com/Top/Health/Nutrition/**
- Healthnotes: **http://www.healthnotes.com/**
- Open Directory Project: **http://dmoz.org/Health/Nutrition/**
- Yahoo.com: **http://dir.yahoo.com/Health/Nutrition/**
- WebMD®Health: **http://my.webmd.com/nutrition**
- WholeHealthMD.com: **http://www.wholehealthmd.com/reflib/0,1529,,00.html**

The following is a specific Web list relating to human immunodeficiency virus; please note that any particular subject below may indicate either a therapeutic use, or a contraindication (potential danger), and does not reflect an official recommendation (some Web sites are subscription based):

- **Vitamins**

  Vitamin B12
  Source: Healthnotes, Inc. www.healthnotes.com

  Vitamin B12 (Cobalamin)
  Source: Integrative Medicine Communications; www.drkoop.com

  Vitamin D
  Alternative names: Calciferol, Calcitrol, Cholecalciferol, Erocalciferol
  Source: Integrative Medicine Communications; www.drkoop.com

- **Minerals**

  Retinol
  Source: Integrative Medicine Communications; www.drkoop.com

  Stinging Nettle
  Alternative names: Urtica dioica, Urtica urens, Nettle
  Source: Integrative Medicine Communications; www.drkoop.com

  Vitamin A (Retinol)
  Source: Integrative Medicine Communications; www.drkoop.com

- **Food and Diet**

  Gluten-Free Diet
  Source: Healthnotes, Inc. www.healthnotes.com

CHAPTER 3. ALTERNATIVE MEDICINE AND HUMAN IMMUNODEFICIENCY VIRUS

Overview

In this chapter, we will begin by introducing you to official information sources on complementary and alternative medicine (CAM) relating to human immunodeficiency virus. At the conclusion of this chapter, we will provide additional sources.

The Combined Health Information Database

The Combined Health Information Database (CHID) is a bibliographic database produced by health-related agencies of the U.S. federal government (mostly from the National Institutes of Health) that can offer concise information for a targeted search. The CHID database is updated four times a year at the end of January, April, July, and October. Check the titles, summaries, and availability of CAM-related information by using the "Simple Search" option at the following Web site: **http://chid.nih.gov/simple/simple.html**. In the drop box at the top, select "Complementary and Alternative Medicine." Then type "human immunodeficiency virus" (or synonyms) in the second search box. We recommend that you select 100 "documents per page" and to check the "whole records" options. The following was extracted using this technique:

- **Psychosocial Aspects of Complementary and Alternative Medicine**

  Source: Pharmacotherapy. 20(11): 1289-1294. November 11, 2000.

  Summary: This journal article reviews patterns of complementary and alternative medicine (CAM) use in the United States. Between 1990 and 1997, the proportion of consumers using CAM increased from 33.8 percent to 42.1 percent. Among users, 46.3 percent saw a CAM practitioner and 53.7 percent used CAM on their own. CAM users tend to have high incomes and high levels of education. They are likely to have medical conditions such as chronic pain, poor mental health, **human immunodeficiency virus** infection, and cancer that are not easily treated by conventional medicine. Many of the most commonly used therapies are noninvasive, but dietary supplements also have become popular. Some therapies such as lifestyle modification, behavior modification, and relaxation techniques are routine parts of treatment plans. Others, such as

acupuncture, chiropractic, and massage, are gaining acceptance from the medical community. Only 38.5 percent of CAM users reported this use to their physicians, often because they anticipated disinterest or disapproval from the doctor. More recent data suggest that physicians are more open to discussing CAM than patients perceive. With growing evidence of potential herb-drug interactions, the authors suggest that discussing CAM with patients is becoming even more important. The article has 2 figures and 24 references.

- **Complementary Therapies and HIV Infection**

  Source: American Journal of Nursing. 99(2): 42-45. February 1999.

  Summary: This journal article provides an overview of complementary therapies for **human immunodeficiency virus** (HIV) infection and acquired immunodeficiency syndrome (AIDS). First, it describes two cases in which complementary therapies were used to improve the quality of life of patients with HIV infection. Then, it briefly discusses the role of the National Center for Complementary and Alternative Medicine in investigating these practices, and compares the healing approaches of conventional and alternative medical systems. The main body of the article describes the major alternative therapies that are being used for patients with HIV infection and AIDS. These include Ayurvedic medicine, traditional Chinese medicine, acupuncture, naturopathic medicine, nutritional and dietary supplements, homeopathy, manual healing, and mind-body therapies. Finally, the article discusses the implications for nursing practice and education. The article lists 10 selected references.

- **Most Frequently Used Alternative and Complementary Therapies and Activities by Participants in the AMCOA Study**

  Source: Journal of the Association of Nurses in AIDS Care. 10(3): 60-73. May-June 1999.

  Summary: This journal article reviews the literature on the 10 most commonly used alternative complementary and alternative therapies reported by the first 1,016 eligible participants in the Alternative Medical Care Outcomes in AIDS Study. The most frequently used therapies are aerobic exercise (64 percent), prayer (56 percent), massage (54 percent), needle acupuncture (48 percent), meditation (46 percent), support groups (42 percent), visualization and imagery (34 percent), breathing exercises (33 percent), spiritual activities (33 percent), and other exercise (33 percent). The literature search was restricted to published peer-reviewed articles indexed in MEDLINE. Despite the reported frequency of use, this review indicates that clinical research supporting the use of most of these therapies for **human immunodeficiency virus** or acquired immunodeficiency syndrome is not available on MEDLINE. The article has 2 tables and 116 references.

National Center for Complementary and Alternative Medicine

The National Center for Complementary and Alternative Medicine (NCCAM) of the National Institutes of Health (**http://nccam.nih.gov/**) has created a link to the National Library of Medicine's databases to facilitate research for articles that specifically relate to human immunodeficiency virus and complementary medicine. To search the database, go to the following Web site: **http://www.nlm.nih.gov/nccam/camonpubmed.html**. Select "CAM on PubMed." Enter "human immunodeficiency virus" (or synonyms) into the search box.

Click "Go." The following references provide information on particular aspects of complementary and alternative medicine that are related to human immunodeficiency virus:

- **12-O-acetylphorbol-13-decanoate potently inhibits cytopathic effects of human immunodeficiency virus type 1 (HIV-1), without activation of protein kinase C.**
  Author(s): el-Mekkawy S, Meselhy MR, Nakamura N, Hattori M, Kawahata T, Otake T.
  Source: Chemical & Pharmaceutical Bulletin. 1999 September; 47(9): 1346-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10517016&dopt=Abstract

- **A clinical protocol for the study of traditional medicine and human immunodeficiency virus-related illness.**
  Author(s): Chaudhury RR.
  Source: Journal of Alternative and Complementary Medicine (New York, N.Y.). 2001 October; 7(5): 553-66.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11719948&dopt=Abstract

- **A comparison of human immunodeficiency virus type 1 inhibition by partially purified aqueous extracts of Chinese medicinal herbs.**
  Author(s): Collins RA, Ng TB, Fong WP, Wan CC, Yeung HW.
  Source: Life Sciences. 1997; 60(23): Pl345-51.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9180371&dopt=Abstract

- **A comparison of human immunodeficiency virus type-1 protease inhibition activities by the aqueous and methanol extracts of Chinese medicinal herbs.**
  Author(s): Lam TL, Lam ML, Au TK, Ip DT, Ng TB, Fong WP, Wan DC.
  Source: Life Sciences. 2000 October 27; 67(23): 2889-96.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11106004&dopt=Abstract

- **A holistic life view of human immunodeficiency virus-infected African American women.**
  Author(s): Russell JM, Smith KV.
  Source: Journal of Holistic Nursing : Official Journal of the American Holistic Nurses' Association. 1999 December; 17(4): 331-45.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10818846&dopt=Abstract

- **A new caffeoyl quinic acid from aster scaber and its inhibitory activity against human immunodeficiency virus-1 (HIV-1) integrase.**
  Author(s): Kwon HC, Jung CM, Shin CG, Lee JK, Choi SU, Kim SY, Lee KR.
  Source: Chemical & Pharmaceutical Bulletin. 2000 November; 48(11): 1796-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11086919&dopt=Abstract

- **A new flavonol glycoside gallate ester from Acer okamotoanum and its inhibitory activity against human immunodeficiency virus-1 (HIV-1) integrase.**
  Author(s): Kim HJ, Woo ER, Shin CG, Park H.

Source: Journal of Natural Products. 1998 January; 61(1): 145-8.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9461665&dopt=Abstract

- **A randomized controlled clinical trial of a bereavement support group intervention in human immunodeficiency virus type 1-seropositive and -seronegative homosexual men.**
  Author(s): Goodkin K, Blaney NT, Feaster DJ, Baldewicz T, Burkhalter JE, Leeds B.
  Source: Archives of General Psychiatry. 1999 January; 56(1): 52-9. Erratum In: Arch Gen Psychiatry 1999 August; 56(8): 693.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9892256&dopt=Abstract

- **A randomized, placebo-controlled trial of combined insulin-like growth factor I and low dose growth hormone therapy for wasting associated with human immunodeficiency virus infection.**
  Author(s): Lee PD, Pivarnik JM, Bukar JG, Muurahainen N, Berry PS, Skolnik PR, Nerad JL, Kudsk KA, Jackson L, Ellis KJ, Gesundheit N.
  Source: The Journal of Clinical Endocrinology and Metabolism. 1996 August; 81(8): 2968-75. Erratum In: J Clin Endocrinol Metab 1996 October; 81(10): 3696.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8768860&dopt=Abstract

- **A survey of some Indian medicinal plants for anti-human immunodeficiency virus (HIV) activity.**
  Author(s): Premanathan M, Rajendran S, Ramanathan T, Kathiresan K, Nakashima H, Yamamoto N.
  Source: The Indian Journal of Medical Research. 2000 September; 112: 73-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11094851&dopt=Abstract

- **A xylanase from roots of sanchi ginseng (Panax notoginseng) with inhibitory effects on human immunodeficiency virus-1 reverse transcriptase.**
  Author(s): Lam SK, Ng TB.
  Source: Life Sciences. 2002 May 10; 70(25): 3049-58.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12138018&dopt=Abstract

- **Activation of human immunodeficiency virus long terminal repeat by arachidonic acid.**
  Author(s): Carini R, Leonarduzzi G, Camandola S, Musso T, Varesio L, Baeuerle PA, Poli G.
  Source: Free Radical Biology & Medicine. 1997; 22(1-2): 195-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8958144&dopt=Abstract

- **Addressing the spiritual needs of a drug user living with human immunodeficiency virus: a case study.**
  Author(s): Marcotte D, Margolin A, Avants SK.

Source: Journal of Alternative and Complementary Medicine (New York, N.Y.). 2003 February; 9(1): 169-75.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12676045&dopt=Abstract

- **Alternative treatment modalities in human immunodeficiency virus/acquired immune deficiency syndrome.**
  Author(s): Ernst J.
  Source: Clinical Infectious Diseases : an Official Publication of the Infectious Diseases Society of America. 2003; 37 Suppl 2: S150-3. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12942390&dopt=Abstract

- **Antenatal vitamin A supplementation increases birth weight and decreases anemia among infants born to human immunodeficiency virus-infected women in Malawi.**
  Author(s): Kumwenda N, Miotti PG, Taha TE, Broadhead R, Biggar RJ, Jackson JB, Melikian G, Semba RD.
  Source: Clinical Infectious Diseases : an Official Publication of the Infectious Diseases Society of America. 2002 September 1; 35(5): 618-24. Epub 2002 August 02.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12173139&dopt=Abstract

- **Anti-human immunodeficiency virus activity of oligosaccharides from rooibos tea (Aspalathus linearis) extracts in vitro.**
  Author(s): Nakano M, Nakashima H, Itoh Y.
  Source: Leukemia : Official Journal of the Leukemia Society of America, Leukemia Research Fund, U.K. 1997 April; 11 Suppl 3: 128-30.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9209319&dopt=Abstract

- **Anti-human immunodeficiency virus type 1 (HIV-1) activity of lectins from Narcissus species.**
  Author(s): Lopez S, Armand-Ugon M, Bastida J, Viladomat F, Este JA, Stewart D, Codina C.
  Source: Planta Medica. 2003 February; 69(2): 109-12.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12624813&dopt=Abstract

- **Antiviral activity against human immunodeficiency virus type 1 (HIV-1) and type 2 (HIV-2) of ethnobotanically selected Ethiopian medicinal plants.**
  Author(s): Asres K, Bucar F, Kartnig T, Witvrouw M, Pannecouque C, De Clercq E.
  Source: Phytotherapy Research : Ptr. 2001 February; 15(1): 62-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11180526&dopt=Abstract

- **Antiviral activity of Rwandan medicinal plants against human immunodeficiency virus type-1 (HIV-1).**
  Author(s): Cos P, Hermans N, De BT, Apers S, Sindambiwe JB, Witvrouw M, De CE, Vanden BD, Pieters L, Vlietinck AJ.

Source: Phytomedicine : International Journal of Phytotherapy and Phytopharmacology. 2002 January; 9(1): 62-8.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11924766&dopt=Abstract

- **Breast enlargement in 13 men who were seropositive for human immunodeficiency virus.**
  Author(s): Evans DL, Pantanowitz L, Dezube BJ, Aboulafia DM.
  Source: Clinical Infectious Diseases : an Official Publication of the Infectious Diseases Society of America. 2002 November 1; 35(9): 1113-9. Epub 2002 October 14.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12384846&dopt=Abstract

- **Chemical trapping of ternary complexes of human immunodeficiency virus type 1 integrase, divalent metal, and DNA substrates containing an abasic site. Implications for the role of lysine 136 in DNA binding.**
  Author(s): Mazumder A, Neamati N, Pilon AA, Sunder S, Pommier Y.
  Source: The Journal of Biological Chemistry. 1996 November 1; 271(44): 27330-8.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8910309&dopt=Abstract

- **Chinese herbal formula XQ-9302: pilot study of its clinical and in vitro activity against human immunodeficiency virus.**
  Author(s): Kang LY, Pan XZ, Yang WX, Pan QC, Weng XH, Yang WQ.
  Source: Hong Kong Medical Journal = Xianggang Yi Xue Za Zhi / Hong Kong Academy of Medicine. 1999 June; 5(2): 135-139.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11821581&dopt=Abstract

- **Clinical trials update in human immunodeficiency virus wasting.**
  Author(s): Muurahainen N, Mulligan K.
  Source: Seminars in Oncology. 1998 April; 25(2 Suppl 6): 104-11. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9625392&dopt=Abstract

- **Comparison of blood collected in acid-citrate-dextrose and EDTA for use in human immunodeficiency virus peripheral blood mononuclear cell cultures.**
  Author(s): Fiscus SA, Chakraborty H, Shepard R, Goodman M.
  Source: Journal of Clinical Microbiology. 2000 February; 38(2): 858-60.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10655398&dopt=Abstract

- **Considerations relating to the epidemiology of human immunodeficiency virus infection: the impact of bacterial antigens and consequences for treatment.**
  Author(s): Danninger T, Gallenberger K, Kraeling J.
  Source: Journal of Alternative and Complementary Medicine (New York, N.Y.). 2003 April; 9(2): 299-309.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12804083&dopt=Abstract

- **Controlled clinical trials evaluating the homeopathic treatment of people with human immunodeficiency virus or acquired immune deficiency syndrome.**
  Author(s): Ullman D.
  Source: Journal of Alternative and Complementary Medicine (New York, N.Y.). 2003 February; 9(1): 133-41. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12676041&dopt=Abstract

- **Current lead natural products for the chemotherapy of human immunodeficiency virus (HIV) infection.**
  Author(s): De Clercq E.
  Source: Medicinal Research Reviews. 2000 September; 20(5): 323-49. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10934347&dopt=Abstract

- **DC-SIGN interactions with human immunodeficiency virus type 1 and 2 and simian immunodeficiency virus.**
  Author(s): Pohlmann S, Baribaud F, Lee B, Leslie GJ, Sanchez MD, Hiebenthal-Millow K, Munch J, Kirchhoff F, Doms RW.
  Source: Journal of Virology. 2001 May; 75(10): 4664-72.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11312337&dopt=Abstract

- **Detection of apoptotic T lymphocytes in peripheral blood of human immunodeficiency virus (HIV)-infected subjects by apostain.**
  Author(s): Kunkl A, Paola Terranova M, Ferlini C, Astegiano G, Mazzarello G, Scambia G, Fattorossi A.
  Source: Cytometry : the Journal of the Society for Analytical Cytology. 2000 February 15; 42(1): 67-73.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10679745&dopt=Abstract

- **Determinants of the human immunodeficiency virus type 1 p15NC-RNA interaction that affect enhanced cleavage by the viral protease.**
  Author(s): Sheng N, Pettit SC, Tritch RJ, Ozturk DH, Rayner MM, Swanstrom R, Erickson-Viitanen S.
  Source: Journal of Virology. 1997 August; 71(8): 5723-32.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9223458&dopt=Abstract

- **Development of an in vitro blood-brain barrier model to study molecular neuropathogenesis and neurovirologic disorders induced by human immunodeficiency virus type 1 infection.**
  Author(s): Mukhtar M, Pomerantz RJ.
  Source: Journal of Human Virology. 2000 November-December; 3(6): 324-34.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11100913&dopt=Abstract

- **Diarrhea and human immunodeficiency virus: Western and Eastern perspectives [corrected]**
  Author(s): Anastasi JK, Dawes NC, Li YM.
  Source: Journal of Alternative and Complementary Medicine (New York, N.Y.). 1997 Summer; 3(2): 163-8. Erratum In: J Altern Complement Med 1997 Fall; 3(3): 302.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9395707&dopt=Abstract

- **Dietary fish oil and cytokine and eicosanoid production during human immunodeficiency virus infection.**
  Author(s): Bell SJ, Chavali S, Bistrian BR, Connolly CA, Utsunomiya T, Forse RA.
  Source: Jpen. Journal of Parenteral and Enteral Nutrition. 1996 January-February; 20(1): 43-9.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8788262&dopt=Abstract

- **Differential effects of p-glycoprotein and multidrug resistance protein-1 on productive human immunodeficiency virus infection.**
  Author(s): Speck RR, Yu XF, Hildreth J, Flexner C.
  Source: The Journal of Infectious Diseases. 2002 August 1; 186(3): 332-40. Epub 2002 July 08.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12134229&dopt=Abstract

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  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12766696&dopt=Abstract

- **The anti-human immunodeficiency virus agent 3'-fluorothymidine induces DNA damage and apoptosis in human lymphoblastoid cells.**
  Author(s): Sundseth R, Joyner SS, Moore JT, Dornsife RE, Dev IK.
  Source: Antimicrobial Agents and Chemotherapy. 1996 February; 40(2): 331-5.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8834875&dopt=Abstract

- **The effects of massage therapy alone and in combination with other complementary therapies on immune system measures and quality of life in human immunodeficiency virus.**
  Author(s): Birk TJ, McGrady A, MacArthur RD, Khuder S.
  Source: Journal of Alternative and Complementary Medicine (New York, N.Y.). 2000 October; 6(5): 405-14.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11059502&dopt=Abstract

- **The enzymatic antioxidant system in blood and glutathione status in human immunodeficiency virus (HIV)-infected patients: effects of supplementation with selenium or beta-carotene.**
  Author(s): Delmas-Beauvieux MC, Peuchant E, Couchouron A, Constans J, Sergeant C, Simonoff M, Pellegrin JL, Leng B, Conri C, Clerc M.
  Source: The American Journal of Clinical Nutrition. 1996 July; 64(1): 101-7. Erratum In: Am J Clin Nutr 1996 December; 64(6): 971.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8669404&dopt=Abstract

- **The etiology of community-acquired pneumonia at an urban public hospital: influence of human immunodeficiency virus infection and initial severity of illness.**
  Author(s): Park DR, Sherbin VL, Goodman MS, Pacifico AD, Rubenfeld GD, Polissar NL, Root RK; Harborview CAP Study Group.
  Source: The Journal of Infectious Diseases. 2001 August 1; 184(3): 268-77. Epub 2001 June 26.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11443551&dopt=Abstract

- **The late-domain-containing protein p6 is the predominant phosphoprotein of human immunodeficiency virus type 1 particles.**
  Author(s): Muller B, Patschinsky T, Krausslich HG.
  Source: Journal of Virology. 2002 February; 76(3): 1015-24.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11773377&dopt=Abstract

- **The prevalence of distress in persons with human immunodeficiency virus infection.**
  Author(s): Cohen M, Hoffman RG, Cromwell C, Schmeidler J, Ebrahim F, Carrera G, Endorf F, Alfonso CA, Jacobson JM.
  Source: Psychosomatics. 2002 January-February; 43(1): 10-5.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11927752&dopt=Abstract

- **The role of ambulatory care information systems in supporting the provision of holistic care for persons infected with the human immunodeficiency virus.**
  Author(s): Henry SB, Costantino M.
  Source: Holistic Nursing Practice. 1996 October; 11(1): 39-47.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8945173&dopt=Abstract

- **Treatment of human immunodeficiency virus-positive patients with complementary and alternative medicine: a survey of practitioners.**
  Author(s): Calabrese C, Wenner CA, Reeves C, Turet P, Standish LJ.
  Source: Journal of Alternative and Complementary Medicine (New York, N.Y.). 1998 Fall; 4(3): 281-7.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9764767&dopt=Abstract

- **Treatment of Kaposi sarcoma with oral administration of shark cartilage in a human herpesvirus 8-seropositive, human immunodeficiency virus-seronegative homosexual man.**
  Author(s): Hillman JD, Peng AT, Gilliam AC, Remick SC.
  Source: Archives of Dermatology. 2001 September; 137(9): 1149-52.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11559209&dopt=Abstract

- **Triple trouble: the role of malnutrition in tuberculosis and human immunodeficiency virus co-infection.**
  Author(s): van Lettow M, Fawzi WW, Semba RD.
  Source: Nutrition Reviews. 2003 March; 61(3): 81-90. Review.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12723640&dopt=Abstract

- **Use of complementary and alternative therapies by patients with human immunodeficiency virus disease in the era of highly active antiretroviral therapy.**
  Author(s): Bica I, Tang AM, Skinner S, Spiegelman D, Knox T, Gorbach S, Wilson IB.
  Source: Journal of Alternative and Complementary Medicine (New York, N.Y.). 2003 February; 9(1): 65-76.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12676036&dopt=Abstract

- **Vincristine as therapy for idiopathic thrombocytopenic purpura in patients infected with human immunodeficiency virus.**
  Author(s): Ena J, Garcia A, de Mar Masia M.

Source: Clinical Infectious Diseases : an Official Publication of the Infectious Diseases Society of America. 1996 May; 22(5): 880-1.
http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8722968&dopt=Abstract

- **Vitamin A supplementation and human immunodeficiency virus load in injection drug users.**
  Author(s): Semba RD, Lyles CM, Margolick JB, Caiaffa WT, Farzadegan H, Cohn S, Vlahov D.
  Source: The Journal of Infectious Diseases. 1998 March; 177(3): 611-6.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9498439&dopt=Abstract

- **Vitamin A supplementation and human immunodeficiency virus type 1 shedding in women: results of a randomized clinical trial.**
  Author(s): Baeten JM, McClelland RS, Overbaugh J, Richardson BA, Emery S, Lavreys L, Mandaliya K, Bankson DD, Ndinya-Achola JO, Bwayo JJ, Kreiss JK.
  Source: The Journal of Infectious Diseases. 2002 April 15; 185(8): 1187-91. Epub 2002 March 22.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11930332&dopt=Abstract

- **Zinc status in human immunodeficiency virus type 1 infection and illicit drug use.**
  Author(s): Baum MK, Campa A, Lai S, Lai H, Page JB.
  Source: Clinical Infectious Diseases : an Official Publication of the Infectious Diseases Society of America. 2003; 37 Suppl 2: S117-23.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12942385&dopt=Abstract

- **Zn2+ promotes the self-association of human immunodeficiency virus type-1 integrase in vitro.**
  Author(s): Lee SP, Xiao J, Knutson JR, Lewis MS, Han MK.
  Source: Biochemistry. 1997 January 7; 36(1): 173-80.
  http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8993331&dopt=Abstract

Additional Web Resources

A number of additional Web sites offer encyclopedic information covering CAM and related topics. The following is a representative sample:

- Alternative Medicine Foundation, Inc.: **http://www.herbmed.org/**
- AOL: **http://search.aol.com/cat.adp?id=169&layer=&from=subcats**
- Chinese Medicine: **http://www.newcenturynutrition.com/**
- drkoop.com®: **http://www.drkoop.com/InteractiveMedicine/IndexC.html**
- Family Village: **http://www.familyvillage.wisc.edu/med_altn.htm**
- Google: **http://directory.google.com/Top/Health/Alternative/**

- Healthnotes: **http://www.healthnotes.com/**
- MedWebPlus: **http://medwebplus.com/subject/Alternative_and_Complementary_Medicine**
- Open Directory Project: **http://dmoz.org/Health/Alternative/**
- HealthGate: **http://www.tnp.com/**
- WebMD®Health: **http://my.webmd.com/drugs_and_herbs**
- WholeHealthMD.com: **http://www.wholehealthmd.com/reflib/0,1529,,00.html**

Yahoo.com: **http://dir.yahoo.com/Health/Alternative_Medicine/**

The following is a specific Web list relating to human immunodeficiency virus; please note that any particular subject below may indicate either a therapeutic use, or a contraindication (potential danger), and does not reflect an official recommendation (some Web sites are subscription based):

- **General Overview**

AIDS and HIV
Source: Integrative Medicine Communications; www.drkoop.com

Brain Inflammation, Meningitis
Source: Integrative Medicine Communications; www.drkoop.com

Brain Inflammation, Viral Encephalitis
Source: Integrative Medicine Communications; www.drkoop.com

Cervical Dysplasia
Source: Integrative Medicine Communications; www.drkoop.com

HIV and AIDS Support
Source: Healthnotes, Inc. www.healthnotes.com

Measles
Source: Integrative Medicine Communications; www.drkoop.com

Meningitis
Source: Integrative Medicine Communications; www.drkoop.com

Nail Disorders
Source: Integrative Medicine Communications; www.drkoop.com

Sexually Transmitted Diseases
Source: Integrative Medicine Communications; www.drkoop.com

Skin Cancer
Source: Integrative Medicine Communications; www.drkoop.com

STDs
Source: Integrative Medicine Communications; www.drkoop.com

Tuberculosis
Source: Integrative Medicine Communications; www.drkoop.com

Vaginal Inflammation
Source: Integrative Medicine Communications; www.drkoop.com

Vaginitis
Source: Integrative Medicine Communications; www.drkoop.com

- **Herbs and Supplements**

AZT
Source: Healthnotes, Inc. www.healthnotes.com

Blue-Green Algae
Source: Healthnotes, Inc. www.healthnotes.com

Blue-green Algae
Source: Integrative Medicine Communications; www.drkoop.com

Bupleurum
Alternative names: Bupleurum chinense, Bupleurum falcatum
Source: Healthnotes, Inc. www.healthnotes.com

Calciferol
Source: Integrative Medicine Communications; www.drkoop.com

Calcitrol
Source: Integrative Medicine Communications; www.drkoop.com

Cholecalciferol
Source: Integrative Medicine Communications; www.drkoop.com

Cobalamin
Source: Integrative Medicine Communications; www.drkoop.com

Dapsone
Source: Healthnotes, Inc. www.healthnotes.com

Didanosine
Source: Healthnotes, Inc. www.healthnotes.com

Erocalciferol
Source: Integrative Medicine Communications; www.drkoop.com

Glutamine
Source: Integrative Medicine Communications; www.drkoop.com

Hypericum perforatum
Source: Integrative Medicine Communications; www.drkoop.com

Hyssop
Alternative names: Hyssopus officinalis
Source: Healthnotes, Inc. www.healthnotes.com

Klamathweed
Source: Integrative Medicine Communications; www.drkoop.com

Lamivudine
Source: Healthnotes, Inc. www.healthnotes.com

Methionine
Source: Healthnotes, Inc. www.healthnotes.com

NAC (N-acetylcysteine)
Source: WholeHealthMD.com, LLC. www.wholehealthmd.com
Hyperlink:
http://www.wholehealthmd.com/refshelf/substances_view/0,1525,809,00.html

Nettle
Source: Integrative Medicine Communications; www.drkoop.com

Spirulina
Alternative names: Blue-green Algae
Source: Integrative Medicine Communications; www.drkoop.com

St. John's Wort
Alternative names: Hypericum perforatum, Klamathweed
Source: Integrative Medicine Communications; www.drkoop.com

Stavudine
Source: Healthnotes, Inc. www.healthnotes.com

Thuja occid
Alternative names: Arbor Vitae; Thuja occidentalis
Source: Alternative Medicine Foundation, Inc. www.amfoundation.org

Turmeric
Alternative names: Curcuma longa
Source: Healthnotes, Inc. www.healthnotes.com

Urtica dioica
Source: Integrative Medicine Communications; www.drkoop.com

Urtica urens
Source: Integrative Medicine Communications; www.drkoop.com

General References

A good place to find general background information on CAM is the National Library of Medicine. It has prepared within the MEDLINEplus system an information topic page

dedicated to complementary and alternative medicine. To access this page, go to the MEDLINEplus site at **http://www.nlm.nih.gov/medlineplus/alternativemedicine.html**. This Web site provides a general overview of various topics and can lead to a number of general sources.

CHAPTER 4. DISSERTATIONS ON HUMAN IMMUNODEFICIENCY VIRUS

Overview

In this chapter, we will give you a bibliography on recent dissertations relating to human immunodeficiency virus. We will also provide you with information on how to use the Internet to stay current on dissertations. **IMPORTANT NOTE:** When following the search strategy described below, you may discover non-medical dissertations that use the generic term "human immunodeficiency virus" (or a synonym) in their titles. To accurately reflect the results that you might find while conducting research on human immunodeficiency virus, we have not necessarily excluded non-medical dissertations in this bibliography.

Dissertations on Human Immunodeficiency Virus

ProQuest Digital Dissertations, the largest archive of academic dissertations available, is located at the following Web address: **http://wwwlib.umi.com/dissertations**. From this archive, we have compiled the following list covering dissertations devoted to human immunodeficiency virus. You will see that the information provided includes the dissertation's title, its author, and the institution with which the author is associated. The following covers recent dissertations found when using this search procedure:

- **A Study of the Factors That Affect the Implementation of Human Immunodeficiency Virus Education Programs in Pennsylvania Schools (immune Deficiency)** by Healey, Bernard Joseph, Phd from University of Pennsylvania, 1990, 242 pages
  http://wwwlib.umi.com/dissertations/fullcit/9112572
- **Adherence to Antiretroviral Therapy among a Sample of Human Immunodeficiency Virus-positive Women in Ontario (immune Deficiency)** by Gahagan, Jacqueline C. Phd from Wayne State University, 1999, 149 pages
  http://wwwlib.umi.com/dissertations/fullcit/9954507
- **An Analysis of the Medical and Legal Aspects Related to the Educational Placement in the Public Schools of Children with Human Immunodeficiency Virus Infection** by Walls, Wemme Ensor, Edd from Virginia Polytechnic Institute and State University, 1988, 354 pages
  http://wwwlib.umi.com/dissertations/fullcit/8817426

- **An Investigation of the Effects of Knowledge of Human Immunodeficiency Virus Antibody Status on High-risk Sexual Behaviors and Safer Sex Practices in a Cohort of Homosexual and Bisexual Men** by Graham, Davis Michael, Phd from The Ohio State University, 1990, 124 pages
  http://wwwlib.umi.com/dissertations/fullcit/9105117
- **An Investigation of the Relationship between the Human Immunodeficiency Virus (hiv) and Special Education (immune Deficiency)** by Smith, Marie Ann, Phd from The University of Southern Mississippi, 1990, 123 pages
  http://wwwlib.umi.com/dissertations/fullcit/9033676
- **Assessing Attitudes of Physicians and Registered Nurses toward the Human Immunodeficiency Virus (hiv) and Acquired Immunodeficiency Syndrome (aids): a Cultural Communication Analysis** by Brown, Geraldine, Phd from Howard University, 1994, 218 pages
  http://wwwlib.umi.com/dissertations/fullcit/9507309
- **Assessing Quality of Life in Women Living with Human Immunodeficiency Virus Infection** by Cowdery, Joan Ellen, Phd from The University of Alabama, 1997, 100 pages
  http://wwwlib.umi.com/dissertations/fullcit/9735693
- **Biochemical and Pharmacological Characterizations of the Structure and Function of Human Immunodeficiency Virus Type 1 Integrase and Its Role during Early Steps of the Viral Life Cycle** by Zhu, Kai; Phd from University of California, Los Angeles, 2002, 173 pages
  http://wwwlib.umi.com/dissertations/fullcit/3063914
- **Broadly Neutralizing Antibodies to Human Immunodeficiency Virus-1 and the Interaction between Recombinant Mannose-binding Lectin and Anti-hiv Antibodies (immune Deficiency)** by Ying, Hongyu; Ms from Rush University, 2002, 48 pages
  http://wwwlib.umi.com/dissertations/fullcit/1407748
- **Characterization and Enhancement of the Interaction between Mannose-binding Lectin and Human Immunodeficiency Virus Type-1** by Hart, Melanie Lynn; Phd from Rush University, 2002, 148 pages
  http://wwwlib.umi.com/dissertations/fullcit/3058984
- **Characterization of C-myc-mediated Repression of the Human Immunodeficiency Virus Type 1 Promoter (immune Deficiency)** by Stojanova, Angelina; Msc from Concordia University (canada), 2002, 143 pages
  http://wwwlib.umi.com/dissertations/fullcit/MQ72884
- **Characterization of Human Immunodeficiency Virus Type 1 Associated with and without Vertical Transmission** by Hahn, Tobias; Phd from The University of Arizona, 2002, 187 pages
  http://wwwlib.umi.com/dissertations/fullcit/3050358
- **Child Sexual Abuse, Alcohol and Drug (mis)use, and Human Immunodeficiency Virus (hiv) Vulnerability among African-american Women: an Exploratory Study** by Purnell, Rogeair Damone, Phd from University of Michigan, 1996, 224 pages
  http://wwwlib.umi.com/dissertations/fullcit/9712063
- **Cis- and Trans-acting Factors Modulating Nuclear Retention of Human Immunodeficiency Virus Type 1 Env Rna** by Suh, Daniel; Msc from University of Toronto (canada), 2002, 110 pages
  http://wwwlib.umi.com/dissertations/fullcit/MQ74094

- **Consequences of Human Immunodeficiency Virus Type 1 Subtype a Genetic Diversity** by Mani, Indu; Sd from Harvard University, 2002
http://wwwlib.umi.com/dissertations/fullcit/f657969
- **Control of Protein Synthesis in Eukaryotes C-myc Oncogene and the Human Immunodeficiency Virus Tat Iii Protein = Controle De La Synthese Proteique Chez Les Cellules Eucaryotes : L'oncogene C-myc Et La Proteine Tat Iii Du Virus De L'immunodeficience Humain** by Darveau, André; Phd from Mcgill University (canada), 1987
http://wwwlib.umi.com/dissertations/fullcit/NL38197
- **Coping Strategies, Psychological Adjustment, and Aids-related Concerns of Women with the Human Immunodeficiency Virus (immune Deficiency)** by Coleman, Christy Lynn, Phd from University of California, Los Angeles, 1994, 285 pages
http://wwwlib.umi.com/dissertations/fullcit/9509857
- **Dogmatic Thinking and Social Reaction of School Board Members toward the Education of Students with Human Immunodeficiency Virus (immune Deficiency)** by Montigros, Patricia, Edd from Rutgers the State University of New Jersey - New Brunswick, 1990, 161 pages
http://wwwlib.umi.com/dissertations/fullcit/9033608
- **Evolution of Human Immunodeficiency Virus Type 1 Genotype and Phenotype in Response to Strong Selective Pressure from Protease Inhibitors** by Resch, Wolfgang; Phd from The University of North Carolina at Chapel Hill, 2002, 179 pages
http://wwwlib.umi.com/dissertations/fullcit/3047060
- **Exploring White Dental Students' Willingness to Provide Dental Care to People with Human Immunodeficiency Virus Disease** by Driscoll, Jeanine M., Phd from University of Maryland College Park, 1996, 180 pages
http://wwwlib.umi.com/dissertations/fullcit/9707590
- **Factors Associated with Appointment and Medication Adherence in Low-income Latinas Living with the Human Immunodeficiency Virus** by Garcia-teague, Lorraine Ann; Phd from University of California, Los Angeles, 2002, 143 pages
http://wwwlib.umi.com/dissertations/fullcit/3063906
- **Generation of High-level Cytotoxic T-lymphocyte Responses to Human Immunodeficiency Virus Proteins Using Live Recombinant Viruses (immune Deficiency)** by Haglund, Karl Erick; Phd from Yale University, 2002, 240 pages
http://wwwlib.umi.com/dissertations/fullcit/3046162
- **Having a Parent with Human Immunodeficiency Virus: Impact on the Surviving Child's Mental Health** by Landman, Wendy Shara; Phd from Temple University, 2000, 99 pages
http://wwwlib.umi.com/dissertations/fullcit/9997275
- **Human Immunodeficiency Virus and Acquired Immune Deficiency: Beliefs, Knowledge, and Behaviors of High School Students Attending Seventh-day Adventist Academies (adolescents)** by Gray, Deborah Louise, Edd from Andrews University, 1994, 247 pages
http://wwwlib.umi.com/dissertations/fullcit/9502652
- **Human Immunodeficiency Virus Prevention Education: an Evaluation of 'slipping and Sliding'. a Small Group Intervention for Gay Men (immune Deficiency)** by Popejoy, Peter Van, Phd from University of Georgia, 1996, 194 pages
http://wwwlib.umi.com/dissertations/fullcit/9624075

- **Human Immunodeficiency Virus Prevention Education: an Evaluation of the Impact of 'aids 101' on Hiv-related Knowledge and Attitudes toward Persons with Hiv/aids** by Campbell, Alan Lloyd; Phd from University of Georgia, 2001, 80 pages
  http://wwwlib.umi.com/dissertations/fullcit/3025260
- **Human Immunodeficiency Virus Type 1 (hiv-1) Gag-pro Genetic Variability Is Related to Therapy Response and Impacts Viral Fitness in Specific Cell Types** by Rose, Stephanie Leigh; Phd from University of Florida, 2002, 194 pages
  http://wwwlib.umi.com/dissertations/fullcit/3069041
- **Human Immunodeficiency Virus Type 1 Diversity in Blood and Oral Fluids during Primary and Chronic Infection** by Freel, Stephanie Alayne; Phd from The University of North Carolina at Chapel Hill, 2002, 115 pages
  http://wwwlib.umi.com/dissertations/fullcit/3070844
- **Human Immunodeficiency Virus Type 1 Reverse Transcriptase: the Role of Template-primer Interactions in Polymerase Function** by Fisher, Timothy Steven; Phd from Yeshiva University, 2002, 327 pages
  http://wwwlib.umi.com/dissertations/fullcit/3036930
- **Human Immunodeficiency Virus Voluntary Counseling and Testing (vct) in Northern Thailand (immune Deficiency)** by Kawichai, Surinda; Phd from The Johns Hopkins University, 2002, 137 pages
  http://wwwlib.umi.com/dissertations/fullcit/3028290
- **Human Immunodeficiency Virus-1 Proteins in Hiv-1 Encephalitis: Detection of Gp120 and Tat in Brain and Their Potential Receptors (immune Deficiency)** by Jones, Melina Viola; Phd from University of Kentucky, 2002, 121 pages
  http://wwwlib.umi.com/dissertations/fullcit/3039119
- **Incidence Trends, Degree of Rurality, and Migration Patterns among Persons with Human Immunodeficiency Virus Infection in the Deep South** by Agee, Bonita Sneed; Phd from The University of Alabama at Birmingham, 2002, 135 pages
  http://wwwlib.umi.com/dissertations/fullcit/3053262
- **Isolation of Two Highly Potent and Non-toxic Inhibitors of Human Immunodeficiency Virus Type 1 (hiv-1) Integrase and Viral Replication** by Abd-elazem, Ibrahim Shawky; Phd from The Johns Hopkins University, 2002, 103 pages
  http://wwwlib.umi.com/dissertations/fullcit/3046408
- **Lipid and Morphologic Abnormalities Associated with Antiretroviral Therapy for Human Immunodeficiency Virus Infection: Prevalence, Incidence, Aetiology and Impact on Treatment Patterns** by Heath, Katherine Valerie; Phd from The University of British Columbia (canada), 2002, 235 pages
  http://wwwlib.umi.com/dissertations/fullcit/NQ75114
- **Longitudinal Evaluation of Subtype-specific Viral Load Variation in an Individual Displaying Inter-subtype Human Immunodeficiency Virus Type-1 Superinfection (immune Deficiency)** by Srinivasan, Priya; Ms from Texas Woman's University, 2003, 60 pages
  http://wwwlib.umi.com/dissertations/fullcit/1413518
- **Male Latino Gay Youth: Insights into Potential Barriers against Human Immunodeficiency Virus Testing** by Berry, Christine Cozad; Phd from Texas Woman's University, 2003, 148 pages
  http://wwwlib.umi.com/dissertations/fullcit/3084173

- **Mechanistic Understanding of Nucleoside Inhibitors of Human Immunodeficiency Virus (hiv) (immune Deficiency)** by Ray, Adrian Staffin; Phd from Yale University, 2002, 297 pages
  http://wwwlib.umi.com/dissertations/fullcit/3046215
- **Parameters That Influence the Binding of Human Immunodeficiency Virus Reverse Transcriptase to Primer-template** by Cristofaro, Jason Vittorio; Phd from University of Maryland College Park, 2002, 131 pages
  http://wwwlib.umi.com/dissertations/fullcit/3070528
- **Phenotypic and Functional Genomic Characterization of Immune Cell Reservoirs for Human Immunodeficiency Virus Type-1** by Coberley, Carter Ray; Phd from University of Florida, 2002, 171 pages
  http://wwwlib.umi.com/dissertations/fullcit/3069024
- **Psychosocial Variables and Disease Progression in Human Immunodeficiency Virus (immune Deficiency)** by Spalding, Alison Dowling, Phd from Virginia Commonwealth University, 1991, 238 pages
  http://wwwlib.umi.com/dissertations/fullcit/9214071
- **Racial/ethnic Variations in the Prevalence of Human Immunodeficiency Virus Type 1 Infection among Injecting Drug Users: Social and Behavioral Risk Factors (racial, Ethnic, Immune Deficiency, Hiv)** by Jose, Benny, Phd from Fordham University, 1996, 193 pages
  http://wwwlib.umi.com/dissertations/fullcit/9628335
- **Risk Factors for Human Immunodeficiency Virus Seropositivity among Puerto Rican Injection Drug Users: Implications for Social Work Practice (immune Deficiency)** by Rodriguez, Gloria M., Dsw from City University of New York, 1995, 181 pages
  http://wwwlib.umi.com/dissertations/fullcit/9530916
- **Role of Chemokine Receptors in Human Immunodeficiency Virus-1 Infection** by Vasudevan, Jayanand; Phd from University of Virginia, 2003, 147 pages
  http://wwwlib.umi.com/dissertations/fullcit/3073583
- **Social Work Students' and Practitioners' Beliefs, Attitudes, and Willingness to Provide Services to People with Human Immunodeficiency Virus Disease (immune Deficiency)** by Segovia-tadehara, Corina D. Phd from The University of Utah, 2000, 158 pages
  http://wwwlib.umi.com/dissertations/fullcit/3001237
- **Stigma, Fear and the Human Immunodeficiency Virus** by Nohava, Jean Ann, Phd from Brigham Young University, 1997, 71 pages
  http://wwwlib.umi.com/dissertations/fullcit/9721506
- **The Association between Polymorphisms in Human Leukocyte Antigen Class I and Transporter Associated with Antigen Presentation Genes with Resistance to Human Immunodeficiency Virus-1 Infection** by Liu, Chenglong; Phd from University of California, Los Angeles, 2002, 99 pages
  http://wwwlib.umi.com/dissertations/fullcit/3063946
- **The Effect of Human Immunodeficiency Virus/acquired Immune Deficiency Syndrome Education Program on Knowledge, Attitudes and Sexual Behavior of Selected College Students (immune Deficiency)** by Montgomery, Arlene Jaine Jackson, Phd from Old Dominion University, 1994, 164 pages
  http://wwwlib.umi.com/dissertations/fullcit/9434854

- **The Effect of Retinoic Acid on Human Immunodeficiency Virus Type-1 Replication in Monocyte/macrophages (immune Deficiency)** by Brown, Xin Qian; Phd from Boston University, 2002, 203 pages
  http://wwwlib.umi.com/dissertations/fullcit/3021050
- **The Forging of a Collective Truth: a Sociological Analysis of the Discovery of the Human Immunodeficiency Virus (immune Deficiency)** by Haritos, Rosa, Phd from Columbia University, 1993, 364 pages
  http://wwwlib.umi.com/dissertations/fullcit/9333784
- **The Role of Sequence Variability in the Biology of the Human Immunodeficiency Virus Type 1 and Simian Immunodeficiency Virus Envelope Protein** by Mcgrath, Kathryn Mary; Phd from The University of North Carolina at Chapel Hill, 2003, 189 pages
  http://wwwlib.umi.com/dissertations/fullcit/3086574
- **The Role of the B7 Co-stimulation Pathway in Feline Immunodeficiency Virus (fiv) and Human Immunodeficiency Virus (hiv) Associated T Cell Depletion** by Bull, Marta Eileen; Phd from North Carolina State University, 2002, 195 pages
  http://wwwlib.umi.com/dissertations/fullcit/3081695
- **The Role of the Human Immunodeficiency Virus-1 in Macrophage Gene Transcription** by Caldwell, Robert Learohn; Phd from Vanderbilt University, 2003, 190 pages
  http://wwwlib.umi.com/dissertations/fullcit/3085752
- **Transcriptional Regulation of the Human Immunodeficiency Virus by Protein Phosphatase 2a** by Faulkner, Neil Esantis; Phd from University of Michigan, 2003, 117 pages
  http://wwwlib.umi.com/dissertations/fullcit/3079440

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Ask the medical librarian at your library if it has full and unlimited access to the *ProQuest Digital Dissertations* database. From the library, you should be able to do more complete searches via **http://wwwlib.umi.com/dissertations**.

CHAPTER 5. CLINICAL TRIALS AND HUMAN IMMUNODEFICIENCY VIRUS

Overview

In this chapter, we will show you how to keep informed of the latest clinical trials concerning human immunodeficiency virus.

Recent Trials on Human Immunodeficiency Virus

The following is a list of recent trials dedicated to human immunodeficiency virus.[8] Further information on a trial is available at the Web site indicated.

- **A Study of Patients Who Develop HIV Infection After Enrolling in HIV Vaccine Trials or HIV Vaccine Preparedness Trials**

  Condition(s): HIV Infections

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

  Purpose - Excerpt: The purpose of this study is to find out more about how persons respond to HIV-1 infection if they have received an experimental HIV-1 vaccine before they became HIV-infected. It is important to study people who have been given experimental **HIV** vaccines and who later became HIV-infected for several reasons. First, if **HIV** infection is found and then cleared, it is important to note the relationship between the virus and the vaccine. This may give an understanding of the immunity. A second reason is to better understand the immune response in those who received a vaccine compared to those who received placebo (no vaccine). If the vaccine does not prevent **HIV** infection, it will be important to study the progression of the disease. Understanding the immune response in vaccinated patients after infection and the impact on symptoms and disease progression may give valuable information for future vaccine trials and the effectiveness of **HIV** vaccines.

  Study Type: Observational

  Contact(s): see Web site below

[8] These are listed at **www.ClinicalTrials.gov**.

Web Site: http://clinicaltrials.gov/ct/show/NCT00029913

- **A Study of Peer Education to Prevent HIV Transmission among Injection Drug Users and Their HIV Risk Contacts**

  Condition(s): HIV Infections

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID); National Institute of Child Health and Human Development (NICHD); National Institutes of Health (NIH); National Institute of Mental Health (NIMH); National Institute on Drug Abuse (NIDA)

  Purpose - Excerpt: Injection drug use is the major mode of **HIV** transmission in many countries. Injection drug users (IDUs) transmit **HIV** not only through shared drug injection equipment but also through heterosexual and homosexual transmission and mother-to-child transmission. Studies have shown that peer education programs can reduce **HIV** risk behavior in IDUs. However, it is not known if reduced **HIV** risk behavior leads to fewer **HIV** infections. The purpose of this study is to find out if a peer education program can reduce the number of new **HIV** infections by changing the behavior of IDUs and their **HIV** risk contacts.

  Phase(s): Phase III

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00038688

- **A Study of the Safety and Effectiveness of an HIV Vaccine for HIV-Positive Patients Receiving Anti-HIV Drugs for at Least 2 Years**

  Condition(s): HIV Infections

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

  Purpose - Excerpt: The purpose of this study is to see if 2 study vaccines, ALVAC-HIV (vCP1452) and gp160 MN/LAI-2, are safe and effective in boosting the body's attacks on **HIV** in HIV-positive patients. HIV-infected patients who have been treated with anti-HIV drugs for a long time may have weakened immune responses. One way to strengthen these responses may be to have a safe and effective vaccine, which will boost immune responses that are specific to **HIV.**

  Phase(s): Phase I

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00006509

- **Evaluation of the Safety of and Immune Response to an HIV Vaccine in Healthy Adults**

  Condition(s): HIV Infections

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

Purpose - Excerpt: This study will examine the safety and immune response to a two-part **HIV** vaccine. Healthy volunteers who are at low risk of **HIV** infection will receive either active vaccine or a placebo.

Phase(s): Phase I; Phase II

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00051454

- **HIV Levels in Cerebrospinal Fluid and Brain Function in Patients Receiving Anti-HIV Drugs**

  Condition(s): Cognitive Disorders; HIV Infections

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID); National Institute of Neurological Disorders and Stroke (NINDS); Neurologic AIDS Research Consortium (NARC)

  Purpose - Excerpt: The purpose of this study is to see whether anti-HIV drugs that reduce **HIV** in the blood also reduce **HIV** in the cerebrospinal fluid (CSF). CSF is the fluid found around the brain and spinal cord. This study also looks at whether reducing **HIV** in the CSF can help protect brain function. **HIV** can be detected in the brain and CSF early in **HIV** disease. Anti-HIV drugs probably reduce **HIV** in the CSF. This may be important because other studies have suggested high CSF **HIV** levels may lead to some loss of brain function.

  Study Type: Observational

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00001103

- **HIV Vaccine Designed for HIV Infected Adults Taking Anti-HIV Drugs**

  Condition(s): HIV Infections

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

  Purpose - Excerpt: This study will evaluate the safety of and immune responses to a dendritic cell vaccination for HIV-1 infection. The vaccine will be made from a patient's own cells combined with small fragments of HIV-1 (made synthetically in a laboratory). These cells will be administered back to the patient either into a vein (intravenously) or the skin (subcutaneously).

  Phase(s): Phase I

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00056758

- **Safety of and Immune System Response to an HIV Vaccine (EP HIV-1090) in HIV Uninfected Adults**

  Condition(s): HIV Infections

Study Status: This study is currently recruiting patients.

Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

Purpose - Excerpt: The purpose of this study is to test the safety of an **HIV** DNA vaccine (EP HIV-1090) and to test whether or not the vaccine can stimulate immune system responses in **HIV** uninfected people. This vaccine uses only parts of the virus's DNA and cannot cause **HIV** infection.

Phase(s): Phase I

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00054860

- **Safety of and Immune System Response to an HIV Vaccine (EP-HIV-1090) in HIV Infected Patients**

  Condition(s): HIV Infections

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

  Purpose - Excerpt: HIV-1-infected patients who have been treated with anti-HIV drugs for a long time may have weakened immune responses to **HIV.** The DNA-based vaccine in this study is designed to boost the immune system's responses against many HIV-1 proteins. The main purposes of this study are to test the safety of this **HIV** vaccine (EP HIV-1090) and to test whether or not the vaccine can stimulate immune system responses in people who have HIV-1 infection.

  Phase(s): Phase I

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00052182

- **Therapeutic HIV Vaccine and Interleukin-2 to Increase the Immune System's Response to HIV**

  Condition(s): HIV Infections

  Study Status: This study is currently recruiting patients.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

  Purpose - Excerpt: This study will evaluate whether the **HIV** vaccine ALVAC vCP1452 given in combination with interleukin-2 (IL-2) can increase immune system function in people with **HIV** infection.

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00056797

- **A Comparison of Two Anti-HIV Triple-Drug Combinations in HIV-Infected Patients**

  Condition(s): HIV Infections

Study Status: This study is no longer recruiting patients.

Sponsor(s): Bristol-Myers Squibb

Purpose - Excerpt: The purpose of this study is to compare the safety and effectiveness of two anti-HIV drug combinations when given to HIV-infected patients who have never been treated with anti-HIV drugs. One drug combination is stavudine (d4T) plus didanosine (ddI) plus Crixivan. The other combination is Retrovir (AZT) plus Epivir (3TC) plus Crixivan.

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00002168

- **A Study of the Effectiveness of an HIV Vaccine (ALVAC vCP205) to Boost Immune Functions in HIV-Negative Volunteers Who Have Already Received an HIV Vaccine**

  Condition(s): HIV Infections; HIV Seronegativity

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

  Purpose - Excerpt: The purpose of this study is to see if it is safe to give an **HIV** vaccine (vCP205) to volunteers who received an **HIV** vaccine at least 2 years ago, and to study how the immune system responds to this vaccine. Vaccines are given to people to try to resist infection or prevent disease. There are a number of different **HIV** vaccines that are currently being tested. The vaccines that seem to be the most promising are canarypox vaccines, known as ALVAC vaccines; the vaccine tested in this study is ALVAC-HIV vCP205. This study will look at the safety of the vaccine and how the immune system responds to it.

  Phase(s): Phase I

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00001136

- **A Study of the Effects of Giving Two Anti-HIV Vaccines to Babies of HIV-Positive Mothers**

  Condition(s): HIV Infections; HIV Seronegativity

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID); National Institute of Child Health and Human Development (NICHD)

  Purpose - Excerpt: The purpose of this study is to see if giving the ALVAC vCP1452 anti-HIV vaccine alone or with another vaccine called AIDSVAX B/B to babies of HIV-positive mothers is safe. The study will also look at how these vaccines affect a baby's immune system. Most HIV-positive children get **HIV** from their mothers during pregnancy or birth. Treatment with anti-HIV drugs can reduce the baby's risk of getting **HIV.** Vaccines also may help prevent **HIV** infection. This study will look at whether the ALVAC vCP1452 vaccine and the AIDSVAX B/B vaccine can help the body fight off **HIV** infection. There is no chance of getting **HIV** infection from the vaccines. (This study has been changed. In earlier versions, ALVAC vCP205 and AIDSVAX B/E were going to be used.)

Phase(s): Phase I

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00000879

- **A Study to Test the Safety of Three Experimental HIV Vaccines**

  Condition(s): HIV Infections; HIV Seronegativity

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

  Purpose - Excerpt: The purpose of this study is to test three experimental **HIV** vaccines. This study will look at whether it is safe to give these vaccines together and how the immune system responds to the vaccines. There are a number of studies being performed to test **HIV** vaccines. The vaccines that seem to be the most promising are canarypox vaccines, known as ALVAC vaccines. The three experimental **HIV** vaccines used in this study are called ALVAC-HIV vCP205, HIV-1 SF-2 p24, and HIV-1 SF-2 rgp120. The HIV-1 SF-2 p24 and HIV-1 SF-2 rgp120 vaccines are mixed with an adjuvant, which is a substance that increases immune response.

  Phase(s): Phase I

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00000946

- **ALVAC-HIV vCP1452 Alone and Combined with MN rgp120**

  Condition(s): HIV Infections; HIV Seronegativity

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

  Purpose - Excerpt: The purpose of this study is to test how the body's immune system responds to the vaccine ALVAC-HIV vCP1452 and to determine if the vaccine is safe when given alone and with MN rgp120. **HIV** infection and AIDS have no cure, in spite of recent advances in anti-HIV drugs. Many worldwide populations cannot afford the antiviral treatments for infected people. **HIV** vaccines offer hope for disease prevention. In this trial, 2 experimental **HIV** vaccines called ALVAC vCP1452 and MN rgp120 will be given to volunteers in Haiti, Brazil, Peru, and Trinidad and Tobago. The study will determine how volunteers' immune systems respond to the vaccines. (This protocol has been changed by adding new international sites.)

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00011037

- **Effectiveness of Giving an HIV Vaccine (Remune) to HIV-Positive Patients Receiving an Anti-HIV Drug Combination**

  Condition(s): HIV Infections

Study Status: This study is no longer recruiting patients.

Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

Purpose - Excerpt: The purpose of this study is to look at the effects of the **HIV** vaccine Remune on viral load (level of **HIV** in the blood) and on the way the immune system responds to **HIV.** This study will also try to see if the effects of the vaccine are different in patients entering the study with a viral load below 50 copies/ml compared to those who have a viral load from 50 to 500 copies/ml. (This study is currently being redesigned and the purpose may be revised.) Treatment with anti-HIV drugs does not always keep **HIV** viral load undetectable (so low that it cannot be measured). This study originally added an **HIV** vaccine called Remune to treat patients. Remune was thought to reduce viral load and improve immune responses. However, new information suggests that Remune may not be as effective as was first believed. The study has been changed to follow people already in the study and to let people enroll only if they participate in the substudy. The substudy will look at the effect of another **HIV** vaccine, vCP1452, on the immune response and how it works in combination with Remune. Information about the safety of these vaccines in HIV-positive patients will be gathered.

Phase(s): Phase III

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00005758

- **Effectiveness of Treating HIV-Positive Patients with an HIV Vaccine (Remune)**

  Condition(s): HIV Infections

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): Agouron Pharmaceuticals

  Purpose - Excerpt: The purpose of this study is to see if it is effective to add an **HIV** vaccine (Remune) to the anti-HIV drug combination of Combivir (zidovudine plus lamivudine) and nelfinavir.

  Phase(s): Phase III

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00005002

- **HIV Candidate Vaccine, ALVAC-HIV-1, Administration in HIV-Negative Adults**

  Condition(s): HIV Infections; HIV Seronegativity

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): Walter Reed Army Institute of Research (WRAIR)

  Purpose - Excerpt: The purpose of this study is to determine the best way to administer the candidate **HIV** vaccine, ALVAC HIV-1 (vCP205).

  Phase(s): Phase I

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00013572

- **Immune Responses in HIV-Positive Patients Receiving an Anti-HIV Drug Combination When Given the HIV Vaccines Remune and vCP1452**

  Condition(s): HIV Infections

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

  Purpose - Excerpt: The purpose of this study is to see how the vaccines Remune (HIV-1 immunogen) and vCP1452 affect immune responses in patients who also are taking anti-HIV medications. This study also will see if these vaccines are safe to use either alone or in combination. Treatment with anti-HIV drugs does not always keep **HIV** viral load low and under control. This study will look at the effect of the **HIV** vaccine, vCP1452, on the immune response and how it works in combination with Remune. Information about immune responses and the safety of these vaccines in HIV-positive patients will be gathered.

  Phase(s): Phase I

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00006495

- **Safety and Immune Response Study of High-Dose Canarypox ALVAC-HIV Vaccine in Healthy, HIV Uninfected Adults**

  Condition(s): HIV Infections; HIV Seronegativity

  Study Status: This study is no longer recruiting patients.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

  Purpose - Excerpt: The purpose of this study is to see if the experimental vaccine, ALVAC-HIV (vCP1452) is safe and to study how the immune system responds to the vaccine. This trial is designed to determine whether a higher vaccine dose (6 times the usual dose) will elicit a higher immune response. As of May 2001, over 200 people received the ALVAC-HIV (vCP1452) vaccine at the lower dose. The higher dose of the vaccine to be used in this study has not been given to humans previously. High doses of a similar vaccine have been given to a few people without serious side effects. In a recent study done in mice, higher doses of ALVAC-HIV produced stronger immune responses. It is possible that the doses of ALVAC-HIV given to humans are below the amount needed for the maximum immune response. Because the exact relationship between an increased immune response and its effectiveness in preventing **HIV** infection is uncertain, the HVTN will use the highest dose that can be manufactured.

  Phase(s): Phase I

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00027261

- **A Multicenter, Double-Blind, Phase III, Adjuvant-Controlled Study of the Effect of 10 Units of HIV-1 Immunogen (Remune) Compared to Incomplete Freund's Adjuvant (IFA) Alone Every 12 Weeks on AIDS-Free Survival in Subjects With HIV Infection and CD4 T-Lymp**

  Condition(s): HIV Infections

  Study Status: This study is completed.

  Sponsor(s): Immune Response

  Purpose - Excerpt: To determine the effect of HIV-1 immunogen (Remune) on AIDS-free survival, defined as the time prior to development of an AIDS-defining condition or death.

  Phase(s): Phase III

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00002359

- **A Multicenter, Randomized, Placebo-Controlled, Double-Blinded, Phase I Trial to Evaluate the Safety and Immunogenicity of Live Recombinant Canarypox ALVAC-HIV vCP205 Combined with GM-CSF in Healthy, HIV-1 Uninfected Volunteers**

  Condition(s): HIV Infections

  Study Status: This study is completed.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

  Purpose - Excerpt: To evaluate the safety and immunogenicity of live recombinant canarypox ALVAC-HIV vCP205 in combination with recombinant human granulocyte-macrophage colony-stimulating factor (GM-CSF) at 80 microg and 250 microg. [AS PER AMENDMENT 4/30/99: To study the safety of following 4 ALVAC immunizations with a nucleic acid gag/pol HIV-1 immunogen (APL-400-047, Wyeth-Lederle). To assess the ability of this sequence of immunization to boost the LTL, T-helper cell, and antibody response.] ALVAC-HIV candidate vaccines have induced HIV-specific CTL responses in more than half of recipients in some protocols. Depending on the HIV-1 gene products expressed by the particular ALVAC-HIV candidate vaccine, volunteers have generated anti-Envelope (vCP125, vCP205, and vCP300), anti-Gag (vCP205 and vCP300), and anti-Nef (vCP300) CTL activity. Although 3 to 4 immunizations with the different ALVAC-HIV experimental vaccines induce anti-HIV-1 neutralizing antibodies in a portion, often the majority, of volunteers, the geometric mean titers of these antibodies are modest, usually less than 50. This study will determine whether there is an increase in the anti-HIV antibody titers when GM-CSF is used as an adjuvant with ALVAC-HIV vCP205 and will also examine the kinetics and magnitude of the HIV-specific CTL response.

  Phase(s): Phase I

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00001090

- **A Study of 1592U89 in Combination with Protease Inhibitors in HIV-Infected Patients Who Have Never Taken Anti-HIV Drugs**

  Condition(s): HIV Infections

  Study Status: This study is completed.

  Sponsor(s): Glaxo Wellcome

  Purpose - Excerpt: The purpose of this study is to see if it is safe and effective to give 1592U89 plus certain protease inhibitors (PIs) to HIV-infected patients who never have been treated with anti-HIV drugs. This study also examines how the body processes these drugs when they are given together.

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00002440

- **A Study of AZT in HIV-Infected Patients with AIDS-Related Kaposi's Sarcoma**

  Condition(s): HIV Infections

  Study Status: This study is completed.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

  Purpose - Excerpt: To determine whether taking zidovudine (AZT) will change the natural course of **HIV** infection in patients with AIDS-associated Kaposi's sarcoma (KS) and whether administering AZT at a similar dose but at different intervals will reduce toxicity in a more manageable treatment plan. Patients infected with AIDS can benefit from therapy with an effective anti-AIDS virus agent. AZT is a drug that is effective in inhibiting the effects of **HIV** infection. The study will show whether toxicity of AZT can be reduced in a more manageable treatment plan, and whether AZT therapy will delay the development of opportunistic infections and/or KS lesions.

  Phase(s): Phase III

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00000994

- **A Study of Dextran Sulfate in HIV-Infected Patients and in Patients with AIDS or AIDS Related Complex (ARC)**

  Condition(s): HIV Infections

  Study Status: This study is completed.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

  Purpose - Excerpt: To determine the effectiveness and safety of dextran sulfate (DS) as a treatment for patients with AIDS, AIDS related complex (ARC), or asymptomatic **HIV** infection with or without persistent generalized lymphadenopathy (PGL), and to determine antiviral activity at different doses of DS. Although zidovudine (AZT) has shown promise in prolonging life in patients with AIDS and severe ARC, it has significant blood toxicities. It would be beneficial to combine AZT with another antiviral agent that does not have the same toxicity. DS might be a suitable drug since it has shown antiviral activity against **HIV** in the laboratory, and in preliminary studies it has

shown little toxicity. Also, the combination of DS with AZT has been shown to be more effective than either alone.

Phase(s): Phase I

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00001009

- **A Study of HIV and Cytomegalovirus (CMV) in HIV-Infected Patients**

  Condition(s): Cytomegalovirus Infections; HIV Infections

  Study Status: This study is completed.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

  Purpose - Excerpt: To define relationships between 1) **HIV** load and risk of CMV disease, 2) CMV load and the risk of developing CMV disease, and 3) CMV load and **HIV** load. To establish threshold CMV and **HIV** load values in peripheral blood fractions that are associated with development of CMV end-organ disease. To define the natural history of CMV diseases in the context of highly active antiretroviral therapy (HAART). Establishment of threshold CMV and **HIV** load values associated with CMV disease would facilitate identification of HIV-infected individuals truly at risk for CMV disease in whom targeted prophylactic interventions to prevent CMV disease would be indicated. These studies would also further the understanding of the natural history of CMV disease within the context of AIDS. Natural history studies conducted prior to the advent of highly active antiretroviral therapy (HAART; i.e., 3-drug regimens that include **HIV** reverse transcriptase and protease inhibitors) have demonstrated that the risk for developing CMV disease increases with progression of **HIV** disease and with declining CD4 counts. Presently the need exists to define the natural history of CMV disease in patients with AIDS within the context of HAART.

  Study Type: Observational

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00001089

- **A Study of Ribavirin in the Treatment of Patients with AIDS and AIDS-Related Problems**

  Condition(s): HIV Infections

  Study Status: This study is completed.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

  Purpose - Excerpt: To determine the maximum long-term dosage of ribavirin (RBV) that is safe and free of serious side effects in patients with AIDS or AIDS related illnesses. Also, to determine what effect different dosage levels have on biologic markers of efficacy, such as the amount of the AIDS virus (HIV) or number of T cells in the patient's blood. RBV is a new drug capable of inhibiting the growth of the AIDS virus in the laboratory with little effect on normal human cells. In earlier tests of RBV in AIDS patients, the drug was well tolerated and safe, and this favorable result suggested that RBV should be more extensively studied in patients with AIDS and advanced AIDS related complex (ARC).

  Phase(s): Phase I

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00001015

- **A Study of Several Anti-HIV Drug Combinations in HIV-Infected Patients Who Have Used Indinavir**

  Condition(s): HIV Infections

  Study Status: This study is completed.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

  Purpose - Excerpt: To compare the proportion of patients whose plasma HIV-1 RNA is below 500 copies/ml after 16 weeks of treatment. To assess the safety, toxicity, and tolerance of each treatment arm. While indinavir is currently the most commonly prescribed protease inhibitor, the optimal therapy for a person on an indinavir-containing regimen who experiences a rebound in viral load or never experiences a decrease in viral load below 500 copies per milliliter is unknown. Current clinical practice for such patients typically involves empiric use of a combination of other protease inhibitors (saquinavir/nelfinavir or saquinavir/ritonavir) and at least 1 other antiretroviral agent to which the patient has had little or no prior exposure. This may involve the use of 1 or more reverse transcriptase inhibitors (RTIs) or nonnucleoside reverse transcriptase inhibitors (NNRTIs). This study attempts to formally evaluate some of these options in indinavir-experienced patients.

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00000892

- **A Study of the Effectiveness of Different Anti-HIV Treatments in HIV-Positive Individuals Who Have Been on a Protease Inhibitor-Containing Drug Regimen for at Least 16 Weeks**

  Condition(s): HIV Infections

  Study Status: This study is completed.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

  Purpose - Excerpt: The purpose of this study is to compare different treatments for **HIV** infection to see which works best to lower **HIV** levels and to raise the number of CD4 cells (cells of the immune system that fight infection), in HIV-positive individuals who have been on a protease inhibitor-containing drug regimen for at least 16 weeks. Researchers have found that combination anti-HIV therapy (multiple drugs given together) can help prevent AIDS-related illnesses and help people with AIDS live longer. In this study, the anti-HIV drug efavirenz (EFV) will be tested with 1 or 2 other protease inhibitors (PIs) to see which combination works best to treat **HIV** infection. EFV has been shown to limit the amount of **HIV** virus produced by infected cells.

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00000914

- **A Study on Amprenavir in Combination with Other Anti-HIV Drugs in HIV-Positive Patients**

  Condition(s): HIV Infections

  Study Status: This study is completed.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

  Purpose - Excerpt: The purpose of this study is to compare 4 different combinations of anti-HIV drugs and to determine the number of people whose **HIV** blood levels decrease to 200 copies/ml or less while on the treatment. This study evaluates the safety of these drug combinations, which include an experimental protease inhibitor (PI), amprenavir. Despite the success that many patients have had with PI treatment regimens, there is still a possibility that patients receiving PIs may continue to have high **HIV** blood levels. Because of this possibility, alternative drug combinations containing PIs are being studied. It appears that amprenavir, when taken with 3 or 4 other anti-HIV drugs, may be effective in patients with prior PI treatment experience.

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00000912

- **A Study on the Safety and Effectiveness of Adefovir Dipivoxil in Combination with Anti-HIV Therapy (HAART) in HIV-Positive Patients**

  Condition(s): HIV Infections

  Study Status: This study is completed.

  Sponsor(s): Gilead Sciences

  Purpose - Excerpt: The purpose of this study is to see if it is safe and effective to give an experimental anti-HIV drug, adefovir dipivoxil (ADV), in combination with other anti-HIV drugs (HAART) to patients who have a viral load (level of **HIV** in the blood) between 50 and 400 copies/ml.

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00002426

- **A Study to Compare The Ability of Different Anti-HIV Drugs to Decrease Viral Load After Nelfinavir (an Anti-HIV Drug)Treatment Failure**

  Condition(s): HIV Infections

  Study Status: This study is completed.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

  Purpose - Excerpt: The purpose of this study is to determine the safety and effectiveness of combining several anti-HIV drugs in order to decrease plasma viral load (level of **HIV** in the blood) in HIV-positive patients who have failed nelfinavir (NFV) treatment. In order to determine the ability of a drug regimen to decrease viral load after drug treatment has failed, it is best to test a variety different of drug "cocktails" (drug regimens). The drug cocktails in this study include 2 new nucleoside reverse transcriptase inhibitors (NRTIs), efavirenz (an NNRTI, non-nucleoside reverse

transcriptase inhibitor), and either 1 or 2 protease inhibitors. It is important to include multiple drugs from different groups in a drug cocktail since combinations containing fewer drugs are likely to fail.

Phase(s): Phase II

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00000918

- **A Study to Evaluate the Effects of Anti-HIV Drugs in HIV-Positive Patients Who Also Have Hepatitis C Infection**

  Condition(s): HIV Infections; Hepatitis C

  Study Status: This study is completed.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

  Purpose - Excerpt: This study evaluates patients infected with both **HIV** and Hepatitis C virus (HCV) who are receiving anti-HIV drugs. The purpose of this study is to learn more about HCV infection in patients whose **HIV** blood level decreases to less than 500 copies/ml.

  Phase(s): Phase II

  Study Type: Observational

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00001117

- **A Study to Evaluate the Safety and Effectiveness of HIV-1 LAI gp120 (an HIV Vaccine) Given With or Without HIV-1 MN rgp120 (Another HIV Vaccine) to HIV-Negative Volunteers**

  Condition(s): HIV Infections; HIV Seronegativity

  Study Status: This study is completed.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

  Purpose - Excerpt: The purpose of this study is to evaluate the safety and effectiveness of giving healthy volunteers a new oral **HIV** vaccine which has been incorporated into a bacterial cell. This oral vaccine (HIV-1 LAI gp120) will be given with or without a different injected **HIV** vaccine (HIV-1 MN rgp120). Vaccines are preparations that are introduced into the body to try to prevent infection or create resistance to infection. This study examines a new oral vaccine to see if it can improve the immune system's ability to fight the **HIV** virus when given alone or with another injected vaccine.

  Phase(s): Phase I

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00000868

- **A Study to Evaluate the Use of Memantine In Combination with Anti-HIV Drugs to Treat AIDS Dementia Complex (ADC)**

  Condition(s): AIDS Dementia Complex; HIV Infections

Study Status: This study is completed.

Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

Purpose - Excerpt: The purpose of this study is to determine the safety and effectiveness of memantine, an experimental drug, in improving AIDS dementia complex (ADC). The symptoms of ADC can be improved with zidovudine (ZDV). However, ZDV therapy has been associated with significant toxicities, and the effectiveness of ZDV seems to decrease during the second and third years of therapy. The effectiveness of other antiretroviral drugs as treatment for ADC is not known, so it is important to explore alternative therapies.

Phase(s): Phase II

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00000867

- **A Study to See Whether Two HIV Vaccines Are Safe and Can Prevent HIV Infection**

  Condition(s): HIV Infections; HIV Seronegativity

  Study Status: This study is completed.

  Sponsor(s): Walter Reed Army Institute of Research (WRAIR)

  Purpose - Excerpt: The purpose of this study is to see whether an **HIV** vaccine, ALVAC vCP205, is safe and can prevent **HIV** infection. The vCP205 vaccine will be tested with another vaccine, gp160MN/LAI-2.

  Phase(s): Phase I

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00004579

- **A Study to Test If Giving Remune (an HIV Vaccine) Can Improve the Immune Systems of HIV-Positive Patients Who Are Also Participating in ACTG 328**

  Condition(s): HIV Infections

  Study Status: This study is completed.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

  Purpose - Excerpt: The purpose of this study is to determine the effects of an **HIV** vaccine (Remune) on the immune system. This study involves patients who have received at least 60 weeks of anti-HIV therapy, either alone or in combination with IL-2, while enrolled in ACTG 328. Remune is an experimental **HIV** vaccine. To see how the body's immune system reacts, this vaccine will be given with 1 to 3 other vaccines, and skin tests will monitor the body's reaction.

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00000943

- **Effectiveness of Adding Remune to Your Current Anti-HIV Drug Combination**

  Condition(s): HIV Infections

Study Status: This study is terminated.

Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID); Immune Response

Purpose - Excerpt: The purpose of this study is to see if giving a vaccine (Remune) is effective in HIV-positive patients who are also taking anti-HIV therapy. Regular treatment of HIV-positive patients with anti-HIV drugs slows the multiplication of the **HIV** virus in the body. A vaccine called Remune works to stop the virus infection by "boosting" the body's immune cell defense against the **HIV** virus before the virus enters cells. It also blocks the virus from entering the cells. This study will see whether Remune will improve the immune cell natural defense in patients who are also taking anti-HIV drugs.

Phase(s): Phase I

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00006153

- **Effectiveness of an HIV Vaccine in HIV-Negative Adults in North America Who Are at Risk of HIV Infection**

  Condition(s): HIV Infections; HIV Seronegativity

  Study Status: This study is completed.

  Sponsor(s): VaxGen

  Purpose - Excerpt: The purpose of this study is to see if an **HIV** vaccine, AIDSVAX B/B, can protect adults who are at risk from becoming infected with **HIV.** Patients who become infected despite immunization will be studied to see if receiving the vaccine before becoming infected will help keep **HIV** levels (viral load) low.

  Phase(s): Phase III

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00002441

- **Effects of Immunization with HIV-1 Immunogen Plus Anti-HIV Treatment Interruption on the Levels of HIV**

  Condition(s): HIV Infections

  Study Status: This study is terminated.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

  Purpose - Excerpt: The purpose of this study is to see whether or not an **HIV** vaccination will help the body control the amount of **HIV** virus in blood (viral load) in patients who are not taking anti-HIV medicines. Doctors are not sure why the body fails to control **HIV** viral load in most people infected with **HIV.** The vaccine Remune has been shown to boost part of the body's immune response to **HIV** in patients whose viral load has been lowered with anti-HIV drugs. This study will test the ability of Remune to improve the body's immune response and to lower **HIV** viral load in patients who stop taking anti-HIV drugs for short periods of time.

  Phase(s): Phase II

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00021762

- **Preventive Treatment Against Tuberculosis (TB) in Patients With Human Immunodeficiency Virus (HIV) Infection and Confirmed Latent Tuberculous Infection**

  Condition(s): HIV Infections; Tuberculosis

  Study Status: This study is completed.

  Sponsor(s): Hoechst Marion Roussel; Lederle Laboratories; National Institute of Allergy and Infectious Diseases (NIAID)

  Purpose - Excerpt: To evaluate and compare the safety and effectiveness of a one-year course of isoniazid (INH) versus a two-month course of rifampin plus pyrazinamide for the prevention of reactivation tuberculosis in individuals infected with both HIV and latent (inactive) Mycobacterium tuberculosis. Current guidelines from the American Thoracic Society and the Centers for Disease Control recommend 6 to 12 months of INH for PPD (purified protein derivative)-positive individuals. Although the effectiveness of this treatment is not known for HIV-infected individuals, several studies using INH to prevent tuberculosis in presumably normal hosts have shown 60 to 80 percent effectiveness. Problems with this treatment include compliance, adverse reaction, and the possibility of not preventing disease due to tuberculosis organisms being resistant to INH. A two-month preventive treatment plan should help in increasing compliance. In addition, the use of two drugs (rifampin / pyrazinamide) may help overcome problems with drug resistance. If this study shows equal or greater effectiveness of the two-month rifampin / pyrazinamide treatment, it could alter the approach to tuberculosis prevention for both HIV-positive and HIV-negative individuals.

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00000638

- **Safety and Effectiveness of Anti-HIV Vaccines in HIV-Negative Adults**

  Condition(s): HIV Infections

  Study Status: This study is completed.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

  Purpose - Excerpt: The purpose of this study is to find out whether three different anti-HIV vaccines are safe and whether they help prevent **HIV** infection. These vaccines are called vCP205, vCP1433, and vCP1452. Some patients also receive another anti-HIV vaccine, gp160. The vaccines are made up of small pieces of **HIV,** which help the body learn to recognize and destroy **HIV.** You cannot get **HIV** from these vaccines. There are two different ways a vaccine can protect the body from infection. First, a vaccine may help the immune system make antibodies, which are proteins that recognize invading viruses or bacteria. Second, a vaccine may help the body make immune cells that destroy infected cells. The second type of vaccine is more powerful against **HIV.** In this study, doctors will see whether vCP205, vCP1433, vCP1452, and gp160 are good vaccines by seeing whether they help the body make immune cells.

  Phase(s): Phase I

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00000904

- **Safety and Effectiveness of the Vaccine ALVAC-HIV vCP205 in HIV-Negative Adult Volunteers in Uganda**

  Condition(s): HIV Infections; HIV Seronegativity

  Study Status: This study is completed.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID); Joint Clinical Research Center; Uganda Virus Research Institute; Joint UN Programme on HIV/AIDS (UNAIDS); John E. Fogarty International Center (FIC); Case Western Reserve University

  Purpose - Excerpt: The purpose of this study is to see if it is safe to give ALVAC-HIV vCP205, a possible **HIV** vaccine, and to study the immune responses in adult HIV-1 uninfected volunteers. Uganda has been severely affected by **HIV** infection and AIDS and has been selected to participate in HIV-vaccine development. The **HIV** viruses commonly isolated from Uganda are 2 kinds that are not used in making current vaccines. Current vaccines generate several kinds of immune responses. Researchers would like to see if a response to the kind of virus in a current vaccine will also protect people from the viruses commonly found in Uganda.

  Phase(s): Phase I

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00007423

- **Safety and Effectiveness of Treating HIV-Positive Patients with an HIV Vaccine (Remune)**

  Condition(s): HIV Infections

  Study Status: This study is completed.

  Sponsor(s): Agouron Pharmaceuticals

  Purpose - Excerpt: The purpose of this study is to see if giving HIV-positive patients an **HIV** vaccine plus anti-HIV drugs can help lower **HIV** levels in the blood (viral load).

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00005001

- **Safety and Effectiveness of Two Different Formulations of an HIV Vaccine in Infants Born to HIV-Infected Women**

  Condition(s): HIV Infections; HIV Seronegativity

  Study Status: This study is terminated.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

  Purpose - Excerpt: The purpose of this study is to test the safety and effectiveness of two different formulations of an **HIV** vaccine in infants born to HIV-infected women.

Phase(s): Phase I

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00000809

- **Safety and Effects of Giving a New HIV Vaccine (GENEVAX-HIV) to HIV-Negative Volunteers**

  Condition(s): HIV Infections; HIV Seronegativity

  Study Status: This study is completed.

  Sponsor(s): Wyeth-Lederle Vaccines

  Purpose - Excerpt: The purpose of this study is to see if it is safe to give GENEVAX-HIV, a new **HIV** vaccine, to HIV-negative volunteers. This study will also look at how this vaccine affects the immune system of these volunteers.

  Phase(s): Phase I

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00002231

- **Safety of and Immune Response to Polyvalent HIV-1 Vaccine in HIV Uninfected Adults**

  Condition(s): HIV Infections

  Study Status: This study is not yet open for patient recruitment.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

  Purpose - Excerpt: This study will evaluate the safety of and immune response to a new **HIV** vaccine. The vaccine in this trial uses pieces of **HIV** DNA and **HIV** proteins. The vaccine itself cannot cause **HIV** infection or AIDS.

  Phase(s): Phase I

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00061243

- **Safety of the Candidate Vaccine C4-V3 Alone or with Interleukin-12 (IL-12) in HIV-Infected Patients Receiving Effective Anti-HIV Drug Therapy**

  Condition(s): HIV Infections

  Study Status: This study is completed.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

  Purpose - Excerpt: The purpose of this study is to see if it is safe to give C4-V3, a possible **HIV** vaccine, alone or in conjunction with 4 different doses of interleukin-12 (IL-12), to HIV-infected patients who are taking anti-HIV drugs that have lowered the amount of **HIV** in patients' blood. (This study has been changed so that vaccine is administered alone or with 4 different doses of IL-12.) Immune cells known as cytotoxic T lymphocytes (CTLs) help destroy HIV-infected cells. However, in most patients, CTLs decrease over time. This allows **HIV** levels to rise and AIDS symptoms to develop. The

C4-V3 vaccine contains small pieces of **HIV** protein that can boost CTL levels, allowing the body's immune system to fight **HIV.** Giving IL-12, a normal part of the immune system, with C4-V3 may make the vaccine more effective.

Phase(s): Phase I

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00005779

- **Tenofovir Disoproxil Fumarate (TDF) in HIV-1 Patients Who Have Never Taken Anti-HIV Drugs**

  Condition(s): HIV Infections

  Study Status: This study is completed.

  Sponsor(s): Gilead Sciences

  Purpose - Excerpt: The purpose of this study is to look at the effectiveness of tenofovir disoproxil fumarate (TDF) in HIV-infected patients who have never taken anti-HIV drugs.

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00016588

- **The Effectiveness of GM-CSF in HIV-Positive Patients Who Are Also Receiving Anti-HIV Therapy**

  Condition(s): HIV Infections

  Study Status: This study is completed.

  Sponsor(s): National Institute of Allergy and Infectious Diseases (NIAID)

  Purpose - Excerpt: The purpose of this study is to see how HIV-positive patients who are taking anti-HIV drugs and have a viral load (level of **HIV** in the blood) of 1,500 copies/ml or more respond to GM-CSF (granulocyte-macrophage colony-stimulating factor). GM-CSF is a medication that is being tested in HIV-positive patients to see if it can improve their immune systems or if it can lower the level of **HIV** in their blood. GM-CSF is often given to patients with leukemia or patients who have received bone marrow transplants to increase their white blood cells and to improve their immune systems. Doctors believe that GM-CSF can increase CD4 counts in HIV-positive patients, but this study will also look at how GM-CSF affects viral load.

  Phase(s): Phase II

  Study Type: Interventional

  Contact(s): see Web site below

  Web Site: http://clinicaltrials.gov/ct/show/NCT00000850

- **The Safety and Effectiveness of Adefovir Dipivoxil Plus Indinavir Combined with Zidovudine or Lamivudine or Stavudine in HIV-Infected Patients Who Have Not Taken Anti-HIV Drugs**

  Condition(s): HIV Infections

Study Status: This study is completed.

Sponsor(s): Gilead Sciences

Purpose - Excerpt: To evaluate the safety and tolerance of adefovir dipivoxil and indinavir administered orally in combination with zidovudine, lamivudine, or stavudine in HIV-infected patients with CD4 cell counts >= 100 cells/mm3 and an HIV-1 RNA baseline copy number >= 5000 copies/ml. To determine the proportion of patients whose plasma HIV-1 RNA level falls below the level of detection (500 copies/ml) by 20 weeks of study therapy and the average reduction in HIV-1 RNA from baseline through study week 20. To evaluate the durability of the antiviral response through 48 weeks of study in patients who continue on study therapy after week 24.

Phase(s): Phase II

Study Type: Interventional

Contact(s): see Web site below

Web Site: http://clinicaltrials.gov/ct/show/NCT00002379

Keeping Current on Clinical Trials

The U.S. National Institutes of Health, through the National Library of Medicine, has developed ClinicalTrials.gov to provide current information about clinical research across the broadest number of diseases and conditions.

The site was launched in February 2000 and currently contains approximately 5,700 clinical studies in over 59,000 locations worldwide, with most studies being conducted in the United States. ClinicalTrials.gov receives about 2 million hits per month and hosts approximately 5,400 visitors daily. To access this database, simply go to the Web site at **http://www.clinicaltrials.gov/** and search by "human immunodeficiency virus" (or synonyms).

While ClinicalTrials.gov is the most comprehensive listing of NIH-supported clinical trials available, not all trials are in the database. The database is updated regularly, so clinical trials are continually being added. The following is a list of specialty databases affiliated with the National Institutes of Health that offer additional information on trials:

- For clinical studies at the Warren Grant Magnuson Clinical Center located in Bethesda, Maryland, visit their Web site: **http://clinicalstudies.info.nih.gov/**
- For clinical studies conducted at the Bayview Campus in Baltimore, Maryland, visit their Web site: **http://www.jhbmc.jhu.edu/studies/index.html**
- For cancer trials, visit the National Cancer Institute: **http://cancertrials.nci.nih.gov/**
- For eye-related trials, visit and search the Web page of the National Eye Institute: **http://www.nei.nih.gov/neitrials/index.htm**
- For heart, lung and blood trials, visit the Web page of the National Heart, Lung and Blood Institute: **http://www.nhlbi.nih.gov/studies/index.htm**
- For trials on aging, visit and search the Web site of the National Institute on Aging: **http://www.grc.nia.nih.gov/studies/index.htm**
- For rare diseases, visit and search the Web site sponsored by the Office of Rare Diseases: **http://ord.aspensys.com/asp/resources/rsch_trials.asp**

- For alcoholism, visit the National Institute on Alcohol Abuse and Alcoholism: **http://www.niaaa.nih.gov/intramural/Web_dicbr_hp/particip.htm**
- For trials on infectious, immune, and allergic diseases, visit the site of the National Institute of Allergy and Infectious Diseases: **http://www.niaid.nih.gov/clintrials/**
- For trials on arthritis, musculoskeletal and skin diseases, visit newly revised site of the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health: **http://www.niams.nih.gov/hi/studies/index.htm**
- For hearing-related trials, visit the National Institute on Deafness and Other Communication Disorders: **http://www.nidcd.nih.gov/health/clinical/index.htm**
- For trials on diseases of the digestive system and kidneys, and diabetes, visit the National Institute of Diabetes and Digestive and Kidney Diseases: **http://www.niddk.nih.gov/patient/patient.htm**
- For drug abuse trials, visit and search the Web site sponsored by the National Institute on Drug Abuse: **http://www.nida.nih.gov/CTN/Index.htm**
- For trials on mental disorders, visit and search the Web site of the National Institute of Mental Health: **http://www.nimh.nih.gov/studies/index.cfm**
- For trials on neurological disorders and stroke, visit and search the Web site sponsored by the National Institute of Neurological Disorders and Stroke of the NIH: **http://www.ninds.nih.gov/funding/funding_opportunities.htm#Clinical_Trials**

CHAPTER 6. PATENTS ON HUMAN IMMUNODEFICIENCY VIRUS

Overview

Patents can be physical innovations (e.g. chemicals, pharmaceuticals, medical equipment) or processes (e.g. treatments or diagnostic procedures). The United States Patent and Trademark Office defines a patent as a grant of a property right to the inventor, issued by the Patent and Trademark Office.[9] Patents, therefore, are intellectual property. For the United States, the term of a new patent is 20 years from the date when the patent application was filed. If the inventor wishes to receive economic benefits, it is likely that the invention will become commercially available within 20 years of the initial filing. It is important to understand, therefore, that an inventor's patent does not indicate that a product or service is or will be commercially available. The patent implies only that the inventor has "the right to exclude others from making, using, offering for sale, or selling" the invention in the United States. While this relates to U.S. patents, similar rules govern foreign patents.

In this chapter, we show you how to locate information on patents and their inventors. If you find a patent that is particularly interesting to you, contact the inventor or the assignee for further information. **IMPORTANT NOTE:** When following the search strategy described below, you may discover non-medical patents that use the generic term "human immunodeficiency virus" (or a synonym) in their titles. To accurately reflect the results that you might find while conducting research on human immunodeficiency virus, we have not necessarily excluded non-medical patents in this bibliography.

Patents on Human Immunodeficiency Virus

By performing a patent search focusing on human immunodeficiency virus, you can obtain information such as the title of the invention, the names of the inventor(s), the assignee(s) or the company that owns or controls the patent, a short abstract that summarizes the patent, and a few excerpts from the description of the patent. The abstract of a patent tends to be more technical in nature, while the description is often written for the public. Full patent

[9]Adapted from the United States Patent and Trademark Office: **http://www.uspto.gov/web/offices/pac/doc/general/whatis.htm**.

descriptions contain much more information than is presented here (e.g. claims, references, figures, diagrams, etc.). We will tell you how to obtain this information later in the chapter. The following is an example of the type of information that you can expect to obtain from a patent search on human immunodeficiency virus:

- **Amino acid DNA sequences related to genomic RNA of human immunodeficiency virus (HIV-1)**

  Inventor(s): Danos; Oliver (Paris, FR), Wain-Hobson; Simon (Montigny Les Bretonneux, FR), Stewart; Cole (Chatillon, FR), Sonigo; Pierre (Paris, FR), Alizon; Marc (Paris, FR)

  Assignee(s): Institut Pasteur and Centre National de la Recherche Scientifique (Paris, FR)

  Patent Number: 5,980,900

  Date filed: August 28, 1991

  Abstract: This invention is in the field of lymphadenopathy virus which has been desogmated Human Immunodeficiency Virus Type 1 (HIV-1) This invention relates to a diagnostic means and method to detect the presence of DNA, RNA or antibodies of the lymphadenopathy retrovirus associated with the acquired immune deficiency syndrome or of the lymphadenopathy syndrome by the use of DNA fragments or the peptides encoded by said DNA fragments. The invention further relates to the DNA fragments, vectors comprising them and the proteins expressed.

  Excerpt(s): This invention relates to cloned DNA sequences indistinguishable from genomic RNA and DNA of lymphadenopathy-associated virus (LAV), a process for their preparation and their uses. It relates more particularly to stable probes including a DNA sequence which can be used for the detection of the LAV virus or related viruses or DNA proviruses in any medium, particularly biological samples containing any of them. The invention also relates to polypepetides, whether glycosylated or not, encoded by said DNA sequences.... Lymphadenopathy-associated virus (LAV) is a human retrovirus first isolated from the lymph node of a homosexual patient with lymphadenopathy syndrome, frequently a prodrome or a benign form of acquired immune deficiency syndrome (AIDS). Subsequently, over LAV isolates were recovered from patients with AIDS or pre-AIDS. All available data are consistent with the virus being the causative agent of AIDS.... A method for cloning such DNA sequences has already been disclosed in British Patent Application Nr. 84 23659, filed on Sep. 19, 1984. Reference is hereafter made to that application as concerns subject matter in common with the further improvements to the invention disclosed herein.

  Web site: http://www.delphion.com/details?pn=US05980900__

- **Apparatus and method for inactivation of human immunodeficiency virus**

  Inventor(s): Wainwright; Basil E. (Fort Lauderdale, FL)

  Assignee(s): Polyatomic Apheresis, Ltd. ()

  Patent Number: 6,027,688

  Date filed: May 2, 1994

  Abstract: An apparatus and method for the inactivation of infectious organisms such as viruses, bacteria, fungi and protozoa, and especially for the inactivation of human immunodeficiency virus in proteinaceous material such as blood and blood products, without adversely affecting the normal physiological activity of the material, by

contacting it for a time interval of only about 16 seconds with an ozone-oxygen mixture having an ozone concentration of only about 27.mu./ml. The apparatus includes a gas-liquid contact apparatus through which the material and ozone-oxygen mixture flow in contacting, counter-current relationship, and an ozone generator which produces an ozone-oxygen mixture having a resonant frequency of about 7.83 Hz. The apparatus and method of the invention provide precise control of the concentration of ozone and the contact time between the material to be treated and the ozone-oxygen mixture.

Excerpt(s): This invention relates to an apparatus and method for the treatment of blood and blood products to inactivate infectious organisms, such as viruses and bacteria, and especially to inactivate the human immunodeficiency virus (HIV) in human blood and blood products.... Infectious diseases which once decimated entire populations are now largely controlled by modern drugs and sanitation methods. One virus, however, has remained elusive to medical science, and is infecting the human population in epidemic proportions. The human immunodeficiency virus (HIV), the etiologic agent of acquired immunodeficiency syndrome (AIDS), once generally regarded as a malady of homosexuals and intravenous drug abusers, has become a threat to all strata of society. In most instances, this virus leads to AIDS, and eventually death. Prior to the present invention, there was no known cure, nor were there any effective treatments for controlling the virus without causing unwanted side effects.... Some scientists believe that HIV may have been introduced into the human population through use of polio vaccines made from the tissue of infectious African green monkeys, many of which have been discovered to be infected with a retrovirus related to HIV. The rapid spread of this disease, however, is generally believed to be transmitted through infected blood and blood products, and through sexual contact. Drug abusers sharing used intravenous needles, persons receiving blood transfusions, and homosexuals and heterosexuals engaging in "unsafe" sexual contact are particularly vulnerable.

Web site: http://www.delphion.com/details?pn=US06027688__

- **Cell lines useful for detection of human immunodeficiency virus**

  Inventor(s): Chesebro; Bruce (Corvallis, MT), Wehrly; Kathy (Hamilton, MT)

  Assignee(s): The Unites States of America as represented by the Secretary of the (Washington, DC)

  Patent Number: 5,811,282

  Date filed: June 7, 1995

  Abstract: The present invention relates to a method for AIDS diagnosis and monitoring of anti-AIDS drug therapy, and more particularly to a method of assaying for human immunodeficiency virus. The present invention uses a focal immunoassay (FIA) which utilizes HIV-specific antibodies and indirect immunoassay techniques to detect local areas of HIV infection in susceptible target cells growing in monolayers on plastic dishes. The present invention further relates to specific cell lines used as the susceptible target cells in the disclosed methods.

  Excerpt(s): The present invention relates to a method for AIDS diagnosis and monitoring of anti-AIDS drug therapy, and more particularly to a method of assaying for human immunodeficiency virus.... Retrovirus infection is known to lead to depressed immune function in animal systems. Analogizing the human response to these non-animal systems, a human retrovirus with a tropism for T-cells was considered a candidate in the etiology of human AIDS.... Several members of a family of human T-

lymphotropic retroviruses (HTLV) have been isolated. One of these isolates was obtained from a patient with an aggressive form of T-cell lymphoma. This virus, designated as HTLV-I, has been etiologically linked to the pathogenesis adult T-cell leukemia/lymphoma (ATLL). In vitro infection with HTLV-I can alter T-cell function and, in some cases, lead to T-cell death. Another member of the HTLV family was isolated from a patient with a T-cell variant of hairy cell leukemia, and was designated HTLV-II. Isolation of the HTLV-I and HTLV-II have been reported from cultured T-cells of patients with AIDS. Isolation of another retrovirus was reported from a homosexual patient with chronic generalized lymphadenopathy, a syndrome that often precedes AIDS and therefore is referred to as "pre-AIDS". Proviral DNA of HTLV-I was detected in the cellular DNA of two AIDS patients, and sera of some patients were shown to react with antigens of HTLV-I. The correlation between AIDS and serum antibodies to HTLV-I protein is weak.

Web site: http://www.delphion.com/details?pn=US05811282__

- **Chimeric immunogenic gag-V3 virus-like particles of the human immunodeficiency virus (HIV)**

  Inventor(s): Kang; Chil-Yong (London, CA), Luo; Lizhong (London, CA)

  Assignee(s): Korea Green Cross Corporation (Kyongki-Do, KR)

  Patent Number: 5,580,773

  Date filed: July 30, 1993

  Abstract: An unprocessed human immunodeficiency virus 2 (HIV-2) gag precursor protein, containing a deficient protease, assembles into virus-like particles by budding through the cytoplasmic domain of baculovirus-infected cells. Chimeric constructs were generated by coupling the truncated HIV-2 gag gene to the neutralizing domain (V3) or the neutralizing and CD4 binding domains (V3+CD4B) of gp120 env gene sequences obtained from HIV-1 or HIV-2. Virus-like particles were formed by chimeric gene products when the env gene sequences were linked to the 3' terminus of the gag gene. The gag-env chimeric proteins displayed immunoreactivity towards anti-gp120 rabbit antisera.

  Excerpt(s): The present invention relates to construction of chimeric proteins useful for an AIDS vaccine and the development of diagnostic reagents, and a process for production thereof. More particularly, the present invention relates to gag chimeric proteins of HIV expressed in a recombinant baculovirus-infected insect cell, and a process for production thereof.... Type 1 and 2 of the human immunodeficiency viruses (HIV) are recognized as the etiologic agents for acquired immunodeficiency syndrome (AIDS). A vaccine against these viruses would be an ideal way of preventing infection with HIV and AIDS. Accordingly, much research has been focused on molecular biological analyses of structures and functions of HIV. The main virion structural proteins of HIV are derived from three structural genes known as gag, pol, and env. The genome of many different isolates of HIV have been completely sequenced, and amino acid sequences have been deduced from the cloned proviral DNA sequences. The envelope gene of HIV codes for a glycoprotein precursor with a molecular weight of 160,000 (gp160). The precursor gp160 in virus-infected cells is processed (or cleaved) to produce envelope glycoprotein gp120 and gp41. The envelope glycoproteins gp120 of HIV has been the major target for developing a candidate vaccine against AIDS. gp120 recognizes the cellular receptor (CD4) on helper T lymphocytes, and carries the V3 loop domain that induces neutralizing antibodies (Putney et al., Science 234, 1392-1395 (1986);

Robey et al., Proc. Natl. Acad. Science, USA 83, 7023-7027 (1986)).... The V3 loop represents the third hypervariable region of HIV-1 gp120 (amino acid residues 308-331) which contains not only a major immunodominant neutralizing epitope but also the epitopes for antigen-dependent cellular cytotoxicity (ADCC) and cytotoxic T-lymphocyte (CTL) recognition. Although the majority of the amino acids in the V3 loop are variable among different strains of HIV, a G-P-G-R motif at the tip of the loop is conserved (LaRosa et al., Science 249, 932-935 (1990)).

Web site: http://www.delphion.com/details?pn=US05580773__

- **CLONED DNA SEQUENCES RELATED TO THE ENTIRE GENOMIC RNA OF HUMAN IMMUNODEFICIENCY VIRUS II (HIV-2), POLYPEPTIDES ENCODED BY THESE DNA SEQUENCES AND USE OF THESE DNA CLONES AND POLYPEPTIDES IN DIAGNOSTIC KITS**

  Inventor(s): Clavel; Francois (Rockville, MD), Sonigo; Pierre (Paris, FR), Geutard; Denise (Paris, FR), Montagnier; Luc (Le Plessis Robinson, FR), Alizon; Marc (Paris, FR), Guyader; Mireille (Paris, FR)

  Assignee(s): Institut Pasteur (Paris, FR)

  Patent Number: 6,355,789

  Date filed: June 6, 1995

  Abstract: The present invention is directed toward nucleic acids containing the full-length human immunodeficiency virus type 2 ROD (HIV-2.sub.ROD) pol gene. HIV-2, which was originally designated lymphadenopathy-associated virus type II (LAV-II), was isolated from AIDS patients in West Africa. The virus is genotypically and phenotypically distinct from HIV-1 and bears a closer genetic relationship to the simian immunodeficiency virus (SIV). The present invention describes the preparation of HIV-2.sub.ROD proviral molecular clones from a genomic lambda phage library of CD4.sup.+ -infected cells. The complete nucleotide sequence of the full-length genome was determined and the putative gag, pol, env, vif (Q), vpr (R), vpx (X), nef (F), tat, and rev (art) genes identified. The claimed invention is directed toward nucleic acids containing the full-length HIV-2.sub.ROD pol gene (nt 1829-4936). These nucleic acids should prove useful as diagnostic reagents for the detection of HIV-2 and facilitate expression of the pol gene product.

  Excerpt(s): The invention relates to cloned DNA sequences analogous to the genomic RNA of a virus known as Lymphadenopathy-Associated Virus II ("LAV-II"), a process for the preparation of these cloned DNA sequences, and their use as probes in diagnostic kits. In one embodiment, the invention relates to a cloned DNA sequence analogous to the entire genomic RNA of HIV-2 and its use as a probe. The invention also relates to polypeptides with amino acid sequences encoded by these cloned DNA sequences and the use of these polypeptides in diagnostic kits.... According to recently adopted nomenclature, as reported in Nature, May 1986, a substantially-identical group of retroviruses which has been identified as one causative agent of AIDS are now referred to as Human Immunodeficiency Viruses I (HIV-1). This previously-described group of retroviruses includes Lymphadenopathy-Associated Virus I (LAV-I), Human T-cell Lymphotropic Virus-III (HTLV-III), and AIDS-Related Virus (ARV).... Lymphadenopathy-Associated Virus II has been described in U.S. application Ser. No. 835,228, which was filed Mar. 3, 1986, and is specifically incorporated herein by reference. Because LAV-II is a second, distinct causative agent of AIDS, LAV-II properly

is classifiable as a Human Immunodeficiency Virus II (HIV-2). Therefore, "LAV-II" as used hereinafter describes a particular genus of HIV-2 isolates.

Web site: http://www.delphion.com/details?pn=US06355789__

- **Composition for suppressing infection and growth of human immunodeficiency virus**

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  Assignee(s): Snow Brand Milk Products Co., Ltd. (Hokkaido, JP)

  Patent Number: 5,725,864

  Date filed: December 22, 1994

  Abstract: The invention relates to compositions and methods for inhibiting infection or suppressing growth of human immunodeficiency virus. The composition comprises, as an effective component, an iron-binding protein (e.g., lactoferrin, transferrin, ovotransferrin), a chemically modified compound of the iron-binding protein, or a hydrolyzed compound of the iron-binding protein. The effective components are safe and can be easily prepared from inexpensive raw materials. The composition can be orally administered, injected or applied to the skin, eye, ear, nose or used as a preparation for vagina affusion, mouth washing or suppositories, and can effectively inhibit infection or suppress growth of human immunodeficiency virus.

  Excerpt(s): The present invention relates to a composition for inhibiting infection or suppressing growth of human immunodeficiency virus, comprising an iron-binding protein, a chemically modified compound of the iron-binding protein, or hydrolysate of an iron-binding protein, as an effective component.... Acquired Immune Deficiency Syndrome (AIDS) is a serious immune deficiency disease caused by infection of human immunodeficiency virus (HIV). As of July 1993, the number of AIDS patients reported to WHO is 370,000 and the actual number of HIV infected patients are supposed to be well over that number. At first, HIV infection was considered to be a characteristic infection disease for homosexuals, drug-abusers, and the like. Nowadays, a heterosexual intercourse is proven to be the most significant infection route.... Methods to cure AIDS which are currently being developed include a reverse transcriptase inhibitor, a virus adsorption inhibitor, a protease inhibitor, a sugar chain synthesis inhibitor, a neutralizing antibody, a passive immunization, vaccine, an antisense agent, an immunomodulator, a gene therapy, and the like. Among them, the method using an adsorption inhibitor is very important, because it can act at the earliest stage of the infection and prevent HIV from entering bodies or infecting other cells in vivo.

  Web site: http://www.delphion.com/details?pn=US05725864__

- **Compositions and methods for inhibiting human immunodeficiency virus infection by down-regulating human cellular genes**

  Inventor(s): Dayn; Andrew (Mountain View, CA), Dunn; Stephen J. (Mountain View, CA), Holzmayer; Tanya A. (Mountain View, CA)

  Assignee(s): Subsidiary No. 3, Inc. (Wilmington, NC)

  Patent Number: 6,326,152

  Date filed: June 5, 2000

  Abstract: The present invention relates to the identification of several human genes as cellular targets for the design of therapeutic agents for suppressing human immunodeficiency virus (HIV) infection. These genes encode intracellular products which appear to be necessary for HIV replication, as evidenced by an inhibition of HIV infection in cells in which the expression of these genes is down-regulated. Therefore, inhibitors of these genes and their encoded products may be used as therapeutic agents for the treatment and/or prevention of HIV infection. In addition, the invention also relates to methods for identifying additional cellular genes as therapeutic targets for suppressing HIV infection, and methods of using such cellular genes and their encoded products in screening assays for selecting additional inhibitors of HIV.

  Excerpt(s): The present invention relates to the identification of several human genes as cellular targets for the design of therapeutic agents for suppressing human immunodeficiency virus (HIV) infection. These genes encode intracellular products which appear to be necessary for HIV replication, as evidenced by an inhibition of HIV infection in cells in which the expression of these genes is down-regulated. Therefore, inhibitors of these genes and their encoded products may be used as therapeutic agents for the treatment and/or prevention of HIV infection. In addition, the invention also relates to methods for identifying additional cellular genes as therapeutic targets for suppressing HIV infection, and methods of using such cellular genes and their encoded products in screening assays for selecting additional inhibitors of HIV.... The primary cause of acquired immunodeficiency syndrome (AIDS) has been shown to be HIV (Barre-Sinoussi et al., 1983, Science 220:868-870; Gallo et al., 1984, Science 224:500-503). HIV causes immunodeficiency in an individual by infecting important cell types of the immune system, which results in their depletion. This, in turn, leads to opportunistic infections, neoplastic growth and death.... Another stage of the HIV life cycle that has been targeted is viral entry into the cells, the earliest stage of HIV infection. This approach has primarily utilized recombinant soluble CD4 protein to inhibit infection of CD4.sup.+ T cells by some HIV-1 strains (Smith et al., 1987, Science 238:1704-1707). Certain primary HIV-1 isolates, however, are relatively less sensitive to inhibition by recombinant CD4 (Daar et al., 1990, Proc. Natl. Acad. Sci. USA 87:6574-6579). To date, clinical trials of recombinant, soluble CD4 have produced inconclusive results (Schooley et al., 1990, Ann. Int. Med. 112:247-253; Kahn et al., 1990, Ann. Int. Med. 112:254-261; Yarchoan et al., 1989, Proc. Vth Int. Conf. on AIDS, p. 564, MCP 137).

  Web site: http://www.delphion.com/details?pn=US06326152__

- **Compositions and methods for inhibiting human immunodeficiency virus infection by down-regulating human cellular genes**

  Inventor(s): Dunn; Stephen J. (Mountain View, CA), Holzmayer; Tanya A. (Mountain View, CA), Dayn; Andrew (Mountain View, CA)

  Assignee(s): Subsidiary No. 3, Inc. (Wilmington, NC)

  Patent Number: 6,436,634

  Date filed: June 5, 2000

  Abstract: The present invention relates to the identification of several human genes as cellular targets for the design of therapeutic agents for suppressing human immunodeficiency virus (HIV) infection. These genes encode intracellular products which appear to be necessary for HIV replication, as evidenced by an inhibition of HIV infection in cells in which the expression of these genes is down-regulated. Therefore, inhibitors of these genes and their encoded products may be used as therapeutic agents for the treatment and/or prevention of HIV infection. In addition, the invention also relates to methods for identifying additional cellular genes as therapeutic targets for suppressing HIV infection, and methods of using such cellular genes and their encoded products in screening assays for selecting additional inhibitors of HIV.

  Excerpt(s): The present invention relates to the identification of several human genes as cellular targets for the design of therapeutic agents for suppressing human immunodeficiency virus (HIV) infection. These genes encode intracellular products which appear to be necessary for HIV replication, as evidenced by an inhibition of HIV infection in cells in which the expression of these genes is down-regulated. Therefore, inhibitors of these genes and their encoded products may be used as therapeutic agents for the treatment and/or prevention of HIV infection. In addition, the invention also relates to methods for identifying additional cellular genes as therapeutic targets for suppressing HIV infection, and methods of using such cellular genes and their encoded products in screening assays for selecting additional inhibitors of HIV.... The primary cause of acquired immunodeficiency syndrome (AIDS) has been shown to be HIV (Barre-Sinoussi et al., 1983, Science 220:868-870; Gallo et al., 1984, Science 224:500-503). HIV causes immunodeficiency in an individual by infecting important cell types of the immune system, which results in their depletion. This, in turn, leads to opportunistic infections, neoplastic growth and death.... Another stage of the HIV life cycle that has been targeted is viral entry into the cells, the earliest stage of HIV infection. This approach has primarily utilized recombinant soluble CD4 protein to inhibit infection of CD4.sup.+ T cells by some HIV-1 strains (Smith et al., 1987, Science 238:1704-1707). Certain primary HIV-1 isolates, however, are relatively less sensitive to inhibition by recombinant CD4 (Daar et al., 1990, Proc Natl. Acad. Sci. USA 87:6574-6579). To date, clinical trials of recombinant, soluble CD4 have produced inconclusive results (Schooley et al., 1990, Ann. Int. Med. 112:247-253; Kahn et al., 1990, Ann. Int. Med. 112:254-261; Yarchoan et al., 1989, Proc Vth Int. Conf. on AIDS, p. 564, MCP 137).

  Web site: http://www.delphion.com/details?pn=US06436634__

- **Detection of antibodies to human immunodeficiency virus by agglutination of antigen coated latex**

  Inventor(s): Riggin; Charles H. (Hopedale, MA), Marciani; Dante J. (Hopkinton, MA)

  Assignee(s): Cambridge Bioscience Corporation (Worcester, MA)

  Patent Number: 4,921,787

  Date filed: May 1, 1987

  Abstract: The present invention relates to an assay for determinng the presence of antibodies in a sample to human immunodeficiency virus (HIV) comprising mixing a sample suspected of containing antibodies to HIV with HIV-specific antigen coated, hydroxylated microbeads, evaluating whether agglutination occurs, and determining therefrom the presence of the antibodies to HIV in the sample.

  Excerpt(s): This invention relates to a latex agglutination assay for the determination of antibodies to human immunodeficiency virus (HIV) with HIV-specific antigen coated, hydroxylated microbeads.... Human immunodeficiency virus (HIV) has been shown to be the etiologic agent for acquired immune deficiency syndrome (AIDS) (Barre-Sinoussi et al., "Isolation of a T-lymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS)," Science, 220:868-871 (1983) and Gallo et al., "Frequent detection and isolation of cytopathic retroviruses (HTLV-III) from patients with AIDS or at risk for AIDS," Science, 224:500-503 (1984)). An antibody response to HIV indicates exposure and infection. Current clinical assays for antibodies to HIV are viral based enzyme immunoassays (EIA). Viral lysate EIAs offer the advantage of high sensitivity but the disadvantage of high rates of false positives, of being slow, requiring several hours to complete a test, and the further disadvantage of requiring sophisticated instrumentation that is not available in all laboratories.... A latex agglutination assay based on purified HIV-specific antigen could offer the advantages of relatively high sensitivity, specificity, speed, and simplicity in situations where the time and technology required for EIA may not be available or appropriate. Latex agglutination is a technology which, unlike EIA, is a direct assay for specific antibodies. This test is based upon cross-linking antigen attached to microbeads with antibodies to form visible aggregates. Latex microbeads are negatively charged and antigen may bind to the microbeads by means of hydrophobic and ionic adsorption rather than by covalent attachment. Because of the fatal nature of HIV infection, it is important that any latex agglutination assay developed for determining the presence of antibodies to HIV in an individual at risk be very accurate.

  Web site: http://www.delphion.com/details?pn=US04921787__

- **Detection of human immunodeficiency virus type 1**

  Inventor(s): Yang; Yeasing (San Diego, CA), Ryder; Thomas B. (Escondido, CA), McDonough; Sherrol H. (San Diego, CA)

  Assignee(s): Gen-Probe Incorporated (San Diego, CA)

  Patent Number: 6,252,059

  Date filed: January 26, 1998

  Abstract: Amplification oligonucleotides and hybridization assay probes which distinguish Human Immunodeficiency Virus type 1 from other viruses.

Excerpt(s): This invention relates to the design and construction of amplification oligonucleotides and probes to Human Immunodeficiency Virus Type 1 (HIV), which allow detection of the organism in a test sample.... This section provides a brief outline of relevant areas. None of the art cited or referred to is admitted to be prior art to the claims. Laboratory diagnosis of Human Immunodeficiency Virus Type 1 in humans is currently performed by demonstration of the presence of viral antigen (p24) or anti-HIV-1 antibodies in serum. Direct detection of viral DNA, however, is a more useful diagnostic tool in some populations, such as infants born to seropositive mothers. Detection of viral DNA is more rapid and less hazardous than culture. Direct hybridization lacks adequate sensitivity in most patients (Shaw et al., Science 226:1165-1171, 1984). Many references mention oligonucleotides said to have use in detection of Human Immunodeficiency Virus. Most of these references also mention the use of polymerase chain reaction (PCR). These references include the following: Kwok et al., J. Virol. 61: 1690-1694, 1987; Agius et al., J. Virol. Meth., 30:141-150, 1990; Albert and Fenyo, J. Clin. Microbiol. 28:1560-1564, 1990; Bell and Ratner, AIDS Res. and Human Retroviruses 5:87-95, 1989; Bruisten et al., Vox Sang 61:24-29, 1991; Clarke et al., AIDS 4:1133-1136, 1990; Coutlee et al., Anal. Biochem. 181:96-105, 1989; Dahlen et al., J. Clin. Microbiol. 29:798-804, 1991; Dudding et al., Biochem. Biophys. Res. Comm. 167:244-250, 1990; Ferrer-Le-Coeur et al., Thrombosis and Haemostasis 65:478-482, 1991; Goswami et al., AIDS 5:797-803, 1991; Grankvist et al., AIDS 5:575-578, 1991; Guatelli et al., J. Virol. 64:4093-4098, 1990; Hart et al., Lancet 2 (8611):596-599, 1988; Holland et al., Proc. Natl. Acad. Sci. USA, 88:7276-7280, 1991; Keller et al., Anal. Biochem. 177:27-32, 1989; Kumar et al., AIDS Res. and Human Retroviruses 5:345-354, 1989; Linz et al., J. Clin. Chem. Clin. Biochem. 28:5-13, 1990; Mano and Chermann, Res. Virol. 142:95-104, 1991; Mariotti et al., AIDS 4:633-637, 1990; Mariotti et al., Transfusion 30:704-706, 1990; Meyerhans et al., Cell 58:901-910, 1989; Mousset et al., AIDS 4:1225-1230, 1990; Ou et al., Science 239:295-297, 1988; Pang et al., Nature 343:85-89, 1990; Paterlini et al., J. Med. Virol. 30:53-57, 1990; Perrin et al., Blood 76:641-645, 1990; Preston et al., J. Virol. Meth. 33:383-390, 1991; Pritchard and Stefano, Ann. Biol. Clin. 48:492-497, 1990; Rudin et al., Eur. J. Clin. Microbiol. Infect. Dis. 10:146-156, 1991; Shoebridge et al., AIDS 5:221-224, 1991; Stevenson et al., J. Virol. 64:3792-3803, 1990; Truckenmiller et al., Res. Immunol. 140:527-544, 1989; Van de Perre, et al., New Eng. J. Med. 325:593-598, 1991; Varas et al., BioTechniques 11:384-391, 1991; Velpandi et al., J. Virol. 65:4847-4852, 1991; Williams et al., AIDS 4:393-398, 1990; Zachar et al., J. Virol. Meth. 33:391-395, 1991; Zack et al., Cell 61:213-222, 1990; Findlay et al., entitled "Nucleic acid test article and its use to detect a predetermined nucleic acid," PCT/US90/00452, Publication No. WO 90/08840; Gingeras et al., entitled "Nucleic acid probe assay methods and compositions," PCT/US87/01966, Publication No. WO 88/01302; Brakel and Spadoro, entitled "Amplification capture assay," EPO application number 90124738.7, publication number 0 435 150 A2; Moncany and Montagnier, entitled "Sequences nucleotidiques issues du genome des retrovirus du typ hiv-1, hiv-2 et siv, et leurs applications notamment pour l'amplification des genomes de ces retrovirus et pour le diagnostic in-vitro des infections dues a ces virus," EPO application number 90401520.3, publication number 0 403 333 A2; Urdea, entitled "DNA-dependent RNA polymerase transcripts as reporter molecules for signal amplification in nucleic acid hybridization assays," PCT/US91/00213, Publication No. WO 91/10746; Musso et al., entitled "Lanthanide chelate-tagged nucleic acid probes," PCT/US88/03735, Publication No. WO 89/04375; Chang, entitled "Cloning and expression of HTLV-III DNA," EPO application number 85307260.1, publication number 0 185 444 A2; and Levenson, entitled "Diagnostic kit and method using a solid phase capture means for detecting nucleic acids," EPO application number 89311862.0, publication number 0 370 694; and Sninsky et al., U.S. Pat. No. 5,008,182.... This invention discloses novel amplification oligonucleotides and detection probes for the

detection of Human Immunodeficiency Virus Type 1. The probes are capable of distinguishing between the Human Immunodeficiency Virus type 1 and its known closest phylogenetic neighbors. The amplification oligonucleotides and probes may be used in an assay for the detection and/or quantitation of Human Immunodeficiency Virus nucleic acid.

Web site: http://www.delphion.com/details?pn=US06252059__

- **DNA fragments obtained from a novel human immunodeficiency virus designated LAV.sub.MAL**

  Inventor(s): Sonigo; Pierre (Paris, FR), Wain-Hobson; Simon (Montigny les Bretonneux, FR), Alizon; Marc (Paris, FR), Montagnier; Luc (Le Plessis Robinson, FR)

  Assignee(s): Institut Pasteur (Paris, FR)

  Patent Number: 5,773,602

  Date filed: November 18, 1993

  Abstract: A novel human immunodeficiency virus type 1 (HIV-1) isolate, designated lymphadenopathy-associated virus strain MAL, or LAV.sub.MAL, was molecularly cloned and characterized. Nucleotide sequence analysis demonstrated that the viral genome of LAV.sub.MAL is 9229 nucleotides long. This retrovirus contains the canonical gag, pol, and env genes, as well as ancillary genes encoding Vif (or Q), Vpr (or R), Tat (or S), and Nef (or F). This virus differs significantly, at both the nucleotide and amino acid sequence levels, from prototypical HIV isolates (e.g., HTLV-III, LAV.sub.BRU, and ARV). DNA fragments corresponding to the various gene products and regulatory regions are disclosed. These fragments are useful, inter alia, as probes in diagnostic assays and for the generation of recombinant proteins.

  Excerpt(s): The present invention relates to a virus capable of inducing lymphadenopathies (hereinafter "LAS") and acquired immuno-depressive syndromes (hereinafter "AIDS"), to antigens of this virus, particularly in a purified form, and to a process for producing these antigens, particularly antigens of the envelope of this virus. The invention also relates to polypeptides, whether glycosylated or not, produced by the virus and to DNA sequences which code for such polypeptides. The invention further relates to cloned DNA sequences hybridizable to genomic RNA and DNA of the lymphadenopathy associated virus (hereinafter "LAV") of this invention and to processes for their preparation and their use. The invention still further relates to a stable probe including a DNA sequence which can be used for the detection of the LAV virus of this invention or related viruses or DNA proviruses in any medium, particularly biological, and in samples containing any of them.... An important genetic polymorphism has been recognized for the human retrovirus which is the cause of AIDS and other diseases like LAS, AIDS-related complex (hereinafter "ARC") and probably some encephalopathies (for review, see Weiss, 1984). Indeed all of the isolates, analyzed until now, have had distinct restriction maps, even those recovered at the same place and time ›Benn et al., 1985!. Identical restriction maps have only been observed for the first two isolates which were designated LAV ›Alizon et al., 1984! and human T-cell lymphotropic virus type 3 (hereinafter "HTLV-3") ›Hahn et al., 1984! and which appear to be exceptions. The genetic polymorphism of the AIDS virus was better assessed after the determination of the complete nucleotide sequence of LAV ›Wain-Hobson et al., 1985!, HTLV-3 ›Ratner et al., 1985; Muesing et al., 1985! and a third isolate designated AIDS-associated retrovirus (hereinafter "ARV2") ›Sanchez-Pescador et al., 1985!. In particular, it appeared that, besides the nucleic acid variations responsible for the

restriction map polymorphism, isolates could differ significantly at the protein level, especially in the envelope (up to 13% of difference between ARV and LAV), by both amino acids substitutions and reciprocal insertions-deletions ›Rabson and Martin, 1985!.... Nevertheless, such differences did not go so far as to destroy the immunological similarity of such isolates as evidenced by the capabilities of their similar proteins, (e.g., core proteins of similar nature, such as the p25 proteins, or similar envelope glycoproteins, such as the 110-120 kD glycoproteins) to immunologically cross-react. Accordingly, the proteins of any of said LAV viruses can be used for the in vitro detection of antibodies induced in vivo and present in biological fluids obtained from individuals infected with the other LAV variants. Therefore, these viruses are grouped together as a class of LAV viruses (hereinafter "LAV-1 viruses").

Web site: http://www.delphion.com/details?pn=US05773602__

- **Expression of human immunodeficiency virus (HIV) reverse transcriptase**

  Inventor(s): Tanese; Naoko (New York, NY), Goff; Stephen P. (Tenafly, NJ), Haseltine; William A. (Cambridge, MA)

  Assignee(s): The Dana Farber Cancer Institute (Boston, MA), The Trustees of Columbia University in the City of New York (New York, NY)

  Patent Number: 5,256,554

  Date filed: December 2, 1991

  Abstract: This invention describes pHRT25, a plasmid containing a modified pol gene of the Human Immunodeficiency Virus Type 1 (HIV-1), formerly HTLV-III, under control of an inducible trp promoter. Methods of expressing reverse transcriptase activity using pHRT25 in E. coli are described.

  Excerpt(s): Within this application several publications are referenced by number within parentheses. Full citations for these publications may be found at the end of the specification immediately preceding the claims. The disclosures of these publications in their entireties are hereby incorporated by reference into this application in order to more fully describe the state of the art to which the invention pertains.... Acquired Immune Deficiency Syndrome (AIDS) is a new epidemic characterized by a marked depletion of the cellular immune response. The causative agent of the disease is now firmly established to be the human retrovirus known as Human Immunodeficiency Virus Type 1 (HIV-1), but was formerly known as Human T-cell lymphotropic virus III or Lymphadenopathy virus (HTLV-III/LAV) (1-4). Efforts to arrest the spread of this virus are being made on two broad fronts: the development of antiviral vaccines which might allow immunized individuals to resist infection, and the development of antiviral drugs which would specifically retard or arrest viral replication. One potentially important target of such drugs is the virion-associated enzyme reverse transcriptase (5-8).... In the early stages of the retroviral life cycle, viral RNA is copied to form a double-stranded DNA, which is integrated into host DNA to generate the provirus (for review, 1). The synthesis of the proviral DNA is catalyzed by the enzyme reverse transcriptase, which may efficiently utilize either RNA or DNA templates for DNA synthesis by the elongation of a primer bearing a paired 3' hydroxyl terminus. Inherent in the same protein is a second activity, RNAse H, which degrades RNA present as a duplex RNA:DNA hybrid. The viral pol gene encodes many enzymatic activities which participate in various steps of the life cycle. The pol gene product is initially expressed as a polyprotein Pr200gag-pol (2,3), containing sequences encoded by the gag gene

fused to sequences encoded by the pol gene; proteolytic processing is required to remove the sequences and to excise the mature products from the pol sequences.

Web site: http://www.delphion.com/details?pn=US05256554__

- **Genetic suppressor elements against human immunodeficiency virus**

  Inventor(s): Dunn; Stephen J. (Mountain View, CA), Holzmayer; Tanya A. (Mountain View, CA)

  Assignee(s): Subsidiary No. 3, Inc. (Wilminton, NC)

  Patent Number: 6,316,210

  Date filed: September 1, 1999

  Abstract: The present invention relates to genetic elements that suppress the activities of the human immunodeficiency virus (HIV). In particular, the invention relates to polynucleotides isolated from the HIV-1 genome, methods for isolating, identifying and designing such polynucleotides, and methods for using them for the protection of human cells against HIV infection and/or replication. The present invention also relates to polynucleotides that prevent tumor cell formation and the use of such polynucleotides to prevent tumorigenesis.

  Excerpt(s): The present invention relates to genetic elements that suppress the activities of the human immunodeficiency virus (HIV). In particular, the invention relates to polynucleotides isolated from the HIV-1 genome, methods for isolating, identifying and designing such polynucleotides, and methods for using them for the protection of human cells against HIV infection and/or replication.... The primary cause of acquired immunodeficiency syndrome (AIDS) has been shown to be HIV (Barre-Sinoussi et al., 1983, Science 220:868-870; Gallo et al., 1984, Science 224:500-503). HIV causes immunodeficiency in an individual by infecting important cell types of the immune system, which results in their depletion. This, in turn, leads to opportunistic infections, neurological dysfunctions, neoplastic growth, and death.... Another stage of the HIV life cycle that has been targeted is viral entry into the cells, the earliest stage of HIV infection. This approach has primarily utilized recombinant soluble CD4 protein to inhibit infection of CD4.sup.30 T cells by some HIV-1 strains (Smith et al., 1987, Science 238:1704-1707). Certain primary HIV-1 isolates, however, are relatively less sensitive to inhibition by recombinant CD4 (Daar et al., 1990, Proc. Natl. Acad. Sci. USA 87:6574-6579). To date, recombinant soluble CD4 clinical trials have produced inconclusive results (Schooley et al., 1990, Ann. Int. Med. 112:247-253; Kahn et al., 1990, Ann. Int. Med. 112:254-261; Yarchoan et al., 1989, Proc. Vth Int. Conf. on AIDS, p. 564, MCP 137).

  Web site: http://www.delphion.com/details?pn=US06316210__

- **Human hybridomas and monoclonal antibodies which bind both gp41 and gp120 envelope proteins of human immunodeficiency virus**

  Inventor(s): Peterson; Eskild A. (Tucson, AZ), Matsumoto; Yoh-ichi (Tokyo, JP), Sugano; Toru (Tokyo, JP), Masuho; Yasuhiko (Tokyo, JP), Hersh; Evan M. (Tucson, AZ)

  Assignee(s): The Arizona Board of Regents on behalf of the University of Arizona (Tucson, AZ), Teijin Limited (Osaka, JP)

  Patent Number: 5,298,419

  Date filed: March 31, 1988

  Abstract: The invention is directed to the human hybridoma designated MCA 86 and having A.T.C.C. Accession No. HB 9669 and human monoclonal antibodies produced by hybridoma MCA 86. Human monoclonal antibodies produced by hybridoma MCA 86 immunologically binds to both gp41 and gp120 envelope glycoproteins of Human Immunodeficiency Virus (HIV). These monoclonal antibodies are useful in the diagnosis of HIV infection.

  Excerpt(s): The present invention relates to human monoclonal antibodies (abbreviated as MCAs hereinafter) specific for human immunodeficiency virus (abbreviated as HIV herein), and hybridomas which produce these MCAs. The human MCAs of this invention are specific for HIV and will be useful in the diagnosis, prevention and therapy of HIV infection.... In light of the above background information regarding HIV and AIDS, it is clear that antibodies specific for the envelope of the virus, which plays such an important role in the establishment of the viral infection, have great significance in the prevention of the infection.... M. Robert-Guroff et al. (J. Immunol. 138: 3731, 1987) reported that the progression of the disease was slower in patients whose blood contained viral-neutralizing antibodies in comparison with patients not having such antibodies. In addition, it has been reported that the neutralizing antibodies in the blood of AIDS patients bind to gp120 (L. A. Lasky et al.: Science 233: 209, 186; and T. J. Mathew et al.: Pro. Natl. Acad. Sci. U.S.A. 83: 9709, 1986). In light of these findings, it is clear that antibodies specific for gp120 must play an important role in the prevention of infection by HIV.

  Web site: http://www.delphion.com/details?pn=US05298419__

- **Human Immunodeficiency Virus (HIV) associated with Acquired Immunual Deficiency Syndrome (AIDS), a diagnostic method for aids and pre-aids, and a kit therefor**

  Inventor(s): Gallo; Robert C. (Bethesda, MD), Popovic; Mikulas (Bethesda, MD), Sarngadharan; Mangalasseril G. (Vienna, VA), Nugeyre; Marie-Therese (Paris, FR), Chamaret; Solange (Paris, FR), Barre-Sinoussi; Francoise (Issy Les Moulineaux, FR), Axler-Blin; Claudine (Paris, FR), Chermann; Jean-Claude (Elancourt, FR), Brun-Vezinet; Francoise (Paris, FR), Rouzioux; Christine (Paris, FR), Rozenbaum; Willy (Paris, FR), Dauguet; Charles (Paris, FR), Gruest; Jacqueline (L'Hay Les Roses, FR), Rey; Francoise (Paris, FR), Montagnier; Luc (Le Plessis Robinson, FR)

  Assignee(s): Institut Pasteur (Paris Cedex, FR), The United States of America as represented by the Secretary of The (Washington, DC)

  Patent Number: 5,135,864

  Date filed: November 5, 1987

Abstract: Retroviruses associated with Acquired Immune Deficiency Syndrome (AIDS), including Lymphadenopathy Associated Virus (LAV), are isolated from the sera of patients afflicted with Lymphadenopathy Syndrome (LAS) or AIDS. LAV is a Human Immunodeficiency Virus (HIV). Viral extract, structural proteins and other fractions of the retrovirus immunologically recognize the sera of such patients. Immunological reaction is used to detect antibodies that specifically bind to antigenic sites of the retrovirus in samples of body fluids from patients with AIDS or risk of AIDS. A kit for in vitro assay of LAS or AIDS is provided.

Excerpt(s): The invention relates to antigens, means and methods for the diagnosis of lymphadenopathy and acquired immune deficiency syndrome.... The acquired immune deficiency syndrome (AIDS) has recently been recognized in several countries. The disease has been reported mainly in homosexual males with multiple partners, and epidemiological studies suggest horizontal transmission by sexual routes as well as by intravenous drug administration, and blood transfusion. The pronounced depression of cellular immunity that occurs in patients with AIDS and the quantitative modifications of subpopulations of their T lymphocytes suggest that T cells or a subset of T cells might be a preferential target for the putative infectious agent. Alternatively, these modifications may result from subsequent infections. The depressed cellular immunity may result in serious opportunistic infections in AIDS patients, many of whom develop Kaposi's sarcoma. However, a picture of persistent multiple lymphadenopathies has also been described in homosexual males and infants who may or may not develop AIDS. The histological aspect of such lymph nodes is that of reactive hyperplasia. Such cases may correspond to an early or a milder form of the disease.... It has been found that one of the major etiological agents of AIDS and of lymphadenopathy syndrome (LAS), which is often considered as a prodromic sign of AIDS, should consist of a T-lymphotropic retrovirus which has been isolated from a lymph node of a homosexual patient with multiple lymphadenopathies. The virus appears to be distinct from the human T-cell leukemia virus (HTLV) family (R. C. Gallo and M. S. Reitz, "J. Natl. Cancer Inst.", 69 (No. 6), 1209 (1982)). The last mentioned virus has been known as belonging to the so-called HTLV-1 subgroup.

Web site: http://www.delphion.com/details?pn=US05135864__

- **Human immunodeficiency virus (HIV) ENV-coded peptide capable of eliciting HIV-inhibiting antibodies in mammals**

  Inventor(s): Durda; Paul J. (Needham, MA), Petteway; Stephen R. (West Chester, PA), Kenealy; William R. (Madison, WI)

  Assignee(s): E. I. Du Pont de Nemours and Company (Wilmington, DE)

  Patent Number: 5,562,905

  Date filed: March 20, 1989

  Abstract: A chemically synthesized 15 amino acid peptide designated peptide 1-69, which has the sequence of amino acids numbers 308 to 322 (RIQRGPGRAFVTIGK) of the human immunodeficiency virus-1 (HIV-1) IIIB env-coded protein, was used to immunize animals. Peptide 1-69 elicited in immunized animals antibodies that block HIV proliferation and block HIV-induced cell fusion in cell culture.

  Excerpt(s): The invention relates to a chemically synthesized peptide corresponding to a segment of the human immunodeficiency virus (HIV) env-coded protein useful as a prophylactic or vaccine for HIV infection and disease, and to monoclonal antibodies to

the env-coded segment of HIV.... Antibodies specific for human immunodeficiency virus-1 (HIV-1), the causative agent of acquired immunodeficiency syndrome (AIDS), are found in the sera of HIV-infected individuals (Sarngadharan et al. (1984) Science 224,506-508; Schupbach et al. (1984) Science 224,503-505; Chang et al. (1985) Biotechnoloy 3, 905-911; Kenealy et al. (1987) AIDS Research and Human Retroviruses 3, 95-105). The level of serum antibodies that block HIV-1 proliferation (HIV-neutralizing antibodies) or block the fusion of HIV-infected and noninfected cells in cell culture (fusion-blocking antibodies) is relatively low when compared to the overall humoral response to the virus (i.e., total levels of HIV-specific antibodies) (Weiss et al. (1985) Nature 316,69-74; Robert-Guroff et al. (1985) Nature 316,72-74; Weiss et al. (1986) Nature 324,572-575). The role of HIV-neutralizing and fusion-blocking antibodies in the pathogenesis of HIV-1 infection and the structure of the epitopes responsible for this biological activity remain to be determined. The exterior envelope glycoprotein of HIV-1 (gp120) is known to bind human neutralizing antibodies and has been used as an immunogen capable of eliciting HIV-neutralizing antibodies in animals (Lasky et al. (1986) Science 233,209-212; Matthews et al. (1986) Proc. Natl. Acad. Sci. USA 83,9709-9713; Robey et al. (1986) Proc. Natl. Acad. Sci. USA 84,7023-7927). Notably, these neutralizing antibodies are reported to be type-specific, i.e., the antibodies only block proliferation of the HIV-1 subtype or isolate from which the immunogen was derived.... A number of HIV-1 peptides and proteins have been identified which elicit neutralizing antibodies in animals. These include synthetic peptides corresponding to sequences from the gag-coded protein, the env-coded transmembrane protein (gp41), and several peptides corresponding to conserved regions of the env-coded gp120 protein (Putney et al. (1986) Science 234,1392-1395; Sarin et al. (1986) Science 232,1135-1137; Kennedy et al. (1987) J. Biol. Chem. 262,5769-5774; Taylor et al. (1987) Proc. Natl. Acad. Sci. USA 84,2951-2955; Chanh et al. (1986) EMBO J. 5,3065-3071; Ho et al. (1987) J. of Virol. 61,2024-2028). Particularly high levels of neutralizing and fusion-blocking antibodies have been shown to be induced in animals by two recombinant proteins. One of these is a glycosylated full length env-coded protein produced using an insect cell expression system, designated gp160 (Rusehe et al. (1987) Proc. Natl. Acad. Sci. USA 84,6924-6928) and a second is a nonglycosylated Escherichia coli produced protein, designated PB1, representing a region of gp120 (amino acids number 288 to 472 of HIV-1 IIIB) (Putney et al. (1986) Science 234,1392-1395). In spite of the strong antibody responses using these proteins as immunogens, the neutralizing activity remained restricted to and specific for the HIV-1 subtype or isolate from which the immunogen was derived, i.e., IIIB.

Web site: http://www.delphion.com/details?pn=US05562905__

- **Human immunodeficiency virus type 1 (HIV-1) GP160 epitopes that are immunologically homologous to epitopes located in the class I major histocompatibility complex (MHC) heavy chain.alpha.-1 domain**

  Inventor(s): Beretta; Alberto (Milan, IT)

  Assignee(s): La Fondation Mondiale Recherche et Prevention Sida (Cedex)

  Patent Number: 6,042,831

  Date filed: November 10, 1994

  Abstract: This invention is directed toward human immunodeficiency virus type 1 (HIV-1) peptidic epitopes derived from the envelope glycoprotein gp160 which are immunologically homologous to epitopes located in the class I major histocompatibility

complex (MHC) heavy chain.alpha.-1 domain. These peptides should prove useful in the preparation of immunodiagnostic reagents.

Excerpt(s): The invention concerns epitopes of the HIV virus gp160 protein, that are immunologically homologous to epitopes of the protein family of the human major histocompatibilty complex HLA, to be used for diagnosing and immunization.... Among the mechanisms thought to be responsible of AIDS, it has been suggested that auto-immunity, namely auto-antibody induction mechanism, may play a major role (Hebeshaw J. A and Dalgleish A. G., J. Acquired Immun. Defic. Syndrome, 2, 457, 1989). The homology of portions of virus components with endogenous proteins of the human body could reduce the self-tolerance immunity mechanisms, thus causing the synthesis of antibodies, and activating cytotoxic T lymphocytes.... The gp120 protein is used to produce vaccines for immunization of HIV infection, as a complex with the gp41 protein, such complex being defined as gp160 (ref.).

Web site: http://www.delphion.com/details?pn=US06042831__

- **Human lymphoid cells expressing human immunodeficiency virus envelope protein gp160**

  Inventor(s): Trulli; Stephen (Havertown, PA), Debouck; Christine (Wayne, PA), Jonak; Zdenka L. (Devon, PA), Clark; Robert (Woodstown, NJ)

  Assignee(s): SmithKline Beecham Corporation (Philadelphia, PA)

  Patent Number: 5,580,720

  Date filed: June 2, 1995

  Abstract: The present invention provides mammalian cells modified to stably express at least the entire human immunodeficiency virus-1 envelope protein gp160. The invention provides a vaccine comprising the cells of the invention. The invention also provides methods for screening compounds for their ability to inhibit formation of syncytia between cells that express HIV-1 gp160 and cells that express CD4 comprising mixing cells of invention, cells that express CD4 on their surfaces, and a test compound for a length of time sufficient for syncytia to form; and then determining the amount of syncytia formation.

  Excerpt(s): The present invention relates to the field of cells transfected by recombinant DNA techniques to express heterologous proteins. More particularly, the present invention relates to cells transfected by recombinant DNA techniques to express viral proteins, and their use as vaccines for prevention of disease, and in assay systems in the drug discovery process.... Infection begins as gp120 on the viral particle binds tightly to the CD4 receptor on the surface of T4 lymphocytes or other target cells. The virus then merges with the target cell and reverse transcribes its RNA genome into double-stranded DNA. The viral DNA becomes incorporated into the genetic material in the cell's nucleus and directs the production of new viral RNA and viral proteins, which combine to form new virus particles. These particles bud from the target cell membrane and infect other cells.... Destruction of T4 lymphocytes, which are critical to immune defense, is the major cause of the progressive immune dysfunction that is the hallmark of HIV infection. The loss of target cells seriously impairs the body's ability to fight most invaders, but it has a particularly severe impact on the defenses against viruses, fungi, parasites and certain bacteria, including mycobacteria.

  Web site: http://www.delphion.com/details?pn=US05580720__

- **Human monoclonal antibodies directed against the transmembrane glycoprotein (gp41) of human immunodeficiency virus-1 (HIV-1) and detection of antibodies against epitope (GCSGKLIC)**

  Inventor(s): Cotropia; Joseph P. (Philadelphia, PA)

  Assignee(s): BioClonetics (Philadelphia, PA)

  Patent Number: 6,008,044

  Date filed: July 1, 1998

  Abstract: A method for neutralizing the retrovirus Human Immunodeficiency Virus-1 (HIV-1) through free virus neutralization or fusion inhibition, comprises adding to a cell mixture of HIV-infected and uninfected cells, a neutralizing agent which specifically binds to at least a portion of the amino acid sequence R-Leu-Ile-Cys-R', where R is either absent or a sequence of 1 to 5 amino acids selected from the group consisting of Lys, Gly-Lys, Ser-Gly-Lys, Cys-Ser-Gly-Lys and Gly-Cys-Ser-Gly-Lys, and R' is either absent or a sequence of 1 to 2 amino acids selected from the group consisting of Thr and Thr-Thr, under conditions effective for allowing said neutralizing agent to inhibit fusion between said HIV-1 infected cells or free HIV-1 and said uninfected cells or administering the neutralizing agent orally, intravenously, or intramuscularly under conditions effective for allowing said neutralizing agent to inhibit fusion between HIV-1 infected cells and uninfected cells. In one embodiment, the neutralizing agent is a novel human monoclonal antibody.

  Excerpt(s): This invention relates to anti-HIV-1 monoclonal antibodies and specifically to monoclonal antibodies which bind to a viral epitope, thereby neutralizing the virus. The invention also relates to continuous cell lines capable of producing the antibodies and to the peptides recognizable by the antibodies. The antibodies and antigens of this invention are useful for diagnosis, prognosis, prophylaxis and therapy. This invention also relates to prognostic tests for viral diseases, and particularly prognostic tests for Acquired Immunodeficiency Syndrome (AIDS).... The human immunodeficiency virus (HIV-1) has been established as the primary etiologic agent in the pathogenesis of acquired immunodeficiency syndrome (AIDS) and related disorders. (Barre-Sinoussi, et al. Science (1983) 220:868-871; Gallo, et al., Science (1984) 224:500-503; Levy, et al., Science (1984) 225:840-842).... The CD4+ cells play a central role in HIV infection. (Fauci, Science (1988) 239:617-622). CD4 is a molecule present on the surface of certain lymphocytes and, to a lesser degree, macrophages. The CD4 molecule plays a significant role in the function of T4 helper lymphocytes and serves as a marker for such cells. (Gallo, R. C. and Montagnier, L., Scientific American (1988) 259:41-48.) The virus uses the CD4 receptor to gain entry into a number of cells. (Dalgleish, et al., Nature (1984) 312:763-767). The envelope glycoprotein, gp160, is the precursor to the gp120, which specifically binds to the surface receptor (CD4) of CD4+ cells, and the gp41, the transmembrane (TM) glycoprotein which initiates cell membrane fusion, leading to the formation of multinucleated giant cells commonly called syncytia. (Kowalski, science (1987) 237:1351-1355). Fusion leads to the death of the syncytial cells. While HIV-1 may also cause cell death through mechanisms independent of cell fusion, data suggest that the formation of syncytia contributes to the progressive depletion of CD4+ cells (T4 helper lymphocytes), quantitatively and functionally. (Lifson, et al., Nature (1986) 323:725-728). This is the most profound hematologic feature and hallmark associated with acquired immunodeficiency syndrome (AIDS) (Broder, S. M. and Gallo, R. C., N. Eng. J. Med. (1984) 311:1292-1297), as demonstrated by impaired cell-mediated immunity.

Web site: http://www.delphion.com/details?pn=US06008044__

- **Human monoclonal antibodies to human immunodeficiency virus**

  Inventor(s): Gorny; Miroslaw K. (Forest Hills, NY), Zolla-Pazner; Susan (New York, NY)

  Assignee(s): New York University (New York, NY)

  Patent Number: 5,731,189

  Date filed: December 27, 1994

  Abstract: Disclosed herein are eleven human lymphoblastoid cell lines producing monoclonal antibodies directed against human immunodeficiency virus (HIV) proteins gp41 and p24. Also disclosed are methods for treating HIV-infected individuals using the human monoclonal antibodies and pharmaceutical formulations comprising effective amounts of the human monoclonal antibodies.

  Excerpt(s): The human immunodeficiency virus (HIV) has been implicated as the causative agent of acquired immune deficiency syndrome (AIDS). Two different serotypes of the virus have been identified to date: HIV-1 and HIV-2. It is currently believed that the majority of individuals that become infected with HIV eventually will develop AIDS and are likely to succumb to fatal infections and/or malignancies. At this time it is estimated that approximately 1.5 million individuals have been infected by HIV in the United States alone.... Several avenues have been explored to treat individuals afflicted with AIDS or HIV infections. The antiviral drug azidothymidine (AZT) has been found to produce both clinical and immunological improvements upon short term administration to patients afflicted with AIDS and ARC (AIDS Related Complex--a prodrome of the disease) and to decrease the mortality rate and frequency of opportunistic infections. Although clinical benefits are achieved with AZT, it is costly. A further drawback is that significant drug toxicity often accompanies administration of AZT. This may necessitate blood transfusions and/or reduction of the AZT dosage, or in some instances, discontinuance of AZT therapy altogether. Nonetheless, AZT is the only drug currently authorized for the treatment of AIDS.... An alternative treatment that is currently under evaluation involves administration of one or more lymphokines. Interferon (particularly gamma-interferon) and interleukin-2 are currently being studied for possible use in the treatment of HIV infections. However, the preliminary results of early clinical trials are not promising. Patients receiving lymphokine therapy often suffer serious side effects including low blood pressure, nausea and diarrhea.

  Web site: http://www.delphion.com/details?pn=US05731189__

- **Human neutralizing monoclonal antibodies to human immunodeficiency virus**

  Inventor(s): Barbas; Carlos F. (San Diego, CA), Lerner; Richard A. (La Jolla, CA), Burton; Dennis R. (La Jolla, CA)

  Assignee(s): The Scripps Research Institute (La Jolla, CA)

  Patent Number: 5,804,440

  Date filed: July 24, 1997

  Abstract: The present invention describes human monoclonal antibodies which immunoreact with and neutralize human immunodeficiency virus (HIV). Also disclosed

are immunotherapeutic and diagnostic methods of using the monoclonal antibodies, as well as cell line for producing the monoclonal antibodies.

Excerpt(s): The present invention relates generally to the field of immunology and specifically to human monoclonal antibodies which bind and neutralize human immunodeficiency virus (HIV).... Passive immunization of HIV-1 infected humans using human sera containing polyclonal antibodies immunoreactive with HIV has been reported. See for example, Jackson et al., Lancet, September 17:647-652, (1988); Karpas et al., Proc. Natl. Acad. Sci., USA, 87:7613-7616 (1990).... Numerous groups have reported the preparation of human monoclonal antibodies that neutralize HIV isolates in vitro. The described antibodies typically have immunospecificities for epitopes on the HIV glycoprotein gp120 or the related external surface envelope glycoprotein gp120 or the transmembrane glycoprotein gp41. See, for example Levy, Micro. Rev., 57:183-289 (1993); Karwowska et al., Aids Research and Human Retroviruses, 8:1099-1106 (1992); Takeda et al., J. Clin. Invest., 89:1952-1957 (1992); Tilley et al., Aids Research and Human Retroviruses, 8:461-467 (1992); Laman et al., J. Virol., 66:1823-1831 (1992); Thali et al., J. Virol., 65:6188-6193 (1991); Ho et al., Proc. Natl. Acad. Sci. USA, 88:8949-8952 (1991); D'Souza et al., AIDS, 5:1061-1070 (1991); Tilley et al., Res. Virol., 142:247-259 (1991); Broliden et al., Immunol., 73:371-376. (1991); Matour et al., J. Immunol., 146:4325-4332 (1991); and Gorny et al., Proc. Natl. Acad. Sci., USA, 88:3238-3242 (1991).

Web site: http://www.delphion.com/details?pn=US05804440__

- **Immunogenic compositions comprising dimeric forms of the human immunodeficiency virus type 2 (HIV-2) and simian immunodeficiency virus (SIV) envelope glycoproteins**

  Inventor(s): Laurent; Anne G. (Paris, FR), Montagnier; Luc (Le Plessis-Robinson, FR), Rey; Marie-Anne (Paris, FR), Hovanessian; Ara G. (Montreuil, FR), Krust; Bernard (Paris, FR)

  Assignee(s): Institute Pasteur (Paris, FR)

  Patent Number: 6,261,571

  Date filed: December 27, 1994

  Abstract: The invention relates to an isolated immune complex comprising a protein and an antibody that binds with said protein, wherein the protein is selected from the group consisting of gp80 of HIV-2 and gp65 of SIV, wherein said gp80 is a glycoprotein having an apparent molecular weight of 80 kDa, as determined by SDS-PAGE, and further wherein said gp65 is a glycoprotein having an apparent molecular weight of 65 kDa as determined by SDS-PAGE. Also provided are an immunogenic composition comprising an amount of gp80 protein of human immunodeficiency virus type 2 (HIV-2) sufficient to induce an immune response and a pharmaceutically acceptible carrier, and a composition comprising at least one antigen selected from the group consisting of gp80 protein of HIV-2 and gp65.sub.SIV.

  Excerpt(s): This invention relates to viral proteins and glycoproteins, to compositions containing these proteins, to methods of preparing the proteins, and to their use in detecting viral inection.... Human immunodeficiency virus (HIV) is the etiological agent of acquired immunodeficiency syndrome (AIDS) (Montagnier et al., 1984). To date, two related but distinct viruses HIV-1 and HIV-2, have been identified (Barre-Sinoussi et al., 1983; Brun-Vezinet et al., 1987; Clavel et al., 1986a, 1986b; Guyader et al., 1987; Popovic et al., 1984; Ratner et al., 1985; Wain-Hobson et al., 1985). HIV-2 is closely related to

simian immunodeficiency virus (SIV-mac), which causes an AIDS-like disease in macaques (Daniel et al., 1985; Fultz et al., 1986; Chakrabarti et al., 1987). Alignments of the nucleotide sequences of HIV-1, HIV-2, and SIV reveal a considerable homology between HIV-2 and SIV-mac. These two viruses share about 75% overall nucleotide sequence homology, but both of them are only distantly related to HIV-1 with about 40% overall homology (Guyader et al., 1987; Chakrabarti et al., 1977).... In addition to the genes that encode structural proteins (the virion capsid and envelope glycoproteins) and the enzymes required for proviral synthesis and integration common to all retroviruses, HIV-1, HIV-2, and SIV encode genes that regulate virus replication as well as genes that encode proteins of yet unknown function. The only notable difference in the genetic organizations of HIV-1, HIV-2, and SIV resides in the open reading frame referred to as vpx, which is absent in HIV-1 and vpu in HIV-1 but not in HIV-2 and SIV (Cohen et al., 1988; Guyader et al., 1987). These viruses are both tropic and cytopathic for CD4 positive T lymphocytes (Klatzmann et al., 1984; Clavel et al., 1985a; Dalgleish et al., 1984; Daniel et al., 1985). A great number of studies have indicated that CD4 functions as the cellular receptor of HIV (Weiss, 1988).

Web site: http://www.delphion.com/details?pn=US06261571__

- **Inactivation of human immunodeficiency virus (HIV) in protein-containing solutions by phenols**

  Inventor(s): Hilfenhaus; Joachim (Marburg, DE)

  Assignee(s): Behringwerke Aktiengesellschaft (Marburg/Lahn, DE)

  Patent Number: 4,886,779

  Date filed: March 10, 1988

  Abstract: A procedure for the inactivation of human immunodeficiency virus (HIV) in protein solutions as described, which process comprises addition of a phenol to a solution of this type, and allowing it to act. It is possible in this way, for example, to prepare products for human use which are free of any infectious HIV and thus do not transmit AIDS. Phenol is used at a low concentration and can be used at a ph of 3.5 to 4.5.

  Excerpt(s): The invention relates to a process for the inactivation of human immunodeficiency virus (HIV) in protein-containing solutions by the action of a phenol. Preparations treated in this way do not carry the risk of AIDS transmission.... Besides other origins, donated human blood and human plasma proteins given to patients represent a potential source of transmitted in this way of AIDS. The AIDS pathogens which are transmitted in this way are retroviruses the first isolates of which were called LAV, HTLV-III or ARV and are now designated as human immunodeficiency viruses (HIV). There have been described various HIV serotypes. Within the scope of the invention, HIV is to be understood to mean all viruses belonging to this virus group. Whereas the transmission of HIV by human blood as well as by factor VIII concentrates not specially treated for virus inactivation has unequivocally been demonstrated to date HIV transmission by human immunoglobulins has not been found.... However, irrespective of these findings, it is desirable to include process steps leading to inactivation of HIV into the manufacturing procedure of human plasma proteins used for the therapy of human patients. The use of HIV inactivating process steps remains desirable even when there is routine testing of blood donors for antibodies against HIV and the exclusive use of anti-HIV negative donations in order to rule out any potential risk of AIDS transmission due to administration of human plasma protein products. The

use of every possible HIV inactivating step when manufacturing human immunoglobulins is desirable in addition to a customary alcohol precipitation.

Web site: http://www.delphion.com/details?pn=US04886779__

- **Kits for the detection of human immunodeficiency virus type 2 (HIV-2) antigens**

  Inventor(s): Guetard; Denise (Paris, FR), Brun-Vezinet; Francoise (Paris, FR), Montagnier; Luc (Le Plessis Robinson, FR), Clavel; Francois (Paris, FR)

  Assignee(s): Institut Pasteur (Paris, FR)

  Patent Number: 6,296,807

  Date filed: August 28, 1998

  Abstract: The invention relates to a novel retrovirus isolated from patients in West Africa that is capable of causing lymphadenopathies and the acquired immune deficiency syndrome (AIDS). This virus, which was originally designated "LAV type II", "LAV-II", or "West African AIDS retrovirus", has been subsequently renamed the human immunodeficiency virus type 2 (HIV-2). Two isolates were obtained, characterized, and designated HIV-2.sub.MIR and HIV-2.sub.ROD (C.N.C.M. deposit nos. I-502 and I-532, respectively). Radioimmunoprecipitation (RIPA) and Western blot analyses involving patient antisera identified viral proteins with molecular weights of 16 Kd (p16), 26 Kd (p26), 130-140 Kd (gp130-140), and 36 Kd (gp36). The claimed invention is directed toward kits for the detection of HIV-2 antigens comprising polyclonal and monoclonal antisera directed against these proteins.

  Excerpt(s): The invention relates to new virus forms capable of causing lymphadenopathies which are capable of then developing into acquired immunodeficiency syndrome (AIDS). The invention also applies to antigens which may be obtained from these viruses and other viruses having certain properties in common with them. It also concerns antibodies which may be induced against these various antigens. Lastly, the invention relates to using these antigens or antibodies in diagnosing certain AIDS forms and, with respect to some of these AIDS forms, to producing immunizing and vaccinating compositions against these retroviruses such as purified proteins, glycoproteins, recombinant proteins or synthetic peptides.... An article by F. Barre-Sinoussi et al. in Science, Vol 220: pp 868-871 [1983] describes the isolation of the first retrovirus which was known to be responsible for AIDS. European Patent Application 138,667 specifically describes diagnosis of AIDS and pre-AIDS by detection of the presence of antibodies against the virus through the use of certain virus extracts and particularly through the use of some of the viral proteins. This retrovirus is known generally as LAV. Since that time, other similar strains and variations of LAV have been isolated. Illustrative strains include HTLV-III and ARV. The expression "LAV-I" has been coined to cover these designations and the corresponding viral strains. Thus, the set of viruses which are identical with or close to the initial isolate shall be called herein "LAV type 1" or "LAV-I".... The "LAV" set may be defined as a set of viruses either causing generalized and persistent polyadenopathies, or AIDS, and having in vitro a tropism for T4 cells wherein this retrovirus induces a cytopathogenic effect. These retroviruses have been found to be distinct from the other already known human retoviruses (HTLV-I and HTLV-II).

  Web site: http://www.delphion.com/details?pn=US06296807__

- **Method for ameliorating muscle weakness/wasting in a patient infected with human immunodeficiency virus-type 1**

  Inventor(s): Berger; Joseph R. (Miami, FL)

  Assignee(s): BTG Pharmaceuticals Corp. (Iselin, NJ)

  Patent Number: 6,090,799

  Date filed: June 22, 1995

  Abstract: A method for attenuating the HIV-associated myopathy and muscle wasting associated with infection by human immunodeficiency virus-Type 1. Administration of oxandrolone in a daily dosage of about 2.5 to about 20 milligrams is described.

  Excerpt(s): The invention relates to the use of oxandrolone to attenuate myopathy and muscle weakness/wasting associated with infection by human immune deficiency virus-Type 1.... Human immunodeficiency virus (HIV) associated myopathy and/or muscle weakness/wasting is a relatively common clinical manifestation of acquired immunodeficiency syndrome (AIDS). This is one of a number of neuromuscular disorders associated with the disease. There is some evidence to indicate that direct HIV infection of muscle may be at least partly responsible, occasionally resulting in a polymyositis-like disorder. In addition, zidovudine (AZT), an antiviral agent that is used widely in the clinical management of AIDS, has been associated with a toxic myopathy, presumably related to an inhibition of mitochondrial metabolism. In any event, the loss of muscle mass commonly observed in AIDS victims negatively impacts muscle function, however caused.... Individuals with HIV-associated myopathy or muscle weakness or wasting typically experience significant weight loss, generalized or proximal muscle weakness, tenderness, and muscle atrophy. Laboratory tests of samples from such individuals often reveal elevated levels of enzymes associated with muscle degeneration and necrosis, such as creatine kinase, aldolase, and aspartate amino transferase. Electromyographic test results for individuals with HIV-associated myopathy are typically consistent with myopathic changes. Histopathologic tests may reveal muscle fiber necrosis associated with lymphocytic inflammatory infiltrates. In AZT myotoxicity, ragged red fibers are often observed.

  Web site: http://www.delphion.com/details?pn=US06090799__

- **Method for inhibiting disease associated with the human immunodeficiency virus through the use of monoclonal antibodies directed against anti-self cytotoxic T-lymphocytes or their lytics**

  Inventor(s): Allen; Allen D. (4236 Longridge Ave., Penthouse 302, Studio City, CA 91604)

  Assignee(s): none reported

  Patent Number: 5,651,970

  Date filed: June 7, 1995

  Abstract: Methods for treating and inhibiting disease and symptoms associated with the human immunodeficiency virus (HIV) are provided. The method includes transforming the human immunodeficiency virus (HIV) infection into a nonserious disease through the infusion of monoclonal antibodies directed against particular antigens on anti-self, anti-CD4 cytotoxic T-lymphocytes.

Excerpt(s): The present invention relates generally to methods for treating human disease conditions associated with the human immunodeficiency virus (HIV) and more particularly to the use of monoclonal antibodies directed against anti-self cytotoxic T-lymphocytes or their lytics in order to inhibit or treat HIV and related HIV diseases.... Several viruses produce latent infection in humans and can reactivate to produce recrudescent or persistent disease. One such disease is the human immunodeficiency virus (HIV). HIV is associated with a progressive catastrophic disease in certain primates, including humans. Humans infected with HIV experience proliferation of a certain class of white blood cells known as cytotoxic T-lymphocytes (CTL). The final stage of this disease is commonly known as acquired immune deficiency syndrome (AIDS).... It is well known in the art that the clinical signs and symptoms of AIDS are primarily due to a profound loss of all lymphocytes marked with the CD3 and CD4 antigens (CD4+ T-lymphocytes). It is also generally accepted that the infectious agent in AIDS is the human immunodeficiency virus (HIV). Although HIV infects and destroys CD4+ cells, the number of cells infected is inadequate to account for the profound and indiscriminate loss of these cells that occurs in individuals infected with HIV. It has been suggested by those in the field that autoimmunity may play a role in the pathogenesis of AIDS. However, few have suspected a pathogenic cytotoxic T-lymphocyte (CTL).

Web site: http://www.delphion.com/details?pn=US05651970__

- **Method for the identification of compounds capable of abrogating human immunodeficiency virus (HIV) infection of dendritic cells and T-lymphocytes**

  Inventor(s): Betjes; Michiel (Amsterdam, NL), Hoffman; Lloyd (Great Neck, NY), Pope; Melissa (New York, NY), Steinman; Ralph M. (Westport, CT)

  Assignee(s): The Rockefeller University (New York, NY)

  Patent Number: 5,627,025

  Date filed: August 12, 1994

  Abstract: The present invention relates to the role of dendritic cells in facilitating productive human immunodeficiency virus (HIV) infection. Experimentally, productive infection with HIV-1 requires that virus be administered to T cells that are activated by mitogens. This application describes a productive milieu for HIV-1 infection within the confines of normal epithelial tissue that does not require standard stimuli. The milieu consists of dendritic cells and T cells that emigrate from skin and produce distinctive stable, nonproliferating conjugates. These conjugates, upon exposure to HIV-1, begin to release high levels of virus progeny. Numerous infected syncytia, comprised of both dendritic cells and T cells, rapidly develop. A method is disclosed for the identification of agents capable of inhibiting HIV transmission and chronic infection of dendritic cells and T lymphocytes found in epithelial tissues.

  Excerpt(s): The present invention relates to the role of dendritic cells in immune responses, and the transmission and infectivity of the human immunodeficiency virus. The invention further relates to identification of agents capable of modulating the immunological functional activity of dendritic cells, and agents capable of inhibiting the transmission or infectivity, or both, of HIV.... Amongst the distinctive features of dendritic cells are their migratory properties. Migration has been studied to a large extent in skin. During contact sensitivity, dendritic cells (Langerhans cells) are noted in the afferent lymph (Lens et al., 1983; Silberberg-Sinakin et al., 1976) and in the draining lymph node (Kripke et al., 1990; Macatonia et al., 1987). Following skin transplantation, dendritic cells leave the epidermis and undergo changes that include increased

expression of MHC class II (Larsen et al., 1990). Since dendritic cells are known to gain access to afferent lymphatics (Knight et al., 1982; Lens et al., 1983; Pugh et al., 1983; Rhodes et al., 1989), the migration of these potent antigen presenting cells into the lymph and then to the draining lymph node, may account for the need for intact, cutaneous afferent lymphatics during the primary response to transplants (Barker and Billingham, 1968) and contact allergens (Frey & Wenk, 1957) in situ. In recall or delayed type hypersensitivity reactions, dendritic cells also are juxtaposed to the infiltrates of dermal mononuclear cells (Kaplan et al., 1987).... When dendritic cells are pulsed with antigens ex vivo and are injected into mice, CD4.sup.+ T cells are primed in the draining lymphoid organs (Inaba et al., 1990; Liu and MacPherson, 1993; Sornasse et al., 1992). Austyn et al. showed that dendritic cells, when placed into the blood stream or paws of mice, migrate to the T cell areas in the draining lymphoid tissue, i.e., spleen and lymph node respectively (Austyn et al., 1988). If antigens are deposited intramuscularly, the dendritic cells from the corresponding afferent lymphatics carry that antigen in a form stimulatory for T cells (Bujdoso et al., 1989). Therefore, the migratory properties of dendritic cells likely interface with their antigen presenting functions to sensitize T cells in situ.

Web site: http://www.delphion.com/details?pn=US05627025__

- **Method of delaying the progression of an infection with the human immunodeficiency virus**

  Inventor(s): Tsoukas; Christos M. (Montreal, CA), Woloski; Barry Michael (Winnipeg, CA)

  Assignee(s): Cangene Corporation (Winnipeg, CA)

  Patent Number: 5,993,812

  Date filed: April 7, 1997

  Abstract: Therapeutic and prophylactic methods using Rh antibodies for delaying the progression of infection with the Human Immunodeficiency Virus (HIV) in a subject who is exposed to HIV, or infected by HIV.

  Excerpt(s): Acquired Immunodeficiency Syndrome (AIDS) is a transmissible disease caused by a retrovirus. The retrovirus responsible for AIDS was first identified by Barre-Sinoussi, F., et al, Science 220, 868-871, 1983 and Gallo, R. C., et al., Science 224:500-503, 1984, and related retroviruses have been isolated from patients in different areas. The accepted terminology for these isolates is human immunodeficiency virus (HIV), which has subtypes e.g. HIV type-1 and HIV type-2.... The mechanisms by which HIV infection produces immunodeficiency is the subject of intensive investigations. It has been suggested that the decrease in CD4+ lymphocyte number and function involves direct effects of viral infection on mature and progenitor CD4 cells, as well as the destruction by cellular or humoral mechanisms of uninfected CD4 cells that display absorbed or processed viral antigens on their surface. Monocytes and macrophages which express the CD4 antigen are also targets for HIV infection. These cells of the reticuloendothelial system probably represent a major reservoir for virus production in vivo (Gendelman et al., 1989, AIDS 2:475; Embretson et al, 1993, Nature 362:359). Monocytes play a central role in the processing and presenting of antigens to T and B lymphocytes and they are able to migrate to the central nervous system. Therefore, infection of monocytes by HIV may play a role in the development of both immunologic and neurologic disease in infected individuals.... The use of intravenous immunoglobulin in the treatment of patients with HIV infections has been widely documented (See Schrappe-Bacher, M.,

Vox-Sang, 1990; Suppl 1:3-14; Wagner , N., et al. Arch. Dis. Child. 1992, Oct., 67(10): 1267-71; Brunkhorst, U. et al., Infection, 1990, 18(2):86-90; De Simone, C., et al, Immunopharmacol Immunotoxicol. 1991 13(3) 447-58; Gungor, T. et al., Eur. J. Pediatr., 1993 152(8): 650-4; Mofenson, L. M. et al., J. Acquir. Immune Defic. Syndr. 1993, 6(10): 1103-13; Mofenson, L. M. and Moye, J, Pediatr. Res. 1993 33(I Suppl): S80-7; discussion S87-9; Ersoy et al., Turk. J. Pediatr. 1992 34(4): 203-9; Shearer, W. T. et al, Ann N.Y. cad. Sci. 1993, 693:35-51; and WO 89/01339 to Cummins et al.). Intravenous immunoglobulin administration has been reported to be beneficial in reducing the rate of secondary opportunistic bacterial or viral infections in HIV-positive adults and children. It has also been reported to temporarily increase and/or maintain CD4+T-lymphocyte profiles in HIV-infected patients. However, this activity has not been consistently observed.

Web site: http://www.delphion.com/details?pn=US05993812__

- **Method of inhibiting the activity of human immunodeficiency virus (HIV) in vivo**

  Inventor(s): Davis; Michael H. (3020 E. Inglewood Ct., Springfield, MO 65804)

  Assignee(s): none reported

  Patent Number: 5,278,173

  Date filed: December 10, 1992

  Abstract: A method for inhibiting the activity of human immunodeficiency virus (HIV) in vivo comprises administering to a human host an antimalarial drug, which is capable of exhibiting a protective effect, a curative effect, or of preventing transmission of malaria in humans. The antimalarial drug is selected from the group consisting of(a) alkaloids;(b) 9-amino-acridines;(c) 4-aminoquinolines;(d) 8-aminoquinolines;(e) biguanides;(f) dihyrofolate reductase inhibitors;(g) sulfones;(h) sulfonamides;(i) mefloquine;(i) halofantrine;(k) hydroxyanilino-benzo-naphtyridines; and(l) sesquiterpene lactones.The antimalarial drug is administered to the human in an amount sufficient to prevent or at least inhibit infection of T lymphocytes by HIV in vivo or to prevent or at least inhibit replication of HIV in vivo.

  Excerpt(s): This invention relates to the use of anti-malarial drugs for inhibiting infection of susceptible cells by human immunodeficiency virus (HIV). This invention also relates to a method of inhibiting proliferation of HIV.... Acquired immune deficiency syndrome (AIDS) is a condition which is now of major importance in North America, Europe, and Central Africa. The casual agent of AIDS is believed to be a retrovirus. Recent estimates suggest that approximately 1.5 million Americans may have been exposed to the AIDS virus. The individuals affected show severe immunosuppression, which may be followed by the onset of degenerative and even fatal diseases.... The isolation and characterization of the first AIDS retrovirus, known as LAV, was described in a paper by F. Barre-Sinoussi, et al. Science, 220:868-871 (1983). The use of some extracts of this virus and some of its proteins to detect antibodies against the virus is described in U.S. Pat. No. 4,708,818 issued to Dr. Luc Montagnier, et al.

  Web site: http://www.delphion.com/details?pn=US05278173__

- **Method of prevention or treatment of AIDS by inhibition of human immunodeficiency virus**

  Inventor(s): Gallaher; William R. (New Orleans, LA)

  Assignee(s): Research Corporation Technologies, Inc. (Tucson, AZ)

  Patent Number: 4,880,779

  Date filed: July 31, 1987

  Abstract: The present invention relates to a method of prevention or treatment of AIDS by inhibition of the human immunodeficiency virus (HIV). Inhibition of the virus is achieved by administration of an inhibitory peptide containing the sequence Phe-X-Gly, wherein X is an amino acid.

  Excerpt(s): The present invention relates to a method of prevention or treatment of acquired immune deficiency syndrome (AIDS). More specifically, the invention relates to a method of inhibiting infection by the viral etiologic agent of AIDS through administration of an inhibitory peptide.... A wide variety of different types of viruses are well-known as being the etiologic agents for a number of diseases in both animals and man. Because of the large number of potentially widespread epidemics, e.g. influenza, herpes, and AIDS, to name but a few, methods are constantly being sought for either prevention or cure of the diseases caused by these entities. This effort has been hampered to a large extent by the unusual structural and functional aspects of viruses, which are quite unlike any other known infectious agents, such as bacteria or fungi. The virus itself consists essentially of nucleic acid surrounded by a lipid-protein envelope; the virus does not replicate in the host by simple division like a bacterium, but rather multiplies by invading a host cell and, by virture of the action of the viral nucleic acid, reprogramming the cell to synthesize the viral components. The extensive use of mimicry of cellular mechanisms by the virus makes it especially difficult to generate drugs which are selectively toxic to viral infection.... In more recent years, an increased understanding of the structure, and related function of different viruses has provided an insight into the detailed mechanisms by which a viral particle invades a cell. The protein elements of the envelope, which generally consist of matrix proteins and glycoproteins, may play an integral role in the infection process. In fact it is now known that the glycoprotein components of the envelopes of many viruses are absolutely critical to the successful entry of the virus into the host cell. For example, in a large number of essentially unrelated types of virus, such as paramyxoviruses, influenza viruses and retroviruses, a common pattern exists. Attachment or adsorption of the virus to the host cell membrane is achieved by the interaction of an "attachment" or "receptor-binding" viral glycoprotein with a specific receptor on the host cell surface. Following attachment of the virus, fusion of the target cell membrane with the viral envelope occurs via the mediation of a fusion glycoprotein of the virus, which probably penetrates the host cell at a particular site, and then may shorten, drawing the two entities in closer proximity. Once fusion occurs, the cytoplasm of the cell is merged with the contents of the virus and the viral nucleic acid may then begin to direct the cell machinery.

  Web site: http://www.delphion.com/details?pn=US04880779__

- **Method of treating human immunodeficiency virus infection using a cyclic protease inhibitor in combination with a reverse transcriptase inhibitor**

  Inventor(s): Otto; Michael J. (West Chester, PA)

  Assignee(s): The Dupont Merck Pharmaceutical Company (Wilmington, DE)

  Patent Number: 5,616,578

  Date filed: August 26, 1993

  Abstract: This invention relates to a method of treating human immunodeficiency virus (HIV) infection in a mammal comprising administering to the mammal a therapeutically effective amount of a combination of: (i) at least one cyclic HIV protease inhibitor and (ii) at least one HIV reverse transcriptase inhibitor.

  Excerpt(s): This invention relates to a method of treating human immunodeficiency virus (HIV) infection in a mammal comprising administering to the mammal a therapeutically effective amount of a combination of: (i) at least one cyclic HIV protease inhibitor and (ii) at least one HIV reverse transcriptase inhibitor.... Two distinct retroviruses, human immunodeficiency virus (HIV) type-1 (HIV-1) or type-2 (HIV-2), have been etiologically linked to the immunosuppressive disease, acquired immunodeficiency syndrome (AIDS). HIV seropositive individuals are initially asymptomatic but typically develop AIDS related complex (ARC) followed by AIDS. Affected individuals exhibit severe immunosuppression which predisposes them to debilitating and ultimately fatal opportunistic infections.... No treatment is currently available to prevent or reverse the immunodeficiency of AIDS and ARC. Moreover, it is generally believed that an effective vaccine or therapy must be developed in order to prevent the transmission of HIV.

  Web site: http://www.delphion.com/details?pn=US05616578__

- **Method of treatment of human immunodeficiency virus**

  Inventor(s): Gupta; Phalguni (Pittsburgh, PA), Ho; Monto (Pittsburgh, PA)

  Assignee(s): University of Pittsburgh of the Commonwealth System of Higher Education (Pittsburgh, PA)

  Patent Number: 4,923,895

  Date filed: October 24, 1988

  Abstract: A method of treating a patient for human immunodeficiency virus (HIV) inces administering to the individual patient intravenously a therapeutically effective dosage of oxyphenarshine (3 amino-4 hydroxyphenyl-arsineoxide hydrochloride). The dose emplyed may be up to about 1 milligram per kilogram of body weight administered 1 to 2 times weekly. The oxyphenarsine is preferably administered in such an amount as to achieve in said patient a blood serum concentration of about 0.12 to 6.0 micrograms per milliliter.

  Excerpt(s): It has been known to employ organic arsenicals for therapeutic purposes. See, for example, U.S. Pat. No. 986,148.... It has also been known to employ oxyphenarsine (3 amino-4 hydroxyphenyl-arsineoxide hydrochloride) in the treatment of syphilis.... Human immunodeficiency virus type 1 or HIV causes acquired immunodeficiency syndrome ("AIDS") and is a fatal disease which has approached epidemic proportions both within the U.S. and elsewhere. The problem has reached

sufficiently serious proportions that by Executive order, the President of the U.S. established Presidential Commission on the Human Immunodeficiency Virus Epidemic.

Web site: http://www.delphion.com/details?pn=US04923895__

- **Methodologies for the detection of human immunodeficiency virus nucleic acids employing oligonucleotide primer derived from the HIV-1 MVP5180/91 genome**

  Inventor(s): Knapp; Stefan (Marburg, DE), Brust; Stefan (Marburg-Michelbach, DE), Guertler; Lutz G. (Munich, DE), Gerken; Manfred (Marburg, DE)

  Assignee(s): Dade Behring Marburg GmbH (Marburg, DE)

  Patent Number: 6,335,158

  Date filed: August 10, 1998

  Abstract: The present invention is directed toward nucleic-acid based methodologies for the detection of human immunodeficiency virus (HIV) nucleic acids in a sample. A novel HIV-1 isolate, designated MVP5180/91, was isolated from a West African Cameroonian patient with immunodeficiency. Nucleic acid and amino acid sequence comparisons of this isolate, with other HIV-1 strains of subtypes A-E and HIV-2 isolates, demonstrated that this virus shares only limited homology with other known HIV-1 and -2 isolates. However, this virus does display some genetic relatedness to another Cameroonian isolate designated ANT-70. These viruses form the basis for a new HIV-1 group which has been designated subtype O. An immunologically important epitope, corresponding to amino acids 601-623 of the MVP5180/91 transmembrane envelope glycoprotein, was identified. Labeled nucleic acids can be prepared from the nucleotide sequence encoding this region and employed in standard hybridization assays to detect HIV-1 nucleic acids. Alternatively, oligonucleotide primers can also be prepared from this region and employed in polymerase chain reaction (PCR) assays to detect viral-specific nucleic acids.

  Excerpt(s): The present invention relates immunologically active peptides derived from a novel retrovirus of the HIV group, MVP5180/91. The invention further relates to the use of these peptides in diagnostic compositions and as immunogens.... Retroviruses which belong to the HIV group give rise, in humans infected with them, to disease symptoms which are summarized under the collective term immune deficiency or AIDS (acquired immune deficiency syndrome). Epidemiological studies demonstrate that the human immunodeficiency virus (HIV) represents the etiological agent for the overwhelming majority of AIDS cases. A retrovirus which was isolated from a patient and characterized in 1983 was given the designation HIV-1 (Barre-Sinoussi, F. et al., Science 220: 868-871 (1983)). A variant of HIV-1 is described in WO 86/02383.... Until 1993, the known HIV-1 isolates were categorized into the five subtypes A-E on the basis of sequence comparisons and epidemiological standpoints (G. Myers et al., Human Retroviruses and AIDS 1992. "A compilation and analysis of nucleic acid and amino acid sequences." Los Alamos Laboratory, Los Alamos, USA (1992)).

  Web site: http://www.delphion.com/details?pn=US06335158__

- **Methods for stimulating immune responses in a host through the administration of superantigen peptides derived from human immunodeficiency virus type 1 Nef**

  Inventor(s): Johnson; Howard M. (Gainesville, FL), Torres; Barbara A. (Gainesville, FL), Yamamoto; Janet K. (Gainesville, FL)

  Assignee(s): University of Florida (Gainesville, FL)

  Patent Number: 5,968,514

  Date filed: October 31, 1994

  Abstract: The human immunodeficiency virus (HIV) contains, in addition to the canonical genes gag, pol, and env, an open reading frame in the 3' region of the genome that overlaps with the 3' long terminal repeat (LTR). Initial studies on the protein encoded by this ORF revealed a negative effect on HIV replication in vitro and this gene product was subsequently designated the negative factor, or Nef. The nef gene product is 25-29 kDa protein that localizes primarily to the cytoplasm of HIV-infected cells. The subject of this invention pertains to the discovery of a superantigen activity associated with this peptide and peptidic fragments derived therefrom. Superantigens are powerful T-cell mitogens that bind directly to major histocompatibility complex (MHC) class II molecules and form a binary complex with the variable.beta. (V.sub..beta.) region of the T-cell antigen receptor (TCR). It was demonstrated that Nef induces the rapid proliferation of human peripheral mononuclear cells and T-lymphocyte cytokine production. Nef peptidic fragments were also identified that display major histocompatibility complex (MHC) class II binding activity. These peptides can be utilized to generate suitable immune responses in the desired host.

  Excerpt(s): Normally, when a person's immune system encounters a protein made by a virus or other microbe, fewer than one in 10,000 of the white blood cells known as T lymphocytes react. Although their number is small, these T lymphocytes orchestrate an attack that specifically targets the alien protein, or antigen, without harming healthy tissue. In contrast, proteins called superantigens highly activate the immune system and can cause an unproductive, even destructive, immune response.... Superantigens are the most powerful T cell mitogens known (Johnson, H. M., H. I. Magazine [1988] Int. Arch Allergy Appl. Immunol. 87:87-90). As explained below, these unique antigens stimulate T cells by first binding to class II major histocompatibility (MHC) molecules (Carlsson, R., H. Fischer, H. O. Sjogren [1988] J. Immunol. 140:2484-2488; Fleischer, B., H. Schrezenmeier [1988] J. Exp. Med. 167:1697-1707; Mollick, J. A., R. G. Cook, R. R. Rich [1989] Science 244:817-820) forming a binary complex which binds in a V.sub..beta. -specific manner to the T cell antigen receptor (TCR) (Janeway, C. A., J. Yagi, P. J. Conrad, M. E. Katz, B. Jones, S. Vroegop, S. Buxser [1989] Immunol. Rev. 107:61-88; White, J., A. Herman, A. M. Pullen, R. Kubo, J. W. Kappler, P. Marrack [1989] Cell 56:27-35).... Superantigens can arouse as many as one in five T cells, most of which are useless for fighting a current infection. What is worse, certain of the activated cells may unleash an autoimmune attack which targets tissues of the host organism. At times, superantigens may even have the opposite effect: they somehow trigger the death of the cells they excite.

  Web site: http://www.delphion.com/details?pn=US05968514__

- **Monoclonal antibodies to specific antigenic regions of the human immunodeficiency virus and methods for use**

  Inventor(s): Flesher; Alan R. (Seattle, WA), Shriver; Mary K. (Bellevue, WA)

  Assignee(s): Genetic Systems Corporation (Redmond, WA)

  Patent Number: 5,104,790

  Date filed: October 7, 1987

  Abstract: Monoclonal antibodies capable of binding antigenic determinants within regions of the core proteins of the Human Immunodeficiency Virus and immortalized cell lines producing those monoclonal antibodies are provided. The monoclonal antibodies find use in a variety of ways, including HIV antigen detection in biological samples. Using these methods, individuals may be identified who are infected with HIV but who have not yet developed anti-HIV antibodies. The methods also find use in monitoring in vitro growth of HIV, and the efficacy of therapeutic agents and vaccines.

  Excerpt(s): The present invention relates generally to novel immunological materials useful in diagnosing and monitoring infections caused by the Human Immunodeficiency Virus (HIV), the etiologic agent of AIDS. More particularly, the invention provides cell lines which produce monoclonal antibodies to antigenic determinants of the core proteins of HIV. These antibodies are useful in the diagnosis of HIV infection and monitoring the efficacy of pharmaceutical formulations and vaccine compositions.... The etiologic agent of Acquired Immune Deficiency Syndrome (AIDS) is a novel lymphotropic retrovirus termed the Human Immunodeficiency Virus (HIV), which may also be referred to in the literature as LAV, HTLV-III, or ARV. As the spread of HIV reaches pandemic proportions, preventing its transmission has become a paramount concern. To reduce the risk of transfusion-associated HIV infection, hospitals, blood banks, and other users or manufacturers of blood-related products now routinely screen blood donors for the presence of antibodies to HIV. The screening tests typically employ disrupted preparations of purified HIV which have been adsorbed onto a solid surface, such as a microwell or bead. Other screening tests use HIV polypeptides produced by recombinant means, or chemically synthesized peptides which contain immunodominant antigenic regions of HIV. Using such screening tests, the vast majority of the potentially infective units of blood in the donor pool are identified and removed.... Despite the high sensitivity and specificity of the HIV antibody screening tests, a small but significant number of infected blood products still pass undetected into the blood supply. Of primary concern are donors who are infected with HIV at the time they donate blood or plasma but have not yet developed antibodies to the virus. Antibodies may not rise to detectable titers until 3-4 weeks or more after infection. Recent evidence puts the window between time of infection and development of detectable antibody at six weeks to six months. If an infected individual donates blood or plasma during this period, the public blood supply is threatened with an undetected contamination.

  Web site: http://www.delphion.com/details?pn=US05104790__

- **Nucleic acids and pepties of human immunodeficiency virus type-1 (HIV-1).**

  Inventor(s): Danos; Olivier (Paris, FR), Wain-Hobson; Simon (Montigny les Bretonneux, FR), Clavel; Fran.cedilla.ois (Paris, FR), Cole; Stewart (Chatillon, FR), Montagnier; Luc (Le Plessis Robinson, FR), Sonigo; Pierre (Paris, FR), Krust; Bernard (Paris, FR), Chamaret; Solange (Paris, FR), Barre-Sinoussi; Fran.cedilla.oise (Issy les Moulineaux, FR), Chermann; Jean-Claude (Elancourt, FR), Alizon; Marc (Paris, FR)

  Assignee(s): Institut Pasteur and Centre National de la Recherche Scientifique (Paris, FR)

  Patent Number: 5,843,638

  Date filed: June 6, 1995

  Abstract: This invention is directed to nucleic acids derived from the pol region of the genome of human immunodeficiency virus type 1 (HIV-1). The nucleic acids are useful as probes for the detection of HIV-1. More particularly, this invention is directed to nucleic acids encoding a pol region of HIV-1 extending from about nucleotide 1856 to about 1906 and extending from about nucleotide 2048 to about nucleotide 2797.

  Excerpt(s): The present invention relates to antigens, particularly in a purified form, of the virus of lymphadenopathies (denoted below by the abbreviation LAS) and of the acquired immuno-depressive syndrome (denoted below by the abbreviation AIDS), to a process for producing these antigens, particularly antigens of the envelopes of these viruses. The invention also relates to polypeptides, whether glycosylated or not, encoded by said DNA sequences.... The causative agent of LAS or AIDS, a retrovirus, has been identified by F. BARRE-SINOUSSI et al, Science, 220, 868 (1983). It has the following characteristics. It is T-lymphotropic; its prefered target is constituted by Leu 3 cells (or T4 lymphocytes); it has reverse transcriptase activity necessitating the presence of Mg.sup.++ and exhibits strong affinity for poly(adenylate-oligodeoxy-thymidylate)(poly(A)-oligo(dT)12-18). It has a density of 1.16-1.17 in a sucrose gradient, an average diameter of 139 nanometers; and a nucleus having an average diameter of 41 nanometers. Antigens of said virus, particularly a protein p25 are recognised immunologically by antibodies contained in serum obtained from patients afflicted with LAS or AIDS. The p25 protein, which is a core protein, is not immunologically related to the p24 protein of the HTLVI and II viruses. The virus is also free of a p19 protein which is immunologically cross-reactive with the p19 proteins of HTLVI and HTLVII.... Retroviruses of this type (sometimes denoted by the generic abbreviation LAV) have been deposited in the National Collection of Micro-organism Cultures of the INSTITUT PASTEUR of Paris, under numbers I-232, I-240 and I-241. Virus strains similar to LAV in all respects from the morphological and immunological point of view have been isolated in other laboratories. Reference is made by way of example to the retrovirus strains named HTLV-III isolated by R. C. GALLO et al., Science, 224, 500 (1984) and by M. G. SARNGADHARAN et al., Science 224, 506 (1984) respectively and to the retrovirus isolated by M. JAY LEVY et al., Science, 225, 840-842 (1984), which was designated ARV. For the ease of language the last mentioned viruses, as well as others which have equivalent morphological and immunological properties, will be designated hereafter under the generic designation "LAV". Reference is also made to European patent application filed 14 Sep. 1984, with the priority of British patent application number 83 24800 filed 15 Sep. 1983 as regards a more detailed description of the LAV retroviruses or the like and of the uses to which extracts of these viruses give rise.

  Web site: http://www.delphion.com/details?pn=US05843638__

- **Nucleic acids encoding mutated human immunodeficiency virus matrix proteins**

  Inventor(s): Lee; Tun-Hou (Newton, MA), Yu; Xiaofang (Columbia, MD), Essex; Myron E. (Sharon, MA)

  Assignee(s): President and Fellows of Harvard College (Cambridge, MA)

  Patent Number: 5,707,864

  Date filed: November 23, 1992

  Abstract: Nucleic acid constructs encoding mutated human immunodeficiency virus matrix proteins are described. The mutated proteins lower the incorporation of envelope polypeptides in viral particles, disrupt viral assembly or disrupt viral entry into uninfected cells.

  Excerpt(s): This invention relates to the treatment of infection with the human immunodeficiency virus (HIV) by which we mean to include all of the various viral types and strains denominated by that term, such as HTLV-III, LAV, ARV, HIV-1, HIV-2, and LAV-2.... A second virus related to HIV-1 has been isolated and termed HIV-2. This virus is reported by Guyader et al., Nature 326:662, 1987; Brun-Vezinet et al., The Lancet 1:128, 1987; and Clavel et al., Science 233:343, 1986, each of which is hereby incorporated by reference. The genetic organization of HIV-2 is similar to that of HIV-1.... A group of viruses isolated from monkeys, termed simian immunodeficiency virus (SIV or STLV-III), is related to HIV-1 and HIV-2, particularly the latter. See Daniel et al., Science 228:1201-1204 (1985); Kanki et al., Science 230:951-954 (1985); Chakrabarti et al., Nature 328:543-547 (1987); and Ohta et al., Int'l. J. Cancer 41:115-222 (1988), each of which is hereby incorporated by reference. Members of this viral group exhibit minor variations in their genomic sequences, and have some differences in their restriction enzyme maps.

  Web site: http://www.delphion.com/details?pn=US05707864__

- **Nucleic acids of a human immunodeficiency virus type 2 (HIV-2)**

  Inventor(s): Guyader; Mireille (Paris, FR), Sonigo; Pierre (Paris, FR), Clavel; Fran.cedilla.ois (Paris, FR), Alizon; Marc (Paris, FR), Guetard; Denise (Paris, FR), Montagnier; Luc (Le Plessis Robinson, FR), Brun-Vezinet; Fran.cedilla.oise (Paris, FR)

  Assignee(s): Institut Pasteur (FR)

  Patent Number: 6,429,306

  Date filed: February 22, 1995

  Abstract: The present invention is directed toward a novel human retrovirus isolated from West African AIDS patients. This virus was originally designated lymphadenopathy associated virus (LAV) type II and subsequently renamed the human immunodeficiency virus type 2, or HIV-2. This virus is genotypically and phenotypically distinct from both human immunodeficiency virus type 1 (HIV-1) and the simian immunodeficiency virus (SIV). A recombinant.lambda. phage library was prepared by subjecting HIV-2-infected CEM genomic DNA to digestion with Sau3AI. The library was screened with an HIV-2-specific cDNA probe and molecular clones of the virus were obtained. Restriction maps and the nucleotide sequences of these clones were ascertained. These nucleic acids should prove useful, inter alia, as probes for the detection of HIV-2 in biological samples and for the expression of HIV-2 gene products.

Excerpt(s): The invention relates to a new class of viruses having the capacity to cause lymphadenopathies, which are then capable of being replaced by acquired immune deficiency syndrome (AIDS) in man. The invention also relates to antigens capable of being recognized by antibodies induced in man by this new class of virus. It also relates to the antibodies induced by antigens obtained from these viruses.... This invention relates, furthermore, to cloned DNA sequences possessing sequence analogy or complementarity with the genomic RNA of the above-mentioned virus. It also relates to the methods for preparing these cloned DNA sequences.... The invention also relates to polypeptides containing amino acid sequences encoded by the cloned DNA sequences.

Web site: http://www.delphion.com/details?pn=US06429306__

- **Nucleotide sequence encoding a human immunodeficiency virus antigen**

  Inventor(s): Petteway; Steven R. (Hockessin, DE), Ivanoff; Lucinda A. (Springfield, PA)

  Assignee(s): E. I. Du Pont de Nemours and Company (Wilmington, DE)

  Patent Number: 5,141,867

  Date filed: May 4, 1989

  Abstract: A nucleotide sequence encoding a recombinant peptide displaying the antigenicity of Human Immunodeficiency Virus (HIV) viral antigens is disclosed. The peptide comprises an antigenic segment having about 150 to about 400 amino acids corresponding to at least about 30 amino acids of the C-terminal of the gp120 domain and at least about 120 amino acids of the N-terminal of the gp41 domain.

  Excerpt(s): The present invention concerns antigens and vaccines for infectious diseases and, more particularly, to antigens useful in the diagnosis and treatment of Human Immunodeficiency Virus.... Human Immunodeficiency Virus (HIV, also HTLV-III, LAV, ARV), a cytopathic lymphotropic retrovirus, is considered the probable causative agent of Acquired Immunodeficiency Syndrome (AIDS) in humans. [Gallo, et al., Science, 224:500 (1984); Popovic, et al., Science, 224:497 (1984); Sarngadharan, et al., Science, 224:506 (1984)]. The underlying disease state involves a tropism of HIV for the T4+ lymphocyte subset resulting in a selective depletion of the helper/inducer cells of the immune system, leaving the individual defenseless against a number of opportunistic infections.... There are currently more than 27,700 diagnosed cases of AIDS in the United States and the U.S. Public Health Service predicts that by the end of 1991 more than 179,000 persons will have the disease. It is believed that only 10 to 15 percent of those with clinical symptoms and 1 to 2 percent of those infected with HIV suffer the clinical syndrome of AIDS. The development of diagnostics and vaccines to HIV is the subject of intense medical research.

  Web site: http://www.delphion.com/details?pn=US05141867__

- **Oligonucleotide phosphonates and method of inhibiting a human immunodeficiency virus in vitro utilizing said oligonucleotide phosphonates**

  Inventor(s): Rossi; John J. (Glendora, CA), Zaia; John A. (Arcadia, CA), Cantin; Edouard M. (Los Angeles, CA), Wallace; R. Bruce (South Pasadena, CA)

  Assignee(s): City of Hope (Duarte, CA)

  Patent Number: 5,110,802

  Date filed: July 14, 1987

  Abstract: A method of inhibiting human immunodeficiency virus (HIV) comprising administering a therapeutically effective amount of an antiviral agent to attack the first splice acceptor site of the tat III gene of HIV.

  Excerpt(s): This invention relates to a method of treating Acquired Immune Deficiency Syndrome (AIDS) in humans using antisense oligodeoxynucleoside methylphosphonates.....sup.1/ A., Hollander, H. and Stobo, J. Ann. Rev. Med. 36, 545-562 (1985); Wong-Staal, F. and Gallo, R. C., Nature 317, 395-403 (1985); Rabson, A. B. and Martin, M. A. Cell 40, 477-480 (1985).....sup.2/ Dalgleish, A. B. et al., Nature 312, 277-284 (1985); Maddon, P. J., et al., Cell 47, 333-348 (1986); McDougal, J. S., et al., J. Immunol. 135, 3151-3162 (1985).

  Web site: http://www.delphion.com/details?pn=US05110802__

- **Oligonucleotide primers for efficient multiplex detection of hepatitis C virus (HCV) and human immunodeficiency virus (HIV) and methods of use thereof**

  Inventor(s): Song; Keming (Ballwin, MO), Linnen; Jeffrey M. (San Diego, CA), Gorman; Kevin M. (Penfield, NY), Patterson; David R. (San Diego, CA)

  Assignee(s): Ortho-Clinical Diagnostics, INC (Raritan, NJ)

  Patent Number: 6,623,919

  Date filed: January 28, 2000

  Abstract: Disclosed herein are methods and kits for the simultaneous detection of hepatitis C virus and human immunodeficiency virus in biological samples from human subjects.

  Excerpt(s): The present invention pertains to improved methods for detecting nucleic acid sequences in biological samples, particularly sequences derived from infectious microorganisms.... Human Immunodeficiency Virus (HIV) infects millions of individuals world-wide and consequently represents a serious public health concern. Spread of HIV infection via contaminated blood products means that there is a need for screening methods that can detect small amounts of HIV RNA in patient samples. Furthermore, the increasing availability of ameliorative treatments for HIV infection means that early detection of infection in a patient is vital in order to initiate appropriate therapeutic interventions.... Hepatitis C Virus (HCV) is a parenterally transmitted virus responsible for the majority of cases of post-transfusion hepatitis and a substantial portion of sporadic (or community acquired) hepatitis cases worldwide. It is estimated that more than 1% of the world's population is infected with HCV. HCV infection is associated with acute hepatitis, chronic hepatitis, cirrhosis, and subsequent hepatocellular carcinoma.

  Web site: http://www.delphion.com/details?pn=US06623919__

- **Oligonucleotides and methods for inhibiting propagation of human immunodeficiency virus**

  Inventor(s): Ryder; Thomas B. (Escondido, CA), Kwoh; Theodore Jesse (Carlsbad, CA)

  Assignee(s): Gen-Probe Incorporated (San Diego, CA)

  Patent Number: 5,733,781

  Date filed: July 19, 1994

  Abstract: The present invention concerns the use of oligonucleotides to inhibit propagation of human immunodeficiency virus (HIV). Preferred HIV target sites are identified and oligonucleotides designed to hybridize to a target site, or be analogous to a target site, are described. The preferred use of the oligonucleotides is to inhibit HIV propagation in a patient infected with HIV.

  Excerpt(s): The present invention features compounds and methods for inhibiting propagation of human immunodeficiency virus.... Oligonucleotides such as antisense oligonucleotides can hybridize to a target RNA, such as mRNA, and inhibit protein production from that RNA. Numerous mechanisms have been proposed to explain the effects of antisense oligonucleotides. For example, see Helene, C. and Toulme, J. Biochimica et Biophysica Acta 1049:99 (1990), and Uhlmann, E. and Peyman, A. Chemical Reviews 90:543 (1990). Proposed mechanisms include forming a DNA: RNA substrate for cellular RNase H, hybridization of an antisense oligonucleotide to nascent mRNA leading to premature transcription termination and interfering with mRNA processing by hybridizing to a pre-mRNA intron/exon junction. These and several other proposed mechanisms for inhibiting nucleic acid activity by antisense oligonucleotides are based upon the ability of antisense oligonucleotides to hybridize to a target nucleic acid sequence.... Tullis, U.S. Pat. No. 5,023,243, provides a general description of using antisense oligonucleotides to inhibit protein translation. Kaji, U.S. Pat. No. 4,689,320, provides data showing a decrease in mortality in mice infected with Herpes Simplex Virus by administering an antisense oligonucleotide targeted to herpes simplex virus. Goodchild et al., U.S. Pat. No. 4,806,463, provides data concerning the ability of antisense oligonucleotides to inhibit HTLV-III (HIV) replication and gene expression in cultured cells infected with HIV. Cantin et al., U.S. Pat. No. 5,110,802, describe the use of a methylphosphonate-linked oligonucleotide to inhibit HIV replication. These U.S. patents are hereby incorporated by reference herein. Matsukura et al., Proc. Natl. Acad. Sci. 86:4244 (1989) describe inhibiting HIV expression using a phosphorothioate-linked oligonucleotide targeted to a rev nucleotide sequence.

  Web site: http://www.delphion.com/details?pn=US05733781__

- **Oligonucleotides with activity against human immunodeficiency virus**

  Inventor(s): Velarde, Jr. Jorge (San Diego, CA), Peterson; Todd C. (Chula Vista, CA)

  Assignee(s): Gen-Probe Incorporated (San Diego, CA)

  Patent Number: 5,919,701

  Date filed: June 2, 1997

  Abstract: The present invention features compounds and methods for inhibiting propagation of human immunodeficiency virus (HIV). Preferred HIV target sites are identified and oligonucleotides designed to hybridize to a target site are described. The

preferred use of the oligonucleotides is as an anti-HIV agent to inhibit HIV propagation in a patient infected with HIV. Other uses of the present invention include detecting the presence of HIV by using the oligonucleotides as detection probes or amplification primers, and measuring the ability of an oligonucleotide to inhibit HIV propagation to evaluate its suitability as an anti-HIV agent for a phenotype of HIV or diagnose the presence of HIV in a patient.

Excerpt(s): This invention relates to oligonucleotides particularly useful in inhibiting replication of the human immunodeficiency virus (HIV).... Antisense oligonucleotides can hybridize with viral mRNA and inhibit translation or processing of mRNA, thereby inhibiting viral replication. Hybridization of antisense oligonucleotides to viral mRNA (antisense:mRNA) occurs by hydrogen bonding between complementary nucleotides present on an antisense oligonucleotide and viral mRNA. Adenine (A) is complementary to thymidine (T) and uracil (U), while cytosine (C) is complementary to guanine (G). Along the antisense:mRNA chain classical base pairs AU, TA or UA, GC, or CG are present. Additionally, some mismatched base pairs (e.g., AG, GU) may be present.... The ability to form hydrogen bonds between nucleotides enables antisense oligonucleotides to be targeted to specific viral nucleic acid sequences. Thus, antisense oligonucleotides can be targeted to nucleic acid sequences present only in viral nucleic acid, and viral gene expression can be selectively inhibited.

Web site: http://www.delphion.com/details?pn=US05919701__

- **Peptide derived from human immunodeficiency virus type 1 (HIV-1), isolate Ant70, containing an immunodominant epitope and it's use in immunodiagnostic assays**

  Inventor(s): De Leys; Robert (Grimbergen, BE)

  Assignee(s): N. V. Innogenetics S. A. (Ghent, BE)

  Patent Number: 6,210,903

  Date filed: July 9, 1998

  Abstract: This invention is directed toward a peptide corresponding to an immunologically important viral epitope. Specifically, the peptide corresponds to an immunodominant epitope identified in the gp120 region of the human immunodeficiency virus type 1 (HIV-1), strain Ant70. This peptide has the following amino acid sequence: NH.sub.2 -Gln-Ile-Asp-Ile-Gln-Glu-Met-Arg-Ile-Gly-Pro-Met-Ala-Trp-Tyr-Ser-Met-Gly-I le-Gly-Gly-CO.sub.2 H. The invention also relates to the use of this peptide, particularly when biotinylated in the form of complexes of streptavidin-biotinylated peptides or of avidin-biotinylated peptides, for the in vitro determination of HIV-1-specific antibodies.

  Excerpt(s): The technical problem underlying the present invention is to provide peptides corresponding to immunologically important epitopes on bacterial and viral proteins, as well as the use of said peptides in diagnostic or immunogenic compositions.... Recent developments in genetic engineering as well as the chemistry of solid phase peptide synthesis have led to the increasingly wider use of synthetic peptides in biochemistry and immunology. Protein sequences which become available as a result of molecular cloning techniques can be synthesized chemically in large quantities for structural, functional, and immunological studies. Peptides corresponding to immunologically important epitopes found on viral and bacterial proteins have also proven to be highly specific reagents which can be used for antibody detection and the diagnosis of infection.... Despite the many advantages synthetic peptides offer, there are

a number of disadvantages associated with their use. Because of their relatively short size (generally less than 50 amino acids in length), their structure may fluctuate between many different conformations in the absence of the stabilizing influence of intramolecular interactions present in the full-length protein. Furthermore, the small size of these peptides means that their chemical properties and solubilities will frequently be quite different from those of the full-length protein and that the contribution of individual amino acids in the peptide sequence toward determining the overall chemical properties of the peptide will be proportionally greater.

Web site: http://www.delphion.com/details?pn=US06210903__

- **Peptides derived from human immunodeficiency virus-1 GP160**

Inventor(s): Greene; Mark I. (Penn Valley, PA), Williams; William V. (Havertown, PA), Weiner; David B. (Penn Wynne, PA)

Assignee(s): Trustees of the University of Pennsylvania (Philadelphia, PA)

Patent Number: 5,338,829

Date filed: October 19, 1992

Abstract: This invention discloses novel polypeptides having an antigenic determinant or determinants immunologically cross-reactive with determinants of a glycoprotein having a molecular weight of approximately 41,000 daltons, and determinants of a glycoprotein having a molecular weight of approximately 160,000 daltons which are obtained from cells infected with human immunodeficiency virus-1. The invention further discloses novel polypeptides having an antigenic determinant or determinants specific for a glycoprotein having a molecular weight of approximately 41,000 daltons obtained from cells infected with human immunodeficiency virus-1, the polypeptides further having an antigenic determinant or determinants immunologically cross-reactive with at least one glycoprotein having a molecular weight of 25,000 to 35,000 daltons, 45,000 daltons to 60,000 daltons, 80,000 to 100,000 daltons or 180,000 or 220,000 daltons, which are obtained from HSB, St, HeLa and human cells. The novel polypeptides of the invention are useful in methods of interfering with the effects of HIV-1 upon host cells having cell surface polypeptides capable of binding HIV-1. Methods of assay for HIV-1 infection are also disclosed. The invention also discloses peptides having amino acid sequences of about 10 to about 50 amino acids that correspond to at least a portion of an epitope of HIV and methods for developing such biologically active peptides.

Excerpt(s): The present invention relates to the field of treatments and diagnostics for vital infection. More particularly, this invention relates to the field of treatments and diagnostics for infection by the human immunodeficiency virus-1.... This application is a continuation-in-part application of U.S. patent application Ser. No. 183,840 filed Apr. 20, 1988 in the names of Mark I. Greene, William V. Williams and David Weiner, entitled "Methods of Modulating Retro-Virus Host Cell Interactions", which application is specifically incorporated as if fully set forth herein.... Acquired Immune Deficiency Syndrome (AIDS) is one of the most feared diseases in the world today. Infection with the human immunodeficiency virus (HIV-1), believed to be the cause of AIDS is almost always fatal. Symptoms of the disease can take years to develop, thus facilitating the spread of this fatal disease by persons unknowingly harboring the virus. Treatments for AIDS are limited and have been unsuccessful in controlling the disease.

Web site: http://www.delphion.com/details?pn=US05338829__

- **Peptides for induction of neutralizing antibodies against human immunodeficiency virus**

  Inventor(s): Jeansson; Stig (Goteborg, SE), Horal; Peter (Goteborg, SE), Rymo; Lars (Hovas, SE), Svennerholm; Bo (Goteborg, SE), Vahlne; Anders (Hovas, SE)

  Assignee(s): Syntello Vaccine Development KB (Goteborg, SE)

  Patent Number: 5,589,175

  Date filed: March 27, 1995

  Abstract: In accordance with the present invention, novel peptides corresponding to epitopes of human immunodeficiency virus-1 gp120 protein and analogues and homologs thereof are provided. These peptides can be utilized alone or in combination, uncoupled or coupled to other molecules or substrates. The peptides are useful in immunization against human immunodeficiency virus infection and in production of polyclonal and monoclonal antibodies.

  Excerpt(s): The present invention relates to peptides suitable for use in vaccination against AIDS.... The human immunodeficiency virus (HIV) is responsible for the disease that has come to be known as acquired immune deficiency syndrome (AIDS). Although initially recognized in 1981, no cure has yet been found for this inevitably fatal disease. HIV is spread by a variety of means such as sexual contact, infected blood or blood products and perinatally. Due to the complexity of HIV infection and the paucity of effective therapies, eradication of AIDS will most likely occur by preventing new infections rather than curing those persons already infected. To this end a great deal of effort has been expended in developing methods for detecting and preventing infection. Diagnostic procedures have been developed for identifying infected persons, blood and other biological products.... Like most viruses, HIV often elicits the production of neutralizing antibodies, unlike many other viruses and other infectious agents for which infection leads to protective immunity, however, HIV specific antibodies are insufficient to halt the progression of the disease. Therefore, in the case of HIV, a vaccine that elicits the immunity of natural infection could prove to be ineffective. In fact, vaccines prepared from the HIV protein gp160 appear to provide little immunity to HIV infection although they elicit neutralizing antibodies. The failure to produce an effective anti-HIV vaccine has led to the prediction that an effective vaccine will not be available until the end of the 1990's.

  Web site: http://www.delphion.com/details?pn=US05589175__

- **Peptides of human immunodeficiency virus type 1 (HIV-1)**

  Inventor(s): Danos; Oliver (Paris, FR), Wain-Hobson; Simon (Montigny les Bretonneux, FR), Stewart; Cole (Chatillon, FR), Sonigo; Pierre (Paris, FR), Alizon; Marc (Paris, FR)

  Assignee(s): Centre National de la Recherche Scientifique (Paris, FR), Institut Pasteur (Paris, FR)

  Patent Number: 6,261,564

  Date filed: December 31, 1997

  Abstract: This invention is in the field of lymphadenopathy virus, which has been designated Human Immunodeficiency Virus Type 1 (HIV-1). This invention relates to a diagnostic means and method to detect the presence of DNA, RNA or antibodies of the lymphadenopathy retrovirus associated with the acquired immune deficiency syndrome

or of the lymphadenopathy syndrome by the use of DNA fragments or the peptides encoded by said DNA fragments. The invention further relates to the DNA fragments, vectors comprising them and the proteins expressed.

Excerpt(s): This invention relates to cloned DNA sequences indistinguishable from genomic RNA and DNA of lymphadenopathy-associated virus (LAV), a process for their preparation and their uses. It relates more particularly to stable probes including a DNA sequence which can be used for the detection of the LAV virus or related viruses or DNA proviruses in any medium, particularly biological samples containing any of them. The invention also relates to polypeptides, whether glycosylated or not, encoded by said DNA sequences.... Lymphadenopathy-associated virus (LAV) is a human retrovirus first isolated from the lymph node of a homosexual patient with lymphadenopathy syndrome, frequently a prodrome or a benign form of acquired immune deficiency syndrome (AIDS). Subsequently, other LAV isolates were recovered from patients with AIDS or pre-AIDS. All available data are consistent with the virus being the causative agent of AIDS.... A method for cloning such DNA sequences has already been disclosed in British Patent Application Nr. 84 23659, filed on Sep. 19, 1984. Reference is hereafter made to that application as concerns subject matter in common with the further improvements to the invention disclosed herein.

Web site: http://www.delphion.com/details?pn=US06261564__

- **Peptides of human immunodeficiency virus type 2 (HIV-2) and in vitro diagnostic methods and kits employing the peptides for the detection of HIV-2**

Inventor(s): Clavel; Francois (Rockville, MD), Sonigo; Pierre (Paris, FR), Geutard; Denise (Paris, FR), Montagnier; Luc (Le Plessis Robinson, FR), Alizon; Marc (Paris, FR), Guyader; Mireille (Paris, FR)

Assignee(s): Institut Pasteur (Paris, FR)

Patent Number: 5,580,739

Date filed: March 17, 1994

Abstract: A novel lentivirus, designated the human immunodeficiency virus type 2 (HIV-2.sub.ROD), was isolated from West African patients with acquired immune deficiency syndrome (AIDS). A recombinant lambda phage library was constructed from HIV-2.sub.ROD -infected CEM genomic DNA. Overlapping molecular clones were obtained and the nucleotide sequence of the complete 9.5-kilobase (kb) HIV-2.sub.ROD genome ascertained. The genetic organization of HIV-2 is analogous to that of other retroviruses and consists of the 5'LTR-gag-pol-central region-env-nef-3'LTR. The central region also encodes for the regulatory proteins Tat and Rev, as well as the ancillary proteins Vif, Vpr, and Vpx. The proteins encoded by this proviral clone will provide novel immunologic, biochemic, and diagnostic reagents useful for the detection of HIV-2.

Excerpt(s): The disclosures of each of these predecessor applications are expressly incorporated herein by reference.... The invention relates to cloned DNA sequences analogous to the genomic RNA of a virus known as Lymphadenopathy-Associated Virus II ("LAV-II"), a process for the preparation of these cloned DNA sequences, and their use as probes in diagnostic kits. In one embodiment, the invention relates to a cloned DNA sequence analogous to the entire genomic RNA of HIV-2 and its use as a probe. The invention also relates to polypeptides with amino acid sequences encoded by these cloned DNA sequences and the use of these polypeptides in diagnostic kits....

According to recently adopted nomenclature, as reported in Nature, May 1986, a substantially-identical group of retroviruses which has been identified as one causative agent of AIDS are now referred to as Human Immunodeficiency Viruses I (HIV-1). This previously-described group of retroviruses includes Lymphadenopathy-Associated Virus I (LAV-I), Human T-cell Lymphotropic Virus-III (HTLV-III), and AIDS-Related Virus (ARV).

Web site: http://www.delphion.com/details?pn=US05580739__

- **Preventing agent for human immunodeficiency virus infection comprising menfegol**

  Inventor(s): Igarashi; Hisanaga (Nagasaki, JP), Sugiyama; Hidenori (Tokyo, JP), Miyamoto; Tsutomu (Nagasaki, JP)

  Assignee(s): Eisai Co., Ltd. (Tokyo, JP)

  Patent Number: 5,078,706

  Date filed: July 3, 1990

  Abstract: Preventing agent for a human immunodeficiency virus infection contains menfegol as an active ingredient. The preventing agent may be in the form of a foaming tablet, a jelly preparation, vaginal suppository, or ointment. A condom applied with the jelly preparation is also disclosed.

  Excerpt(s): This invention relates to a an agent for preventing human immunodeficiency virus (HIV) infection suitable for external application, which comprises menfegol as an active ingredient. More specifically, this invention is concerned with a preventing agent for HIV infection which contains menfegol as an active ingredient in a form of a gel preparation, foaming tablets, an ointment, vaginal suppositories or the like. This invention also embraces therein condoms with said gel preparation applied thereto.... Acquired immunodeficiency syndrome (AIDS) is a disease caused by cytopathogenicity and a decrease of helper T cells (Cluster of Differentiation type 4 antigen positive cells) due to infection by HIV. AIDS patients will go on to develop opportunistic infections such as pneumocytis carinii pneumonia, and malignant tumors like Kaposi's sarcoma, etc., resulting in their deaths eventually. Although HIV infection may take place by breast-feeding, the administration of an agent for blood preparation, etc., it occurs above all by heterosexual or homosexual intercourse. Thus, the increase of AIDS patients has become a serious social problem in recent years. A wide variety of research has been conducted for the prevention and treatment of AIDS, but no AIDS drug whose effectiveness has been confirmed has yet been developed. For the prevention of AIDS, it is hence important to avoid HIV infection. Use of condoms is recommended for this purpose. Condoms are however accompanied by a potential danger of breakage or slip-off and are not considered to be perfect for the prevention of HIV infection.... An object of this invention is to provide an agent for preventing HIV infection suitable for external application.

  Web site: http://www.delphion.com/details?pn=US05078706__

- **Rapid, easy, and economical screening test for antibodies to human immunodeficiency virus**

  Inventor(s): Yee; Joann L. (Sacramento, CA), Mertens; Steve C. (Davis, CA), Carlson; James R. (Davis, CA)

  Assignee(s): Virotest, Inc. (Lodi, CA)

  Patent Number: 5,149,623

  Date filed: February 1, 1989

  Abstract: A new dot enzyme immunoassay (EIA) with a conserved portion of the envelope protein of the human immunodeficiency virus (HIV) as antigen has been designed for use in areas with few laboratory facilities and by personnel with little laboratory experience. Sera were tested in 263 subjects who had AIDS or AIDS-related complex or were at -risk or not-at-risk of AIDS from the USA, Africa, and Asia/Oceania. The dot EIA was 100% sensitive in the American subjects, and there were only 2 false negatives in the others, both of which were negative by commerical EIA. The test is simple to perform, economical, rapid (30 min), and stable.

  Excerpt(s): This invention relates to a new dot enzyme immunoassay (EIA) with a conserved portion of the envelope protein of the human immunodeficiency virus (HIV) as antigen. The immunoassay has been designed for use in areas with few laboratory facilities and by personnel with little laboratory experience. The test is simple to perform, economical, rapid (30 min), and stable.... Immunoassays for the detection of human antibodies against HIV are currently being used in laboratories to diagnose individuals infected with the AIDs virus. Carlson, J.R. et al. AIDS Serology Testing in Low- and High-Risk groups, JAMA, 253:3405-3408 (1985).... The dot enzyme immunoassay is known. Lin T-M, and Halbert, S.P., Rapid Dot Enzyme Immunoassay for the Detection of Antibodies to Cytomegalovirus, J. of Clin. Microbiol. 24:7-11 (1986).

  Web site: http://www.delphion.com/details?pn=US05149623__

- **Recombinant human immunodeficiency virus producing cell lines**

  Inventor(s): Kuma; Hidekazu (Ibaraki-ken, JP), Akiyama; Katsuhiko (Ibaraki-ken, JP), Shimada; Takashi (Tokyo, JP), Suzuki; Yosuke (Ibaraki-ken, JP)

  Assignee(s): Hisamitsu Pharmaceutical Co., Inc. (Saga, JP)

  Patent Number: 6,048,725

  Date filed: September 12, 1997

  Abstract: Recombinant human immunodeficiency virus producing cell that is obtained by introducing into an animal cell a recombinant human immunodeficiency virus helper plasmid containing at least the sequences of gag, pol and env genes encoded by a human immunodeficiency virus genome and being deficient of a packaging signal and which sustains said genes stably.The human immunodeficiency virus producing cell of the invention is capable of large-scale and consistent preparation of HIV vectors more efficiently than in the prior art.

  Excerpt(s): This invention relates to recombinant human immunodeficiency virus vectors (hereinafter, HIV vectors), a process for producing said vectors, and productive cells capable of sustaining said vectors stably.... The recent rapid advances in genetic engineering triggered the development of various techniques in molecular biology. This has been commensurate with remarkable advances in the analysis of genetic

information and the unravelling of functions of genes and many attempts are being made to exploit these achievements in practical therapeutic settings. One of the areas that have seen the most remarkable advances is that of gene therapy. Etiological genes of various genetic diseases have been discovered and deciphered on one hand, and procedures for transferring such genes into cells by physical and chemical techniques have been developed on the other; as a result, gene therapy has progressed from the stage of preclinical experimentation to practical clinical applications.... Depending on the type of cells (target cells) for gene transfer, gene therapy is classified as either germline cell gene therapy or somatic cell gene therapy. Another way of classification is into augmentation gene therapy which involves the addition of a new (normal) gene, with an abnormal (etiological) gene left intact, and replacement gene therapy for replacing an abnormal gene by a normal gene. At the present stage, only augmentation gene therapy of somatic cells is being practised in consideration of ethical and technological restraints. More specifically, a method of gene therapy in current practice is one by autotransplantation (ex vivo gene therapy) in which a target cell is taken out of the patient and a gene to be inserted is transferred into the target cell, which is then replaced into the patient's body. A method under review for future possibility is one that involves direct gene administration into the patient (in vivo gene therapy).

Web site: http://www.delphion.com/details?pn=US06048725__

- **Reference clones and sequences for non-subtype B isolates of human immunodeficiency virus type 1**

  Inventor(s): Gao; Feng (Hoover, AL), Shaw; George M. (Birmingham, AL), Hahn; Beatrice H. (Birmingham, AL)

  Assignee(s): UAB Research Foundation (Birmingham, AL)

  Patent Number: 6,492,110

  Date filed: November 2, 1998

  Abstract: The nucleotide sequences of the genomes of eleven molecular clones for non-subtype B isolates of human immunodeficiency virus type 1 are disclosed. The invention relates to the nucleic acids and peptides encoded by and/or derived from these sequences and their use in diagnostic methods and as immunogens.

  Excerpt(s): The present invention is in the field of virology. The invention relates to the nucleotide sequences of the genomes of 11 molecular clones for non-subtype B isolates of human immunodeficiency virus type 1 (HIV-1), and nucleic acids derived therefrom. This invention also relates to peptides encoded by and/or derived from the nucleic acid sequences of these molecular clones, and host cells containing these nucleic acid sequences and peptides. The invention also relates to diagnostic methods, kits and immunogens which employ the nucleic acids, peptides and/or host cells of the invention.... A critical question facing current AIDS vaccine development efforts is to what extent HIV-1 genetic variation has to be considered in the design of candidate vaccines (11,21,42,72). Phylogenetic analyses of globally circulating viral strains have identified two distinct groups of HIV-1, a major M group and an O group (33,45,61,62). Within the M group, ten sequence subtypes (A-J) have been proposed (29,30,45,72). Sequence variation among viruses belonging to these different lineages is extensive, with envelope amino acid sequence variation ranging from 24% between different subtypes to 47% between the two different groups. Given this extent of diversity, the question has been raised whether immunogens based on a single virus strain can be expected to elicit immune responses effective against a broad spectrum of viruses, or

whether vaccine preparations should include mixtures of genetically divergent antigens and/or be tailored toward locally circulating strains (11, 21, 42, 72). This is of particular concern in developing countries where multiple subtypes of HIV-1 are known to co-circulate and where subtype B viruses, which have been the source for most current candidate vaccine preparations (10, 21), are rare or nonexistent (5, 24, 40, 72).... Although the extent of global HIV-1 variation is well defined, little is known about the biological consequences of this genetic diversity and its impact on cellular and humoral immune responses in the infected host. In particular, it remains unknown whether subtype specific differences in virus biology exist that need to be considered for vaccine design. Only a comprehensive analysis of genetically defined representatives of the various groups and subtypes will address the question of whether certain variants differ in fundamental viral properties and whether such differences will need to be incorporated into vaccine strategies. Obviously, such studies require well-characterized reference reagents, in particular full length and replication competent molecular clones that can be used for functional and biological studies.

Web site: http://www.delphion.com/details?pn=US06492110__

- **Short polypeptide sequences useful in the production and detection of antibodies against human immunodeficiency virus**

  Inventor(s): Papsidero; Lawrence D. (Orchard Park, NY)

  Assignee(s): Cellular Products, Inc. (Buffalo, NY)

  Patent Number: 5,185,147

  Date filed: August 19, 1988

  Abstract: Polypeptides in the size range 6-11 amino acids from discrete regions of the human immunodeficiency virus p17 protein are immunogenic and form the basis for diagnosis and therapy of HIV-related disease.

  Excerpt(s): This invention relates to polypeptides useful in the therapy and diagnosis of diseases, especially acquired immunodeficiency disease (AIDS), for which human immunodeficiency virus (HIV) is the etiological agent.... Human Immunodeficiency Virus, type 1 (HIV) is the etiologic agent associated with acquired immunodeficiency syndrome (AIDS). It is lymphotropic for cells expressing the CD4 molecule.... In vitro infection by HIV can be blocked by serum antibodies obtained from infected individuals (1-3), although a precise relationship between antibody titers and disease course is not presently apparent. Several reports have also demonstrated that HIV-neutralizing antibodies can be developed against various immunogens, including glycoprotein extracts (4), recombinant proteins (5-6), and synthetic peptides (1, 7-8). These antibodies react with HIV env gene products, thus solidifying the role of viral surface glycoproteins and cell receptor interactions. In addition, antibodies to the CD4 molecule are capable of inhibiting viral binding activity, as are antiidiotypic reagents to these antibodies (9).

  Web site: http://www.delphion.com/details?pn=US05185147__

- **Synthetic human neutralizing monoclonal antibodies to human immunodeficiency virus**

  Inventor(s): Lerner; Richard A. (La Jolla, CA), Burton; Dennis R. (La Jolla, CA), Barbas; Carlos F. (San Diego, CA)

  Assignee(s): The Scripps Research Institute (La Jolla, CA)

  Patent Number: 6,395,275

  Date filed: July 6, 2000

  Abstract: The present invention describes synthetic human monoclonal antibodies that immunoreact with and neutralize human immunodeficiency virus (HIV). The synthetic monoclonal antibodies of this invention exhibit enhanced binding affinity and neutralization ability to gp120. Also disclosed are immunotherapeutic and diagnostic methods of using the monoclonal antibodies, as well as cell lines for producing the monoclonal antibodies.

  Excerpt(s): The present invention relates generally to the field of immunology and specifically to synthetic human monoclonal antibodies that bind and neutralize human immunodeficiency virus (HIV).... Passive immunization of HIV-1 infected humans using human sera containing polyclonal antibodies immunoreactive with HIV has been reported. See for example, Jackson et al., Lancet, Sep. 17:647-652, (1988); Karpas et al., Proc. Natl. Acad. Sci., USA, 87:7613-7616 (1990).... Numerous groups have reported the preparation of human monoclonal antibodies that neutralize HIV isolates in vitro. The described antibodies typically have immunospecificities for epitopes on the HIV glycoprotein gp160 or the related glycoproteins gp120 or gp41. See, for example Karwowska et al., Aids Research and Human Retroviruses, 8:1099-1106 (1992); Takeda et al., J. Clin. Invest., 89:1952-1957 (1992); Tilley et al., Aids Research and Human Retroviruses, 8:461-467 (1992); Laman et al., J. Virol., 66:1823-1831 (1992); Thali et al., J. Virol., 65:6188-6193 (1991); Ho et al., Proc. Natl. Acad. Sci., USA, 88:8949-8952 (1991); D'Souza et al., AIDS, 5:1061-1070 (1991); Tilley et al., Res. Virol., 142:247-259 (1991); Broliden et al., Immunol., 73:371-376 (1991); Matour et al., J. Immunol., 146:4325-4332 (1991); and Gorny et al., Proc. Natl. Acad. Sci., USA, 88:3238-3242 (1991). For a current review of pathogenesis of HIV infection and therapeutic modalities including the use of passive immunity with anti-HIV antibodies, see Levy, Microbiol. Rev., 57:183-289 (1993).

  Web site: http://www.delphion.com/details?pn=US06395275__

- **Synthetic peptides and process of using same for the detection of antibodies to human immunodeficiency virus (HIV) gp120 envelope protein, diagnosis of AIDS and pre-AIDS conditions and as vaccines**

  Inventor(s): Wang; Chang Yi (Greak Neck, NY)

  Assignee(s): United Biomedical, Inc. (Hauppauge, NY)

  Patent Number: 5,763,160

  Date filed: June 7, 1995

  Abstract: This invention relates to a method using synthetic peptides as the solid phase immunoadsorbent for the detection and elicitation of antibodies to Human Immunodeficiency Virus (HIV) gp120, and, in particular, antibodies having HIV neutralizing capabilities. The amino acid sequences of the peptides correspond to segments of the external envelope protein gp120 of HIV. These peptides have been

found to be highly immunogenic, and are reactive with antibodies in sera of patients with AIDS, ARC or HIV infected individuals. They can also be used to elicit the production of neutralizing antibodies to HIV. More specifically, the present invention is directed to the use of a synthetic peptide selected from the groups consisting of peptides containing thirty-three amino acids in a prescribed sequence derived from the HIV-gp120 external protein, analogues, mixtures and poly-L-lysine polymers thereof, for the detection and elicitation of antibodies to HIV-gp120. It is particularly useful for the detection and elicitation of antibodies having HIV neutralizing capabilities. The detection method includes an enzyme linked immunoassay and other forms of immunoassay procedures. The present invention also relates to a method for generating high titer neutralizing antibodies to HIV gp120 protein in healthy mammals, including humans, by the use of the synthetic peptides, their analogues or mixtures in either a conjugated or a polymeric form as a key component in a synthetic vaccine for the prevention of AIDS.

Excerpt(s): This invention relates to a method using synthetic peptides for the detection of antibodies to Human Immunodeficiency Virus (HIV) gp120, in particular, antibodies having HIV neutralizing capabilities and as vaccines. The amino acid sequences of the peptides correspond to segments of the external envelope protein gp120 of HIV. These peptides have been found to be highly immunogenic, and are reactive with antibodies in sera of patients with AIDS, ARC, or HIV infection. They can also be used to elicit the production of neutralizing antibodies to HIV. More specifically, the present invention is directed to the use of a synthetic peptide selected from the groups consisting of peptides, with from about 15 to 40 amino acids, in a prescribed sequence, their analogues and mixtures, corresponding to a part of the HIV gp120 external protein for the detection and elicitation of antibodies to HIV gp120. It is particularly useful for the detection and elicitation of antibodies having HIV neutralizing capabilities. The detection method includes an enzyme linked immunoassay and other forms of immunoassay procedures. The present invention also relates to a method for generating high titer antibodies to HIV gp120 protein in healthy mammals, including humans, by the use of the synthetic peptides, in either a conjugated or a polymeric form, and analogues or mixtures thereof as the key component in a synthetic vaccine for the prevention of AIDS.... Since the human immunodeficiency virus (HIV) started its spread through the human population, the AIDS epidemic has steadily increased worldwide for the lack of any therapeutic or preventive means for intervention. The unique pathogenicity and the variability of HIV have raised new challenges in the design, testing and evaluation of therapeutics and vaccines for HIV. It appears, for the moment, that the development of an effective method for the detection of HIV infection and an effective vaccine remain the only means by which the disease is to be controlled and eradicated.... An ideal vaccine against HIV infection should be highly immunogenic, induce both T and B cell mediated virus-specific immunity, and be free of irrelevant carrier proteins. Although traditional approaches using whole virus or viral protein subunits can generally achieve this goal, practical considerations, such as the safety and availability of native antigen, have led many to consider other highly engineered vaccine constructs for AIDS.

Web site: http://www.delphion.com/details?pn=US05763160__

- **Whole blood method and kit for the detection of antibodies against human immunodeficiency virus (HIV) in HIV-seronegative individuals**

  Inventor(s): Jehuda-Cohen; Tamar (Rehovot, IL)

  Assignee(s): Shiloov Medical Technologies, Ltd. (Rehovot, IL)

  Patent Number: 5,637,453

  Date filed: July 15, 1994

  Abstract: The present invention relates to an improved method and kit for the detection of antibodies directed against the human immunodeficiency virus (HIV) in whole blood obtained from individuals who are HIV-seronegative as determined by conventional assay techniques. Whole blood is isolated from these individuals and cultured directly with mitogen to stimulate the proliferation of B-lymphocytes producing immunoglobulin specific for HIV. This method provides a rapid, simple, and inexpensive means for screening large numbers of blood samples for HIV infection while minimizing exposure of the technician to infectious blood components.

  Excerpt(s): The present invention relates to an improved method and kit for detecting antibodies in whole blood of individuals who test seronegative by conventional assay techniques. More particularly, the present invention relates to an assay for detecting possible retrovirus infection, such as infection by the HIV virus, which utilizes a mitogen in whole blood to stimulate antibody production by peripheral blood mononuclear cells. The present invention also relates to an improved assay kit which does not require the separation of peripheral blood mononuclear cells from whole blood prior to culture with pokeweed mitogen.... As used herein, mitogen means any substance capable of activating B-cells and/or T-cells. The term "whole blood" means blood collected with heparin, EDTA, or any other substance that prevents coagulation and clotting. The term whole blood as used herein also includes blood collected from an animal or human with heparin, ethylenediaminetetraacetate, or any other substance that prevents coagulation and clotting. "Whole blood" can also mean blood wherein the red blood cells have been lysed while maintaining the viability of the remaining white blood cells.... Serological detection of antibodies against a variety of infectious disease agents is considered evidence of exposure to and/or active infection by the agent. Serological detection of antibodies could also be useful for early detection of cancer and for predicting the success of organ or tissue transplants. Enzyme-linked immunosorbent assay (ELISA) commercial kits are commonly used as screening tests for serological detection of antibodies. The western blot technique has been the method most widely used to confirm ELISA-reactive serum samples, although other methods such as immunofluorescence, may also be applicable. Polymerase chain reaction (PCR) technique may also be used to confirm results of a preliminary assay.

  Web site: http://www.delphion.com/details?pn=US05637453__

Patent Applications on Human Immunodeficiency Virus

As of December 2000, U.S. patent applications are open to public viewing.[10] Applications are patent requests which have yet to be granted. (The process to achieve a patent can take

[10] This has been a common practice outside the United States prior to December 2000.

several years.) The following patent applications have been filed since December 2000 relating to human immunodeficiency virus:

- **Compositions and methods for inhibiting human immunodeficiency virus infection by down-regulating human cellular genes**

  Inventor(s): Dunn, Stephen J. (Mountain View, CA), Holzmayer, Tanya A. (Mountain View, CA), Dayn, Andrew; (Mountain View, CA)

  Correspondence: MCDONNELL BOEHNEN HULBERT & BERGHOFF; 300 SOUTH WACKER DRIVE; SUITE 3200; CHICAGO; IL; 60606; US

  Patent Application Number: 20030109477

  Date filed: August 20, 2002

  Abstract: The present invention relates to the identification of several human genes as cellular targets for the design of therapeutic agents for suppressing human immunodeficiency virus (HIV) infection. These genes encode intracellular products which appear to be necessary for HIV replication, as evidenced by an inhibition of HIV infection in cells in which the expression of these genes is down-regulated. Therefore, inhibitors of these genes and their encoded products may be used as therapeutic agents for the treatment and/or prevention of HIV infection. In addition, the invention also relates to methods for identifying additional cellular genes as therapeutic targets for suppressing HIV infection, and methods of using such cellular genes and their encoded products in screening assays for selecting additional inhibitors of HIV.

  Excerpt(s): The present invention relates to the identification of several human genes as cellular targets for the design of therapeutic agents for suppressing human immunodeficiency virus (HIV) infection. These genes encode intracellular products which appear to be necessary for HIV replication, as evidenced by an inhibition of HIV infection in cells in which the expression of these genes is down-regulated. Therefore, inhibitors of these genes and their encoded products may be used as therapeutic agents for the treatment and/or prevention of HIV infection. In addition, the invention also relates to methods for identifying additional cellular genes as therapeutic targets for suppressing HIV infection, and methods of using such cellular genes and their encoded products in screening assays for selecting additional inhibitors of HIV.... The primary cause of acquired immunodeficiency syndrome (AIDS) has been shown to be HIV (Barre-Sinoussi et al., 1983, Science 220:868-870; Gallo et al., 1984, Science 224:500-503). HIV causes immunodeficiency in an individual by infecting important cell types of the immune system, which results in their depletion. This, in turn, leads to opportunistic infections, neoplastic growth and death.... HIV is a member of the lentivirus family of retroviruses (Teich et al., 1984, RNA Tumor Viruses, Weiss et al., eds., CSH-Press, pp. 949-956). Retroviruses are small enveloped viruses that contain a diploid, single-stranded RNA genome, and replicate via a DNA intermediate produced by a virally-encoded reverse transcriptase, an RNA-dependent DNA polymerase (Varmus, 1988, Science 240:1427-1439). There are at least two distinct subtypes of HIV: HIV-1 (Barre-Sinoussi et al., 1983, Science 220:868-870; Gallo et al., 1984, Science 224:500-503) and HIV-2 (Clavel et al., 1986, Science 233:343-346; Guyader et al., 1987, Nature 326:662-669). Genetic heterogeneity exists within each of these HIV subtypes.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Detection of Human Immunodeficiency Virus type 1**

  Inventor(s): Yang, Yeasing; (San Diego, CA), Ryder, Thomas B. (Escondido, CA), McDonough, Sherrol H. (San Diego, CA)

  Correspondence: Douglas C. Murdock; BROBECK, PHLEGER & HARRISON LLP; 12390 El Camino Real; San Diego; CA; 92130; US

  Patent Application Number: 20020062016

  Date filed: January 20, 2001

  Abstract: Amplification oligonucleotides and hybridization assay probes which distinguish Human Immunodeficiency Virus type 1 from other viruses.

  Excerpt(s): This application is a continuation in part of Kacian and Fultz, entitled "Nucleic Acid Sequence Amplification Methods," U.S. Ser. No. 07/379,501, filed Jul. 11, 1989, and Kacian and Fultz, entitled "Nucleic Acid Sequence Amplification Methods," U.S. Ser. No. 07/550,837, filed Jul. 10, 1990, both hereby incorporated by reference herein.... This invention relates to the design and construction of amplification oligonucleotides and probes to Human Immunodeficiency Virus Type 1 (HIV), which allow detection of the organism in a test sample.... This section provides a brief outline of relevant areas. None of the art cited or referred to is admitted to be prior art to the claims. Laboratory diagnosis of Human Immunodeficiency Virus Type 1 in humans is currently performed by demonstration of the presence of viral antigen (p24) or anti-HIV-1 antibodies in serum. Direct detection of viral DNA, however, is a more useful diagnostic tool in some populations, such as infants born to seropositive mothers. Detection of viral DNA is more rapid and less hazardous than culture. Direct hybridization lacks adequate sensitivity in most patients (Shaw et al. Science 226:1165-1171, 1984). Many references mention oligonucleotides said to have use in detection of Human Immunodeficiency Virus. Most of these references also mention the use of polymerase chain reaction (PCR). These references include the following: Kwok et al., J. Virol. 61: 1690-1694, 1987; Agius et al., J. Virol. Meth., 30:141-150, 1990; Albert and Fenyo, J. Clin. Microbiol. 28:1560-1564, 1990; Bell and Ratner, AIDS Res. and Human Retroviruses 5:87-95, 1989; Bruisten et al., Vox Sang 61:24-29, 1991; Clarke et al., AIDS 4:1133-1136, 1990; Coutlee et al., Anal. Biochem. 181:96-105, 1989; Dahlen et al., J. Clin. Microbiol. 29:798-804, 1991; Dudding et al., Biochem. Biophys. Res. Comm. 167:244-250, 1990; Ferrer-Le-Coeur et al., Thrombosis and Haemostasis 65:478-482, 1991; Goswami et al., AIDS 5:797-803, 1991; Grankvist et al., AIDS 5:575-578, 1991; Guatelli et al., J. Virol. 64:4093-4098, 1990; Hart et al., Lancet 2 (8611):596-599, 1988; Holland et al., Proc. Natl. Acad. Sci. USA, 88:7276-7280, 1991; Keller et al., Anal. Biochem. 177:27-32, 1989; Kumar et al., AIDS Res. and Human Retroviruses 5:345-354, 1989; Linz et al., J. Clin. Chem. Clin. Biochem. 28:5-13, 1990; Mano and Chermann, Res. Virol. 142:95-104, 1991; Mariotti et al., AIDS 4:633-637, 1990; Mariotti et al., Transfusion 30:704-706, 1990; Meyerhans et al., Cell 58:901-910, 1989; Mousset et al., AIDS 4:1225-1230, 1990; Ou et al., Science 239:295-297, 1988; Pang et al., Nature 343:85-89, 1990; Paterlini et al., J. Med. Virol. 30:53-57, 1990; Perrin et al., Blood 76:641-645, 1990; Preston et al., J. Virol. Meth. 33:383-390, 1991; Pritchard and Stefano, Ann. Biol. Clin. 48:492-497, 1990; Rudin et al., Eur. J. Clin. Microbiol. Infect. Dis. 10:146-156, 1991; Shoebridge et al., AIDS 5:221-224, 1991; Stevenson et al., J. Virol. 64:3792-3803, 1990; Truckenmiller et al., Res. Immunol. 140:527-544, 1989; Van de Perre, et al., New Eng. J. Med. 325:593-598, 1991; Varas et al., BioTechniques 11:384-391, 1991; Velpandi et al., J. Virol. 65:4847-4852, 1991; Williams et al., AIDS 4:393-398, 1990; Zachar et al., J. Virol. Meth. 33:391-395, 1991; Zack et al. Cell 61:213-222, 1990; Findlay et al., entitled "Nucleic acid test article and its use to detect a predetermined nucleic acid," PCT/US90/00452; Gingeras et al., entitled "Nucleic acid

probe assay methods and compositions," PCT/US87/01966; Brakel and Spadoro, entitled "Amplification capture assay," EPO application number 90124738.7, publication number 0 435 150 A2; Moncany and Montagnier, entitled "Squences nuclotidiques issues du gnome des rtrovirus du typ hiv-1, hiv-2 et siv, et leurs applications notamment pour 1'amplification des gnomes de ces rtrovirus et pour le diagnostic in-vitro des infections dues ces virus," EPO application number 90401520.3, publication number 0 403 333 A2; Urdea, entitled "DNA-dependent RNA polymerase transcripts as reporter molecules for signal amplification in nucleic acid hybridization assays," PCT/US91/00213; Musso et al., entitled "Lanthanide chelate-tagged nucleic acid probes," PCT/US88/03735; Chang, entitled "Cloning and expression of HTLV-III DNA," EPO application number 85307260.1, publication number 0 185 444 A2; and Levenson, entitled "Diagnostic kit and method using a solid phase capture means for detecting nucleic acids," EPO application number 89311862.0, publication number 0 370 694; and Sninsky et al., U.S. Pat. No. 5,008,182.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Genetic suppressor elements against human immunodeficiency virus**

  Inventor(s): Park, Suk W. (Mountain View, CA), Dayn, Andrew; (Mountain View, CA), Dunn, Stephen J. (Mountain View, CA), Holzmayer, Tanya A. (Mountain View, CA)

  Correspondence: MCDONNELL BOEHNEN HULBERT & BERGHOFF; 300 SOUTH WACKER DRIVE; SUITE 3200; CHICAGO; IL; 60606; US

  Patent Application Number: 20030108909

  Date filed: July 29, 2002

  Abstract: The present invention relates to genetic elements that suppress the activities of the human immunodeficiency virus (HIV). In particular, the invention relates to polynucleotides isolated from the HIV-1 genome, methods for isolating and identifying such polynucleotides, and methods for using them for the protection of human cells against HIV infection and/or replication.

  Excerpt(s): The present invention relates to genetic elements that suppress the activities of the human immunodeficiency virus (HIV). In particular, the invention relates to polynucleotides isolated from the HIV-1 genome, methods for isolating and identifying such polynucleotides, and methods for using them for the protection of human cells against HIV infection and/or replication.... The primary cause of acquired immunodeficiency syndrome (AIDS) has been shown to be HIV (Barre-Sinoussi et al., 1983, Science 220:868-870; Gallo et al., 1984, Science 224:500-503). HIV causes immunodeficiency in an individual by infecting important cell types of the immune system, which results in their depletion. This, in turn, leads to opportunistic infections, neurological dysfunctions, neoplastic growth, and death.... HIV is a member of the lentivirus family of retroviruses (Teich et al., 1984, RNA Tumor Viruses, Weiss et al., eds., CSH-Press, pp. 949-956). Retroviruses are small enveloped viruses that contain a diploid, single-stranded RNA genome, and replicate via a DNA intermediate produced by a virally-encoded reverse transcriptase, an RNA-dependent DNA polymerase (Varmus, 1988, Science 240:1427-1439). There are at least two distinct subtypes of HIV: HIV-1 (Barre-Sinoussi et al., 1983, Science 220:868-870; Gallo et al., 1984, Science 224:500-503) and HIV-2 (Clavel et al., 1986, Science 233:343-346; Guyader et al., 1987, Nature 326:662-669). Genetic heterogeneity exists within each of these HIV subtypes.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Genetic vaccine against human immunodeficiency virus**

  Inventor(s): Wang, Danher; (Mt. Pleasant, SC)

  Correspondence: WILSON SONSINI GOODRICH & ROSATI; 650 PAGE MILL ROAD; PALO ALTO; CA; 943041050

  Patent Application Number: 20020155127

  Date filed: November 1, 2001

  Abstract: Recombinant adenovirus and methods of administration to a host are provided for eliciting immune response of the host to human immunodeficiency virus (HIV). The recombinant adenovirus is capable of expressing multiple wild type or mutant HIV antigens such as HIV envelope proteins without the cleavage site or the cytosolic domain, structural proteins such as Gag and its proteolytical fragments in a natural, secreted or membrane-bound form, and regulatory proteins such as Tat, Rev and Nef. Immuno-stimulators such as cytokines can also be expressed by the recombinant adenovirus to further enhance the immunogenicity of the HIV antigens.

  Excerpt(s): This application is a continuation-in-part of PCT application entitled "GENETIC VACCINE THAT MIMICS NATURAL VIRAL INFECTION AND INDUCES LONG-LASTING IMMUNITY TO PATHOGEN", application Ser. No.: PCT US01/18238, Filed: Jun. 4, 2001, which is a continuation-in-part of U.S. patent application entitled "GENETIC VACCINE THAT MIMICS NATURAL VIRAL INFECTION AND INDUCES LONG-LASTING IMMUNITY TO PATHOGEN", application Ser. No.: 09/585,599, Filed: Jun. 2, 2000. The above applications are incorporated herein by reference.... 1. Field of the Invention This invention relates to vaccines for stimulating immune responses in human and other hosts, and, in particular, relates to recombinant viruses that express heterologous antigens of human immunodeficiency virus (HIV) in a host and elicit immune response to HIV infection.... Current techniques for developing vaccines are largely based on the concept of using denatured virus or purified viral proteins made from bacteria. These types of vaccines may be effective for only a limited number of infectious agents, and the protection rates are limited.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Human immunodeficiency virus vaccine**

  Inventor(s): Haynes, Barton F. (Durham, NC), Liao, Hua-Xin; (Chapel Hill, NC)

  Correspondence: NIXON & VANDERHYE P.C. 1100 North Glebe Road, 8th Floor; Arlington; VA; 22201; US

  Patent Application Number: 20010036461

  Date filed: February 5, 2001

  Abstract: The present invention relates, in general, to human immunodeficiency virus (HIV) and, in particular, to an HLA-based HIV vaccine.

  Excerpt(s): This is a continuation-in-part of application Ser. No. 09/497,497, filed Feb. 4, 2000, now pending, the entire contents of which is incorporated herein by reference.... The present invention relates, in general, to human immunodeficiency virus (HIV) and, in particular, to an HLA-based HIV vaccine.... As the HIV epidemic continues to spread world-wide, the need for an effective HIV vaccine remains urgent. The extraordinary

ability of HIV to mutate, the inability of many currently known specificities of anti-HIV antibodies to consistently neutralize HIV primary isolates, and the lack of a complete understanding of the correlates of protective immunity to HIV infection have impeded efforts to develop an HIV vaccine having the desired effectiveness.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Human monoclonal antibody against coreceptors for human immunodeficiency virus**

  Inventor(s): Zhu, Li; (Palo Alto, CA), Hua, Shaobing; (Cupertino, CA), Pauling, Michelle H. (San Mateo, CA)

  Correspondence: WILSON SONSINI GOODRICH & ROSATI; 650 PAGE MILL ROAD; PALO ALTO; CA; 943041050

  Patent Application Number: 20030152913

  Date filed: February 8, 2002

  Abstract: Compositions are provided that comprise antibody against coreceptors for human immunodeficiency virus such as CCR5 and CXCR4. In particular, monoclonal human antibodies against human CCR5 are provided that bind to CCR5 with high affinity and are capable of inhibiting HIV infection at low concentrations. The antibodies can be used as prophylactics or therapeutics to prevent and treat HIV infection, for screening drugs, and for diagnosing diseases or conditions associated with interactions with HIV coreceptors.

  Excerpt(s): This application is a continuation of U.S. application Ser. No. 10/_____, filed Feb. 8, 2002, entitled "High throughput generation of human monoclonal antibody against peptide fragments derived from membrane protein", [Attorney Docket No. 25636-717]. The above application is hereby incorporated by reference.... This invention relates to methods for generating monoclonal antibody against cell membrane proteins, and, more particularly, to methods for generating human monoclonal antibodies against cell surface coreceptors for human immunodeficiency virus (HIV) and using these antibodies for diagnostic or therapeutic purposes.... HIV infection has been implicated as the primary cause of the slowly degenerate disease of the immune system termed acquired immune deficiency syndrome (AIDS). Barre-Sinoussi et al. (1983) Science 220:868-870; and Gallo et al. (1984) Science 224:500-503. Infection of the CD4+ subclass of T-lymphocytes with the HIV-1 virus leads to depletion of this essential lymphocyte subclass which inevitably leads to opportunistic infections, neurological disease, neoplastic growth and eventually death. HIV-1 infection and HIV-1 associated diseases represent a major health problem and considerable attention is currently being directed towards the successful design of effective therapeutics.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Hyperbaric oxigenation (HBO) as the method for enhancement efficiency of anti-HIV substances in inhibition the human immunodeficiency virus (HIV) reproduction and reduction of the cytotoxic effect of those substances as well**

  Inventor(s): Kornilaeva, Galina Vladimirovna; (Moscow, Ru), Shtshelkanov, Mikhail Yurevich; (Ekaterinburg, Ru), Sokolov, Alexandr Evgenevich; (Moscow, Ru), Karamov, Eduard Vladimirovich; (Moscow, Ru), Pakhomov, Vladimir Ilich; (Moscow, Ru), Kostyunin, Vladimir Nikolaevich; (Moscow, Ru)

  Correspondence: ROTHWELL FIGG; ERNST & KURZ P C; 555 13TH STREET N W SUITE 701-E; WASHINGTON; DC; 20004

  Patent Application Number: 20020019356

  Date filed: May 3, 1999

  Abstract: A method of increasing efficiency and/or decreasing the cytotoxic effect of a human immunodeficiency virus (HIV) reproduction-suppressing drug such as Azidothimidin (AZT) involves administering the drug to an HIV-positive patient and subjecting the patient to hyperbaric oxygenation (HBO).

  Excerpt(s): The present invention relates to the methods of prophylactics and therapeutics of Human Immunodeficiency Virus (HIV) infection well as to the Acquired Immunodeficiency Syndrome (AIDS), which is etiologically connected therewith.... More specifically this invention permits to increase the Azidothimidin's (AZT) inhibition effect to the HIV reproduction and simultaneously, to decrease the cytotoxic effect.... It is known the way for suppression of reproduction HIV with the help of 3-azido-2,3-didezoxythimidim (Karamov E. V., Lukahev V. V., Gorbacheva A. P. etc. <<Inhibition of reproduction of Human Immunodeficiency Virus in cell's culture with 5-phosfatum 2,3-didezoxynukleozidov>>. Molecular biology, 1992, volume 26, p.201-206).

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Immunological reagents and diagnostic methods for the detection of human immunodeficiency virus type 2 utilizing multimeric forms of the envelope proteins GP300, P200, and P90/80**

  Inventor(s): Rey-Cuille, Marie-Anne; (Paris, FR), Hovanessian, Ara G. (Bourg-la-Reine, FR), Krust, Bernard; (Paris, FR), Laurent-Crawford, Anne G. (Paris, FR), Montagnier, Luc; (Le Plessis Robinson, FR)

  Correspondence: FINNEGAN, HENDERSON, FARABOW,; GARRETT and DUNNER, L.L.P. 1300 I Street, N.W. Washington; DC; 20005-3315; US

  Patent Application Number: 20010006641

  Date filed: December 19, 2000

  Abstract: Four glycoproteins of apparent molecular weights 300,000, 140,000, 125,000, and 36,000 (gp300, gp140, gp125, and gp36) are detectable in human immunodeficiency virus type 2 (HIV-2) infected cells. The gp125 and gp36 are the external and transmembrane components, respectively, of the envelope glycoproteins of HIV-2 mature virions. The gp300, which is a dimeric form of gp14O, the precursor of HIV-2 envelope glycoprotein, is probably formed by a pH dependent fusion in the endoplasmic reticulum. Such a doublet is also observed in cells infected with simian immunodeficiency virus (SIV), a virus closely related to HIV-2. On the other hand, the

envelope glycoprotein precursor of HIV-1 does not form a dimer during its processing. Experiments carried out with various inhibitors of oligosaccharide trimming enzymes suggest that transient dimerization of the glycoprotein precursor is required for its efficient transport to the Golgi apparatus and for its processing. The gp300 is useful for detecting antibodies to HIV-2 antigens in human body fluids and for raising antibodies to gp300.

Excerpt(s): This application is a continuation-in-part of application Ser. No. 08/002,756, filed Jan. 13, 1993 (pending), which is a division of application Ser. No. 07/356,459, filed May 25, 1989, now U.S. Pat. No. 5,208,321. Ser. No. 08/002,756 is also a continuation-in-part of application Serial No. 07/204,346, filed Jun. 9, 1988 (abandoned), which is a continuation application of Ser. No. 07/804,712, filed Dec. 6, 1991, now U.S. Pat. No. 5,312,902. The related applications are specifically incorporated by reference.... This invention relates to viral proteins and glycoproteins, to compositions containing these proteins, to methods of preparing the proteins, and to their use in detecting viral infection.... The etiological agent of acquired immunodeficiency syndrome (AIDS) is the retrovirus referred to as human immunodeficiency virus (HIV) (Montagnier et al., 1984). To date, two related but distinct viruses, HIV-1 and HIV-2, have been identified (Barre-Sinoussi et al., 1983; Popovic et al., 1984; Levy et al., 1984; Wain-Hobson et al., 1985a; Clavel et al., 1986a; Brun-Vezinet et al., 1987; Guyader et al., 1987). HIV-2 is closely related to simian immunodeficiency virus (SIV), which causes an AIDS-like disease in macaques (Daniel et al, 1985; Sonigo et al., 1985; Chakrabarti et al., 1987).

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Inhibition of human immunodeficiency virus reverse transcriptase**

  Inventor(s): Hung, Paul Porwen; (Bryn Mawr, PA)

  Correspondence: Y. ROCKY TSAO; Fish & Richardson P.C. 225 Franklin Street; Boston; MA; 02110-2804; US

  Patent Application Number: 20020187944

  Date filed: March 21, 2002

  Abstract: A method of inhibiting a human immunodeficiency virus reverse transcriptase by contacting the reverse transcriptase with an effective amount of 9-O-methyl oxime erythromycin A.

  Excerpt(s): This application claims priority from U.S. Provisional Patent Application Serial No. 60/277,583, filed Mar. 21, 2001.... Human immunodeficiency virus (HIV) has proven to be an intractable pathogen. One strategy has been to target the reverse transcriptase of this virus.... The invention is based on the unexpected discovery that 9-O-methyl oxime erythromycin A inhibits HIV reverse transcriptase and thereby blocks HIV replication at low concentrations, as compared with previous studies on other retroviruses.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Method for ameliorating muscle weakness/wasting in a patient infected with human immunodeficiency virus-type 1**

  Inventor(s): Berger, Joseph R. (Miami, FL)

  Correspondence: John P. White; Cooper & Dunham LLP; 1185 Avenue of the Americas; New York; NY; 10036; US

  Patent Application Number: 20020091155

  Date filed: January 18, 2002

  Abstract: A method for attenuating the HIV-associated myopathy and muscle wasting associated with infection by human immunodeficiency virus-Type 1. Administration of oxandrolone in a daily dosage of about 2.5 to about 20 milligrams is described.

  Excerpt(s): The invention relates to the use of oxandrolone to attenuate myopathy and muscle weakness/wasting associated with infection by human immunodeficiency virus-Type 1.... Human immunodeficiency virus (HIV) associated myopathy and/or muscle weakness/wasting is a relatively common clinical manifestation of acquired immunodeficiency syndrome (AIDS). This is one of a number of neuromuscular disorders associated with the disease. There is some evidence to indicate that direct HIV infection of muscle may be at least partly responsible, occasionally resulting in a polymyositis-like disorder. In addition, zidovudine (AZT), an antiviral agent that is used widely in the clinical management of AIDS, has been associated with a toxic myopathy, presumably related to an inhibition of mitochondrial metabolism. In any event, the loss of muscle mass commonly observed in AIDS victims negatively impacts muscle function, however caused.... Individuals with HIV-associated myopathy or muscle weakness or wasting typically experience significant weight loss, generalized or proximal muscle weakness, tenderness, and muscle atrophy. Laboratory tests of samples from such individuals often reveal elevated levels of enzymes associated with muscle degeneration and necrosis, such as creating kinase, aldolase, and aspartate amino transferase. Electromyographic test results for individuals with HIV-associated myopathy are typically consistent with myopathic changes. Histopathologic tests may reveal muscle fiber necrosis associated with lymphocytic inflammatory infiltrates. In AZT myotoxicity, ragged red fibers are often observed.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Monoclonal antibodies to human immunodeficiency virus and uses thereof**

  Inventor(s): Konrath, John G. (Lake Villa, IL), Tyner, Joan D. (Beach Park, IL), Qiu, Xiaoxing; (Gurnee, IL), Hunt, Jeffrey C. (Mundelein, IL), Lou, Sheng C. (Libertyville, IL), Scheffel, James W. (Mundelein, IL)

  Correspondence: Steven F. Weinstock; ABBOTT LABORATORIES; CHAD 0377/AP6D-2; 100 Abbott Park Road; Abbott Park; IL; 60064-6050; US

  Patent Application Number: 20020106636

  Date filed: December 6, 2000

  Abstract: The present invention relates to novel monoclonal antibodies which may be used in the detection of Human Immunodeficiency Virus (HIV). These antibodies exhibit an unusually high degree of sensitivity, a remarkably broad range of specificity, and bind to novel shared, non-cross-reactive epitopes. In particular, the monoclonal

antibodies of the present invention may be utilized to detect HIV-1 antigen and HIV-2 core antigen in a patient sample.

Excerpt(s): The present invention relates to novel monoclonal antibodies which may be used in the detection of Human Immunodeficiency Virus (HIV). These antibodies exhibit an unusually high degree of sensitivity, a remarkably broad range of specificity, and bind to novel shared, non-cross-reactive epitopes. In particular, the monoclonal antibodies of the present invention may be utilized to detect HIV-1 and HIV-2 core antigens in a patient sample.... Acquired Immunodeficiency Syndrome (AIDS) is an infectious and incurable disease transmitted through sexual contact from HIV infected individuals or by exposure to HIV contaminated blood or blood products. HIV-1 includes the formerly named viruses Human T-cell Lymphotrophic Virus Type III (HTLV III), Lymphadenopathy Associated Virus (LAV), and AIDS Associated Retrovirus (ARV). HIV is a retrovirus related to a group of cytopathic retroviruses, namely lentiviruses, on the basis of morphologic features, genomic organization, and nucleotide sequence (Gonda et al., Science (1985) 277:177-179; Stephan et al., Science (1986) 231:589-594; Korber, B. (ed.) et al., Human Retroviruses and AIDS. A Compilation and Analysis of Nucleic Acid and Amino Acid Sequences. Published by Theoretical Biology and Biophysics, Los Alamos National Laboratory, Los Alamos, N. Mex. Reviewed in, Schochetman, G. and George, J. R., (1994) AIDS Testing. Springer-Verlag, N.Y., Berlin, Heidelberg). HIV is an enveloped virus containing several structural proteins. Of particular relevance, the core of the virus is formed by condensation of cleavage products from a highly processed gag-pol polyprotein precursor (Pr180gag-pol) which is cleaved into a pol precursor and a gag precursor (Pr55gag). Subsequently, the core precursor Pr55gag is cleaved into p17 (myristilated gag protein), p24 (major structural protein), p7 (nucleic acid binding protein), and p9 (proline-rich protein). The envelope contains two structural proteins, gp120 (envelope glycoprotein) and gp41 (transmembrane protein) which are cleavage products of the envelope polyprotein precursor, gp160.... The most common markers of HIV infection are antibodies against viral structural proteins (Dawson, et.al., J. Infect. Dis. (1988) 157:149-155; Montagnier, et al. Virology (1985) 144:283-289; Barin, et al., Science (1985) 228:1094-1096; Schulz, T. F., et al., Lancet (1986) 2:111-112; Sarngadharan, et al., Science (1984) 224:506-508; Allan, et al., Science (1985) 228:1091-1093) and viremia in the form of detectable viral core antigen (antigenemia) (Kessler, et. al., JAMA (1987) 258:1196-1199; Phair, JAMA (1987) 258:p1218; Allain, et al., The Lancet (1986) ii:1233-1236; Kenny, et al., The Lancet (1987) 1 (8532):565-566; Wall, et al., The Lancet (1987) 1(8532):p566; Stute, The Lancet (1987) 1(8532):p566; Goudsmit, et al., The Lancet (1986) ii: 177-180; vonSydow, et al., Brit. Med. J. (1988) 296:238-240; Bowen, et al. Ann. of Int. Med. (1988) 108:46-48) or detectable viral nucleic acid (Mellors, et al., Science (1996) 272: 1167-1170; Saag, et al. Nat. Med. (1996) 2: 625-629; Mulder, et al. J. Clin. Microbiol. (1994) 32:292-300; Zhang, et al., AIDS (1991) 5(6):675-681; Simmonds, et al., J. Virology (1990) 64(2):864-872). For example, in the United States, screening of blood and blood products by tests to detect antibody or antigen is mandated (Federal Food, Drug, and Cosmetic Act, 21 U.S.C..sctn..sctn.301 et. seq., Public Health Service Act 42 U.S.C..sctn..sctn.201 et. seq.). Nucleic acid testing recently has been implemented in order to attain maximal reduction of the HIV seroconversion window (www.fda.gov). As a further example, various countries in Europe have begun to evaluate and use tests that detect antibody and antigen simultaneously (Ly, et al. J. Clin. Microbiol. (2000) 38(6): 2459-2461; Gurtler, et al., J. Virol. Methods (1998) 75: 27-38; Weber, et al., J. Clin. Microbiol (1998) 36(8): 2235-2239; Courouce', et al., La Gazette de la Transfusion (1999) N.degree.155-Mars-Avril; Van Binsbergen, et al., J. Virol. Methods (1999) 82: 77-84), in addition to European implementation of nucleic acid testing. Serologic assays that combine antibody and

antigen detection exhibit superior seroconversion sensitivity compared to assays that detect only antibody, because detection of antigen, which appears prior to antibody, reduces the seroconversion window. An early version of an HIV combo assay is described in Gallarda, et al., 1992, WO93/21346, Assay for Detection of HIV Antigen and Antibody.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Mouse monoclonal antibody (5-21-3) to human immunodeficiency virus gp41 protein**

  Inventor(s): Wray, Larry K. (Highland Park, IL), Falk, Lawrence A. (Waukegan, IL), Webber, J. Scott; (Waukegan, IL), Sarin, Virender K. (Libertyville, IL), Dawson, George J. (Libertyville, IL), Hunt, Jeffrey C. (Lindenhurst, IL), Devare, Sushil G. (Northbrook, IL)

  Correspondence: Cheryl L. Becker; Abbott Laboratories; D-377, AP6D; 100 Abbott Park Road; Abbott Park; IL; 60064; US

  Patent Application Number: 20030118985

  Date filed: November 19, 2001

  Abstract: The present invention discloses a monoclonal antibody capable of demonstrating specific reactivity with a conformational epitope on the Human Immunodeficiency Virus I protein gp41. The present invention also provides for a cell line capable of producing such a monoclonal antibody as well as immunological procedures for the detection in biological samples of exposure to HIV. The invention further provides for the use of the monoclonal antibody as a probe against native antigens and synthetic peptides of HIV.

  Excerpt(s): The present invention relates to the detection in body fluids such as blood or other blood products of exposure to the etiological agent of acquired immunodeficiency syndrome (AIDS). The etiological agent of AIDS is the human exogenous retrovirus termed Human Immunodeficiency Virus (HIV I), formerly named Human T-Cell Lymphotrophic Virus Type III (HTLV III), Lymphadenopathy Associated Virus (LAV), or AIDS Associated Retrovirus (ARV). In particular, a mouse monoclonal antibody, 5-21-3, and its native, conformation-dependent epitope within HIV I gp41 are provided which form the basis of an immunoassay used for the detection of exposure to HIV I. In another aspect, the invention relates to a monoclonal antibody for use as a probe against native antigens and synthetic peptides of HIV I.... Because AIDS is an infectious disease transmitted by parenteral exposure to contaminated blood or blood products (or intimate sexual contact), there is an established need to screen all blood and blood products prior to transfusion to detect and eliminate those derived from individuals exposed to HIV I. (See, for example Curran et al., Science (1985) 229:1352-1357; Council on Scientific Affairs, JAMA (1985) 254:1342-1345; Fauci et al., Ann. Int. Med. (1985) 102:800-813; Fauci et al., Int. Arch. Allergy Appl. Immun. (1985) 77:81-88. Diagnostic tests may determine if an individual is infected with HIV I by in vitro recovery of infectious virus from the individual. In addition, diagnostic tests may detect HIV I proteins or nucleic acid in body fluid or tissue, indicating possible HIV I infection. However, most diagnostic tests which are presently used for mass screening of blood and blood products are designed to detect antibody to HIV I, thus establishing prior exposure to HIV I.... The most widely used antibody test is the enzyme-linked immunoabsorbent assay (ELISA) employing inactivated whole virus cultured in a cell line capable of virus replication as the antigen reagent. While this method is quite sensitive, and there is a high likelihood that a truly infected person will be detected,

there is also the possibility that persons never exposed to the virus may occasionally give positive results.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Reference clones and sequences for non-subtype B isolates of human immunodeficiency virus type 1**

  Inventor(s): Gao, Feng; (Hoover, AL), Shaw, George M. (Birmingham, AL), Hahn, Beatrice H. (Birmingham, AL)

  Correspondence: Dr. Benjamin Adler; Adler & Associates; 8011 Candle Lane; Houston; TX; 77071; US

  Patent Application Number: 20030148266

  Date filed: November 8, 2002

  Abstract: The nucleotide sequences of the genomes of eleven molecular clones for non-subtype B isolates of human immunodeficiency virus type 1 are disclosed. The invention relates to the nucleic acids and peptides encoded by and/or derived from these sequences and their use in diagnostic methods and as immunogens.

  Excerpt(s): This is a divisional application of non-provisional U.S. Ser. No. 09/184,418, filed Nov. 2, 1998.... The present invention is in the field of virology. The invention relates to the nucleotide sequences of the genomes of 11 molecular clones for non-subtype B isolates of human immunodeficiency virus type 1 (HIV-1), and nucleic acids derived therefrom. This invention also relates to peptides encoded by and/or derived from the nucleic acid sequences of these molecular clones, and host cells containing these nucleic acid sequences and peptides. The invention also relates to diagnostic methods, kits and immunogens which employ the nucleic acids, peptides and/or host cells of the invention.... A critical question facing current AIDS vaccine development efforts is to what extent HIV-1 genetic variation has to be considered in the design of candidate vaccines (11,21,42,72). Phylogenetic analyses of globally circulating viral strains have identified two distinct groups of HIV-1, a major M group and an O group (33,45,61,62). Within the M group, ten sequence subtypes (A-J) have been proposed (29,30,45,72). Sequence variation among viruses belonging to these different lineages is extensive, with envelope amino acid sequence variation ranging from 24% between different subtypes to 47% between the two different groups. Given this extent of diversity, the question has been raised whether immunogens based on a single virus strain can be expected to elicit immune responses effective against a broad spectrum of viruses, or whether vaccine preparations should include mixtures of genetically divergent antigens and/or be tailored toward locally circulating strains (11, 21, 42, 72). This is of particular concern in developing countries where multiple subtypes of HIV-1 are known to co-circulate and where subtype B viruses, which have been the source for most current candidate vaccine preparations (10, 21), are rare or nonexistent (5, 24, 40, 72).

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Selective destruction of cells infected with human immunodeficiency virus**

  Inventor(s): Keener, William K. (Idaho Falls, ID), Ward, Thomas E. (Idaho Falls, ID)

  Correspondence: Stephen R Christian; Bechtel BWXT Idaho, LLC; P O Box 1625; Idaho Falls; ID; 83415-3899; US

  Patent Application Number: 20020094334

  Date filed: June 15, 2001

  Abstract: Compositions and methods for selectively killing a cell containing a viral protease are disclosed. The composition is a variant of a protein synthesis inactivating toxin wherein a viral protease cleavage site is interposed between the A and B chains. The variant of the type II ribosome-inactivating protein is activated by digestion of the viral protease cleavage site by the specific viral protease. The activated ribosome-inactivating protein then kills the cell by inactivating cellular ribosomes. A preferred embodiment of the invention is specific for human immunodeficiency virus (HIV) and uses ricin as the ribosome-inactivating protein. In another preferred embodiment of the invention, the variant of the ribosome-inactivating protein is modified by attachment of one or more hydrophobic agents. The hydrophobic agent facilitates entry of the variant of the ribosome-inactivating protein into cells and can lead to incorporation of the ribosome-inactivating protein into viral particles. Still another preferred embodiment of the invention includes a targeting moiety attached to the variants of the ribosome-inactivating protein to target the agent to HIV infectable cells.

  Excerpt(s): This application claims priority from U.S. provisional application Ser. No. 60/182,759 filed Feb. 16, 2000 and is incorporated by reference.... This invention relates to antiviral agents and methods of use thereof. More particularly, the invention relates to antiviral agents that specifically destroy cells infected by viruses that produce a protease in such infected cells. The antiviral agents are activated by the viral protease, thereby specifically targeting the infected cells for destruction. Toxins that target cell surface receptors or antigens on tumor cells have attracted considerable attention for treatment of cancer. E.g., I. Pastan & D. FitzGerald, Recombinant Toxins for Cancer Treatment, 254 Science 1173-1177 (1991); Anderson et al., U.S. Pat. Nos. 5,169,933 and 5,135,736; Thorpe et al., U.S. Pat. No. 5,165,923; Jansen et al., U.S. Pat. No. 4,906,469; Frankel, U.S. Pat. No. 4,962,188; Uhr et al., U.S. Pat. No. 4,792,447; Masuho et al., U.S. Pat. Nos. 4,450,154 and 4,350,626. These agents include a cell-targeting moiety, such as an antigen-binding protein or a growth factor, linked to a plant or bacterial toxin. They kill cells by mechanisms different from conventional chemotherapy, thus potentially reducing or eliminating cross resistance to conventional chemotherapeutic agents.... Ricin and other similar plant toxins, such as abrin, modeccin and viscumin, comprise two polypeptide chains (known as the A and B chains) linked by a disulfide bridge, one chain (the A chain) being primarily responsible for the cytotoxicity and the other chain (the B chain) having sites that enable the molecule to bind to cell surfaces. Such toxins are known as type II ribosome-inactivating proteins or RIPs. F. Stirpe et al., Ribosome-inactivating Proteins from Plants: Present Status and Future Prospects, 10 Biotechnology 405-412 (1992).

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

Keeping Current

In order to stay informed about patents and patent applications dealing with human immunodeficiency virus, you can access the U.S. Patent Office archive via the Internet at the following Web address: **http://www.uspto.gov/patft/index.html**. You will see two broad options: (1) Issued Patent, and (2) Published Applications. To see a list of issued patents, perform the following steps: Under "Issued Patents," click "Quick Search." Then, type "human immunodeficiency virus" (or synonyms) into the "Term 1" box. After clicking on the search button, scroll down to see the various patents which have been granted to date on human immunodeficiency virus.

You can also use this procedure to view pending patent applications concerning human immunodeficiency virus. Simply go back to **http://www.uspto.gov/patft/index.html**. Select "Quick Search" under "Published Applications." Then proceed with the steps listed above.

CHAPTER 7. BOOKS ON HUMAN IMMUNODEFICIENCY VIRUS

Overview

This chapter provides bibliographic book references relating to human immunodeficiency virus. In addition to online booksellers such as **www.amazon.com** and **www.bn.com**, excellent sources for book titles on human immunodeficiency virus include the Combined Health Information Database and the National Library of Medicine. Your local medical library also may have these titles available for loan.

Book Summaries: Federal Agencies

The Combined Health Information Database collects various book abstracts from a variety of healthcare institutions and federal agencies. To access these summaries, go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. You will need to use the "Detailed Search" option. To find book summaries, use the drop boxes at the bottom of the search page where "You may refine your search by." Select the dates and language you prefer. For the format option, select "Monograph/Book." Now type "human immunodeficiency virus" (or synonyms) into the "For these words:" box. You should check back periodically with this database which is updated every three months. The following is a typical result when searching for books on human immunodeficiency virus:

- **Combating AIDS: Communication Strategies in Action**

  Contact: SAGE Publications, 6 Bonhill St, London.

  Summary: This monograph synthesizes important lessons learned about effective **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) prevention programs, focusing on the role of communication strategies that could mobilize political action, target high-risk groups, and overcome stigma. The monograph begins with a chapter on the history of the AIDS epidemic. This is followed by a chapter on AIDS advocacy and policies, which focuses on the responses to the AIDS epidemic by national governments, international agencies, nongovernmental organizations, and advocacy groups. The monograph also discusses whether antiretroviral drugs are the solution to the worldwide AIDS epidemic. Other chapters deal with the lessons learned

about targeting HIV/AIDS programs to populations such as gay men, Indian commercial sex workers, and truck drivers; the role of cultural values in HIV prevention programs to stop the spread of HIV/AIDS; the nature of the stigma associated with HIV/AIDS and communication strategies for overcoming this stigma. In addition, the monograph analyzes the contributions of the entertainment-education strategy to HIV prevention, focusing on the use of television and radio soap operas to engage audiences emotionally and to encourage public discussion. It describes how HIV/AIDS programs are monitored and evaluated and reviews the lessons learned about combating HIV/AIDS in the past 20 years.

- **Tuberculosis Prevention Guide for Homeless Service Providers**

  Contact: Homeless Health Care Los Angeles, 2330 Beverly Blvd, Los Angeles, CA, 90057, (213) 744-0724, http://www.hhcla.org.

  Summary: This monograph, for health professionals who serve homeless persons, can be used as a guide in developing policies and procedures to decrease the risk of tuberculosis (TB) in homeless person facilities. The monograph discusses the epidemiology of TB among homeless persons in Los Angeles. It outlines how TB is transmitted, the difference between TB infection (LTBI) and TB disease, and TB risk factors. It examines treatments for persons with TB, persons co-infected with TB and the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS), pregnant women with TB, and individuals with multidrug-resistant TB.

- **Workplace HIV/AIDS Program: An Action Guide for Managers**

  Contact: Family Health International, AIDS Control and Prevention Project, HIV/AIDS Department, 2101 Wilson Blvd Ste 700, Arlington, VA, 22201, (703) 516-9779, http://www.fhi.org.

  Summary: This monograph provides practical steps for developing and implementing workplace **human immunodeficiency virus** (HIV)/acquired immunodeficiency syndrome (AIDS) prevention and care programs that will serve both employees and managers. It contains guidance in assessing the real and potential impact of HIV/AIDS on the company, in developing an HIV/AIDS policy to cover the workplace, and on designing and implementing HIV/AIDS prevention and care programs in the workplace. The monograph includes a series of checklists to aid in decision-making about particular components of workplace HIV/AIDS programs and suggests strategies for company managers and union leaders to obtain assistance for their HIV/AIDS programs. It also includes examples and case studies of how other companies have responded to the epidemic.

- **Guidelines for the Use of Antiretroviral Medications: Treatment and Prophylaxis for Adults, Pregnant Women, Adolescents, and Children**

  Contact: New York Department of Health, AIDS Institute, Empire State Plz, Corning Tower Rm 1483, Albany, NY, 12237-0684, (518) 473-7238, http://www.health.state.ny.us/nysdoh/aids/hivtesti.htm.

  Summary: This monograph provides guidelines for the treatment of adolescents, children, adults, and pregnant women, with antiretroviral therapy (ARV) for the **human immunodeficiency virus** (HIV)/acquired immunodeficiency syndrome (AIDS). The monograph discusses possible side effects and drug-drug interactions related to use of ARV drugs, prevention of perinatal HIV transmission, HIV post-exposure prophylaxis

(PEP) following exposure for children beyond the perinatal period, and PEP for adults following occupational and non-occupational exposure.

- **Federal HIV/AIDS Spending: Budget Chartbook: Fiscal Year 2001**

  Contact: Henry J Kaiser Family Foundation, 2400 Sand Hill Rd, Menlo Park, CA, 94025, (650) 854-9400, http://www.kff.org.

  Summary: This monograph reviews United States (US) government spending on **human immunodeficiency virus** (HIV)/acquired immunodeficiency syndrome (AIDS) programs for fiscal year (FY) 2001. The monograph presents financial figures showing federal HIV/AIDS spending, mandatory and discretionary spending, categories of federal spending, spending across departments and agencies, spending on HIV/AIDS programs, and spending on services and benefits. Federal HIV/AIDS spending is divided into four categories: Care and Assistance, Research, Prevention, and International. Total federal HIV/AIDS spending in FY 2001 is estimated to be $13.9 billion, which is approximately 0.7 percent of total federal spending.

- **Be Safe: NMAETC Cultural Competency Model**

  Contact: National Minority AIDS Education and Training Center, 2041 Georgia Ave NW Rm 2300, Washington, DC, 20060, (202) 865-3300, http://www.nmaetc.org/.

  Summary: This monograph outlines a cultural competency model for treating minorities with the **human immunodeficiency virus** (HIV)/acquired immunodeficiency syndrome (AIDS). The monograph explains the role of and the importance of cultural competency in treating minorities with HIV/AIDS, and discusses the BESAFE framework that uses culturally pluralistic content and perspectives based on the following six elements: barriers, ethics, sensitivity of the provider, assessment, facts, and encounters. The monograph explains these elements and how their use can help health care professionals toward becoming culturally competent.

- **Employers' Handbook on HIV/AIDS: A Guide for Action**

  Contact: World Health Organization, Joint United Nations Programme on HIV/AIDS, 20 Avenue Appia, CH-1211 Geneva, http://www.unaids.org.

  Summary: This monograph serves as a handbook to guide employers' organizations and their members in creating programs to deal with the impact of **human immunodeficiency virus** (HIV)/acquired immunodeficiency syndrome (AIDS) on their companies. The monograph gives basic facts about HIV/AIDS transmission, prevention, and progress from HIV to AIDS, and regional trends on HIV/AIDS. It discusses whether employers and their organizations should be involved in the fight against HIV/AIDS by examining the effect of HIV/AIDS on the business environment and on individual companies. The monograph provides guidelines for employers' organizations and companies on responding to HIV/AIDS in the workplaceand gives the outline of workplace policy, including provision of HIV-prevention education as well as community involvement. The monograph also gives examples of initiatives taken by employers' organizations and individual companies.

- **Glossary of HIV/AIDS-Related Terms**

  Contact: US Department of Health and Human Services, AIDSinfo, PO Box 6303, Rockville, MD, 20849-6303, (301) 519-6616, http://www.aidsinfo.nih.gov.

Summary: This monograph is an alphabetical glossary of **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) related terms. It defines words that are commonly used to describe the HIV virus, its pathogenesis, its associated treatments, and the medical management of related conditions. A list of federal resources that can be contacted for additional information on HIV/AIDS is included.

- **Monitoring the Declaration of Commitment on HIV/AIDS: Guidelines on Construction of Core Indicators**

  Contact: World Health Organization, Joint United Nations Programme on HIV/AIDS, 20 Avenue Appia, CH-1211 Geneva, http://www.unaids.org.

  Summary: This monograph contains guidelines to provide countries participating in the Declaration of Commitment on **human immunodeficiency virus** (HIV)/acquired immunodeficiency syndrome (AIDS) with technical guidance on the detailed specifications of the indicators for monitoring measurable aspects of actions, programme outcomes, and national impact objectives of the Declaration of Commitment. The Declaration established goals for the achievement of specific quantified and time-bound targets. The guidelines aim to increase the validity, internal consistency, and comparability across countries and over time of the indicator estimates obtained and to ensure consistency in the types of data and methods of calculation used. National commitment and action indicators include amount of national funds spent by governments on HIV/AIDS and the National Composite Policy Index, which is comprised of strategic plan, prevention, human rights, and care and support. The national return forms are included. Although specifications of the global indicators are included in the guidelines, global indicators will be measured by UNAIDS and its partners.

- **Many Threads One Weave: A Program to Assist Parish Communities in Responding to the HIV/AIDS Pandemic**

  Contact: National Catholic AIDS Network, PO Box 422984, San Francisco, CA, 94142-2984, (707) 874-3031, http://www.ncan.org/resources/index.html.

  Summary: This monograph discusses the role of the Roman Catholic Church in the provision of information about the **human immunodeficiency virus** (HIV)/acquired immunodeficiency syndrome (AIDS). The monograph discusses church roles in providing care and support to persons with HIV/AIDS and their caregivers, the basic facts about HIV/AIDS, the epidemiology of this pandemic, the emotional impact of being HIV-positive on individuals and their loved ones, and how to educate congregations about HIV/AIDS.

- **Ryan White CARE Act Title I Manual**

  Contact: US Department of Health and Human Services, Public Health Service, Health Resources and Services Administration, HIV/AIDS Bureau, Division of Training and Technical Assistance, 5600 Fishers Ln Rm 7-13, Rockville, MD, 20857, (301) 443-4092, http://www.hrsa.dhhs.gov/hab.

  Summary: This monograph explains the Ryan White Comprehensive AIDS Resources Emergency (CARE) ACT I, which funds primary health care and support services that enhance access to and retention in care for people living with the **human immunodeficiency virus** (HIV). Title I of the CARE Act funds eligible metropolitan areas. The monograph contains nine sections. Section1 presents general information including an overview of the CARE Act, CARE Act 2000 legislation, summary of

changes to the program and an overview of technical assistance for grantees and planning councils. The other 8 sections present information on grants administration; reporting requirements, including sample report forms; policies, including a list of Program Policy Guidance and Policy notes that have been issued by the US Department of Health and Human Services HIV/AIDS Bureau (HAB) and Division of Service Systems (DSS) since the inception of the CARE Act; a Chief Elected Official Guide, which gives a better understanding of the relationship of the CEO to the grantee and planning council; Planning Council Operations; program guidance; and a listing of Health Resources and Services Administration (HRSA)/HAB offices and Title I Grantees. The appendices provide definitions, acronyms, and a listing of approved service category contacts.

- **Ryan White CARE Act Title III Manual**

  Contact: US Department of Health and Human Services, Public Health Service, Health Resources and Services Administration, HIV/AIDS Bureau, Division of Training and Technical Assistance, 5600 Fishers Ln Rm 7-13, Rockville, MD, 20857, (301) 443-4092, http://www.hrsa.dhhs.gov/hab.

  Summary: This monograph is a manual that provides information to assist grantees in complying with legislative and program requirements of the Ryan White CARE Act of 1996. The monograph contains information about the Ryan White CARE Act and **human immunodeficiency virus** (HIV)/acquired immunodeficiency syndrome (AIDS) Bureau (HAB), Title III program expectations, Title III early intervention and planning grants, grants administration and technical assistance resources, as well as general information about contact listings for HAB and CARE Act grantees. The monograph is divided into six sections. Section I contains an overview of the ACT, information on legislation, the federal agencies concerned with the ACT, and overview of community based programs and other HAB programs; Section II describes program expectations; Section III discusses reporting issues and grants administration; Section IV explains technical assistance; and Section V gives contact information including listings of program offices, program staff, regional coordinators, and CARE Act grantees. Section VI provides information on Statewide Coordinated Statement of Need guidelines and a listing of CARE Act- definitions and acronyms.

- **Positive Negative: A Collection of Plays: Women of Color and HIV/AIDS**

  Contact: Aunt Lute Books, PO Box 410687, San Francisco, CA, 94141-0687, (800) 949-5883, http://www.auntlute.com.

  Summary: This monograph features a collection of plays, poems, and monologues that demonstrate how the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) pandemic has affected the lives of both HIV-positive and HIV-negative people, particularly women of color with HIV or AIDS. The monograph is divided into three thematic sections: love/relationships, sex/sexuality, and danger/death. The works in the love/relationships section include six short plays that deal with how the AIDS crisis has been experienced in the Latina community. The plays, monologues, and poetry in the section on sex/sexuality challenge conflicts and concerns about the expression and meaning of one's sexuality, one's identity as a sexual person, and the consequences of that expression. The works in the danger/death section deal with the emotions that accompany loss and demonstrate how to reclaim life and human connectedness in the context of death and loss.

- **AIDS**

  Contact: Rosen Publishing Group, Incorporated, 29 E 21st St, New York, NY, 10010, (212) 777-3017.

  Summary: This monograph, for adolescents, discusses the general facts and the history of the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) epidemic. It discusses HIV; its effects on the immune system; its development into AIDS; the history of HIV/AIDS; HIV diagnosis; how to understand HIV test results; and HIV treatment, research, and prevention.

- **No Time to Lose: The AIDS Crisis is Not Over: Getting More From HIV Prevention**

  Contact: National Academy Press, 2101 Constitution Ave NW, Box 285, Washington, DC, 20055, (202) 334-3313.

  Summary: This report, for health professionals, government agencies, and organizations, makes recommendations on how to develop a comprehensive, effective, and efficient strategy for prevention of the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) in the United States. It discusses the AIDS epidemic including epidemiological data; developing an accurate surveillance system focused on averting new HIV infections (e.g., by targeting prevention activities to those individuals who are most likely to transmit or acquire HIV); allocating resources to prevent as many new HIV infections as possible; using the clinical setting for prevention; investing in the development of new tools and technologies for HIV prevention; and overcoming social barriers (e.g., by increasing drug abuse treatment funding and removing legal and policy barriers that limit access to sterile drug injection equipment). The appendices provide an overview of the history of the AIDS epidemic, interventions used to help to prevent HIV/AIDS, information on federal spending on HIV/AIDS programs, the HIV prevention resource allocation model, data gathering activities, and possible agendas for public committee meetings.

- **2001-2002 Medical Management of HIV Infection**

  Contact: Johns Hopkins University, Department of Medicine, Division of Infectious Diseases, Baltimore, MD, 21205.

  Summary: This monograph focuses on issues of primary concern for health professionals and caregivers of people with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). It discusses the development of HIV into AIDS; HIV transmission; laboratory tests used to monitor the development of HIV in patients; disease prevention including prophylactic antimicrobial agents and vaccines; antiretroviral therapy; management of opportunistic infections in patients with HIV and miscellaneous conditions by organ systems; drugs used in HIV therapy, their side effects, and drug interactions; psychiatric and substance abuse disorders; and pulmonary complications, nervous system complications, gastrointestinal complications, dermatologic complications, wasting syndrome, cytomegalovirus retinitis, and fever.

- **2001 Delaware HIV/AIDS Resource Guide**

  Contact: Delaware HIV Consortium, 100 W 10th St Ste 415, Wilmington, DE, 19801, (302) 654-3869, http://delawarehiv.org.

  Summary: This directory provides contact information for **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) programs and services in

the state of Delaware (DE). The services are listed by categories and by county and include HIV counseling and testing, medical resources, wellness counseling, supportive services, housing including emergency shelters and transitional homes, and prevention and treatment education. The directory also provides information on the Delaware HIV Consortium; the Hope for Tomorrow Resources, a coalition of people living with HIV/AIDS (PLWH); and the HIV/AIDS Resource Centers Program. An alphabetical list of service providers is also supplied.

- **Evaluating CDC-Funded Health Department HIV Prevention Programs: Volume 1 Guidance and Volume 2 Supplemental Handbook**

  Contact: CDC National Prevention Information Network, PO Box 6003, Rockville, MD, 20849-6003, (800) 458-5231, http://cdcnpin.org.

  Summary: These two monographs provide evaluation guidance for federal, State, and local agencies involved in **human immunodeficiency virus** (HIV) prevention. Specifically, Volume 1 provides a description of the minimum Center for Disease Control and Prevention (CDC) evaluation requirements for health department HIV prevention programs funded by the CDC, and Volume 2 provides supplemental information on obtaining additional data and conducting evaluation activities not addressed in Volume 1. Topics of the two volumes include evaluating the HIV prevention community planning process; designing and evaluating intervention plans; monitoring and evaluating the implementation of HIV prevention programs; evaluating linkages between the comprehensive HIV prevention plan, CDC funding application, and resource allocation; monitoring outcomes of health education/risk reduction individual- and group-level HIV prevention interventions; evaluating outcomes of HIV prevention programs; and developing an evaluation plan.

- **HIV/AIDS and STD Lesson Plans : Suggested Lesson Plans and Learning Activities to Accompany the STD Poster Series**

  Contact: Campaign for Our Children, 120 W Fayette Street, Suite 1200, Baltimore, MD, 21201, (410) 576-9015.

  Summary: This teaching guide provides community organizations, schools, and educators with a curriculum to teach adolescents about sexually transmitted diseases (STDs), including the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). The guide outlines the lesson plan and the materials required for each lesson. It discusses HIV and AIDS, methods of transmission, persons at high risk, prevention through the practice of sexual abstinence, and the use of refusal skills. The guide describes refusal skills and provides role-playing exercises in which adolescents can participate to reinforce the use of refusal skills. Other activities show youth how easy it is for anyone to contract HIV if they practice high-risk behaviors. The guide presents adolescents with the task of developing a personal plan for HIV prevention.

- **Promoting Gyn Care for HIV-Infected Women**

  Contact: New York Department of Health, AIDS Institute, Room 359, Corning Tower, Albany, NY, 12237, (518) 486-1383.

  Summary: This monograph provides information about how to promote gynecological care for women with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). It covers the following topics: (1) Why Routine Pelvic Exams Are Important; (2) Best Practices in Patient Care; (3) Facilities in New York State

with a focus on access and client comfort, enhancing access to care, and offering incentives; and (4) Storyboard Presentation: Improvement of GYN Care for HIV-Infected Women.

- **The Next Generation of AIDS Patients : Service Needs and Vulnerabilities**

  Contact: Haworth Press, 10 Alice Street, Binghamton, NY, 13904-9981, (800) 342-9678.

  Summary: This monograph provides health professionals and organizations with pooled data from the efforts of several clusters of projects within the Special Projects of National Significance Program, which is composed of diverse organizations with the common goals to improve access to care, health, and quality of life for traditionally underserved populations living with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). One group includes programs identified as community-based organizations who share the goal of providing care for HIV-positive individuals who belong to groups that are traditionally underserved because of linguistic, cultural, racial, and economic barriers that prevent their integration into the traditional hospital-based system. Another group includes projects that developed specialized medical care models within the context of a continuum of services in a medical clinic. A third group includes models that focused on providing healthcare to HIV/AIDS-positive persons under capitated systems of reimbursement. The monograph also discusses the analysis methodology used to evaluate the programs, Exhaustive CHAID (Chi-squared Automatic Interaction Detector).

- **Street Smart**

  Contact: Center for HIV Identification and Treatment Services, 10920 Wilshire Blvd Ste 350, Los Angeles, CA, 90024, (310) 794-8278.

  Summary: This teaching guide, for educators and community organizations, provides a curriculum that can be used to educate high-risk youth about the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) and other sexually transmitted diseases (STDs). The teaching guide discusses HIV and other STDs; it advises adolescents about high risk behavior and how they can set their own personal limits to reduce their risks; it describes how to use male and female condoms properly; it discusses safer sex; and it examines the role of substance abuse in the transmission of HIV/STDs, how to cope with feelings in peer pressure or high-risk situations, and how to communicate to partners about sex. The teaching guide directs the facilitator about how to handle individual counseling sessions with youth.

- **Facilitating Meetings: A Guide for Community Planning Groups**

  Contact: CDC National Prevention Information Network, PO Box 6003, Rockville, MD, 20849-6003, (800) 458-5231, http://cdcnpin.org.

  Summary: This guide, written for community planning group (CPG) co-chairs, committee chairs, members, external facilitators, and anyone else interested in facilitating CPG meetings, presents meeting facilitation skills and tools to encourage productive CPG meetings, which play a critical role in developing effective **human immunodeficiency virus** (HIV) prevention plans. Section I provides an introduction to the guide. Section II gives an overview of the skills and tools that individuals will use throughout most meetings. Sections III, IV, and V each suggest specific tools to use during a particular part of a meeting, namely the opening, the discussions and decisions section, and the conclusion. Section VI presents tools for coping with challenging situations, such as members carrying on private conversations during the meeting.

Appendices A through F provide assistance with pre- and post-meeting tasks, such as deciding whether or not to use external facilitators and assessing one's facilitation skills.

- **Together We Can : Leadership in a World of AIDS**

  Contact: World Health Organization, Joint United Nations Programme on HIV/AIDS, 20 Avenue Appia, CH-1211 Geneva, http://www.unaids.org.

  Summary: This monograph makes recommendations regarding **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS)-related policy development worldwide. It emphasizes the importance of good leadership at every level to overcome this epidemic. The monograph reviews the global epidemiology and overall impact of HIV/AIDS. It makes recommendations about how to improve HIV/AIDS care and prevention programs through healthcare and political policies and emphasizes the need to protect human rights and solve, nationally and internationally, the many disparities that fuel this epidemic.

- **Working Together : A Guide to Collaborative Research in HIV Prevention**

  Contact: University of California San Francisco, Center for AIDS Prevention Studies, 74 New Montgomery St Ste 600, San Francisco, CA, 94105, (415) 597-9100, http://www.caps.ucsf.edu/capsweb.

  Summary: This monograph presents information about forming collaborations to research **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) prevention strategies. The monograph discusses why organizations should collaborate, how to start collaborating, how to conduct research in a community-based organization (CBO) setting, and developing a research thesis. It explains how to conduct HIV prevention research and applying research findings to prevention strategies.

- **Compendium of HIV Prevention Interventions With Evidence of Effectiveness from CDC's HIV/AIDS Prevention Research Synthesis Project**

  Contact: CDC National Prevention Information Network, PO Box 6003, Rockville, MD, 20849-6003, (800) 458-5231, http://www.cdcnpin.org.

  Summary: This monograph, which provides information on interventions found to be efficacious for the prevention of the **human immunodeficiency virus** (HIV), was developed by the Centers for Disease Control and Prevention (CDC) to respond to prevention service providers, planners, and others who requested science-based interventions that work. All interventions selected for this monograph came from behavioral or social studies that had both intervention and control/comparison groups and positive results for behavioral or health outcomes. The monograph is organized into four sections. Section one contains summaries or 'one-pagers' of prevention interventions, which met CDC's criteria for inclusion, written to emphasize the intervention content and methods. Specific summary information includes the title, authors, reference for the source report, intervention goals, intervention setting, population, comparison conditions, intervention description, behavioral/health findings, and the contact person. Summaries are grouped by target populations: drug users, heterosexual adults, men who have sex with men, and youth. Section two provides tables. For all interventions, Table 1 highlights characteristics of the populations and interventions. For selected interventions, Table 2 provides information about access to intervention materials. Section three provides an intervention checklist designed as a tool to help assess existing interventions. Section four contains two

appendices: (1) a description of CDC's HIV/AIDS Prevention Research Synthesis (PRS) project, the criteria used to select primary studies, and the additional criteria used to select a subset of primary studies for the monograph, and (2) the bibliography, which references each study in the monograph, along with additional or supplemental citations that pertain to that study.

- **The Chicago Comprehensive HIV Prevention Plan 2001-2003**

  Contact: Chicago Department of Public Health, Division of STD/HIV/AIDS, 333 S State St Rm 200, Chicago, IL, 60604-3972, (312) 747-9867, http://www.ci.chi.il.us/Health/.

  Summary: This monograph presents information about a collaborative program to prevent the spread of the **human immunodeficiency virus** (HIV)/acquired immunodeficiency syndrome (AIDS) in Chicago, Illinois. The monograph discusses the development, management, and evaluation of the program; how technical assistance was arranged; how collaborations were formed; and how research and surveillance were conducted.

- **Accessing Difficult-To Reach Populations: Community Assessment Survey Methods: Particpatory Methods**

  Contact: University of Texas, Southwestern Medical Center of Dallas, Division of Maternal Health and Family Planning, 2330 Butler St Ste 103, Dallas, TX, 75235-9081, (214) 905-2100, http://www.swmed.edu.

  Summary: This monograph describes techniques for contacting hidden populations for information gathering. The manual is divided into three sections: (1) making contact, which deals with how to recruit people from difficult-to-reach populations for focus groups, interviews and/or surveys; (2) using community knowledge, which addresses methods for community identification and assessment; and (4) methods. The monograph discusses strengths, weaknesses, and implementation of the methods presented. The manual also includes tools, such as an interview guide and diagrams, that make educational sessions more interactive; create opportunities for assessing participants' knowledge about issues related to **human immunodeficiency virus** (HIV) and other sexually transmitted diseases (STDs); and encourage problem-solving to devise effective ways of changing risk-taking behavior.

- **Leading the Way: USAID Responds to HIV/AIDS**

  Contact: US Agency for International Development, Bureau for Global Programs, Field Support and Research, Center for Population Health and Nutrition, Ronald Reagan Bldg, Washington, DC, 20523-0016, (202) 712-4120, http://www.info.usaid.gov. Synergy Project, 1101 Vermont Ave NW, Washington, DC, 20005, (202) 842-2939, http://www.synergyaids.com.

  Summary: This monograph discusses the work of the US Agency for International Development (USAID) toward preventing and lessening the impact of the **human immunodeficiency virus** (HIV)/acquired immunodeficiency syndrome (AIDS) in the developing world. The monograph begins by presenting data on AIDS and its impact in the developing world. This is followed by the USAID response from the beginning of the epidemic to the present. The monograph describes USAID's current HIV/AIDS strategy, discusses the change in the way countries view the AIDS epidemic and efforts to contain it, and the challenge involved in continuing the fight against AIDS in some of the poorer regions of the world. It presents maps showing the prevalence of HIV among urban populations at high risk, HIV prevalence among women of childbearing age, and

data on USAID HIV/AIDS funding for fiscal years 1997-2000 in the developing countries of the world.

- **A Collection of NIDA Notes: Articles That Address Drugs and AIDS**

  Contact: US Department of Health and Human Services, Public Health Service, National Institutes of Health, National Institute on Drug Abuse, Center on AIDS and Other Medical Consequences of Drug Abuse, 6001 Executive Blvd Rm 5798, Bethesda, MD, 20892-9593, (301) 443-1801, http://www.nida.nih.gov/ooa/ooahome.html.

  Summary: This monograph presents a collection of National Institute on Drug Abuse (NIDA) articles that focus on the relationship between drug use and **human immunodeficiency virus** (HIV)/acquired immunodeficiency syndrome (AIDS). Topics include the prevention of drug abuse-related infectious diseases, the role of gender in drug abuse research, NIDA research, conferences on the link between drug abuse and infectious diseases, an information network on HIV prevention, and drug abuse treatment and outreach.

- **Knowledge, Action, Health: A Woman's Guide to HIV Treatments**

  Contact: Women Alive, 1566 S Burnside Ave, Los Angeles, CA, 90019-4016, (323) 965-1564, http://www.women-alive.org.

  Summary: This monograph, for women with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS), provides information on the treatment of HIV/AIDS. It discusses the development of HIV into AIDS, how HIV affects women specifically, combination therapy, and the different drugs used in HIV treatment. It addresses considerations for treating HIV-positive women including pregnancy, side effects, and the development of opportunistic infections. The monograph provides readers with tables and surveys they can use to rate treatment effectiveness and to keep track of different therapies and the development of any side effects. A list of resources is provided.

- **Evaluating HIV/AIDS Treatment Programs: Innovative Methods and Findings**

  Contact: Haworth Press, 10 Alice Street, Binghamton, NY, 13904-9981, (800) 342-9678.

  Summary: This monograph examines organizing **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) treatment programs for a variety of populations infected or affected by HIV/AIDS, and provides an impressive case study of the potential value and challenges in implementing large-scale, cross-cutting evaluations. The monograph discusses the evaluation methods used to assess the programs' effectiveness, its implementation and practicality, as well as the findings from each evaluation. It includes an evaluation of the national AIDS care project run by the Health Resources and Services Administration (HRSA), a community-based organization, which aims to reduce the barriers to care in the community. It includes other examples of programs and evaluation types including an evaluation in comprehensive HIV care programs, a continuum of care model for adolescents living with HIV, a substance abuse program for Haitians in Boston, a model of comprehensive HIV care for ex-inmates, and an intervention program for HIV-positive women.

- **HIV Treatment: Mental Health Aspects of Antiviral Therapy**

  Contact: University of California San Francisco, AIDS Health Project, 1855 Folsom St Ste 670, San Francisco, CA, 94103-4241, (415) 502-8378, http://www.ucsf-ahp.org.

Summary: This monograph, for mental health professionals, examines the mental health aspects of antiretroviral treatment for individuals with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). It discusses combination antiretroviral therapy including barriers to successful combination therapy and implications of new treatment for HIV prevention; how to make decisions about antiviral treatment (e.g., the risks and benefits and culture and countertransference); psychosocial issues of successful antiviral treatment including returning to work, financial concerns, and starting relationships with significant others; and responding to treatment-related psychosocial issues.

- **People Living With HIV (PLWH) Sourcebook: Describing the Involvement of PLWH in the Ryan White CARE Act**

  Contact: US Department of Health and Human Services, Public Health Service, Health Resources and Services Administration, HIV/AIDS Bureau, Division of Training and Technical Assistance, 5600 Fishers Ln Rm 7-13, Rockville, MD, 20857, (301) 443-4092, http://www.hrsa.dhhs.gov/hab.

  Summary: This sourcebook provides materials about the involvement of people living with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) (PLWH) in the Ryan White Comprehensive AIDS Resources Emergency (CARE) Act and primarily was written for CARE Act grantees, planning councils and consortia, PLWH who are members of planning bodies, and PLWH committees and caucuses. The sourcebook contains the following information: (1) how CARE Act programs are administered within the federal government, including background information about the Health Resources and Services Administration's (HRSA) HIV/AIDS Bureau (HAB) organizational structure; (2) contact information for current HAB CARE Act grantees and PLWH groups; (3) what has been learned about PLWH involvement in CARE Act activities, including field-based lessons from CARE Act experience with PLWH recruitment, involvement, and retention as planning body members and ways to obtain non-member PLWH input to the planning process; (4) HAB policies on PLWH involvement; (5) HAB activities to strengthen PLWH involvement; (6) sources of information about PLWH involvement presented through an annotated bibliography of materials prepared by or with the support of HAB, both directly or through grantees, and a listing of Public Health Service publications; and (7) a glossary of HIV/AIDS and CARE Act terms and acronyms.

- **Handbook of HIV Prevention**

  Contact: Plenum Publishing Corporation, Plenum Medical Book Company, 233 Spring St, New York, NY, 10013-1578, (888) 640-7378, http://www.wkap.nl.

  Summary: This handbook provides a compilation of behavioral **human immunodeficiency virus** (HIV) prevention research. It contains 17 chapters: (1) Theoretical Approaches to Individual-Level Change in HIV Risk Behavior; (2) Diffusion Theory: A Theoretical Approach to Promote Community-Level Change; (3) Methodological Issues in HIV Behavioral Interventions; (4) School-Based Interventions to Prevent Unprotected Sex and HIV Among Adolescents; (5) HIV Behavioral Interventions for Adolescents in Community Settings; (6) Interventions for High-Risk Youth; (7) The Role of Drug Abuse Treatment in the Prevention of HIV Infection; (8) HIV/AIDS Prevention for Drug Users in Natural Settings; (9) Interventions for Sexually Active Heterosexual Women; (10) Interventions to Reduce HIV Transmission in Homosexual Men; (11) HIV Prevention Among African-American and Latino Men Who Have Sex With Men; (12) HIV Prevention in Developing Countries; (13) HIV Prevention

in Industrialized Countries; (14) Technology Transfer: Achieving the Promise of HIV Prevention; (15) The Economics of HIV Primary Prevention; (16) Ethical Issues of Behavioral Interventions for HIV Prevention; and (17) Looking Forward: Future Directions for HIV Prevention Research.

- **Texas Resource Guide for HIV/STD Education for Health Education Professionals**

  Contact: Texas Department of Health, Bureau of HIV and STD Prevention, 1100 W 49th St, Austin, TX, 78756-9987, (512) 490-2500, http://www.tdh.state.tx.us/hivstd/.

  Summary: This directory, for health education professionals, provides a comprehensive listing of **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) and sexually transmitted disease (STD) resources in Texas. It discusses what individuals can do to become involved in HIV/STD prevention; legal mandates related to health education; STDs; HIV transmission; risk-factors; information on diseases including chlamydia, hepatitis, syphilis, and vaginitis; model education programs and other training opportunities; school-aged HIV/STD education resources; legal resources; special resources (e.g., on sexual abstinence, self-esteem, and sexual education); statistics; HIV/STD resources including treatment resources and training centers; and other resources on abuse, condoms, hemophilia, pharmacies, sex workers, and special populations. It provides helpful telephone numbers for HIV/STD resources in Texas.

- **Resource Guide to HIV/AIDS Related Resources : You Don't Have to go it Alone**

  Contact: Project Inform, HIV Treatment Hotline, 205 13th St Ste 2001, San Francisco, CA, 94103, (415) 558-8669, http://www.projectinform.org.

  Summary: This directory, for individuals with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS), provides listings for national and government services and organizations. The directory includes Web sites, telephone numbers, and addresses for organizations that can direct individuals to the appropriate local services. Organizations that deal specifically with HIV/AIDS testing; treatment and support such as clinical trials, treatment information dissemination, nutrition, mental and emotional support, age and gender specific support and, racial and ethnic support are listed.

- **AIDS : An Incredibly Easy MiniGuide**

  Contact: Springhouse Corporation, 1111 Bethlehem Pike, Springhouse, PA, 19477, (800) 346-7844, http://www.springnet.com.

  Summary: This monograph, for nurses and nursing students, provides information on the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). The monograph discusses HIV's effect on the immune system, the pathogenesis of HIV to AIDS, HIV transmission (e.g., through oral, anal, and vaginal sex; from a mother to her infant; and through occupational exposures), prevention, diagnosis, and AIDS-related conditions such as opportunistic infections. The monograph provides advice on educating HIV-positive patients about HIV.

- **HIV/AIDS Prevention : Current Issues in Community Practice**

  Contact: Haworth Press, 10 Alice Street, Binghamton, NY, 13904-9981, (800) 342-9678.

  Summary: This monograph contains four research articles examining current issues in communities' efforts to prevent the further spread of the **human immunodeficiency**

virus (HIV)/acquired immune deficiency syndrome (AIDS): (1) Building Collaborative Partnerships to Improve Community-Based HIV Prevention Research: The University-CBO Collaborative Partnership (UCCP) Model; (2) Ongoing Evaluation in AIDS-Service Organizations: Building Meaningful Evaluation Activities; (3) Influence of Health Beliefs, Attitudes, and Concern About HIV/AIDS on Condom Use in College Women; and (4) Psychological Distress Among HIV-Impacted African-American and Latino Males.

- **Safe, Fast and Reliable: A New Generation of HIV Testing**

  Contact: AIDS Action Foundation, 1875 Connecticut Ave NW, Ste 700, Washington, DC, 20009, (202) 986-1300. CDC National Prevention Information Network, PO Box 6003, Rockville, MD, 20849-6003, (800) 458-5231, http://cdcnpin.org.

  Summary: This brochure provides general information on the state of **human immunodeficiency virus** (HIV) testing including information on standard (non-rapid) HIV antibody testing and the rapid test (Single Use Diagnostic System [SUDS]). Topics discussed are the accuracy of the rapid test, its impact, and issues for community-based organizations (CBOs) regarding rapid testing. Standard HIV antibody tests require blood, saliva, or urine samples at the testing site. The samples are normally sent to an outside laboratory because the standard tests use specialized equipment to evaluate the presence or absence of HIV antibodies. Rapid tests detect HIV antibodies within five to 30 minutes, enabling results to be given during the same visit at which the sample is drawn. The sensitivity and specificity of the rapid HIV test are just as good as enzyme immunoassays (EIA). As with the EIA, rapid tests are only screening tests, and a reactive screening test must be confirmed by a follow-up test. The feasibility of rapid testing by smaller CBOs may largely depend on which of the rapid tests are approved by the Food and Drug Administration (FDA). Although all of the rapid tests currently under consideration by the FDA are far simpler to administer than standard antibody tests, some are more complicated than others. Considerations include costs and pre- and post-test counseling requirements. The brochure also discusses findings from a study on the use of enzyme-linked immunosorbent assay (ELISA) versus SUDS and rapid testing accessibility, implications for anonymous testing and easier discrimination, and potential national impact. The brochure contains five appendices: (1) The Standard HIV Test vs. the Rapid; (2) Positive Predictive Value of Rapid HIV Test Combinations; (3) Positive Predictive Value of a single Rapid HIV Test Result; (4) CDC Guidelines Regarding Rapid HIV Tests: Issues for Counselors Providing HIV Prevention Counseling; and (5) Resources for More Information.

- **HIV**

  Contact: American College of Physicians - American Society of Internal Medicine, 190 N Independence Mall W, Philadelphia, PA, 19106-1572, (215) 351-2400, http://www.acponline.org.

  Summary: This monograph, for health professionals, discusses providing high-quality primary medical care to adults with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). It addresses major clinical issues including antiretroviral therapy and prophylaxis of opportunistic infections and offers up-to-date practical advice on HIV disease management. The monograph provides tables, charts, and photographs to make this information easily accessible; illustrative clinical vignettes on HIV infection during pregnancy; and an appendix with information on drugs used in HIV treatment. It covers the epidemiology and transmission of HIV, its pathogenesis and natural history, HIV prevention in clinical practice, primary care of

HIV disease, the prevention of opportunistic infections, diagnostic approaches to common clinical syndromes, diagnosis and management of opportunistic infections, diagnosis and management of opportunistic cancers, and infection control and risk reduction for health care workers.

- **HIV/AIDS at Year 2000 : A Source book for Social Workers**

  Contact: Allyn and Bacon Publishing Company, 160 Gould St, Needham Heights, MA, 02494, (800) 922-0579, http://vig.abacon.com.

  Summary: This monograph, for social workers, provides information about the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). It shows how the disease affects communities, how social workers work within these communities, and with those affected with HIV/AIDS. It brings together the latest medical, psychosocial, and ethical issues surrounding HIV, through vignettes that illustrate the problems and challenges social workers face. The monograph begins by discussing the key medical, psychosocial, and ethical contexts within which social work with HIV/AIDS clients takes place, then looks at who in the U.S. today is most impacted by the disease. Taking an ecosystem perspective, it examines in particular how the epidemic has ravaged poor communities and communities of color. Finally, the various roles of the social worker are presented, including prevention, social advocacy and policy issues, treatment, mental health issues, bereavement, and spirituality.

- **STD: Educator's Guide to HIV/AIDS and Other STD's**

  Contact: Health Education Consultants, 1284 Manor Park, Lakewood, OH, 44107, (216) 521-1766.

  Summary: This guide is a classroom-ready, activity-oriented, behavioral approach to sexually transmitted disease (STD) education, which was developed by students, teachers, parents, disease intervention specialists, medical experts, and persons with STDs, including those with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). The goal of the guide is to provide accurate and timely methods and materials to help students gain the knowledge, attitudes, and life skills needed for realistic decision-making regarding STD prevention. Basic information is presented as Teacher Keys with corresponding Student Activity worksheets, which are ready for use as reproduction masters or overhead transparencies. The guide contains an STD pre-/post-questionnaire, which measures student STD knowledge, attitudes, and behavioral intentions, with a Teacher's Key to be used for student evaluation before and after the STD education program. The guide presents HIV/AIDS and other STDs as communicable diseases within a chain of infection disease concept. It emphasizes that HIV/AIDS and other STDs are like all other communicable diseases; they follow a chain of infection, need prompt medical care, and can be prevented. Abstinence is presented as the most effective way to prevent STDs, and responsible sexual behavior and drug use prevention are emphasized. The four objectives of the guide are that students will be able to (1) describe the communicable disease chain of infection concept, (2) identify basic STD information and attitudes needed to break the chain of infection, (3) plan actions for persons with STDs, and (4) analyze and practice strategies to prevent STDs and drug use. The guide provides an organizational plan for teaching STD education.

- **Treat Yourself Right : Information for Women With HIV and AIDS**

  Contact: National Association of People Living With AIDS, PO Box 876, Darlinghurst, http://www.napwa.org.au.

  Summary: This monograph, written for women with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS), discusses this infection/disease and what woman can do to remain healthy. It discusses the effect of HIV on the body, living with HIV, disclosure of serostatus, sex and HIV, choosing and working with health care providers, and monitoring HIV. Other topics include HIV treatments, complementary therapies, menstrual irregularities, pregnancy, gynecological conditions, opportunistic infections, other transmissible infections, and co-infection with HIV and hepatitis C. The monograph provides contact information for services in Australia from which individuals can learn more about HIV/AIDS.

- **On Beating HIV : Why Knowing Is Better : Getting Tested, Getting Treated**

  Contact: Channing L. Bete Company Incorporated, 200 State Rd, South Deerfield, MA, 01373-0200, (800) 477-4776, http://www.channing-bete.com.

  Summary: This study guide, for young people and educators, discusses the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) and sexually transmitted diseases (STDs). The study guide discusses STDs, HIV/STD transmission and diagnosis, risk factors for contracting HIV/STDs, the media's influence on societal attitudes about sex, healthy relationships, condom use, and sexual abstinence. Condom negotiation skills and ways to say no to partners who ask for sex are addressed. The guide provides a chronological history of the HIV epidemic. It recommends that individuals get tested for HIV and other STDs and discusses what individuals can do if they test positive. The guide provides hotline phone numbers for individuals diagnosed with STDs and Web sites that support the guide. Questions to assess the readers' knowledge about sex are included as well as a teaching guide, which provides ideas for educators.

- **Lifting the Burden of Secrecy: A Manual for HIV-Positive People Who Want to Speak Out in Public**

  Contact: Asia-Pacific Network, 628 Race Course Rd.

  Summary: This monograph, for individuals with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS), discusses how to become an effective public speaker on HIV/AIDS. It discusses the motivating factors for wanting to speak out about HIV/AIDS including fighting discrimination, preventing new infections, protecting human rights, and promoting public health; how to prepare for a speech (e.g., getting support from peers and family, building partnerships, understanding legal issues, and deciding whether to sign a contract); how to speak effectively; and how to answer the audiences' questions. The appendices identify regional networks of people living with HIV/AIDS, resource manuals for HIV-positive speakers, and a Positive Speakers' Bureau sample booking form.

- **Guia de Recursos Relacionados con el VIH/SIDA : Usted no Tiene que Arreglarselas Solo!. [Resource Guide to HIV/AIDS Related Resources : You Don't Have to Go It Alone]**

  Contact: Project Inform, HIV Treatment Hotline, 205 13th St Ste 2001, San Francisco, CA, 94103, (415) 558-8669, http://www.projectinform.org.

Summary: This directory, for individuals with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS), provides listings for national and government services and organizations. The directory includes Web sites, telephone numbers, and addresses for organizations that can direct individuals to the appropriate local services. Organizations that deal specifically with HIV/AIDS testing; treatment and support such as clinical trials, treatment information dissemination, nutrition, mental and emotional support, age and gender specific support and, racial and ethnic support are listed.

- **Perspectives on Returning to Work : Changing Legal Issues and the HIV/AIDS Epidemic**

  Contact: American Bar Association/AIDS Coordination Project, American Bar Association, AIDS Coordination Project, 740 15th St NW, Washington, DC, 20005-1009, (202) 662-1030, http://www.abanet.org/home.html.

  Summary: This monograph --for employees and potential employees with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS), and employers--discusses the legal and ethical issues related to the return of HIV-positive individuals to the workforce. The monograph, through the story of a male and female pair of fictitious employees, Carmen and Ralph, examines these topics. The monograph reviews the medical and disability benefits provided to employees who discover that they are HIV-positive, how private group disability coverage interacts with these benefits. The terms of these coverage plans are identified and described. Different insurance options are explored and outcomes are contrasted between group and individuals disability plans. Social Security and Disability Insurance (SSDI) offered by the federal government is explained, as is the timeline for when individuals become eligible for different benefits. Insurance policy options regarding medical relapses resulting from HIV, supplemental security income (SSI), and Medicaid are outlined. Legal issues pertaining to the employment and termination of workers with HIV/AIDS, confidentiality, reasonable accommodation, the Americans with Disabilities Act (ADA), and the Families and Medical Leave Act are reviewed.

- **Discovering Global Success: Future Directions for HIV Prevention in the Developing World**

  Contact: University of California San Francisco, Center for AIDS Prevention Studies, 74 New Montgomery St Ste 600, San Francisco, CA, 94105, (415) 597-9100, http://www.caps.ucsf.edu/capsweb.

  Summary: This monograph presents information about the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) prevention efforts in developing nations from the Fogarty Workshop on International HIV/AIDS Prevention Research Opportunities that took place on April 18-27, 1998. The main products of the workshop are presented in this monograph including essential HIV prevention strategies, a model for country-level HIV prevention planning, and a listing of priorities for international HIV prevention research. The plans developed by the workshop participants are included in the appendix.

- **The Emergence of AIDS: The Impact of Immunology, Microbiology and Public Health**

  Contact: American Public Health Association, 800 I St NW, Washington, DC, 20001, (301) 893-1894, http://www.apha.org.

Summary: This monograph examines the global impact of the **human immunodeficiency virus** (HIV)/acquired immunodeficiency syndrome (AIDS). The monograph begins with the history of HIV/AIDS and discusses the scientific advances in microbiology and immunology since the discovery of the AIDS virus. It also examines the social impact of HIV/AIDS, including high-risk behaviors, and the social inequalities of infection rates and of access to clinical trials for women. The monograph identifies how HIV/AIDS has forced changes in public and healthcare policies.

- **Tuberculosis Control Program Staff Handbook**

  Contact: New York City Department of Health and Mental Hygiene, Bureau of Tuberculosis Control, PO Box 74, New York, NY, 10013-0061, (212) 788-4155, http://www.ci.nyc.ny.us/nyclink/html/doh/html/tb/tb.html.

  Summary: This monograph provides health professionals with information on tuberculosis (TB) drugs, treating latent TB infection, and TB direct care and field services. It contains a listing of TB-related resources and services in New York City along with their contact information. It includes information for chest clinics, outreach programs, relevant local government offices, housing services, and programs for persons with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS).

- **HIV Anonymous: Positive Attitudes: A 12-Step Workbook for Men, Women, and Children with HIV, and Their Families and Friends**

  Contact: HIV Anonymous World Service Organization, HIV Anonymous, 129 W Canada, San Clemente, CA, 92672-4602, (949) 218-6793, http://www.hivanonymous.com.

  Summary: This monograph presents a twelve-step program that has been tailored to meet the needs of people infected with or affected by the **human immunodeficiency virus** (HIV). The program has adapted the twelve steps and twelve traditions of Alcoholics Anonymous (AA), and is described as a continuing education and recovery process that helps its participants develop spiritually. The monograph contains inspirational reading and writing exercises for each step and guidelines for different meeting formats.

- **Module 3: Nursing Care: Pharmacologic Treatment of HIV/AIDS: Update October 2000**

  Contact: Canadian Association of Nurses in AIDS Care, 3840 St-Urbain, Pavillon Cooper, (514) 843-2712.

  Summary: This monograph serves as a guide for the care of persons with **human immunodeficiency virus** (HIV) disease. It focuses on medications commonly used in the prevention and treatment of HIV infection and the treatment of most bacterial, parasitic, fungal, and viral opportunistic infections. HIV infection drug categories include nucleoside reverse transcriptase inhibitors, nonnucleoside reverse transcriptase inhibitors, ribonucleotide reductase inhibitors, protease inhibitors, and nonnucleotide reverse transcriptase inhibitors. For each drug, the monograph provides generic and trade names, adult dosage guidelines, general side effects, drug interactions, and some specific recommendations.

- **HIV Vaccine Handbook: Community Perspectives on Participating in Research, Advocacy, and Progress**

  Contact: CDC National Prevention Information Network, PO Box 6003, Rockville, MD, 20849-6003, (800) 458-5231, http://cdcnpin.org.

  Summary: This monograph is an anthology of articles on the **human immunodeficiency virus** (HIV) vaccines from the perspective of communities affected by the acquired immune deficiency syndrome (AIDS) to be used as a resource and reference, particularly for potential trial participants and advocates. It contains over 30 articles dealing with complex science, policy, and economic issues of vaccine development. The articles are grouped under four headings: (1) background information on vaccine development and advocacy, (2) participant issues in vaccine development, (3) advocacy, and (4) approaches to vaccine development. Specific topics include phases of clinical trials, efficacy trials, vaccine preparedness studies, reducing risk in HIV vaccine trials, vulnerable populations in research, and participant rights. Other topics include animal studies for AIDS vaccines, VaxGen, the ALVAC vaccine, and nonprofits that support AIDS vaccines.

- **Teenagers Health Care and the Law : A Guide to the Law on Minors' Rights in New York**

  Contact: New York Civil Liberties Union, 125 Broad St 17th Fl, New York, NY, 10004, (212) 344-3005, http://www.nyclu.org.

  Summary: This monograph discusses New York State law that regulates the medical treatment of adolescents and who has the right to grant consent for medical care. The monograph defines legal terms such as adult, minor, informed consent, and confidentiality. It examines the general laws surrounding minors and consent, confidentiality, as well as medicaid or private insurance coverage. It explains how a minor's legal status such as being married, parents, pregnant, emancipated, or mature, affects one's legal right to care. It identifies the types of care for which minors can give consent such as emergencies, sexually transmitted diseases (STD), the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS), family planning, pregnancy, abortion, sterilization, mental health issues, and substance abuse. The monograph lists those persons who can authorize care for minors under New York State law such as parents, guardians, and State social services.

- **Integrating Cultural, Observational, and Epidemiological Approaches in the Prevention of Drug Abuse and HIV/AIDS**

  Contact: National Institute on Drug Abuse, Division of Epidemiology Services and Prevention Research, 6001 Executive Blvd, Rm 5153 MSC 9589, Bethesda, MD, 20892-9589, (301) 443-6504, http://www.nida.nih.gov/DESPR.

  Summary: This monograph provides both a historical and future perspective on the evolving substantive and methodological dialog between epidemiologists and ethnographers who focus on risk behaviors, the **human immunodeficiency virus** (HIV) transmission, and strategies to prevent further spread of the infection. The following topics are covered: Frontiers in acquired immune deficiency syndrome (AIDS) and Drug Abuse Prevention Research; Toward a Critical Biocultural Model of Drug Use and Health Risk; Anthropological Research in Drugs and AIDS; Interdisciplinary Research on the Transmission of Blood-Borne Pathogens in Drug Injection Practices; Complexities in the Lives of Female Drug Users in the AIDS Era; Prevention Research on Substance Abuse, Sexual Behavior, and HIV/AIDS in Asia and Australia; Neighborhood Violence

in New York City and Indigenous Attempts to Contain It; Access and Adherence to Combination Antiretroviral Therapy for HIV/AIDS in Injection Drug Users; Ethics, Ethnography, Drug Use, and AIDS; An Approach to Ethical Decision Making in Ethnographic Research on HIV Prevention and Drug Use; and the Ethnography of Street Drug Use Before AIDS.

- **A Guide to HIV/AIDS Education in Religious Settings**

  Contact: New York State Department of Health, AIDS Institute, AIDS Education and Training Center, ESP - Corning Tower Rm 372, Albany, NY, 12237, (518) 473-8815. New York State Department of Health Publication Distribution Center, PO Box 2000, Albany, NY, 12220, (518) 465-0432.

  Summary: This teaching guide is designed for religious organizations and spiritual leaders to educate their members and others about the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) and its prevention. It discusses the epidemiology of HIV/AIDS in the state of New York; the role of religious organizations and spiritual leaders in the prevention of HIV/AIDS; and HIV transmission, its effect on the immune system, and its treatment. It provides guidelines for educating children, preteens, adolescents, and parents on HIV/AIDS and resources, educational materials, and suggestions for group activities.

- **Working With AIDS Bereavement: A Comprehensive Approach for Mental Health Providers**

  Contact: University of California San Francisco, AIDS Health Project, 1855 Folsom St Ste 670, San Francisco, CA, 94103-4241, (415) 502-8378, http://www.ucsf-ahp.org.

  Summary: This monograph, for mental health professionals, discusses bereavement counseling for individuals whose loved ones have died as a result of the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). It reviews the history of the HIV/AIDS epidemic and the cultural and psychological contexts of mourning. It discusses the meaning of AIDS bereavement; AIDS bereavement disease; and how to help the AIDS mourner.

- **AIDS and Mental Health Practice : Clinical and Policy Issues**

  Contact: Haworth Press, Incorporated, Harrington Park Press, Incorporated, 12 W 32 St, New York, NY, 10001, (212) 563-4247.

  Summary: This book provides psychologists, psychiatrists, social workers, and counselors with research and case studies that offer models for effective clinical practice with persons with the **human immunodeficiency virus** (HIV) and the acquired immune deficiency syndrome (AIDS) (PWAs). The book has 28 chapters. Topics include the role of mental health professionals in medical decision making regarding protease inhibitors, intrapsychic and systemic issues concerning returning to work for PWAs, the influence of combination therapies on PWA support groups, telephone support groups for HIV-positive bereaved mothers of children, HIV prevention for women and the kitchen sink model, the death of a child in a residential child welfare facility, issues in counseling homeless persons with HIV, support groups for HIV-negative gay men, and spiritual issues and HIV/AIDS in the Latino community. Other topics include HIV/AIDS mental health services for Black men, clinical issues for HIV-positive slow and nonprogressors from a self-psychology perspective, care for male-to-female pre-operative transsexuals, internalized homophobia in the psychotherapy of gay men with HIV/AIDS, counseling end-stage clients with AIDS, and 'storytelling' in a bereavement support group for

pediatric HIV/AIDS case managers. The book also covers social work with hospitalized AIDS patients, Black women and clinical cultural competence, immigrants with HIV, couples of mixed HIV status, HIV-associated cognitive/motor complex, racism in AIDS service organizations, HIV/AIDS education and training for mental health professionals, the New York Peer AIDS Education Coalition community empowerment model, suicide and hastened death, and HIV prevention for homosexual and bisexual youth.

- **School Health Education to Prevent AIDS and STD : A Resource Package for Curriculum Planners : Students' Activities**

  Contact: World Health Organization, Joint United Nations Programme on HIV/AIDS, 20 Avenue Appia, CH-1211 Geneva, http://www.unaids.org.

  Summary: This study guide provides 53 student activities related to the prevention of the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) and other sexually transmitted diseases (STDs). Activities are categorized under four headings: (1) Basic Knowledge on HIV/AIDS/STD; (2) Responsible Behaviour: Delaying Sex; (3) Responsible Behavior: Protected Sex; and (4) Care and Support. Specific topics include HIV transmission, high-risk behaviors, antibody testing, sexual abstinence, partner communication, peer pressure, decision-making, condom use, condom negotiation, discrimination against persons with HIV/AIDS (PWAs), universal precautions, caregiving, and attitudes toward PWAs.

- **Florida HIV Community Resource Directory**

  Contact: Florida Department of Health, Bureau of HIV/AIDS, 2020 Capital Cir SE BIN A09, Tallahassee, FL, 32399-1700, (850) 922-6675.

  Summary: This directory provides a listing of **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) services in Florida (FL). For each organization, the directory supplies the address, phone number(s), hours of operation, and type(s) of services offered. The types of services/service providers listed include state and local government health programs, HIV antibody testing facilities, counseling centers, drug abuse treatment programs, dental services, case management, housing, home health care agencies, transportation programs, and pharmaceutical services.

- **Abstinence: Making Responsible Decisions**

  Contact: Macmillan/McGraw-Hill, Glencoe Division, 936 Eastwind Drive, Westerville, OH, 43081.

  Summary: This study guide covers teen sexuality and promotes sexual abstinence in the prevention of unplanned pregnancies and sexually transmitted diseases (STDs). It discusses making good decisions; various aspects of dating and relationship building; the physical, emotional, and social consequences of having sex as an adolescent; and the transmission, symptoms, possible long-term effects, and treatment of STDs including chlamydia, gonorrhea, syphilis, genital herpes, vaginitis, the human papillomavirus (HPV), parasitic infections, and the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS).

- **Helping Adolescents With HIV Adhere to HAART**

  Contact: US Department of Health and Human Services, Public Health Service, Health Resources and Services Administration, HIV/AIDS Bureau, Division of Training and

Technical Assistance, 5600 Fishers Ln Rm 7-13, Rockville, MD, 20857, (301) 443-4092, http://www.hrsa.dhhs.gov/hab.

Summary: This monograph, written for health professionals, provides information about assisting adolescents living with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) adhere to the complex regimens of highly active antiretroviral therapies (HAART). The monograph outlines a series of strategies and techniques with which clinicians can tailor antiretroviral regimens to teens individual requirements, address the obstacles to adherence in their lives, provide them with opportunities to practice medicine-taking behaviors, and give them continuing support when they finally initiate HAART. The monograph outlines the five stages of the behavioral change model used in the intervention: pre-contemplation stage, the contemplation stage, the preparation stage, the action stage, and the maintenance stage. The monograph also discusses the process of relapse and provides recommendations for assisting with adherence to HAART.

- **Starter Facts**

  Contact: American Red Cross National Headquarters, American Red Cross, National Headquarters, Health and Safety Services, Office of HIV/AIDS Education, 8111 Gatehouse Rd 6th Fl, Falls Church, VA, 22042-1203, (703) 206-6707, http://www.redcross.org/.

  Summary: This teaching guide, for educators and community organizations, provides an overview of the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). It discusses the difference between HIV, HIV infection, and AIDS; how HIV infection progresses; how HIV is transmitted and not transmitted; and how to prevent the spread of HIV. It illustrates and describes prevention methods including practicing safer sex with condoms and sterilizing needles before and after injection drug use. The guide also contains worksheets and handouts for the training course.

- **American Red Cross : African American HIV/AIDS Instructor's Manual**

  Contact: American Red Cross National Headquarters, American Red Cross, National Headquarters, Health and Safety Services, Office of HIV/AIDS Education, 8111 Gatehouse Rd 6th Fl, Falls Church, VA, 22042-1203, (703) 206-6707, http://www.redcross.org/.

  Summary: This teaching guide provides information about setting up a **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) education program in African-American communities. The teaching manual examines the impact of HIV/AIDS on the Black community and the community's response to the disease/infection. It discusses the need for the creation of culturally sensitive HIV/AIDS education/prevention programs for Black communities, and provides tips on how to effectively plan for a community education session. The teaching manual presents specific information on the impact of HIV/AIDS and special needs of youth, women, substance abusers, and homosexuals in the African-American community. The teaching manual supplies the readers with strategies about how to effectively facilitate a community HIV/AIDS education session and provides two separate modules from which the readers can draw their information for these events. These modules contain information concerning HIV/AIDS such as methods of transmission, its prevention, and what African Americans can do as a community to help to protect themselves from it. The teaching guide advises the readers in the use of supporting materials and resources

for these sessions and provides a number of planning tools, handouts, reprints, and supplemental readings that they can use during these HIV/AIDS education programs.

- **The River : A Journey to the Source of HIV and AIDS**

  Contact: Little, Brown and Company, PO Box 9131, Waltham, MA, 02254, (617) 890-2125.

  Summary: Based on over a decade of research, involving more than 600 interviews and analysis of more than 4,000 scientific texts, this monograph examines the myriad theories about the origin of the acquired immune deficiency syndrome (AIDS) epidemic. The author posits that the transfer of the **human immunodeficiency virus** (HIV) from chimps to human may be the result of American and European medical interventions in Africa during the 1950s; specifically the administration of more than a million doses of an experimental oral polio vaccine, some batches of which may have been manufactured from chimp kidneys.

- **Living Positively : A Guide to HIV Resources and Services in Idaho**

  Contact: Idaho Department of Health and Welfare, Division of Health, Bureau of Clinical and Preventive Services, STD/AIDS Program, PO Box 83720, Boise, ID, 83720-3720, (208) 334-5500, http://www2.state.id.us/dhw.

  Summary: This guide provides a listing of the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) services and programs in the state of Idaho (ID). It provides general information about HIV/AIDS, its transmission, its prevention, and the maintenance of mental and physical health by persons living with HIV/AIDS. A brief description of the Idaho AIDS Drug Assistance Program is provided. The guide discusses nutritional problems, kitchen sanitation and food preparation safety, safer sex practices, and condom negotiation. It reviews state, federal, and private financial, medical, and legal benefits and assistance programs and how to enroll in them. Contact information is given for Idaho health districts and community-based AIDS service organizations as well as national and statewide hotlines.

- **Learning About AIDS : An Active Learning Program for Children in Grades 5 and 6 : Teacher's Guide**

  Contact: Canadian Public Health Association, Canadian HIV/AIDS Clearinghouse, 400-1565 Carling Ave Ste 400, Ottawa, (613) 725-3434, http://www.cpha.ca.

  Summary: This teacher's guide instructs elementary educators how to inform their students about the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). The teaching guide explains the need to teach children about HIV/AIDS and the advantages of doing so in a school environment. It suggests ways that basic, age appropriate information could be taught concerning the transmission and prevention of HIV/AIDS. The teaching guide also answers possible questions that may arise from the students. It provides the readers with activities to help to instill in the students this new knowledge concerning HIV/AIDS.

- **Caring for People With AIDS at Home**

  Contact: International Federation of Red Cross and Red Crescent Societies, PO Box 372, Geneva 19.

  Summary: This monograph provides information for volunteers and home health care workers about caring for persons with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). The monograph examines issues

such as the role of the health care volunteer or caregiver, how to access and use community resources to their fullest, and how caregivers can care for themselves emotionally and physically. Other topics include general HIV/AIDS information, the stigma associated with HIV/AIDS, confidentiality, hygiene in the home, and HIV/AIDS prevention. The monograph also discusses common problems experienced by persons with HIV/AIDS: nutritional problems, skin problems, sore mouth and throat, pain, tiredness/weakness, fevers, chronic diarrhea, cough/difficulty in breathing, confusion, and fear/anxiety/depression. It also discusses care of the person who is dying.

- **Reducing the Odds : Preventing Perinatal Transmission of HIV in the United States**

  Contact: National Academy Press, 2101 Constitution Ave NW, Box 285, Washington, DC, 20055, (202) 334-3313.

  Summary: This monograph discusses the perinatal transmission of the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). It examines the current status of public health HIV/AIDS screening, and makes recommendations on how to improve these programs. It discusses HIV diagnosis for pregnant women and treatments available to prevent transmission to unborn babies and infants. It describes treatment and care services available for women, infants, and children living with HIV/AIDS, and it reviews and analyzes the effectiveness of public health services, including HIV/AIDS testing and counseling, the implementation of primary HIV prevention programs, the increased participation of pregnant women in prenatal care programs, and the use of comprehensive HIV prevention programs in correctional facilities.

- **Life Is What You Make It : Live Life! : Video Discussion Guide**

  Contact: Motivational Educational Entertainment Productions, HIV Campaign, Community Network, 340 N 12th St Ste 503, Philadelphia, PA, 19107, (215) 829-0558, http://www.meeproductions.com.

  Summary: This teaching guide, designed for African Americans and Hispanics with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS), provides information in support of the video by the same title (see record AD0023061) concerning informed decision making about treatments for HIV/AIDS. The discussion guide explores the cultural aspects associated with Blacks and Hispanics that affect how they cope with having HIV/AIDS. It reviews the characters in the video and its plot. The teaching guide supplies the readers with ideas about how to facilitate an effective discussion session before and after the video, by providing a series of discussion topics, warm-up activities and themes for exploration among the video viewers. It also lists the materials that should be provided to participants to aid in the delivery of the video's message during these periods. The teaching guide has a glossary of HIV-related terms.

- **Faithful, Free, or Both? : Tools for Maximizing Long Term HIV Treatment Efficacy**

  Contact: Mosby-Yearbook Europe Ltd., Torrington Place, London.

  Summary: This monograph, written for persons with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS), discusses this infection/disease and its treatment. For newly diagnosed patients, it advises individuals on how to start taking therapeutic drugs and to keep taking them properly in order to achieve the best results. For individuals already taking medications, it helps them understand why continuing to take the medications correctly is so important, what they can do to enhance the effectiveness of their medications, and how to overcome any

difficulties they may encounter. Topics include drug scheduling, seroconversion, chronic infection, advanced disease, CD4 cells, viral load, resistance assays, treatment options, the initiation of therapy, reasons for drug failure, and body changes with therapy.

- **My Grandma Has AIDS : Annisha's Story**

  Contact: Motivational Educational Entertainment Productions, HIV Campaign, Community Network, 340 N 12th St Ste 503, Philadelphia, PA, 19107, (215) 829-0558, http://www.meeproductions.com.

  Summary: Throught the use of a personal anecdote, this monograph, written for children and their parents, discusses the fact that there is no danger for children to engage in normal activities with persons who have the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). Annisha is a young girl whose grandmother has HIV. Annisha recounts all of the things that she does with her grandmother such as making breakfast and going rollerblading. Annisha states that HIV-negative individuals can hold hands, be friends, hug, talk on the phone, and play together with HIV-positive persons. Both Annisha and her grandmother speak to groups about the importance of treating HIV-positive persons with compassion. A note at the end of the monograph stresses the need for parents to explain HIV/AIDS to their children and to emphasize that they must show compassion to HIV-positive persons. This monograph comes with a bookmark and an order form to obtain free copies of this publication.

- **Living With HIV : A Personal Handbook**

  Contact: New Zealand AIDS Foundation, PO Box 6663, Wellesley St, Auckland.

  Summary: This monograph provides information to individuals who have recently been diagnosed with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). Section topics include general information about HIV/AIDS, emotions that are commonly experience after individuals discover that they are HIV-positive, communication about an HIV-positive status, maintenance of a healthy immune system, medical treatment, communication with sex partners, and caregivers. The monograph also provides information about legal issues (i.e., power of attorney, wills, guardianship, property ownership, life insurance) for residents of New Zealand.

- **HIV Affected and Vulnerable Youth: Prevention Issues and Approaches**

  Contact: Haworth Press, 10 Alice Street, Binghamton, NY, 13904-9981, (800) 342-9678.

  Summary: This monograph, for health professionals, government agencies, and organizations, addresses the needs of women, children, and adolescents affected by the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). It contains personal anecdotes of a child and a mother affected by HIV, and it examines a longitudinal study of psychological distress symptoms in HIV-positive, school-aged children; the psychosocial impact on individuals living with HIV-positive family members; the impact of current prevention programs aimed at adolescents at high-risk for HIV transmission; the concept of minors' legal rights and their relationship to HIV prevention, testing, and treatment; how to help maintain family cohesion when a parent or child has become infected with HIV; and the challenges faced by HIV-positive mothers in parenting.

- **HIV Prevention Community Planning: An Orientation Guide**

  Contact: Academy for Educational Development, 1825 Connecticut Ave NW, Washington, DC, 20009-5721, (202) 884-8000, http://www.aed.org. CDC National Prevention Information Network, PO Box 6003, Rockville, MD, 20849-6003, (800) 458-5231, http://www.cdcnpin.org.

  Summary: This guidebook provides an orientation to the principal components of **human immunodeficiency virus** (HIV) prevention community planning for members of community planning groups (CPGs). The objectives of the guide are (1) to furnish useful information on HIV prevention community planning that is needed by all CPG members and CPG co-chairs; (2) to provide 'stand-alone' materials for continuing orientation needs, independent of outside technical assistance (TA) providers; and (3) to promote enthusiasm about participating in the community planning process. The guide is divided into several parts: (1) a brief history of HIV prevention community planning; (2) roles and responsibilities of CPG members, co-chairs, and staff; (3) the nine steps and 15 principles of community planning; (4) a side-by-side companion to the supplemental guidance; (5) technical assistance for CPGs; and (6) technical resources for CPGs.

- **The AIDS Dictionary : Concise : Easy to Use : Indispensable : The First Comprehensive Resource for Nonspecialists**

  Contact: Facts on File, Inc., 460 Park Avenue South, New York, NY, 10016.

  Summary: This dictionary serves as a reference for nonspecialists about the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). The dictionary defines many of the terms associated with the HIV/AIDS (such as opportunistic infections and symptoms), as well as many terms associated with the social and personal side of HIV/AIDS (such as emotional and social issues). It also describes many related issues, such as how to organize a group for political or social activism/advocacy.

- **Use and Interpretation of Laboratory Tests in Infectious Disease**

  Contact: Specialty Laboratories, 2211 Michigan Ave, Santa Monica, CA, 90404-3900, (310) 828-6543, http://www.speciality.com.

  Summary: This monograph discusses the laboratory diagnosis, research concerning, and epidemiology of infectious diseases. The monograph covers these topics for the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) and sexually transmitted diseases (STD), as well as parasitic, respiratory, bloodborne, and neurological disorders or infections. For each disease discussed, the monograph examines its global epidemiology and the commonly used diagnostic tests. The monograph explains how to interpret test results to make a proper dianosis of the disorder. For some of the infectious diseases, it explains treatment and what current research is being done to aid in patient care or eradication of the infection/disease.

- **The Alcohol and Drug Wild Card: Substance Use and Psychiatric Problems in People With HIV**

  Contact: University of California San Francisco, AIDS Health Project, 1855 Folsom St Ste 670, San Francisco, CA, 94103-4241, (415) 502-8378, http://www.ucsf-ahp.org.

  Summary: This monograph, for mental health professionals, discusses substance abuse and its effect on the mental health of individuals with the **human immunodeficiency virus** (HIV)/acquired immunodeficiency syndrome (AIDS). It provides information on

approaches to triple disorders (substance abuse, HIV disease, and psychiatric conditions); assessment and diagnosis; addiction treatment; and integrating treatment for triple disorders.

- **Critical Issues in HIV Prevention Evaluation**

  Contact: Academy for Educational Development, 1825 Connecticut Ave NW, Washington, DC, 20009-5721, (202) 884-8000, http://www.aed.org. CDC National Prevention Information Network, PO Box 6003, Rockville, MD, 20849-6003, (800) 458-5231, http://www.cdcnpin.org.

  Summary: This monograph provides information concerning a national forum held to discuss the purpose for and methods of conducting an evaluation of state and local **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) prevention/intervention programs. The monograph examines the factors that can affect the strategic planning for an evaluation and provides case studies to show how to properly prepare for an HIV/AIDS prevention assessment survey. The case studies present state level programs from a wide range of communities for which contact information is provided. For each program evaluation, the monograph discusses target audience, program objectives, the evaluation's goals, who conducted the survey and its methodology, and how the results of the assessment survey affected the program's policies. The monograph supplies the readers with many supporting materials covering issues such as conducting an evaluation, getting the community and program staff involved in the assessment process, and conducting an evaluation with limited resources.

- **Teen-Agers : Safe Sex Isn't, But Abstinence Is..**

  Contact: Huard Publications, 1549 Oriole Pl, Prescott, AZ, 86303, (520) 717-0043.

  Summary: This monograph explains to the reader that sexual abstinence is the only path for teenagers to follow. The monograph examines peer pressures surrounding adolescent sex. It describes 'safer sex' and explains that safer sex is not safe for teens because it only reduces the chances for contracting **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS), sexually transmitted diseases (STDs), and unexpected pregnancies. The monograph provides similar arguments about why sex with condoms is unsafe, especially compared to sexual abstinence. It discusses reasons why it is wrong to have premarital sex, safer or unprotected, as a teen or young adult. The monograph takes the reader through a scenario, showing the emotions, lifestyle changes, and problems of a teen couple who have protected sex which results in an unexpected pregnancy. The monograph empahsizes that, though adolescence is a time of exploration, the reader should not 'follow the crowd' but instead, should choose abstinence over safer sex.

- **Breaking the Walls of Silence**

  Contact: Overlook Press, Lewis Hollow Rd, Woodstock, NY, 12498, http://www.overlookpress.com.

  Summary: This monograph examines the history of the Acquired Immune Deficiency Syndrome (AIDS) Counseling and Education (ACE) program of the Bedford Hills Correctional Facility for women in New York and its **human immunodeficiency virus** (HIV)/AIDS curricula. It is the story of women, those who are living/lived with HIV/AIDS and their commitment to cope with the AIDS epidemic. It provides a brief overview of the history of the ACE and its challenges; it reviews the ACE curriculum, its

development, lessons, and teaching plans; it discusses the universality of HIV/AIDS and the social disease of stigma, blame, and prejudice faced by infected individuals; it describes HIV/AIDS' effect on the body and the social and medical issues regarding treatment; and it discusses transmission and risk-reducing activities, HIV/AIDS testing, women and HIV/AIDS, and how to live with AIDS. The appendices provide a sample orientation to the program, an outline of a seminar, teaching plans for the 'Women and Our Bodies' workshops, medical advocacy forms, and answers to some commonly asked questions.

- **In the Center of the Ring : A Guide for HIV Housing Advocates on How to Improve Your Act**

  Contact: AIDS Housing Corporation, 29 Stanhope St, Boston, MA, 02116, (617) 927-0088, http://www.ahc.org.

  Summary: This guide provides information and instructions to individuals and organizations whose mission is to assist homeless people with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) find safe, stable, affordable housing. The guide identifies a number of sources from which individuals can learn more about finding housing for HIV-positive homeless persons and offers recommendations about organizing a workplan, linking consumers with HIV housing, and subsidizing mainstream housing for individuals with HIV/AIDS. Other topics include the tenant selection process, households with children, working from an outreach site, the avoidance of stress and burn-out, and after-care and homelessness prevention. The guide supplies prototypes of forms for implementing services.

- **Let's Get Cooking! A Practical Guide to Community Kitchens for People Living with and Affected by HIV/AIDS**

  Contact: Canadian Public Health Association, Canadian HIV/AIDS Clearinghouse, 400-1565 Carling Ave Ste 400, Ottawa, (613) 725-3434, http://www.cpha.ca.

  Summary: This cookbook, for community organizations that serve individuals with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS), contains recipes for inexpensive, nutritious meals and discusses the concept of a community kitchen and how to establish one. The cookbook contains recipes for beef, poultry, pork, fish, and vegetarian dishes as well as desserts that are safe for consumption by HIV-positive persons.

- **Becoming a Responsible Teen : An HIV Risk Reduction Program for Adolescents : CDC Identified as a Program That Works**

  Contact: Education Training and Research Associates, PO Box 1830, Santa Cruz, CA, 95061-1830, (800) 321-4407, http://www.etr.org.

  Summary: This teacher's guide provides prevention information and activities for presentation to adolescents concerning the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). The teacher's guide explains the principles and theories behind Becoming a Responsible Team (BART). It explains HIV/AIDS, its modes of transmission, and how it works in the immune system. The teacher's guide identifies the high-risk behaviors associated with HIV transmissions and uses techniques to build solid decision-making skills among the teens taking part in the program so that they will avoid such activities thereby reducing their risks. It instructs the readers on how to present condom negotiation techniques to adolescents, and how to instill in them the knowledge to use one every time during sexual activities. The

teacher's guide works to develop good partner communication skills among adolescents to help them to avoid unwanted sexual encounters or unsafe intercourse. The teacher's guide asks teens to assess their risks for HIV/AIDS and provides the readers with information resources that can be used during the BART program.

- **African American : American Indian Alaska Native : Asian American : Hispanic : Pacific Islander : Sources of Health Materials**

  Contact: US Department of Health and Human Services, Public Health Service, Office of Minority Health Resource Center, PO Box 37337, Washington, DC, 20013-7337, (800) 444-6472, http://www.omhrc.gov.

  Summary: This directory provides a listing of health education information sources for minorities. The directory supplies the reader with the names, addresses, and phone numbers for minority health organizations that can provide information concerning specific health topics. It includes resource listings for health topics such as adolescent pregnancy prevention, aging, the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS), cancer, child health, cultural awareness, diabetes, digestive diseases, disabilities, exercise, family planning, general health education, heart disease, high blood pressure, kidney disease, lung disease, lupus, mental health, nutrition, organ transplants, osteoporosis, parenting, prenatal care, sickle cell disease, smoking, stress, stroke, substance abuse, violence, weight control, and women's health. The health information provided is tailored for minorities such as: African Americans, Asian Americans, American Indians, Alaskan Natives, Hispanics, and Pacific Islanders.

- **La Tardeada : Discussion Guide : Educating Youth about HIV/AIDS**

  Contact: National Alliance for Hispanic Health, Community HIV/AIDS Technical Assistance Network, 1501 16th St NW, Washington, DC, 20036-1401, (202) 387-5000, http://www.hispanichealth.org.

  Summary: This teaching guide reinforces the messages concerning the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) presented in the video 'La Tardeada' (AD0023022). The teaching guide instructs the readers in conducting information sessions for Hispanic adolescents and young adults in conjunction with the video. It provides information concerning HIV/AIDS, its epidemiology among Hispanics in the United States (US), and methods of transmission. To prevent the sexual transmission of HIV, the teaching guide recommends abstinence or safer sex practices such as condom use. It suggests avoiding injection drug use, cleaning or sterilizing needles, and if possible, using new needles each time one injects. It examines the perinatal transmission of HIV and the use of AZT to prevent HIV transmission to the infant. It describes the HIV antibody testing process and makes recommendations about making decisions soundly and effectively to avoid high-risk situations. The teaching guide examines psycho-social dynamics that can reduce or increase one's risks for contracting HIV/AIDS.

- **Towards a European Standard : A Standard of Care for HIV and AIDS**

  Contact: European AIDS Treatment Group, Mindener Strasse 33, Duesseldorf, http://www.eatg.org.

  Summary: This proceedings reports on speeches and presentations given at a conference hosted by the European Acquired Immune Deficiency Syndrome Group (EATG) concerning the standardization of new medical treatments for persons with the **human immunodeficiency virus** (HIV)/AIDS across Europe. The proceedings presents the

results of a study in Hamburg, Germany that examines the number of HIV/AIDS patients seen per week per physician, the accessibility of viral load tests to doctors, the different combinations of therapy inclusive of protease inhibitors that are prescribed, types of salvage therapy undertaken, and physician satisfaction with the care options they can offer to their patients. It discusses various sources of information available concerning new developments in HIV/AIDS treatment, and which sources are the most reliable. The proceedings produced the results of another survey that explores issues such as new developments that have led to a change in the phyicians' HIV/AIDS medical practice, methods of learning about new treatments, the number of drugs used per patient, the number of patients not on protease inhibitors, the perceived role of treatment, and possible steps that can be taken to avoid or delay resistance. It compares the accessibility of urban areas and smaller towns to the latest HIV/AIDS treatment developments. The proceedings discusses the challenges of creating a standard of clinical care based upon new developments in HIV/AIDS treatments. It reports the results of a study covering topics such as the number of viral load tests a physician can give a patient per year, the frequency of use of viral load testing, the waiting period for the outcomes of a viral load test, and perceived facility restrictions that inhibit a doctor's ability to treat patients effectively.

- **Handbook of Economic Evaluation of HIV Prevention Programs**

  Contact: Plenum Publishing Corporation, Plenum Medical Book Company, 233 Spring St, New York, NY, 10013-1578, (888) 640-7378, http://www.wkap.nl.

  Summary: This monograph discusses the economic evaluation of **human immunodeficiency virus** (HIV) prevention programs. It includes 15 chapters: (1) An Overview of Economic Evaluation Methodologies and Selected Issues in Methods Standardization; (2) The Bernoulli-Process Model of HIV Transmission: Applications and Implications; (3) Assessing the Cost-Effectiveness of HIV Prevention Interventions: A Primer; (4) Economic Evaluation of Primary HIV Prevention in Injection Drug Users; (5) Economic Evaluation of HIV Counseling and Testing Programs: The Influence of Program Goals on Evaluation; (6) Economic Evaluation of HIV Screening Interventions; (7) Changing Public Policy to Prevent HIV Transmission: The Role of Structural and Environmental Interventions; (8) The Cost-Effectiveness of Small Group and Community-Level Interventions; (9) The Cost-Effectiveness of the Components of a Comprehensive HIV Prevention Program: A Road Map of the Literature; (10) Resource Allocation and the Funding of HIV Prevention; (11) Economic Evaluation and HIV Prevention Decision Making: The State Perspective; (12) Adapting Cost Analytic Techniques to Local HIV Prevention Programs; (13) Economic Evaluation and HIV Prevention Community Planning: A Policy Analyst's Perspective; (14) Threshold Analysis of AIDS Outreach and Intervention; and (15) A Few Reflections on the Practicality of Economic Evaluation Methods and Conclusions. Appendices titles include (1) A method to Measure the Costs of Counseling for HIV Prevention, (2) Updates of Cost of Illness and Quality of Life Estimates for Use in Economic Evaluations of HIV Prevention Programs, (3) Cost-Effectiveness of a Community-Level HIV Risk Reduction Intervention, and (4) HIV Prevention and Cost-Effectiveness Resources on the World Wide Web.

Book Summaries: Online Booksellers

Commercial Internet-based booksellers, such as Amazon.com and Barnes&Noble.com, offer summaries which have been supplied by each title's publisher. Some summaries also include customer reviews. Your local bookseller may have access to in-house and commercial databases that index all published books (e.g. Books in Print®). **IMPORTANT NOTE:** Online booksellers typically produce search results for medical and non-medical books. When searching for "human immunodeficiency virus" at online booksellers' Web sites, you may discover non-medical books that use the generic term "human immunodeficiency virus" (or a synonym) in their titles. The following is indicative of the results you might find when searching for "human immunodeficiency virus" (sorted alphabetically by title; follow the hyperlink to view more details at Amazon.com):

- **AIDS Sourcebook: Basic Consumer Health Information About Acquired Immune Deficiency Syndrome (Aids) and Human Immunodeficiency Virus (Hiv) Infection)** by Dawn D. Matthews; ISBN: 078080631X; http://www.amazon.com/exec/obidos/ASIN/078080631X/icongroupinterna
- **AIDS Sourcebook: Basic Consumer Health Information About Acquired Immune Deficiency Syndrome (Aids) and Human Immunodeficiency Virus (Hiv) Infection, Featuring updated (Health Reference Series)** by Karen Bellenir (Editor) (1999); ISBN: 078080225X; http://www.amazon.com/exec/obidos/ASIN/078080225X/icongroupinterna
- **AIDS: A Catholic Educational Approach to Hiv (Human Immunodeficiency Virus: Implementation Guide)** by Carleen, Ph.D. Reck (Editor) (1992); ISBN: 1558331123; http://www.amazon.com/exec/obidos/ASIN/1558331123/icongroupinterna
- **Dideoxynucleoside Analogues as Inhibitors of the Replication of Human Immunodeficiency Virus (HIV)** by P. Herdewijn (1989); ISBN: 9061863538; http://www.amazon.com/exec/obidos/ASIN/9061863538/icongroupinterna
- **Guidelines for Nursing Management of People Infected With Human Immunodeficiency Virus**; ISBN: 9241210036; http://www.amazon.com/exec/obidos/ASIN/9241210036/icongroupinterna
- **Guidelines for Prevention of Transmission Human Immunodeficiency Virus and Hepatitis B**; ISBN: 0016002539; http://www.amazon.com/exec/obidos/ASIN/0016002539/icongroupinterna
- **Guidelines for Prevention of Transmission of Human Immunodeficiency Virus & Hepatitis Virus to Health-Care & Public-Safety Workers** (1989); ISBN: 0788136224; http://www.amazon.com/exec/obidos/ASIN/0788136224/icongroupinterna
- **Guidelines for Prevention of Transmission of Human Immunodeficiency Virus and Hepatitis B Virus to Health-Care and Public Safety Workers Response to p** (1989); ISBN: 9990470073; http://www.amazon.com/exec/obidos/ASIN/9990470073/icongroupinterna
- **Guidelines on Sterilization and Disinfection Methods Effective Against Human Immunodeficiency Virus (Hiv)** (1990); ISBN: 9241212020; http://www.amazon.com/exec/obidos/ASIN/9241212020/icongroupinterna
- **Human Immunodeficiency Virus and the Lung** by Mark J. Rosen (Editor), James M. Beck (Editor); ISBN: 082479883X; http://www.amazon.com/exec/obidos/ASIN/082479883X/icongroupinterna

- **Human Immunodeficiency Virus: Innovative Techniques for Isolation and Identification (Monographs in Virology, Vol 18)** by Narayan C. Khan, Joseph L. Melnick (Editor) (1990); ISBN: 3805551827; http://www.amazon.com/exec/obidos/ASIN/3805551827/icongroupinterna
- **Immunobiology of Proteins and Peptides VI: Human Immunodeficiency Virus, Antibody Immunoconjugates, Bacterial Vaccines, and Immunomodulators (Advances in Experimental Medicine and Biology, 303)** by M. Zouhair Atassi (Editor) (1992); ISBN: 0306440385; http://www.amazon.com/exec/obidos/ASIN/0306440385/icongroupinterna
- **Management of Kaposi's sarcoma associated with human immunodeficiency virus infection : report** by Frances A. Shepherd; ISBN: 0662581415; http://www.amazon.com/exec/obidos/ASIN/0662581415/icongroupinterna
- **Medical Analysis & Reviews of Human Immunodeficiency Virus (Hiv): Index of Synthesis of New Information by Research Scientists** by Gleen H. Parks (1998); ISBN: 0788318926; http://www.amazon.com/exec/obidos/ASIN/0788318926/icongroupinterna
- **Medical Analysis and Reviews of Human Immunodeficiency Virus: Index of Syntheses of New Information by Research Scientists** by Glenn H. Parks (1998); ISBN: 0788308173; http://www.amazon.com/exec/obidos/ASIN/0788308173/icongroupinterna
- **Mode of Action and Development of Resistance to Human Immunodeficiency Virus Inhibitors That Are Targeted at Early Stages of Infection (Acta Biomedica Lovaniensia, 190)** by Jose Andres Este (1999); ISBN: 9061869439; http://www.amazon.com/exec/obidos/ASIN/9061869439/icongroupinterna
- **Nursing and the Human Immunodeficiency Virus Guide for Nursings Response to AIDS**; ISBN: 9999914152; http://www.amazon.com/exec/obidos/ASIN/9999914152/icongroupinterna
- **Oral Health Care Guidelines: Patients With Human Immunodeficiency Virus (Hiv Infection and Acquired Immune Deficiency Syndrome)** (1992); ISBN: 999363008X; http://www.amazon.com/exec/obidos/ASIN/999363008X/icongroupinterna
- **Pediatric Human Immunodeficiency Virus (Hiv) Infection: A Compendium of Aap Guidelines on Pediatric HIV Infection** by American Academy of Pediatrics; ISBN: 1581100272; http://www.amazon.com/exec/obidos/ASIN/1581100272/icongroupinterna
- **Preventing the transmission of the human immunodeficiency virus (HIV) : hearing before the Subcommittee on Health and Environment of the Committee on Commerce, House of Representatives, One Hundred Fifth Congress, second session, February 5, 1998**; ISBN: 0160564883; http://www.amazon.com/exec/obidos/ASIN/0160564883/icongroupinterna
- **Prevention of Sexual Transmission of Human Immunodeficiency Virus** (1990); ISBN: 9241210060; http://www.amazon.com/exec/obidos/ASIN/9241210060/icongroupinterna
- **Report of the Presidential Commission on the Human Immunodeficiency Virus Epidemic Submitted to the President of the United States** by 40000005293, Watkins; ISBN: 9998187842; http://www.amazon.com/exec/obidos/ASIN/9998187842/icongroupinterna

- **The Human Immunodeficiency Virus: Biology, Immunology, and Therapy.** by Emilio A. Emini (Editor); ISBN: 0691004544; http://www.amazon.com/exec/obidos/ASIN/0691004544/icongroupinterna
- **Transmission of the human immunodeficiency virus (HIV) through blood transfusions between 1978 and 1985 : information document for Québec's physicians**; ISBN: 2550282051; http://www.amazon.com/exec/obidos/ASIN/2550282051/icongroupinterna

The National Library of Medicine Book Index

The National Library of Medicine at the National Institutes of Health has a massive database of books published on healthcare and biomedicine. Go to the following Internet site, **http://locatorplus.gov/**, and then select "Search LOCATORplus." Once you are in the search area, simply type "human immunodeficiency virus" (or synonyms) into the search box, and select "books only." From there, results can be sorted by publication date, author, or relevance. The following was recently catalogued by the National Library of Medicine:[11]

- **Blood donation and human immunodeficiency virus infection: do new and regular donors present different risks?** Author: Jones, M. E.; Year: 1994; Canberra, A.C.T., Australia: National Centre for Epidemiology and Population Health, Australian National University, [1991]; ISBN: 0731513282
- **Euthanasia and assisted suicide in persons with acquired immunodeficiency syndrome (AIDS) or human immunodeficiency virus (HIV)** Author: Ogden, Russel D.,; Year: 1997; New Wesminster, B.C.: Peroglyphics Pub., [1994]; ISBN: 0969823509 http://www.amazon.com/exec/obidos/ASIN/0969823509/icongroupinterna
- **Guidelines on sterilization and high-level disinfection methods effective against human immunodeficiency virus (HIV).** Author: World Health Organization.; Year: 1989; Geneva: World Health Organization; Albany, N.Y.: WHO Publications Center USA [distributor], 1988; ISBN: 9241210028
- **Hospitalization for community-acquired pneumonia in Alberta patients with human immunodeficiency virus infection: a case control study** Author: Johnson, David,; Year: 1988; [Edmonton]: Alberta Centre for Health Services Utilization Research, [2003]
- **Human immunodeficiency virus (HIV) testing for pregnant women: final report** Author: Minnesota. Health Technology Advisory Committee.; Year: 1989; St. Paul, Minn.: Health Technology Advisory Committee, Minnesota Health Care Commission, [1997]
- **Management of health care workers or others exposed to blood from a person infected or suspected to be infected with human immunodeficiency virus.** Author: Australian National Council on AIDS.; Year: 1993; Canberra, ACT: Australian National Council on AIDS, [1990]

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[11] In addition to LOCATORPlus, in collaboration with authors and publishers, the National Center for Biotechnology Information (NCBI) is currently adapting biomedical books for the Web. The books may be accessed in two ways: (1) by searching directly using any search term or phrase (in the same way as the bibliographic database PubMed), or (2) by following the links to PubMed abstracts. Each PubMed abstract has a "Books" button that displays a facsimile of the abstract in which some phrases are hypertext links. These phrases are also found in the books available at NCBI. Click on hyperlinked results in the list of books in which the phrase is found. Currently, the majority of the links are between the books and PubMed. In the future, more links will be created between the books and other types of information, such as gene and protein sequences and macromolecular structures. See **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Books**.

- **Medical evaluation of persons at risk of human immunodeficiency virus infection: including acquired immunodeficiency syndrome (AIDS) and related conditions** Author: Bay Area Physicians for Human Rights. Scientific Affairs Committee.; Year: 1990; San Francisco, Calif.: Bay Area Physicians for
- **Nursing and the human immunodeficiency virus: a guide for nursing's response to AIDS.** Author: American Nurses' Association. Task Force to Develop Guidelines for the Care of People with AIDS.; Year: 1988; Kansas City, Mo. (2420 Pershing Rd., Kansas City 64108): American Nurses' Association, c1988
- **Patients with human immunodeficiency virus (HIV) infection and acquired immune deficiency syndrome (AIDS).** Author: Council on Community Health, Hospital, Institutional, and Medical Affairs.; Year: 1994; Chicago, Ill.: American Dental Association, Council on Community Health, Hospital, Institutional, and Medical Affairs, [1993]
- **Pediatric human immunodeficiency virus (HIV) infection: a compendium of AAP guidelines on pediatric HIV infection: a compilation of AAP policy statements and excerpts from manuals published through August 1994.** Author: American Academy of Pediatrics.; Year: 1998; Elk Grove Village, IL: American Academy of Pediatrics, c1994; ISBN: 0910761515
  http://www.amazon.com/exec/obidos/ASIN/0910761515/icongroupinterna
- **Prevalence of antibodies to human immunodeficiency virus (HIV) in prostitutes in Guadalajara, Mexico** Author: Torres-Mendoza, M. B.; Year: 1991; 1988
- **Prospects for vaccines against HIV infection: report of the Conference on Promoting Development of Vaccines Against Human Immunodeficiency Virus Infection and Acquired Immune Deficiency Syndrome, December 14-15, 1987** Author: Institute of Medicine (U.S.); Year: 1990; Washington, D.C.: National Academy Press, 1988
- **Report of the Presidential Commission on the Human Immunodeficiency Virus Epidemic: submitted to the President of the United States.** Author: United States. Presidential Commission on the Human Immunodeficiency Virus Epidemic.; Year: 1988; Washington, D.C.: The Commission, [1988]
- **Strategic plan for prevention of human immunodeficiency virus (HIV) infection: 1990 and beyond: draft for public review and comment.** Author: Centers for Disease Control (U.S.); Year: 1992; Atlanta, Ga.: Centers for Disease Control, Public Health Service, Dept. of Health and
- **The AIDS manual: a comprehensive reference on the human immunodeficiency virus (HIV)** Author: Albion Street Centre (Sydney, N.S.W.); Year: 1976; Ultimo: Stateprint, 1989; ISBN: 0724087338
- **The AIDS manual: a comprehensive reference on the human immunodeficiency virus (HIV)**; Year: 1997; Sydney; Philadelphia: MacLennan + Petty, 1994; ISBN: 0864330898
  http://www.amazon.com/exec/obidos/ASIN/0864330898/icongroupinterna
- **The Epidemiology of AIDS: expression, occurrence, and control of human immunodeficiency virus type 1 infection** Author: Kaslow, Richard A.; Year: 1989; New York: Oxford University Press, 1989; ISBN: 0195050584
  http://www.amazon.com/exec/obidos/ASIN/0195050584/icongroupinterna
- **The FAHEC clinical manual for the care of patients with human immunodeficiency virus (HIV) infection or acquired immune deficiency syndrome (AIDS)** Author: Ellenbogen, Charles.; Year: 1994; [Fayetteville, N.C.]: Fayetteville Area Health Education Center, c1992
- **The HIV epidemic and topics for the U.S. valuation actuary: presented at Society of Actuaries Annual Meeting, Boston, October 23-26, 1988. Observations on the human**

immunodeficiency virus epidemic and managing uncertainty in insurance: presented at 23rd Actuarial Research Conference, University of Connecticut, August 25-27, 1988 papers Author: Holland, David M.; Year: 1996; [Itasca, Ill.]: The Society, c1988

Chapters on Human Immunodeficiency Virus

In order to find chapters that specifically relate to human immunodeficiency virus, an excellent source of abstracts is the Combined Health Information Database. You will need to limit your search to book chapters and human immunodeficiency virus using the "Detailed Search" option. Go to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. To find book chapters, use the drop boxes at the bottom of the search page where "You may refine your search by." Select the dates and language you prefer, and the format option "Book Chapter." Type "human immunodeficiency virus" (or synonyms) into the "For these words:" box. The following is a typical result when searching for book chapters on human immunodeficiency virus:

- **Renal Complications of Human Immunodeficiency Virus-Type I**

  Source: in Andreucci, V.E. International Yearbook of Nephrology 1990. Hingham, MA: Kluwer Academic Publishers. 1990. p. 73-88.

  Contact: Available from Kluwer Academic Publishers. P.O. Box 358, Accord Station, Hingham, MA02018-0358. (617) 871-6600.

  Summary: This review examines the electrolyte disorders and renal complications observed in patients with human immunodeficiency virus (HIV-1) infection, which is (with neoplasms) the dominant clinical manifestation of AIDS. Topics include: electrolyte and acid-base disturbances (hyponatremia; hyperkalemia; hypocalcemia; hypercalcemia; hypouricemia); the nephropathology in patients with HIV-1 infection; and acute renal failure in AIDS patients. The clinical aspects, pathology, and treatment of HIV-associated nephropathy also are discussed. 73 references.

- **Human Immunodeficiency Virus Disease**

  Source: in Scully, C. and Cawson, R.A. Oral Disease: Colour Guide. 2nd ed. Edinburgh, Scotland: Churchill Livingstone. 1999. p. 159-162.

  Contact: Available from W.B. Saunders Company, A Harcourt Health Sciences Company. Book Order Fulfillment Department, 11830 Westline Industrial Drive, St Louis, MO 63146-9988. (800) 545-2522. Fax (800) 568-5136. E-mail: wbsbcs@harcourt.com. Website: www.wbsaunders.com. PRICE: $19.95 plus shipping and handling. ISBN: 044306170X.

  Summary: This chapter on human immunodeficiency virus (HIV) disease is from a book that is intended as an aid to oral medicine and the diagnosis and treatment of oral disease. The chapter includes 6 full color photographs demonstrating the oral manifestations of HIV, with textual information accompanying them. Conditions include erythematous candidosis, linear gingivitis (inflamed gums), necrotizing ulcerative gingivitis, swelling of the submandibular (lower jaw) salivary glands, candidosis, and hairy leukoplakia. The text briefly covers incidence, clinical features, diagnosis and diagnostic tests, and treatment options.

- **Oral Manifestations of Human Immunodeficiency Virus Infection**

  Source: in Eisen, D. and Lynch, D.P. Mouth: Diagnosis and Treatment. St. Louis, MO: Mosby, Inc. 1998. p. 237-254.

  Contact: Available from Harcourt Health Sciences. Book Order Fulfillment Department, 11830 Westline Industrial Drive, St. Louis, MO 63146-9988. Website: www.mosby.com. PRICE: $79.95 plus shipping and handling. ISBN: 0815131054.

  Summary: The identification of the oral manifestations of HIV (human immunodeficiency virus) infection is of great significance because they may be the first signs of the disease and, furthermore, are highly predictive markers of severe immune deterioration and disease progression. This chapter on the oral manifestations of HIV infection is from a textbook on the mouth that offers information to primary care physicians and to many specialists in medicine and dentistry. The chapter begins with a discussion of the epidemiology of oral manifestations of HIV. The authors then describe how the oral manifestations of AIDS are divided into three groups and discuss each one. Group 1 lesions are strongly associated with HIV infection and include candidiasis, hairy leukoplakia, HIV associated periodontal diseases, Kaposi's sarcoma, and nonHodgkin's lymphoma. Group 2 lesions are less commonly associated with HIV infection and include a variety of bacterial and viral infections, salivary gland dysfunction, and oral mucosal disorders. Group 3 lesions are composed of conditions that have been reported in HIV infected patients but are not strongly linked to either HIV infection or AIDS. The chapter is illustrated with numerous full color photographs of the conditions under discussion. 15 figures. 1 table. 99 references.

Directories

In addition to the references and resources discussed earlier in this chapter, a number of directories relating to human immunodeficiency virus have been published that consolidate information across various sources. The Combined Health Information Database lists the following, which you may wish to consult in your local medical library:[12]

- **National Organizations Working for Healthy Youth: 1998 Project Summaries**

  Source: Atlanta, GA, Centers for Disease Control and Prevention, 233 p., 1999.

  Contact: Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Division of Adolescent and School Health, Atlanta, GA. (770) 488-3253.

  Summary: National Organizations Working for Healthy Youth: 1998 Project Summaries describes the work of the 34 organizations funded by the Centers for Disease Control and Prevention, Division of Adolescent and School Health (DASH). Each description includes a brief profile of the organization's overall activities, an overview of its project, its target audience, and detailed descriptions of its current activities or products. The DASH-funded organizations prevent behaviors that place young people at risk for

[12] You will need to limit your search to "Directory" and "human immunodeficiency virus" using the "Detailed Search" option. Go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. To find directories, use the drop boxes at the bottom of the search page where "You may refine your search by." For publication date, select "All Years." Select your preferred language and the format option "Directory." Type "human immunodeficiency virus" (or synonyms) into the "For these words:" box. You should check back periodically with this database as it is updated every three months.

human immunodeficiency virus (HIV) infection and other serious health problems. These organizations can be grouped into three general categories of constituencies targeted for HIV prevention activities: (1) School programs, (2) institutions of higher education, and (3) youth in high-risk situations. Topics covered by these organizations include (1) assessment, (2) barriers, (3) college health, (4) comprehensive health education, (5) culturally specific activities, (6) incarcerated youth, (7) mass media, (8) migrants, (9) nurses, (10) parents, (11) peer education, (12) physicians, (13) pregnancy prevention, (14) religious institutions, (15) sexual orientation, (16) sexually transmitted diseases, and (17) teacher training.

- **Models That Work: Compendium of Innovative Primary Health Care Programs for Underserved and Vulnerable Populations, 1996**

  Source: Bethesda, MD, US Department of Health and Human Services, Health Resources and Services Administration, Bureau of Primary Health Care, 223 p., 1996.

  Contact: National Clearinghouse for Primary Health Care Information, 8201 Greensboro Drive, Suite 600, McLean, VA 22102. (703) 821-8955.

  Summary: Models That Work: Compendium of Innovative Primary Health Care Programs for Underserved and Vulnerable Populations, 1996, profiles programs selected by the Models That Work (MTW) Campaign as examples of outstanding grassroots efforts to improve access to primary health care for underserved persons. The purpose of the MTW Campaign is to identify exemplary programs and encourage their replication in other communities. Applicants are judged on five criteria: Community responsiveness, innovation, partnerships and collaboration between participating organizations, evidence of improved access to primary health care services and health-related outcomes, and program replication or sustainability. This compendium describes the 5 winning programs and the 10 special honorees selected in 1996. It also outlines applicant programs in 15 self-selected categories: Business participation, city-level or county-level participation, dental health, farmworker health, health professions program participation, **human immunodeficiency virus** (HIV)/acquired immunodeficiency syndrome (AIDS), the health of the homeless, hospital participation, low-budget programs, managed care, maternal and child health, religious organization participation, rural health, state-level coordination, and substance abuse prevention and treatment. Each description includes the program name, address, telephone and fax numbers, contact person, and information about the services provided, populations served, linkages to other community organizations, and outcomes. The two appendixes contain an order form for additional information and a request form for presentations or workshops.

CHAPTER 8. MULTIMEDIA ON HUMAN IMMUNODEFICIENCY VIRUS

Overview

In this chapter, we show you how to keep current on multimedia sources of information on human immunodeficiency virus. We start with sources that have been summarized by federal agencies, and then show you how to find bibliographic information catalogued by the National Library of Medicine.

Video Recordings

An excellent source of multimedia information on human immunodeficiency virus is the Combined Health Information Database. You will need to limit your search to "Videorecording" and "human immunodeficiency virus" using the "Detailed Search" option. Go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. To find video productions, use the drop boxes at the bottom of the search page where "You may refine your search by." Select the dates and language you prefer, and the format option "Videorecording (videotape, videocassette, etc.)." Type "human immunodeficiency virus" (or synonyms) into the "For these words:" box. The following is a typical result when searching for video recordings on human immunodeficiency virus:

- **Update on Rapid Testing for HIV: CDC National Health Training Network Satellite Broadcast, April 24, 2003**

  Contact: CDC National Prevention Information Network, PO Box 6003, Rockville, MD, 20849-6003, (800) 458-5231, http://www.cdcnpin.org.

  Summary: This videotape discusses the use of the rapid tests for **human immunodeficiency virus** (HIV) antibodies. Results of these tests are available in twenty minutes thus eliminating the need to return for results. The videotape discusses the availability and administration of the tests, the benefits and limitations of rapid tests, implementation and considerations for counseling and testing, including HIV testing for pregnant women and women in labor and the ability to take the test to vunlnerable populations who will not go to a clinic.

- **Occupational Exposure to HIV: Recommendations for PEP**

  Contact: University of Washington Center for Health Education and Research, Northwest AIDS Education and Training Center, 901 Boren Ave Ste 1100, Seattle, WA, 98104-3596, (206) 221-4964, http://depts.washington.edu/nwaetc/.

  Summary: This video provides guidelines for the prevention of occupational exposure to the **human immunodeficiency virus** (HIV)/acquired immunodeficiency syndrome (AIDS). The video examines the Centers for Disease Control Prevention (CDC) guidelines for post-exposure prophylaxis (PEP) treatments available to workers exposed to HIV as well as the role of universal precautions in HIV prevention.

- **Priests With AIDS**

  Contact: American Broadcasting Company, 1330 Ave of the Americas, New York, NY, 10019-5499, (212) 456-7777.

  Summary: This video, for the general public, discusses the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) among Catholic priests in the United States. In the video, 'Father Roger', an unidentified gay priest, talks about his secret life as a gay man of the clergy. He describes how he contracted HIV, and how his homosexuality and medical condition affected his spirituality and position in the priesthood. The video demonstrates the conflicting views among Catholic Church leaders regarding HIV/AIDS epidemiological data. It outlines several new programs within the Catholic Church, which address how to maintain vows of celibacy and deal with sexual issues.

- **The Impact of Stigma on HIV Prevention Programs**

  Contact: CDC National Prevention Information Network, PO Box 6003, Rockville, MD, 20849-6003, (800) 458-5231, http://www.cdcnpin.org.

  Summary: This video, for organizations and individuals working in **human immunodeficiency virus** (HIV) prevention, reviews the impact of stigma on health and HIV prevention efforts and how public health programs may send mixed messages that contribute to stigma. It provides an update on public health resources and innovative strategies to reduce or eliminate stigmatizing attitudes. Viewers will be able to describe the impact of stigma on health and HIV prevention efforts; identify innovative strategies used by HIV prevention programs and other health-related services to reduce or eliminate stigmatizing attitudes; and discuss how public health programs may send mixed messages that contribute to stigma.

- **HIV/AIDS and the Latino Community**

  Contact: National Minority AIDS Council, 1931 13th St NW, Washington, DC, 20009-4432, (202) 483-6622, http://www.nmac.org.

  Summary: This video provides information about the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) epidemic in Latino communities in the United States (US) including 1) how HIV is transmitted; 2) the symptoms of HIV; 3) a review of the epidemiology among Hispanic/Latino communities in the US; 4) identified high risk behaviors practiced by this population; and 5) HIV transmission patterns in Latino communities.

- **Ignorarlo es Fomentarlo: Centros Para el Control y la Prevencion de las Enfermedades: Anuncios de Servicio Publico**

  Contact: CDC National Prevention Information Network, PO Box 6003, Rockville, MD, 20849-6003, (800) 458-5231, http://www.cdcnpin.org.

  Summary: This VHS videotape contains six television public service announcements (PSAs) concerning **human immunodeficiency virus** (HIV) prevention developed for youth and adults. These spots were designed to highlight awareness of the epidemic among Latinos, and were adapted from the Centers for Disease Control and Prevention's (CDC) America Responds to AIDS campaign. The PSAs deliver science-based information that can help Latinos make informed choices about how to reduce their risk of HIV infection. The spots range in content from a how to talk to your children about HIV/AIDS message to a message promoting condom use. All of the PSAs encourage listeners to call the National AIDS Spanish-language Hotline for more information about how they can protect themselves..

- **Pill Burden: Medications and the Role of the Pharmacist**

  Contact: University of Washington Center for Health Education and Research, Northwest AIDS Education and Training Center, 901 Boren Ave Ste 1100, Seattle, WA, 98104-3596, (206) 221-4964, http://depts.washington.edu/nwaetc/.

  Summary: This video examines the role of pharmacists in the formulation of an antiretroviral drug therapy regimen for persons with the **human immunodeficiency virus** (HIV)/acquired immunodeficiency syndrome (AIDS). The video discusses antiretroviral drugs, and how pharmacists can help persons with HIV/AIDS and their physicians to devise a safe and effective drug regimen or to change regimens that are ineffective. The video features two HIV specialists and two HIV-positive clients, one who is beginning an HIV regimen and one whose regimen is failing.

- **High Impact: Substance Abuse and HIV Care**

  Contact: University of Washington Center for Health Education and Research, Northwest AIDS Education and Training Center, 901 Boren Ave Ste 1100, Seattle, WA, 98104-3596, (206) 221-4964, http://depts.washington.edu/nwaetc/.

  Summary: This video examines issues related to the medical care of substance abusers with the **human immunodeficiency virus** (HIV)/acquired immunodeficiency syndrome (AIDS). The video provides information about harm reduction among HIV-positive substance abusers, initiating antiretroviral therapy, possible drug interactions between illicit and anti-HIV drugs, pain management, and ways to promote and support regimen adherence among HIV-positive substance abusers.

- **Undetectable: The New Face of AIDS**

  Contact: Fanlight Productions, 47 Halifax St, Boston, MA, 02130, (617) 524-0980.

  Summary: This video examines how society has dealt with the **human immunodeficiency virus** (HIV)/acquired immunodeficiency syndrome (AIDS) and its treatment of HIV-positive individuals. The video examines the history of HIV/AIDS, how public and healthcare policies regarding HIV/AIDS have changed over time, and how society has coped with and treated individuals with HIV/AIDS since the beginning of this pandemic. It features the personal stories of six HIV-positive individuals of various races and socioeconomic/sociocultural backgrounds and their response to HIV medication regimens.

- **Adults: Coping With HIV and AIDS**

  Contact: Aquarius Health Care Videos, Olde Medfield Sq, 266 Main St Ste 33B, Medfield, MA, 02052-2099, (888) 440-2963, http://www.aquariusproductions.com.

  Summary: This videotape presents information about coping with the **human immunodeficiency virus** (HIV)/acquired immunodeficiency syndrome (AIDS). The video discusses how to get past denial after the initial diagnosis, adherence to the treatment regimen, coping with mental health disorders for both the HIV positive individuals and their caregivers. The video presents information on how to disclose HIV status and to whom, and the benefits of patient support groups and counseling.

- **Update on CDC's Revised Guidelines for HIV Counseling, Testing and Referral, NCHSTP Satellite Broadcast, November 15, 2001**

  Contact: CDC National Prevention Information Network, PO Box 6003, Rockville, MD, 20849-6003, (800) 458-5231, http://www.cdcnpin.org.

  Summary: This video, for policy developers and service providers, includes the key recommendations in the "Revised Guidelines for HIV (human immunodeficiency virus) Counseling, Testing and Referral." It provides information on implementation issues, resources, and recommended readings. At the completion of the broadcast, viewers were able to describe why quality HIV counseling, testing, and referral are critical to prevention and care services.

- **HIV Vaccine PSAs**

  Contact: Johns Hopkins Center for Immunization Research, Johns Hopkins University, Center for Immunization Research, Vaccine Evaluation Unit, 624 N Broadway Rm 117, Baltimore, MD, 21205, (410) 955-7283, http://www.jhsph.edu/cir.

  Summary: This video contains two public service announcements (PSA) that advise urban-dwelling minorities, often the groups hit hardest by the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS), to participate in clinical research to develop a vaccine for HIV/AIDS. The first PSA, 'Doing My Part,' shows an African-American man talking about the effects of HIV/AIDS among men in his community. Because he wants to reduce the incidences of HIV/AIDS and eventually eliminate this pandemic among this population, he has decided to take part in research for the HIV/AIDS vaccine and encourages people like himself to participate for the betterment of their communities. The second PSA, 'Pulse of the City,',depicts children playing in the park representing cities everywhere. It states that cities can only be strong if they are free of diseases, such as HIV/AIDS, that can keep populations from reaching their full potential. Therefore, the viewers are encouraged to participate in clinical research programs to create a vaccine for this pandemic.

- **Cable Positive Public Service Announcements : Reel #10**

  Contact: Cable Positive, East Coast Office, 250 West 54th St Ste 903, New York, NY, 10036-4015, (212) 459-1502, http://www.cablepositive.org.

  Summary: This videocassette contains public service announcements (PSAs) that promote National **human immunodeficiency virus** (HIV) Testing Day on June 27. These PSAs encourage individuals to get tested for HIV and present facts about the transmission and prevention of HIV/acquired immune deficiency syndrome (AIDS). The PSAs also discuss the pain and guilt that HIV-infected individuals may feel if unknowingly pass HIV to their loved ones. The PSAs feature well-known individuals

such as actor Billy Bob Thornton, former head of the NAACP and African-American civil rights leader Julian Bond, poet Maya Angelou, and recording artists Joe McIntyre, Monica, and 'N SYNC.

- **S.T.A.R. Theatre Video Series**

  Contact: NiteStar Program, Saint Lukes Roosevelt Hospital, 1090 Amsterdam Ave #10A, New York, NY, 10025, (212) 523-3599.

  Summary: This video series, designed for adolescents and educators, discusses life issues and growing up in the age of the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) pandemic. The videos portray the lives of adolescents dealing with HIV/AIDS-related issues such as sexual abstinence, safer sex, condom negotiation, peer pressure, decision-making, drug abuse, homosexuality, sexuality, bereavement, and teen pregnancy, and encourage youth to explore and voice their opinions and beliefs. Each video provides a teaching guide to assist facilitators in leading discussions, activities, and question and answer sessions.

- **Death By Denial**

  Contact: Columbia Broadcasting System News, 555 W 57th St, New York, NY, 10019, (212) 975-4321.

  Summary: This video, for the general public, investigates government actions in response to the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) epidemic in the African countries of Zimbabwe, South Africa, and Uganda. Reports from Zimbabwe and South Africa show that the governments of these countries have, for the most part ignored this epidemic. It shows examples of some of the misconceptions held by government officials in these two countries. In contrast, the video shows what efforts Uganda has made to address the HIV/AIDS epidemic in that country including prevention efforts that have included HIV/AIDS education, the provision of HIV antibody testing, and the promotion of safer sex practices. The video discusses the high prices of anti-HIV medications and how it is financially difficult for many developing nations to treat infected individuals. The video states that pharmaceutical companies are refusing to lower their prices for their medications for HIV/AIDS, but are negotiating with a number of African countries and the United Nations for a price that is economically feasible for the companies and the developing nations.

- **Hopes and Fears: Rusti's Story**

  Contact: Aquarius Productions, Incorporated, 5 Powderhouse Ln, Sherborn, MA, 01770, (508) 651-2963.

  Summary: This video, for individuals with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS), presents the true story of a woman faced with the decision of whether or not to take medications for HIV. The video features a woman, Rusti Miller, who has been infected with HIV for five years. Rusti explains how she used to be a drug user and how her drug use caused her to spend time in prison; how she learned that she was HIV-positive and how she initially decided against taking medicine for treatment; she talks about her current life as a mother, future wife, and future grandmother; her job as a housing coordinator for persons with HIV/AIDS; and her fears about starting medical treatment for HIV. At the end of the video Rusti chooses medical treatment to improve the quality of her life and her health.

- **Under the Mupundu Tree**

  Contact: ActionAid, Hamlyn House, Archway, (011) 999999. TALC, PO Box 49, St. Albans.

  Summary: This video, for health and development professionals, addresses the dual epidemic of the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) and tuberculosis (TB) in sub-Saharan Africa, particularly Zambia. It discusses the challenges faced by Zambia in addressing the needs (e.g. medical, material, social, psychological, and spiritual support) of people affected by this dual epidemic. The video describes an innovative home care program, which has been implemented in 23 low-income townships in Zambia's Copperbelt. The program has achieved high coverage at reasonable costs and have integrated TB control into home care for people with HIV/AIDS and their families. The video discusses how 500 mostly women volunteers are key to the success of the program. The video provides information about the impact of the HIV epidemic on the Zambian working class, the use of Directly Observed Therapy Short Course (DOTS) to attack the TB epidemic, and the history and effectiveness of this home care health service. Information on the results of this outreach strategy, volunteer recruitment, health services, benefits to the communities served, and projections for the future of these Zambian communities is provided. The video includes numerous interviews with volunteers and families that they visit.

- **Epidemic Africa**

  Contact: Moxie Firecracker Films, 180 Varcik St Ste 1302, New York, NY, 10014, (212) 620-7727.

  Summary: This video examines the impact of the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) on the African population, particularly on children. The video states that HIV is the worst epidemic to hit Africa and that the majority of the world's children whom have been orphaned by HIV/AIDS live in Africa. The video shows footage of a large orphanage in Africa that is full of children whose parents have died as a result of HIV/AIDS. The video also shows a clip of a family whose child has just died from AIDS. Despite the facts surrounding the child's death and because of the stigma associated with HIV/AIDS, the family claims that he died of malaria. The video also contains a clip of a grandmother who cares for thirty-five grandchildren because ten of her eleven adult children have died of HIV/AIDS. To help care for the children and to provide medical care for the five grandchildren who have been diagnosed with HIV, the woman receives state and international funding. Despite the fact that HIV prevention efforts have been effective in certain regions, social service agencies are still trying to mobilize to meet the needs of children who have been affected by HIV/AIDS. The video features an introduction and epilogue by former Nobel Peace Prize winner, Archbishop Desmond Tutu of South African, and is narrated by actress, Jamie Lee Curtis.

- **Kaiser's PSA's : 'Homeboy' : 'Friends'**

  Contact: Kaiser Family Foundation, AIDS Public Information Project, 1450 G Street NW Ste 250, Washington, DC, 20005, (800) 656-4533, http://www.kff.org.

  Summary: This video contains public service announcements (PSAs) that advise the viewers to use condoms to prevent the transmission of the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) and sexually transmitted diseases (STDs). The PSAs discuss the epidemiology of HIV/AIDS and STDs and shows

the fear that one, who is knowledgeable of how to avoid contracting these diseases, may experience after having unprotected sex influenced by alcohol or drugs.

- **Sister's Keeper**

  Contact: National Association for the Advancement of Colored People, National Health Committee, 4805 Mount Hope Dr, Baltimore, MD, 21215, (410) 358-8900, http://www.naacp.org.

  Summary: This video, for African American women, illustrates the impact of the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). The video contains interviews with women whose lives have been impacted by HIV/AIDS as grandmothers, partners, and wives. It examines the risks associated with breastfeeding and substance abuse, perinatal transmission of HIV, HIV testing, and the need for women to protect themselves and their partners by using condoms during sex.

- **God Cares, We Care : Congregations Concerned About HIV/AIDS**

  Contact: Presbyterian Church USA, Presbyterian AIDS Network, 100 Witherspoon St Rm 3041, Louisville, KY, 40202-1396, (800) 524-2612, http://www.pcusa.org.

  Summary: This video discusses the role of the church in the prevention of the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) and in the care for those persons with this disease. The video provides personal anecdotes from persons with HIV/AIDS and their families about the emotional effects of living with HIV/AIDS. It emphasizes the need for the church to express compassion towards persons with HIV/AIDS and asserts that this can be achieved only through education and volunteerism. It states that ecclesiastical and congregational HIV/AIDS education is necessary to break down any discriminatory attitudes and misconceptions held in the church. The video examines the positive spiritual aspects of volunteerism in HIV/AIDS-related community services and the church's direct role in care, counseling, and support for persons with HIV/AIDS. Volunteers from congregations discuss the personal and spiritual growth they have undergone because of their HIV/AIDS-related community services.

- **Preventing Communicable Diseases: Colds, Flu, AIDS, STDs (Condom Version)**

  Contact: AIMS Multimedia, 9710 DeSoto Ave, Chatsworth, CA, 91311-4409, (818) 773-4300, http://www.aims-multimedia.com.

  Summary: This video, for adolescents, provides information on preventing communicable and sexually transmitted diseases (STDs). It explains how bacteria and germs enter the human body and how the immune system has the ability to fight germs and bacteria. It states that a person's immune system works best if they do not abuse substances and if they take good physical care of themselves. It provides proper sanitation and hygiene tips and examines the causes, transmission, and prevention of colds and the flu; it provides information on STDs and how they are transmitted; it describes how to use condoms properly to help prevent STDs; and it discusses the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS), its transmission and prevention. The video stresses that sexual abstinence is the best way to prevent the transmission of STDs such as HIV.

- **Protect Yourself So You Can Protect Others**

  Contact: Resource, 615 Clay Lane, State College, PA, 16801, (814) 237-6462.

Summary: This video, for fire fighters and other safety professionals, discusses hepatitis B, hepatitis C, and the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). It examines common attitudes towards personal protection equipment (PPE) such as gloves. It shows how occupational exposures to these diseases can be avoided by following universal precautions and by using gloves and other PPE. The video describes the exposure reporting process and stresses the importance of following common workplace procedures and workers' legal rights to keep workers' medical status confidential.

- **Friends for Life Living With AIDS**

  Contact: Walt Disney Company, 500 S Buena Vista, Burbank, CA, 91521, (818) 560-1000.

  Summary: This videocassette documents the lives of children living with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). The video includes children telling their stories of how they live and cope with HIV/AIDS. Many of the children explain how they contracted the virus and how they handle the daily discrimination from other children and adults. These HIV-positive children express their need for acceptance and educate other children and adolescents about HIV/AIDS. The HIV-positive children express their emotions concerning HIV/AIDS and death. HIV-negative children tell of their views concerning HIV/AIDS before and after learning about this infection/disease. The video provides general information about HIV transmission and prevention.

- **The Positive Workplace: Managing HIV at Work**

  Contact: National AIDS Fund, 1400 Eye St NW Ste 1220, Washington, DC, 20005-2208, (202) 408-4848, http://www.aidsfund.org/.

  Summary: This video, designed for employers and employees, discusses the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) in the workplace. The video discusses HIV transmission, how HIV affects the immune system, how HIV develops into AIDS, HIV prevention, and recommendations on avoiding occupational exposures to HIV. It reviews important ethical and legal issues related to HIV-positive individuals in the workplace. The video concludes with a series of short skits and encourages discussion periods between vignettes.

- **Safe Sex: Girl Chat**

  Contact: Pyramid Media, PO Box 1048, Santa Monica, CA, 90406-1048, (310) 828-7577, http://www.pyramidmedia.com.

  Summary: This video, for young women, examines their views on relationships and the prevention of the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). The video shows several women discussing past relationships and safe and unsafe sexual experiences; it examines how dating has changed in the age of HIV/AIDS and the kinds of commitment women are making when they have sex; and it discusses HIV/AIDS and other sexually transmitted diseases (STDs), their modes of transmission, and how to prevent these infectious diseases through the practice of sexual abstinence or safer sex with condoms. It makes recommendations about how to talk to partners about the decision to be abstinent or to practice safer sex.

- **The Female Condom : Progress Around the World**

  Contact: Female Health Company, 875 N Michigan Ave Ste 3660, Chicago, IL, 60611, (800) 275-6601, http://www.femaleheatlh.com.

  Summary: This video, for health professionals and organizations, discusses the use of the female condoms in the prevention of the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). The video discusses reasons for using the female condom such as it gives women more control when protecting themselves against HIV/AIDS, and it increases safer sex practices as compared to the male condom. The video profiles a community outreach program in Philadelphia, which offers free female condoms and educational materials to educators. It discusses the United Nations Joint Program on HIV/AIDS' (UNAIDS) efforts to support the productivity of and accessibility to female condoms through partnerships with female condom manufacturers and female condom promotion programs.

- **I'm Having a Baby**

  Contact: New York Department of Health, AIDS Institute, Room 359, Corning Tower, Albany, NY, 12237, (518) 486-1383.

  Summary: This video, for women, discusses the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). It tells the story of a woman, Angela, who learns she is pregnant and is advised to get tested for HIV. The story provides information on high-risk behaviors associated with HIV transmission, how condoms can be used to help prevent HIV, the importance of HIV antibody testing, how to communicate with partners about practicing safer sex behaviors and getting tested for HIV, and the physical and emotional consequences associated with contracting HIV.

- **The Sex Talk: Exclusively Abstinence**

  Contact: Legacy Resource Group, PO Box 700, Carlisle, IA, 50047, (515) 989-3360, http://www.members.aol.com/legacyrgl/legacy.html.

  Summary: This video, for adolescents, parents, and educators, discusses the benefits of practicing sexual abstinence before marriage. It introduces adolescents to the possible consequences of having premarital sex including pregnancy, the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS), and other sexually transmitted diseases (STDs). It examines what it means to be a teen parent; it discusses HIV/AIDS and other STDs transmission and their possible long-term physical and emotional effects; it describes ways individuals can show affection without sex; and it provides information about how to cope with and overcome peer, media, and social pressures to have sex. The video discusses the characteristics of a healthy relationship and how abstinence helps to build them into a safe dating relationship.

- **Knowing the Facts**

  Contact: University of Connecticut, Center for HIV Intervention and Prevention, 406 Babbidge Rd U-20, Storrs, CT, 06269-1020, (860) 486-5917, http://www.uconn.edu.

  Summary: This videocassette presents information to the general public, including adolescents, about the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). HIV is a virus that attacks the immune system, weakens it, and develops into AIDS. The video identifies the body fluids in which HIV is carried and the ways by which it is transmitted from person to person. Sexual abstinence is the

only sure way to prevent HIV while safer sex with condoms can only help to prevent viral transmissions. The video classifies a number of sexual practices into high-, low-, and no-risk categories for the transmission of HIV/AIDS. The viewers should always avoid substance abuse because it can affect decision-making capabilities. The video advises viewers always to use condoms during sexual encounters and tells viewers where they can obtain prophylactics. It also recommends getting tested approximately six months after practicing a risky behavior.

- **Creando Nuestro Futuro: Apego a los Medicamentos del VIH/SIDA**

  Contact: University of Washington MedEd Media, Campus Box 359932, Seattle, WA, 98195, (206) 685-9680.

  Summary: This videotape makes recommendations regarding adherence to medical regimens for the **human immunodeficiency virus** (HIV)/acquired immunodeficiency syndrome (AIDS). The video provides information about each of the different categories of antiretroviral medications, their effect on the body, and their possible adverse reactions. It suggests ways for HIV-positive individuals to practice adherence and what they should do if they fail to adhere to the regimen.

- **Brothers...To Thy Own Self Be True**

  Contact: Motivational Educational Entertainment Productions, HIV Campaign, Community Network, 340 N 12th St Ste 503, Philadelphia, PA, 19107, (215) 829-0558, http://www.meeproductions.com.

  Summary: This video, for African-American and Hispanic men who have sex with men (MSM), provides information about the impact of the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). The video examines the epidemiology of HIV/AIDS among minority MSM and how this infectious disease has added to the discrimination against minority MSM. Several HIV-infected and uninfected MSM discuss what they have done to promote public awareness of HIV/AIDS.

- **Just Thought You Oughta Know PSAs**

  Contact: Medical Institute for Sexual Health, PO Box 162306, Austin, TX, 78716-2306, (512) 328-6268, http://www.medinstitute.org.

  Summary: This video, for adolescents and young adults, provides information on the prevention of the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS), other sexually transmitted diseases (STDs), and pregnancy. The video contains public service announcements (PSAs) designed for mass viewing via television broadcasts. It illustrates the disadvantages of using condoms and how to avoid peer pressure. The video stresses that sexual abstinence is the only way to completely prevent HIV/AIDS, STDs, and pregnancy.

- **Teens and Chastity: Public School Program**

  Contact: Easton Publishing Company Incorporated, PO Box 1064, Jefferson City, MO, 65102, (888) 635-0609, http://www.eastonpublishing.com. The Center for Learning, PO Box 910, Villa Maria, PA, 16155, (800) 767-9090.

  Summary: This video, for adolescents, promotes sexual abstinence. It examines the physical and emotional consequences of sex, pregnancy, and sexually transmitted diseases (STDs); it provides statistics showing the incidence rates of pregnancy, STDs, abortion, and the **human immunodeficiency virus** (HIV)/acquired immune deficiency

syndrome (AIDS) among adolescents; it reviews the effectiveness of condoms against pregnancy and STDs; it defines sexual abstinence; and it makes recommendations on dealing with peer pressure. The video highlights the physical and emotional benefits of sexual abstinence and outlines a plan to help teens remain sexually abstinent.

- **Steps Toward Health : Second in a Series : HIV Treatment Issues**

  Contact: GlaxoSmithKline, Oncology/HIV, PO Box 13398, Research Triangle Park, NC, 27709, (919) 248-2100, http://www.imgw.com/forms/GWcoform.html.

  Summary: This video discusses issues concerning the medical treatment of person with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). In the video, persons living with HIV/AIDS discuss their emotional responses when learning their serostatus. It defines viral load and dispels some common myths concerning the medical treatments available for HIV/AIDS. The video emphasizes the importance of changing one's sexual and social behaviors in order to live a long life with the disease. According to the video, another important component of living with HIV/AIDS is medical treatment in which one learns about HIV/AIDS and maintains a close relationship with one's physician. It identifies the types of therapeutic drugs involved in the medical treatment of HIV/AIDS and the side effects of the medications. The video stresses the importance of patient adherence to the drug regimens and lists the reasons why adherence is so important to a person living with HIV/AIDS.

- **Before It's Too Late**

  Contact: Aquarius Productions, Incorporated, 5 Powderhouse Ln, Sherborn, MA, 01770, (508) 651-2963.

  Summary: This video, which is a documentary, discusses the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) and how it affects the people who have contracted it, and presents interviews and performances by the AIDS Theater Project, which features actors with HIV/AIDS who perform a play about AIDS for high school and college students. The video supplies the viewers with the personal anecdotes of HIV-positive persons who share how they found out their serostatus and how the disease has affected their lives. It explains the window period for the formation of HIV antibodies in the immune system after the initial infection. It identifies the symptoms of some opportunistic infections such as kaposi's sarcoma (KS). The video profiles volunteer organizations that provide services to persons with HIV/AIDS or raise public awareness about HIV prevention, and a hospital program that provides comprehensive psychosocial and physical care for adolescents who are HIV-positive.

- **Taking Control : Adherence and HIV/AIDS Medication : Provider Version**

  Contact: Northwest AIDS Education and Training Center Program, University of Washington, 1001 Broadway Ste 217, Seattle, WA, 98122-4304.

  Summary: This videocassette, designed for health professionals, discusses treatment adherence by patients with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). The video defines patient adherence and examines how patients can fit adherence practices into their lives. The consequences of non-adherence, particularly the development of multidrug-resistant HIV/AIDS and its emotional impact, are discussed. Some of the barriers to patient adherence and treatment are identified. These barriers include fear of a doctor's judgement by patients who fail to remain adherent, unsupportive doctors, the rigorous dosage schedules

demanded by many contemporary drugs, fear or weariness of side effects, weight gain or loss, access to food to take with medications, mental health issues, substance abuse, and homelessness. Adherence can be improved through clinic support for patients; the development of more flexible, individualized regimens; effective case management; and peer support. The video includes clips of HIV-positive individuals describing the benefits of treatment adherence.

- **Sharing Stories : Getting the Most Out of Your Therapy With Crixivan (Indinavir Sulfate)**

  Contact: Merck and Company, PO Box 4, West Point, PA, 19486-0004, (215) 652-5000, http://www.merck.com.

  Summary: This video, through the personal anecdotes of persons with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS), explains the therapeutic drug crixivan and its treatment regimen. The video examines the way that crixivan has affected the lives HIV-positive persons. It explains how HIV affects the immune system and how crixivan, a protease inhibitor, helps to prevent the virus from replicating. The video advises the viewers to maintain adherence to their drug regimen in order to prevent the development of multidrug-resistant. It emphasizes the importance of exercise and a balanced diet and explains dosing information for crixivan. The video identifies some of the side effects of crixivan.

- **Just Like Me**

  Contact: University of Connecticut, Center for HIV Intervention and Prevention, 406 Babbidge Rd U-20, Storrs, CT, 06269-1020, (860) 486-5917, http://www.uconn.edu.

  Summary: This video, for adolescents and young adults, shows the impact of the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) on young people. It contains the personal stories of several individuals in their teens and early twenties who contracted HIV during high school. These individuals recount what their lives were like before they became HIV-positive, how they believed they contracted the virus, and how HIV/AIDS has affected their lives. The participants explain how their life plans have been forever altered and lament about how they will not get to do many things in their life. The stories provide information on HIV transmission and HIV prevention by practicing sexual abstinence and using condoms.

- **Tuberculosis 2000: Fundamentals of Clinical Tuberculosis and Tuberculosis Control: Part III**

  Contact: Francis J Curry National Tuberculosis Center, 3180 18th St Ste 101, San Francisco, CA, 94110-2042, (415) 502-4600, http://www.nationaltbcenter.edu.

  Summary: This video, for health professionals, examines issues related to the medical treatment of tuberculosis (TB) in children and persons with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS), as well as topics related to general TB prevention. It examines the challenges involved in treating adults and children with HIV/AIDS and TB and what to consider when treating children (i.e., dosage procedures and patient adherence); and it identifies current public health measures, including public education and the screening of high-risk groups in order to control the spread of TB. It provides information about and makes recommendations for current and future healthcare policies and policy development for TB control.

- **Vinetas de Discusion Sobre VIH/SIDA en el Lugar de Trabajo. [Workplace HIV/AIDS Discussion Vignettes]**

  Contact: American Red Cross National Headquarters, American Red Cross, National Headquarters, Health and Safety Services, Office of HIV/AIDS Education, 8111 Gatehouse Rd 6th Fl, Falls Church, VA, 22042-1203, (703) 206-6707, http://www.redcross.org/.

  Summary: This video, for employees and employers, presents a number of situations related to working with individuals infected or affected by the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). The video encourages viewers to discuss their feelings about HIV/AIDS. The six vignettes examine HIV transmission, how to avoid HIV transmission while applying first aid to a co-worker, and workplace discrimination.

- **Stakes Are High**

  Contact: University of Connecticut, Center for HIV Intervention and Prevention, 406 Babbidge Rd U-20, Storrs, CT, 06269-1020, (860) 486-5917, http://www.uconn.edu.

  Summary: This video, for adolescents, promotes the prevention of the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) and other sexually transmitted diseases (STDs). It examines the basic facts about HIV and other STDs through the stories of two groups of teens. It provides information on proper condom use and makes recommendations regarding condom negotiation skills. The video demonstrates how to diffuse potentially risky or tempting situations through partner communication.

- **What You Don't Know About Tuberculosis... Could Kill You**

  Contact: Texas Department of Health, Tuberculosis Elimination Division, 1100 W 49th St, Austin, TX, 78756-3199, (512) 458-7447, http://www.tdh.state.tx.us/tb/default.htm.

  Summary: This video, for incarcerated person, discusses tuberculosis (TB). It identifies populations at risk for TB, methods of transmission, the tuberculin skin test, and the symptoms of active TB. It differentiates between active TB and latent TB infection (LTBI). The video discusses available treatments for tuberculosis and their possible side effects; it reviews how individuals with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) and TB are treated; and stresses the importance of patient adherence to TB medicines.

- **Living With AIDS : Dispelling the Myths of How Long People Live With AIDS**

  Contact: Aquarius Productions, Incorporated, 5 Powderhouse Ln, Sherborn, MA, 01770, (508) 651-2963.

  Summary: This video documents the lives of persons with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) who have had the virus for 8, 12, and 15 years; how this infection/disease has affected their lives; and methods, thoughts, and support these individuals have employed to maintain their health. The video examines the emotion of guilt commonly experienced by mothers who pass HIV on to their infants through perinatal transmission, and identifies high-risk behaviors associated with the spread of HIV/AIDS. It dispels the myth of immortality sometimes felt by adolescents and adults. It also explains the general effects of the infection/disease, side effects of anti-HIV medications, and the effects of taking

these medications on the daily lives of HIV-positive persons. The video discusses the benefits of counseling for persons who have HIV/AIDS and their families.

- **101 Ways to Make Love Without Doin' It**

  Contact: Education Training and Research Associates, PO Box 1830, Santa Cruz, CA, 95061-1830, (800) 321-4407, http://www.etr.org.

  Summary: This video presents 101 ideas for demonstrating affection without engaging in sexual relations, thereby promoting sexual absteinence as ameans of preventing unwanted pregnancies and the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) and other sexually transmitted diseases (STDs). In a compilation of fast-paced interviews, dialogues, and vignettes, adolescents and young adults offer their creative suggestions for showing love and commitment without facing the risks involved with premarital sex.

- **Abstinence**

  Contact: Syndistar Incorporated, 5801 River Rd, New Orleans, LA, 70123-5106, (504) 733-9887, http://www.syndistar.com.

  Summary: This video provides information about the advantages of sexual abstinence. The video discusses the facts about abstinence and the consequences of adolescent pregnancy, the **human immunodeficiency virus** (HIV)/acquired immunodeficiency syndrome (AIDS) and other sexually transmitted diseases (STDs). The video also includes two vignettes in which a teen mother and father explain the difficulties of teen parenthood and advise young people to postpone sex. The leaders' guide outlines how to use this video in the context of a small group setting or in a classroom.

- **Reasons to Care: The Many Faces of HIV**

  Contact: American Red Cross National Headquarters, American Red Cross, National Headquarters, Health and Safety Services, Office of HIV/AIDS Education, 8111 Gatehouse Rd 6th Fl, Falls Church, VA, 22042-1203, (703) 206-6707, http://www.redcross.org/.

  Summary: This videorecording makes the point that the **human immunodeficiency virus** (HIV) can affect everyone. It uses a mix of narration, personal stories by Persons with AIDS (PWA's), and interviews with health professionals to make points about the need for compassion, caring, and HIV prevention. The first PWA to speak is Jose Perez, who has had HIV infection for four years but continues to hold down a productive job with an Hispanic Health Organization. Perez' presentation makes points about the spectrum of HIV illness. Next, Pat, who has been living with Acquired immunodeficiency syndrome (AIDS) for a year, talks about the support he receives from his housemates. After outlining the methods of HIV transmission, the videorecording cuts to an interview with Candy Fleming, a Black woman who formerly practiced risky behaviors, and who now works in a street outreach program with the Whitman-Walker Clinic in Washington, D.C. Ledia Martinez, an HIV/AIDS educator, provides an extensive explanation of condom use. Narration points out that women are increasingly at risk, and that many of them don't know they are infected until they give birth to an infected child. Ellen, whose husband died of AIDS, talks about her struggle to maintain her health and raise her 7-year-old son, Andrew, who is not infected. Louis Sullivan, former Secretary of Health and Human Services, speaks of the need for support from the community and church; Gordon, a Black man who discovered he was HIV-positive when hospitalized for pneumonia, discusses his feelings of embarrassment, shame, and

withdrawl after his diagnosis. Gordon lost his job playing in a gospel band, and now composes songs and serves as a peer educator. The final story is told by Cheryl, a 16-year-old former Injecting drug user (IDU). A runaway who supported herself through prostitution and petty crime, Cheryl went straight and learned to cope with her diagnosis a year ago when she was sent to a youth detention facility. The videorecording concludes by talking about the disproportionate effect that AIDS has on the Black community, and the need for churches and parents to take a strong role in education.

- **Changing Attitudes: Union Members Talk About AIDS**

  Contact: George Meany Center for Labor Studies, HIV/AIDS Workplace Education Program, 10000 New Hampshire Ave, Silver Spring, MD, 20903, (301) 431-6400, http://www.georgemeany.org. Service Employees International Union, 1313 L St NW, Washington, DC, 20005, (202) 898-3200.

  Summary: This videorecording looks at how several unions deal with the problem of Acquired immunodeficiency syndrome (AIDS). It opens with a number of people telling their thoughts about AIDS; some show knowledge of the subject, while others don't. It then uses interviews with union members with **human immunodeficiency virus** (HIV) infection and with union officials and AIDS educators to present its message. The Persons with AIDS (PWA's) talk of their desire to keep working and their interest in educating other union members. Educators and officials talk of the need to educate workers and to help PWA's keep their jobs. The videorecording addresses the topics of fear and discrimination, pointing out that PWA's are in need of support and caring from their friends and co-workers. It looks at the need for infection control and discusses health-care workers' need for support after needlestick injuries. The videorecording also examines the need for strong medical plans and for policies that protect the rights of PWA's.

- **Peer Education Not Fear Education**

  Contact: AIDS Community Television, 12 Wooster St, New York, NY, 10013.

  Summary: This video discusses the benefits of sexuality education and contrasts it to abstinence-based education as a means of preventing the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) among adolescents and young adults. The video presents adolescents discussing sex as a natural act and states that adolescence is a time of sexual exploration. It shows clips of videos and television interviews in which abstinence-based education is explained by religious leaders and parochial school teachers. Peer educators examine the meaning of sexual abstinence and the effectiveness of condoms. The peer educators offer their opinions on the benefits of sexuality education and state that condom efficacy can be improved if teens are taught how to use them. Persons who advocate peer sexuality education for adolescents state that abstinence-based education is popular because it plays on the fears of parents and educators, whereas sexuality education addresses issues based on contemporary realities. Adolescents identify the persons from whom they have learned the most about HIV/AIDS, sexuality, and sex. The peer educators discuss the reasons why they think it is important for teens to learn about sex, sexuality, and HIV/AIDS from other teens. The video also looks at the controversies around what some view as fear-based abstinence-only curricula, which exclude birth control and disease prevention information, that were implemented in Jacksonville, FL and Vista, CA. Various professionals in the fields of sex education and reproductive issues discuss the legal challenge to the adoption of the curriculum in Jacksonville, FL.

- **Journey Home : First Nations Living With HIV/AIDS**

  Contact: Gryphon Productions, PO Box 93009, 5331 Headland Dr, W. Vancouver.

  Summary: This videocassette examines how Native Americans in Canada are dealing with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). The video, through personal anecdotes of Native Americans with HIV/AIDS, explains the importance of spirituality and community involvement in medical treatments. It discusses the incorporation of traditional medicines and healing techniques by Native Americans into their HIV/AIDS treatments. The video focuses on the need for support from the Native-American community for its ill members and shows how some nations are providing support. The video explores the cultural factors that affect the treatment of HIV-positive Native Americans. The video includes a discussion guide to assist facilitators in leading a discussion of the video.

- **Learning to Care: An Introduction to HIV Psychiatry**

  Contact: Canadian Public Health Association, Canadian HIV/AIDS Clearinghouse, 400-1565 Carling Ave Ste 400, Ottawa, (613) 725-3434, http://www.cpha.ca. Canadian Psychiatric Association, 260-441 MacLaren St, Ottawa, http://cpa.medical.org.

  Summary: This video, for mental health professionals, examines treating individuals with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) for psychiatric disorders. The objectives of the video are to review the basic principles of psychiatric intervention with individuals living with HIV/AIDS, including drug therapy and psychotherapy strategies; to build on the viewer's existing knowledge; and to suggest ways of augmenting specific learning. The video features four patients affected by HIV/AIDS to illustrate how common psychiatric disorders and their treatment differ compared to regular psychiatric patients. It covers anxiety disorder, mood disorder, mania/bipolar disorders, psychosis, delirium, cognitive/motor disorders, and bereavement. It provides suggestions for specific psychotherapy and medications for each disorder.

- **Sexuality Education for the 21st Century**

  Contact: Sexuality Information and Education Council of the US, Public Policy Office, 1638 R St NW, Washington, DC, 20009, (202) 265-2405.

  Summary: This videocassette informs the audience about sexuality education in schools as a means of helping to prevent pregnancy, the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS), and other sexually transmitted diseases (STDs). Comprehensive sexuality education can help children develop into sexually healthy adults because human sexuality is taught in an age appropriate manner beginning in kindergarten and running through high school. Public opinion polls show that the majority of parents want comprehensive sexuality education for their children and most states support or require that it be taught; however, this type of education is only taught to a small percentage of children nationwide. Many people who are not in favor of comprehensive sexuality education fear that it encourages children and adolescents to engage in sexual intercourse. However, the World Health Organization (WHO) has conducted studies that show that comprehensive sexuality education may actually delay sex in most instances. Comprehensive sexuality education consists of several educational elements concerning human biology and anatomy, sexual health, sexual behavior, reproduction, relationships, and sexuality and culture.

- **Relapse and HIV Risk**

  Contact: Hazelden Foundation, Hazelden Renewal Center, PO Box 176, Center City, MN, 55012-0176, (651) 213-4000, http://www.hazelden.org.

  Summary: This video provides information about the relationship between a substance abuse relapse and the **human immunodeficiency virus** (HIV)/acquired immunodeficiency syndrome (AIDS). The video discusses how substance abuse puts individuals at risk for HIV; how to avoid relapses as well as HIV transmission; and how to garner peer support to prevent substance abuse relapses, to prevent HIV, and to be tested for HIV.

- **America at Work: Living with HIV**

  Contact: American Red Cross National Headquarters, American Red Cross, National Headquarters, Health and Safety Services, Office of HIV/AIDS Education, 8111 Gatehouse Rd 6th Fl, Falls Church, VA, 22042-1203, (703) 206-6707, http://www.redcross.org/.

  Summary: This videorecording is for use in a workplace education program about Acquired immunodeficiency syndrome (AIDS) and **human immunodeficiency virus** (HIV) infection. The major portion of the videorecording provides education about HIV and the workplace. Narrated by James Earl Jones, this segment discusses HIV transmission, its prevention through condom use, and how American workplaces are coping with HIV-related discrimination. A large portion of this segment features interviews with two persons with HIV infection, their co-workers, and their supervisors. The six remaining tracks use brief dramatizations to address issues of discrimination, casual contact transmission, fear, first aid, and HIV transmission. Their titles are Todd and Cindy, Teamwork, Restaurant Kitchen, Fran Returns to Work, Mother and Son, and Happy Hour.

- **Saying No to AIDS**

  Contact: Altschul Group Corporation Educational Media, 1560 Sherman Ave Ste 100, Evanston, IL, 60201, (847) 328-6700, http://www.agcmedia.com.

  Summary: This video, for adolescents, discusses sexual abstinence as a means to prevent the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS) and other sexually transmitted diseases (STDs). It stresses that self-control and the ability to resist peer pressure are very important attributes. Teens interviewed provide information about how they handle peer pressure from friends or partners to have sex or to engage in drug use. The video explains how to diffuse peer pressure by asking questions and identifying situations that could lead them to contract HIV or another STD.

- **Crosslink: HIV/AIDS Forum #5 - Everybody's Business HIV/AIDS on Campus**

  Contact: Media Associates, Incorporated, PO Box 5747, Springfield, VA, 22150-5747, (703) 379-8160.

  Summary: This videorecording presents a teleconference workplace training program that addressed the issues of Acquired immunodeficiency syndrome (AIDS), and its etiologic agent the **human immunodeficiency virus** (HIV), on the campuses of community colleges nationwide. Over 500 sites participated in a workplace training program given by Russ Williams, American Red Cross trainer, which specifically looked at the issues that would be encountered by community colleges, their staff, and

students. An abbreviated version of the ARC video "America At Work Living With HIV", with James Earl Jones is shown. Two HIV-positive individuals, Christina Lewis and Jim Kirby, share their experiences with HIV. A third video segment illustrates the different responses "Fran" receives when she returns to her work after an AIDS-related absence. The videorecording continues with a discussion of reasonable accommodations, the impact of the Americans with Disabilities Act, and how colleges can treat an HIV-positive individual in terms of a disability. The teleconference is then opened for questions and answers from participating sites, and concludes with a mention of referral numbers for further information.

- **The AIDS Issue: Guidelines for the Foodservice Manager; a Videotape for Management**

  Contact: National Restaurant Association, 1200 17th St NW, Washington, DC, 20036-3097, (202) 331-5900, http://www.restaurant.org.

  Summary: This videorecording, narrated by Ron Sarasin of the National Restaurant Association, deals with how Acquired immunodeficiency syndrome (AIDS) can affect food-service establishments. Sarasin says that the public has many erroneous ideas that **human immunodeficiency virus** (HIV) can be transmitted through food, and that panic often results when rumors surface about HIV-infected people working in a restaurant. He gives an example of a potential problem: Employees begin circulating a rumor that the chef has AIDS, and it spreads to the customers. The customers call the restaurant owner in a panic, and he or she then receives a call from a newspaper. Because the owner is caught offguard, he or she tells the newspaper no comment. The restaurant then loses business because of the rumors. To prevent problems, Sarasin says, restaurant owners should become prepared to deal with such a situation before it arises. First, the National Restaurant Association suggests becoming familiar with the legal status of an employee with AIDS. Sarasin explains that in most states, AIDS is considered a handicap, and employment discrimination is unlawful. Medical evidence has shown there is no danger of a customer or another employee contracting HIV through casual contact in a restaurant. Restaurants should also follow a four-step approach to dealing with AIDS: One, assemble an AIDS crisis team, including a lawyer and a spokesperson; two, have them develop an AIDS policy statement which protects the rights of an employees infected with AIDS; three, educate employees about the lack of danger from casual contact transmission; and four, develop a strategy for communicating with the media.

- **Haven**

  Contact: North Eastern Wisconsin In School Telecommunication, Cooperative Educational Services Agency 7, 2420 Nicolet Dr, Green Bay, WI, 54311-7001, (800) 633-7445, http://weba.uwgb.edu/newist.

  Summary: This videorecording, narrated by Tom Pederson, focuses on the experiences of a few Injecting drug users (IDU's) and how they contracted **human immunodeficiency virus** (HIV) and Acquired immunodeficiency syndrome (AIDS). It describes the ways in which HIV/AIDS is transmitted including: 1) IV needle sharing; 2) breastfeeding 3) mother to fetus; and 4) infected sex partners. It is said that using condoms and the sterilization of needles lowers the risk of contracting HIV/AIDS. There are many community health service providers out there who want to help IDU's, it says.

- **AIDS: A Rural Perspective**

  Contact: Montana State University, Continuing Education for the Health Professional, 318 Montana Hall, Montana State U, Bozeman, MT, 59717, (406) 994-4930.

  Summary: Set against the backdrop of a typical Montana landscape, this videorecording addresses the issue that Acquired immunodeficiency syndrome (AIDS), and its etiologic agent, the **human immunodeficiency virus** (HIV) affects not only residents of urban areas but those in rural communities as well. It discusses the fact that the challenges facing rural communities may be greater than those facing urban communities as individuals return to their family homes to live with HIV. Three health educators offer ideas and techniques for the rural communities to deal with this crisis. An HIV-positive individual, and also the parents of a person who died from AIDS share their experiences with their communities and the reactions they experienced when they shared this with them. The videorecording ends with the emphasis that effective community response involves all members of the community. The accompanying study guide provides the facilitator and discussion leader of the program with many options. Handouts and State and national resources are included in the Appendix.

- **A Visible Symbol. Translated title**

  Contact: NAMES Project Foundation, AIDS Memorial Quilt, 310 Townsend St Ste 310, San Francisco, CA, 94107, (415) 882-5500, http://www.aidsquilt.org.

  Summary: This videorecording presents an overall view of The Names Project's AIDS Memorial Quilt, which honors the more than 44,000 people who have died from Acquired immunodeficiency syndrome (AIDS). It explains that the quilt project began in June 1987, inspired by a candlelight march in San Francisco two years earlier where people taped the names of friends and loves ones to walls. The organizers of The Names Project saw the creation of the six-by-six foot panels as a positive step in remembering those who died in the **human immunodeficiency virus** (HIV) epidemic. Now, thousands of volunteers organize sewing shops and centers around the world to help create the panels, and they also organize displays of the quilt. The panels toured more than 20 cities in the spring of 1988, the videorecording says, with a larger tour planned for 1989. It concludes with footage from the October 1988 display of the entire 8,288-panel quilt in Washington, D.C. The display covered an area the size of eight football fields and had six miles of walkway fabric between panels; a reading of the names from the quilt took more than 11 hours. The same videorecording, with Spanish narration, follows the English version.

- **AIDS Project Los Angeles PSA: 11 Spots Tied**

  Contact: Dubs, Incorporated, 1200 N Highland Ave, Hollywood, CA, 90038, (213) 461-3726.

  Summary: This videorecording consists of 11 public service announcements (PSA's) that urge individuals with the **human immunodeficiency virus** (HIV) or Acquired immunodeficiency syndrome (AIDS) to contact the AIDS Project Los Angeles (APLA) for information and support. A series of celebrities, including Natalie Cole, Liza Minnelli, Aaron Neville, John Goodman, Shirley McLaine, Clint Black, and Cindy Crawford are featured delivering this message on PSA's that address general audiences; African Americans; gay men; and adolescents. Miss America, Leanza Cornett, appears on one PSA; Lyle Lovett and Naomi Judd are on a PSA appealing to country-music fans; and Marlee Matlin appears on one PSA signing the message for deaf viewers.

- **AIDS and Chemical Dependency**

  Contact: Hazelden Foundation, Educational Materials, PO Box 176, Center City, MN, 55012-0176, (651) 213-4000, http://www.hazelden.org.

  Summary: This is a videorecording of a lecture given by a physician to an audience of health professionals, explaining the relationship between chemical dependency and Acquired immunodeficiency syndrome (AIDS). Both drug addiction and alcoholism increase the risk of **human immunodeficiency virus** (HIV) transmission, either by needle sharing or by decreased awareness of safer sexual practices. In addition, they weaken the immune system, increasing opportunistic infections in HIV-positive persons. The use of antibody testing to identify HIV-positive persons and get them into treatment programs which strengthen their immune systems is also discussed.

- **Les Visages Du SIDA.. [The Faces of AIDS]**

  Contact: Media for Development International, PO Box 281, Columbia, MD, 21045, (410) 964-0037.

  Summary: In this videorecording, individuals from Cameroon and Zimbabwe describe their personal experiences with **human immunodeficiency virus** (HIV) and Acquired immunodeficiency syndrome (AIDS). They recount the effects of the disease on themselves, their families, and their friends. Cultural obstacles, such as abandonment and rejection, are cited as major problems in coping with HIV. The need for family and community support is emphasized.

- **AIDS in Your School**

  Contact: Altschul Group Corporation, 1560 Sherman Ave Ste 100, Evanston, IL, 60201, (847) 328-6700.

  Summary: The program is a general presentation on Acquired immunodeficiency syndrome (AIDS). The people are real, the information is basic, and it conveys all aspects of the disease. It includes the following: Dr. Mervyn Silverman, president of the American Foundation for AIDS Research (AmFAR), explains how AIDS affects the immune system and defines risky behaviors; Dr. Nicollette Collins, a health consultant, reviews **human immunodeficiency virus** (HIV) transmission; and Magic Johnson's press conference where he reveals he is HIV-positive. It combines interviews, computer animation, art work, and pop music to entice viewers.

- **TASO: Living Positively With AIDS**

  Contact: TALC, PO Box 49, St. Albans.

  Summary: This videorecording discusses the effect Acquired immunodeficiency syndrome (AIDS), and its etiologic agent the **human immunodeficiency virus** (HIV), is having on individuals and families in the African county of Uganda. The first segment depicts the activities of the AIDS Support Organization (TASO) in Uganda and describes how TASO provides help in meeting the needs of HIV-positive individuals. The second segment discusses TASO's approach to AIDS counseling. It presents three HIV-positive individuals as they discuss the support it has provided. The skills and attitudes needed to become an AIDS counselor are explored. Typical counseling situations are illustrated.

- **Positive People Discuss HIV and Dentistry**

  Contact: University of Southern California Los Angeles, School of Dentistry, Los Angeles, CA, 90033.

  Summary: This videorecording, hosted by Gayle McDonald, features interviews with three persons with **human immunodeficiency virus** (HIV) infection: Mike Reynolds, Melody Waltz, and Channon Phipps. Reynolds, a long-term survivor who has had Acquired immunodeficiency syndrome (AIDS) since 1979, tells his story first. Reynolds, a 40-year-old homosexual, talks of his brush with death from Pneumocystis carinii pneumonia (PCP) in 1987, his subsequent abandonment by his mother and support from his father, and his present job as director of West Hollywood Cares, an AIDS education and support organization. His father also appears in the video, but his mother does not speak to him. He concludes his story with a brief plea to dentists for compassion and understanding. Melody Waltz begins her presentation by telling of her visit to a dentist who scolded her like a child for not telling his staff about her HIV status. She also talks about other incidents of discrimination suffered by both her and her children, and how, through her older son, she has become involved in peer education for teenagers. The final story is that of Phipps, who became infected through contaminated Factor VIII in 1983. Now 17, he tells of his relationship with his girlfriend, Lisa. He talks about their being counseled about safer sex by a physician, and their decision to be married after finishing school. He asks that dental professionals treat him and other Persons with AIDS (PWA's) just like their other patients.

- **Capital Punishment**

  Contact: After Stonewall Productions, PO Box 21016, Kingston.

  Summary: This videorecording explores issues surrounding infection with the **human immunodeficiency virus** (HIV) in the prison environment at the Kingston Penitentiary in Kingston, Ontario, Canada. Three inmates share their experiences as HIV-positive individuals. Sharing needles among inmates, both for drug use and tattooing, is a major mode of transmission. Tattoing is also explored as a major factor in the inmate subculture. The Kingston AIDS Project is featured as conditions for HIV education, treatment, and support are compared within and without the prison setting.

- **Family Photo**

  Contact: Parents Families and Friends of Lesbians and Gays, National Office, PO Box 66363, Washington, DC, 20035, (202) 638-3852, http://www.pflag.org.

  Summary: This videorecording shows a public service announcement (PSA) that is for parents of gays and lesbians. It presents a scene of families together while a narrator discusses the issues that parents of gays and lesbians face. A toll-free phone number is provided for individuals wishing to get more information. (Large numbers of homosexual men have been infected with the **human immunodeficiency virus** (HIV)).

- **Bloodborne Pathogens Standard for Environmental Workers**

  Contact: Medfilms, Incorporated, 6841 N Cassim Pl, Tucson, AZ, 85704, (520) 575-8900.

  Summary: This videorecording covers the universal precautions to be practiced by environmental workers in hospitals and health-care settings. It points out that following these precautions is required by the Occupational Safety and Health Administration (OSHA) standards on bloodborne pathogens. It looks at four aspects of universal precautions: Proper work practices, use of protective equipment, housekeeping

procedures, and handling an occupational exposure. Viewers are assured they cannot become infected with the **human immunodeficiency virus** (HIV) or Hepatitis B through casual contact.

- **Women and AIDS: A Growing Problem**

  Contact: Alfred Higgins Productions, Incorporated, 6350 Laurel Canyon Blvd, N. Hollywood, CA, 91606, (818) 762-3300.

  Summary: This videorecording recounts the experiences of six women who have been infected with the **human immunodeficiency virus** (HIV), the etiologic agent of Acquired immunodeficiency syndrome (AIDS). Many of the women engaged in high risk behaviors while they were still adolescents, through heterosexual transmission. The myth that women cannot get HIV is dispelled. The importance of safer sexual behavior is emphasized. Methods to prevent heterosexual transmission are explained. The importance of the HIV antibody test and early treatment are discussed. Finally, the early symptoms that HIV may manifest in women are detailed.

- **AIDS Risk: It's Your Choice**

  Contact: American Institute for Teen AIDS Prevention, Teen Choice, PO Box 395, Oberlin, OH, 44074-0395, (440) 774-3353.

  Summary: This videorecording shows Acquired immunodeficiency syndrome (AIDS) educator Duane Crumb giving a speech at an assembly at Polytechnic High School in Fort Worth, TX. Crumb addresses their fears about **human immunodeficiency virus** (HIV) infection, and stresses the need for compassion toward Persons with AIDS (PWA's). He gives the students a summary of AIDS information, starting with what the letters in AIDS stand for, and HIV as the causative agent of the disease. He presents statistics on infection and uses the iceberg analogy to show the numbers of HIV-infected persons. Crumb outlines the routes of HIV transmission, emphasizing the risks through pregnancy, IV-needle sharing, and sexual intercourse. He tells the students that it's not the drugs that transmit HIV, it's the needles, and that the danger is just as great from shooting steroids, piercing ears, or being tattooed. He mentions sterilizing needles with bleach. The students hear that abstinence from sex is the best method of HIV prevention, along with statistics on adolescent pregnancy and Sexually transmitted diseases (STD's). He explains condom use, emphasizing that the failure rate is about 10 percent. Crumb tells the students that HIV is not transmitted through casual contact, presenting details on families who live together but do not contract AIDS; therefore, sitting next to an infected person in class poses no danger. He urges them to be friends with PWA's. The speech concludes with a question-and-answer session, where students ask about opportunistic infections; the risks from kissing, sharing drinking glasses, mosquitoes, and swimming pools; symptoms; and treatments.

- **Here for a Brief Moment: The Thoughts and Feelings of Five People Who Live With a Life Threatening Illness**

  Contact: Rites of Passage, AIDS Care and Assistance, PO Box 161461, Austin, TX, 78716, (512) 476-5831. Rainmaker Productions, Austin, TX, 78710.

  Summary: This videorecording delves into the thoughts and feelings of five persons who face life-threatening illnesses. They include three cancer patients and two with Acquired immunodeficiency syndrome (AIDS). One of those infected with the **human immunodeficiency virus** (HIV) is Mike, a middle-aged white man, and the other is Jason, a white infant; Jason's caregivers tell his story. The five stories carry a common

theme of reaction to diagnosis with feelings of anger, denial, and fear; several speak of a spiritual coming-to-terms with their illness. Emphasis is placed on enjoying the small things in life and in living each day to the fullest. Mike tells of his grief in watching his friends die of AIDS. All five speak of their need for, and appreciation of, support from their families and friends.

- **Who's Going to Care for These Children? Babies With AIDS**

  Contact: Filmakers Library, Incorporated, 124 East 40th St, New York, NY, 10016, (212) 808-4980.

  Summary: This videorecording examines the situation of children and infants with Acquired immunodeficiency syndrome (AIDS). It says that many children who are born with **human immunodeficiency virus** (HIV) infection live out their lives as boarder babies in the hospitals where they are born, because their mothers are unable to care for them. It tells about University Hospital in New Jersey, where volunteers come to hug and play with the boarder babies every day, and about the Incarnation Children's Center in New York City, a group home where volunteers also care for children. It then profiles a foster mother who cares for a blind infant with AIDS, and a foster family that has taken in two small boys with AIDS. The mother and father from that family discuss their feelings of grief when their first foster child died, and of their struggle for acceptance from family and friends.

- **Three Faces of AIDS**

  Contact: Office of Consultation and Research in Medical Education, 2351 Steindler Bldg, Iowa City, IA, 52242, (319) 335-8902.

  Summary: This videorecording presents three Acquired immunodeficiency syndrome (AIDS) case histories through interviews with three Persons with AIDS (PWA's). They include Tom, a young homosexual man; Judy, a single mother with two children; and Tony, a family man with three children. Each of the three tell their own story of coping, but they touch on common themes of fear, discrimination, effects on family members and friends, and facing death. Tom tells of his rejection by his family, who could not deal with his homosexuality. Judy, whose ex-husband contracted **human immunodeficiency virus** (HIV) infection through hemophilia treatment, discusses her fears for her then-unborn son, and her relief when he tested negative at 13 months. Tony, an independent trucker, talks about losing work when the farmers who hired him learned of his illness.

- **Myths About AIDS. Translated title**

  Contact: Hispanic AIDS Awareness Program, 2350 Coral Way Ste 301, Miami, FL, 33145, (305) 860-0780, http://www.emservices.com.

  Summary: This videorecording of a public service announcement (PSA), with some dialogue in English and some in Spanish, dispels myths of casual contact transmission. It features an Hispanic family discussing ways in which they believe the **human immunodeficiency virus** (HIV) can be transmitted; the mother produces a pamphlet on Acquired immunodeficiency syndrome (AIDS) and urges them to become informed.

- **AIDS: A Salvationist Response**

  Contact: Salvation Army, Office of Media Ministries, PO Box 3608, Dallas, TX, 75221.

Summary: This videorecording consists of four separate segments (An Overview, Transmission and Prevention, Working With Persons At Risk, and How Do We Minister?), each 28 minutes and 30 seconds in length. The programs are hosted by Major Paul Bollwahn, Social Services Secretary for the USA Central Territory, and feature interviews with Salvation Army officers who minister to persons with **human immunodeficiency virus** (HIV) infection. The programs are designed to be used by Salvation Army officers, Corps leaders, and professional staff. In Program 1, Captain Christine MacMillan of Vancouver, British Columbia, director of a Salvation Army drug outreach program; Captain Ian Campbell, MD, medical director at International Headquarters; and Major Herbert Rader, MD, of Booth Memorial Medical Center, in NY; present general information. Topics addressed include HIV transmission and prevention, research needs, the spectrum of HIV disease, and the lack of a cure. It points out that the Salvation Army has always practiced a practical application of the Gospel, following Christ's mandate to feed the hungry and care for the sick. Acquired immunodeficiency syndrome (AIDS) has added a new dimension to this ministry, it says. In Program 2, Dr. Rader; Major Charles Gillies of Fairbanks, AK; Captain Stephen Langford, of The Bronx; and MacMillan discuss HIV prevention and transmission, and how lack of understanding of this information results in fear and discrimination. Risky behaviors, and what motivates people to practice them, are analyzed. Cindy Flachmeier, Salvation Army Social Services director in Miami, dispels myths of casual contact transmission. They also discuss teaching adolescents how to deal with their sexuality in positive ways. Program 3 focuses on providing Salvation Army services to persons who practice risky behaviors. Speakers include Eunice Swayers, who supervises a youth shelter in Atlanta; Gillies; Flachmeier; and Captain Deborah Wilson, who supervises a street outreach program in Vancouver. They discuss working with at-risk youth, Injecting drug users (IDU's), and sex workers. The conflict between teaching morality versus teaching preventive measures is discussed; it is pointed out that it is important to save their lives before preaching a sermon. This program als.

- **People Like Us**

  Contact: Pennsylvania/Mid - Atlantic AIDS Education and Training Center, 130 DeSoto St G15 Parron Hall, Pittsburgh, PA, 15261, (412) 624-1895, http://www.pitt.edu/~paaids/paaids.html.

  Summary: This videorecording uses a series of short interviews with persons with **human immunodeficiency virus** (HIV) infection or Acquired immunodeficiency syndrome (AIDS) and health care professionals to analyze the psychosocial issues involved in the epidemic. The Persons with AIDS (PWA's) speak of the stress related to their illness, their feelings of the loss of future, rejection by friends and family, and a loss of support. The videorecording points out that AIDS is spreading rapidly among women, children, Intravenous drug users (IVDU's), and minorities, especially Blacks and Hispanics. These groups have special needs that they present to health care workers. The videorecording urges viewers to think of PWA's as PLU's -- People Like Us. AIDS is compared to diabetes before the discovery of insulin: An always fatal disease. Now, viewers are urged to see HIV as a chronic and progressive condition with patients who need a range of services. Some of the PWA's tell stories of being treated badly by a health-care worker because of fear of AIDS or disapproval of past drug-use. The videorecording discusses medical, psychological, and social issues and how health-care workers can treat them.

- **Staying Well in the Age of AIDS: A Holistic Guide to Health Empowerment**

  Contact: Dr. Rodney W. Dennis Institute for Health Empowerment Incorporated, PO Box 65256, Washington, DC, 20035-5256.

  Summary: This video, for African Americans with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS), discusses holistic treatment options. It examines the epidemiology of AIDS among African Americans and how individuals with HIV and other diseases can take care of themselves using holistic therapies in addition to their regular medical regimens. It discusses the power of the mind-body relationship and what lessons can be learned from using holistic medicine.

- **Sharing the Challenge. Translated title**

  Contact: Caribbean Epidemiology Centre, PO Box 164, Port of Spain, (868) 622-4261, http://www.carec.org.

  Summary: This videorecording features the song, "Sharing the Challenge," written by Marilyn Jones and sung by David Rudder, Melanie Hudson, and Yolande Joseph. The song calls on listeners to be aware that everyone is vulnerable to **human immunodeficiency virus** (HIV) infection, and to join in the fight against Acquired immunodeficiency syndrome (AIDS). The song is sung over background shots of people strolling about in a park, clippings of newspaper headlines about AIDS, and activities in a hospital. Although the majority of the song is in English, one verse is sung in French.

- **No Second Chance**

  Contact: Jeremiah Films, PO Box 1710, Hemet, CA, 92546, (800) 828-2290. Capital Communications, 3807 Dickerson Rd, Nashville, TN, 37207, (615) 868-2040.

  Summary: This videorecording advocates sexual abstinence and monogamy as the best ways to prevent **human immunodeficiency virus** (HIV) infection. It starts out with a section taking place in the home of a 6-year-old boy with Acquired immunodeficiency syndrome (AIDS); one of his parents became infected through premarital intercourse, and both subsequently died. His grandparents provide round-the-clock care to the small boy, who is unable to eat and suffers a great deal of pain. The videorecording then switches to a segment hosted by Cathy Kay, a registered nurse and executive director of California Healthcare Advocates. First, a number of researchers and physicians make brief statements about the epidemiology of **human immunodeficiency virus** (HIV) infection; graphics of the HIV are shown. Persons with AIDS (PWA's) make brief statements about their illnesses. It then shows Kay in a classroom setting, discussing the methods of HIV transmission with her teenage audience. She de-emphasizes using condoms as a means of HIV prevention, saying that their failure rate is high. After discussing the risks involved in having sex with multiple partners, she emphasizes sexual abstinence and developing a monogamous relationship within marriage. Adolescents who have already had intercourse are encouraged to stop until marriage. She concludes her presentation by dispelling myths of casual contact transmission, and encouraging her audience to care for, not alienate, friends with AIDS.

- **What About Me?**

  Contact: Halstead Hospital, 328 Poplar, Halstead, KS, 67056, (316) 835-2651.

  Summary: In this videorecording, a man's feelings of denial upon learning of his positive result on the test for **human immunodeficiency virus** (HIV) antibodies are explored. In the first scene, his doctor informs him of the result, and assures him that it

doesn't mean that he has Acquired immunodeficiency syndrome (AIDS). The doctor explains what HIV is, and how it can lie dormant for years. The doctor tells his patient that the virus may not be passed through casual contact, but that his wife should come in for a test. The man also insists on a second test for himself because he doubts the original results. A week later, the man learns that his wife's test is negative, because they have been using condoms as a form of birth control. However, his second test also came back positive. The doctor tells him to inform his other sexual contacts, and the patient says he has none; apparently he contracted the virus through a blood transfusion received eight years earlier. Though he has no other sexual contacts to notify, the doctor tells him to inform his dentist and other health professionals who routinely come into contact with his blood. After explaining about possible means of treatment and urging the patient to live a healthy lifestyle, the doctor urges viewers to get more information about HIV and AIDS.

- **Neuropsychiatric Aspects of HIV/AIDS**

  Contact: University of Washington, Northwest AIDS Education and Training Center, 901 Boren Ave Ste 1100, Seattle, WA, 98104-3596, (800) 677-4799, http://depts.washington.edu/nwaetc/.

  Summary: This videorecording is a lecture by Dr. Terence C. Gayle, a clinical assistant professor at the University of Washington/Harborview Medical Center. Aimed at first-year residents in psychiatry, it covers neuropsychological disorders commonly found in **human immunodeficiency virus** (HIV) disease. He begins his lecture by discussing the epidemiology of Acquired immunodeficiency syndrome (AIDS). He then examines, in detail, the three types of neurological disorders: Organic problems such as delirium and dementia, psychoses, and mood disorders such as mania and major depression. The majority of the lecture focuses on AIDS Dementia Commplex, with detailed information on early and late stage signs and symptoms, possible causes, and types of treatment. He delves into the ethical dilemmas of caring for a patient who has a pressing need for treatment, but may die soon. Gayle then goes on to take less detailed looks at psychoses and depression.

- **Turnarounds: New Haven Needle Exchange Program**

  Contact: Filmakers Library, Incorporated, 124 East 40th St, New York, NY, 10016, (212) 808-4980.

  Summary: This videorecording profiles the needle-exchange program for **human immunodeficiency virus** (HIV) prevention in New Haven, CT. It shows the outreach van and its staff members at work on the streets as they collect used needles from Injecting drug users (IDU's) and give them clean ones. The director of the program, Elaine O'Keefe, explains that they started out by distributing bleach kits, condoms, and Acquired immunodeficiency syndrome (AIDS) literature, but that the Mayor's Task Force on AIDS fought to have possession of syringes decriminalized. A staff worker points out that most of the IDU's enrolled in New Haven treatment programs are white men, but that many of the people who use the needle-exchange program are Black. The van provides an alternative and a hope for these people who feel they are barred from treatment, the videorecording says.

- **Now That You Know: Living Healthy With HIV; Part 2 - Understanding HIV**

  Contact: Kaiser Permanente, National Video Communications, 825 Colorado Blvd Ste 301, Los Angeles, CA, 90041, (323) 259-4776, http://www.kaiserpermanente.org/locations/index.html.

  Summary: This videorecording, part of a series, advises persons with **human immunodeficiency virus** (HIV) infection that education is the best way to take control of their health. Viewers are advised to know their treatment options so they can choose the best program for them. Bob Goen and Susan Campos serve as narrators for the program, which is intercut with short-burst interviews with infected persons. The HIV-positive persons speak of how knowledge quells their fears and makes them feel in control of their health. The videorecording features two embedded segments, one on how HIV affects the immune system, and the other on the importance and meaning of various blood tests, including the HIV-antibody test. Physicians discuss the best time to begin medication, and point out that how a patient feels physically is also important. The narrators emphasize the importance of a strong physician-patient relationship.

- **Now That You Know: Living Healthy With HIV; Part 3 - Lifestyle Choices and Changes**

  Contact: Kaiser Permanente, National Video Communications, 825 Colorado Blvd Ste 301, Los Angeles, CA, 90041, (323) 259-4776, http://www.kaiserpermanente.org/locations/index.html.

  Summary: This videorecording, part of a series, deals with the lifestyle changes made necessary by a diagnosis of **human immunodeficiency virus** (HIV) infection. Co-hosts Bob Goen and Susan Campos provide narration, interspersed with presentations by experts in various fields and short-burst interviews with infected persons. The videorecording starts by saying that stress is the biggest problem in life today, and that it can suppress the immune system. Viewers are told to become aware that not all stress is caused by bad events, and are urged to learn how to cope with and reduce all types of stress. Different people have different ways of dealing with stress, and it's important for each person to determine what is right. Next, the videorecording discusses primary goals for nutrition. The importance of vitamins, minerals, calories, and protein is emphasized. Questions of supplements and dealing with illness, such as diarrhea, are addressed. Next, the videorecording looks at the importance of exercise, particularly aerobic exercise. Viewers are cautioned not to overexercise. Examples of the best types are given, and the importance of having a positive attitude is stressed. The theme then switches to drug and alcohol abuse as an escape mechanism that is harmful to the body. The videorecording points out how smoking suppresses the immune system; the narrators point out that risky sex may be a consequence of getting high. Signs of addiction are listed. The final portion of the videorecording looks at the ramifications of sexuality, including safer sexual conduct, abstinence, and loss of desire. The possibility that other Sexually transmitted diseases (STD's) may be co-factors in progression from HIV infection to full-blown Acquired immunodeficiency syndrome (AIDS), is pointed out. The videorecording discusses condom use and how to overcome the initial awkwardness of using a condom. It also examines the difficulty of telling potential partners about HIV status.

- **Nutrition Strategies in HIV Management Teleconference**

  Contact: TKN - TV, 2000 5th Ave R-101, River Grove, IL, 60171.

Summary: This videorecording documents a teleconference on the subject of nutrition and **human immunodeficiency virus** (HIV) infection. Hosted by Novella Dudley, it features a panel of four experts from various areas of the field who discuss aspects of HIV and nutrition; they then field questions from both the studio audience and over the telephone. Short video segments introduce each new topic. The panel includes Dr. Donald Kotler, of St. Luke's - Roosevelt Hospital; Joyce Fitzpatrick, a nursing consultant; Frank San Miguel, coordinator of HIV services for travelers and immigrants in Chicago; and Annette Smerko of Caremark. The teleconference opens by considering nutrition as part of the psychosocial needs of a Person with AIDS (PWA). The symptoms of malnutrition are discussed, such as weight loss, anorexia, diarrhea, fever, and painful chewing or swallowing. It addresses financial issues of the cost of medication being so great that some patients cannot afford food. It looks at the different nutritional needs of PWA's, who must avoid weight loss by eating extra calories. The panel addresses the philosophy behind providing nutritional care for someone who is dying, and looks at the effect of alcohol use on nutrition. Case studies are examined; they say that the lack of ability to eat may be due to neurologic disease, drugs, or local pathology. PWA's are encouraged to consult with a dietitian, a physican, and a social worker. The connection between depression and malnutrition is established. The panel looks at specific opportunistic infections that may affect the appetite, such as hepatitis, thrush, and candida. A demonstration is given on safe handling of food to prevent salmonella and other foodborne diseases. The videorecording examines the devastating effects of weight loss on a patient, and looks at the barriers to motivating a patient to eat. It studies ethical concerns in treatment and legal issues involved in refusal to treat. The concluding segment studies the diagnosis and management of gastrointestinal disorders. It touches on steroid use and the use of nutritional supplements. At the end of the videorecording, viewers are urged to complete an evaluation.

- **HIV Disease Patient Health Care**

  Contact: Blue Cross and Blue Shield Association, 676 N St Clair St, Chicago, IL, 60611.

  Summary: This videorecording explains the resources and patient management programs available to people in Rochester, NY, who have **human immunodeficiency virus** (HIV) infection or Acquired immunodeficiency syndrome (AIDS). Infection-control procedures and HIV-transmission routes are described. Several physicians discuss medications, including experimental drugs and clinical trials. Antibiotic prophylaxis is explained, and the use of aerosolized pentamidine to prevent pneumocystis carinii pneumonia (PCP) is demonstrated. A social worker lists various agencies which provide assistance, and analyzes financial and insurance issues. A primary-care physician tells how such physicians provide care for Persons with AIDS (PWA's), including health precautions for these patients.

- **(In)Visible Women. Translated title**

  Contact: Video Data Bank, 22 Warren St, New York, NY, 10007, (212) 233-3441.

  Summary: This videorecording recounts the personal experiences of three women of color who are infected with the **human immunodeficiency virus** (HIV), the etiologic agent of Acquired immunodeficiency syndrome (AIDS). The women share their stories through poetry, art, activism, and dance. The importance of support, community acceptance, and positive attitudes is emphasized.

- **Protecting Yourself From AIDS: What Everyone Needs to Know**

  Contact: SAVANT Audiovisuals, Inc., PO Box 3670, Fullerton, CA, 92634, (714) 870-7880.

  Summary: This videorecording presents an overview of **human immunodeficiency virus** (HIV) infection, including statistical data, signs and symptoms, and ways in which it is, and is not transmitted. It examines the causes of Acquired immunodeficiency syndrome (AIDS), how HIV affects the immune system and similarities AIDS shares with other infectious diseases such as hepatitis B. It also looks at the nature and reliability of clinical detection tests, and provides other general information. An accompanying teaching guide includes the script and self-tests.

- **FBI World AIDS Day Program**

  Contact: US Department of Justice, Federal Bureau of Investigation, 1900 Half St SW, Washington, DC, 20535, (202) 324-3299.

  Summary: This videorecording is a speech given by Henry Nichols, an 18-year-old man with hemophilia and Acquired immunodeficiency syndrome (AIDS), at the Federal Bureau of Investigation (FBI) World AIDS Day program in 1991. His sister, Jennifer Curtis, introduces his presentation and assists in a question-and-answer session following his speech. In a presentation sprinkled with humor, Nichols talks about his stubborn struggle to be a normal child in spite of the hemophilia, his 1985 infection with the **human immunodeficiency virus** (HIV) through contaminated clotting factor, and his family's decision to keep the infection secret for six years. Since being diagnosed with AIDS in March of 1991, Nichols and his family have gone public with his illness, and he and Curtis have traveled the country making presentations, mainly at high schools and colleges. While his life has mainly been free of discrimination, treating all Persons with AIDS (PWA's) with acceptance and compassion is one of the main points of his speech. He also speaks of the growing number of infections among the 16-25 age group, and how members of this group continue to practice risky behaviors because they believe themselves to be invulnerable. Questions in the discussion period cover the whole range of general AIDS information.

- **The Time to Know : Women, Children, and AIDS**

  Contact: Eastern Maine AIDS Network, PO Box 2038, Bangor, ME, 04402-2038, (207) 990-3626, http://www.maineaidsnetwork.com.

  Summary: This video examines the social and medical issues surrounding women and children with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). The video explains the social factors surrounding women with HIV/AIDS that lead them to decide whether or not to have children. It discusses how HIV can be transmitted perinatally. Women offer their personal anecdotes about how they contracted the virus and how they arrived at the decision concerning children in the video. The women explore their feelings concerning the affect the virus has had on their lives as well as the lives of their children. The video participants examine their emotions about their own death and/or the death of their HIV-positive child and each make recommendations to the viewer about the practice of safer sex to prevent HIV/AIDS.

- **Rappin'**

  Contact: Multicultural Training Resource Center, Multicultural AIDS Resource Center, 1540 Market St Ste 320, San Francisco, CA, 94102, (415) 861-2142.

Summary: This videorecording, utilizing a format of cartoon drawings and voiceover narration, uses a dialogue between two teenage girls, one of whom is sexually active, to explain the transmission of **human immunodeficiency virus** (HIV) and the need for all sexually active people to use condoms. Their discussion with the school's health educator also emphasizes that all types of people can get Acquired immunodeficiency syndrome (AIDS), that abstinence is desirable until both partners are more responsible and ready for the possibility of pregnancy, that condoms are important for preventing all types of Sexually transmitted diseases (STD's), and that the **human immunodeficiency virus** (HIV) is not transmitted through casual contact.

- **HIV Education for Adults Literacy Programs: Providing a Supportive and Sensitive Environment**

  Contact: Albany Educational Television, 27 Western Ave, Albany, NY, 12203, (518) 465-4741.

  Summary: This videorecording discusses the importance of adult **human immunodeficiency virus** (HIV)/Acquired immunodeficiency syndrome (AIDS) education. The classroom is the primary environment where AIDS will be addressed. It says there are certain elements involved when discussing this topic that an educator should tune into before providing information about AIDS: Know oneself, create a context of awareness, have sensitivity, and finally, provide support in a nonjudgmental way.

- **Universal Precautions for Child Care Facilities**

  Contact: Indiana Board of Health, Division of Acquired Diseases, PO Box 1964, Indianapolis, IN, 46206-1964, (317) 633-0842.

  Summary: This vidorecording tells those who provide child care that they need to use universal precautions in any situation where blood is present. It gives background information on **human immunodeficiency virus** (HIV) prevention, and dispels myths of transmission through casual contact. Viewers are warned they need to use universal precautions not only to protect themselves from HIV, but also from Hepatitis B and other infectious diseases. The videorecording points out that a 1988 Indiana law requires all employees who may come into contact with blood or body fluids to have training in universal precautions, and to use them on the job. It demonstrates how to give first aid to an injured child, and how to diaper a child when blood is present in the urine or stool. These techniques emphasize wearing gloves, cleaning up spills with bleach, and handwashing.

- **Born in Africa: A Frontline/AIDS Quarterly Special Report**

  Contact: WGBH Boston, Health Quarterly, 125 Western Ave, Allston, MA, 02134, (617) 492-2777. Public Broadcasting Service, PBS Video, 1320 Braddock Pl, Alexandria, VA, 22314-1698, (703) 739-5380.

  Summary: This videorecording, a special Public Television report, profiles singer Philly Lutaya of Uganda, who died of Acquired immunodeficiency syndrome (AIDS) on December 15, 1989. The producers of the videorecording explain that they originally set out to produce an installment on the epidemic's effects on the African continent, but ran into government opposition on all fronts. Only Uganda, with a number of restrictions, would cooperate, and the Ugandan government originally balked at their filming Lutaya in his homeland. Statistics presented at the beginning of the videorecording say that while Africa has only 150,000 officially diagnosed AIDS cases, estimates say that 4-5

million people are infected with the **human immunodeficiency virus** (HIV). The videorecording follows the story of the closing weeks of Lutaya's life, after he publicly declared that he had AIDS. It explains that AIDS has been a painful and taboo subject throughout Africa, where heterosexual transmission predominates. The storyline shows Lutaya receiving treatment in Sweden, where he lived as a political exile for four years. He decides to write a song, "Alone," about the feelings of being a Person with AIDS (PWA). The videorecording then follows him back to Uganda and shows him touring the nation, promoting HIV education in schools and communities. It explains that the educational emphasis needs to be placed on the 5-15 age group, which is relatively virus-free, and on women, who are often forced into prostitution to support themselves and their families. The love and support Lutaya receives from his peers is sharply contrasted with the discrimination that most Ugandan PWA's face. It looks at the role the church plays in Ugandan society, the inability of the government to fund medical treatment, and the biased attitudes that prevail toward AIDS. The videorecording concludes with Lutaya's death.

Audio Recordings

The Combined Health Information Database contains abstracts on audio productions. To search CHID, go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. To find audio productions, use the drop boxes at the bottom of the search page where "You may refine your search by." Select the dates and language you prefer, and the format option "Sound Recordings." Type "human immunodeficiency virus" (or synonyms) into the "For these words:" box. The following is a typical result when searching for sound recordings on human immunodeficiency virus:

- **Diagnosis and Treatment of Latent Tuberculosis Infection in the 21st Century: An Audio Recording for Clinicians**

  Contact: Francis J Curry National Tuberculosis Center, 3180 18th St Ste 101, San Francisco, CA, 94110-2042, (415) 502-4600, http://www.nationaltbcenter.edu.

  Summary: This CD and study guide, designed for health professionals, discusses the diagnosis and treatment of latent tuberculosis (TB) infection (LTBI), especially in special populations including individuals with the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). It discusses the major risk factors for developing active TB once LTBI has been contracted; the tuberculin skin test process and how to evaluate the results of this diagnostic test; the medical treatment options for individuals with LTBI and HIV-infected patients; and how patients being treated for LTBI should be monitored. It provides an overview of the drugs used to treat LTBI and their possible side effects.

- **HIV/AIDS Information : Understanding and Preventing HIV and AIDS/What You Should Know About Taking an HIV Test. [HIV/AIDS Information : Understanding and Preventing HIV and AIDS /What You**

  Contact: California Department of Health Services, Office of AIDS, California AIDS Clearinghouse, 1443 N Martel Ave, Los Angeles, CA, 90046, (323) 845-4180, http://www.hivinfo.org.

  Summary: This cassette provides information about the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). The cassette discusses

HIV's attack on the immune system, HIV's development into AIDS, and how infected persons can look and feel healthy for years. It discusses HIV transmission, diagnosis, and prevention (e.g., practicing sexual abstinence, practicing safer sex, and avoiding substance abuse). It dispels myths about how HIV is spread and provides information about HIV testing such as how and where tests are administered, what the results mean, and the difference between anonymous and confidential testing.

- **Autoestima/Viva Tu Vida! Hazte la Prueba. [HIV/AIDS Information for Gay Men : Pride/Take Control, Take the Test]**

  Contact: California Department of Health Services, Office of AIDS, California AIDS Clearinghouse, 1443 N Martel Ave, Los Angeles, CA, 90046, (323) 845-4180, http://www.hivinfo.org.

  Summary: This cassette, for gay and bisexual men, provides information on the **human immunodeficiency virus** (HIV)/acquired immune deficiency syndrome (AIDS). The cassette covers topics such as HIV transmission, prevention methods (i.e., safer sex, how to choose and use condoms, and how to engage in anal intercourse safely), risk factor identification, and partner communication. The cassette covers topics on HIV testing such as how and where the test is administered, what test results mean, and the difference between anonymous and confidential testing.

- **Heart-to-Heart**

  Contact: Kairos Support for Caregivers, 2128 15th St, San Francisco, CA, 94114-1213, (415) 861-0877, http://www.cyberpark.com/kairos.

  Summary: This sound recording consists of guided visualization and affirmations designed for the caregivers of individuals with the **human immunodeficiency virus** (HIV) and Acquired immunodeficiency syndrome (AIDS). It leads the listener through a journey at the beach which contains affirmations that enable the caregiver to gain strength and peace. By describing a series of natural scenes, it guides the listener into examining the circumstances of caregiving, including dealing with unforeseen setbacks, decision-making, and meeting the needs of the caregiver. It continues with a series of affirmations that stress hope, courage, strength, and wisdom.

- **Denial and Death**

  Contact: National Public Radio, 2025 M St NW, Washington, DC, 20036, (202) 822-2000.

  Summary: This sound recording of a National Public Radio (NPR) program covers the impact of Acquired immunodeficiency syndrome (AIDS) on the Cuban community in Miami. Although these immigrants are usually well-off financially, many cultural myths and beliefs have contributed to the rapid spread of **human immunodeficiency virus** (HIV) infection in the community. The reporter, Cecilia Vaisman, first visits a group of four mothers whose adult sons have died of AIDS. They meet to tell their stories and give each other support. The women talk about the difficulty that the community and the Catholic church have in dealing with homosexuality. The program also tells the story of Lenny, a young HIV-positive man who has not told his family of his AIDS diagnosis or his homosexuality because he fears ostracism. By contrast, the reporter interviews extremists who have prejudicial attitudes about HIV-infected persons. Yolanda, a 45-year-old woman with AIDS, talks about her feelings of isolation from her family and friends. The program also profiles Pedro Zamora, a young man with AIDS who has embraced the role of peer educator.

- **Using Churches to Teach About AIDS**

  Contact: National Public Radio, 2025 M St NW, Washington, DC, 20036, (202) 822-2000.

  Summary: This sound recording of a National Public Radio (NPR) program looks at the efforts of Hispanic ministers in Chicago, through the AIDS Pastoral Care Network, in educating members of their community about the Acquired immunodeficiency syndrome (AIDS) epidemic. It tells several stories of young gay men with **human immunodeficiency virus** (HIV) infection, and the difficulties that the traditional church and the community have in dealing with their homosexuality. The sound recording says that the ministers of the Pastoral Care Network are practicing a philosophy of compassion and caring; the group includes representatives of a wide range of theologies and perspectives. They emphasize that they do not condemn homosexuality.

- **A Migrant Legacy: The Yakima Valley, Part One**

  Contact: National Public Radio, 2025 M St NW, Washington, DC, 20036, (202) 822-2000.

  Summary: This sound recording of a National Public Radio (NPR) program, reported by Isabel Alegria, looks at the efforts of a male-female outreach team that visit a bar frequented by migrant workers in the Yakima Valley of Washington State. Roberto and Becky have kept up this effort of distributing condoms and bleach kits because of the high rates of **human immunodeficiency virus** (HIV) infection seen at the local clinic. Roberto says risk factors include low condom use, the transient status of the population, and unacknowledged sex among men. The sound recording also points out that members of this population refuse to seek medical help until they are extremely ill. Since many of these migrant workers are in this country illegally, this also hinders their efforts to seek medical help. The program includes individual stories.

- **The Hardest Hit Americans: AIDS in Puerto Rico**

  Contact: National Public Radio, 2025 M St NW, Washington, DC, 20036, (202) 822-2000.

  Summary: This sound recording of a National Public Radio (NPR) program examines the high incidence of Acquired immunodeficiency syndrome (AIDS) in Puerto Rico. Reporter Maria Martin visits the island to talk to residents about the epidemic. She hears stories about government indifference, failure to target Injecting drug users (IDU's), cultural barriers to condom use, and poverty. The program points out that the Catholic church in Puerto Rico opposes the use of condoms. It also points out that although Puerto Ricans are United States citizens, the island's territorial status means they do not have all the benefits that mainland citizens do. Limitations on Medicaid are explained; the program points out that the average income in Puerto Rico is less than half that in Mississippi, the poorest of the 50 states. Because Puerto Ricans are so poor and they have such limited access to health care, their health declines rapidly after diagnosis. The reporter profiles a hospice where Persons with AIDS (PWA's) can live out their lives in dignity. The hospice is run by a woman named Mariana, whose husband, Jorge, is one of the patients. They speak of the need to break down the myths of casual contact transmission that pervade the island and to stop the rapid spread of **human immunodeficiency virus** (HIV) infection.

- **BE SAFE**

  Contact: Advantage Life Products, Incorporated, 26052 Merit Cir #106, Laguna Hills, CA, 92653, (714) 582-0035.

Summary: This sound recording recapitulates the accompanying study guide to discuss with adolescents, their parents, schools, or counselors the consequences of sexual activity, including the **human immunodeficiency virus** (HIV) and Sexually transmitted diseases (STD's). The progression of HIV to Acquired immunodeficiency syndrome (AIDS) is presented. Adolescents are given information to encourage responsible decision-making. The development of strong self esteem is emphasized. It discusses the HIV-antibody test and who should consider taking the test. It also lists phone numbers of organizations that can provide further information or referrals.

- **Asylum and AIDS: Central Americans in Washington, DC**

  Contact: National Public Radio, 2025 M St NW, Washington, DC, 20036, (202) 822-2000.

  Summary: This sound recording of a National Public Radio (NPR) broadcast looks at the social and cultural conditions that make the community of El Salvadoran and other Central American refugees living in Washington, D.C. especially vulnerable to **human immunodeficiency virus** (HIV) infection. Reporter Brenda Wilson uses interviews with a doctor at a clinic to paint a picture of the life he and his patients left behind when they fled, and the life they lead now. A social worker tells how many men feel left out and alienated because their women can find work as domestics, but they have difficulties finding employment in the recessionary economy. This often leads to a deteriorating relationship and the breakup of a marriage. These men also carry with them memories of fleeing war and other conflicts, and turn to alcohol, drugs, and sex with prostitutes. An outreach worker describes the difficulties in providing them with information about **human immunodeficiency virus** (HIV) prevention; he says many of them believe they can become infected through needles used at clinics, and they say they will take their own needles with them to be used in treatment. Outreach to women, and the role they need to take in negotiating condom use, is discussed. The sound recording points out that many Hispanic men are equally comfortable in sexual relationships with either sex, but do not think of themselves as homosexual. These men often carry HIV infection home to their wives and their children. Personal stories are presented to illustrate many of these points.

- **Lucha Contra el HIV: Un Curso de Supervivencia Contra el SIDA.. [Fight Back Against HIV: An AIDS Survival Course.]**

  Contact: Image Enhancement, Incorporated, Glendale, CA, 92109.

  Summary: This sound recording is hosted by Bill Roberts, who was diagnosed with AIDS-related complex (ARC) in 1987, but says he is now symptom-free. He says that a diagnosis of **human immunodeficiency virus** (HIV) infection is no longer a death sentence, because of early intervention and the effective treatments that are now in place. He discusses diagnostic tests and preventive treatment for Pneumocystis carinii pneumonia (PCP). The sound recording discusses the spectrum of HIV disease and the symptoms that accompany each stage. Roberts points out that many people are infected with the virus, but do not realize it because of the slow progression of the disease. Without treatment, 87 percent of those infected will progress to ARC or Acquired immunodeficiency syndrome (AIDS) within 7 to 10 years of infection. But, the sound recording says, with treatment this statistic can be lowered drastically. It urges people to take the HIV-antibody test and then to have their immune systems monitored regularly. The sound recording explains how HIV affects the immune system, and the effect that stress can have on the brain and on the immune system. The importance of thinking positively is emphasized, and the role of visualization in fighting disease is explained.

Side two demonstrates a visualization session, emphasizing the importance of sleep, exercise, nutrition, and effective treatment.

- **The Healthcare Worker: HIV Risk, Prevention & Management**

  Contact: Health Impact, PO Box 9443, Seattle, WA, 98109-9443, (206) 284-3865, http://www.healthimpact.org/.

  Summary: This sound recording, with accompanying pre-test and post-test material, comprises a course on preventing **human immunodeficiency virus** (HIV) transmission in the healthcare setting. The course teaches listeners to identify the risk of HIV transmission through blood exposure, outlines the use of universal precautions, explains methods of HIV prevention and transmission, demonstrates cleaning and disinfection of instruments and equipment, and looks at case management for HIV-infected health-care workers.

- **Babies: Drugs, Alcohol, & AIDS**

  Contact: Sunrise Media, 96 Inverness Dr E, Englewood, CO, 80112, (303) 792-3822.

  Summary: This sound recording offers a panel discussion dealing with problems involving mothers who are dependent on drugs or alcohol during pregnancy and after their babies are born. A growing number of these women are infected with the **human immunodeficiency virus** (HIV), which they may pass on to their infants. The first speaker is an attorney, who analyzes the legal problems such mothers may face in retaining custody of their children. They also face grave difficulties finding treatment programs which will accept them, and child care to attend any they do find. Poor and Black women are the ones who most frequently lose custody of their children. The next two speakers are legislators who discuss new treatment approaches for such women and their children. Innovative funding for such programs is also examined.

- **Motivating People to Use Condoms**

  Contact: Mary Ann Liebert, Incorporated, 2 Madison Ave, Larchmont, NY, 10538, (914) 834-3100.

  Summary: This sound recording gives instructions on counseling clients about the use of condoms. It says the counselors need to fulfill the role of educating, counseling, and motivating individuals to use condoms. The sound recording suggests beginning a session by presenting basic facts about Acquired immunodeficiency syndrome (AIDS); it emphasizes the importance of establishing a comfortable and personal relationship with the clients. After the informational portion of the interview, it says counselors should conduct a personal interview to assess the client's risk factors. Clients should be encouraged to be tested for **human immunodeficiency virus** (HIV) antibodies if they are at risk. It also talks about using different approaches in different settings, and being aware of the differing needs of women and minorities. The sound recording says the interview should include with information on the correct way to use a condom, and methods for negotiating condom use with partners.

- **AIDS in Adolescents and Women. Building an Economic Framework, Prevention '91: Baltimore, MD, March 16-19, 1991**

  Contact: Chesapeake Audio/Video Communications, 6330 Howard Ave, Elkridge, MD, 21227, (410) 796-0040.

Summary: This sound recording of proceedings, from Building an Economic Framework: Prevention '91, held March 16-19, 1991, in Baltimore, MD, examines issues related to women, adolescents, and **human immunodeficiency virus** (HIV) infection. The primary speaker is Larry D'Angelo, chairman of Adolescent Health at Children's National Medical Center in Washington, D.C. He gives a general overview of Acquired immunodeficiency syndrome (AIDS) in women and adolescents, and says that both are similar in that they represent a small, but rapidly growing, percentage of HIV infections. D'Angelo says it is important to count the AIDS cases that will be seen in the future, not the AIDS cases that are being seen now. He presents statistics from high prevalence areas throughout the United States, and takes a look at testing, confidentiality, and support issues for both groups. The second speaker discusses a study of AIDS risk and risk-reduction behaviors among young Black and white women in California. She says that the nationwide rate of heterosexual transmission has more than doubled in the past eight years, and that AIDS is spreading to women who are dating, not just to sex workers or Intravenous drug users (IVDU's). She presents the results of research questions which determined risk, perception of risk, and risk-reducing behavior. The study showed that Black women had more partners and more incidence of Sexually transmitted diseases (STD's), but there was no difference in risk between the two groups. Their perceptions of risk were related to their actual risk, but there was no correlation between this and risk-reducing behavior. A final speaker presents models of HIV trends among Black and Hispanic women in New York City. The model uses 32 different parameters to examine AIDS incidence, testing, pregnancy, and serostatus of infants.

- **The Role of Schools in Promoting Adolescent Health. Building an Economic Framework, Prevention '91: Baltimore, MD, March 16-19, 1991**

  Contact: Chesapeake Audio/Video Communications, 6330 Howard Ave, Elkridge, MD, 21227, (410) 796-0040.

  Summary: This sound recording of proceedings, from Building an Economic Framework: Prevention '91, held March 16-19, 1991, in Baltimore, MD, deals with the health needs of adolescents. The speakers, John Santelli and Candace Sullivan, discuss the many problems faced by today's adolescents, including pregnancy, suicide, homicide, and Sexually transmitted diseases (STD's) such as **human immunodeficiency virus** (HIV) infection and Acquired immunodeficiency syndrome (AIDS). Santelli presents statistics and studies about these behaviorally based problems; he takes a look at the implications of peer pressure and compares the United States to other Western nations. Sullivan examines health education programs and their attendant problems, such as parental disapproval of curriculum and lack of staff and funds. The success of school-based clinics in preventing pregnancy and other sexual problems is discussed at length. Cooperation among agencies and guaranteed access to health care for all adolescents are called for.

- **Don't Lose the Magic**

  Contact: Lieberman Appalucci, 4635 Crackersport Rd, Allentown, PA, 18104-9597, (610) 395-7111.

  Summary: This sound recording, by a group called The Valley Voices, pays tribute to National Basketball Association (NBA) player Magic Johnson, who announced that he had tested positive for **human immunodeficiency virus** (HIV) antibodies in November 1991. The chorus urges listeners to realize that Acquired immunodeficiency syndrome (AIDS) can affect everyone. Because of the subject, it is related to sports.

- **Living, Dying, and Healing With AIDS**

  Contact: King's College, Center for Education about Death and Bereavement, 266 Epworth Ave, London, (519) 432-7946.

  Summary: This videorecording presents a speech by Virginia Duffy on the need for healing for persons who are dying of Acquired immunodeficiency syndrome (AIDS). Duffy, a nurse-practitioner and the director of the HIV Clinic in Psychiatry at Strong Memorial Hospital, talks about healing taking on a new meaning when death is inevitable. She discusses the psychological factors involved, including the difference between psychological and spiritual healing. According to Duffy, Persons with AIDS (PWA's) often lead a hidden lifestyle, contributing to their sense of isolation. For healing to take place, isolation must be replaced by a sense of belonging and acceptance. She speaks about faith by saying that everyone has his or her own definition, but that it is basically a trust in God, in oneself, and in others, and a belief that there is a purpose in life. Duffy includes a 15-minute videorecording in her presentation, in which a developmentally disabled gay man with **human immunodeficiency virus** (HIV) infection speaks about his spiritiual and psychological beliefs, and the need for healing. A question-and-answer period concludes the presentation.

- **Prevention of HIV Infections and AIDS in Drug Abuser**

  Contact: Audio Visual, Incorporated, 5542 Tuxedo Rd, Cheverly, MD, 20781, (301) 322-5600.

  Summary: This sound recording of a National Institute on Drug Abuse Conference session held on January 13, 1991, presents a panel discussion of intervention strategies to prevent **human immunodeficiency virus** (HIV) infection and Acquired immunodeficiency syndrome (AIDS) in drug abusers. The first speaker discusses drug buying and IV-needle sharing behavior. The second speaker describes two culturally sensitive programs for women of color in Los Angeles, who must overcome poverty and illiteracy. The third speaker examines a study of two types of intervention used for heroin addicts. The panel extensively analyzes the effects of paid interviews.

- **Psychological Aspects of AIDS and Drug Abuse Clients**

  Contact: Audio Visual, Incorporated, 5542 Tuxedo Rd, Cheverly, MD, 20781, (301) 322-5600.

  Summary: This sound recording of a National Institute on Drug Abuse Conference on January 13, 1991, examines the psychological and psychosocial aspects of **human immunodeficiency virus** (HIV) infection and drug abuse. The first speaker describes the psychological continuum of Acquired immunodeficiency syndrome (AIDS) from diagnosis to death. It analyzes the characteristics, needs, and treatment of each phase of the disease. The second speaker continues this discussion and examines the need for support groups and counseling.

- **Infectious Diseases and HIV Drug Abusers**

  Contact: Audio Visual, Incorporated, 5542 Tuxedo Rd, Cheverly, MD, 20781, (301) 322-5600.

  Summary: This sound recording of a National Institute on Drug Abuse Conference presents a panel discussion held January 15, 1991 of a variety of infectious diseases which affect people with **human immunodeficiency virus** (HIV) infection or Acquired immunodeficiency syndrome (AIDS). The first speaker describes the diseases, besides

HIV, which he found in a cohort of 800 Intravenous drug users (IVDU's) in the Bronx. Tuberculosis (TB), bacterial pneumonia, and pneumocystis carinii pneumonia (PCP) were among the most common ones found. The second speaker examines vaccines which HIV-positive people may take without ill effects. These include hepatitis, pneumococcal, and various influenza vaccines. Oral polio vaccine should never be given. The third speaker discusses results of examining the death certificates of drug addicts.

- **AIDS and Substance Abuse - Closing Remarks**

  Contact: Audio Visual, Incorporated, 5542 Tuxedo Rd, Cheverly, MD, 20781, (301) 322-5600.

  Summary: This sound recording of the proceedings of a session of the National Institute on Drug Abuse Conference held January 15, 1991, deals with the spread of the **human immunodeficiency virus** (HIV) from Intravenous drug users (IVDU's) to others. Heterosexual transmission is rising in this group, and consequently, the number of children with Acquired immunodeficiency syndrome (AIDS).

- **A Service Delivery System Model for AIDS Prevention**

  Contact: Audio Visual, Incorporated, 5542 Tuxedo Rd, Cheverly, MD, 20781, (301) 322-5600.

  Summary: This sound recording of a National Institute on Drug Abuse Conference held Jan. 13, 1991, deals with a variety of service delivery systems for prevention of Acquired immunodeficiency syndrome (AIDS). The first speaker discusses early problems with treating patients with **human immunodeficiency virus** (HIV) infection. These included staff morale problems from working with dying patients, and problems with confidentiality and privacy. This speaker describes an outreach program for which she now works. Clinical procedures have been streamlined so that patients' waiting periods are not as long. In certain cases, street outreach and counseling is done in cars. She stresses the need for cultural understanding and bilingual programs. The second speaker describes the situation in Boston, where a van is used for street outreach, and offers antibody tests and counseling. This speaker explains the need for common treatment facilities for both mothers and their HIV-positive children, and for daycare for HIV-positive children. The third speaker describes street-outreach programs through methadone-maintenance clinics in Los Angeles. He analyzes barriers to women's seeking treatment, and examines the need for additional help for crack-addicted women.

- **AIDS Outreach - Behavior Change Strategies**

  Contact: Audio Visual, Incorporated, 5542 Tuxedo Rd, Cheverly, MD, 20781, (301) 322-5600.

  Summary: This sound recording of a National Institute on Drug Abuse Conference held January 13, 1991, deals with outreach and behavior modification programs to prevent **human immunodeficiency virus** (HIV) infection. The first speaker explains the need to develop site-specific strategies. Since HIV transmission is rising rapidly among Intravenous drug users (IVDU's), intervention strategies which meet their needs are of paramount importance. Demonstration projects which provide both qualitative and quantitative information are needed. She describes a project in San Francisco, including information about five types of IVDU's and the effects of street crime on the outreach workers. The second project described aims to change the sexual behavior of IVDU's

and their partners in Paterson, NJ. There were attendance problems despite child care's being provided. The project paid patients for testing. Hispanics were the most difficult to attract. Females came to support and educational groups more frequently than males, and sex partners came more than IVDU's. The most successful groups had case managers with certain characteristics. Taking interventions to the neighborhoods proved more successful than asking clients to travel. A discussion of drug-use patterns follows the presentations on outreach and behavior modification programs.

- **Be a Hero**

  Summary: This sound recording advocates the use of condoms to prevent the spread of **human immunodeficiency virus** (HIV). It emphasizes that no group is immune from Acquired immunodeficiency syndrome (AIDS), and tells listeners to feel free to say no to sexual intercourse.

- **AIDS & Education**

  Contact: InfoMedix, 12800 Garden Grove Blvd, Ste F, Garden Grove, CA, 92643, (714) 530-3454.

  Summary: This sound recording features several speakers whose subject is the need to integrate education about the **human immunodeficiency virus** (HIV) and Acquired immunodeficiency syndrome (AIDS) into sex education courses. The first speaker deals with discrimination against homosexuals and bisexuals, and suggests including some civil rights information in these courses. Church policies and roles in creating or dispelling such discrimination are explained. The second speaker describes the program she has developed to teach adolescents about sex. She emphasizes that they must understand that their decisions about sex can have deadly consequences. The third speaker discusses sexual behavior on college campuses and how HIV is transmitted there. A question-and answer session follows.

- **Rural AIDS Network: 13th Annual Conference on Rural Health, New Orleans, LA, May 16-19, 1990**

  Contact: Convention Recorders, 2645 Financial Ct Ste P, Ste C, San Diego, CA, 92117, (619) 274-7100.

  Summary: This sound recording of the 13th Annual Conference on Rural Health, May 16-19, 1990, in New Orleans, LA, covers a session on the Rural AIDS Network. Jeremy Landau describes the beginnings of the Rural AIDS Network and its work, particularly outreach services. Issues of incidence of Acquired immunodeficiency syndrome (AIDS) and **human immunodeficiency virus** (HIV) infection in rural communities, confidentiality, application of urban models of AIDS health-care delivery to rural environments, and training of staff and health officials to overcome fear of HIV are examined. Development of models, covering needs assessment, funding sources, networking, and training and education of staff are then discussed. Scott Austin, a trainer with Rural AIDS Network and a staff worker with the NAMES Project, provides more details about the education aspects, needs assessment, training, and education in local AIDS service organizations, and the importance of local networking and coalition building.

- **Women & AIDS, AIDS & Blood**

  Contact: National Public Radio, 2025 M St NW, Washington, DC, 20036, (202) 822-2000.

Summary: This sound recording deals with the problems of the **human immunodeficiency virus** (HIV) in the blood supply, and also with the problems of HIV in young Black women, where it ranks as the number one killer. There have been 230 reports of Acquired immunodeficiency syndrome (AIDS) related to transfusions among blood recipients in the Washington, D.C., region. The need for community health education programs for Black communities and the need to promote condom use to combat HIV is stressed.

- **Aloe Vera: Advanced Immune Discoveries Symposium**

  Contact: Human Energy Press, 493 Beach Park Blvd Ste 210, Foster City, CA, 94404, (415) 349-0718.

  Summary: This sound recording deals with the long-term survival of persons with **human immunodeficiency virus** (HIV) infection or Acquired immunodeficiency syndrome (AIDS) who receive a patented oral aloe vera extract. The speaker gives a brief history of the use of aloe vera in folk medicine, including how the extract is made, and of how his research began. He describes the patients treated, the means the researchers used to evaluate them, and their compliance rate. Difficulties in isolating the extract and maintaining it are also discussed.

- **Passive Immunotherapy: Advanced Immune Discoveries Symposium**

  Contact: Human Energy Press, 493 Beach Park Blvd Ste 210, Foster City, CA, 94404, (415) 349-0718.

  Summary: This sound recording describes what passive immunotherapy is and how it is used to treat persons with **human immunodeficiency virus** (HIV) infection or Acquired immunodeficiency syndrome (AIDS). Blood plasma is drawn from an HIV-positive person, who is otherwise well. The plasma is then treated and injected into a Person with AIDS (PWA) in an attempt to pass on the antibodies the blood contains. Criteria for donors are listed, and a brief history of passive immunotherapy is given. Information about the clinical trial licensed by California is also included.

- **Total Body Hyperthermia: Advanced Immune Discoveries Symposium**

  Contact: Human Energy Press, 493 Beach Park Blvd Ste 210, Foster City, CA, 94404, (415) 349-0718.

  Summary: This sound recording describes the use of hyperthermia to treat Acquired immunodeficiency syndrome (AIDS) and **human immunodeficiency virus** (HIV) infection. Hyperthermia is already recognized as an anticancer therapy. Criteria for patients selected included a growing Kaposis sarcoma and a tumor responsive to therapy. Research methodology is described, including the use of interferon along with hyperthermia. Several case studies are presented.

- **Thymus Extracts: Advanced Immune Discoveries Symposium**

  Contact: Human Energy Press, 493 Beach Park Blvd Ste 210, Foster City, CA, 94404, (415) 349-0718.

  Summary: This sound recording deals with treatment of Acquired immunodeficiency syndrome (AIDS) and **human immunodeficiency virus** (HIV) infection with thymus extracts. An explanation of the way the human immune system works is included. The effect of the thymus extract on several patients is discussed. The sound track of a film on immunodeficiency and the human immune system is included.

- **Electromagnetics: Advanced Immune Discoveries Symposium**

  Contact: Human Energy Press, 493 Beach Park Blvd Ste 210, Foster City, CA, 94404, (415) 349-0718.

  Summary: This sound recording deals with the use of electromagnetic energy to treat various diseases, including Acquired immunodeficiency syndrome (AIDS). The first part of the presentation explains the theory of how electromagnetic fields affect the human body. Experimentation using several different electromagnetic fields together is being undertaken in an effort to ascertain which ones work synergisticly and which ones work antagonisticly. Tissue culture cell research is being done to find which frequencies of electromagnetic energy have the most effect on the **human immunodeficiency virus** (HIV) and what dosage affects the Deoxyribonucleic acid (DNA) of the virus, but not the DNA of the host cell. The subject of other research is how electromagnetic energy can stimulate the body's own systems to repair themselves from injuries from burns and wounds. A brief history of phototherapy and its healing properties is also included.

- **AIDS 101: Basic Facts and Important Issues**

  Source: Taking Action on AIDS.

  Contact: Walker Trieschman Center, Child Welfare League of America, 300 Congress St Ste 305, Quincy, MA, 02169, (617) 769-4010, http://www.cwla.org.

  Summary: This sound recording, the first in a series, presents basic background information on Acquired immunodeficiency syndrome (AIDS) and **human immunodeficiency virus** (HIV) infection. Divided into five parts, it opens with the definition of AIDS as a medical condition. It emphasizes that HIV is a bloodborne, not an airborne, virus, and discusses the long latency period that may follow HIV infection. It covers the difference between HIV infection, AIDS-related complex (ARC), and AIDS, then adds that many physicians now favor dropping the ARC designation and regarding HIV as a continuum of disease. Part II looks at the HIV-antibody test and its reliability, while Part III examines working with prevalence statistics. It says that 21 percent of all Persons with AIDS (PWA's) are between 20-29, and most were probably infected as adolescents. The sound recording points out that the rate of infection among gay males is leveling off, while heterosexual transmission increases. In Part IV, the sound recording explains routes of HIV transmission and methods of prevention, looking at transmission through IV-needle sharing and sexual intercourse, and from a mother to her unborn child. Detailed instructions for condom use are given. The fifth and final part looks at the impact of AIDS on society, and says that there is a need to examine thought, behaviors, and attitudes, and to work to prevent the spread of the disease.

- **Herbal DANN Treatment: Advanced Immune Discoveries Symposium**

  Contact: Human Energy Press, 493 Beach Park Blvd Ste 210, Foster City, CA, 94404, (415) 349-0718.

  Summary: This sound recording deals with Korean and American research into a system of herbology to cure Acquired immunodeficiency syndrome (AIDS) and **human immunodeficiency virus** (HIV) infection. The recording describes patients admitted to the study, the side effects they experienced, and toxicity levels. The treatment is designed to extract internal body heat and poisons to the outside.

- **Eclectic Protocols/Live Cell Therapy: Advanced Immune Discoveries Symposium**

  Contact: Human Energy Press, 493 Beach Park Blvd Ste 210, Foster City, CA, 94404, (415) 349-0718.

  Summary: This sound recording explains live-cell therapy and how it is used to treat Acquired immunodeficiency syndrome (AIDS), which is caused by the **human immunodeficiency virus** (HIV). Live cells from bovine fetus and embryo tissue are injected into patients in an effort to bolster the immune system. Therapeutic drugs, such as Azidothymidine (AZT) and cortisone, must be discontinued since they cause immune disturbances. The speaker feels that HIV is not the sole cause of AIDS. Since HIV is newly discovered, many problems for which there seem to be no other explanation are assigned to it. Deaths, he points out, come from a variety of opportunistic infections which are not new. Problems for obtaining funding for alternative-therapy research are also discussed.

- **Compound Q: Advanced Immune Discoveries Symposium**

  Contact: Human Energy Press, 493 Beach Park Blvd Ste 210, Foster City, CA, 94404, (415) 349-0718.

  Summary: This sound recording deals with Compound Q, which is a plant protein that has been used in China for many years for medicinal purposes. It is now being used as a treatment for Acquired immunodeficiency syndrome (AIDS) and **human immunodeficiency virus** (HIV) infection. The speaker explains that it can be used externally as a dry root, or taken orally. She also discusses the difference between its use as a cytotoxin and its use as an immune toxin.

- **Protect Your Body, Protect Your Mind**

  Contact: American Correctional Association, Training and Contracts Division, 4321 Hartwick Rd, College Park, MD, 20740, (301) 206-5100.

  Summary: This sound recording presents a rap song for adolescents pertaining to **human immunodeficiency virus** (HIV) and Acquired immunodeficiency syndrome (AIDS) prevention. It endorses practicing safer sex and avoiding IV-drug use.

- **Ascorbate Therapy: Advanced Immune Discoveries Symposium**

  Contact: Human Energy Press, 493 Beach Park Blvd Ste 210, Foster City, CA, 94404, (415) 349-0718.

  Summary: This sound recording deals with the use of ascorbate as a free radical scavenger in treating a variety of diseases, including Acquired immunodeficiency syndrome (AIDS), which is caused by the **human immunodeficiency virus** (HIV). Included is a brief history of the use of ascorbates in curing disease and the researcher's own experience in using it to treat allergies. He explains how a free radical scavenger works and how to prevent side effects of massive doses of ascorbates.

- **Fungal Extracts: Advanced Immune Discoveries Symposium**

  Contact: Human Energy Press, 493 Beach Park Blvd Ste 210, Foster City, CA, 94404, (415) 349-0718.

  Summary: This sound recording deals with the use of fungal extracts in treating diseases, including Acquired immunodeficiency syndrome (AIDS), which is caused by the **human immunodeficiency virus** (HIV). A brief history of such research is given, as

well as a discussion of the difficulties encountered in isolating the microbes which these researchers feel are involved in the disease. Isopathy and living blood analysis are described. Samples of blood from a wide variety of patients are examined.

- **The Child With Immunodeficiency: Evaluation and Management**

  Contact: InfoMedix, 12800 Garden Grove Blvd, Ste F, Garden Grove, CA, 92643, (714) 530-3454.

  Summary: This sound recording from the American Academy of Allergy and Immunology's 45th Annual Meeting, held February 24 - March 1, 1989, in San Antonio, TX, presents a session on various treatment modalities of immune deficiencies, such as **human immunodeficiency virus** (HIV) infection or Acquired immunodeficiency syndrome (AIDS) in children. It covers responses to antigen immunizations, donor T- and B-cells, treating patients with severe combined immune deficiency (SKID) with half-matched bone marrow transplants; and T-cell deficiencies, such as De George's syndrome. Examples of the use of recombinant interleukin II and fetal thymus transplant for T-cell deficiencies are cited and discussed. Questions from the audience address anaphylactic reactions, patient and family selection for home therapy, B-cell dysfunction, subcutaneous infusion versus intramuscular gamma globulin injection, immunoglobulin G subclass deficiencies, and evaluation of patients.

- **Prophecy Band: Going to a Go Go**

  Contact: District of Columbia Department of Health, HIV/AIDS Administration, 717 14th St NW Ste 600, Washington, DC, 20005-3212, (202) 727-2500, http://www.dchealth.com/hiv/welcome.htm.

  Summary: This sound recording is a series of disco songs which have lyrics dealing with drug abuse, IV-needle sharing, and safer sexual conduct to prevent transmission of the **human immunodeficiency virus** (HIV), the etiologic agent of Acquired immunodeficiency syndrome (AIDS).

- **Drug Abuse & AIDS**

  Contact: US Department of Health and Human Services, Public Health Service, National Institutes of Health, National Institute on Drug Abuse, Center on AIDS and Other Medical Consequences of Drug Abuse, Rm 5213 MSC 9561, 6001 Executive Blvd, Bethesda, MD, 20892-9561, (301) 443-1124, http://www.nida.nih.gov.

  Summary: This sound recording of three public service announcements (PSA's) addresses the topic of alcohol and drug abuse and Acquired immunodeficiency syndrome (AIDS). The three PSA's look at how substance abuse can impair judgment and lead to risky sexual behaviors, which may result in **human immunodeficiency virus** (HIV) transmission. These PSA's are part of a campaign aimed at reducing AIDS risk among adolescents. They are titled Tony (60 seconds), Denise (60 seconds), and Denise (30 seconds).

- **Facing Our Fears: Helping Staff Deal With AIDS Issues**

  Source: Taking Action on AIDS.

  Contact: Walker Trieschman Center, Child Welfare League of America, 300 Congress St Ste 305, Quincy, MA, 02169, (617) 769-4010, http://www.cwla.org.

Summary: This sound recording, part of a series, addresses the fears of staff who work in group care facilities for adolescents. It says that workers need to overcome these fears about Acquired immunodeficiency syndrome (AIDS) so that they can better work with clients, and that a sound **human immunodeficiency virus** (HIV) policy and an ongoing education program should help. Most people resist talking openly about their lifestyles and their personal risks due to fears of discrimination and labeling. The AIDS educator should tell staff it's all right to think about themselves first, and clients later. Through anonymous questions and small-group discussion, a good AIDS education program should address personal risk factors and condom use. The sound recording mentions a classroom visit by a Person with AIDS (PWA) and videos as good teaching tools. The remainder of the sound recording briefly looks at some of the fears that staff may face, such as concern about universal precautions and HIV transmission in the workplace. It says that staff should be taught to talk about subjects they feel uneasy about, such as condom use and sexual intercourse. Staff should learn to admit when they don't know the answer to a client's question, and should be taught where to go for more information. The sound recording also says it is important for staff to feel that the administration is doing all it can to protect clients and staff. Also, it says, staff need to learn to understand adolescent subcultures. Often they feel some clients are simply impossible to reach, while the difficulty really stems from a lack of knowledge of the cultural context of the client's lifestyle. Financial worries are also considered.

- **Education and Training: Effective Resources and Strategies for Clients, Staff and Board**

  Contact: Walker Trieschman Center, Child Welfare League of America, 300 Congress St Ste 305, Quincy, MA, 02169, (617) 769-4010, http://www.cwla.org.

  Summary: This sound recording, part of a series, outlines principles and guidelines for Acquired immunodeficiency syndrome (AIDS) education in group care facilities for adolescents. Part I of the presentation gives seven reasons for AIDS education: One, it is the best method of **human immunodeficiency virus** (HIV) prevention; two, it is the best way to fulfill the legal obligation of duty to warn; three, it minimizes fears and maximizes productivity among the staff; four, adolescents usually trust the direct care staff, and they learn best from people they trust; five, it helps update an agency's entire curriculum in the areas of sex, drugs, science, and history; six, it demonstrates willingness to respond to the impact of AIDS on society; and seven, an ongoing agencywide educational approach reinforces principles of safety. In Part II, the sound recording outlines eight guidelines on AIDS education, beginning with the theory that people need to be exposed to AIDS education five times before they really comprehend it. Secondly, the program should begin at the top of the agency, with its board members, then come down through the administration, middle management, staff, and parents. AIDS education should become incorporated into different disciplines, such as biology, statistics, and history. Educators should avoid moralizing and teach that AIDS is a medical condition. The fifth guideline encourages educators to examine their own values; if they feel uncomfortable talking about sex or drug use, the clients will sense this. Therefore, staff should work through their own fears first. Educators should use language that their clients will understand, and should also use appropriate materials and methods. Part III of the sound recording gives nine training tips on AIDS education. Everyone needs to understand that AIDS cannot be transmitted through casual contact, how to prevent HIV transmission, Persons with AIDS (PWA's) need love and support, and AIDS leads to death. Secondly, educators should start out with something nonthreatening, such as statistics or the history of the epidemic. Statistical analysis is

necessary to explain the risk to children, since the latency period lasts so long. The fourth tip tells educators to talk about HIV transmission and prevention, but they.

- **Living Foods: Advanced Immune Discoveries Symposium**

  Contact: Human Energy Press, 493 Beach Park Blvd Ste 210, Foster City, CA, 94404, (415) 349-0718.

  Summary: This sound recording deals with the need for living foods in the human diet and their effect on various diseases, including Acquired immunodeficiency syndrome (AIDS) and **human immunodeficiency virus** (HIV) infection. Greens, for example, are energy foods which cleanse the blood. Disease means an individual needs to rebuild health. In order to do this, fresh fruits and vegetables are needed. There may be a need to create indoor gardens in order to insure freshness. No foods should be cooked, since this destroys the health-restoring properties. Bread is dehydrated and certain other foods may be fermented.

- **Policy Implications Preventing and Treating AIDS: Part B**

  Contact: Convention Cassettes, 1-550 Eclectic St, Ste C-140, Palm Desert, CA, 92260, (415) 776-5454.

  Summary: This sound recording covers a session on the effects of **human immunodeficiency virus** (HIV) prevention and treatment programs on policy development at the Public Health 1990 Conference in California. The first speaker, Dr. Robert Hyatt, describes a study (Archives of Internal Medicine, vol. 150, April 1, 1990) analyzing the medical care costs of Persons with AIDS (PWA's) on the Kaiser Health plan in Northern California. Utilization data presented covers survival time, life time, inpatient hospitalizations, hospital days, average length of stay, and outpatient clinic visits, whereas cost analysis data includes drugs and services. Other issues addressed are additional components of future programs such as counseling and education for behavior modification, increase in infant PWA's, increase in hospital days, inadequate funding, health insurance issues covering attendant care for patients at home, and experimental drugs status. Beverly Bradlee, a San Francisco school district supervisor of health education and health services, talks about teaching Acquired immunodeficiency syndrome (AIDS) in school, in particular the development of HIV prevention programs. She explains what she has learned from the process, and what schools could and need to do about providing sex and AIDS education.

- **Policy Implications Preventing and Treating AIDS: Part A**

  Contact: Convention Cassettes, 1-550 Eclectic St, Ste C-140, Palm Desert, CA, 92260, (415) 776-5454.

  Summary: This sound recording of the New Public Health 1990 conference in California covers a session on the prevalence of **human immunodeficiency virus** (HIV) infection and Acquired immunodeficiency syndrome (AIDS) in California and analyzes the weakness of the public health responses to AIDS. It focuses on deficiencies in government leadership, organizational structure, funding, and resources, and proposes a response to HIV encompassing communicability and behavior changes for prevention and care. Issues discussed include: Surveillance and evaluation, general school information education, targeted community knowing change program, and continuum of care with psychosocial and behavioral support for HIV-infected persons. Early intervention prevention with behavioral and psychosocial counseling, acute hospital care, extended hospital care, and out of hospital care are discussed. It also explains why

the development of programs have been unsuccessful. Frank Kappel, an epidemiologist, presents projections of the incidence of AIDS in California according to region. Statistics of the incidence are reviewed, and data is provided from population-based surveys on seroprevalence and HIV infection. Particular focus is placed on children with AIDS and neonatal analysis of HIV-risk behaviors.

- **Relaxation and Visualization**

  Contact: University of California San Francisco, AIDS Health Project, PO Box 0884, San Francisco, CA, 94143-0884, (415) 476-6430.

  Summary: This sound recording presents a session on relaxation and visualization produced by the University of California at San Francisco, for a project on Acquired immunodeficiency syndrome (AIDS), which is caused by the **human immunodeficiency virus** (HIV). In a 20-minute session, the leader conducts the listening audience through a series of deep breathing and relaxation exercises. He tells his listeners to close their eyes and concentrate on their breathing. Synthesizer music is played in the background throughout most of the sound recording. After the breathing exercises, he moves slowly up the body, starting with the feet and suggests relaxation of each muscle group in turn. He then suggests that his listeners form a mental image of themselves, unstressed, confident, and at peace. Then he counts from one to ten, and tells his listeners that they are becoming present and alert before they open their eyes.

- **America Responds to AIDS -- Radio PSA's: Los Angeles**

  Contact: US Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National AIDS Information and Education Program, Bldg 1 Rm 2122, 1600 Clifton Rd NE, Atlanta, GA, 30333, (404) 639-2928.

  Summary: In this radio public service announcement (PSA), three residents of Los Angeles urge wider discussion of problems associated with **human immunodeficiency virus** (HIV) and Acquired immunodeficiency syndrome (AIDS). One, an AIDS counselor, says there is no way to avoid talking about sex in this connection. An AIDS educator says to talk about AIDS would be to talk about uncomfortable topics like homosexuality, and so people don't do it enough. A volunteer says it's necessary to discuss sex and AIDS to save a life, possibly one's own. An announcer urges listeners to take responsibility for keeping AIDS out of their lives, and to learn the facts about AIDS and tell others.

- **America Responds to AIDS -- Radio PSA's: New York**

  Contact: US Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National AIDS Information and Education Program, Bldg 1 Rm 2122, 1600 Clifton Rd NE, Atlanta, GA, 30333, (404) 639-2928.

  Summary: In this sound recording of a radio public service announcement (PSA), three New Yorkers give warnings about the dangers of contracting **human immunodeficiency virus** (HIV) and/or Acquired immunodeficiency syndrome (AIDS) from sexual partners. An AIDS counselor notes that deciding to have sex is potentially exposing oneself to HIV, but that unlike gonorrhea and syphilis, there is no cure for AIDS. A nurse counselor says that even one sexual encounter could lead to infection. A minority AIDS project worker says there is a problem with young people not knowing how to protect themselves against AIDS, and so efforts must be made to inform them. An announcer notes that AIDS affects everyone, and urges listeners to learn the facts about AIDS to protect themselves and their families.

- **Art Against AIDS**

  Contact: Sunrise Media, 96 Inverness Dr E, Englewood, CO, 80112, (303) 792-3822.

  Summary: This sound recording deals with the contributions made by artists and arts organizations to fighting Acquired immunodeficiency syndrome (AIDS). The presentation begins with a discussion of the number of people in the arts who have succumbed to **human immunodeficiency virus** (HIV), the arts as a tool to reduce discrimination, and the therapeutic and political value of the arts. Excerpts from the play "Heartstrings" which toured the United States raising funds for AIDS research, are included.

- **Working With Substance Abusers - Intervention**

  Contact: Health Impact, PO Box 9443, Seattle, WA, 98109-9443, (206) 284-3865, http://www.healthimpact.org/.

  Summary: This sound recording deals with intervention to change and eliminate patterns of drug or alcohol abuse. Such abuse is associated with high rates of infection with the **human immunodeficiency virus** (HIV), which is the etiologic agent of Acquired immunodeficiency syndrome (AIDS). A variety of intervention strategies are presented, generally based on explaining the risks associated with continuing abuse. Barriers to behavioral modification are also discussed, along with suggestions for surmounting these barriers. Of paramount importance in all these methods is the need to establish a trusting, nonjudgemental relationship with the clients. References and a post-test questionnaire are given in the booklet that accompanies this sound recording.

- **Zidovudine and Alternative Therapies for HIV/AIDS**

  Contact: Health Impact, PO Box 9443, Seattle, WA, 98109-9443, (206) 284-3865, http://www.healthimpact.org/.

  Summary: This sound recording deals with the use of Zidovudine, and other drugs and alternative therapies, in treating **human immunodeficiency virus** (HIV) infection and Acquired immunodeficiency syndrome (AIDS). Experience using Zidovudine alone and in combination with other drugs is explained, and other antiviral drugs which show potential are discussed. Experimental treatment of children with AIDS with Zidovudine has been approved by the Food and Drug Administration (FDA). Criteria for using Zidovudine to prevent or treat opportunistic infections are listed. A wide variety of alternative therapies are described, and recommendations for health professionals to assist HIV-positive persons to use them are given. References and a post-test questionnaire are given in the booklet which accompanies the recording.

- **Oferta de un Paquete de Informacion :10.. [With a Guide Offer :10.]**

  Source: America Responds to AIDS, Parents & Youth Campaign, 12 Public Service Announcements: Track no. 5 (Eng.), track no. 12 (Span.).

  Contact: America Responds to AIDS, 1901 L St NW Ste300, Washington, DC, 20036, (202) 452-9412.

  Summary: This videorecording of a sound track for a public service announcement (PSA) offers a free guide to prevention of **human immunodeficiency virus** (HIV) infection and to communicating with children about this disease. This track is on a videorecording with other PSA's.

- **Introduction to Testing and Counseling**

  Contact: Health Impact, PO Box 9443, Seattle, WA, 98109-9443, (206) 284-3865, http://www.healthimpact.org/.

  Summary: This sound recording deals with three types of antibody tests: the ELISA, the Western blot, and the Immunofluorescent Assay. The functions of each type are described, and the advantages and disadvantages of having testing for **human immunodeficiency virus** (HIV) antibodies are discussed, as are the pre- and post-test counseling needs. Individuals in Washington who are legally required to be offered testing, and those who are legally required to undergo testing, are listed. Review questions and a post-test are given in the booklet that accompanies this recording.

- **Clinical Manifestations and Introduction to Treatment**

  Contact: Health Impact, PO Box 9443, Seattle, WA, 98109-9443, (206) 284-3865, http://www.healthimpact.org/.

  Summary: This sound recording deals with the clinical manifestations of, and treatment for, **human immunodeficiency virus** (HIV) infection and Acquired immunodeficiency syndrome (AIDS). Symptoms of each stage of disease and the appropriate treatments are described. Signs identifying potential asymptomatic carriers are listed. Various opportunistic infections are described, along with recommended treatment programs for each. Visuals, references, review questions, and a post-test are given in the booklet that accompanies this recording.

- **Transmission and Infection Control**

  Contact: Health Impact, PO Box 9443, Seattle, WA, 98109-9443, (206) 284-3865, http://www.healthimpact.org/.

  Summary: This sound recording deals with the modes by which the **human immunodeficiency virus** (HIV) is transmitted, and ways to prevent its spread. Transmission by sexual means, by blood transfer in transfusion or IV-needle sharing, and in-utero and perinatal routes are discussed. Evidence disproving casual contact transmission is explained. Public-health measures to control HIV and Acquired immunodeficiency virus (AIDS) are listed, and the role health professionals play in its control is analyzed. Review questions, references, and a post-test are given in the booklet that accompanies this recording.

- **Living With AIDS Instead of Dying From It. First International Conference on Traditional and Complementary Therapies in the Prevention and Treatment of AIDS; Washington, D.C., February 17-19,**

  Contact: Institute for Learning Mastery, PO Box 314, Baltimore, MD, 21203, (410) 366-7373.

  Summary: This sound recording presentation given at the First International Conference on Traditional and Complementary Therapies in the Prevention and Treatment of AIDS, held in Washington, D.C. on February 17 - 19, 1989, deals with living with Acquired immunodeficiency syndrome (AIDS) or infection with the **human immunodeficiency virus** (HIV). The speaker points out that health is more than the absence of disease. He fears that the names HIV and AIDS are locking thoughts into a certain progression, e.g., full-blown AIDS. The population may then fail to see that HIV-positive persons are not, and do not necessarily become, Persons with AIDS (PWA's). Antibody tests have mixed value for otherwise apparently healthy people. A positive result may lead people to

follow a more healthy life style, but it may also cause discrimination. PWA's must tell someone of their disease if they are to survive and they need to experience their own healing anger. They must also learn to discriminate between news and treatments that may help them and those which will only upset them. A rule of thumb suggested by the speaker is that if the information will improve the immune system or the quality of life, pay attention.

- **A Conversation About National AIDS Policy: Part 1 & Part 2**

  Contact: Institute for Learning Mastery, PO Box 314, Baltimore, MD, 21203, (410) 366-7373.

  Summary: In this sound recording, several individuals discuss what they would do about Acquired immunodeficiency syndrome (AIDS), caused by the **human immunodeficiency virus** (HIV), if they were President of the United States. The first speaker says that he would provide a plurality of health systems; that we do not have enough diversity of health care. He said he would make a 25 percent cut in the Department of Defense funds and would redistribute the money to health care and research. The next speaker, Kelly Dunn, says that she would decrease the cost of azidothymidine, and provide research money to identify the cofactors that turn HIV into into full-blown AIDS. She says that she would provide financial support to the small pharmaceutical companies and would educate the public through all of the media. The next speaker is a hemophiliac, who describes what it was like growing up with hemophilia in the 60's. He says that many things which happened to hemophiliacs then are happening to Persons with AIDS (PWA's) today. He says that as soon as health becomes cost effective, that we will see a great change. Next, Dr. Joan Priestley, from California, makes a few suggestions to improve the country. She says that any company convicted of fraud should be forever barred from doing business with the government. She says the government should also stop subsidizing the growing of tobacco, and that single-parent families should have a place to leave children during the day while the parent works. She says that more money should be put into alternative treatments for AIDS. The final speaker emphasizes the need for a massive expansion of drug treatment centers.

- **Legal and Ethical Issues**

  Contact: Health Impact, PO Box 9443, Seattle, WA, 98109-9443, (206) 284-3865, http://www.healthimpact.org/.

  Summary: This sound recording deals with the legal and ethical issues involved in testing and treating persons with **human immunodeficiency virus** (HIV) infection and Acquired immunodeficiency syndrome (AIDS). The legal issues surrounding antibody tests, confidentiality of the results, discrimination against HIV-positive persons or Persons with AIDS (PWA's), and contact tracing are discussed. The right to pre- and post-test counseling is also explained. Legal requirements for accommodating handicapped employees, such as those who have AIDS, are described. Ethical issues concerning medical treatment of HIV-positive persons and PWA's are analyzed. Review questions and visuals are included in the booklet that accompanies this recording.

- **Pharmacologic Treatment of HIV - Related Illness**

  Contact: Health Impact, PO Box 9443, Seattle, WA, 98109-9443, (206) 284-3865, http://www.healthimpact.org/.

Summary: This sound recording describes the three major types of therapeutic drugs needed to treat persons with **human immunodeficiency virus** (HIV) infection or Acquired immunodeficiency syndrome (AIDS). These types are those used to treat opportunistic infections, those antiviral drugs used to combat HIV itself, and the drugs used to combat the side effects of other drugs or the symptoms of HIV. Various opportunistic infections and HIV-related cancers are listed, along with suggested treatments and possible side effects. Sample drug cards are included in the booklet that accompanies this recording.

- **Tres Hombres sin Fronteras.. [Three Men Without Frontiers.]**

  Contact: University of Washington, Novela Health Education, 901 Boren St Ste 1100, Seattle, WA, 98104, (800) 677-4799. Radio KDNA, Northwest Communities Education Center, PO Box 800, Granger, WA, 98932, (509) 854-2222.

  Summary: This audiorecording is targeted toward Hispanic migrant farmworkers, to inform, discuss, educate, and alert them about Acquired immunodeficiency syndrome (AIDS) in a way they can relate to and understand. This is done by narrating the story of three men as they leave Mexico and go to the U.S. to look for work opportunities. Victor and Sergio are married, and their wives are pregnant. Both have been through the journey before. Marco is single, and this is his first time away from home. Victor warns Marco about Sexually transmitted diseases (STD's), especially about AIDS, and the use of condoms when they encounter the offer of a prostitute. Victor chooses to remain celibate as he has done before. Sergio and Marco both have unprotected sexual relations. They then develop gonorrhea and learn the prostitute was also an Intravenous drug user (IVDU). Sergio, as the macho man, seeks treatment from a local woman who gives penicillin injections. Marco, with Victor's guidance, seeks help through the local health clinic. The doctor there explains to him about STD's and **human immunodeficiency virus** (HIV), reviews issues such as how it is contracted and transmitted, symptoms, high-risk groups, lack of cure or vaccine, and testing, and emphasizes the importance of the use of condoms. Sergio continues in his risky lifestyle. Marco learns to use condoms, falls in love, and is considering marriage. Sergio's health is not good, and when he receives news of his family, he returns to find both his wife and newborn son have AIDS. The issues of mother-to-child transmission, symptoms, and lack of cure are stressed. The importance of prevention is reinforced. He seeks help from his friends and the myth of transmission by casual contact is dispelled. He returns home to die. Marco marries after having a negative antibody test. Victor's celibacy is rewarded with a healthy wife and son.

- **Rappin' on AIDS; Volume II**

  Contact: AIDS Prevention Project, City of Toronto, Department of Public Health, City Hall 7th Fl, E Tower 100 Queen St, Toronto, (800) 668-2437.

  Summary: This sound recording is a series of rap songs dealing with safer sexual behavior, avoiding drug abuse and IV-needle sharing, and the need for drug and sex education to prevent transmission of the **human immunodeficiency virus** (HIV), the etiologic agent of Acquired immunodeficiency syndrome (AIDS).

- **AIDS Update: ED Management, Part II**

  Contact: California Medical Association, Audio Digest Foundation, 1577 E Chevy Chase Dr, Glendale, CA, 91206, (213) 245-8505.

Summary: This sound recording, along with accompanying pre-test and post-test questions, comprises part of an ongoing series of educational activities. The first speaker, George F. Risi Jr., Assistant Professor of Medicine at Louisiana State University School of Medicine in New Orleans, looks at the evolution of the Acquired immunodeficiency syndrome (AIDS) epidemic between 1981 and 1986. He discusses the test for **human immunodeficiency virus** (HIV) antibodies, HIV transmission, early theories about the origin of the illness, and the Centers for Disease Control and Prevention (CDC) classification system for AIDS patients. David F. Dreis, of the Section of Chest and Infectious Diseases at Virginia Mason Medical Center in Seattle, looks at symptoms and opportunistic infections associated with AIDS in the second presentation. He examines Pneumocystis carinii pneumonia (PCP), Candida Albicans, Kaposi's sarcoma, decreased vision, headache, unexplained fever, leukoplakia, pulmonary diseases, cryptosporidium, toxoplasmosis, and tuberculosis (TB). Asymptomatic carriers are discussed.

- **Developing a Continuum of Care for Persons With HIV/AIDS**

  Contact: Health Impact, PO Box 9443, Seattle, WA, 98109-9443, (206) 284-3865, http://www.healthimpact.org/.

  Summary: This sound recording explains the range of care that may be required for persons with **human immunodeficiency virus** (HIV) infection or Acquired immunodeficiency syndrome (AIDS), and why policies and provisions for such care should be developed. Individual case management is the cornerstone of such care. The range of care encompasses in-home, multi-site, community, physician-directed, and institutional. The type of care required is generally determined by the case manager. Whether it is performed by volunteers or by paid personnel is determined by the community and its resources. References and a post-test questionnaire are included in the booklet that accompanies this sound recording.

- **Self - Care for Providers**

  Contact: Health Impact, PO Box 9443, Seattle, WA, 98109-9443, (206) 284-3865, http://www.healthimpact.org/.

  Summary: This sound recording deals with the stress experienced by caregivers of persons with **human immunodeficiency virus** (HIV) infection or Acquired immunodeficiency syndrome (AIDS). Stress management is vitally important so that caregivers do not experience burnout. Causes and symptoms of stress are listed, along with recommendations for overcoming these problems. Review questions and references are listed in the booklet that accompanies this recording.

- **Living With AIDS: Personal Perspectives**

  Contact: Health Impact, PO Box 9443, Seattle, WA, 98109-9443, (206) 284-3865, http://www.healthimpact.org/.

  Summary: This sound recording is the story of two Persons with AIDS (PWA's). The first is Pat, a married woman whose husband was infected with the **human immunodeficiency virus** (HIV) in a sexual encounter several years ago. She is HIV positive and he has been diagnosed with Acquired immunodeficiency syndrome (AIDS). During the course of his illness, he has been unable to work and she has become the primary source of income. She explains how her expectations have changed from the time before the illness struck when they had two cars, a boat, and a lovely home, and expected to have children. Now, because of her HIV infection, she will not have

children, and their standard of living has been reduced. She explains that she does not resent her husband's infecting her with HIV because she feels it was just very bad luck that he became infected. The second story is Michael's. He is a 26-year old homosexual male, and explains that he copes with AIDS by using humor and drawing cartoons which are published in a newsletter. His family has not been supportive, but he realizes that many people are in the same situation. He tells of a friend who, although hospitalized himself with AIDS, managed to replace Michael's pills with M & M's during Michael's visit to him in the hospital. References and a post-test questionnaire are included in the booklet that accompanies this recording.

- **AIDS and Other Transmissible Diseases: Protecting Yourself in the Operating Room**

  Contact: California Medical Association, Audio Digest Foundation, 1577 E Chevy Chase Dr, Glendale, CA, 91206, (213) 245-8505.

  Summary: This sound recording, along with accompanying pre-test and post-test questions, is part of an ongoing series of educational activities. The first speaker, Elizabeth A. Donegan, Assistant Professor of Clinical Laboratory Medicine, University of California, San Francisco, School of Medicine, discusses the major infections transmitted by blood transfusions which include cytomegalovirus (CMV), **human immunodeficiency virus** (HIV) infection, and HTLV-1. Nancy B. Bjerke, Major, United States Air Force, in North Carolina, and course supervisor/instructor of Sheppard Air Force Base in Texas, talks about the mechanisms for health care worker protection. Her presentation deals with the most frequent occupational injuries to health-care workers, disease transmission, safety precautions and hepatitis B immunization for health-care workers. The third speaker, Arnold J. Berry, Associate Professor of Anesthesiology, Emory University School of Medicine in Atlanta, looks at disease transmission in the operating room. His presentation deals with the implementation of universal precautions, risks to anesthesiologists other than Acquired immunodeficiency syndrome (AIDS) and Hepatitis B, specific recommendations for anesthesia equipment, handwashing, and infections from intravenous lines. The final speaker, C. Daniel Sooy, Assistant Professor of Otolaryngology, University of California in San Francisco, School of Medicine; and Director of Otolaryngology Clinic, San Francisco General Hospital, discusses policies for protecting the anesthesiologist. This presentation includes universal precautions, preoperative testing for HIV, and exposed health care workers.

- **CDC/AIDS Task Force :60 Radio Koop, Windom, Bowen**

  Contact: US Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National AIDS Information and Education Program, Bldg 1 Rm 2122, 1600 Clifton Rd NE, Atlanta, GA, 30333, (404) 639-2928.

  Summary: In this sound recording, U.S. Surgeon General C. Everett Koop asks if Americans know how **human immunodeficiency virus** (HIV) and Acquired immunodeficiency syndrome (AIDS) affect them as individuals. Robert Windom, U.S. Public Health Service director, states that more than one million Americans are infected with HIV. Otis Bowen, Secretary of Health and Human Services, announces the national mailing of "Understanding AIDS," and urges everyone to read it and discuss it, to get the information needed to prevent the spread of AIDS.

- **AIDS: At Last the Good News, Tape 1 and Tape 2**

  Contact: Hypnodyne Foundation, PO Box 17353, Clearwater, FL, 34622, (813) 536-2960.

Summary: These sound recordings provide resources for learning about Persons with **human immunodeficiency virus** (HIV) infection or Acquired immunodeficiency syndrome (AIDS) who have survived significantly longer than expected, or who have been cured. Many case studies in a variety of alternative and holistic therapies are examined, including one of a child with AIDS. The importance of exercise and good nutrition are stressed. Psychological factors impacting health are analyzed. The second sound recording contains a self-hypnosis session on one side and a guided imagery session on the other. Both of these sessions are set to soothing instrumental music.

- **No One Surviving**

  Source: Sir Justice Emcee, Life of the Future.

  Contact: God N Hop Records International, PO Box 11764, Tampa, FL, 33680, (813) 321-0622.

  Summary: This videorecording deals with **human immunodeficiency virus** (HIV) and other Sexually transmitted diseases (STD's). The song describes an attractive young woman who develops Acquired immunodeficiency syndrome (AIDS) and goes on to tell of other STD's. The song is on a videorecording called Life of the Future, which includes other songs not about AIDS.

- **The AIDS Epidemic: Implications for Mental and Public Health. American Public Health Association, 116th Annual Meeting**

  Contact: American Public Health Association, 800 I St NW, Washington, DC, 20001, (301) 893-1894, http://www.apha.org.

  Summary: This sound recording presents four papers on advancement of knowledge about Acquired immunodeficiency syndrome (AIDS) delivered at the School Health Education and Services (SHES) sponsored session on AIDS education and health services with Robert McDermott from the University of South Florida, College of Public Health, as the presiding chairman. The first paper, titled AIDS in Comprehensive School Health Education K-12 - If Not Now, When?, is presented in two parts by Cheryl Vince and Charles Deutsch from the Educational Development Center in Newton, MA. The first part discusses the comprehensive health education approach, whereas the second describes the national training program. The second paper, "AIDS Transmission Changes in Knowledge and Behavior Among Adolescents by Gender" is by Ralph Hinson from the Boston University School of Public Health. It presents the findings of a 1986 and 1988 survey investigating adolescent attitudes about **human immunodeficiency virus** (HIV) infection, and knowledge of HIV transmission and HIV prevention. The third paper deals with development of a Self-efficacy Scale for AIDS Education with high-risk groups. It presents a study of behavior predictors in 58 pregnant females between 15 and 18 years of age, such as condom use, IV-needle sharing, and multiple sex partners. The last paper, titled "Persons With AIDS as Presenters of San Francisco AIDS Prevention Education for School-Age Youth at Risk for HIV Infection" is presented by Kimberly Cox of the San Francisco Department of Public Health, and a family life health educator and AIDS teacher trainer for the San Francisco Unified School District. It describes the four one-hour sessions of the Wedge Program, which provides information and education about AIDS to adolescents through peer teaching.

- **AIDS and Public Hospitals. American Public Health Association, 116th Annual Meeting**

  Contact: American Public Health Association, 800 I St NW, Washington, DC, 20001, (301) 893-1894, http://www.apha.org.

  Summary: This sound recording presents a panel discussion of the impact of Acquired immunodeficiency syndrome (AIDS) on public hospitals. Dr. Constance Williams, from Orange County, CA, discusses the impact of AIDS on residency and teaching programs in public hospitals from a resident physician's perspective. It examines the relationship between the Person with AIDS (PWA) and the resident physician in a public hospital, and presents two case studies, one of the Committee of Interns and Residents (CIR) in Newark, NJ, and the other from the San Francisco Association of Interns and Residents (SFIR), dealing with issues such as health hazards of needlestick injuries and their reporting, and state legislation regarding results of tests for **human immunodeficiency virus** (HIV) antibodies. Dr. Dennis Andrulis, vice president of the National Association of Public Hospitals, then talks about the financial and organizational impact of AIDS on public hospitals. He presents the results of a study of utilization and cost of public hospital health care for PWA's. He then draws conclusions about the reality of the financial crisis public hospitals are facing with increasing numbers of PWA's without insurance coverage and presents solutions to the problem, specifically a Federal government policy providing continuum of care for PWA's, as well as financial support from private foundations such as the Robert Wood Johnson Foundation.

- **Workshop for Support Staff and Others**

  Source: 3rd National Forum on AIDS and Hepatitis B. Washington, DC, November 21-22, 1988.

  Contact: National Foundation for Infectious Diseases, 4733 Bethesda Ave Ste 750, Bethesda, MD, 20814-5228, (301) 656-0003, http://www.nfid.org. Sound Solution, PO Box 566074, Dallas, TX, 75356, (214) 258-6144.

  Summary: This sound recording contains proceedings of the 3rd National Forum on AIDS and Hepatitis B held in Washington, DC on November 21-22, 1988. It covers the workshop on support staff and others, and their need for general education on Acquired immunodeficiency syndrome (AIDS) and specific education on protection against the **human immunodeficiency virus** (HIV). Current programs and problems are discussed. The problems that are encountered include language barriers, high turnover of employees, and fear.The importance of targeting the information to specific groups is emphasized. Note: Audio quality on the sound recording is not consistent. Some of the discussion is difficult to hear.

Bibliography: Multimedia on Human Immunodeficiency Virus

The National Library of Medicine is a rich source of information on healthcare-related multimedia productions including slides, computer software, and databases. To access the multimedia database, go to the following Web site: **http://locatorplus.gov/**. Select "Search LOCATORplus." Once in the search area, simply type in human immunodeficiency virus (or synonyms). Then, in the option box provided below the search box, select "Audiovisuals and Computer Files." From there, you can choose to sort results by publication date, author, or relevance. The following multimedia has been indexed on human immunodeficiency virus:

- Etiology and immunopathogenesis of the acquired immunodeficiency syndrome; Epidemiology and clinical classification of human immunodeficiency virus (HIV) infection [videorecording] Source: [presented by] CMESAT; Year: 1987; Format: Videorecording; [Sarasota, Fla.]: CMESAT, c1987
- **Human immunodeficiency virus infections [videorecording]: new insights** Source: American Society for Microbiology; Year: 1993; Format: Videorecording; Secaucus, N.J.: Network for Continuing Medical Education, [1993?]
- **Tracking human immunodeficiency viruses [videorecording]** Source: Gerald Myers; Year: 1989; Format: Videorecording; Bethesda, MD: National Library of Medicine, 1989

CHAPTER 9. PERIODICALS AND NEWS ON HUMAN IMMUNODEFICIENCY VIRUS

Overview

In this chapter, we suggest a number of news sources and present various periodicals that cover human immunodeficiency virus.

News Services and Press Releases

One of the simplest ways of tracking press releases on human immunodeficiency virus is to search the news wires. In the following sample of sources, we will briefly describe how to access each service. These services only post recent news intended for public viewing.

PR Newswire

To access the PR Newswire archive, simply go to **http://www.prnewswire.com/**. Select your country. Type "human immunodeficiency virus" (or synonyms) into the search box. You will automatically receive information on relevant news releases posted within the last 30 days. The search results are shown by order of relevance.

Reuters Health

The Reuters' Medical News and Health eLine databases can be very useful in exploring news archives relating to human immunodeficiency virus. While some of the listed articles are free to view, others are available for purchase for a nominal fee. To access this archive, go to **http://www.reutershealth.com/en/index.html** and search by "human immunodeficiency virus" (or synonyms). The following was recently listed in this archive for human immunodeficiency virus:

- **Chimeric simian-human immunodeficiency virus persistently infects macaques**
  Source: Reuters Medical News
  Date: October 04, 2000
  http://www.reutershealth.com/archive/2000/10/04/professional/links/20001004scie001.html

The NIH

Within MEDLINEplus, the NIH has made an agreement with the New York Times Syndicate, the AP News Service, and Reuters to deliver news that can be browsed by the public. Search news releases at **http://www.nlm.nih.gov/medlineplus/alphanews_a.html**. MEDLINEplus allows you to browse across an alphabetical index. Or you can search by date at the following Web page: **http://www.nlm.nih.gov/medlineplus/newsbydate.html**. Often, news items are indexed by MEDLINEplus within its search engine.

Business Wire

Business Wire is similar to PR Newswire. To access this archive, simply go to **http://www.businesswire.com/**. You can scan the news by industry category or company name.

Market Wire

Market Wire is more focused on technology than the other wires. To browse the latest press releases by topic, such as alternative medicine, biotechnology, fitness, healthcare, legal, nutrition, and pharmaceuticals, access Market Wire's Medical/Health channel at **http://www.marketwire.com/mw/release_index?channel=MedicalHealth**. Or simply go to Market Wire's home page at **http://www.marketwire.com/mw/home**, type "human immunodeficiency virus" (or synonyms) into the search box, and click on "Search News." As this service is technology oriented, you may wish to use it when searching for press releases covering diagnostic procedures or tests.

Search Engines

Medical news is also available in the news sections of commercial Internet search engines. See the health news page at Yahoo (**http://dir.yahoo.com/Health/News_and_Media/**), or you can use this Web site's general news search page at **http://news.yahoo.com/**. Type in "human immunodeficiency virus" (or synonyms). If you know the name of a company that is relevant to human immunodeficiency virus, you can go to any stock trading Web site (such as **http://www.etrade.com/**) and search for the company name there. News items across various news sources are reported on indicated hyperlinks. Google offers a similar service at **http://news.google.com/**.

BBC

Covering news from a more European perspective, the British Broadcasting Corporation (BBC) allows the public free access to their news archive located at **http://www.bbc.co.uk/**. Search by "human immunodeficiency virus" (or synonyms).

Newsletters on Human Immunodeficiency Virus

Find newsletters on human immunodeficiency virus using the Combined Health Information Database (CHID). You will need to use the "Detailed Search" option. To access CHID, go to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. Limit your search to "Newsletter" and "human immunodeficiency virus." Go to the bottom of the search page where "You may refine your search by." Select the dates and language that you prefer. For the format option, select "Newsletter." Type "human immunodeficiency virus" (or synonyms) into the "For these words:" box. The following list was generated using the options described above:

- **Special Focus: School Health: Reducing the Burden of Chronic Disease: Promoting Healthy Behaviors Among Youth**

  Source: Chronic Disease Notes and Reports. 14(1):1-36, Winter 2001.

  Contact: Centers for Disease Control and Prevention, Mail Stop K-11, 4770 Buford Highway, NE., Atlanta, GA 30341-3717. (770) 488-5050. FAX: (770) 488-5095. INTERNET/EMAIL: http://www.cdc.gov/nccdphp; ccdinfo@cdc.gov.

  Summary: The focus of this newsletter issue is on using school health programs to reduce the impact of chronic disease and risky behavior by promoting healthy lifestyles. Years spent in the education process in the United States could vastly improve the health of the future adults of this nation if additional emphasis and understanding could be placed on the importance of physical activity, fruit and vegetable consumption, and reduced tobacco use. Schools could help prevent cardiovascular diseasse, cancer, and diabetes. The Centers for Disease Control and Prevention (CDC) employs four national strategies to improve young people's health: (1) Monitor critical health events and school policies and programs, (2) synthesize and apply research to improve school policies and programs, (3) enable constituents to help schools implement effective policies and programs, and (4) evaluate to improve policies and programs. Key to monitoring chronic disease risk factors is the Youth Risk Behavior Surveillance System. The School Health Index for Physical Activity and Healthy Eating: A Self-Assessment and Planning Guide, provides a checklist questionnaire to rate school policies and programs against CDC standards. The Fit, Healthy and Ready to Learn tool serves as a guide to school health policy development. The CDC has developed an eight-component model to assist in the development of coordinated school health programs: (1) Health education, (2) physical education, (3) health services, (4) nutrition services, (5) health promotion for staff, (6) counseling and psychological services, (7) healthy school environment, and (8) parent/community involvement. Reaching and protecting young people at risk for **human immunodeficiency virus** infection is also reviewed in this report as it pertains to school health program efforts. State efforts target physical activity, absenteeism linked to asthma attacks, and oral health. Finally, the efforts of the CDC in the area of international school health activities are discussed.

Newsletter Articles

Use the Combined Health Information Database, and limit your search criteria to "newsletter articles." Again, you will need to use the "Detailed Search" option. Go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. Go to the bottom of the search page where "You may refine your search by." Select the dates and language that you prefer. For the format option, select "Newsletter Article." Type "human immunodeficiency virus" (or synonyms) into the "For these words:" box. You should check back periodically with this database as it is updated every three months. The following is a typical result when searching for newsletter articles on human immunodeficiency virus:

- **Understanding the AIDS Dementia Complex**

  Source: Family Survival Project Update. [Newsletter] 10(3): 6. Fall, 1991.

  Contact: Family Survival Project. 425 Bush Street, Suite 500, San Francisco, CA 94108. (415) 434-3388 or (800) 445-8106 (in California). PRICE: Call for price information.

  Summary: This newsletter article for the nonprofessional caregiver reviews the types of neurological problems that may develop in people infected with the **human immunodeficiency virus** (HIV). Neurological disorders in people with acquired immune deficiency syndrome (AIDS) consist of two broad types: opportunistic infections such as Cryptococcal meningitis and Toxoplasmosis, and the AIDS Dementia Complex. The AIDS Dementia Complex is caused by direct infection of the brain by the HIV virus. Early cognitive symptoms include poor concentration, slowed mental processing, impaired initiation, and forgetfulness. Behavioral symptoms include withdrawal, apathy, and personality changes. Early motor problems include difficulty with balance, clumsiness, and leg weakness. There is no treatment for AIDS Dementia Complex, but some patients have benefitted from the anti-viral drug, AZT (Azidothymidine or Retrovir). Caregivers should be aware of the common early signs of cognitive impairment so that patients can be quickly referred for diagnosis and treatment. 4 references.

- **SLE and Infections**

  Source: SLE Newsletter. 3-6; Fall 1997.

  Contact: Bay Area Lupus Foundation, Inc., 3635 North First Street, Suite 206, San Jose, CA 95134. (408) 954-8600.

  Summary: This newsletter article for health professionals and individuals with systemic lupus erythematosus (SLE) discusses the problem of developing infections in SLE. It explains why physicians should be concerned about infections in patients with SLE; provide a typical presentation of an SLE patient with an infection; and identified the risk factors for infection in SLE, including immune system dysfunction, reticuloendothelial system dysfunction, and immunosuppressive therapy. Other risk factors for infections, disease activity and renal diseases are discussed. The article is described clinically infectious syndromes and clues to their diagnosis, focusing on fever, headache, shortness of breath, joint pain, chest pain, abdominal pain, urinary tract infection, and skin infection. In addition, it examines the coexistence of **human immunodeficiency virus** and SLE and considers the controversial preventive measures of antibiotic prophylaxis and immunization. 1 photograph.

Academic Periodicals covering Human Immunodeficiency Virus

Numerous periodicals are currently indexed within the National Library of Medicine's PubMed database that are known to publish articles relating to human immunodeficiency virus. In addition to these sources, you can search for articles covering human immunodeficiency virus that have been published by any of the periodicals listed in previous chapters. To find the latest studies published, go to **http://www.ncbi.nlm.nih.gov/pubmed**, type the name of the periodical into the search box, and click "Go."

If you want complete details about the historical contents of a journal, you can also visit the following Web site: **http://www.ncbi.nlm.nih.gov/entrez/jrbrowser.cgi**. Here, type in the name of the journal or its abbreviation, and you will receive an index of published articles. At **http://locatorplus.gov/**, you can retrieve more indexing information on medical periodicals (e.g. the name of the publisher). Select the button "Search LOCATORplus." Then type in the name of the journal and select the advanced search option "Journal Title Search."

CHAPTER 10. RESEARCHING MEDICATIONS

Overview

While a number of hard copy or CD-ROM resources are available for researching medications, a more flexible method is to use Internet-based databases. Broadly speaking, there are two sources of information on approved medications: public sources and private sources. We will emphasize free-to-use public sources.

U.S. Pharmacopeia

Because of historical investments by various organizations and the emergence of the Internet, it has become rather simple to learn about the medications recommended for human immunodeficiency virus. One such source is the United States Pharmacopeia. In 1820, eleven physicians met in Washington, D.C. to establish the first compendium of standard drugs for the United States. They called this compendium the U.S. Pharmacopeia (USP). Today, the USP is a non-profit organization consisting of 800 volunteer scientists, eleven elected officials, and 400 representatives of state associations and colleges of medicine and pharmacy. The USP is located in Rockville, Maryland, and its home page is located at **http://www.usp.org/**. The USP currently provides standards for over 3,700 medications. The resulting USP DI® Advice for the Patient® can be accessed through the National Library of Medicine of the National Institutes of Health. The database is partially derived from lists of federally approved medications in the Food and Drug Administration's (FDA) Drug Approvals database, located at **http://www.fda.gov/cder/da/da.htm**.

While the FDA database is rather large and difficult to navigate, the Phamacopeia is both user-friendly and free to use. It covers more than 9,000 prescription and over-the-counter medications. To access this database, simply type the following hyperlink into your Web browser: **http://www.nlm.nih.gov/medlineplus/druginformation.html**. To view examples of a given medication (brand names, category, description, preparation, proper use, precautions, side effects, etc.), simply follow the hyperlinks indicated within the United States Pharmacopeia (USP).

Below, we have compiled a list of medications associated with human immunodeficiency virus. If you would like more information on a particular medication, the provided hyperlinks will direct you to ample documentation (e.g. typical dosage, side effects, drug-

interaction risks, etc.). The following drugs have been mentioned in the Pharmacopeia and other sources as being potentially applicable to human immunodeficiency virus:

Abacavir

- **Systemic - U.S. Brands:** Ziagen
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203732.html

Alglucerase

- **Systemic - U.S. Brands:** Ceredase
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202625.html

Alpha 1 -Proteinase Inhibitor, Human

- **Systemic - U.S. Brands:** Prolastin
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202022.html

Amprenavir

- **Systemic - U.S. Brands:** Agenerase
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203778.html

Antihemophilic Factor

- **Systemic - U.S. Brands:** Alphanate; Bioclate; Helixate; Humate-P; Hyate:C; Koate-HP; Kogenate; Monarc-M; Monoclate-P; Recombinate
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202671.html

Azithromycin

- **Systemic - U.S. Brands:** Zithromax
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202642.html

Delavirdine

- **Systemic - U.S. Brands:** Rescriptor
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203521.html

Didanosine

- **Systemic - U.S. Brands:** Videx
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202616.html

Efavirenz

- **Systemic - U.S. Brands:** Sustiva
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203687.html

Factor Ix

- **Systemic - U.S. Brands:** BeneFix; Mononine
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202674.html

Ganciclovir

- **Systemic - U.S. Brands:** Cytovene; Cytovene-IV
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202255.html

Hepatitis B Vaccine Recombinant

- **Systemic - U.S. Brands:** Engerix-B
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202281.html

Indinavir

- **Systemic - U.S. Brands:** Crixivan
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203523.html

Lamivudine

- **Systemic - U.S. Brands:** Epivir; Epivir-HBV
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202292.html
- **Systemic - U.S. Brands:** Epivir; Epivir-HBV
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202791.html
- **Systemic - U.S. Brands:** Epivir; Epivir-HBV
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203689.html

Lamivudine and Zidovudine

- **Systemic - U.S. Brands:** Combivir
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203386.html

Lopinavir and Ritonavir

- **Systemic - U.S. Brands:** Kaletra
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/500251.html

Nelfinavir

- **Systemic - U.S. Brands:** Viracept
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203526.html

Nevirapine

- **Systemic - U.S. Brands:** Viramune
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203527.html

Progesterone Intrauterine Device

- **Iud) - U.S. Brands**: Progestasert
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202774.html

Progestins for Contraceptive Use

- **Systemic - U.S. Brands:** Depo-Provera Contraceptive Injection; Micronor; NORPLANT System; Nor-QD; Ovrette; Plan B
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202757.html

Rifabutin

- **Systemic - U.S. Brands:** Mycobutin
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202683.html

Ritonavir

- **Systemic - U.S. Brands:** Norvir
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203528.html

Saquinavir

- **Systemic - U.S. Brands:** Fortovase; Invirase
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/203529.html

Stavudine

- **Systemic - U.S. Brands:** Zerit
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202728.html

Zalcitabine

- **Systemic - U.S. Brands:** HIVID
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202652.html

Zidovudine

- **Systemic - U.S. Brands:** Retrovir
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202602.html

Commercial Databases

In addition to the medications listed in the USP above, a number of commercial sites are available by subscription to physicians and their institutions. Or, you may be able to access these sources from your local medical library.

Mosby's Drug Consult™

Mosby's Drug Consult™ database (also available on CD-ROM and book format) covers 45,000 drug products including generics and international brands. It provides prescribing information, drug interactions, and patient information. Subscription information is available at the following hyperlink: **http://www.mosbysdrugconsult.com/**.

PDR*health*

The PDR*health* database is a free-to-use, drug information search engine that has been written for the public in layman's terms. It contains FDA-approved drug information adapted from the Physicians' Desk Reference (PDR) database. PDR*health* can be searched by brand name, generic name, or indication. It features multiple drug interactions reports. Search PDR*health* at **http://www.pdrhealth.com/drug_info/index.html**.

Other Web Sites

Drugs.com (**www.drugs.com**) reproduces the information in the Pharmacopeia as well as commercial information. You may also want to consider the Web site of the Medical Letter, Inc. (**http://www.medletter.com/**) which allows users to download articles on various drugs and therapeutics for a nominal fee.

Researching Orphan Drugs

Although the list of orphan drugs is revised on a daily basis, you can quickly research orphan drugs that might be applicable to human immunodeficiency virus by using the database managed by the National Organization for Rare Disorders, Inc. (NORD), at **http://www.rarediseases.org/**. Scroll down the page, and on the left toolbar, click on "Orphan Drug Designation Database." On this page (**http://www.rarediseases.org/search/noddsearch.html**), type "human immunodeficiency virus" (or synonyms) into the search box, and click "Submit Query." When you receive your results, note that not all of the drugs may be relevant, as some may have been withdrawn from orphan status. Write down or print out the name of each drug and the relevant contact information. From there, visit the Pharmacopeia Web site and type the name of each orphan drug into the search box at **http://www.nlm.nih.gov/medlineplus/druginformation.html**. You may need to contact the sponsor or NORD for further information.

NORD conducts "early access programs for investigational new drugs (IND) under the Food and Drug Administration's (FDA's) approval 'Treatment INDs' programs which allow for a limited number of individuals to receive investigational drugs before FDA marketing approval." If the orphan product about which you are seeking information is approved for marketing, information on side effects can be found on the product's label. If the product is not approved, you may need to contact the sponsor.

The following is a list of orphan drugs currently listed in the NORD Orphan Drug Designation Database for human immunodeficiency virus:

- **5a8, monoclonal antibody to CD4**

  http://www.rarediseases.org/nord/search/nodd_full?code=503
- **Immune globulin intravenous, human (trade name: Gamimune N)**

  http://www.rarediseases.org/nord/search/nodd_full?code=57
- **Immune globulin intravenous, human (trade name: Gamimune N)**

  http://www.rarediseases.org/nord/search/nodd_full?code=572

If you have any questions about a medical treatment, the FDA may have an office near you. Look for their number in the blue pages of the phone book. You can also contact the FDA through its toll-free number, 1-888-INFO-FDA (1-888-463-6332), or on the World Wide Web at **www.fda.gov**.

APPENDICES

APPENDIX A. PHYSICIAN RESOURCES

Overview

In this chapter, we focus on databases and Internet-based guidelines and information resources created or written for a professional audience.

NIH Guidelines

Commonly referred to as "clinical" or "professional" guidelines, the National Institutes of Health publish physician guidelines for the most common diseases. Publications are available at the following by relevant Institute[13]:

- Office of the Director (OD); guidelines consolidated across agencies available at **http://www.nih.gov/health/consumer/conkey.htm**
- National Institute of General Medical Sciences (NIGMS); fact sheets available at **http://www.nigms.nih.gov/news/facts/**
- National Library of Medicine (NLM); extensive encyclopedia (A.D.A.M., Inc.) with guidelines: **http://www.nlm.nih.gov/medlineplus/healthtopics.html**
- National Cancer Institute (NCI); guidelines available at **http://www.cancer.gov/cancerinfo/list.aspx?viewid=5f35036e-5497-4d86-8c2c-714a9f7c8d25**
- National Eye Institute (NEI); guidelines available at **http://www.nei.nih.gov/order/index.htm**
- National Heart, Lung, and Blood Institute (NHLBI); guidelines available at **http://www.nhlbi.nih.gov/guidelines/index.htm**
- National Human Genome Research Institute (NHGRI); research available at **http://www.genome.gov/page.cfm?pageID=10000375**
- National Institute on Aging (NIA); guidelines available at **http://www.nia.nih.gov/health/**

[13] These publications are typically written by one or more of the various NIH Institutes.

- National Institute on Alcohol Abuse and Alcoholism (NIAAA); guidelines available at **http://www.niaaa.nih.gov/publications/publications.htm**
- National Institute of Allergy and Infectious Diseases (NIAID); guidelines available at **http://www.niaid.nih.gov/publications/**
- National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS); fact sheets and guidelines available at **http://www.niams.nih.gov/hi/index.htm**
- National Institute of Child Health and Human Development (NICHD); guidelines available at **http://www.nichd.nih.gov/publications/pubskey.cfm**
- National Institute on Deafness and Other Communication Disorders (NIDCD); fact sheets and guidelines at **http://www.nidcd.nih.gov/health/**
- National Institute of Dental and Craniofacial Research (NIDCR); guidelines available at **http://www.nidr.nih.gov/health/**
- National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK); guidelines available at **http://www.niddk.nih.gov/health/health.htm**
- National Institute on Drug Abuse (NIDA); guidelines available at **http://www.nida.nih.gov/DrugAbuse.html**
- National Institute of Environmental Health Sciences (NIEHS); environmental health information available at **http://www.niehs.nih.gov/external/facts.htm**
- National Institute of Mental Health (NIMH); guidelines available at **http://www.nimh.nih.gov/practitioners/index.cfm**
- National Institute of Neurological Disorders and Stroke (NINDS); neurological disorder information pages available at **http://www.ninds.nih.gov/health_and_medical/disorder_index.htm**
- National Institute of Nursing Research (NINR); publications on selected illnesses at **http://www.nih.gov/ninr/news-info/publications.html**
- National Institute of Biomedical Imaging and Bioengineering; general information at **http://grants.nih.gov/grants/becon/becon_info.htm**
- Center for Information Technology (CIT); referrals to other agencies based on keyword searches available at **http://kb.nih.gov/www_query_main.asp**
- National Center for Complementary and Alternative Medicine (NCCAM); health information available at **http://nccam.nih.gov/health/**
- National Center for Research Resources (NCRR); various information directories available at **http://www.ncrr.nih.gov/publications.asp**
- Office of Rare Diseases; various fact sheets available at **http://rarediseases.info.nih.gov/html/resources/rep_pubs.html**
- Centers for Disease Control and Prevention; various fact sheets on infectious diseases available at **http://www.cdc.gov/publications.htm**

NIH Databases

In addition to the various Institutes of Health that publish professional guidelines, the NIH has designed a number of databases for professionals.[14] Physician-oriented resources provide a wide variety of information related to the biomedical and health sciences, both past and present. The format of these resources varies. Searchable databases, bibliographic citations, full-text articles (when available), archival collections, and images are all available. The following are referenced by the National Library of Medicine:[15]

- **Bioethics:** Access to published literature on the ethical, legal, and public policy issues surrounding healthcare and biomedical research. This information is provided in conjunction with the Kennedy Institute of Ethics located at Georgetown University, Washington, D.C.: **http://www.nlm.nih.gov/databases/databases_bioethics.html**
- **HIV/AIDS Resources:** Describes various links and databases dedicated to HIV/AIDS research: **http://www.nlm.nih.gov/pubs/factsheets/aidsinfs.html**
- **NLM Online Exhibitions:** Describes "Exhibitions in the History of Medicine": **http://www.nlm.nih.gov/exhibition/exhibition.html**. Additional resources for historical scholarship in medicine: **http://www.nlm.nih.gov/hmd/hmd.html**
- **Biotechnology Information:** Access to public databases. The National Center for Biotechnology Information conducts research in computational biology, develops software tools for analyzing genome data, and disseminates biomedical information for the better understanding of molecular processes affecting human health and disease: **http://www.ncbi.nlm.nih.gov/**
- **Population Information:** The National Library of Medicine provides access to worldwide coverage of population, family planning, and related health issues, including family planning technology and programs, fertility, and population law and policy: **http://www.nlm.nih.gov/databases/databases_population.html**
- **Cancer Information:** Access to cancer-oriented databases: **http://www.nlm.nih.gov/databases/databases_cancer.html**
- **Profiles in Science:** Offering the archival collections of prominent twentieth-century biomedical scientists to the public through modern digital technology: **http://www.profiles.nlm.nih.gov/**
- **Chemical Information:** Provides links to various chemical databases and references: **http://sis.nlm.nih.gov/Chem/ChemMain.html**
- **Clinical Alerts:** Reports the release of findings from the NIH-funded clinical trials where such release could significantly affect morbidity and mortality: **http://www.nlm.nih.gov/databases/alerts/clinical_alerts.html**
- **Space Life Sciences:** Provides links and information to space-based research (including NASA): **http://www.nlm.nih.gov/databases/databases_space.html**
- **MEDLINE:** Bibliographic database covering the fields of medicine, nursing, dentistry, veterinary medicine, the healthcare system, and the pre-clinical sciences: **http://www.nlm.nih.gov/databases/databases_medline.html**

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[14] Remember, for the general public, the National Library of Medicine recommends the databases referenced in MEDLINE*plus* (**http://medlineplus.gov/** or **http://www.nlm.nih.gov/medlineplus/databases.html**).

[15] See **http://www.nlm.nih.gov/databases/databases.html**.

- **Toxicology and Environmental Health Information (TOXNET):** Databases covering toxicology and environmental health: **http://sis.nlm.nih.gov/Tox/ToxMain.html**
- **Visible Human Interface:** Anatomically detailed, three-dimensional representations of normal male and female human bodies: **http://www.nlm.nih.gov/research/visible/visible_human.html**

The Combined Health Information Database

A comprehensive source of information on clinical guidelines written for professionals is the Combined Health Information Database. You will need to limit your search to one of the following: Brochure/Pamphlet, Fact Sheet, or Information Package, and "human immunodeficiency virus" using the "Detailed Search" option. Go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. To find associations, use the drop boxes at the bottom of the search page where "You may refine your search by." For the publication date, select "All Years." Select your preferred language and the format option "Fact Sheet." Type "human immunodeficiency virus" (or synonyms) into the "For these words:" box. The following is a sample result:

- **CDC Guidelines for National Human Immunodeficiency Virus Case Surveillance, Including Monitoring for Human Immunodeficiency Virus Infection and Acquired Immunodeficiency Syndrome**

  Source: MMWR Morbidity and Mortality Weekly Report December 10 1999;48(RR-13):1-31.

  Contact: US Government Printing Office, PO Box 371954, Pittsburgh, PA, 15250-7954, (202) 512-1800, http://www.access.gpo.gov. CDC National Prevention Information Network, PO Box 6003, Rockville, MD, 20849-6003, (800) 458-5231, http://www.cdcnpin.org.

  Summary: This report includes the Centers for Disease Control and Prevention's (CDC)revised case definition for the human immunodeficiency virus (HIV) infection in adults and children, recommended surveillance program practices, and performance and security standards for conducting HIV/acquired immunodeficiency syndrome (AIDS) surveillance by local, state, and territorial health departments. The revised surveillance recommendations became effective January 1, 2000. The CDC recommends that all states and territories conduct case surveillance for HIV as an extension of current AIDS surveillance activities. The expansion of national surveillance to include both HIV infection and AIDS cases is a necessary response to the impact of advances in antiretroviral therapy, the implementation of new HIV treatment guidelines, and the increased need for epidemiologic data regarding persons at all stages of HIV disease. Expanded surveillance will provide additional data about HIV-infected populations to enhance local, state, and federal efforts to prevent HIV transmission, improve allocation of resources for treatment services, and assist in evaluating the impact of public health interventions. CDC will provide technical assistance to all state and territorial health departments to continue or establish HIV and AIDS case surveillance systems and to evaluate the performance of their surveillance programs. Other topics discussed in the report include the history of AIDS and HIV case surveillance, considerations in implementing nationwide HIV case surveillance, HIV surveillance using non-name-based unique identifiers, and the effect of national HIV case surveillance on reporting trends.

The NLM Gateway[16]

The NLM (National Library of Medicine) Gateway is a Web-based system that lets users search simultaneously in multiple retrieval systems at the U.S. National Library of Medicine (NLM). It allows users of NLM services to initiate searches from one Web interface, providing one-stop searching for many of NLM's information resources or databases.[17] To use the NLM Gateway, simply go to the search site at **http://gateway.nlm.nih.gov/gw/Cmd**. Type "human immunodeficiency virus" (or synonyms) into the search box and click "Search." The results will be presented in a tabular form, indicating the number of references in each database category.

Results Summary

Category	Items Found
Journal Articles	66336
Books / Periodicals / Audio Visual	6623
Consumer Health	1839
Meeting Abstracts	47928
Other Collections	58
Total	122784

HSTAT[18]

HSTAT is a free, Web-based resource that provides access to full-text documents used in healthcare decision-making.[19] These documents include clinical practice guidelines, quick-reference guides for clinicians, consumer health brochures, evidence reports and technology assessments from the Agency for Healthcare Research and Quality (AHRQ), as well as AHRQ's Put Prevention Into Practice.[20] Simply search by "human immunodeficiency virus" (or synonyms) at the following Web site: **http://text.nlm.nih.gov**.

Coffee Break: Tutorials for Biologists[21]

Coffee Break is a general healthcare site that takes a scientific view of the news and covers recent breakthroughs in biology that may one day assist physicians in developing treatments. Here you will find a collection of short reports on recent biological discoveries.

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[16] Adapted from NLM: **http://gateway.nlm.nih.gov/gw/Cmd?Overview.x**.

[17] The NLM Gateway is currently being developed by the Lister Hill National Center for Biomedical Communications (LHNCBC) at the National Library of Medicine (NLM) of the National Institutes of Health (NIH).

[18] Adapted from HSTAT: **http://www.nlm.nih.gov/pubs/factsheets/hstat.html**.

[19] The HSTAT URL is **http://hstat.nlm.nih.gov/**.

[20] Other important documents in HSTAT include: the National Institutes of Health (NIH) Consensus Conference Reports and Technology Assessment Reports; the HIV/AIDS Treatment Information Service (ATIS) resource documents; the Substance Abuse and Mental Health Services Administration's Center for Substance Abuse Treatment (SAMHSA/CSAT) Treatment Improvement Protocols (TIP) and Center for Substance Abuse Prevention (SAMHSA/CSAP) Prevention Enhancement Protocols System (PEPS); the Public Health Service (PHS) Preventive Services Task Force's *Guide to Clinical Preventive Services*; the independent, nonfederal Task Force on Community Services' *Guide to Community Preventive Services*; and the Health Technology Advisory Committee (HTAC) of the Minnesota Health Care Commission (MHCC) health technology evaluations.

[21] Adapted from **http://www.ncbi.nlm.nih.gov/Coffeebreak/Archive/FAQ.html**.

Each report incorporates interactive tutorials that demonstrate how bioinformatics tools are used as a part of the research process. Currently, all Coffee Breaks are written by NCBI staff.[22] Each report is about 400 words and is usually based on a discovery reported in one or more articles from recently published, peer-reviewed literature.[23] This site has new articles every few weeks, so it can be considered an online magazine of sorts. It is intended for general background information. You can access the Coffee Break Web site at the following hyperlink: **http://www.ncbi.nlm.nih.gov/Coffeebreak/**.

Other Commercial Databases

In addition to resources maintained by official agencies, other databases exist that are commercial ventures addressing medical professionals. Here are some examples that may interest you:

- **CliniWeb International:** Index and table of contents to selected clinical information on the Internet; see **http://www.ohsu.edu/cliniweb/**.
- **Medical World Search:** Searches full text from thousands of selected medical sites on the Internet; see **http://www.mwsearch.com/**.

The Genome Project and Human Immunodeficiency Virus

In the following section, we will discuss databases and references which relate to the Genome Project and human immunodeficiency virus.

Online Mendelian Inheritance in Man (OMIM)

The Online Mendelian Inheritance in Man (OMIM) database is a catalog of human genes and genetic disorders authored and edited by Dr. Victor A. McKusick and his colleagues at Johns Hopkins and elsewhere. OMIM was developed for the World Wide Web by the National Center for Biotechnology Information (NCBI).[24] The database contains textual information, pictures, and reference information. It also contains copious links to NCBI's Entrez database of MEDLINE articles and sequence information.

To search the database, go to **http://www.ncbi.nlm.nih.gov/Omim/searchomim.html**. Type "human immunodeficiency virus" (or synonyms) into the search box, and click "Submit Search." If too many results appear, you can narrow the search by adding the word "clinical." Each report will have additional links to related research and databases. In particular, the option "Database Links" will search across technical databases that offer an

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[22] The figure that accompanies each article is frequently supplied by an expert external to NCBI, in which case the source of the figure is cited. The result is an interactive tutorial that tells a biological story.

[23] After a brief introduction that sets the work described into a broader context, the report focuses on how a molecular understanding can provide explanations of observed biology and lead to therapies for diseases. Each vignette is accompanied by a figure and hypertext links that lead to a series of pages that interactively show how NCBI tools and resources are used in the research process.

[24] Adapted from **http://www.ncbi.nlm.nih.gov/**. Established in 1988 as a national resource for molecular biology information, NCBI creates public databases, conducts research in computational biology, develops software tools for analyzing genome data, and disseminates biomedical information--all for the better understanding of molecular processes affecting human health and disease.

abundance of information. The following is an example of the results you can obtain from the OMIM for human immunodeficiency virus:

- **Human Immunodeficiency Virus Type 1 Enhancer-binding Protein 1**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?194540
- **Human Immunodeficiency Virus Type 1 Enhancer-binding Protein 2**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?143054
- **Human Immunodeficiency Virus Type 1 Enhancer-binding Protein 3**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?606649
- **Human Immunodeficiency Virus Type 1 Expression 1**
  Web site: http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?143055

Genes and Disease (NCBI - Map)

The Genes and Disease database is produced by the National Center for Biotechnology Information of the National Library of Medicine at the National Institutes of Health. This Web site categorizes each disorder by system of the body. Go to **http://www.ncbi.nlm.nih.gov/disease/**, and browse the system pages to have a full view of important conditions linked to human genes. Since this site is regularly updated, you may wish to revisit it from time to time. The following systems and associated disorders are addressed:

- **Cancer:** Uncontrolled cell division.
  Examples: Breast and ovarian cancer, Burkitt lymphoma, chronic myeloid leukemia, colon cancer, lung cancer, malignant melanoma, multiple endocrine neoplasia, neurofibromatosis, p53 tumor suppressor, pancreatic cancer, prostate cancer, Ras oncogene, RB: retinoblastoma, von Hippel-Lindau syndrome.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Cancer.html**
- **Immune System:** Fights invaders.
  Examples: Asthma, autoimmune polyglandular syndrome, Crohn's disease, DiGeorge syndrome, familial Mediterranean fever, immunodeficiency with Hyper-IgM, severe combined immunodeficiency.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Immune.html**
- **Metabolism:** Food and energy.
  Examples: Adreno-leukodystrophy, atherosclerosis, Best disease, Gaucher disease, glucose galactose malabsorption, gyrate atrophy, juvenile-onset diabetes, obesity, paroxysmal nocturnal hemoglobinuria, phenylketonuria, Refsum disease, Tangier disease, Tay-Sachs disease.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Metabolism.html**
- **Muscle and Bone:** Movement and growth.
  Examples: Duchenne muscular dystrophy, Ellis-van Creveld syndrome, Marfan syndrome, myotonic dystrophy, spinal muscular atrophy.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Muscle.html**
- **Nervous System:** Mind and body.
  Examples: Alzheimer disease, amyotrophic lateral sclerosis, Angelman syndrome, Charcot-Marie-Tooth disease, epilepsy, essential tremor, fragile X syndrome, Friedreich's ataxia, Huntington disease, Niemann-Pick disease, Parkinson disease,

Prader-Willi syndrome, Rett syndrome, spinocerebellar atrophy, Williams syndrome.
Web site: **http://www.ncbi.nlm.nih.gov/disease/Brain.html**

- **Signals:** Cellular messages.
  Examples: Ataxia telangiectasia, Cockayne syndrome, glaucoma, male-patterned baldness, SRY: sex determination, tuberous sclerosis, Waardenburg syndrome, Werner syndrome.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Signals.html**
- **Transporters:** Pumps and channels.
  Examples: Cystic fibrosis, deafness, diastrophic dysplasia, Hemophilia A, long-QT syndrome, Menkes syndrome, Pendred syndrome, polycystic kidney disease, sickle cell anemia, Wilson's disease, Zellweger syndrome.
  Web site: **http://www.ncbi.nlm.nih.gov/disease/Transporters.html**

Entrez

Entrez is a search and retrieval system that integrates several linked databases at the National Center for Biotechnology Information (NCBI). These databases include nucleotide sequences, protein sequences, macromolecular structures, whole genomes, and MEDLINE through PubMed. Entrez provides access to the following databases:

- **3D Domains:** Domains from Entrez Structure,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=geo**
- **Books:** Online books,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=books**
- **Genome:** Complete genome assemblies,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Genome**
- **NCBI's Protein Sequence Information Survey Results:**
  Web site: **http://www.ncbi.nlm.nih.gov/About/proteinsurvey/**
- **Nucleotide Sequence Database (Genbank):**
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Nucleotide**
- **OMIM:** Online Mendelian Inheritance in Man,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM**
- **PopSet:** Population study data sets,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Popset**
- **ProbeSet:** Gene Expression Omnibus (GEO),
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=geo**
- **Protein Sequence Database:**
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Protein**
- **PubMed:** Biomedical literature (PubMed),
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed**
- **Structure:** Three-dimensional macromolecular structures,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Structure**
- **Taxonomy:** Organisms in GenBank,
  Web site: **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Taxonomy**

To access the Entrez system at the National Center for Biotechnology Information, go to **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=genome**, and then select the database that you would like to search. The databases available are listed in the drop box next to "Search." Enter "human immunodeficiency virus" (or synonyms) into the search box and click "Go."

Jablonski's Multiple Congenital Anomaly/Mental Retardation (MCA/MR) Syndromes Database[25]

This online resource has been developed to facilitate the identification and differentiation of syndromic entities. Special attention is given to the type of information that is usually limited or completely omitted in existing reference sources due to space limitations of the printed form.

At **http://www.nlm.nih.gov/mesh/jablonski/syndrome_toc/toc_a.html**, you can search across syndromes using an alphabetical index**.** Search by keywords at **http://www.nlm.nih.gov/mesh/jablonski/syndrome_db.html**.

The Genome Database[26]

Established at Johns Hopkins University in Baltimore, Maryland in 1990, the Genome Database (GDB) is the official central repository for genomic mapping data resulting from the Human Genome Initiative. In the spring of 1999, the Bioinformatics Supercomputing Centre (BiSC) at the Hospital for Sick Children in Toronto, Ontario assumed the management of GDB. The Human Genome Initiative is a worldwide research effort focusing on structural analysis of human DNA to determine the location and sequence of the estimated 100,000 human genes. In support of this project, GDB stores and curates data generated by researchers worldwide who are engaged in the mapping effort of the Human Genome Project (HGP). GDB's mission is to provide scientists with an encyclopedia of the human genome which is continually revised and updated to reflect the current state of scientific knowledge. Although GDB has historically focused on gene mapping, its focus will broaden as the Genome Project moves from mapping to sequence, and finally, to functional analysis.

To access the GDB, simply go to the following hyperlink: **http://www.gdb.org/**. Search "All Biological Data" by "Keyword." Type "human immunodeficiency virus" (or synonyms) into the search box, and review the results. If more than one word is used in the search box, then separate each one with the word "and" or "or" (using "or" might be useful when using synonyms).

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[25] Adapted from the National Library of Medicine: **http://www.nlm.nih.gov/mesh/jablonski/about_syndrome.html**.

[26] Adapted from the Genome Database: **http://gdbwww.gdb.org/gdb/aboutGDB.html - mission**.

APPENDIX B. PATIENT RESOURCES

Overview

Official agencies, as well as federally funded institutions supported by national grants, frequently publish a variety of guidelines written with the patient in mind. These are typically called "Fact Sheets" or "Guidelines." They can take the form of a brochure, information kit, pamphlet, or flyer. Often they are only a few pages in length. Since new guidelines on human immunodeficiency virus can appear at any moment and be published by a number of sources, the best approach to finding guidelines is to systematically scan the Internet-based services that post them.

Patient Guideline Sources

The remainder of this chapter directs you to sources which either publish or can help you find additional guidelines on topics related to human immunodeficiency virus. Due to space limitations, these sources are listed in a concise manner. Do not hesitate to consult the following sources by either using the Internet hyperlink provided, or, in cases where the contact information is provided, contacting the publisher or author directly.

The National Institutes of Health

The NIH gateway to patients is located at **http://health.nih.gov/**. From this site, you can search across various sources and institutes, a number of which are summarized below.

Topic Pages: MEDLINEplus

The National Library of Medicine has created a vast and patient-oriented healthcare information portal called MEDLINEplus. Within this Internet-based system are "health topic pages" which list links to available materials relevant to human immunodeficiency virus. To access this system, log on to **http://www.nlm.nih.gov/medlineplus/healthtopics.html**. From there you can either search using the alphabetical index or browse by broad topic areas. Recently, MEDLINEplus listed the following when searched for "human immunodeficiency virus":

- Other Guides

  AIDS
  http://www.nlm.nih.gov/medlineplus/aids.html

  AIDS and Infections
  http://www.nlm.nih.gov/medlineplus/aidsandinfections.html

  AIDS and Pregnancy
  http://www.nlm.nih.gov/medlineplus/aidsandpregnancy.html

  Hearing Disorders & Deafness
  http://www.nlm.nih.gov/medlineplus/hearingdisordersdeafness.html

Within the health topic page dedicated to human immunodeficiency virus, the following was listed:

- General/Overviews

  AIDS/HIV
  Source: Mayo Foundation for Medical Education and Research
  http://www.mayoclinic.com/invoke.cfm?id=DS00005

  Frequently Asked Questions
  Source: Centers for Disease Control and Prevention
  http://www.ashastd.org/nah/tty/ttyfaq.html

  Frequently Asked Questions (FAQs) about HIV and AIDS
  Source: National Center for HIV, STD, and TB Prevention
  http://www.cdc.gov/hiv/pubs/faqs.htm

  What You Need to Know About HIV and AIDS
  Source: American Society for Clinical Pathology
  http://www.ascp.org/general/pub_resources/aids/

- Diagnosis/Symptoms

  FDA Approves New Rapid HIV Test Kit
  Source: Food and Drug Administration
  http://www.fda.gov/bbs/topics/NEWS/2002/NEW00852.html

  HHS Extends Use of Rapid HIV Test to New Sites Nationwide
  Source: Dept. of Health and Human Services
  http://www.hhs.gov/news/press/2003pres/20030131b.html

  HIV Antibody Test
  Source: American Association for Clinical Chemistry
  http://www.labtestsonline.org/understanding/analytes/hiv_antibody/test.html

  OraQuick Rapid HIV-1 Antibody Test: Frequently Asked Questions
  Source: National Center for HIV, STD, and TB Prevention
  http://www.cdc.gov/hiv/pubs/rt-faq.htm

  p24 Antigen Test
  Source: American Association for Clinical Chemistry
  http://www.labtestsonline.org/understanding/analytes/p24/test.html

Testing Your Blood for HIV, the Virus that Causes AIDS
http://www.cc.nih.gov/ccc/patient_education/pepubs/hiv.pdf

Testing Yourself for HIV-1, the Virus that Causes AIDS
Source: Food and Drug Administration
http://www.fda.gov/cber/infosheets/hiv-home2.htm

- Treatment

AIDS-Related Lymphoma (PDQ): Treatment
Source: National Cancer Institute
http://www.cancer.gov/cancerinfo/pdq/treatment/AIDS-related-lymphoma/patient/

Antiretroviral Drugs
Source: Dept. of Health and Human Services
http://aidsinfo.nih.gov/drugs/

Approved Drugs for HIV/AIDS or AIDS-related Conditions
Source: Food and Drug Administration
http://www.fda.gov/oashi/aids/stat_app.html

FDA Approves First Drug in New Class of HIV Treatments for HIV Infected Adults and Children with Advanced Disease
Source: Food and Drug Administration
http://www.fda.gov/bbs/topics/NEWS/2003/NEW00879.html

HIV/AIDS Treatment Guidelines
Source: Dept. of Health and Human Services
http://aidsinfo.nih.gov/guidelines/

Immune Globulin Intravenous Injection
Source: American Society of Health-System Pharmacists
http://www.safemedication.com/displaydrug.cfm?id=695

Important Interim Results from a Phase III, Randomized, Double Blind Comparison of Three Protease-Inhibitor-Sparing Regimens
http://www.niaid.nih.gov/daids/pdf/aactg_a5095.pdf

Patient Assistance Programs - HIV/AIDS Drugs
Source: University of California, San Francisco
http://hivinsite.ucsf.edu/InSite.jsp?page=li-05-19&doc=2098.2a90

Revised Guidelines Will Ease Selection of HIV/AIDS Treatments
Source: National Institute of Allergy and Infectious Diseases
http://www.nih.gov/news/pr/jul2003/niaid-14.htm

Treatment of HIV Infection
Source: National Institute of Allergy and Infectious Diseases
http://www.niaid.nih.gov/factsheets/treat-hiv.htm

- Alternative Therapy

AIDS Research Center
Source: Bastyr University
http://www.bastyr.edu/research/buarc/

Garlic Supplements Can Impede HIV Medication
Source: National Institute of Allergy and Infectious Diseases
http://www.nih.gov/news/pr/dec2001/niaid-05.htm

- Specific Conditions/Aspects

  Alcohol Alert: Alcohol and HIV/AIDS
  Source: National Institute on Alcohol Abuse and Alcoholism
  http://www.niaaa.nih.gov/publications/aa57.htm

  HIV/AIDS Prevention: Health Information for International Travel, 2001-2002
  Source: Centers for Disease Control and Prevention
  http://www.cdc.gov/travel/hivaids.htm

  HIV: What Is Acute HIV Syndrome?
  Source: American Academy of Family Physicians
  http://familydoctor.org/handouts/451.html

  Human Immunodeficiency Virus and Travel: Health Information for International Travel, 2001-2002
  Source: Centers for Disease Control and Prevention
  http://www.cdc.gov/travel/hivtrav.htm

  Human Immunodeficiency Virus Type 2
  Source: National Center for HIV, STD, and TB Prevention
  http://www.cdc.gov/hiv/pubs/facts/hiv2.htm

  Neurological Manifestations of AIDS
  http://www.ninds.nih.gov/health_and_medical/disorders/aids.htm

  Occupational Exposure to HIV: Advice for Health Care Workers
  Source: American Academy of Family Physicians
  http://familydoctor.org/handouts/004.html

  Oral Polio Vaccine and HIV / AIDS
  Source: National Immunization Program
  http://www.cdc.gov/nip/vacsafe/concerns/aids/poliovac-hiv-aids.htm

  What Are Asian and Pacific Islander HIV Prevention Needs?
  Source: Asian & Pacific Islander American Health Forum
  http://www.apiahf.org/programs/hivcba/hivresource/factsheets/facthiv1.html

- Children

  HIV and AIDS
  Source: Nemours Foundation
  http://kidshealth.org/kid/health_problems/infection/hiv.html

  HIV Infection in Infants and Children
  Source: National Institute of Allergy and Infectious Diseases
  http://www.niaid.nih.gov/newsroom/simple/background.htm

- From the National Institutes of Health

  Focus On: The HIV-AIDS Connection
  Source: National Institute of Allergy and Infectious Diseases
  http://www.niaid.nih.gov/newsroom/focuson/hiv00/default.htm

HIV Infection and AIDS
Source: National Institute of Allergy and Infectious Diseases
http://www.niaid.nih.gov/factsheets/hivinf.htm

How HIV Causes AIDS
Source: National Institute of Allergy and Infectious Diseases
http://www.niaid.nih.gov/factsheets/howhiv.htm

- Latest News

AIDS Chief Calls for More Vaccine Cooperation
Source: 09/19/2003, Reuters Health
http://www.nlm.nih.gov//www.nlm.nih.gov/medlineplus/news/fullstory_14036.html

AIDS Galloping Faster Than Global Plans to Stop It
Source: 09/22/2003, Reuters Health
http://www.nlm.nih.gov//www.nlm.nih.gov/medlineplus/news/fullstory_14048.html

Experts Express Hope for AIDS Vaccine
Source: 09/18/2003, Reuters Health
http://www.nlm.nih.gov//www.nlm.nih.gov/medlineplus/news/fullstory_14019.html

More News on AIDS
http://www.nlm.nih.gov//www.nlm.nih.gov/medlineplus/alphanews_a.html#AIDS

National HIV Prevention Conference Echoes Themes of HHS' New HIV Prevention Initiative
Source: 07/28/2003, Centers for Disease Control and Prevention
http://www.cdc.gov/od/oc/media/pressrel/r030728.htm

Revised Guidelines Will Ease Selection of HIV/AIDS Treatments
Source: 07/14/2003, National Institute of Allergy and Infectious Diseases
http://www.nih.gov/news/pr/jul2003/niaid-14.htm

- Law and Policy

Medicaid and Acquired Immunodeficiency Syndrome (AIDS) and Human Immunodeficiency Virus (HIV) Infection
Source: Centers for Medicare and Medicaid Services
http://www.cms.gov/hiv/hivfs.asp

- Men

What About Men's Health? HIV and AIDS
Source: National Women's Health Information Center
http://www.4women.gov/mens/index.cfm?page=116&text=no

- Organizations

AEGIS
http://www.aegis.com/

AIDS Treatment Data Network
http://www.atdn.org/

AIDSinfo
Source: Dept. of Health and Human Services
http://aidsinfo.nih.gov/

American Social Health Association
http://www.ashastd.org/

CDC Divisions of HIV/AIDS Prevention
Source: National Center for HIV, STD, and TB Prevention
http://www.cdc.gov/hiv/dhap.htm

CDC National Prevention Information Network (NPIN)
Source: National Center for HIV, STD, and TB Prevention
http://www.cdcnpin.org/

Center for AIDS Prevention Studies
Source: University of California, San Francisco
http://www.caps.ucsf.edu/index.html

National Institutes of Health, Office of AIDS Research
http://www.nih.gov/od/oar/index.htm

NIAID Division of AIDS
Source: National Institute of Allergy and Infectious Diseases
http://www.niaid.nih.gov/daids/

Project Inform
http://www.projinf.org/

- Prevention/Screening

Can I Get HIV from Getting a Tattoo or through Body Piercing?
Source: Centers for Disease Control and Prevention
http://www.cdc.gov/hiv/pubs/faq/faq27.htm

Can I Get Infected with HIV from Mosquitoes?
Source: Centers for Disease Control and Prevention
http://www.cdc.gov/hiv/pubs/faq/faq32.htm

Drug-Associated HIV Transmission Continues in the United States
Source: National Center for HIV, STD, and TB Prevention
http://www.cdc.gov/hiv/pubs/facts/idu.htm

HIV and AIDS: Are You at Risk?
Source: National Center for HIV, STD, and TB Prevention
http://www.cdc.gov/hiv/pubs/brochure/atrisk.htm

How to Protect Yourself from AIDS
http://www.fda.gov/opacom/lowlit/aids.html

Need for Sustained HIV Prevention Among Men who Have Sex with Men
Source: National Center for HIV, STD, and TB Prevention
http://www.cdc.gov/hiv/pubs/facts/msm.htm

On the Front Lines: Fighting HIV/AIDS in African American Communities
http://www.cdc.gov/hiv/pubs/brochure/african-american.pdf

Prevention Program for HIV-Positive Youths Reduces Risks of Further HIV Transmission
Source: National Institute on Drug Abuse
http://www.nida.nih.gov/NIDA_Notes/NNVol17N1/Prevention.html

Primary HIV Infection Associated with Oral Transmission
Source: National Center for HIV, STD, and TB Prevention
http://www.cdc.gov/hiv/pubs/facts/oralsexqa.htm

Principles of HIV Prevention in Drug-Using Populations: Frequently Asked Questions: Effectiveness of Strategies
Source: National Institute on Drug Abuse
http://www.nida.nih.gov/POHP/FAQ_2.html

Principles of HIV Prevention in Drug-Using Populations: Frequently Asked Questions: Prevention Strategies
Source: National Institute on Drug Abuse
http://www.nida.nih.gov/POHP/FAQ_1.html

Protecting the Health of Latino Communities: Combating HIV/AIDS
http://www.cdc.gov/hiv/pubs/brochure/latino-report.pdf

Right Way to Use a Condom
Source: American Social Health Association
http://www.ashastd.org/stdfaqs/condom_a.html

Truth about Condoms
http://www.siecus.org/pubs/fact/FS_truth_condoms_02.pdf

What Are U.S. Latinos' HIV Prevention Needs?
Source: Center for AIDS Prevention Studies, UCSF
http://www.caps.ucsf.edu/Latinorev.html

- Research

Alternating Drug Regimens to Treat HIV Infection
Source: American College of Physicians
http://www.annals.org/cgi/content/full/139/2/I-16

Anal Cancer Precursors in Persons with HIV Infection
Source: American College of Physicians
http://www.annals.org/cgi/content/full/138/6/I-44

Black and Hispanic HIV Patients Are Less Likely to Get Experimental Medication
Source: Agency for Healthcare Research and Quality
http://www.ahrq.gov/news/press/pr2002/hivmedpr.htm

Does Marijuana Affect Viral Loads in People with HIV?
Source: American College of Physicians
http://www.annals.org/cgi/content/full/139/4/I-44

Drug Abuse and AIDS
Source: National Institute on Drug Abuse
http://www.drugabuse.gov/Infofax/DrugAbuse.html

Evidence That HIV Causes AIDS
Source: National Institute of Allergy and Infectious Diseases
http://www.niaid.nih.gov/factsheets/evidhiv.htm

High-Risk Sex Is Main Factor in HIV Infection for Men and Women Who Inject Drugs
Source: National Institute on Drug Abuse
http://www.nida.nih.gov/NIDA_Notes/NNVol17N2/HighRisk.html

HIV Infection in Minority Populations
Source: National Institute of Allergy and Infectious Diseases
http://www.niaid.nih.gov/factsheets/Minor.htm

HIV Selectively Suppresses Anti-HIV Defense Cells
Source: National Institute of Allergy and Infectious Diseases
http://www.nih.gov/news/pr/may2002/niaid-01.htm

HIV Vaccines Explained--Making HIV Vaccines a Reality
http://www.niaid.nih.gov/publications/pdf/HIVvaccinebrochure.pdf

Infection by Closely Related HIV Strains Possible
Source: National Institute of Allergy and Infectious Diseases
http://www.nih.gov/news/pr/nov2002/niaid-27.htm

Molecular Fingerprint Predicts HIV-Associated Dementia
Source: National Institutes of Health
http://www.nih.gov/news/pr/jun2003/ninds-23.htm

NIAID Teams with Wyeth on HIV/AIDS Vaccine
Source: National Institute of Allergy and Infectious Diseases
http://www.nih.gov/news/pr/may2002/niaid-17.htm

Relationship between Levels of the Anti-HIV Drug Indinavir in Patients' Hair and Response to Treatment
Source: American College of Physicians
http://www.annals.org/cgi/content/full/137/8/I-48

Researchers Identify Shift Towards More Treatable AIDS-Related Lymphomas
Source: National Cancer Institute
http://www.nih.gov/news/pr/jun2003/nci-10.htm

Structure of HIV-Neutralizing Antibody Solved
Source: National Institute of General Medical Sciences
http://www.nih.gov/news/pr/jun2003/nigms-26.htm

Study Sheds Light on Cause of an AIDS Treatment Side Effect
Source: National Cancer Institute
http://www.cancer.gov/newscenter/HIVmitochondrion

TrialScope
Source: University of California, San Francisco
http://hivinsite.ucsf.edu/tscope?page=ts-01-00

- Statistics

AIDS Cases in Adolescents and Adults, by Age - United States, 1994-2000
Source: National Center for HIV, STD, and TB Prevention
http://www.cdc.gov/hiv/stats/hasrsuppvol9No1.htm

AIDS Cases Reported July 1991 Through June 2001, by Area of Residence
Source: National Center for HIV, STD, and TB Prevention
http://www.cdc.gov/hiv/stats/hasrsupp83/table1.htm

Basic HIV/AIDS Statistics
Source: Centers for Disease Control and Prevention
http://www.cdc.gov/hiv/stats.htm

Countries & Regions
Source: University of California, San Francisco
http://hivinsite.ucsf.edu/InSite.jsp?page=Country

Eliminate Disparities in HIV and AIDS
Source: Centers for Disease Control and Prevention, Office of Minority Health
http://www.cdc.gov/omh/AMH/factsheets/hiv.htm

HIV/AIDS Among African Americans Key Facts
Source: National Center for HIV, STD, and TB Prevention
http://www.cdc.gov/hiv/pubs/Facts/afam.pdf

HIV/AIDS Among Hispanics in the United States
Source: National Center for HIV, STD, and TB Prevention
http://www.cdc.gov/hiv/pubs/facts/hispanic.htm

HIV/AIDS Statistics
Source: National Institute of Allergy and Infectious Diseases
http://www.niaid.nih.gov/factsheets/aidsstat.htm

HIV/AIDS Surveillance Report
Source: Centers for Disease Control and Prevention
http://www.cdc.gov/hiv/stats/hasrlink.HTM

Percent of Adults Aged 18 Years and Over Who Had Ever Been Tested for HIV: United States, 1997 - 2002
Source: National Center for Health Statistics
http://www.cdc.gov/nchs/about/major/nhis/released200212/figures10_1-10_3.htm

Surveillance of Healthcare Personnel with HIV/AIDS, as of December 2001
Source: National Center for Infectious Diseases
http://www.cdc.gov/ncidod/hip/BLOOD/hivpersonnel.htm

- Teenagers

HIV and AIDS
Source: Nemours Foundation
http://kidshealth.org/teen/sexual_health/stds/std_hiv.html

HIV Infection in Adolescents
Source: National Institute of Allergy and Infectious Diseases
http://www.niaid.nih.gov/factsheets/hivadolescent.htm

How do People Get AIDS?
Source: Nemours Foundation
http://kidshealth.org/teen/sexual_health/stds/AIDS.html

National Survey of Teens on HIV/AIDS
http://www.kff.org/content/2000/3092/Teensurveyonhiv.pdf

Young People at Risk: HIV/AIDS Among America's Youth
Source: National Center for HIV, STD, and TB Prevention
http://www.cdc.gov/hiv/pubs/facts/youth.htm

- Women

HIV Infection in Women
Source: National Institute of Allergy and Infectious Diseases
http://www.niaid.nih.gov/factsheets/womenhiv.htm

HIV/AIDS & U.S. Women who Have Sex with Women
Source: Centers for Disease Control and Prevention
http://www.cdc.gov/hiv/pubs/facts/wsw.htm

HIV/AIDS Among US Women: Minority and Young Women at Continuing Risk
Source: Centers for Disease Control and Prevention
http://www.cdc.gov/hiv/pubs/facts/women.htm

What Are Women's HIV Prevention Needs?
Source: Center for AIDS Prevention Studies, UCSF
http://www.caps.ucsf.edu/womenrev.html

Women and HIV/AIDS
http://www.kff.org/content/2001/1631/1631.pdf

You may also choose to use the search utility provided by MEDLINEplus at the following Web address: **http://www.nlm.nih.gov/medlineplus/**. Simply type a keyword into the search box and click "Search." This utility is similar to the NIH search utility, with the exception that it only includes materials that are linked within the MEDLINEplus system (mostly patient-oriented information). It also has the disadvantage of generating unstructured results. We recommend, therefore, that you use this method only if you have a very targeted search.

The Combined Health Information Database (CHID)

CHID Online is a reference tool that maintains a database directory of thousands of journal articles and patient education guidelines on human immunodeficiency virus. CHID offers summaries that describe the guidelines available, including contact information and pricing. CHID's general Web site is **http://chid.nih.gov/**. To search this database, go to **http://chid.nih.gov/detail/detail.html**. In particular, you can use the advanced search options to look up pamphlets, reports, brochures, and information kits. The following was recently posted in this archive:

- **Treatment of Tuberculosis (TB) in Adult and Adolescent Patients Co-Infected With the Human Immunodeficiency Virus (HIV)**

  Contact: University of Medicine and Dentistry of New Jersey, New Jersey Medical School, National Tuberculosis Center, Second Fl E Wing, 225 Warren St, Newark, NJ, 07103-3620, (973) 972-3270, http://www.umdnj.edu/ntbc.

  Summary: This brochure provides health professionals with information on the treatment of drug-susceptible tuberculosis (TB) in children and adolescents who have

the human immunodeficiency virus (HIV). Specifically it discusses three types of antiretroviral therapy (ART) regimens: (1) Rifabutin-based regimen, high dose; (2) Rifabutin-based regimen, low dose; and (3) Streptomycin-based regimen. It also provides general TB treatment information.

The National Guideline Clearinghouse™

The National Guideline Clearinghouse™ offers hundreds of evidence-based clinical practice guidelines published in the United States and other countries. You can search this site located at **http://www.guideline.gov/** by using the keyword "human immunodeficiency virus" (or synonyms). The following was recently posted:

- **(1) Prevention and treatment of tuberculosis among patients with infected human immunodeficiency virus: Principles of therapy and revised recommendations**

  Source: Centers for Disease Control and Prevention - Federal Government Agency [U.S.]; 1998 October 30 (updated 2000 Mar); 59 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2157&nbr=1383&string=human+AND+immunodeficiency+AND+virus

- **2001 USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus**

  Source: Centers for Disease Control and Prevention - Federal Government Agency [U.S.]; 1999 August (updated 2001 November 28); 64 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3080&nbr=2306&string=human+AND+immunodeficiency+AND+virus

- **Adolescents and human immunodeficiency virus infection: the role of the pediatrician in prevention and intervention**

  Source: American Academy of Pediatrics - Medical Specialty Society; 2001 January; 3 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2776&nbr=2002&string=human+AND+immunodeficiency+AND+virus

- **American Gastroenterological Association medical position statement: guidelines for the management of malnutrition and cachexia, chronic diarrhea, and hepatobiliary disease in patients with human immunodeficiency virus infection**

  Source: American Gastroenterological Association - Medical Specialty Society; 1996 December (reviewed 2001); 31 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=837&nbr=41&string=human+AND+immunodeficiency+AND+virus

- **Guidelines for performing single-platform absolute CD4+ T-Cell determinations with CD45 Gating for persons infected with human immunodeficiency virus**

  Source: Centers for Disease Control and Prevention - Federal Government Agency [U.S.]; 2003 January 31; 13 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=3617&nbr=2843&string=human+AND+immunodeficiency+AND+virus

- **Primary care of patients infected with human immunodeficiency virus**

  Source: Infectious Diseases Society of America - Medical Specialty Society; 1998

  http://www.guideline.gov/summary/summary.aspx?doc_id=1469&nbr=695&string=human+AND+immunodeficiency+AND+virus

Healthfinder™

Healthfinder™ is sponsored by the U.S. Department of Health and Human Services and offers links to hundreds of other sites that contain healthcare information. This Web site is located at **http://www.healthfinder.gov**. Again, keyword searches can be used to find guidelines. The following was recently found in this database:

- **Depression and HIV/AIDS**

  Summary: Research has enabled many men and women, and young people living with human immunodeficiency virus (HIV), the virus that causes acquired immunodeficiency syndrome (AIDS), to lead fuller, more

  Source: National Institute of Mental Health, National Institutes of Health

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=6899

- **Evidence That HIV Causes AIDS**

  Summary: This fact sheet provides background and numerous kinds of evidence that the human immunodeficiency virus (HIV) causes AIDS.

  Source: National Institute of Allergy and Infectious Diseases, National Institutes of Health

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=225

The NIH Search Utility

The NIH search utility allows you to search for documents on over 100 selected Web sites that comprise the NIH-WEB-SPACE. Each of these servers is "crawled" and indexed on an ongoing basis. Your search will produce a list of various documents, all of which will relate in some way to human immunodeficiency virus. The drawbacks of this approach are that the information is not organized by theme and that the references are often a mix of information for professionals and patients. Nevertheless, a large number of the listed Web sites provide useful background information. We can only recommend this route, therefore, for relatively rare or specific disorders, or when using highly targeted searches. To use the NIH search utility, visit the following Web page: **http://search.nih.gov/index.html**.

Additional Web Sources

A number of Web sites are available to the public that often link to government sites. These can also point you in the direction of essential information. The following is a representative sample:

- AOL: **http://search.aol.com/cat.adp?id=168&layer=&from=subcats**
- Family Village: **http://www.familyvillage.wisc.edu/specific.htm**
- Google: **http://directory.google.com/Top/Health/Conditions_and_Diseases/**
- Med Help International: **http://www.medhelp.org/HealthTopics/A.html**
- Open Directory Project: **http://dmoz.org/Health/Conditions_and_Diseases/**
- Yahoo.com: **http://dir.yahoo.com/Health/Diseases_and_Conditions/**
- WebMD®Health: **http://my.webmd.com/health_topics**

Associations and Human Immunodeficiency Virus

The following is a list of associations that provide information on and resources relating to human immunodeficiency virus:

- **American Social Health Association**

  Telephone: (919) 361-8400

  Fax: (919) 361-8425

  Email: allkal@ashastd.org

  Web Site: http://www.ashastd.org

  Background: The American Social Health Association (ASHA) is a not-for-profit voluntary organization dedicated to stopping sexually transmitted diseases (STDs) and their harmful consequences to individuals, families, and communities. Established in 1914, ASHA provides direct patient support through the Herpes Resource Center/National Herpes Hotline and the HPV Support Group, which coordinate a network of over 100 local support groups and publish quarterly journals. ASHA also operates the National AIDS Hotline and the National STD Hotline, both under contract with the Centers for Disease Control and Prevention (CDC), as well as the FIRST STEP Hotline and Health Check Hotline, components of North Carolina's effort to improve the health and development of children in the state. In addition, ASHA advocates for increased funding for STD programs and public policies on STD control, working through its office in Washington D.C. provides leadership for the National Coalition to Fight Sexually Transmitted Diseases; and operates the Women s Health Matters program. The organization also administers the ASHA Research Fund, the only privately funded training program for STD research. ASHA s materials include an annual report, quarterly catalog, and pamphlets.

Finding Associations

There are several Internet directories that provide lists of medical associations with information on or resources relating to human immunodeficiency virus. By consulting all of

associations listed in this chapter, you will have nearly exhausted all sources for patient associations concerned with human immunodeficiency virus.

The National Health Information Center (NHIC)

The National Health Information Center (NHIC) offers a free referral service to help people find organizations that provide information about human immunodeficiency virus. For more information, see the NHIC's Web site at **http://www.health.gov/NHIC/** or contact an information specialist by calling 1-800-336-4797.

Directory of Health Organizations

The Directory of Health Organizations, provided by the National Library of Medicine Specialized Information Services, is a comprehensive source of information on associations. The Directory of Health Organizations database can be accessed via the Internet at **http://www.sis.nlm.nih.gov/Dir/DirMain.html**. It is composed of two parts: DIRLINE and Health Hotlines.

The DIRLINE database comprises some 10,000 records of organizations, research centers, and government institutes and associations that primarily focus on health and biomedicine. To access DIRLINE directly, go to the following Web site: **http://dirline.nlm.nih.gov/**. Simply type in "human immunodeficiency virus" (or a synonym), and you will receive information on all relevant organizations listed in the database.

Health Hotlines directs you to toll-free numbers to over 300 organizations. You can access this database directly at **http://www.sis.nlm.nih.gov/hotlines/**. On this page, you are given the option to search by keyword or by browsing the subject list. When you have received your search results, click on the name of the organization for its description and contact information.

The Combined Health Information Database

Another comprehensive source of information on healthcare associations is the Combined Health Information Database. Using the "Detailed Search" option, you will need to limit your search to "Organizations" and "human immunodeficiency virus". Type the following hyperlink into your Web browser: **http://chid.nih.gov/detail/detail.html**. To find associations, use the drop boxes at the bottom of the search page where "You may refine your search by." For publication date, select "All Years." Then, select your preferred language and the format option "Organization Resource Sheet." Type "human immunodeficiency virus" (or synonyms) into the "For these words:" box. You should check back periodically with this database since it is updated every three months.

The National Organization for Rare Disorders, Inc.

The National Organization for Rare Disorders, Inc. has prepared a Web site that provides, at no charge, lists of associations organized by health topic. You can access this database at the following Web site: **http://www.rarediseases.org/search/orgsearch.html**. Type "human immunodeficiency virus" (or a synonym) into the search box, and click "Submit Query."

APPENDIX C. FINDING MEDICAL LIBRARIES

Overview

In this Appendix, we show you how to quickly find a medical library in your area.

Preparation

Your local public library and medical libraries have interlibrary loan programs with the National Library of Medicine (NLM), one of the largest medical collections in the world. According to the NLM, most of the literature in the general and historical collections of the National Library of Medicine is available on interlibrary loan to any library. If you would like to access NLM medical literature, then visit a library in your area that can request the publications for you.[27]

Finding a Local Medical Library

The quickest method to locate medical libraries is to use the Internet-based directory published by the National Network of Libraries of Medicine (NN/LM). This network includes 4626 members and affiliates that provide many services to librarians, health professionals, and the public. To find a library in your area, simply visit **http://nnlm.gov/members/adv.html** or call 1-800-338-7657.

Medical Libraries in the U.S. and Canada

In addition to the NN/LM, the National Library of Medicine (NLM) lists a number of libraries with reference facilities that are open to the public. The following is the NLM's list and includes hyperlinks to each library's Web site. These Web pages can provide information on hours of operation and other restrictions. The list below is a small sample of

[27] Adapted from the NLM: **http://www.nlm.nih.gov/psd/cas/interlibrary.html**.

libraries recommended by the National Library of Medicine (sorted alphabetically by name of the U.S. state or Canadian province where the library is located)[28]:

- **Alabama:** Health InfoNet of Jefferson County (Jefferson County Library Cooperative, Lister Hill Library of the Health Sciences), **http://www.uab.edu/infonet/**
- **Alabama:** Richard M. Scrushy Library (American Sports Medicine Institute)
- **Arizona:** Samaritan Regional Medical Center: The Learning Center (Samaritan Health System, Phoenix, Arizona), **http://www.samaritan.edu/library/bannerlibs.htm**
- **California:** Kris Kelly Health Information Center (St. Joseph Health System, Humboldt), **http://www.humboldt1.com/~kkhic/index.html**
- **California:** Community Health Library of Los Gatos, **http://www.healthlib.org/orgresources.html**
- **California:** Consumer Health Program and Services (CHIPS) (County of Los Angeles Public Library, Los Angeles County Harbor-UCLA Medical Center Library) - Carson, CA, **http://www.colapublib.org/services/chips.html**
- **California:** Gateway Health Library (Sutter Gould Medical Foundation)
- **California:** Health Library (Stanford University Medical Center), **http://www-med.stanford.edu/healthlibrary/**
- **California:** Patient Education Resource Center - Health Information and Resources (University of California, San Francisco), **http://sfghdean.ucsf.edu/barnett/PERC/default.asp**
- **California:** Redwood Health Library (Petaluma Health Care District), **http://www.phcd.org/rdwdlib.html**
- **California:** Los Gatos PlaneTree Health Library, **http://planetreesanjose.org/**
- **California:** Sutter Resource Library (Sutter Hospitals Foundation, Sacramento), **http://suttermedicalcenter.org/library/**
- **California:** Health Sciences Libraries (University of California, Davis), **http://www.lib.ucdavis.edu/healthsci/**
- **California:** ValleyCare Health Library & Ryan Comer Cancer Resource Center (ValleyCare Health System, Pleasanton), **http://gaelnet.stmarys-ca.edu/other.libs/gbal/east/vchl.html**
- **California:** Washington Community Health Resource Library (Fremont), **http://www.healthlibrary.org/**
- **Colorado:** William V. Gervasini Memorial Library (Exempla Healthcare), **http://www.saintjosephdenver.org/yourhealth/libraries/**
- **Connecticut:** Hartford Hospital Health Science Libraries (Hartford Hospital), **http://www.harthosp.org/library/**
- **Connecticut:** Healthnet: Connecticut Consumer Health Information Center (University of Connecticut Health Center, Lyman Maynard Stowe Library), **http://library.uchc.edu/departm/hnet/**

[28] Abstracted from **http://www.nlm.nih.gov/medlineplus/libraries.html**.

- **Connecticut:** Waterbury Hospital Health Center Library (Waterbury Hospital, Waterbury), **http://www.waterburyhospital.com/library/consumer.shtml**
- **Delaware:** Consumer Health Library (Christiana Care Health System, Eugene du Pont Preventive Medicine & Rehabilitation Institute, Wilmington), **http://www.christianacare.org/health_guide/health_guide_pmri_health_info.cfm**
- **Delaware:** Lewis B. Flinn Library (Delaware Academy of Medicine, Wilmington), **http://www.delamed.org/chls.html**
- **Georgia:** Family Resource Library (Medical College of Georgia, Augusta), **http://cmc.mcg.edu/kids_families/fam_resources/fam_res_lib/frl.htm**
- **Georgia:** Health Resource Center (Medical Center of Central Georgia, Macon), **http://www.mccg.org/hrc/hrchome.asp**
- **Hawaii:** Hawaii Medical Library: Consumer Health Information Service (Hawaii Medical Library, Honolulu), **http://hml.org/CHIS/**
- **Idaho:** DeArmond Consumer Health Library (Kootenai Medical Center, Coeur d'Alene), **http://www.nicon.org/DeArmond/index.htm**
- **Illinois:** Health Learning Center of Northwestern Memorial Hospital (Chicago), **http://www.nmh.org/health_info/hlc.html**
- **Illinois:** Medical Library (OSF Saint Francis Medical Center, Peoria), **http://www.osfsaintfrancis.org/general/library/**
- **Kentucky:** Medical Library - Services for Patients, Families, Students & the Public (Central Baptist Hospital, Lexington), **http://www.centralbap.com/education/community/library.cfm**
- **Kentucky:** University of Kentucky - Health Information Library (Chandler Medical Center, Lexington), **http://www.mc.uky.edu/PatientEd/**
- **Louisiana:** Alton Ochsner Medical Foundation Library (Alton Ochsner Medical Foundation, New Orleans), **http://www.ochsner.org/library/**
- **Louisiana:** Louisiana State University Health Sciences Center Medical Library-Shreveport, **http://lib-sh.lsuhsc.edu/**
- **Maine:** Franklin Memorial Hospital Medical Library (Franklin Memorial Hospital, Farmington), **http://www.fchn.org/fmh/lib.htm**
- **Maine:** Gerrish-True Health Sciences Library (Central Maine Medical Center, Lewiston), **http://www.cmmc.org/library/library.html**
- **Maine:** Hadley Parrot Health Science Library (Eastern Maine Healthcare, Bangor), **http://www.emh.org/hll/hpl/guide.htm**
- **Maine:** Maine Medical Center Library (Maine Medical Center, Portland), **http://www.mmc.org/library/**
- **Maine:** Parkview Hospital (Brunswick), **http://www.parkviewhospital.org/**
- **Maine:** Southern Maine Medical Center Health Sciences Library (Southern Maine Medical Center, Biddeford), **http://www.smmc.org/services/service.php3?choice=10**
- **Maine:** Stephens Memorial Hospital's Health Information Library (Western Maine Health, Norway), **http://www.wmhcc.org/Library/**

- **Manitoba, Canada:** Consumer & Patient Health Information Service (University of Manitoba Libraries), **http://www.umanitoba.ca/libraries/units/health/reference/chis.html**
- **Manitoba, Canada:** J.W. Crane Memorial Library (Deer Lodge Centre, Winnipeg), **http://www.deerlodge.mb.ca/crane_library/about.asp**
- **Maryland:** Health Information Center at the Wheaton Regional Library (Montgomery County, Dept. of Public Libraries, Wheaton Regional Library), **http://www.mont.lib.md.us/healthinfo/hic.asp**
- **Massachusetts:** Baystate Medical Center Library (Baystate Health System), **http://www.baystatehealth.com/1024/**
- **Massachusetts:** Boston University Medical Center Alumni Medical Library (Boston University Medical Center), **http://med-libwww.bu.edu/library/lib.html**
- **Massachusetts:** Lowell General Hospital Health Sciences Library (Lowell General Hospital, Lowell), **http://www.lowellgeneral.org/library/HomePageLinks/WWW.htm**
- **Massachusetts:** Paul E. Woodard Health Sciences Library (New England Baptist Hospital, Boston), **http://www.nebh.org/health_lib.asp**
- **Massachusetts:** St. Luke's Hospital Health Sciences Library (St. Luke's Hospital, Southcoast Health System, New Bedford), **http://www.southcoast.org/library/**
- **Massachusetts:** Treadwell Library Consumer Health Reference Center (Massachusetts General Hospital), **http://www.mgh.harvard.edu/library/chrcindex.html**
- **Massachusetts:** UMass HealthNet (University of Massachusetts Medical School, Worchester), **http://healthnet.umassmed.edu/**
- **Michigan:** Botsford General Hospital Library - Consumer Health (Botsford General Hospital, Library & Internet Services), **http://www.botsfordlibrary.org/consumer.htm**
- **Michigan:** Helen DeRoy Medical Library (Providence Hospital and Medical Centers), **http://www.providence-hospital.org/library/**
- **Michigan:** Marquette General Hospital - Consumer Health Library (Marquette General Hospital, Health Information Center), **http://www.mgh.org/center.html**
- **Michigan:** Patient Education Resouce Center - University of Michigan Cancer Center (University of Michigan Comprehensive Cancer Center, Ann Arbor), **http://www.cancer.med.umich.edu/learn/leares.htm**
- **Michigan:** Sladen Library & Center for Health Information Resources - Consumer Health Information (Detroit), **http://www.henryford.com/body.cfm?id=39330**
- **Montana:** Center for Health Information (St. Patrick Hospital and Health Sciences Center, Missoula)
- **National:** Consumer Health Library Directory (Medical Library Association, Consumer and Patient Health Information Section), **http://caphis.mlanet.org/directory/index.html**
- **National:** National Network of Libraries of Medicine (National Library of Medicine) - provides library services for health professionals in the United States who do not have access to a medical library, **http://nnlm.gov/**
- **National:** NN/LM List of Libraries Serving the Public (National Network of Libraries of Medicine), **http://nnlm.gov/members/**

- **Nevada:** Health Science Library, West Charleston Library (Las Vegas-Clark County Library District, Las Vegas), **http://www.lvccld.org/special_collections/medical/index.htm**
- **New Hampshire:** Dartmouth Biomedical Libraries (Dartmouth College Library, Hanover), **http://www.dartmouth.edu/~biomed/resources.htmld/conshealth.htmld/**
- **New Jersey:** Consumer Health Library (Rahway Hospital, Rahway), **http://www.rahwayhospital.com/library.htm**
- **New Jersey:** Dr. Walter Phillips Health Sciences Library (Englewood Hospital and Medical Center, Englewood), **http://www.englewoodhospital.com/links/index.htm**
- **New Jersey:** Meland Foundation (Englewood Hospital and Medical Center, Englewood), **http://www.geocities.com/ResearchTriangle/9360/**
- **New York:** Choices in Health Information (New York Public Library) - NLM Consumer Pilot Project participant, **http://www.nypl.org/branch/health/links.html**
- **New York:** Health Information Center (Upstate Medical University, State University of New York, Syracuse), **http://www.upstate.edu/library/hic/**
- **New York:** Health Sciences Library (Long Island Jewish Medical Center, New Hyde Park), **http://www.lij.edu/library/library.html**
- **New York:** ViaHealth Medical Library (Rochester General Hospital), **http://www.nyam.org/library/**
- **Ohio:** Consumer Health Library (Akron General Medical Center, Medical & Consumer Health Library), **http://www.akrongeneral.org/hwlibrary.htm**
- **Oklahoma:** The Health Information Center at Saint Francis Hospital (Saint Francis Health System, Tulsa), **http://www.sfh-tulsa.com/services/healthinfo.asp**
- **Oregon:** Planetree Health Resource Center (Mid-Columbia Medical Center, The Dalles), **http://www.mcmc.net/phrc/**
- **Pennsylvania:** Community Health Information Library (Milton S. Hershey Medical Center, Hershey), **http://www.hmc.psu.edu/commhealth/**
- **Pennsylvania:** Community Health Resource Library (Geisinger Medical Center, Danville), **http://www.geisinger.edu/education/commlib.shtml**
- **Pennsylvania:** HealthInfo Library (Moses Taylor Hospital, Scranton), **http://www.mth.org/healthwellness.html**
- **Pennsylvania:** Hopwood Library (University of Pittsburgh, Health Sciences Library System, Pittsburgh), **http://www.hsls.pitt.edu/guides/chi/hopwood/index_html**
- **Pennsylvania:** Koop Community Health Information Center (College of Physicians of Philadelphia), **http://www.collphyphil.org/kooppg1.shtml**
- **Pennsylvania:** Learning Resources Center - Medical Library (Susquehanna Health System, Williamsport), **http://www.shscares.org/services/lrc/index.asp**
- **Pennsylvania:** Medical Library (UPMC Health System, Pittsburgh), **http://www.upmc.edu/passavant/library.htm**
- **Quebec, Canada:** Medical Library (Montreal General Hospital), **http://www.mghlib.mcgill.ca/**

- **South Dakota:** Rapid City Regional Hospital Medical Library (Rapid City Regional Hospital), **http://www.rcrh.org/Services/Library/Default.asp**
- **Texas:** Houston HealthWays (Houston Academy of Medicine-Texas Medical Center Library), **http://hhw.library.tmc.edu/**
- **Washington:** Community Health Library (Kittitas Valley Community Hospital), **http://www.kvch.com/**
- **Washington:** Southwest Washington Medical Center Library (Southwest Washington Medical Center, Vancouver), **http://www.swmedicalcenter.com/body.cfm?id=72**

ONLINE GLOSSARIES

The Internet provides access to a number of free-to-use medical dictionaries. The National Library of Medicine has compiled the following list of online dictionaries:

- ADAM Medical Encyclopedia (A.D.A.M., Inc.), comprehensive medical reference: **http://www.nlm.nih.gov/medlineplus/encyclopedia.html**
- MedicineNet.com Medical Dictionary (MedicineNet, Inc.): **http://www.medterms.com/Script/Main/hp.asp**
- Merriam-Webster Medical Dictionary (Inteli-Health, Inc.): **http://www.intelihealth.com/IH/**
- Multilingual Glossary of Technical and Popular Medical Terms in Eight European Languages (European Commission) - Danish, Dutch, English, French, German, Italian, Portuguese, and Spanish: **http://allserv.rug.ac.be/~rvdstich/eugloss/welcome.html**
- On-line Medical Dictionary (CancerWEB): **http://cancerweb.ncl.ac.uk/omd/**
- Rare Diseases Terms (Office of Rare Diseases): **http://ord.aspensys.com/asp/diseases/diseases.asp**
- Technology Glossary (National Library of Medicine) - Health Care Technology: **http://www.nlm.nih.gov/nichsr/ta101/ta10108.htm**

Beyond these, MEDLINEplus contains a very patient-friendly encyclopedia covering every aspect of medicine (licensed from A.D.A.M., Inc.). The ADAM Medical Encyclopedia can be accessed at **http://www.nlm.nih.gov/medlineplus/encyclopedia.html**. ADAM is also available on commercial Web sites such as drkoop.com (**http://www.drkoop.com/**) and Web MD (**http://my.webmd.com/adam/asset/adam_disease_articles/a_to_z/a**). The NIH suggests the following Web sites in the ADAM Medical Encyclopedia when searching for information on human immunodeficiency virus:

- **Basic Guidelines for Human Immunodeficiency Virus**

  AIDS
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/000594.htm

  Renal failure
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/000501.htm

  TB
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/000077.htm

- **Signs & Symptoms for Human Immunodeficiency Virus**

  Diarrhea
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003126.htm

  Fever
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003090.htm

Headache
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003024.htm

Sore throat
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003053.htm

- **Diagnostics and Tests for Human Immunodeficiency Virus**

ELISA
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003332.htm

Western blot
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003538.htm

- **Background Topics for Human Immunodeficiency Virus**

Acute
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002215.htm

PCP
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/001945.htm

Renal
Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002289.htm

Online Dictionary Directories

The following are additional online directories compiled by the National Library of Medicine, including a number of specialized medical dictionaries:

- Medical Dictionaries: Medical & Biological (World Health Organization): **http://www.who.int/hlt/virtuallibrary/English/diction.htm#Medical**
- MEL-Michigan Electronic Library List of Online Health and Medical Dictionaries (Michigan Electronic Library): **http://mel.lib.mi.us/health/health-dictionaries.html**
- Patient Education: Glossaries (DMOZ Open Directory Project): **http://dmoz.org/Health/Education/Patient_Education/Glossaries/**
- Web of Online Dictionaries (Bucknell University): **http://www.yourdictionary.com/diction5.html#medicine**

HUMAN IMMUNODEFICIENCY VIRUS DICTIONARY

The definitions below are derived from official public sources, including the National Institutes of Health [NIH] and the European Union [EU].

Abacavir: A nucleoside analog reverse transcriptase inhibitor (NARTIs) developed by Glaxo Wellcome. [NIH]

Abdominal: Having to do with the abdomen, which is the part of the body between the chest and the hips that contains the pancreas, stomach, intestines, liver, gallbladder, and other organs. [NIH]

Abdominal Pain: Sensation of discomfort, distress, or agony in the abdominal region. [NIH]

Abortion: 1. The premature expulsion from the uterus of the products of conception - of the embryo, or of a nonviable fetus. The four classic symptoms, usually present in each type of abortion, are uterine contractions, uterine haemorrhage, softening and dilatation of the cervix, and presentation or expulsion of all or part of the products of conception. 2. Premature stoppage of a natural or a pathological process. [EU]

Abrin: A toxic lectin from the seeds of jequirity, Abrus precatorius L. Very active poison. Five different proteins have so far been isolated: Abrus agglutinin, the component responsible for hemagglutininating activity, & abrins a-d, the toxic principles each consisting of two peptide chains are held together by disulfide bonds. [NIH]

Abscess: Accumulation of purulent material in tissues, organs, or circumscribed spaces, usually associated with signs of infection. [NIH]

Absenteeism: Chronic absence from work or other duty. [NIH]

Acceptor: A substance which, while normally not oxidized by oxygen or reduced by hydrogen, can be oxidized or reduced in presence of a substance which is itself undergoing oxidation or reduction. [NIH]

Accommodation: Adjustment, especially that of the eye for various distances. [EU]

Acetylgalactosamine: The N-acetyl derivative of galactosamine. [NIH]

Acetylglucosamine: The N-acetyl derivative of glucosamine. [NIH]

Acidemia: Increased acidity of blood. [NIH]

Acidity: The quality of being acid or sour; containing acid (hydrogen ions). [EU]

Acidosis: A pathologic condition resulting from accumulation of acid or depletion of the alkaline reserve (bicarbonate content) in the blood and body tissues, and characterized by an increase in hydrogen ion concentration. [EU]

Acquired Immunodeficiency Syndrome: An acquired defect of cellular immunity associated with infection by the human immunodeficiency virus (HIV), a CD4-positive T-lymphocyte count under 200 cells/microliter or less than 14% of total lymphocytes, and increased susceptibility to opportunistic infections and malignant neoplasms. Clinical manifestations also include emaciation (wasting) and dementia. These elements reflect criteria for AIDS as defined by the CDC in 1993. [NIH]

Acute myelogenous leukemia: AML. A quickly progressing disease in which too many immature blood-forming cells are found in the blood and bone marrow. Also called acute myeloid leukemia or acute nonlymphocytic leukemia. [NIH]

Acute myeloid leukemia: AML. A quickly progressing disease in which too many immature blood-forming cells are found in the blood and bone marrow. Also called acute myelogenous leukemia or acute nonlymphocytic leukemia. [NIH]

Acute nonlymphocytic leukemia: A quickly progressing disease in which too many immature blood-forming cells are found in the blood and bone marrow. Also called acute myeloid leukemia or acute myelogenous leukemia. [NIH]

Acute renal: A condition in which the kidneys suddenly stop working. In most cases, kidneys can recover from almost complete loss of function. [NIH]

Adaptability: Ability to develop some form of tolerance to conditions extremely different from those under which a living organism evolved. [NIH]

Adenine: A purine base and a fundamental unit of adenine nucleotides. [NIH]

Adenocarcinoma: A malignant epithelial tumor with a glandular organization. [NIH]

Adenosine: A nucleoside that is composed of adenine and d-ribose. Adenosine or adenosine derivatives play many important biological roles in addition to being components of DNA and RNA. Adenosine itself is a neurotransmitter. [NIH]

Adenovirus: A group of viruses that cause respiratory tract and eye infections. Adenoviruses used in gene therapy are altered to carry a specific tumor-fighting gene. [NIH]

Adipocytes: Fat-storing cells found mostly in the abdominal cavity and subcutaneous tissue. Fat is usually stored in the form of tryglycerides. [NIH]

Adolescence: The period of life beginning with the appearance of secondary sex characteristics and terminating with the cessation of somatic growth. The years usually referred to as adolescence lie between 13 and 18 years of age. [NIH]

Adrenal Cortex: The outer layer of the adrenal gland. It secretes mineralocorticoids, androgens, and glucocorticoids. [NIH]

Adrenal Glands: Paired glands situated in the retroperitoneal tissues at the superior pole of each kidney. [NIH]

Adrenal insufficiency: The reduced secretion of adrenal glands. [NIH]

Adsorption: The condensation of gases, liquids, or dissolved substances on the surfaces of solids. It includes adsorptive phenomena of bacteria and viruses as well as of tissues treated with exogenous drugs and chemicals. [NIH]

Adsorptive: It captures volatile compounds by binding them to agents such as activated carbon or adsorptive resins. [NIH]

Adverse Effect: An unwanted side effect of treatment. [NIH]

Aerobic: In biochemistry, reactions that need oxygen to happen or happen when oxygen is present. [NIH]

Aerobic Exercise: A type of physical activity that includes walking, jogging, running, and dancing. Aerobic training improves the efficiency of the aerobic energy-producing systems that can improve cardiorespiratory endurance. [NIH]

Afferent: Concerned with the transmission of neural impulse toward the central part of the nervous system. [NIH]

Affinity: 1. Inherent likeness or relationship. 2. A special attraction for a specific element, organ, or structure. 3. Chemical affinity; the force that binds atoms in molecules; the tendency of substances to combine by chemical reaction. 4. The strength of noncovalent chemical binding between two substances as measured by the dissociation constant of the complex. 5. In immunology, a thermodynamic expression of the strength of interaction between a single antigen-binding site and a single antigenic determinant (and thus of the

stereochemical compatibility between them), most accurately applied to interactions among simple, uniform antigenic determinants such as haptens. Expressed as the association constant (K litres mole -1), which, owing to the heterogeneity of affinities in a population of antibody molecules of a given specificity, actually represents an average value (mean intrinsic association constant). 6. The reciprocal of the dissociation constant. [EU]

Albumin: 1. Any protein that is soluble in water and moderately concentrated salt solutions and is coagulable by heat. 2. Serum albumin; the major plasma protein (approximately 60 per cent of the total), which is responsible for much of the plasma colloidal osmotic pressure and serves as a transport protein carrying large organic anions, such as fatty acids, bilirubin, and many drugs, and also carrying certain hormones, such as cortisol and thyroxine, when their specific binding globulins are saturated. Albumin is synthesized in the liver. Low serum levels occur in protein malnutrition, active inflammation and serious hepatic and renal disease. [EU]

Algorithms: A procedure consisting of a sequence of algebraic formulas and/or logical steps to calculate or determine a given task. [NIH]

Alimentary: Pertaining to food or nutritive material, or to the organs of digestion. [EU]

Alkaline: Having the reactions of an alkali. [EU]

Alkaloid: A member of a large group of chemicals that are made by plants and have nitrogen in them. Some alkaloids have been shown to work against cancer. [NIH]

Alkylating Agents: Highly reactive chemicals that introduce alkyl radicals into biologically active molecules and thereby prevent their proper functioning. Many are used as antineoplastic agents, but most are very toxic, with carcinogenic, mutagenic, teratogenic, and immunosuppressant actions. They have also been used as components in poison gases. [NIH]

Alleles: Mutually exclusive forms of the same gene, occupying the same locus on homologous chromosomes, and governing the same biochemical and developmental process. [NIH]

Allergens: Antigen-type substances that produce immediate hypersensitivity (hypersensitivity, immediate). [NIH]

Allografts: A graft of tissue obtained from the body of another animal of the same species but with genotype differing from that of the recipient; tissue graft from a donor of one genotype to a host of another genotype with host and donor being members of the same species. [NIH]

Aloe: A genus of the family Liliaceae containing anthraquinone glycosides such as aloin-emodin or aloe-emodin (emodin). [NIH]

Alpha-helix: One of the secondary element of protein. [NIH]

Alphavirus: A genus of Togaviridae, also known as Group A arboviruses, serologically related to each other but not to other Togaviridae. The viruses are transmitted by mosquitoes. The type species is the sindbis virus. [NIH]

Alternative medicine: Practices not generally recognized by the medical community as standard or conventional medical approaches and used instead of standard treatments. Alternative medicine includes the taking of dietary supplements, megadose vitamins, and herbal preparations; the drinking of special teas; and practices such as massage therapy, magnet therapy, spiritual healing, and meditation. [NIH]

Ambulatory Care: Health care services provided to patients on an ambulatory basis, rather than by admission to a hospital or other health care facility. The services may be a part of a hospital, augmenting its inpatient services, or may be provided at a free-standing facility. [NIH]

Ambulatory Care Information Systems: Information systems, usually computer-assisted, designed to store, manipulate, and retrieve information for planning, organizing, directing, and controlling administrative activities associated with the provision and utilization of ambulatory care services and facilities. [NIH]

Ameliorating: A changeable condition which prevents the consequence of a failure or accident from becoming as bad as it otherwise would. [NIH]

Amenorrhea: Absence of menstruation. [NIH]

Amino acid: Any organic compound containing an amino (-NH2 and a carboxyl (- COOH) group. The 20 a-amino acids listed in the accompanying table are the amino acids from which proteins are synthesized by formation of peptide bonds during ribosomal translation of messenger RNA; all except glycine, which is not optically active, have the L configuration. Other amino acids occurring in proteins, such as hydroxyproline in collagen, are formed by posttranslational enzymatic modification of amino acids residues in polypeptide chains. There are also several important amino acids, such as the neurotransmitter y-aminobutyric acid, that have no relation to proteins. Abbreviated AA. [EU]

Amino Acid Motifs: Commonly observed structural components of proteins formed by simple combinations of adjacent secondary structures. A commonly observed structure may be composed of a conserved sequence which can be represented by a consensus sequence. [NIH]

Amino Acid Sequence: The order of amino acids as they occur in a polypeptide chain. This is referred to as the primary structure of proteins. It is of fundamental importance in determining protein conformation. [NIH]

Amino Acid Substitution: The naturally occurring or experimentally induced replacement of one or more amino acids in a protein with another. If a functionally equivalent amino acid is substituted, the protein may retain wild-type activity. Substitution may also diminish or eliminate protein function. Experimentally induced substitution is often used to study enzyme activities and binding site properties. [NIH]

Aminoquinolines: Quinolines substituted in any position by one or more amino groups. [NIH]

Ammonia: A colorless alkaline gas. It is formed in the body during decomposition of organic materials during a large number of metabolically important reactions. [NIH]

Amphetamines: Analogs or derivatives of amphetamine. Many are sympathomimetics and central nervous system stimulators causing excitation, vasopression, bronchodilation, and to varying degrees, anorexia, analepsis, nasal decongestion, and some smooth muscle relaxation. [NIH]

Amplification: The production of additional copies of a chromosomal DNA sequence, found as either intrachromosomal or extrachromosomal DNA. [NIH]

Anabolic: Relating to, characterized by, or promoting anabolism. [EU]

Anaerobic: 1. Lacking molecular oxygen. 2. Growing, living, or occurring in the absence of molecular oxygen; pertaining to an anaerobe. [EU]

Anaesthesia: Loss of feeling or sensation. Although the term is used for loss of tactile sensibility, or of any of the other senses, it is applied especially to loss of the sensation of pain, as it is induced to permit performance of surgery or other painful procedures. [EU]

Anal: Having to do with the anus, which is the posterior opening of the large bowel. [NIH]

Analog: In chemistry, a substance that is similar, but not identical, to another. [NIH]

Analogous: Resembling or similar in some respects, as in function or appearance, but not in origin or development;. [EU]

Analytes: A component of a test sample the presence of which has to be demonstrated. The term "analyte" includes where appropriate formed from the analyte during the analyses. [NIH]

Anaphylatoxins: The family of peptides C3a, C4a, C5a, and C5a des-arginine produced in the serum during complement activation. They produce smooth muscle contraction, mast cell histamine release, affect platelet aggregation, and act as mediators of the local inflammatory process. The order of anaphylatoxin activity from strongest to weakest is C5a, C3a, C4a, and C5a des-arginine. The latter is the so-called "classical" anaphylatoxin but shows no spasmogenic activity though it contains some chemotactic ability. [NIH]

Anaplasia: Loss of structural differentiation and useful function of neoplastic cells. [NIH]

Anatomical: Pertaining to anatomy, or to the structure of the organism. [EU]

Androgenic: Producing masculine characteristics. [EU]

Androgens: A class of sex hormones associated with the development and maintenance of the secondary male sex characteristics, sperm induction, and sexual differentiation. In addition to increasing virility and libido, they also increase nitrogen and water retention and stimulate skeletal growth. [NIH]

Anemia: A reduction in the number of circulating erythrocytes or in the quantity of hemoglobin. [NIH]

Anergy: Absence of immune response to particular substances. [NIH]

Anesthesia: A state characterized by loss of feeling or sensation. This depression of nerve function is usually the result of pharmacologic action and is induced to allow performance of surgery or other painful procedures. [NIH]

Animal model: An animal with a disease either the same as or like a disease in humans. Animal models are used to study the development and progression of diseases and to test new treatments before they are given to humans. Animals with transplanted human cancers or other tissues are called xenograft models. [NIH]

Annealing: The spontaneous alignment of two single DNA strands to form a double helix. [NIH]

Anorexia: Lack or loss of appetite for food. Appetite is psychologic, dependent on memory and associations. Anorexia can be brought about by unattractive food, surroundings, or company. [NIH]

Anovulation: Suspension or cessation of ovulation in animals and humans. [NIH]

Antibacterial: A substance that destroys bacteria or suppresses their growth or reproduction. [EU]

Antibiotic: A drug used to treat infections caused by bacteria and other microorganisms. [NIH]

Antibiotic Prophylaxis: Use of antibiotics before, during, or after a diagnostic, therapeutic, or surgical procedure to prevent infectious complications. [NIH]

Antibodies: Immunoglobulin molecules having a specific amino acid sequence by virtue of which they interact only with the antigen that induced their synthesis in cells of the lymphoid series (especially plasma cells), or with an antigen closely related to it. [NIH]

Antibodies, Anticardiolipin: Antiphospholipid antibodies found in association with systemic lupus erythematosus (lupus erythematosus, systemic), antiphospholipid syndrome, and in a variety of other diseases as well as in healthy individuals. The antibodies are detected by solid-phase immunoassay employing the purified phospholipid antigen cardiolipin. [NIH]

Antibodies, Antiphospholipid: Autoantibodies directed against phospholipids. These antibodies are characteristically found in patients with systemic lupus erythematosus, antiphospholipid syndrome, related autoimmune diseases, some non-autoimmune diseases, and also in healthy individuals. [NIH]

Antibody: A type of protein made by certain white blood cells in response to a foreign substance (antigen). Each antibody can bind to only a specific antigen. The purpose of this binding is to help destroy the antigen. Antibodies can work in several ways, depending on the nature of the antigen. Some antibodies destroy antigens directly. Others make it easier for white blood cells to destroy the antigen. [NIH]

Anticoagulant: A drug that helps prevent blood clots from forming. Also called a blood thinner. [NIH]

Anticonvulsant: An agent that prevents or relieves convulsions. [EU]

Antidepressant: A drug used to treat depression. [NIH]

Antifungal: Destructive to fungi, or suppressing their reproduction or growth; effective against fungal infections. [EU]

Antigen: Any substance which is capable, under appropriate conditions, of inducing a specific immune response and of reacting with the products of that response, that is, with specific antibody or specifically sensitized T-lymphocytes, or both. Antigens may be soluble substances, such as toxins and foreign proteins, or particulate, such as bacteria and tissue cells; however, only the portion of the protein or polysaccharide molecule known as the antigenic determinant (q.v.) combines with antibody or a specific receptor on a lymphocyte. Abbreviated Ag. [EU]

Antigen-Antibody Complex: The complex formed by the binding of antigen and antibody molecules. The deposition of large antigen-antibody complexes leading to tissue damage causes immune complex diseases. [NIH]

Antigen-presenting cell: APC. A cell that shows antigen on its surface to other cells of the immune system. This is an important part of an immune response. [NIH]

Anti-inflammatory: Having to do with reducing inflammation. [NIH]

Antimetabolite: A chemical that is very similar to one required in a normal biochemical reaction in cells. Antimetabolites can stop or slow down the reaction. [NIH]

Antimicrobial: Killing microorganisms, or suppressing their multiplication or growth. [EU]

Antimutagenic Agents: Agents that reduce the frequency or rate of spontaneous or induced mutations independently of the mechanism involved. [NIH]

Antineoplastic: Inhibiting or preventing the development of neoplasms, checking the maturation and proliferation of malignant cells. [EU]

Antineoplastic Agents: Substances that inhibit or prevent the proliferation of neoplasms. [NIH]

Antioxidant: A substance that prevents damage caused by free radicals. Free radicals are highly reactive chemicals that often contain oxygen. They are produced when molecules are split to give products that have unpaired electrons. This process is called oxidation. [NIH]

Antiphospholipid Syndrome: The presence of antibodies directed against phospholipids (antibodies, antiphospholipid). The condition is associated with a variety of diseases, notably systemic lupus erythematosus and other connective tissue diseases, thrombopenia, and arterial or venous thromboses. In pregnancy it can cause abortion. Of the phospholipids, the cardiolipins show markedly elevated levels of anticardiolipin antibodies (antibodies, anticardiolipin). Present also are high levels of lupus anticoagulant (lupus coagulation inhibitor). [NIH]

Antiviral: Destroying viruses or suppressing their replication. [EU]

Antiviral Agents: Agents used in the prophylaxis or therapy of virus diseases. Some of the ways they may act include preventing viral replication by inhibiting viral DNA polymerase; binding to specific cell-surface receptors and inhibiting viral penetration or uncoating; inhibiting viral protein synthesis; or blocking late stages of virus assembly. [NIH]

Anus: The opening of the rectum to the outside of the body. [NIH]

Anxiety: Persistent feeling of dread, apprehension, and impending disaster. [NIH]

Apathy: Lack of feeling or emotion; indifference. [EU]

Apoptosis: One of the two mechanisms by which cell death occurs (the other being the pathological process of necrosis). Apoptosis is the mechanism responsible for the physiological deletion of cells and appears to be intrinsically programmed. It is characterized by distinctive morphologic changes in the nucleus and cytoplasm, chromatin cleavage at regularly spaced sites, and the endonucleolytic cleavage of genomic DNA (DNA fragmentation) at internucleosomal sites. This mode of cell death serves as a balance to mitosis in regulating the size of animal tissues and in mediating pathologic processes associated with tumor growth. [NIH]

Aqueous: Having to do with water. [NIH]

Arachidonic Acid: An unsaturated, essential fatty acid. It is found in animal and human fat as well as in the liver, brain, and glandular organs, and is a constituent of animal phosphatides. It is formed by the synthesis from dietary linoleic acid and is a precursor in the biosynthesis of prostaglandins, thromboxanes, and leukotrienes. [NIH]

Archaea: One of the three domains of life (the others being bacteria and Eucarya), formerly called Archaebacteria under the taxon Bacteria, but now considered separate and distinct. They are characterized by: 1) the presence of characteristic tRNAs and ribosomal RNAs; 2) the absence of peptidoglycan cell walls; 3) the presence of ether-linked lipids built from branched-chain subunits; and 4) their occurrence in unusual habitats. While archaea resemble bacteria in morphology and genomic organization, they resemble eukarya in their method of genomic replication. The domain contains at least three kingdoms: crenarchaeota, euryarchaeota, and korarchaeota. [NIH]

Arginine: An essential amino acid that is physiologically active in the L-form. [NIH]

Arsenicals: Inorganic or organic compounds that contain arsenic. [NIH]

Arterial: Pertaining to an artery or to the arteries. [EU]

Arteries: The vessels carrying blood away from the heart. [NIH]

Arterioles: The smallest divisions of the arteries located between the muscular arteries and the capillaries. [NIH]

Arteriosclerosis: Thickening and loss of elasticity of arterial walls. Atherosclerosis is the most common form of arteriosclerosis and involves lipid deposition and thickening of the intimal cell layers within arteries. Additional forms of arteriosclerosis involve calcification of the media of muscular arteries (Monkeberg medial calcific sclerosis) and thickening of the walls of small arteries or arterioles due to cell proliferation or hyaline deposition (arteriolosclerosis). [NIH]

Artery: Vessel-carrying blood from the heart to various parts of the body. [NIH]

Aseptic: Free from infection or septic material; sterile. [EU]

Aspartate: A synthetic amino acid. [NIH]

Assay: Determination of the amount of a particular constituent of a mixture, or of the biological or pharmacological potency of a drug. [EU]

Astrocytes: The largest and most numerous neuroglial cells in the brain and spinal cord. Astrocytes (from "star" cells) are irregularly shaped with many long processes, including those with "end feet" which form the glial (limiting) membrane and directly and indirectly contribute to the blood brain barrier. They regulate the extracellular ionic and chemical environment, and "reactive astrocytes" (along with microglia) respond to injury. Astrocytes have high- affinity transmitter uptake systems, voltage-dependent and transmitter-gated ion channels, and can release transmitter, but their role in signaling (as in many other functions) is not well understood. [NIH]

Asymptomatic: Having no signs or symptoms of disease. [NIH]

Ataxia: Impairment of the ability to perform smoothly coordinated voluntary movements. This condition may affect the limbs, trunk, eyes, pharnyx, larnyx, and other structures. Ataxia may result from impaired sensory or motor function. Sensory ataxia may result from posterior column injury or peripheral nerve diseases. Motor ataxia may be associated with cerebellar diseases; cerebral cortex diseases; thalamic diseases; basal ganglia diseases; injury to the red nucleus; and other conditions. [NIH]

Atmospheric Pressure: The pressure at any point in an atmosphere due solely to the weight of the atmospheric gases above the point concerned. [NIH]

ATP: ATP an abbreviation for adenosine triphosphate, a compound which serves as a carrier of energy for cells. [NIH]

Atrophy: Decrease in the size of a cell, tissue, organ, or multiple organs, associated with a variety of pathological conditions such as abnormal cellular changes, ischemia, malnutrition, or hormonal changes. [NIH]

Autoantibodies: Antibodies that react with self-antigens (autoantigens) of the organism that produced them. [NIH]

Autoantigens: Endogenous tissue constituents that have the ability to interact with autoantibodies and cause an immune response. [NIH]

Autoimmune disease: A condition in which the body recognizes its own tissues as foreign and directs an immune response against them. [NIH]

Autoimmune Hepatitis: A liver disease caused when the body's immune system destroys liver cells for no known reason. [NIH]

Autoimmunity: Process whereby the immune system reacts against the body's own tissues. Autoimmunity may produce or be caused by autoimmune diseases. [NIH]

Autologous: Taken from an individual's own tissues, cells, or DNA. [NIH]

Autonomic: Self-controlling; functionally independent. [EU]

Autopsy: Postmortem examination of the body. [NIH]

Avian: A plasmodial infection in birds. [NIH]

Avidin: A specific protein in egg albumin that interacts with biotin to render it unavailable to mammals, thereby producing biotin deficiency. [NIH]

Axonal: Condition associated with metabolic derangement of the entire neuron and is manifest by degeneration of the distal portion of the nerve fiber. [NIH]

Bacillus: A genus of Bacillaceae that are spore-forming, rod-shaped cells. Most species are saprophytic soil forms with only a few species being pathogenic. [NIH]

Back Injuries: General or unspecified injuries to the posterior part of the trunk. It includes injuries to the muscles of the back. [NIH]

Bacteremia: The presence of viable bacteria circulating in the blood. Fever, chills, tachycardia, and tachypnea are common acute manifestations of bacteremia. The majority of

cases are seen in already hospitalized patients, most of whom have underlying diseases or procedures which render their bloodstreams susceptible to invasion. [NIH]

Bacteria: Unicellular prokaryotic microorganisms which generally possess rigid cell walls, multiply by cell division, and exhibit three principal forms: round or coccal, rodlike or bacillary, and spiral or spirochetal. [NIH]

Bacterial Proteins: Proteins found in any species of bacterium. [NIH]

Bacterial toxin: A toxic substance, made by bacteria, that can be modified to kill specific tumor cells without harming normal cells. [NIH]

Bacteriophage: A virus whose host is a bacterial cell; A virus that exclusively infects bacteria. It generally has a protein coat surrounding the genome (DNA or RNA). One of the coliphages most extensively studied is the lambda phage, which is also one of the most important. [NIH]

Bacteriophage lambda: A temperate inducible phage and type species of the genus lambda-like Phages, in the family Siphoviridae. Its natural host is E. coli K12. Its virion contains linear double-stranded DNA, except for 12 complementary bases at the 5'-termini of the polynucleotide chains. The DNA circularizes on infection. [NIH]

Bacteriostatic: 1. Inhibiting the growth or multiplication of bacteria. 2. An agent that inhibits the growth or multiplication of bacteria. [EU]

Bacterium: Microscopic organism which may have a spherical, rod-like, or spiral unicellular or non-cellular body. Bacteria usually reproduce through asexual processes. [NIH]

Basal Ganglia: Large subcortical nuclear masses derived from the telencephalon and located in the basal regions of the cerebral hemispheres. [NIH]

Basal Ganglia Diseases: Diseases of the basal ganglia including the putamen; globus pallidus; claustrum; amygdala; and caudate nucleus. Dyskinesias (most notably involuntary movements and alterations of the rate of movement) represent the primary clinical manifestations of these disorders. Common etiologies include cerebrovascular disease; neurodegenerative diseases; and craniocerebral trauma. [NIH]

Base: In chemistry, the nonacid part of a salt; a substance that combines with acids to form salts; a substance that dissociates to give hydroxide ions in aqueous solutions; a substance whose molecule or ion can combine with a proton (hydrogen ion); a substance capable of donating a pair of electrons (to an acid) for the formation of a coordinate covalent bond. [EU]

Base Sequence: The sequence of purines and pyrimidines in nucleic acids and polynucleotides. It is also called nucleotide or nucleoside sequence. [NIH]

Basophils: Granular leukocytes characterized by a relatively pale-staining, lobate nucleus and cytoplasm containing coarse dark-staining granules of variable size and stainable by basic dyes. [NIH]

Behavior Therapy: The application of modern theories of learning and conditioning in the treatment of behavior disorders. [NIH]

Benign: Not cancerous; does not invade nearby tissue or spread to other parts of the body. [NIH]

Bereavement: Refers to the whole process of grieving and mourning and is associated with a deep sense of loss and sadness. [NIH]

Beta carotene: A vitamin A precursor. Beta carotene belongs to the family of fat-soluble vitamins called carotenoids. [NIH]

Beta-Thromboglobulin: A platelet-specific protein which is released when platelets aggregate. Elevated plasma levels have been reported after deep venous thrombosis, pre-

eclampsia, myocardial infarction with mural thrombosis, and myeloproliferative disorders. Measurement of beta-thromboglobulin in biological fluids by radioimmunoassay is used for the diagnosis and assessment of progress of thromboembolic disorders. [NIH]

Bilateral: Affecting both the right and left side of body. [NIH]

Bile: An emulsifying agent produced in the liver and secreted into the duodenum. Its composition includes bile acids and salts, cholesterol, and electrolytes. It aids digestion of fats in the duodenum. [NIH]

Binding Sites: The reactive parts of a macromolecule that directly participate in its specific combination with another molecule. [NIH]

Bioavailability: The degree to which a drug or other substance becomes available to the target tissue after administration. [EU]

Bioavailable: The ability of a drug or other substance to be absorbed and used by the body. Orally bioavailable means that a drug or other substance that is taken by mouth can be absorbed and used by the body. [NIH]

Biochemical: Relating to biochemistry; characterized by, produced by, or involving chemical reactions in living organisms. [EU]

Biological response modifier: BRM. A substance that stimulates the body's response to infection and disease. [NIH]

Biomarkers: Substances sometimes found in an increased amount in the blood, other body fluids, or tissues and that may suggest the presence of some types of cancer. Biomarkers include CA 125 (ovarian cancer), CA 15-3 (breast cancer), CEA (ovarian, lung, breast, pancreas, and GI tract cancers), and PSA (prostate cancer). Also called tumor markers. [NIH]

Biopsy: Removal and pathologic examination of specimens in the form of small pieces of tissue from the living body. [NIH]

Biotechnology: Body of knowledge related to the use of organisms, cells or cell-derived constituents for the purpose of developing products which are technically, scientifically and clinically useful. Alteration of biologic function at the molecular level (i.e., genetic engineering) is a central focus; laboratory methods used include transfection and cloning technologies, sequence and structure analysis algorithms, computer databases, and gene and protein structure function analysis and prediction. [NIH]

Biotin: Hexahydro-2-oxo-1H-thieno(3,4-d)imidazole-4-pentanoic acid. Growth factor present in minute amounts in every living cell. It occurs mainly bound to proteins or polypeptides and is abundant in liver, kidney, pancreas, yeast, and milk.The biotin content of cancerous tissue is higher than that of normal tissue. [NIH]

Bipolar Disorder: A major affective disorder marked by severe mood swings (manic or major depressive episodes) and a tendency to remission and recurrence. [NIH]

Bladder: The organ that stores urine. [NIH]

Blood Banks: Centers for collecting, characterizing, and storing human blood. [NIH]

Blood Coagulation: The process of the interaction of blood coagulation factors that results in an insoluble fibrin clot. [NIH]

Blood Glucose: Glucose in blood. [NIH]

Blood Platelets: Non-nucleated disk-shaped cells formed in the megakaryocyte and found in the blood of all mammals. They are mainly involved in blood coagulation. [NIH]

Blood pressure: The pressure of blood against the walls of a blood vessel or heart chamber. Unless there is reference to another location, such as the pulmonary artery or one of the heart chambers, it refers to the pressure in the systemic arteries, as measured, for example,

in the forearm. [NIH]

Blood transfusion: The administration of blood or blood products into a blood vessel. [NIH]

Blood vessel: A tube in the body through which blood circulates. Blood vessels include a network of arteries, arterioles, capillaries, venules, and veins. [NIH]

Blood-Brain Barrier: Specialized non-fenestrated tightly-joined endothelial cells (tight junctions) that form a transport barrier for certain substances between the cerebral capillaries and the brain tissue. [NIH]

Blot: To transfer DNA, RNA, or proteins to an immobilizing matrix such as nitrocellulose. [NIH]

Body Composition: The relative amounts of various components in the body, such as percent body fat. [NIH]

Body Fluids: Liquid components of living organisms. [NIH]

Bone Marrow: The soft tissue filling the cavities of bones. Bone marrow exists in two types, yellow and red. Yellow marrow is found in the large cavities of large bones and consists mostly of fat cells and a few primitive blood cells. Red marrow is a hematopoietic tissue and is the site of production of erythrocytes and granular leukocytes. Bone marrow is made up of a framework of connective tissue containing branching fibers with the frame being filled with marrow cells. [NIH]

Bowel: The long tube-shaped organ in the abdomen that completes the process of digestion. There is both a small and a large bowel. Also called the intestine. [NIH]

Bowel Movement: Body wastes passed through the rectum and anus. [NIH]

Bradykinin: A nonapeptide messenger that is enzymatically produced from kallidin in the blood where it is a potent but short-lived agent of arteriolar dilation and increased capillary permeability. Bradykinin is also released from mast cells during asthma attacks, from gut walls as a gastrointestinal vasodilator, from damaged tissues as a pain signal, and may be a neurotransmitter. [NIH]

Branch: Most commonly used for branches of nerves, but applied also to other structures. [NIH]

Breakdown: A physical, metal, or nervous collapse. [NIH]

Breathing Exercises: Therapeutic exercises aimed to deepen inspiration or expiration or even to alter the rate and rhythm of respiration. [NIH]

Buccal: Pertaining to or directed toward the cheek. In dental anatomy, used to refer to the buccal surface of a tooth. [EU]

Burns: Injuries to tissues caused by contact with heat, steam, chemicals (burns, chemical), electricity (burns, electric), or the like. [NIH]

Burns, Electric: Burns produced by contact with electric current or from a sudden discharge of electricity. [NIH]

Cachexia: General ill health, malnutrition, and weight loss, usually associated with chronic disease. [NIH]

Calcification: Deposits of calcium in the tissues of the breast. Calcification in the breast can be seen on a mammogram, but cannot be detected by touch. There are two types of breast calcification, macrocalcification and microcalcification. Macrocalcifications are large deposits and are usually not related to cancer. Microcalcifications are specks of calcium that may be found in an area of rapidly dividing cells. Many microcalcifications clustered together may be a sign of cancer. [NIH]

Calcium: A basic element found in nearly all organized tissues. It is a member of the

alkaline earth family of metals with the atomic symbol Ca, atomic number 20, and atomic weight 40. Calcium is the most abundant mineral in the body and combines with phosphorus to form calcium phosphate in the bones and teeth. It is essential for the normal functioning of nerves and muscles and plays a role in blood coagulation (as factor IV) and in many enzymatic processes. [NIH]

Candidiasis: Infection with a fungus of the genus Candida. It is usually a superficial infection of the moist cutaneous areas of the body, and is generally caused by C. albicans; it most commonly involves the skin (dermatocandidiasis), oral mucous membranes (thrush, def. 1), respiratory tract (bronchocandidiasis), and vagina (vaginitis). Rarely there is a systemic infection or endocarditis. Called also moniliasis, candidosis, oidiomycosis, and formerly blastodendriosis. [EU]

Candidosis: An infection caused by an opportunistic yeasts that tends to proliferate and become pathologic when the environment is favorable and the host resistance is weakened. [NIH]

Canonical: A particular nucleotide sequence in which each position represents the base more often found when many actual sequences of a given class of genetic elements are compared. [NIH]

Capsid: The outer protein protective shell of a virus, which protects the viral nucleic acid. [NIH]

Carbohydrate: An aldehyde or ketone derivative of a polyhydric alcohol, particularly of the pentahydric and hexahydric alcohols. They are so named because the hydrogen and oxygen are usually in the proportion to form water, (CH2O)n. The most important carbohydrates are the starches, sugars, celluloses, and gums. They are classified into mono-, di-, tri-, poly- and heterosaccharides. [EU]

Carcinogen: Any substance that causes cancer. [NIH]

Carcinogenic: Producing carcinoma. [EU]

Carcinoid: A type of tumor usually found in the gastrointestinal system (most often in the appendix), and sometimes in the lungs or other sites. Carcinoid tumors are usually benign. [NIH]

Carcinoma: Cancer that begins in the skin or in tissues that line or cover internal organs. [NIH]

Cardiac: Having to do with the heart. [NIH]

Cardiolipins: Acidic phospholipids composed of two molecules of phosphatidic acid covalently linked to a molecule of glycerol. They occur primarily in mitochondrial inner membranes and in bacterial plasma membranes. They are the main antigenic components of the Wassermann-type antigen that is used in nontreponemal syphilis serodiagnosis. [NIH]

Cardiomyopathy: A general diagnostic term designating primary myocardial disease, often of obscure or unknown etiology. [EU]

Cardiorespiratory: Relating to the heart and lungs and their function. [EU]

Cardiovascular: Having to do with the heart and blood vessels. [NIH]

Cardiovascular disease: Any abnormal condition characterized by dysfunction of the heart and blood vessels. CVD includes atherosclerosis (especially coronary heart disease, which can lead to heart attacks), cerebrovascular disease (e.g., stroke), and hypertension (high blood pressure). [NIH]

Carnitine: Constituent of striated muscle and liver. It is used therapeutically to stimulate gastric and pancreatic secretions and in the treatment of hyperlipoproteinemias. [NIH]

Carotene: The general name for a group of pigments found in green, yellow, and leafy

vegetables, and yellow fruits. The pigments are fat-soluble, unsaturated aliphatic hydrocarbons functioning as provitamins and are converted to vitamin A through enzymatic processes in the intestinal wall. [NIH]

Carotenoids: Substance found in yellow and orange fruits and vegetables and in dark green, leafy vegetables. May reduce the risk of developing cancer. [NIH]

Carrier Proteins: Transport proteins that carry specific substances in the blood or across cell membranes. [NIH]

Case report: A detailed report of the diagnosis, treatment, and follow-up of an individual patient. Case reports also contain some demographic information about the patient (for example, age, gender, ethnic origin). [NIH]

Caspase: Enzyme released by the cell at a crucial stage in apoptosis in order to shred all cellular proteins. [NIH]

Castor Oil: Oil obtained from seeds of Ricinus communis that is used as a cathartic and as a plasticizer. [NIH]

Catalyse: To speed up a chemical reaction. [EU]

Catheters: A small, flexible tube that may be inserted into various parts of the body to inject or remove liquids. [NIH]

Cause of Death: Factors which produce cessation of all vital bodily functions. They can be analyzed from an epidemiologic viewpoint. [NIH]

Cell: The individual unit that makes up all of the tissues of the body. All living things are made up of one or more cells. [NIH]

Cell Count: A count of the number of cells of a specific kind, usually measured per unit volume of sample. [NIH]

Cell Death: The termination of the cell's ability to carry out vital functions such as metabolism, growth, reproduction, responsiveness, and adaptability. [NIH]

Cell Differentiation: Progressive restriction of the developmental potential and increasing specialization of function which takes place during the development of the embryo and leads to the formation of specialized cells, tissues, and organs. [NIH]

Cell Division: The fission of a cell. [NIH]

Cell Fusion: Fusion of somatic cells in vitro or in vivo, which results in somatic cell hybridization. [NIH]

Cell membrane: Cell membrane = plasma membrane. The structure enveloping a cell, enclosing the cytoplasm, and forming a selective permeability barrier; it consists of lipids, proteins, and some carbohydrates, the lipids thought to form a bilayer in which integral proteins are embedded to varying degrees. [EU]

Cell proliferation: An increase in the number of cells as a result of cell growth and cell division. [NIH]

Cell Size: The physical dimensions of a cell. It refers mainly to changes in dimensions correlated with physiological or pathological changes in cells. [NIH]

Cell Transplantation: Transference of cells within an individual, between individuals of the same species, or between individuals of different species. [NIH]

Cellulose: A polysaccharide with glucose units linked as in cellobiose. It is the chief constituent of plant fibers, cotton being the purest natural form of the substance. As a raw material, it forms the basis for many derivatives used in chromatography, ion exchange materials, explosives manufacturing, and pharmaceutical preparations. [NIH]

Central Nervous System: The main information-processing organs of the nervous system, consisting of the brain, spinal cord, and meninges. [NIH]

Central Nervous System Infections: Pathogenic infections of the brain, spinal cord, and meninges. DNA virus infections; RNA virus infections; bacterial infections; mycoplasma infections; Spirochaetales infections; fungal infections; protozoan infections; helminthiasis; and prion diseases may involve the central nervous system as a primary or secondary process. [NIH]

Cerebellar: Pertaining to the cerebellum. [EU]

Cerebral: Of or pertaining of the cerebrum or the brain. [EU]

Cerebral Cortex: The thin layer of gray matter on the surface of the cerebral hemisphere that develops from the telencephalon and folds into gyri. It reaches its highest development in man and is responsible for intellectual faculties and higher mental functions. [NIH]

Cerebrospinal: Pertaining to the brain and spinal cord. [EU]

Cerebrospinal fluid: CSF. The fluid flowing around the brain and spinal cord. Cerebrospinal fluid is produced in the ventricles in the brain. [NIH]

Cerebrovascular: Pertaining to the blood vessels of the cerebrum, or brain. [EU]

Cerebrum: The largest part of the brain. It is divided into two hemispheres, or halves, called the cerebral hemispheres. The cerebrum controls muscle functions of the body and also controls speech, emotions, reading, writing, and learning. [NIH]

Cervical: Relating to the neck, or to the neck of any organ or structure. Cervical lymph nodes are located in the neck; cervical cancer refers to cancer of the uterine cervix, which is the lower, narrow end (the "neck") of the uterus. [NIH]

Cervical intraepithelial neoplasia: CIN. A general term for the growth of abnormal cells on the surface of the cervix. Numbers from 1 to 3 may be used to describe how much of the cervix contains abnormal cells. [NIH]

Cervix: The lower, narrow end of the uterus that forms a canal between the uterus and vagina. [NIH]

Character: In current usage, approximately equivalent to personality. The sum of the relatively fixed personality traits and habitual modes of response of an individual. [NIH]

Chemical Warfare: Tactical warfare using incendiary mixtures, smokes, or irritant, burning, or asphyxiating gases. [NIH]

Chemical Warfare Agents: Chemicals that are used to cause the disturbance, disease, or death of humans during war. [NIH]

Chemokines: Class of pro-inflammatory cytokines that have the ability to attract and activate leukocytes. They can be divided into at least three structural branches: C (chemokines, C), CC (chemokines, CC), and CXC (chemokines, CXC), according to variations in a shared cysteine motif. [NIH]

Chemotactic Factors: Chemical substances that attract or repel cells or organisms. The concept denotes especially those factors released as a result of tissue injury, invasion, or immunologic activity, that attract leukocytes, macrophages, or other cells to the site of infection or insult. [NIH]

Chemotherapeutic agent: A drug used to treat cancer. [NIH]

Chemotherapy: Treatment with anticancer drugs. [NIH]

Chest Pain: Pressure, burning, or numbness in the chest. [NIH]

Child Care: Care of children in the home or institution. [NIH]

Child Welfare: Organized efforts by communities or organizations to improve the health and well-being of the child. [NIH]

Chimera: An individual that contains cell populations derived from different zygotes. [NIH]

Chimeric Proteins: Proteins in individuals that are derived from genetically different zygotes. [NIH]

Chin: The anatomical frontal portion of the mandible, also known as the mentum, that contains the line of fusion of the two separate halves of the mandible (symphysis menti). This line of fusion divides inferiorly to enclose a triangular area called the mental protuberance. On each side, inferior to the second premolar tooth, is the mental foramen for the passage of blood vessels and a nerve. [NIH]

Chiropractic: A system of treating bodily disorders by manipulation of the spine and other parts, based on the belief that the cause is the abnormal functioning of a nerve. [NIH]

Cholelithiasis: Presence or formation of gallstones. [NIH]

Cholera: An acute diarrheal disease endemic in India and Southeast Asia whose causative agent is vibrio cholerae. This condition can lead to severe dehydration in a matter of hours unless quickly treated. [NIH]

Cholesterol: The principal sterol of all higher animals, distributed in body tissues, especially the brain and spinal cord, and in animal fats and oils. [NIH]

Chorioretinitis: Inflammation of the choroid in which the sensory retina becomes edematous and opaque. The inflammatory cells and exudate may burst through the sensory retina to cloud the vitreous body. [NIH]

Choroid: The thin, highly vascular membrane covering most of the posterior of the eye between the retina and sclera. [NIH]

Chromatin: The material of chromosomes. It is a complex of DNA, histones, and nonhistone proteins (chromosomal proteins, non-histone) found within the nucleus of a cell. [NIH]

Chromosomal: Pertaining to chromosomes. [EU]

Chromosome: Part of a cell that contains genetic information. Except for sperm and eggs, all human cells contain 46 chromosomes. [NIH]

Chronic: A disease or condition that persists or progresses over a long period of time. [NIH]

Chronic Disease: Disease or ailment of long duration. [NIH]

Chronic leukemia: A slowly progressing cancer of the blood-forming tissues. [NIH]

Chronic renal: Slow and progressive loss of kidney function over several years, often resulting in end-stage renal disease. People with end-stage renal disease need dialysis or transplantation to replace the work of the kidneys. [NIH]

Cirrhosis: A type of chronic, progressive liver disease. [NIH]

CIS: Cancer Information Service. The CIS is the National Cancer Institute's link to the public, interpreting and explaining research findings in a clear and understandable manner, and providing personalized responses to specific questions about cancer. Access the CIS by calling 1-800-4-CANCER, or by using the Web site at http://cis.nci.nih.gov. [NIH]

Civil Rights: Legal guarantee protecting the individual from attack on personal liberties, right to fair trial, right to vote, and freedom from discrimination on the basis of race, religion, national origin, age, or gender. [NIH]

Clathrin: The main structural coat protein of coated vesicles which play a key role in the intracellular transport between membranous organelles. Clathrin also interacts with cytoskeletal proteins. [NIH]

Clear cell carcinoma: A rare type of tumor of the female genital tract in which the inside of the cells looks clear when viewed under a microscope. [NIH]

Clinical Medicine: The study and practice of medicine by direct examination of the patient. [NIH]

Clinical study: A research study in which patients receive treatment in a clinic or other medical facility. Reports of clinical studies can contain results for single patients (case reports) or many patients (case series or clinical trials). [NIH]

Clinical trial: A research study that tests how well new medical treatments or other interventions work in people. Each study is designed to test new methods of screening, prevention, diagnosis, or treatment of a disease. [NIH]

Clone: The term "clone" has acquired a new meaning. It is applied specifically to the bits of inserted foreign DNA in the hybrid molecules of the population. Each inserted segment originally resided in the DNA of a complex genome amid millions of other DNA segment. [NIH]

Cloning: The production of a number of genetically identical individuals; in genetic engineering, a process for the efficient replication of a great number of identical DNA molecules. [NIH]

Coagulation: 1. The process of clot formation. 2. In colloid chemistry, the solidification of a sol into a gelatinous mass; an alteration of a disperse phase or of a dissolved solid which causes the separation of the system into a liquid phase and an insoluble mass called the clot or curd. Coagulation is usually irreversible. 3. In surgery, the disruption of tissue by physical means to form an amorphous residuum, as in electrocoagulation and photocoagulation. [EU]

Coated Vesicles: Vesicles formed when cell-membrane coated pits invaginate and pinch off. The outer surface of these vesicles are covered with a lattice-like network of coat proteins, such as clathrin, coat protein complex proteins, or caveolins. [NIH]

Coca: Any of several South American shrubs of the Erythroxylon genus (and family) that yield cocaine; the leaves are chewed with alum for CNS stimulation. [NIH]

Cocaine: An alkaloid ester extracted from the leaves of plants including coca. It is a local anesthetic and vasoconstrictor and is clinically used for that purpose, particularly in the eye, ear, nose, and throat. It also has powerful central nervous system effects similar to the amphetamines and is a drug of abuse. Cocaine, like amphetamines, acts by multiple mechanisms on brain catecholaminergic neurons; the mechanism of its reinforcing effects is thought to involve inhibition of dopamine uptake. [NIH]

Codons: Any triplet of nucleotides (coding unit) in DNA or RNA (if RNA is the carrier of primary genetic information as in some viruses) that codes for particular amino acid or signals the beginning or end of the message. [NIH]

Cofactor: A substance, microorganism or environmental factor that activates or enhances the action of another entity such as a disease-causing agent. [NIH]

Cognition: Intellectual or mental process whereby an organism becomes aware of or obtains knowledge. [NIH]

Coliphages: Viruses whose host is Escherichia coli. [NIH]

Colitis: Inflammation of the colon. [NIH]

Collagen: A polypeptide substance comprising about one third of the total protein in mammalian organisms. It is the main constituent of skin, connective tissue, and the organic substance of bones and teeth. Different forms of collagen are produced in the body but all consist of three alpha-polypeptide chains arranged in a triple helix. Collagen is

differentiated from other fibrous proteins, such as elastin, by the content of proline, hydroxyproline, and hydroxylysine; by the absence of tryptophan; and particularly by the high content of polar groups which are responsible for its swelling properties. [NIH]

Colloidal: Of the nature of a colloid. [EU]

Colon: The long, coiled, tubelike organ that removes water from digested food. The remaining material, solid waste called stool, moves through the colon to the rectum and leaves the body through the anus. [NIH]

Combination Therapy: Association of 3 drugs to treat AIDS (AZT + DDC or DDI + protease inhibitor). [NIH]

Combinatorial: A cut-and-paste process that churns out thousands of potentially valuable compounds at once. [NIH]

Communicable disease: A disease that can be transmitted by contact between persons. [NIH]

Communis: Common tendon of the rectus group of muscles that surrounds the optic foramen and a portion of the superior orbital fissure, to the anterior margin of which it is attached at the spina recti lateralis. [NIH]

Competency: The capacity of the bacterium to take up DNA from its surroundings. [NIH]

Complement: A term originally used to refer to the heat-labile factor in serum that causes immune cytolysis, the lysis of antibody-coated cells, and now referring to the entire functionally related system comprising at least 20 distinct serum proteins that is the effector not only of immune cytolysis but also of other biologic functions. Complement activation occurs by two different sequences, the classic and alternative pathways. The proteins of the classic pathway are termed 'components of complement' and are designated by the symbols C1 through C9. C1 is a calcium-dependent complex of three distinct proteins C1q, C1r and C1s. The proteins of the alternative pathway (collectively referred to as the properdin system) and complement regulatory proteins are known by semisystematic or trivial names. Fragments resulting from proteolytic cleavage of complement proteins are designated with lower-case letter suffixes, e.g., C3a. Inactivated fragments may be designated with the suffix 'i', e.g. C3bi. Activated components or complexes with biological activity are designated by a bar over the symbol e.g. C1 or C4b,2a. The classic pathway is activated by the binding of C1 to classic pathway activators, primarily antigen-antibody complexes containing IgM, IgG1, IgG3; C1q binds to a single IgM molecule or two adjacent IgG molecules. The alternative pathway can be activated by IgA immune complexes and also by nonimmunologic materials including bacterial endotoxins, microbial polysaccharides, and cell walls. Activation of the classic pathway triggers an enzymatic cascade involving C1, C4, C2 and C3; activation of the alternative pathway triggers a cascade involving C3 and factors B, D and P. Both result in the cleavage of C5 and the formation of the membrane attack complex. Complement activation also results in the formation of many biologically active complement fragments that act as anaphylatoxins, opsonins, or chemotactic factors. [EU]

Complement Activation: The sequential activation of serum components C1 through C9, initiated by an erythrocyte-antibody complex or by microbial polysaccharides and properdin, and producing an inflammatory response. [NIH]

Complementary and alternative medicine: CAM. Forms of treatment that are used in addition to (complementary) or instead of (alternative) standard treatments. These practices are not considered standard medical approaches. CAM includes dietary supplements, megadose vitamins, herbal preparations, special teas, massage therapy, magnet therapy, spiritual healing, and meditation. [NIH]

Complementary medicine: Practices not generally recognized by the medical community as standard or conventional medical approaches and used to enhance or complement the

standard treatments. Complementary medicine includes the taking of dietary supplements, megadose vitamins, and herbal preparations; the drinking of special teas; and practices such as massage therapy, magnet therapy, spiritual healing, and meditation. [NIH]

Compliance: Distensibility measure of a chamber such as the lungs (lung compliance) or bladder. Compliance is expressed as a change in volume per unit change in pressure. [NIH]

Computational Biology: A field of biology concerned with the development of techniques for the collection and manipulation of biological data, and the use of such data to make biological discoveries or predictions. This field encompasses all computational methods and theories applicable to molecular biology and areas of computer-based techniques for solving biological problems including manipulation of models and datasets. [NIH]

Conception: The onset of pregnancy, marked by implantation of the blastocyst; the formation of a viable zygote. [EU]

Condoms: A sheath that is worn over the penis during sexual behavior in order to prevent pregnancy or spread of sexually transmitted disease. [NIH]

Cone: One of the special retinal receptor elements which are presumed to be primarily concerned with perception of light and color stimuli when the eye is adapted to light. [NIH]

Conjugated: Acting or operating as if joined; simultaneous. [EU]

Conjunctiva: The mucous membrane that lines the inner surface of the eyelids and the anterior part of the sclera. [NIH]

Connective Tissue: Tissue that supports and binds other tissues. It consists of connective tissue cells embedded in a large amount of extracellular matrix. [NIH]

Connective Tissue: Tissue that supports and binds other tissues. It consists of connective tissue cells embedded in a large amount of extracellular matrix. [NIH]

Connective Tissue Diseases: A heterogeneous group of disorders, some hereditary, others acquired, characterized by abnormal structure or function of one or more of the elements of connective tissue, i.e., collagen, elastin, or the mucopolysaccharides. [NIH]

Consciousness: Sense of awareness of self and of the environment. [NIH]

Consensus Sequence: A theoretical representative nucleotide or amino acid sequence in which each nucleotide or amino acid is the one which occurs most frequently at that site in the different sequences which occur in nature. The phrase also refers to an actual sequence which approximates the theoretical consensus. A known conserved sequence set is represented by a consensus sequence. Commonly observed supersecondary protein structures (amino acid motifs) are often formed by conserved sequences. [NIH]

Conserved Sequence: A sequence of amino acids in a polypeptide or of nucleotides in DNA or RNA that is similar across multiple species. A known set of conserved sequences is represented by a consensus sequence. Amino acid motifs are often composed of conserved sequences. [NIH]

Constitutional: 1. Affecting the whole constitution of the body; not local. 2. Pertaining to the constitution. [EU]

Constriction: The act of constricting. [NIH]

Consultation: A deliberation between two or more physicians concerning the diagnosis and the proper method of treatment in a case. [NIH]

Consumption: Pulmonary tuberculosis. [NIH]

Contact Tracing: Identification of those persons (or animals) who have had such an association with an infected person, animal, or contaminated environment as to have had the opportunity to acquire the infection. Contact tracing is a generally accepted method for

the control of sexually transmitted diseases. [NIH]

Contamination: The soiling or pollution by inferior material, as by the introduction of organisms into a wound, or sewage into a stream. [EU]

Continuum: An area over which the vegetation or animal population is of constantly changing composition so that homogeneous, separate communities cannot be distinguished. [NIH]

Contraindications: Any factor or sign that it is unwise to pursue a certain kind of action or treatment, e. g. giving a general anesthetic to a person with pneumonia. [NIH]

Controlled clinical trial: A clinical study that includes a comparison (control) group. The comparison group receives a placebo, another treatment, or no treatment at all. [NIH]

Controlled study: An experiment or clinical trial that includes a comparison (control) group. [NIH]

Coordination: Muscular or motor regulation or the harmonious cooperation of muscles or groups of muscles, in a complex action or series of actions. [NIH]

Coreceptors: Invariant receptor of the helper T-cells. [NIH]

Cornea: The transparent part of the eye that covers the iris and the pupil and allows light to enter the inside. [NIH]

Corneum: The superficial layer of the epidermis containing keratinized cells. [NIH]

Coronary: Encircling in the manner of a crown; a term applied to vessels; nerves, ligaments, etc. The term usually denotes the arteries that supply the heart muscle and, by extension, a pathologic involvement of them. [EU]

Coronary Arteriosclerosis: Thickening and loss of elasticity of the coronary arteries. [NIH]

Coronary heart disease: A type of heart disease caused by narrowing of the coronary arteries that feed the heart, which needs a constant supply of oxygen and nutrients carried by the blood in the coronary arteries. When the coronary arteries become narrowed or clogged by fat and cholesterol deposits and cannot supply enough blood to the heart, CHD results. [NIH]

Coronary Thrombosis: Presence of a thrombus in a coronary artery, often causing a myocardial infarction. [NIH]

Corpus: The body of the uterus. [NIH]

Corpus Luteum: The yellow glandular mass formed in the ovary by an ovarian follicle that has ruptured and discharged its ovum. [NIH]

Cortex: The outer layer of an organ or other body structure, as distinguished from the internal substance. [EU]

Cortical: Pertaining to or of the nature of a cortex or bark. [EU]

Corticosteroids: Hormones that have antitumor activity in lymphomas and lymphoid leukemias; in addition, corticosteroids (steroids) may be used for hormone replacement and for the management of some of the complications of cancer and its treatment. [NIH]

Cortisone: A natural steroid hormone produced in the adrenal gland. It can also be made in the laboratory. Cortisone reduces swelling and can suppress immune responses. [NIH]

Coumarin: A fluorescent dye. [NIH]

Cowpox: A mild, eruptive skin disease of milk cows caused by cowpox virus, with lesions occurring principally on the udder and teats. Human infection may occur while milking an infected animal. [NIH]

Cowpox Virus: A species of orthopoxvirus that is the etiologic agent of cowpox. It is closely

related to but antigenically different from vaccina virus. [NIH]

Cranial: Pertaining to the cranium, or to the anterior (in animals) or superior (in humans) end of the body. [EU]

Craniocerebral Trauma: Traumatic injuries involving the cranium and intracranial structures (i.e., brain; cranial nerves; meninges; and other structures). Injuries may be classified by whether or not the skull is penetrated (i.e., penetrating vs. nonpenetrating) or whether there is an associated hemorrhage. [NIH]

Creatine: An amino acid that occurs in vertebrate tissues and in urine. In muscle tissue, creatine generally occurs as phosphocreatine. Creatine is excreted as creatinine in the urine. [NIH]

Creatine Kinase: A transferase that catalyzes formation of phosphocreatine from ATP + creatine. The reaction stores ATP energy as phosphocreatine. Three cytoplasmic isoenzymes have been identified in human tissues: MM from skeletal muscle, MB from myocardial tissue, and BB from nervous tissue as well as a mitochondrial isoenzyme. Macro-creatine kinase refers to creatine kinase complexed with other serum proteins. EC 2.7.3.2. [NIH]

Creatinine: A compound that is excreted from the body in urine. Creatinine levels are measured to monitor kidney function. [NIH]

Crossing-over: The exchange of corresponding segments between chromatids of homologous chromosomes during meiosia, forming a chiasma. [NIH]

Cryptococcosis: Infection with a fungus of the species Cryptococcus neoformans. [NIH]

Cryptosporidiosis: Parasitic intestinal infection with severe diarrhea caused by a protozoan, Cryptosporidium. It occurs in both animals and humans. [NIH]

Cryptosporidium: A genus of coccidian parasites of the family Cryptosporidiidae, found in the intestinal epithelium of many vertebrates including humans. [NIH]

Cultured cells: Animal or human cells that are grown in the laboratory. [NIH]

Curative: Tending to overcome disease and promote recovery. [EU]

Cutaneous: Having to do with the skin. [NIH]

Cyanide: An extremely toxic class of compounds that can be lethal on inhaling of ingesting in minute quantities. [NIH]

Cyclic: Pertaining to or occurring in a cycle or cycles; the term is applied to chemical compounds that contain a ring of atoms in the nucleus. [EU]

Cyclin: Molecule that regulates the cell cycle. [NIH]

Cyst: A sac or capsule filled with fluid. [NIH]

Cystitis: Inflammation of the urinary bladder. [EU]

Cytokine: Small but highly potent protein that modulates the activity of many cell types, including T and B cells. [NIH]

Cytomegalovirus: A genus of the family Herpesviridae, subfamily Betaherpesvirinae, infecting the salivary glands, liver, spleen, lungs, eyes, and other organs, in which they produce characteristically enlarged cells with intranuclear inclusions. Infection with Cytomegalovirus is also seen as an opportunistic infection in AIDS. [NIH]

Cytomegalovirus Infections: Infection with Cytomegalovirus, characterized by enlarged cells bearing intranuclear inclusions. Infection may be in almost any organ, but the salivary glands are the most common site in children, as are the lungs in adults. [NIH]

Cytomegalovirus Retinitis: Infection of the retina by cytomegalovirus characterized by retinal necrosis, hemorrhage, vessel sheathing, and retinal edema. Cytomegalovirus retinitis

is a major opportunistic infection in AIDS patients and can cause blindness. [NIH]

Cytoplasm: The protoplasm of a cell exclusive of that of the nucleus; it consists of a continuous aqueous solution (cytosol) and the organelles and inclusions suspended in it (phaneroplasm), and is the site of most of the chemical activities of the cell. [EU]

Cytosine: A pyrimidine base that is a fundamental unit of nucleic acids. [NIH]

Cytotoxic: Cell-killing. [NIH]

Cytotoxic chemotherapy: Anticancer drugs that kill cells, especially cancer cells. [NIH]

Cytotoxicity: Quality of being capable of producing a specific toxic action upon cells of special organs. [NIH]

Data Collection: Systematic gathering of data for a particular purpose from various sources, including questionnaires, interviews, observation, existing records, and electronic devices. The process is usually preliminary to statistical analysis of the data. [NIH]

De novo: In cancer, the first occurrence of cancer in the body. [NIH]

Deamination: The removal of an amino group (NH2) from a chemical compound. [NIH]

Death Certificates: Official records of individual deaths including the cause of death certified by a physician, and any other required identifying information. [NIH]

Decision Making: The process of making a selective intellectual judgment when presented with several complex alternatives consisting of several variables, and usually defining a course of action or an idea. [NIH]

Decontamination: The removal of contaminating material, such as radioactive materials, biological materials, or chemical warfare agents, from a person or object. [NIH]

Degenerative: Undergoing degeneration : tending to degenerate; having the character of or involving degeneration; causing or tending to cause degeneration. [EU]

Delavirdine: A potent, non-nucleoside reverse transcriptase inhibitor with activity specific for HIV-1. [NIH]

Deletion: A genetic rearrangement through loss of segments of DNA (chromosomes), bringing sequences, which are normally separated, into close proximity. [NIH]

Delirium: (DSM III-R) an acute, reversible organic mental disorder characterized by reduced ability to maintain attention to external stimuli and disorganized thinking as manifested by rambling, irrelevant, or incoherent speech; there are also a reduced level of consciousness, sensory misperceptions, disturbance of the sleep-wakefulness cycle and level of psychomotor activity, disorientation to time, place, or person, and memory impairment. Delirium may be caused by a large number of conditions resulting in derangement of cerebral metabolism, including systemic infection, poisoning, drug intoxication or withdrawal, seizures or head trauma, and metabolic disturbances such as hypoxia, hypoglycaemia, fluid, electrolyte, or acid-base imbalances, or hepatic or renal failure. Called also acute confusional state and acute brain syndrome. [EU]

Delusions: A false belief regarding the self or persons or objects outside the self that persists despite the facts, and is not considered tenable by one's associates. [NIH]

Dementia: An acquired organic mental disorder with loss of intellectual abilities of sufficient severity to interfere with social or occupational functioning. The dysfunction is multifaceted and involves memory, behavior, personality, judgment, attention, spatial relations, language, abstract thought, and other executive functions. The intellectual decline is usually progressive, and initially spares the level of consciousness. [NIH]

Denaturation: Rupture of the hydrogen bonds by heating a DNA solution and then cooling it rapidly causes the two complementary strands to separate. [NIH]

Dendrites: Extensions of the nerve cell body. They are short and branched and receive stimuli from other neurons. [NIH]

Dendritic: 1. Branched like a tree. 2. Pertaining to or possessing dendrites. [EU]

Dendritic cell: A special type of antigen-presenting cell (APC) that activates T lymphocytes. [NIH]

Density: The logarithm to the base 10 of the opacity of an exposed and processed film. [NIH]

Dental Care: The total of dental diagnostic, preventive, and restorative services provided to meet the needs of a patient (from Illustrated Dictionary of Dentistry, 1982). [NIH]

Dentists: Individuals licensed to practice dentistry. [NIH]

Deoxyribonucleic: A polymer of subunits called deoxyribonucleotides which is the primary genetic material of a cell, the material equivalent to genetic information. [NIH]

Deoxyribonucleic acid: A polymer of subunits called deoxyribonucleotides which is the primary genetic material of a cell, the material equivalent to genetic information. [NIH]

Depolarization: The process or act of neutralizing polarity. In neurophysiology, the reversal of the resting potential in excitable cell membranes when stimulated, i.e., the tendency of the cell membrane potential to become positive with respect to the potential outside the cell. [EU]

Dermal: Pertaining to or coming from the skin. [NIH]

Dermatitis: Any inflammation of the skin. [NIH]

DES: Diethylstilbestrol. A synthetic hormone that was prescribed from the early 1940s until 1971 to help women with complications of pregnancy. DES has been linked to an increased risk of clear cell carcinoma of the vagina in daughters of women who used DES. DES may also increase the risk of breast cancer in women who used DES. [NIH]

Deuterium: Deuterium. The stable isotope of hydrogen. It has one neutron and one proton in the nucleus. [NIH]

Developing Countries: Countries in the process of change directed toward economic growth, that is, an increase in production, per capita consumption, and income. The process of economic growth involves better utilization of natural and human resources, which results in a change in the social, political, and economic structures. [NIH]

Dextroamphetamine: The d-form of amphetamine. It is a central nervous system stimulant and a sympathomimetic. It has also been used in the treatment of narcolepsy and of attention deficit disorders and hyperactivity in children. Dextroamphetamine has multiple mechanisms of action including blocking uptake of adrenergics and dopamine, stimulating release of monamines, and inhibiting monoamine oxidase. It is also a drug of abuse and a psychotomimetic. [NIH]

Diabetes Mellitus: A heterogeneous group of disorders that share glucose intolerance in common. [NIH]

Diagnostic procedure: A method used to identify a disease. [NIH]

Diaphragm: The musculofibrous partition that separates the thoracic cavity from the abdominal cavity. Contraction of the diaphragm increases the volume of the thoracic cavity aiding inspiration. [NIH]

Diarrhea: Passage of excessively liquid or excessively frequent stools. [NIH]

Diarrhoea: Abnormal frequency and liquidity of faecal discharges. [EU]

Dietitian: An expert in nutrition who helps people plan what and how much food to eat. [NIH]

Digestion: The process of breakdown of food for metabolism and use by the body. [NIH]

Digestive system: The organs that take in food and turn it into products that the body can use to stay healthy. Waste products the body cannot use leave the body through bowel movements. The digestive system includes the salivary glands, mouth, esophagus, stomach, liver, pancreas, gallbladder, small and large intestines, and rectum. [NIH]

Digestive tract: The organs through which food passes when food is eaten. These organs are the mouth, esophagus, stomach, small and large intestines, and rectum. [NIH]

Dihydrotestosterone: Anabolic agent. [NIH]

Dilatation: The act of dilating. [NIH]

Dilution: A diluted or attenuated medicine; in homeopathy, the diffusion of a given quantity of a medicinal agent in ten or one hundred times the same quantity of water. [NIH]

Dimerization: The process by which two molecules of the same chemical composition form a condensation product or polymer. [NIH]

Diphtheria: A localized infection of mucous membranes or skin caused by toxigenic strains of Corynebacterium diphtheriae. It is characterized by the presence of a pseudomembrane at the site of infection. Diphtheria toxin, produced by C. diphtheriae, can cause myocarditis, polyneuritis, and other systemic toxic effects. [NIH]

Diphtheria Toxin: A 60 kD single chain protein elaborated by Corynebacterium diphtheriae that causes the sign and symptoms of diphtheria; it can be broken into two unequal fragments, the smaller (A fragment) inhibits protein synthesis and is the lethal moiety that needs the larger (B fragment) for entry into cells. [NIH]

Diploid: Having two sets of chromosomes. [NIH]

Direct: 1. Straight; in a straight line. 2. Performed immediately and without the intervention of subsidiary means. [EU]

Discrete: Made up of separate parts or characterized by lesions which do not become blended; not running together; separate. [NIH]

Discrimination: The act of qualitative and/or quantitative differentiation between two or more stimuli. [NIH]

Disease Progression: The worsening of a disease over time. This concept is most often used for chronic and incurable diseases where the stage of the disease is an important determinant of therapy and prognosis. [NIH]

Disease Transmission: The transmission of infectious disease or pathogens. When transmission is within the same species, the mode can be horizontal (disease transmission, horizontal) or vertical (disease transmission, vertical). [NIH]

Disease Transmission, Horizontal: The transmission of infectious disease or pathogens from one individual to another in the same generation. [NIH]

Disease Transmission, Vertical: The transmission of infectious disease or pathogens from one generation to another. It includes transmission in utero or intrapartum by exposure to blood and secretions, and postpartum exposure via breastfeeding. [NIH]

Disinfection: Rendering pathogens harmless through the use of heat, antiseptics, antibacterial agents, etc. [NIH]

Disorientation: The loss of proper bearings, or a state of mental confusion as to time, place, or identity. [EU]

Dissociation: 1. The act of separating or state of being separated. 2. The separation of a molecule into two or more fragments (atoms, molecules, ions, or free radicals) produced by the absorption of light or thermal energy or by solvation. 3. In psychology, a defense mechanism in which a group of mental processes are segregated from the rest of a person's

mental activity in order to avoid emotional distress, as in the dissociative disorders (q.v.), or in which an idea or object is segregated from its emotional significance; in the first sense it is roughly equivalent to splitting, in the second, to isolation. 4. A defect of mental integration in which one or more groups of mental processes become separated off from normal consciousness and, thus separated, function as a unitary whole. [EU]

Distal: Remote; farther from any point of reference; opposed to proximal. In dentistry, used to designate a position on the dental arch farther from the median line of the jaw. [EU]

DNA Topoisomerase: An enzyme catalyzing ATP-independent breakage of single-stranded DNA, followed by passage and rejoining of another single-stranded DNA. This enzyme class brings about the conversion of one topological isomer of DNA into another, e.g., the relaxation of superhelical turns in DNA, the interconversion of simple and knotted rings of single-stranded DNA, and the intertwisting of single-stranded rings of complementary sequences. (From Enzyme Nomenclature, 1992) EC 5.99.1.2. [NIH]

Dopamine: An endogenous catecholamine and prominent neurotransmitter in several systems of the brain. In the synthesis of catecholamines from tyrosine, it is the immediate precursor to norepinephrine and epinephrine. Dopamine is a major transmitter in the extrapyramidal system of the brain, and important in regulating movement. A family of dopaminergic receptor subtypes mediate its action. Dopamine is used pharmacologically for its direct (beta adrenergic agonist) and indirect (adrenergic releasing) sympathomimetic effects including its actions as an inotropic agent and as a renal vasodilator. [NIH]

Dosage schedule: A scheme set up to determine and regulate size, frequency and number of doses. [EU]

Dose-dependent: Refers to the effects of treatment with a drug. If the effects change when the dose of the drug is changed, the effects are said to be dose dependent. [NIH]

Double-blind: Pertaining to a clinical trial or other experiment in which neither the subject nor the person administering treatment knows which treatment any particular subject is receiving. [EU]

Double-blinded: A clinical trial in which neither the medical staff nor the person knows which of several possible therapies the person is receiving. [NIH]

Drug Information Services: Services providing pharmaceutic and therapeutic drug information and consultation. [NIH]

Drug Interactions: The action of a drug that may affect the activity, metabolism, or toxicity of another drug. [NIH]

Drug Resistance: Diminished or failed response of an organism, disease or tissue to the intended effectiveness of a chemical or drug. It should be differentiated from drug tolerance which is the progressive diminution of the susceptibility of a human or animal to the effects of a drug, as a result of continued administration. [NIH]

Drug Tolerance: Progressive diminution of the susceptibility of a human or animal to the effects of a drug, resulting from its continued administration. It should be differentiated from drug resistance wherein an organism, disease, or tissue fails to respond to the intended effectiveness of a chemical or drug. It should also be differentiated from maximum tolerated dose and no-observed-adverse-effect level. [NIH]

Drug Toxicity: Manifestations of the adverse effects of drugs administered therapeutically or in the course of diagnostic techniques. It does not include accidental or intentional poisoning for which specific headings are available. [NIH]

Duct: A tube through which body fluids pass. [NIH]

Dura mater: The outermost, toughest, and most fibrous of the three membranes (meninges)

covering the brain and spinal cord; called also pachymeninx. [EU]

Duty to Warn: The legal, moral, or ethical responsibility of a health professional to warn an intended victim of specific threats of harm or to warn a person of potential risk for acquiring a disease as the result of a relationship to a patient. [NIH]

Dyes: Chemical substances that are used to stain and color other materials. The coloring may or may not be permanent. Dyes can also be used as therapeutic agents and test reagents in medicine and scientific research. [NIH]

Dynorphins: A class of opioid peptides including dynorphin A, dynorphin B, and smaller fragments of these peptides. Dynorphins prefer kappa-opioid receptors (receptors, opioid, kappa) and have been shown to play a role as central nervous system transmitters. [NIH]

Dyslipidemia: Disorders in the lipoprotein metabolism; classified as hypercholesterolemia, hypertriglyceridemia, combined hyperlipidemia, and low levels of high-density lipoprotein (HDL) cholesterol. All of the dyslipidemias can be primary or secondary. Both elevated levels of low-density lipoprotein (LDL) cholesterol and low levels of HDL cholesterol predispose to premature atherosclerosis. [NIH]

Dysplasia: Cells that look abnormal under a microscope but are not cancer. [NIH]

Dystrophy: Any disorder arising from defective or faulty nutrition, especially the muscular dystrophies. [EU]

Echocardiography: Ultrasonic recording of the size, motion, and composition of the heart and surrounding tissues. The standard approach is transthoracic. [NIH]

Ecosystem: A dynamic complex of plant, animal and micro-organism communities and their non-living environment interacting as a functional unit. [NIH]

Edema: Excessive amount of watery fluid accumulated in the intercellular spaces, most commonly present in subcutaneous tissue. [NIH]

Effector: It is often an enzyme that converts an inactive precursor molecule into an active second messenger. [NIH]

Efficacy: The extent to which a specific intervention, procedure, regimen, or service produces a beneficial result under ideal conditions. Ideally, the determination of efficacy is based on the results of a randomized control trial. [NIH]

Effusion: The escape of fluid into a part or tissue, as an exudation or a transudation. [EU]

Ehrlichiosis: A tick-borne disease characterized by fever, headache, myalgias, anorexia, and occasionally rash. In humans the disease is caused by Ehrlichia chaffeensis, in dogs it is caused by E. canis, and in horses, E. equi. [NIH]

Ejaculation: The release of semen through the penis during orgasm. [NIH]

Elective: Subject to the choice or decision of the patient or physician; applied to procedures that are advantageous to the patient but not urgent. [EU]

Electrocoagulation: Electrosurgical procedures used to treat hemorrhage (e.g., bleeding ulcers) and to ablate tumors, mucosal lesions, and refractory arrhythmias. [NIH]

Electrolyte: A substance that dissociates into ions when fused or in solution, and thus becomes capable of conducting electricity; an ionic solute. [EU]

Electromagnetic Fields: Fields representing the joint interplay of electric and magnetic forces. [NIH]

Electrophoresis: An electrochemical process in which macromolecules or colloidal particles with a net electric charge migrate in a solution under the influence of an electric current. [NIH]

Emaciation: Clinical manifestation of excessive leanness usually caused by disease or a lack of nutrition. [NIH]

Embryo: The prenatal stage of mammalian development characterized by rapid morphological changes and the differentiation of basic structures. [NIH]

Emodin: Purgative anthraquinone found in several plants, especially Rhamnus frangula. It was formerly used as a laxative, but is now used mainly as tool in toxicity studies. [NIH]

Encephalitis: Inflammation of the brain due to infection, autoimmune processes, toxins, and other conditions. Viral infections (see encephalitis, viral) are a relatively frequent cause of this condition. [NIH]

Encephalitis, Viral: Inflammation of brain parenchymal tissue as a result of viral infection. Encephalitis may occur as primary or secondary manifestation of Togaviridae infections; Herpesviridae infections; Adenoviridae infections; Flaviviridae infections; Bunyaviridae infections; Picornaviridae infections; Paramyxoviridae infections; Orthomyxoviridae infections; Retroviridae infections; and Arenaviridae infections. [NIH]

Encephalopathy: A disorder of the brain that can be caused by disease, injury, drugs, or chemicals. [NIH]

Endemic: Present or usually prevalent in a population or geographical area at all times; said of a disease or agent. Called also endemial. [EU]

Endocarditis: Exudative and proliferative inflammatory alterations of the endocardium, characterized by the presence of vegetations on the surface of the endocardium or in the endocardium itself, and most commonly involving a heart valve, but sometimes affecting the inner lining of the cardiac chambers or the endocardium elsewhere. It may occur as a primary disorder or as a complication of or in association with another disease. [EU]

Endocardium: The innermost layer of the heart, comprised of endothelial cells. [NIH]

Endocytosis: Cellular uptake of extracellular materials within membrane-limited vacuoles or microvesicles. Endosomes play a central role in endocytosis. [NIH]

Endogenous: Produced inside an organism or cell. The opposite is external (exogenous) production. [NIH]

Endometrium: The layer of tissue that lines the uterus. [NIH]

Endopeptidases: A subclass of peptide hydrolases. They are classified primarily by their catalytic mechanism. Specificity is used only for identification of individual enzymes. They comprise the serine endopeptidases, EC 3.4.21; cysteine endopeptidases, EC 3.4.22; aspartic endopeptidases, EC 3.4.23, metalloendopeptidases, EC 3.4.24; and a group of enzymes yet to be assigned to any of the above sub-classes, EC 3.4.99. EC 3.4.-. [NIH]

Endorphins: One of the three major groups of endogenous opioid peptides. They are large peptides derived from the pro-opiomelanocortin precursor. The known members of this group are alpha-, beta-, and gamma-endorphin. The term endorphin is also sometimes used to refer to all opioid peptides, but the narrower sense is used here; opioid peptides is used for the broader group. [NIH]

Endothelial cell: The main type of cell found in the inside lining of blood vessels, lymph vessels, and the heart. [NIH]

Endotoxemia: A condition characterized by the presence of endotoxins in the blood. If endotoxemia is the result of gram-negative rod-shaped bacteria, shock may occur. [NIH]

Endotoxin: Toxin from cell walls of bacteria. [NIH]

End-stage renal: Total chronic kidney failure. When the kidneys fail, the body retains fluid and harmful wastes build up. A person with ESRD needs treatment to replace the work of

the failed kidneys. [NIH]

Energy balance: Energy is the capacity of a body or a physical system for doing work. Energy balance is the state in which the total energy intake equals total energy needs. [NIH]

Enkephalins: One of the three major families of endogenous opioid peptides. The enkephalins are pentapeptides that are widespread in the central and peripheral nervous systems and in the adrenal medulla. [NIH]

Enteropeptidase: A specialized proteolytic enzyme secreted by intestinal cells. It converts trypsinogen into its active form trypsin by removing the N-terminal peptide. EC 3.4.21.9. [NIH]

Environmental Exposure: The exposure to potentially harmful chemical, physical, or biological agents in the environment or to environmental factors that may include ionizing radiation, pathogenic organisms, or toxic chemicals. [NIH]

Environmental Health: The science of controlling or modifying those conditions, influences, or forces surrounding man which relate to promoting, establishing, and maintaining health. [NIH]

Enzymatic: Phase where enzyme cuts the precursor protein. [NIH]

Enzyme: A protein that speeds up chemical reactions in the body. [NIH]

Enzyme Inhibitors: Compounds or agents that combine with an enzyme in such a manner as to prevent the normal substrate-enzyme combination and the catalytic reaction. [NIH]

Enzyme-Linked Immunosorbent Assay: An immunoassay utilizing an antibody labeled with an enzyme marker such as horseradish peroxidase. While either the enzyme or the antibody is bound to an immunosorbent substrate, they both retain their biologic activity; the change in enzyme activity as a result of the enzyme-antibody-antigen reaction is proportional to the concentration of the antigen and can be measured spectrophotometrically or with the naked eye. Many variations of the method have been developed. [NIH]

Eosinophil: A polymorphonuclear leucocyte with large eosinophilic granules in its cytoplasm, which plays a role in hypersensitivity reactions. [NIH]

Eosinophilia: Abnormal increase in eosinophils in the blood, tissues or organs. [NIH]

Eosinophilic: A condition found primarily in grinding workers caused by a reaction of the pulmonary tissue, in particular the eosinophilic cells, to dust that has entered the lung. [NIH]

Epidemic: Occurring suddenly in numbers clearly in excess of normal expectancy; said especially of infectious diseases but applied also to any disease, injury, or other health-related event occurring in such outbreaks. [EU]

Epidemiological: Relating to, or involving epidemiology. [EU]

Epidermal: Pertaining to or resembling epidermis. Called also epidermic or epidermoid. [EU]

Epidermis: Nonvascular layer of the skin. It is made up, from within outward, of five layers: 1) basal layer (stratum basale epidermidis); 2) spinous layer (stratum spinosum epidermidis); 3) granular layer (stratum granulosum epidermidis); 4) clear layer (stratum lucidum epidermidis); and 5) horny layer (stratum corneum epidermidis). [NIH]

Epidermoid carcinoma: A type of cancer in which the cells are flat and look like fish scales. Also called squamous cell carcinoma. [NIH]

Epithelial: Refers to the cells that line the internal and external surfaces of the body. [NIH]

Epithelial Cells: Cells that line the inner and outer surfaces of the body. [NIH]

Epithelium: One or more layers of epithelial cells, supported by the basal lamina, which covers the inner or outer surfaces of the body. [NIH]

Epitope: A molecule or portion of a molecule capable of binding to the combining site of an antibody. For every given antigenic determinant, the body can construct a variety of antibody-combining sites, some of which fit almost perfectly, and others which barely fit. [NIH]

Equine Infectious Anemia: Viral disease of horses caused by the equine infectious anemia virus (EIAV). It is characterized by intermittent fever, weakness, and anemia. Chronic infection consists of acute episodes with remissions. [NIH]

Erectile: The inability to get or maintain an erection for satisfactory sexual intercourse. Also called impotence. [NIH]

Erythrocyte Volume: Volume of circulating erythrocytes. It is usually measured by radioisotope dilution technique. [NIH]

Erythrocytes: Red blood cells. Mature erythrocytes are non-nucleated, biconcave disks containing hemoglobin whose function is to transport oxygen. [NIH]

Erythromycin: A bacteriostatic antibiotic substance produced by Streptomyces erythreus. Erythromycin A is considered its major active component. In sensitive organisms, it inhibits protein synthesis by binding to 50S ribosomal subunits. This binding process inhibits peptidyl transferase activity and interferes with translocation of amino acids during translation and assembly of proteins. [NIH]

Esophagus: The muscular tube through which food passes from the throat to the stomach. [NIH]

Essential Tremor: A rhythmic, involuntary, purposeless, oscillating movement resulting from the alternate contraction and relaxation of opposing groups of muscles. [NIH]

Estradiol: The most potent mammalian estrogenic hormone. It is produced in the ovary, placenta, testis, and possibly the adrenal cortex. [NIH]

Estrogen: One of the two female sex hormones. [NIH]

Estrone: 3-Hydroxyestra-1,3,5(10)-trien-17-one. A metabolite of estradiol but possessing less biological activity. It is found in the urine of pregnant women and mares, in the human placenta, and in the urine of bulls and stallions. According to the Fourth Annual Report on Carcinogens (NTP 85-002, 1985), estrone may reasonably be anticipated to be a carcinogen (Merck, 11th ed). [NIH]

Excitation: An act of irritation or stimulation or of responding to a stimulus; the addition of energy, as the excitation of a molecule by absorption of photons. [EU]

Exhaustion: The feeling of weariness of mind and body. [NIH]

Exogenous: Developed or originating outside the organism, as exogenous disease. [EU]

Exon: The part of the DNA that encodes the information for the actual amino acid sequence of the protein. In many eucaryotic genes, the coding sequences consist of a series of exons alternating with intron sequences. [NIH]

Expiration: The act of breathing out, or expelling air from the lungs. [EU]

Extracellular: Outside a cell or cells. [EU]

Extraction: The process or act of pulling or drawing out. [EU]

Eye Infections: Infection, moderate to severe, caused by bacteria, fungi, or viruses, which occurs either on the external surface of the eye or intraocularly with probable inflammation, visual impairment, or blindness. [NIH]

Facial: Of or pertaining to the face. [EU]

Facial Nerve: The 7th cranial nerve. The facial nerve has two parts, the larger motor root which may be called the facial nerve proper, and the smaller intermediate or sensory root.

Together they provide efferent innervation to the muscles of facial expression and to the lacrimal and salivary glands, and convey afferent information for taste from the anterior two-thirds of the tongue and for touch from the external ear. [NIH]

Faecal: Pertaining to or of the nature of feces. [EU]

Family Planning: Programs or services designed to assist the family in controlling reproduction by either improving or diminishing fertility. [NIH]

Fat: Total lipids including phospholipids. [NIH]

Fatal Outcome: Death resulting from the presence of a disease in an individual, as shown by a single case report or a limited number of patients. This should be differentiated from death, the physiological cessation of life and from mortality, an epidemiological or statistical concept. [NIH]

Fatty acids: A major component of fats that are used by the body for energy and tissue development. [NIH]

Feces: The excrement discharged from the intestines, consisting of bacteria, cells exfoliated from the intestines, secretions, chiefly of the liver, and a small amount of food residue. [EU]

Femoral: Pertaining to the femur, or to the thigh. [EU]

Femur: The longest and largest bone of the skeleton, it is situated between the hip and the knee. [NIH]

Fermentation: An enzyme-induced chemical change in organic compounds that takes place in the absence of oxygen. The change usually results in the production of ethanol or lactic acid, and the production of energy. [NIH]

Fetus: The developing offspring from 7 to 8 weeks after conception until birth. [NIH]

Fibrinogen: Plasma glycoprotein clotted by thrombin, composed of a dimer of three non-identical pairs of polypeptide chains (alpha, beta, gamma) held together by disulfide bonds. Fibrinogen clotting is a sol-gel change involving complex molecular arrangements: whereas fibrinogen is cleaved by thrombin to form polypeptides A and B, the proteolytic action of other enzymes yields different fibrinogen degradation products. [NIH]

Fibroblasts: Connective tissue cells which secrete an extracellular matrix rich in collagen and other macromolecules. [NIH]

Fibroid: A benign smooth muscle tumor, usually in the uterus or gastrointestinal tract. Also called leiomyoma. [NIH]

Fibrosis: Any pathological condition where fibrous connective tissue invades any organ, usually as a consequence of inflammation or other injury. [NIH]

Filgrastim: A colony-stimulating factor that stimulates the production of neutrophils (a type of white blood cell). It is a cytokine that belongs to the family of drugs called hematopoietic (blood-forming) agents. Also called granulocyte colony-stimulating factor (G-CSF). [NIH]

Flatus: Gas passed through the rectum. [NIH]

Flow Cytometry: Technique using an instrument system for making, processing, and displaying one or more measurements on individual cells obtained from a cell suspension. Cells are usually stained with one or more fluorescent dyes specific to cell components of interest, e.g., DNA, and fluorescence of each cell is measured as it rapidly transverses the excitation beam (laser or mercury arc lamp). Fluorescence provides a quantitative measure of various biochemical and biophysical properties of the cell, as well as a basis for cell sorting. Other measurable optical parameters include light absorption and light scattering, the latter being applicable to the measurement of cell size, shape, density, granularity, and stain uptake. [NIH]

Fluorescence: The property of emitting radiation while being irradiated. The radiation emitted is usually of longer wavelength than that incident or absorbed, e.g., a substance can be irradiated with invisible radiation and emit visible light. X-ray fluorescence is used in diagnosis. [NIH]

Fluorescent Dyes: Dyes that emit light when exposed to light. The wave length of the emitted light is usually longer than that of the incident light. Fluorochromes are substances that cause fluorescence in other substances, i.e., dyes used to mark or label other compounds with fluorescent tags. They are used as markers in biochemistry and immunology. [NIH]

Focus Groups: A method of data collection and a qualitative research tool in which a small group of individuals are brought together and allowed to interact in a discussion of their opinions about topics, issues, or questions. [NIH]

Forearm: The part between the elbow and the wrist. [NIH]

Foscarnet: An antiviral agent used in the treatment of cytomegalovirus retinitis. Foscarnet also shows activity against human herpesviruses and HIV. [NIH]

Fractionation: Dividing the total dose of radiation therapy into several smaller, equal doses delivered over a period of several days. [NIH]

Frameshift: A type of mutation which causes out-of-phase transcription of the base sequence; such mutations arise from the addition or delection of nucleotide(s) in numbers other than 3 or multiples of 3. [NIH]

Fraud: Exploitation through misrepresentation of the facts or concealment of the purposes of the exploiter. [NIH]

Free Radical Scavengers: Substances that influence the course of a chemical reaction by ready combination with free radicals. Among other effects, this combining activity protects pancreatic islets against damage by cytokines and prevents myocardial and pulmonary perfusion injuries. [NIH]

Free Radicals: Highly reactive molecules with an unsatisfied electron valence pair. Free radicals are produced in both normal and pathological processes. They are proven or suspected agents of tissue damage in a wide variety of circumstances including radiation, damage from environment chemicals, and aging. Natural and pharmacological prevention of free radical damage is being actively investigated. [NIH]

Fructose: A type of sugar found in many fruits and vegetables and in honey. Fructose is used to sweeten some diet foods. It is considered a nutritive sweetener because it has calories. [NIH]

Fungi: A kingdom of eukaryotic, heterotrophic organisms that live as saprobes or parasites, including mushrooms, yeasts, smuts, molds, etc. They reproduce either sexually or asexually, and have life cycles that range from simple to complex. Filamentous fungi refer to those that grow as multicelluar colonies (mushrooms and molds). [NIH]

Fungus: A general term used to denote a group of eukaryotic protists, including mushrooms, yeasts, rusts, moulds, smuts, etc., which are characterized by the absence of chlorophyll and by the presence of a rigid cell wall composed of chitin, mannans, and sometimes cellulose. They are usually of simple morphological form or show some reversible cellular specialization, such as the formation of pseudoparenchymatous tissue in the fruiting body of a mushroom. The dimorphic fungi grow, according to environmental conditions, as moulds or yeasts. [EU]

Gallate: Antioxidant present in tea. [NIH]

Gallbladder: The pear-shaped organ that sits below the liver. Bile is concentrated and stored in the gallbladder. [NIH]

Gallstones: The solid masses or stones made of cholesterol or bilirubin that form in the gallbladder or bile ducts. [NIH]

Gamma irradiation: A type of radiation therapy that uses gamma radiation. Gamma radiation is a type of high-energy radiation that is different from x-rays. [NIH]

Gamma-interferon: Interferon produced by T-lymphocytes in response to various mitogens and antigens. Gamma interferon appears to have potent antineoplastic, immunoregulatory and antiviral activity. [NIH]

Ganglia: Clusters of multipolar neurons surrounded by a capsule of loosely organized connective tissue located outside the central nervous system. [NIH]

Ganglion: 1. A knot, or knotlike mass. 2. A general term for a group of nerve cell bodies located outside the central nervous system; occasionally applied to certain nuclear groups within the brain or spinal cord, e.g. basal ganglia. 3. A benign cystic tumour occurring on a aponeurosis or tendon, as in the wrist or dorsum of the foot; it consists of a thin fibrous capsule enclosing a clear mucinous fluid. [EU]

Gangrenous: A circumscribed, deep-seated, suppurative inflammation of the subcutaneous tissue of the eyelid discharging pus from several points. [NIH]

Gas: Air that comes from normal breakdown of food. The gases are passed out of the body through the rectum (flatus) or the mouth (burp). [NIH]

Gastric: Having to do with the stomach. [NIH]

Gastrin: A hormone released after eating. Gastrin causes the stomach to produce more acid. [NIH]

Gastroenteritis: An acute inflammation of the lining of the stomach and intestines, characterized by anorexia, nausea, diarrhoea, abdominal pain, and weakness, which has various causes, including food poisoning due to infection with such organisms as Escherichia coli, Staphylococcus aureus, and Salmonella species; consumption of irritating food or drink; or psychological factors such as anger, stress, and fear. Called also enterogastritis. [EU]

Gastrointestinal: Refers to the stomach and intestines. [NIH]

Gastrointestinal tract: The stomach and intestines. [NIH]

Gelatin: A product formed from skin, white connective tissue, or bone collagen. It is used as a protein food adjuvant, plasma substitute, hemostatic, suspending agent in pharmaceutical preparations, and in the manufacturing of capsules and suppositories. [NIH]

Gene: The functional and physical unit of heredity passed from parent to offspring. Genes are pieces of DNA, and most genes contain the information for making a specific protein. [NIH]

Gene Expression: The phenotypic manifestation of a gene or genes by the processes of gene action. [NIH]

Gene Therapy: The introduction of new genes into cells for the purpose of treating disease by restoring or adding gene expression. Techniques include insertion of retroviral vectors, transfection, homologous recombination, and injection of new genes into the nuclei of single cell embryos. The entire gene therapy process may consist of multiple steps. The new genes may be introduced into proliferating cells in vivo (e.g., bone marrow) or in vitro (e.g., fibroblast cultures) and the modified cells transferred to the site where the gene expression is required. Gene therapy may be particularly useful for treating enzyme deficiency diseases, hemoglobinopathies, and leukemias and may also prove useful in restoring drug sensitivity, particularly for leukemia. [NIH]

Generator: Any system incorporating a fixed parent radionuclide from which is produced a

daughter radionuclide which is to be removed by elution or by any other method and used in a radiopharmaceutical. [NIH]

Genetic Code: The specifications for how information, stored in nucleic acid sequence (base sequence), is translated into protein sequence (amino acid sequence). The start, stop, and order of amino acids of a protein is specified by consecutive triplets of nucleotides called codons (codon). [NIH]

Genetic Engineering: Directed modification of the gene complement of a living organism by such techniques as altering the DNA, substituting genetic material by means of a virus, transplanting whole nuclei, transplanting cell hybrids, etc. [NIH]

Genetic testing: Analyzing DNA to look for a genetic alteration that may indicate an increased risk for developing a specific disease or disorder. [NIH]

Genetics: The biological science that deals with the phenomena and mechanisms of heredity. [NIH]

Genistein: An isoflavonoid derived from soy products. It inhibits protein-tyrosine kinase and topoisomerase-ii (dna topoisomerase (atp-hydrolysing)) activity and is used as an antineoplastic and antitumor agent. Experimentally, it has been shown to induce G2 phase arrest in human and murine cell lines. [NIH]

Genital: Pertaining to the genitalia. [EU]

Genotype: The genetic constitution of the individual; the characterization of the genes. [NIH]

Gestation: The period of development of the young in viviparous animals, from the time of fertilization of the ovum until birth. [EU]

Giant Cells: Multinucleated masses produced by the fusion of many cells; often associated with viral infections. In AIDS, they are induced when the envelope glycoprotein of the HIV virus binds to the CD4 antigen of uninfected neighboring T4 cells. The resulting syncytium leads to cell death and thus may account for the cytopathic effect of the virus. [NIH]

Gingivitis: Inflammation of the gingivae. Gingivitis associated with bony changes is referred to as periodontitis. Called also oulitis and ulitis. [EU]

Ginseng: An araliaceous genus of plants that contains a number of pharmacologically active agents used as stimulants, sedatives, and tonics, especially in traditional medicine. [NIH]

Gland: An organ that produces and releases one or more substances for use in the body. Some glands produce fluids that affect tissues or organs. Others produce hormones or participate in blood production. [NIH]

Glomerular: Pertaining to or of the nature of a glomerulus, especially a renal glomerulus. [EU]

Glomerulus: A tiny set of looping blood vessels in the nephron where blood is filtered in the kidney. [NIH]

Glucocorticoid: A compound that belongs to the family of compounds called corticosteroids (steroids). Glucocorticoids affect metabolism and have anti-inflammatory and immunosuppressive effects. They may be naturally produced (hormones) or synthetic (drugs). [NIH]

Glucose: D-Glucose. A primary source of energy for living organisms. It is naturally occurring and is found in fruits and other parts of plants in its free state. It is used therapeutically in fluid and nutrient replacement. [NIH]

Glucose Intolerance: A pathological state in which the fasting plasma glucose level is less than 140 mg per deciliter and the 30-, 60-, or 90-minute plasma glucose concentration following a glucose tolerance test exceeds 200 mg per deciliter. This condition is seen

frequently in diabetes mellitus but also occurs with other diseases. [NIH]

Glucuronic Acid: Derivatives of uronic acid found throughout the plant and animal kingdoms. They detoxify drugs and toxins by conjugating with them to form glucuronides in the liver which are more water-soluble metabolites that can be easily eliminated from the body. [NIH]

Glutamic Acid: A non-essential amino acid naturally occurring in the L-form. Glutamic acid (glutamate) is the most common excitatory neurotransmitter in the central nervous system. [NIH]

Glutathione Peroxidase: An enzyme catalyzing the oxidation of 2 moles of glutathione in the presence of hydrogen peroxide to yield oxidized glutathione and water. EC 1.11.1.9. [NIH]

Glycine: A non-essential amino acid. It is found primarily in gelatin and silk fibroin and used therapeutically as a nutrient. It is also a fast inhibitory neurotransmitter. [NIH]

Glycoprotein: A protein that has sugar molecules attached to it. [NIH]

Glycosaminoglycans: Heteropolysaccharides which contain an N-acetylated hexosamine in a characteristic repeating disaccharide unit. The repeating structure of each disaccharide involves alternate 1,4- and 1,3-linkages consisting of either N-acetylglucosamine or N-acetylgalactosamine. [NIH]

Glycoside: Any compound that contains a carbohydrate molecule (sugar), particularly any such natural product in plants, convertible, by hydrolytic cleavage, into sugar and a nonsugar component (aglycone), and named specifically for the sugar contained, as glucoside (glucose), pentoside (pentose), fructoside (fructose) etc. [EU]

Glycosidic: Formed by elimination of water between the anomeric hydroxyl of one sugar and a hydroxyl of another sugar molecule. [NIH]

Glycosylation: The chemical or biochemical addition of carbohydrate or glycosyl groups to other chemicals, especially peptides or proteins. Glycosyl transferases are used in this biochemical reaction. [NIH]

Gonadal: Pertaining to a gonad. [EU]

Gonorrhea: Acute infectious disease characterized by primary invasion of the urogenital tract. The etiologic agent, Neisseria gonorrhoeae, was isolated by Neisser in 1879. [NIH]

Governing Board: The group in which legal authority is vested for the control of health-related institutions and organizations. [NIH]

Government Agencies: Administrative units of government responsible for policy making and management of governmental activities in the U.S. and abroad. [NIH]

Gp120: 120-kD HIV envelope glycoprotein which is involved in the binding of the virus to its membrane receptor, the CD4 molecule, found on the surface of certain cells in the body. [NIH]

GP41: 41-kD HIV transmembrane envelope glycoprotein which mediates the fusion of the viral membrane with the membrane of the target cell. [NIH]

Grade: The grade of a tumor depends on how abnormal the cancer cells look under a microscope and how quickly the tumor is likely to grow and spread. Grading systems are different for each type of cancer. [NIH]

Graft: Healthy skin, bone, or other tissue taken from one part of the body and used to replace diseased or injured tissue removed from another part of the body. [NIH]

Graft Rejection: An immune response with both cellular and humoral components, directed against an allogeneic transplant, whose tissue antigens are not compatible with those of the

recipient. [NIH]

Grafting: The operation of transfer of tissue from one site to another. [NIH]

Gram-negative: Losing the stain or decolorized by alcohol in Gram's method of staining, a primary characteristic of bacteria having a cell wall composed of a thin layer of peptidoglycan covered by an outer membrane of lipoprotein and lipopolysaccharide. [EU]

Gram-positive: Retaining the stain or resisting decolorization by alcohol in Gram's method of staining, a primary characteristic of bacteria whose cell wall is composed of a thick layer of peptidologlycan with attached teichoic acids. [EU]

Granule: A small pill made from sucrose. [EU]

Granulocyte: A type of white blood cell that fights bacterial infection. Neutrophils, eosinophils, and basophils are granulocytes. [NIH]

Granuloma: A relatively small nodular inflammatory lesion containing grouped mononuclear phagocytes, caused by infectious and noninfectious agents. [NIH]

Growth: The progressive development of a living being or part of an organism from its earliest stage to maturity. [NIH]

Growth factors: Substances made by the body that function to regulate cell division and cell survival. Some growth factors are also produced in the laboratory and used in biological therapy. [NIH]

Guanine: One of the four DNA bases. [NIH]

Habitat: An area considered in terms of its environment, particularly as this determines the type and quality of the vegetation the area can carry. [NIH]

Haemorrhage: The escape of blood from the vessels; bleeding. Small haemorrhages are classified according to size as petechiae (very small), purpura (up to 1 cm), and ecchymoses (larger). The massive accumulation of blood within a tissue is called a haematoma. [EU]

Hairy cell leukemia: A type of chronic leukemia in which the abnormal white blood cells appear to be covered with tiny hairs when viewed under a microscope. [NIH]

Half-Life: The time it takes for a substance (drug, radioactive nuclide, or other) to lose half of its pharmacologic, physiologic, or radiologic activity. [NIH]

Handicap: A handicap occurs as a result of disability, but disability does not always constitute a handicap. A handicap may be said to exist when a disability causes a substantial and continuing reduction in a person's capacity to function socially and vocationally. [NIH]

Handwashing: The act of cleansing the hands with water or other liquid, with or without the inclusion of soap or other detergent, for the purpose of removing soil or microorganisms. [NIH]

Haploid: An organism with one basic chromosome set, symbolized by n; the normal condition of gametes in diploids. [NIH]

Haplotypes: The genetic constitution of individuals with respect to one member of a pair of allelic genes, or sets of genes that are closely linked and tend to be inherited together such as those of the major histocompatibility complex. [NIH]

Haptens: Small antigenic determinants capable of eliciting an immune response only when coupled to a carrier. Haptens bind to antibodies but by themselves cannot elicit an antibody response. [NIH]

Headache: Pain in the cranial region that may occur as an isolated and benign symptom or as a manifestation of a wide variety of conditions including subarachnoid hemorrhage; craniocerebral trauma; central nervous system infections; intracranial hypertension; and other disorders. In general, recurrent headaches that are not associated with a primary

disease process are referred to as headache disorders (e.g., migraine). [NIH]

Headache Disorders: Common conditions characterized by persistent or recurrent headaches. Headache syndrome classification systems may be based on etiology (e.g., vascular headache, post-traumatic headaches, etc.), temporal pattern (e.g., cluster headache, paroxysmal hemicrania, etc.), and precipitating factors (e.g., cough headache). [NIH]

Health Education: Education that increases the awareness and favorably influences the attitudes and knowledge relating to the improvement of health on a personal or community basis. [NIH]

Health Policy: Decisions, usually developed by government policymakers, for determining present and future objectives pertaining to the health care system. [NIH]

Health Promotion: Encouraging consumer behaviors most likely to optimize health potentials (physical and psychosocial) through health information, preventive programs, and access to medical care. [NIH]

Health Resources: Available manpower, facilities, revenue, equipment, and supplies to produce requisite health care and services. [NIH]

Health Services: Services for the diagnosis and treatment of disease and the maintenance of health. [NIH]

Heart attack: A seizure of weak or abnormal functioning of the heart. [NIH]

Helminths: Commonly known as parasitic worms, this group includes the acanthocephala, nematoda, and platyhelminths. Some authors consider certain species of leeches that can become temporarily parasitic as helminths. [NIH]

Hematopoietic Stem Cells: Progenitor cells from which all blood cells derive. [NIH]

Heme: The color-furnishing portion of hemoglobin. It is found free in tissues and as the prosthetic group in many hemeproteins. [NIH]

Hemoglobin: One of the fractions of glycosylated hemoglobin A1c. Glycosylated hemoglobin is formed when linkages of glucose and related monosaccharides bind to hemoglobin A and its concentration represents the average blood glucose level over the previous several weeks. HbA1c levels are used as a measure of long-term control of plasma glucose (normal, 4 to 6 percent). In controlled diabetes mellitus, the concentration of glycosylated hemoglobin A is within the normal range, but in uncontrolled cases the level may be 3 to 4 times the normal conentration. Generally, complications are substantially lower among patients with Hb levels of 7 percent or less than in patients with HbA1c levels of 9 percent or more. [NIH]

Hemoglobin A: Normal adult human hemoglobin. The globin moiety consists of two alpha and two beta chains. [NIH]

Hemoglobinopathies: A group of inherited disorders characterized by structural alterations within the hemoglobin molecule. [NIH]

Hemoglobinuria: The presence of free hemoglobin in the urine. [NIH]

Hemolytic: A disease that affects the blood and blood vessels. It destroys red blood cells, cells that cause the blood to clot, and the lining of blood vessels. HUS is often caused by the Escherichia coli bacterium in contaminated food. People with HUS may develop acute renal failure. [NIH]

Hemolytic-Uremic Syndrome: Syndrome of hemolytic anemia, thrombocytopenia, and acute renal failure, with pathological finding of thrombotic microangiopathy in kidney and renal cortical necrosis. [NIH]

Hemophilia: Refers to a group of hereditary disorders in which affected individuals fail to

make enough of certain proteins needed to form blood clots. [NIH]

Hemorrhage: Bleeding or escape of blood from a vessel. [NIH]

Heparin: Heparinic acid. A highly acidic mucopolysaccharide formed of equal parts of sulfated D-glucosamine and D-glucuronic acid with sulfaminic bridges. The molecular weight ranges from six to twenty thousand. Heparin occurs in and is obtained from liver, lung, mast cells, etc., of vertebrates. Its function is unknown, but it is used to prevent blood clotting in vivo and vitro, in the form of many different salts. [NIH]

Hepatic: Refers to the liver. [NIH]

Hepatitis: Inflammation of the liver and liver disease involving degenerative or necrotic alterations of hepatocytes. [NIH]

Hepatitis A: Hepatitis caused by hepatovirus. It can be transmitted through fecal contamination of food or water. [NIH]

Hepatitis B: Hepatitis caused by hepatitis B virus. It may be transmitted by transfusion of contaminated blood or blood products. [NIH]

Hepatitis C: A form of hepatitis, similar to type B post-transfusion hepatitis, but caused by a virus which is serologically distinct from the agents of hepatitis A, B, and E, and which may persist in the blood of chronic asymptomatic carriers. Hepatitis C is parenterally transmitted and associated with transfusions and drug abuse. [NIH]

Hepatitis, Chronic: A collective term for a clinical and pathological syndrome which has several causes and is characterized by varying degrees of hepatocellular necrosis and inflammation. Specific forms of chronic hepatitis include autoimmune hepatitis, chronic hepatitis B, chronic hepatitis C, chronic hepatitis D, indeterminate chronic viral hepatitis, cryptogenic chronic hepatitis, and drug-related chronic hepatitis. [NIH]

Hepatocellular: Pertaining to or affecting liver cells. [EU]

Hepatocellular carcinoma: A type of adenocarcinoma, the most common type of liver tumor. [NIH]

Hepatocytes: The main structural component of the liver. They are specialized epithelial cells that are organized into interconnected plates called lobules. [NIH]

Hepatotoxicity: How much damage a medicine or other substance does to the liver. [NIH]

Hepatovirus: A genus of Picornaviridae causing infectious hepatitis naturally in humans and experimentally in other primates. It is transmitted through fecal contamination of food or water. [NIH]

Hereditary: Of, relating to, or denoting factors that can be transmitted genetically from one generation to another. [NIH]

Heredity: 1. The genetic transmission of a particular quality or trait from parent to offspring. 2. The genetic constitution of an individual. [EU]

Herpes: Any inflammatory skin disease caused by a herpesvirus and characterized by the formation of clusters of small vesicles. When used alone, the term may refer to herpes simplex or to herpes zoster. [EU]

Herpes virus: A member of the herpes family of viruses. [NIH]

Herpes Zoster: Acute vesicular inflammation. [NIH]

Heterogeneity: The property of one or more samples or populations which implies that they are not identical in respect of some or all of their parameters, e. g. heterogeneity of variance. [NIH]

Heterotrophic: Pertaining to organisms that are consumers and dependent on other

organisms for their source of energy (food). [NIH]

Histocompatibility: The degree of antigenic similarity between the tissues of different individuals, which determines the acceptance or rejection of allografts. [NIH]

Histology: The study of tissues and cells under a microscope. [NIH]

Histone Deacetylase: Hydrolyzes N-acetyl groups on histones. [NIH]

HIV: Human immunodeficiency virus. Species of lentivirus, subgenus primate lentiviruses, formerly designated T-cell lymphotropic virus type III/lymphadenopathy-associated virus (HTLV-III/LAV). It is acknowledged to be the agent responsible for the acute infectious manifestations, neurologic disorders, and immunologic abnormalities linked to the acquired immunodeficiency syndrome. [NIH]

HIV-1: The type species of Lentivirus and widely recognized as the etiologic agent of acquired immunodeficiency syndrome (AIDS). It is characterized by its cytopathic effect and affinity for the T4-lymphocyte. [NIH]

HIV-2: An HIV species related to HIV-1 but carrying different antigenic components and with differing nucleic acid composition. It shares serologic reactivity and sequence homology with the simian Lentivirus SIV and infects only T4-lymphocytes expressing the CD4 phenotypic marker. [NIH]

Homeless Persons: Persons who have no permanent residence. The concept excludes nomadic peoples. [NIH]

Homicide: The killing of one person by another. [NIH]

Homogeneous: Consisting of or composed of similar elements or ingredients; of a uniform quality throughout. [EU]

Homologous: Corresponding in structure, position, origin, etc., as (a) the feathers of a bird and the scales of a fish, (b) antigen and its specific antibody, (c) allelic chromosomes. [EU]

Homosexuality: Sexual attraction or relationship between members of the same sex. [NIH]

Hormonal: Pertaining to or of the nature of a hormone. [EU]

Hormone: A substance in the body that regulates certain organs. Hormones such as gastrin help in breaking down food. Some hormones come from cells in the stomach and small intestine. [NIH]

Hormone therapy: Treatment of cancer by removing, blocking, or adding hormones. Also called endocrine therapy. [NIH]

Horny layer: The superficial layer of the epidermis containing keratinized cells. [NIH]

Horseradish Peroxidase: An enzyme isolated from horseradish which is able to act as an antigen. It is frequently used as a histochemical tracer for light and electron microscopy. Its antigenicity has permitted its use as a combined antigen and marker in experimental immunology. [NIH]

Hospice: Institution dedicated to caring for the terminally ill. [NIH]

Host: Any animal that receives a transplanted graft. [NIH]

Housekeeping: The care and management of property. [NIH]

Human growth hormone: A protein hormone, secreted by the anterior lobe of the pituitary, which promotes growth of the whole body by stimulating protein synthesis. The human gene has already been cloned and successfully expressed in bacteria. [NIH]

Human papillomavirus: HPV. A virus that causes abnormal tissue growth (warts) and is often associated with some types of cancer. [NIH]

Humoral: Of, relating to, proceeding from, or involving a bodily humour - now often used

of endocrine factors as opposed to neural or somatic. [EU]

Humour: 1. A normal functioning fluid or semifluid of the body (as the blood, lymph or bile) especially of vertebrates. 2. A secretion that is itself an excitant of activity (as certain hormones). [EU]

Hybrid: Cross fertilization between two varieties or, more usually, two species of vines, see also crossing. [NIH]

Hybridization: The genetic process of crossbreeding to produce a hybrid. Hybrid nucleic acids can be formed by nucleic acid hybridization of DNA and RNA molecules. Protein hybridization allows for hybrid proteins to be formed from polypeptide chains. [NIH]

Hybridoma: A hybrid cell resulting from the fusion of a specific antibody-producing spleen cell with a myeloma cell. [NIH]

Hydrogen: The first chemical element in the periodic table. It has the atomic symbol H, atomic number 1, and atomic weight 1. It exists, under normal conditions, as a colorless, odorless, tasteless, diatomic gas. Hydrogen ions are protons. Besides the common H1 isotope, hydrogen exists as the stable isotope deuterium and the unstable, radioactive isotope tritium. [NIH]

Hydrogen Bonding: A low-energy attractive force between hydrogen and another element. It plays a major role in determining the properties of water, proteins, and other compounds. [NIH]

Hydrolysis: The process of cleaving a chemical compound by the addition of a molecule of water. [NIH]

Hydrophobic: Not readily absorbing water, or being adversely affected by water, as a hydrophobic colloid. [EU]

Hydroxyproline: A hydroxylated form of the imino acid proline. A deficiency in ascorbic acid can result in impaired hydroxyproline formation. [NIH]

Hydroxyurea: An antineoplastic agent that inhibits DNA synthesis through the inhibition of ribonucleoside diphosphate reductase. [NIH]

Hyperbaric: Characterized by greater than normal pressure or weight; applied to gases under greater than atmospheric pressure, as hyperbaric oxygen, or to a solution of greater specific gravity than another taken as a standard of reference. [EU]

Hyperbaric oxygen: Oxygen that is at an atmospheric pressure higher than the pressure at sea level. Breathing hyperbaric oxygen to enhance the effectiveness of radiation therapy is being studied. [NIH]

Hypercalcemia: Abnormally high level of calcium in the blood. [NIH]

Hypercholesterolemia: Abnormally high levels of cholesterol in the blood. [NIH]

Hyperlipidemia: An excess of lipids in the blood. [NIH]

Hyperplasia: An increase in the number of cells in a tissue or organ, not due to tumor formation. It differs from hypertrophy, which is an increase in bulk without an increase in the number of cells. [NIH]

Hypersensitivity: Altered reactivity to an antigen, which can result in pathologic reactions upon subsequent exposure to that particular antigen. [NIH]

Hypersensitivity, Immediate: Hypersensitivity reactions which occur within minutes of exposure to challenging antigen due to the release of histamine which follows the antigen-antibody reaction and causes smooth muscle contraction and increased vascular permeability. [NIH]

Hypertension: Persistently high arterial blood pressure. Currently accepted threshold levels

are 140 mm Hg systolic and 90 mm Hg diastolic pressure. [NIH]

Hyperthermia: A type of treatment in which body tissue is exposed to high temperatures to damage and kill cancer cells or to make cancer cells more sensitive to the effects of radiation and certain anticancer drugs. [NIH]

Hypertriglyceridemia: Condition of elevated triglyceride concentration in the blood; an inherited form occurs in familial hyperlipoproteinemia IIb and hyperlipoproteinemia type IV. It has been linked to higher risk of heart disease and arteriosclerosis. [NIH]

Hypertrophy: General increase in bulk of a part or organ, not due to tumor formation, nor to an increase in the number of cells. [NIH]

Hypoglycaemia: An abnormally diminished concentration of glucose in the blood, which may lead to tremulousness, cold sweat, piloerection, hypothermia, and headache, accompanied by irritability, confusion, hallucinations, bizarre behaviour, and ultimately, convulsions and coma. [EU]

Hypothyroidism: Deficiency of thyroid activity. In adults, it is most common in women and is characterized by decrease in basal metabolic rate, tiredness and lethargy, sensitivity to cold, and menstrual disturbances. If untreated, it progresses to full-blown myxoedema. In infants, severe hypothyroidism leads to cretinism. In juveniles, the manifestations are intermediate, with less severe mental and developmental retardation and only mild symptoms of the adult form. When due to pituitary deficiency of thyrotropin secretion it is called secondary hypothyroidism. [EU]

Hypoxia: Reduction of oxygen supply to tissue below physiological levels despite adequate perfusion of the tissue by blood. [EU]

Id: The part of the personality structure which harbors the unconscious instinctive desires and strivings of the individual. [NIH]

Idiopathic: Describes a disease of unknown cause. [NIH]

Imidazole: C3H4N2. The ring is present in polybenzimidazoles. [NIH]

Immune function: Production and action of cells that fight disease or infection. [NIH]

Immune response: The activity of the immune system against foreign substances (antigens). [NIH]

Immune Sera: Serum that contains antibodies. It is obtained from an animal that has been immunized either by antigen injection or infection with microorganisms containing the antigen. [NIH]

Immune system: The organs, cells, and molecules responsible for the recognition and disposal of foreign ("non-self") material which enters the body. [NIH]

Immunity: Nonsusceptibility to the invasive or pathogenic effects of foreign microorganisms or to the toxic effect of antigenic substances. [NIH]

Immunization: Deliberate stimulation of the host's immune response. Active immunization involves administration of antigens or immunologic adjuvants. Passive immunization involves administration of immune sera or lymphocytes or their extracts (e.g., transfer factor, immune RNA) or transplantation of immunocompetent cell producing tissue (thymus or bone marrow). [NIH]

Immunoassay: Immunochemical assay or detection of a substance by serologic or immunologic methods. Usually the substance being studied serves as antigen both in antibody production and in measurement of antibody by the test substance. [NIH]

Immunodeficiency: The decreased ability of the body to fight infection and disease. [NIH]

Immunodeficiency syndrome: The inability of the body to produce an immune response.

[NIH]

Immunofluorescence: A technique for identifying molecules present on the surfaces of cells or in tissues using a highly fluorescent substance coupled to a specific antibody. [NIH]

Immunogen: A substance that is capable of causing antibody formation. [NIH]

Immunogenic: Producing immunity; evoking an immune response. [EU]

Immunoglobulin: A protein that acts as an antibody. [NIH]

Immunologic: The ability of the antibody-forming system to recall a previous experience with an antigen and to respond to a second exposure with the prompt production of large amounts of antibody. [NIH]

Immunologic Factors: Biologically active substances whose activities affect or play a role in the functioning of the immune system. [NIH]

Immunology: The study of the body's immune system. [NIH]

Immunomodulator: New type of drugs mainly using biotechnological methods. Treatment of cancer. [NIH]

Immunosuppressive: Describes the ability to lower immune system responses. [NIH]

Immunosuppressive therapy: Therapy used to decrease the body's immune response, such as drugs given to prevent transplant rejection. [NIH]

Immunotherapy: Manipulation of the host's immune system in treatment of disease. It includes both active and passive immunization as well as immunosuppressive therapy to prevent graft rejection. [NIH]

Immunotoxin: An antibody linked to a toxic substance. Some immmunotoxins can bind to cancer cells and kill them. [NIH]

Impairment: In the context of health experience, an impairment is any loss or abnormality of psychological, physiological, or anatomical structure or function. [NIH]

In situ: In the natural or normal place; confined to the site of origin without invasion of neighbouring tissues. [EU]

In vitro: In the laboratory (outside the body). The opposite of in vivo (in the body). [NIH]

In vivo: In the body. The opposite of in vitro (outside the body or in the laboratory). [NIH]

Incision: A cut made in the body during surgery. [NIH]

Incubation: The development of an infectious disease from the entrance of the pathogen to the appearance of clinical symptoms. [EU]

Incubation period: The period of time likely to elapse between exposure to the agent of the disease and the onset of clinical symptoms. [NIH]

Indicative: That indicates; that points out more or less exactly; that reveals fairly clearly. [EU]

Indinavir: A potent and specific HIV protease inhibitor that appears to have good oral bioavailability. [NIH]

Indolent: A type of cancer that grows slowly. [NIH]

Induction: The act or process of inducing or causing to occur, especially the production of a specific morphogenetic effect in the developing embryo through the influence of evocators or organizers, or the production of anaesthesia or unconsciousness by use of appropriate agents. [EU]

Induction therapy: Treatment designed to be used as a first step toward shrinking the cancer and in evaluating response to drugs and other agents. Induction therapy is followed by additional therapy to eliminate whatever cancer remains. [NIH]

Infarction: A pathological process consisting of a sudden insufficient blood supply to an area, which results in necrosis of that area. It is usually caused by a thrombus, an embolus, or a vascular torsion. [NIH]

Infection: 1. Invasion and multiplication of microorganisms in body tissues, which may be clinically unapparent or result in local cellular injury due to competitive metabolism, toxins, intracellular replication, or antigen-antibody response. The infection may remain localized, subclinical, and temporary if the body's defensive mechanisms are effective. A local infection may persist and spread by extension to become an acute, subacute, or chronic clinical infection or disease state. A local infection may also become systemic when the microorganisms gain access to the lymphatic or vascular system. 2. An infectious disease. [EU]

Infection Control: Programs of disease surveillance, generally within health care facilities, designed to investigate, prevent, and control the spread of infections and their causative microorganisms. [NIH]

Infertility: The diminished or absent ability to conceive or produce an offspring while sterility is the complete inability to conceive or produce an offspring. [NIH]

Infestation: Parasitic attack or subsistence on the skin and/or its appendages, as by insects, mites, or ticks; sometimes used to denote parasitic invasion of the organs and tissues, as by helminths. [NIH]

Infiltration: The diffusion or accumulation in a tissue or cells of substances not normal to it or in amounts of the normal. Also, the material so accumulated. [EU]

Inflammation: A pathological process characterized by injury or destruction of tissues caused by a variety of cytologic and chemical reactions. It is usually manifested by typical signs of pain, heat, redness, swelling, and loss of function. [NIH]

Influenza: An acute viral infection involving the respiratory tract. It is marked by inflammation of the nasal mucosa, the pharynx, and conjunctiva, and by headache and severe, often generalized, myalgia. [NIH]

Informed Consent: Voluntary authorization, given to the physician by the patient, with full comprehension of the risks involved, for diagnostic or investigative procedures and medical and surgical treatment. [NIH]

Infusion: A method of putting fluids, including drugs, into the bloodstream. Also called intravenous infusion. [NIH]

Initiation: Mutation induced by a chemical reactive substance causing cell changes; being a step in a carcinogenic process. [NIH]

Inlay: In dentistry, a filling first made to correspond with the form of a dental cavity and then cemented into the cavity. [NIH]

Inoculum: The spores or tissues of a pathogen that serve to initiate disease in a plant. [NIH]

Insight: The capacity to understand one's own motives, to be aware of one's own psychodynamics, to appreciate the meaning of symbolic behavior. [NIH]

Insulator: Material covering the metal conductor of the lead. It is usually polyurethane or silicone. [NIH]

Insulin: A protein hormone secreted by beta cells of the pancreas. Insulin plays a major role in the regulation of glucose metabolism, generally promoting the cellular utilization of glucose. It is also an important regulator of protein and lipid metabolism. Insulin is used as a drug to control insulin-dependent diabetes mellitus. [NIH]

Insulin-dependent diabetes mellitus: A disease characterized by high levels of blood glucose resulting from defects in insulin secretion, insulin action, or both. Autoimmune,

genetic, and environmental factors are involved in the development of type I diabetes. [NIH]

Insulin-like: Muscular growth factor. [NIH]

Integrase: An enzyme that inserts DNA into the host genome. It is encoded by the pol gene of retroviruses and also by temperate bacteriophages, the best known being bacteriophage lambda. EC 2.7.7.-. [NIH]

Integrase Inhibitors: Compounds which inhibit or antagonize biosynthesis or actions of integrase. [NIH]

Intensive Care: Advanced and highly specialized care provided to medical or surgical patients whose conditions are life-threatening and require comprehensive care and constant monitoring. It is usually administered in specially equipped units of a health care facility. [NIH]

Interferon: A biological response modifier (a substance that can improve the body's natural response to disease). Interferons interfere with the division of cancer cells and can slow tumor growth. There are several types of interferons, including interferon-alpha, -beta, and -gamma. These substances are normally produced by the body. They are also made in the laboratory for use in treating cancer and other diseases. [NIH]

Interferon-alpha: One of the type I interferons produced by peripheral blood leukocytes or lymphoblastoid cells when exposed to live or inactivated virus, double-stranded RNA, or bacterial products. It is the major interferon produced by virus-induced leukocyte cultures and, in addition to its pronounced antiviral activity, it causes activation of NK cells. [NIH]

Interleukin-1: A soluble factor produced by monocytes, macrophages, and other cells which activates T-lymphocytes and potentiates their response to mitogens or antigens. IL-1 consists of two distinct forms, IL-1 alpha and IL-1 beta which perform the same functions but are distinct proteins. The biological effects of IL-1 include the ability to replace macrophage requirements for T-cell activation. The factor is distinct from interleukin-2. [NIH]

Interleukin-18: Cytokine which resembles IL-1 structurally and IL-12 functionally. It enhances the cytotoxic activity of NK cells and CTLs, and appears to play a role both as neuroimmunomodulator and in the induction of mucosal immunity. [NIH]

Interleukin-2: Chemical mediator produced by activated T lymphocytes and which regulates the proliferation of T cells, as well as playing a role in the regulation of NK cell activity. [NIH]

Interleukin-8: A cytokine that activates neutrophils and attracts neutrophils and T-lymphocytes. It is released by several cell types including monocytes, macrophages, T-lymphocytes, fibroblasts, endothelial cells, and keratinocytes by an inflammatory stimulus. IL-8 is a member of the beta-thromboglobulin superfamily and structurally related to platelet factor 4. [NIH]

Intermittent: Occurring at separated intervals; having periods of cessation of activity. [EU]

International Agencies: International organizations which provide health-related or other cooperative services. [NIH]

Interstitial: Pertaining to or situated between parts or in the interspaces of a tissue. [EU]

Intestinal: Having to do with the intestines. [NIH]

Intestine: A long, tube-shaped organ in the abdomen that completes the process of digestion. There is both a large intestine and a small intestine. Also called the bowel. [NIH]

Intoxication: Poisoning, the state of being poisoned. [EU]

Intracellular: Inside a cell. [NIH]

Intracellular Membranes: Membranes of subcellular structures. [NIH]

Intraepithelial: Within the layer of cells that form the surface or lining of an organ. [NIH]

Intraindividual: Being or occurring within the individual. [EU]

Intramuscular: IM. Within or into muscle. [NIH]

Intravenous: IV. Into a vein. [NIH]

Intrinsic: Situated entirely within or pertaining exclusively to a part. [EU]

Invasive: 1. Having the quality of invasiveness. 2. Involving puncture or incision of the skin or insertion of an instrument or foreign material into the body; said of diagnostic techniques. [EU]

Invasive cervical cancer: Cancer that has spread from the surface of the cervix to tissue deeper in the cervix or to other parts of the body. [NIH]

Involuntary: Reaction occurring without intention or volition. [NIH]

Ion Channels: Gated, ion-selective glycoproteins that traverse membranes. The stimulus for channel gating can be a membrane potential, drug, transmitter, cytoplasmic messenger, or a mechanical deformation. Ion channels which are integral parts of ionotropic neurotransmitter receptors are not included. [NIH]

Ionization: 1. Any process by which a neutral atom gains or loses electrons, thus acquiring a net charge, as the dissociation of a substance in solution into ions or ion production by the passage of radioactive particles. 2. Iontophoresis. [EU]

Ions: An atom or group of atoms that have a positive or negative electric charge due to a gain (negative charge) or loss (positive charge) of one or more electrons. Atoms with a positive charge are known as cations; those with a negative charge are anions. [NIH]

Irradiation: The use of high-energy radiation from x-rays, neutrons, and other sources to kill cancer cells and shrink tumors. Radiation may come from a machine outside the body (external-beam radiation therapy) or from materials called radioisotopes. Radioisotopes produce radiation and can be placed in or near the tumor or in the area near cancer cells. This type of radiation treatment is called internal radiation therapy, implant radiation, interstitial radiation, or brachytherapy. Systemic radiation therapy uses a radioactive substance, such as a radiolabeled monoclonal antibody, that circulates throughout the body. Irradiation is also called radiation therapy, radiotherapy, and x-ray therapy. [NIH]

Ischemia: Deficiency of blood in a part, due to functional constriction or actual obstruction of a blood vessel. [EU]

Isoelectric: Separation of amphoteric substances, dissolved in water, based on their isoelectric behavior. The amphoteric substances are a mixture of proteins to be separated and of auxiliary "carrier ampholytes". [NIH]

Isoelectric Point: The pH in solutions of proteins and related compounds at which the dipolar ions are at a maximum. [NIH]

Isoenzyme: Different forms of an enzyme, usually occurring in different tissues. The isoenzymes of a particular enzyme catalyze the same reaction but they differ in some of their properties. [NIH]

Isoniazid: Antibacterial agent used primarily as a tuberculostatic. It remains the treatment of choice for tuberculosis. [NIH]

Joint: The point of contact between elements of an animal skeleton with the parts that surround and support it. [NIH]

Kaposi: A tumor characterized by development, essentially in men, of violet red patches and nodules on the skin. This disease also affects deeper organs. [NIH]

Kb: A measure of the length of DNA fragments, 1 Kb = 1000 base pairs. The largest DNA

fragments are up to 50 kilobases long. [NIH]

Keratin: A class of fibrous proteins or scleroproteins important both as structural proteins and as keys to the study of protein conformation. The family represents the principal constituent of epidermis, hair, nails, horny tissues, and the organic matrix of tooth enamel. Two major conformational groups have been characterized, alpha-keratin, whose peptide backbone forms an alpha-helix, and beta-keratin, whose backbone forms a zigzag or pleated sheet structure. [NIH]

Keratinocytes: Epidermal cells which synthesize keratin and undergo characteristic changes as they move upward from the basal layers of the epidermis to the cornified (horny) layer of the skin. Successive stages of differentiation of the keratinocytes forming the epidermal layers are basal cell, spinous or prickle cell, and the granular cell. [NIH]

Keratitis: Inflammation of the cornea. [NIH]

Keto: It consists of 8 carbon atoms and within the endotoxins, it connects poysaccharide and lipid A. [NIH]

Kidney Disease: Any one of several chronic conditions that are caused by damage to the cells of the kidney. People who have had diabetes for a long time may have kidney damage. Also called nephropathy. [NIH]

Kidney Failure: The inability of a kidney to excrete metabolites at normal plasma levels under conditions of normal loading, or the inability to retain electrolytes under conditions of normal intake. In the acute form (kidney failure, acute), it is marked by uremia and usually by oliguria or anuria, with hyperkalemia and pulmonary edema. The chronic form (kidney failure, chronic) is irreversible and requires hemodialysis. [NIH]

Kidney Transplantation: The transference of a kidney from one human or animal to another. [NIH]

Kilobase: A measure of the length of DNA fragments, 1 Kb = 1000 base pairs. The largest DNA fragments are up to 50 kilobases long. [NIH]

Kinesin: A microtubule-associated mechanical adenosine triphosphatase, that uses the energy of ATP hydrolysis to move organelles along microtubules toward the plus end of the microtubule. The protein is found in squid axoplasm, optic lobes, and in bovine brain. Bovine kinesin is a heterotetramer composed of two heavy (120 kDa) and two light (62 kDa) chains. EC 3.6.1.-. [NIH]

Kinetics: The study of rate dynamics in chemical or physical systems. [NIH]

Labile: 1. Gliding; moving from point to point over the surface; unstable; fluctuating. 2. Chemically unstable. [EU]

Lamivudine: A reverse transcriptase inhibitor and zalcitabine analog in which a sulfur atom replaces the 3' carbon of the pentose ring. It is used to treat HIV disease. [NIH]

Large Intestine: The part of the intestine that goes from the cecum to the rectum. The large intestine absorbs water from stool and changes it from a liquid to a solid form. The large intestine is 5 feet long and includes the appendix, cecum, colon, and rectum. Also called colon. [NIH]

Latency: The period of apparent inactivity between the time when a stimulus is presented and the moment a response occurs. [NIH]

Latent: Phoria which occurs at one distance or another and which usually has no troublesome effect. [NIH]

Lavage: A cleaning of the stomach and colon. Uses a special drink and enemas. [NIH]

Lectin: A complex molecule that has both protein and sugars. Lectins are able to bind to the

outside of a cell and cause biochemical changes in it. Lectins are made by both animals and plants. [NIH]

Leiomyoma: A benign tumor derived from smooth muscle tissue, also known as a fibroid tumor. They rarely occur outside of the uterus and the gastrointestinal tract but can occur in the skin and subcutaneous tissues, probably arising from the smooth muscle of small blood vessels in these tissues. [NIH]

Leishmaniasis: A disease caused by any of a number of species of protozoa in the genus Leishmania. There are four major clinical types of this infection: cutaneous (Old and New World), diffuse cutaneous, mucocutaneous, and visceral leishmaniasis. [NIH]

Length of Stay: The period of confinement of a patient to a hospital or other health facility. [NIH]

Lens: The transparent, double convex (outward curve on both sides) structure suspended between the aqueous and vitreous; helps to focus light on the retina. [NIH]

Lentivirus: A genus of the family Retroviridae consisting of non-oncogenic retroviruses that produce multi-organ diseases characterized by long incubation periods and persistent infection. Lentiviruses are unique in that they contain open reading frames (ORFs) between the pol and env genes and in the 3' env region. Five serogroups are recognized, reflecting the mammalian hosts with which they are associated. HIV-1 is the type species. [NIH]

Leprosy: A chronic granulomatous infection caused by Mycobacterium leprae. The granulomatous lesions are manifested in the skin, the mucous membranes, and the peripheral nerves. Two polar or principal types are lepromatous and tuberculoid. [NIH]

Leptin: A 16-kD peptide hormone secreted from white adipocytes and implicated in the regulation of food intake and energy balance. Leptin provides the key afferent signal from fat cells in the feedback system that controls body fat stores. [NIH]

Lethal: Deadly, fatal. [EU]

Lethargy: Abnormal drowsiness or stupor; a condition of indifference. [EU]

Leucine: An essential branched-chain amino acid important for hemoglobin formation. [NIH]

Leucocyte: All the white cells of the blood and their precursors (myeloid cell series, lymphoid cell series) but commonly used to indicate granulocytes exclusive of lymphocytes. [NIH]

Leukaemia: An acute or chronic disease of unknown cause in man and other warm-blooded animals that involves the blood-forming organs, is characterized by an abnormal increase in the number of leucocytes in the tissues of the body with or without a corresponding increase of those in the circulating blood, and is classified according of the type leucocyte most prominently involved. [EU]

Leukemia: Cancer of blood-forming tissue. [NIH]

Leukocytes: White blood cells. These include granular leukocytes (basophils, eosinophils, and neutrophils) as well as non-granular leukocytes (lymphocytes and monocytes). [NIH]

Leukoencephalopathy: A condition with spongy holes in the brain's white matter. [NIH]

Leukopenia: A condition in which the number of leukocytes (white blood cells) in the blood is reduced. [NIH]

Leukoplakia: A white patch that may develop on mucous membranes such as the cheek, gums, or tongue and may become cancerous. [NIH]

Leukotrienes: A family of biologically active compounds derived from arachidonic acid by oxidative metabolism through the 5-lipoxygenase pathway. They participate in host defense reactions and pathophysiological conditions such as immediate hypersensitivity and

inflammation. They have potent actions on many essential organs and systems, including the cardiovascular, pulmonary, and central nervous system as well as the gastrointestinal tract and the immune system. [NIH]

Libido: The psychic drive or energy associated with sexual instinct in the broad sense (pleasure and love-object seeking). It may also connote the psychic energy associated with instincts in general that motivate behavior. [NIH]

Library Services: Services offered to the library user. They include reference and circulation. [NIH]

Life cycle: The successive stages through which an organism passes from fertilized ovum or spore to the fertilized ovum or spore of the next generation. [NIH]

Ligament: A band of fibrous tissue that connects bones or cartilages, serving to support and strengthen joints. [EU]

Linkage: The tendency of two or more genes in the same chromosome to remain together from one generation to the next more frequently than expected according to the law of independent assortment. [NIH]

Lipid: Fat. [NIH]

Lipodystrophy: A collection of rare conditions resulting from defective fat metabolism and characterized by atrophy of the subcutaneous fat. They include total, congenital or acquired, partial, abdominal infantile, and localized lipodystrophy. [NIH]

Lipolysis: The hydrolysis of lipids. [NIH]

Lipoprotein: Any of the lipid-protein complexes in which lipids are transported in the blood; lipoprotein particles consist of a spherical hydrophobic core of triglycerides or cholesterol esters surrounded by an amphipathic monolayer of phospholipids, cholesterol, and apolipoproteins; the four principal classes are high-density, low-density, and very-low-density lipoproteins and chylomicrons. [EU]

Liver: A large, glandular organ located in the upper abdomen. The liver cleanses the blood and aids in digestion by secreting bile. [NIH]

Liver Transplantation: The transference of a part of or an entire liver from one human or animal to another. [NIH]

Lobe: A portion of an organ such as the liver, lung, breast, or brain. [NIH]

Local Government: Smallest political subdivisions within a country at which general governmental functions are carried-out. [NIH]

Localization: The process of determining or marking the location or site of a lesion or disease. May also refer to the process of keeping a lesion or disease in a specific location or site. [NIH]

Localized: Cancer which has not metastasized yet. [NIH]

Locomotion: Movement or the ability to move from one place or another. It can refer to humans, vertebrate or invertebrate animals, and microorganisms. [NIH]

Longitudinal Studies: Studies in which variables relating to an individual or group of individuals are assessed over a period of time. [NIH]

Longitudinal study: Also referred to as a "cohort study" or "prospective study"; the analytic method of epidemiologic study in which subsets of a defined population can be identified who are, have been, or in the future may be exposed or not exposed, or exposed in different degrees, to a factor or factors hypothesized to influence the probability of occurrence of a given disease or other outcome. The main feature of this type of study is to observe large numbers of subjects over an extended time, with comparisons of incidence rates in groups

that differ in exposure levels. [NIH]

Long-Term Potentiation: A persistent increase in synaptic efficacy, usually induced by appropriate activation of the same synapses. The phenomenological properties of long-term potentiation suggest that it may be a cellular mechanism of learning and memory. [NIH]

Loop: A wire usually of platinum bent at one end into a small loop (usually 4 mm inside diameter) and used in transferring microorganisms. [NIH]

Low-calorie diet: Caloric restriction of about 800 to 1,500 calories (approximately 12 to 15 kcal/kg of body weight) per day. [NIH]

Low-density lipoprotein: Lipoprotein that contains most of the cholesterol in the blood. LDL carries cholesterol to the tissues of the body, including the arteries. A high level of LDL increases the risk of heart disease. LDL typically contains 60 to 70 percent of the total serum cholesterol and both are directly correlated with CHD risk. [NIH]

Lupus: A form of cutaneous tuberculosis. It is seen predominantly in women and typically involves the nasal, buccal, and conjunctival mucosa. [NIH]

Lymph: The almost colorless fluid that travels through the lymphatic system and carries cells that help fight infection and disease. [NIH]

Lymph node: A rounded mass of lymphatic tissue that is surrounded by a capsule of connective tissue. Also known as a lymph gland. Lymph nodes are spread out along lymphatic vessels and contain many lymphocytes, which filter the lymphatic fluid (lymph). [NIH]

Lymphadenitis: Inflammation of the lymph nodes. [NIH]

Lymphadenopathy: Disease or swelling of the lymph nodes. [NIH]

Lymphatic: The tissues and organs, including the bone marrow, spleen, thymus, and lymph nodes, that produce and store cells that fight infection and disease. [NIH]

Lymphatic system: The tissues and organs that produce, store, and carry white blood cells that fight infection and other diseases. This system includes the bone marrow, spleen, thymus, lymph nodes and a network of thin tubes that carry lymph and white blood cells. These tubes branch, like blood vessels, into all the tissues of the body. [NIH]

Lymphoblastic: One of the most aggressive types of non-Hodgkin lymphoma. [NIH]

Lymphocyte: A white blood cell. Lymphocytes have a number of roles in the immune system, including the production of antibodies and other substances that fight infection and diseases. [NIH]

Lymphocyte Count: A count of the number of lymphocytes in the blood. [NIH]

Lymphocytic: Referring to lymphocytes, a type of white blood cell. [NIH]

Lymphoid: Referring to lymphocytes, a type of white blood cell. Also refers to tissue in which lymphocytes develop. [NIH]

Lymphokine: A soluble protein produced by some types of white blood cell that stimulates other white blood cells to kill foreign invaders. [NIH]

Lymphoma: A general term for various neoplastic diseases of the lymphoid tissue. [NIH]

Lymphopenia: Reduction in the number of lymphocytes. [NIH]

Lymphoproliferative: Disorders characterized by proliferation of lymphoid tissue, general or unspecified. [NIH]

Lymphoproliferative Disorders: Disorders characterized by proliferation of lymphoid tissue, general or unspecified. [NIH]

Lysine: An essential amino acid. It is often added to animal feed. [NIH]

Lytic: 1. Pertaining to lysis or to a lysin. 2. Producing lysis. [EU]

Macroglia: A type of neuroglia composed of astrocytes. [NIH]

Macrophage: A type of white blood cell that surrounds and kills microorganisms, removes dead cells, and stimulates the action of other immune system cells. [NIH]

Maculopapular: Both macular and papular, as an eruption consisting of both macules and papules; sometimes erroneously used to designate a papule that is only slightly elevated. [EU]

Maintenance therapy: Treatment that is given to help a primary (original) treatment keep working. Maintenance therapy is often given to help keep cancer in remission. [NIH]

Major Histocompatibility Complex: The genetic region which contains the loci of genes which determine the structure of the serologically defined (SD) and lymphocyte-defined (LD) transplantation antigens, genes which control the structure of the immune response-associated (Ia) antigens, the immune response (Ir) genes which control the ability of an animal to respond immunologically to antigenic stimuli, and genes which determine the structure and/or level of the first four components of complement. [NIH]

Malabsorption: Impaired intestinal absorption of nutrients. [EU]

Malaria: A protozoan disease caused in humans by four species of the genus Plasmodium (P. falciparum (malaria, falciparum), P. vivax (malaria, vivax), P. ovale, and P. malariae) and transmitted by the bite of an infected female mosquito of the genus Anopheles. Malaria is endemic in parts of Asia, Africa, Central and South America, Oceania, and certain Caribbean islands. It is characterized by extreme exhaustion associated with paroxysms of high fever, sweating, shaking chills, and anemia. Malaria in animals is caused by other species of plasmodia. [NIH]

Malaria, Falciparum: Malaria caused by Plasmodium falciparum. This is the severest form of malaria and is associated with the highest levels of parasites in the blood. This disease is characterized by irregularly recurring febrile paroxysms that in extreme cases occur with acute cerebral, renal, or gastrointestinal manifestations. [NIH]

Malaria, Vivax: Malaria caused by Plasmodium vivax. This form of malaria is less severe than malaria, falciparum, but there is a higher probability for relapses to occur. Febrile paroxysms often occur every other day. [NIH]

Malignancy: A cancerous tumor that can invade and destroy nearby tissue and spread to other parts of the body. [NIH]

Malignant: Cancerous; a growth with a tendency to invade and destroy nearby tissue and spread to other parts of the body. [NIH]

Malignant tumor: A tumor capable of metastasizing. [NIH]

Malnutrition: A condition caused by not eating enough food or not eating a balanced diet. [NIH]

Mammogram: An x-ray of the breast. [NIH]

Mania: Excitement of psychotic proportions manifested by mental and physical hyperactivity, disorganization of behaviour, and elevation of mood. [EU]

Manic: Affected with mania. [EU]

Manic-depressive psychosis: One of a group of psychotic reactions, fundamentally marked by severe mood swings and a tendency to remission and recurrence. [NIH]

Manifest: Being the part or aspect of a phenomenon that is directly observable : concretely expressed in behaviour. [EU]

Mass Media: Instruments or technological means of communication that reach large

numbers of people with a common message: press, radio, television, etc. [NIH]

Mass Screening: Organized periodic procedures performed on large groups of people for the purpose of detecting disease. [NIH]

Mastitis: Inflammatory disease of the breast, or mammary gland. [NIH]

Mediator: An object or substance by which something is mediated, such as (1) a structure of the nervous system that transmits impulses eliciting a specific response; (2) a chemical substance (transmitter substance) that induces activity in an excitable tissue, such as nerve or muscle; or (3) a substance released from cells as the result of the interaction of antigen with antibody or by the action of antigen with a sensitized lymphocyte. [EU]

Medical Staff: Professional medical personnel who provide care to patients in an organized facility, institution or agency. [NIH]

Medicament: A medicinal substance or agent. [EU]

Medicine, Traditional: Systems of medicine based on cultural beliefs and practices handed down from generation to generation. The concept includes mystical and magical rituals, herbal therapy, and other treatments which may not be explained by modern medicine. [NIH]

MEDLINE: An online database of MEDLARS, the computerized bibliographic Medical Literature Analysis and Retrieval System of the National Library of Medicine. [NIH]

Mefloquine: A phospholipid-interacting antimalarial drug (antimalarials). It is very effective against Plasmodium falciparum with very few side effects. [NIH]

Meiosis: A special method of cell division, occurring in maturation of the germ cells, by means of which each daughter nucleus receives half the number of chromosomes characteristic of the somatic cells of the species. [NIH]

Melanocytes: Epidermal dendritic pigment cells which control long-term morphological color changes by alteration in their number or in the amount of pigment they produce and store in the pigment containing organelles called melanosomes. Melanophores are larger cells which do not exist in mammals. [NIH]

Melanoma: A form of skin cancer that arises in melanocytes, the cells that produce pigment. Melanoma usually begins in a mole. [NIH]

Membrane: A very thin layer of tissue that covers a surface. [NIH]

Membrane Fusion: The adherence of cell membranes, intracellular membranes, or artifical membrane models of either to each other or to viruses, parasites, or interstitial particles through a variety of chemical and physical processes. [NIH]

Membrane Proteins: Proteins which are found in membranes including cellular and intracellular membranes. They consist of two types, peripheral and integral proteins. They include most membrane-associated enzymes, antigenic proteins, transport proteins, and drug, hormone, and lectin receptors. [NIH]

Memory: Complex mental function having four distinct phases: (1) memorizing or learning, (2) retention, (3) recall, and (4) recognition. Clinically, it is usually subdivided into immediate, recent, and remote memory. [NIH]

Meninges: The three membranes that cover and protect the brain and spinal cord. [NIH]

Meningitis: Inflammation of the meninges. When it affects the dura mater, the disease is termed pachymeningitis; when the arachnoid and pia mater are involved, it is called leptomeningitis, or meningitis proper. [EU]

Meningoencephalitis: An inflammatory process involving the brain (encephalitis) and meninges (meningitis), most often produced by pathogenic organisms which invade the

central nervous system, and occasionally by toxins, autoimmune disorders, and other conditions. [NIH]

Menstrual Cycle: The period of the regularly recurring physiologic changes in the endometrium occurring during the reproductive period in human females and some primates and culminating in partial sloughing of the endometrium (menstruation). [NIH]

Menstruation: The normal physiologic discharge through the vagina of blood and mucosal tissues from the nonpregnant uterus. [NIH]

Mental: Pertaining to the mind; psychic. 2. (L. mentum chin) pertaining to the chin. [EU]

Mental Disorders: Psychiatric illness or diseases manifested by breakdowns in the adaptational process expressed primarily as abnormalities of thought, feeling, and behavior producing either distress or impairment of function. [NIH]

Mental Health: The state wherein the person is well adjusted. [NIH]

Mental Health Services: Organized services to provide mental health care. [NIH]

Mental Processes: Conceptual functions or thinking in all its forms. [NIH]

Mercury: A silver metallic element that exists as a liquid at room temperature. It has the atomic symbol Hg (from hydrargyrum, liquid silver), atomic number 80, and atomic weight 200.59. Mercury is used in many industrial applications and its salts have been employed therapeutically as purgatives, antisyphilitics, disinfectants, and astringents. It can be absorbed through the skin and mucous membranes which leads to mercury poisoning. Because of its toxicity, the clinical use of mercury and mercurials is diminishing. [NIH]

Mesothelial: It lines the peritonealla and pleural cavities. [NIH]

Metabolite: Any substance produced by metabolism or by a metabolic process. [EU]

Metastasis: The spread of cancer from one part of the body to another. Tumors formed from cells that have spread are called "secondary tumors" and contain cells that are like those in the original (primary) tumor. The plural is metastases. [NIH]

Methamphetamine: A central nervous system stimulant and sympathomimetic with actions and uses similar to dextroamphetamine. The smokable form is a drug of abuse and is referred to as crank, crystal, crystal meth, ice, and speed. [NIH]

Methanol: A colorless, flammable liquid used in the manufacture of formaldehyde and acetic acid, in chemical synthesis, antifreeze, and as a solvent. Ingestion of methanol is toxic and may cause blindness. [NIH]

Methylcholanthrene: A carcinogen that is often used in experimental cancer studies. [NIH]

Methylene Blue: A compound consisting of dark green crystals or crystalline powder, having a bronze-like luster. Solutions in water or alcohol have a deep blue color. Methylene blue is used as a bacteriologic stain and as an indicator. It inhibits Guanylate cyclase, and has been used to treat cyanide poisoning and to lower levels of methemoglobin. [NIH]

MI: Myocardial infarction. Gross necrosis of the myocardium as a result of interruption of the blood supply to the area; it is almost always caused by atherosclerosis of the coronary arteries, upon which coronary thrombosis is usually superimposed. [NIH]

Micelle: A colloid particle formed by an aggregation of small molecules. [EU]

Microbe: An organism which cannot be observed with the naked eye; e. g. unicellular animals, lower algae, lower fungi, bacteria. [NIH]

Microbiology: The study of microorganisms such as fungi, bacteria, algae, archaea, and viruses. [NIH]

Microcalcifications: Tiny deposits of calcium in the breast that cannot be felt but can be

detected on a mammogram. A cluster of these very small specks of calcium may indicate that cancer is present. [NIH]

Microglia: The third type of glial cell, along with astrocytes and oligodendrocytes (which together form the macroglia). Microglia vary in appearance depending on developmental stage, functional state, and anatomical location; subtype terms include ramified, perivascular, ameboid, resting, and activated. Microglia clearly are capable of phagocytosis and play an important role in a wide spectrum of neuropathologies. They have also been suggested to act in several other roles including in secretion (e.g., of cytokines and neural growth factors), in immunological processing (e.g., antigen presentation), and in central nervous system development and remodeling. [NIH]

Microorganism: An organism that can be seen only through a microscope. Microorganisms include bacteria, protozoa, algae, and fungi. Although viruses are not considered living organisms, they are sometimes classified as microorganisms. [NIH]

Micro-organism: An organism which cannot be observed with the naked eye; e. g. unicellular animals, lower algae, lower fungi, bacteria. [NIH]

Microsporidiosis: Infections with protozoa of the phylum Microspora. [NIH]

Microtubules: Slender, cylindrical filaments found in the cytoskeleton of plant and animal cells. They are composed of the protein tubulin. [NIH]

Midwifery: The practice of assisting women in childbirth. [NIH]

Migration: The systematic movement of genes between populations of the same species, geographic race, or variety. [NIH]

Milligram: A measure of weight. A milligram is approximately 450,000-times smaller than a pound and 28,000-times smaller than an ounce. [NIH]

Milliliter: A measure of volume for a liquid. A milliliter is approximately 950-times smaller than a quart and 30-times smaller than a fluid ounce. A milliliter of liquid and a cubic centimeter (cc) of liquid are the same. [NIH]

Mitosis: A method of indirect cell division by means of which the two daughter nuclei normally receive identical complements of the number of chromosomes of the somatic cells of the species. [NIH]

Mitotic: Cell resulting from mitosis. [NIH]

Mode of Transmission: Hepatitis A [NIH]

Modification: A change in an organism, or in a process in an organism, that is acquired from its own activity or environment. [NIH]

Molecular: Of, pertaining to, or composed of molecules : a very small mass of matter. [EU]

Molecule: A chemical made up of two or more atoms. The atoms in a molecule can be the same (an oxygen molecule has two oxygen atoms) or different (a water molecule has two hydrogen atoms and one oxygen atom). Biological molecules, such as proteins and DNA, can be made up of many thousands of atoms. [NIH]

Monitor: An apparatus which automatically records such physiological signs as respiration, pulse, and blood pressure in an anesthetized patient or one undergoing surgical or other procedures. [NIH]

Monoclonal: An antibody produced by culturing a single type of cell. It therefore consists of a single species of immunoglobulin molecules. [NIH]

Monoclonal antibodies: Laboratory-produced substances that can locate and bind to cancer cells wherever they are in the body. Many monoclonal antibodies are used in cancer detection or therapy; each one recognizes a different protein on certain cancer cells.

Monoclonal antibodies can be used alone, or they can be used to deliver drugs, toxins, or radioactive material directly to a tumor. [NIH]

Monocyte: A type of white blood cell. [NIH]

Mononuclear: A cell with one nucleus. [NIH]

Monotherapy: A therapy which uses only one drug. [EU]

Mood Disorders: Those disorders that have a disturbance in mood as their predominant feature. [NIH]

Morale: The prevailing temper or spirit of an individual or group in relation to the tasks or functions which are expected. [NIH]

Morphological: Relating to the configuration or the structure of live organs. [NIH]

Motion Sickness: Sickness caused by motion, as sea sickness, train sickness, car sickness, and air sickness. [NIH]

Mucins: A secretion containing mucopolysaccharides and protein that is the chief constituent of mucus. [NIH]

Mucocutaneous: Pertaining to or affecting the mucous membrane and the skin. [EU]

Mucosa: A mucous membrane, or tunica mucosa. [EU]

Mucositis: A complication of some cancer therapies in which the lining of the digestive system becomes inflamed. Often seen as sores in the mouth. [NIH]

Multicenter study: A clinical trial that is carried out at more than one medical institution. [NIH]

Multidrug resistance: Adaptation of tumor cells to anticancer drugs in ways that make the drugs less effective. [NIH]

Multiple sclerosis: A disorder of the central nervous system marked by weakness, numbness, a loss of muscle coordination, and problems with vision, speech, and bladder control. Multiple sclerosis is thought to be an autoimmune disease in which the body's immune system destroys myelin. Myelin is a substance that contains both protein and fat (lipid) and serves as a nerve insulator and helps in the transmission of nerve signals. [NIH]

Muscle Fibers: Large single cells, either cylindrical or prismatic in shape, that form the basic unit of muscle tissue. They consist of a soft contractile substance enclosed in a tubular sheath. [NIH]

Muscle relaxant: An agent that specifically aids in reducing muscle tension, as those acting at the polysynaptic neurons of motor nerves (e.g. meprobamate) or at the myoneural junction (curare and related compounds). [EU]

Muscle Spindles: Mechanoreceptors found between skeletal muscle fibers. Muscle spindles are arranged in parallel with muscle fibers and respond to the passive stretch of the muscle, but cease to discharge if the muscle contracts isotonically, thus signaling muscle length. The muscle spindles are the receptors responsible for the stretch or myotactic reflex. [NIH]

Muscular Atrophy: Derangement in size and number of muscle fibers occurring with aging, reduction in blood supply, or following immobilization, prolonged weightlessness, malnutrition, and particularly in denervation. [NIH]

Muscular Dystrophies: A general term for a group of inherited disorders which are characterized by progressive degeneration of skeletal muscles. [NIH]

Mutate: To change the genetic material of a cell. Then changes (mutations) can be harmful, beneficial, or have no effect. [NIH]

Myalgia: Pain in a muscle or muscles. [EU]

Mycobacterium: A genus of gram-positive, aerobic bacteria. Most species are free-living in soil and water, but the major habitat for some is the diseased tissue of warm-blooded hosts. [NIH]

Mycobacterium tuberculosis: A species of gram-positive, aerobic bacteria that produces tuberculosis in man, other primates, dogs, and some animals which have contact with man. Growth tends to be in serpentine, cordlike masses in which the bacilli show a parallel orientation. [NIH]

Myelin: The fatty substance that covers and protects nerves. [NIH]

Myeloma: Cancer that arises in plasma cells, a type of white blood cell. [NIH]

Myocardial infarction: Gross necrosis of the myocardium as a result of interruption of the blood supply to the area; it is almost always caused by atherosclerosis of the coronary arteries, upon which coronary thrombosis is usually superimposed. [NIH]

Myocardial Ischemia: A disorder of cardiac function caused by insufficient blood flow to the muscle tissue of the heart. The decreased blood flow may be due to narrowing of the coronary arteries (coronary arteriosclerosis), to obstruction by a thrombus (coronary thrombosis), or less commonly, to diffuse narrowing of arterioles and other small vessels within the heart. Severe interruption of the blood supply to the myocardial tissue may result in necrosis of cardiac muscle (myocardial infarction). [NIH]

Myocarditis: Inflammation of the myocardium; inflammation of the muscular walls of the heart. [EU]

Myocardium: The muscle tissue of the heart composed of striated, involuntary muscle known as cardiac muscle. [NIH]

Myoglobin: A conjugated protein which is the oxygen-transporting pigment of muscle. It is made up of one globin polypeptide chain and one heme group. [NIH]

Myopathy: Any disease of a muscle. [EU]

Myositis: Inflammation of a voluntary muscle. [EU]

Myotonic Dystrophy: A condition presenting muscle weakness and wasting which may be progressive. [NIH]

Myristate: Pharmacological activator of protein kinase C. [NIH]

Naive: Used to describe an individual who has never taken a certain drug or class of drugs (e. g., AZT-naive, antiretroviral-naive), or to refer to an undifferentiated immune system cell. [NIH]

Nasal Mucosa: The mucous membrane lining the nasal cavity. [NIH]

Nausea: An unpleasant sensation in the stomach usually accompanied by the urge to vomit. Common causes are early pregnancy, sea and motion sickness, emotional stress, intense pain, food poisoning, and various enteroviruses. [NIH]

NCI: National Cancer Institute. NCI, part of the National Institutes of Health of the United States Department of Health and Human Services, is the federal government's principal agency for cancer research. NCI conducts, coordinates, and funds cancer research, training, health information dissemination, and other programs with respect to the cause, diagnosis, prevention, and treatment of cancer. Access the NCI Web site at http://cancer.gov. [NIH]

Neck Pain: Discomfort or more intense forms of pain that are localized to the cervical region. This term generally refers to pain in the posterior or lateral regions of the neck. [NIH]

Need: A state of tension or dissatisfaction felt by an individual that impels him to action toward a goal he believes will satisfy the impulse. [NIH]

Needle Sharing: Usage of a single needle among two or more people for injecting drugs.

Needle sharing is a high-risk behavior for contracting infectious disease. [NIH]

Needlestick Injuries: Penetrating stab wounds caused by needles. They are of special concern to health care workers since such injuries put them at risk for developing infectious disease. [NIH]

Needs Assessment: Systematic identification of a population's needs or the assessment of individuals to determine the proper level of services needed. [NIH]

Nelfinavir: A potent HIV protease inhibitor. It is used in combination with other antiviral drugs in the treatment of HIV in both adults and children. [NIH]

Neonatal: Pertaining to the first four weeks after birth. [EU]

Neoplasia: Abnormal and uncontrolled cell growth. [NIH]

Neoplasm: A new growth of benign or malignant tissue. [NIH]

Neoplastic: Pertaining to or like a neoplasm (= any new and abnormal growth); pertaining to neoplasia (= the formation of a neoplasm). [EU]

Nephropathy: Disease of the kidneys. [EU]

Nerve: A cordlike structure of nervous tissue that connects parts of the nervous system with other tissues of the body and conveys nervous impulses to, or away from, these tissues. [NIH]

Nervous System: The entire nerve apparatus composed of the brain, spinal cord, nerves and ganglia. [NIH]

Networks: Pertaining to a nerve or to the nerves, a meshlike structure of interlocking fibers or strands. [NIH]

Neural: 1. Pertaining to a nerve or to the nerves. 2. Situated in the region of the spinal axis, as the neutral arch. [EU]

Neuraminidase: An enzyme that catalyzes the hydrolysis of alpha-2,3, alpha-2,6-, and alpha-2,8-glycosidic linkages (at a decreasing rate, respectively) of terminal sialic residues in oligosaccharides, glycoproteins, glycolipids, colominic acid, and synthetic substrate. (From Enzyme Nomenclature, 1992) EC 3.2.1.18. [NIH]

Neurologic: Having to do with nerves or the nervous system. [NIH]

Neurologic Manifestations: Clinical signs and symptoms caused by nervous system injury or dysfunction. [NIH]

Neuromuscular: Pertaining to muscles and nerves. [EU]

Neuronal: Pertaining to a neuron or neurons (= conducting cells of the nervous system). [EU]

Neurons: The basic cellular units of nervous tissue. Each neuron consists of a body, an axon, and dendrites. Their purpose is to receive, conduct, and transmit impulses in the nervous system. [NIH]

Neuropathy: A problem in any part of the nervous system except the brain and spinal cord. Neuropathies can be caused by infection, toxic substances, or disease. [NIH]

Neuroretinitis: Inflammation of the optic nerve head and adjacent retina. [NIH]

Neurotoxicity: The tendency of some treatments to cause damage to the nervous system. [NIH]

Neurotransmitter: Any of a group of substances that are released on excitation from the axon terminal of a presynaptic neuron of the central or peripheral nervous system and travel across the synaptic cleft to either excite or inhibit the target cell. Among the many substances that have the properties of a neurotransmitter are acetylcholine, norepinephrine, epinephrine, dopamine, glycine, y-aminobutyrate, glutamic acid, substance P, enkephalins, endorphins, and serotonin. [EU]

Neutralization: An act or process of neutralizing. [EU]

Neutrophils: Granular leukocytes having a nucleus with three to five lobes connected by slender threads of chromatin, and cytoplasm containing fine inconspicuous granules and stainable by neutral dyes. [NIH]

Nevirapine: A potent, non-nucleoside reverse transcriptase inhibitor used in combination with nucleoside analogues for treatment of HIV infection and AIDS. [NIH]

Nitric Oxide: A free radical gas produced endogenously by a variety of mammalian cells. It is synthesized from arginine by a complex reaction, catalyzed by nitric oxide synthase. Nitric oxide is endothelium-derived relaxing factor. It is released by the vascular endothelium and mediates the relaxation induced by some vasodilators such as acetylcholine and bradykinin. It also inhibits platelet aggregation, induces disaggregation of aggregated platelets, and inhibits platelet adhesion to the vascular endothelium. Nitric oxide activates cytosolic guanylate cyclase and thus elevates intracellular levels of cyclic GMP. [NIH]

Nitric-Oxide Synthase: An enzyme that catalyzes the conversion of L-arginine, NADPH, and oxygen to citrulline, nitric oxide, and NADP+. The enzyme found in brain, but not that induced in lung or liver by endotoxin, requires calcium. (From Enzyme Nomenclature, 1992) EC 1.14.13.39. [NIH]

Nitrogen: An element with the atomic symbol N, atomic number 7, and atomic weight 14. Nitrogen exists as a diatomic gas and makes up about 78% of the earth's atmosphere by volume. It is a constituent of proteins and nucleic acids and found in all living cells. [NIH]

Non-nucleoside: A member of a class of compounds, including delavirdine, loviride and nevirapine, that acts to directly combine with and block the action of HIV's reverse transcriptase. [NIH]

Nonverbal Communication: Transmission of emotions, ideas, and attitudes between individuals in ways other than the spoken language. [NIH]

Nosocomial: Pertaining to or originating in the hospital, said of an infection not present or incubating prior to admittance to the hospital, but generally occurring 72 hours after admittance; the term is usually used to refer to patient disease, but hospital personnel may also acquire nosocomial infection. [EU]

Nuclear: A test of the structure, blood flow, and function of the kidneys. The doctor injects a mildly radioactive solution into an arm vein and uses x-rays to monitor its progress through the kidneys. [NIH]

Nuclear Localization Signal: Short, predominantly basic amino acid sequences identified as nuclear import signals for some proteins. These sequences are believed to interact with specific receptors at nuclear pores. [NIH]

Nuclear Pore: An opening through the nuclear envelope formed by the nuclear pore complex which transports nuclear proteins or RNA into or out of the cell nucleus and which, under some conditions, acts as an ion channel. [NIH]

Nuclei: A body of specialized protoplasm found in nearly all cells and containing the chromosomes. [NIH]

Nucleic acid: Either of two types of macromolecule (DNA or RNA) formed by polymerization of nucleotides. Nucleic acids are found in all living cells and contain the information (genetic code) for the transfer of genetic information from one generation to the next. [NIH]

Nucleic Acid Hybridization: The process whereby two single-stranded polynucleotides form a double-stranded molecule, with hydrogen bonding between the complementary

bases in the two strains. [NIH]

Nucleic Acid Probes: Nucleic acid which complements a specific mRNA or DNA molecule, or fragment thereof; used for hybridization studies in order to identify microorganisms and for genetic studies. [NIH]

Nucleocapsid: A protein-nucleic acid complex which forms part or all of a virion. It consists of a capsid plus enclosed nucleic acid. Depending on the virus, the nucleocapsid may correspond to a naked core or be surrounded by a membranous envelope. [NIH]

Nucleolus: A small dense body (sub organelle) within the nucleus of eukaryotic cells, visible by phase contrast and interference microscopy in live cells throughout interphase. Contains RNA and protein and is the site of synthesis of ribosomal RNA. [NIH]

Nucleus: A body of specialized protoplasm found in nearly all cells and containing the chromosomes. [NIH]

Nursing Staff: Personnel who provide nursing service to patients in an organized facility, institution, or agency. [NIH]

Nutritional Status: State of the body in relation to the consumption and utilization of nutrients. [NIH]

Occult: Obscure; concealed from observation, difficult to understand. [EU]

Occupational Exposure: The exposure to potentially harmful chemical, physical, or biological agents that occurs as a result of one's occupation. [NIH]

Ocular: 1. Of, pertaining to, or affecting the eye. 2. Eyepiece. [EU]

Ointments: Semisolid preparations used topically for protective emollient effects or as a vehicle for local administration of medications. Ointment bases are various mixtures of fats, waxes, animal and plant oils and solid and liquid hydrocarbons. [NIH]

Oligo: Chemical and mineral elements that exist in minimal (oligo) quantities in the body, in foods, in the air, in soil; name applied to any element observed as a microconstituent of plant or animal tissue and of beneficial, harmful, or even doubtful significance. [NIH]

Oligomenorrhea: Abnormally infrequent menstruation. [NIH]

Oligosaccharides: Carbohydrates consisting of between two and ten monosaccharides connected by either an alpha- or beta-glycosidic link. They are found throughout nature in both the free and bound form. [NIH]

Oncogene: A gene that normally directs cell growth. If altered, an oncogene can promote or allow the uncontrolled growth of cancer. Alterations can be inherited or caused by an environmental exposure to carcinogens. [NIH]

Oncogenic: Chemical, viral, radioactive or other agent that causes cancer; carcinogenic. [NIH]

Opacity: Degree of density (area most dense taken for reading). [NIH]

Open Reading Frames: Reading frames where successive nucleotide triplets can be read as codons specifying amino acids and where the sequence of these triplets is not interrupted by stop codons. [NIH]

Operon: The genetic unit consisting of a feedback system under the control of an operator gene, in which a structural gene transcribes its message in the form of mRNA upon blockade of a repressor produced by a regulator gene. Included here is the attenuator site of bacterial operons where transcription termination is regulated. [NIH]

Opiate: A remedy containing or derived from opium; also any drug that induces sleep. [EU]

Opioid Peptides: The endogenous peptides with opiate-like activity. The three major classes currently recognized are the enkephalins, the dynorphins, and the endorphins. Each of these

families derives from different precursors, proenkephalin, prodynorphin, and pro-opiomelanocortin, respectively. There are also at least three classes of opioid receptors, but the peptide families do not map to the receptors in a simple way. [NIH]

Opportunistic Infections: An infection caused by an organism which becomes pathogenic under certain conditions, e.g., during immunosuppression. [NIH]

Opsin: A protein formed, together with retinene, by the chemical breakdown of meta-rhodopsin. [NIH]

Optic Nerve: The 2nd cranial nerve. The optic nerve conveys visual information from the retina to the brain. The nerve carries the axons of the retinal ganglion cells which sort at the optic chiasm and continue via the optic tracts to the brain. The largest projection is to the lateral geniculate nuclei; other important targets include the superior colliculi and the suprachiasmatic nuclei. Though known as the second cranial nerve, it is considered part of the central nervous system. [NIH]

Oral Health: The optimal state of the mouth and normal functioning of the organs of the mouth without evidence of disease. [NIH]

Oral Manifestations: Disorders of the mouth attendant upon non-oral disease or injury. [NIH]

Organ Culture: The growth in aseptic culture of plant organs such as roots or shoots, beginning with organ primordia or segments and maintaining the characteristics of the organ. [NIH]

Organ Transplantation: Transference of an organ between individuals of the same species or between individuals of different species. [NIH]

Organelles: Specific particles of membrane-bound organized living substances present in eukaryotic cells, such as the mitochondria; the golgi apparatus; endoplasmic reticulum; lysomomes; plastids; and vacuoles. [NIH]

Osteomyelitis: Inflammation of bone caused by a pyogenic organism. It may remain localized or may spread through the bone to involve the marrow, cortex, cancellous tissue, and periosteum. [EU]

Osteonecrosis: Death of a bone or part of a bone, either atraumatic or posttraumatic. [NIH]

Osteoporosis: Reduction of bone mass without alteration in the composition of bone, leading to fractures. Primary osteoporosis can be of two major types: postmenopausal osteoporosis and age-related (or senile) osteoporosis. [NIH]

Otitis: Inflammation of the ear, which may be marked by pain, fever, abnormalities of hearing, hearing loss, tinnitus, and vertigo. [EU]

Outpatient: A patient who is not an inmate of a hospital but receives diagnosis or treatment in a clinic or dispensary connected with the hospital. [NIH]

Ovaries: The pair of female reproductive glands in which the ova, or eggs, are formed. The ovaries are located in the pelvis, one on each side of the uterus. [NIH]

Ovary: Either of the paired glands in the female that produce the female germ cells and secrete some of the female sex hormones. [NIH]

Ovum: A female germ cell extruded from the ovary at ovulation. [NIH]

Ownership: The legal relation between an entity (individual, group, corporation, or-profit, secular, government) and an object. The object may be corporeal, such as equipment, or completely a creature of law, such as a patent; it may be movable, such as an animal, or immovable, such as a building. [NIH]

Oxandrolone: A synthetic hormone with anabolic and androgenic properties. [NIH]

Oxidation: The act of oxidizing or state of being oxidized. Chemically it consists in the increase of positive charges on an atom or the loss of negative charges. Most biological oxidations are accomplished by the removal of a pair of hydrogen atoms (dehydrogenation) from a molecule. Such oxidations must be accompanied by reduction of an acceptor molecule. Univalent o. indicates loss of one electron; divalent o., the loss of two electrons. [EU]

Pachymeningitis: Inflammation of the dura mater of the brain, the spinal cord or the optic nerve. [NIH]

Paclitaxel: Antineoplastic agent isolated from the bark of the Pacific yew tree, Taxus brevifolia. Paclitaxel stabilizes microtubules in their polymerized form and thus mimics the action of the proto-oncogene proteins c-mos. [NIH]

Palate: The structure that forms the roof of the mouth. It consists of the anterior hard palate and the posterior soft palate. [NIH]

Palliative: 1. Affording relief, but not cure. 2. An alleviating medicine. [EU]

Pancreas: A mixed exocrine and endocrine gland situated transversely across the posterior abdominal wall in the epigastric and hypochondriac regions. The endocrine portion is comprised of the Islets of Langerhans, while the exocrine portion is a compound acinar gland that secretes digestive enzymes. [NIH]

Pancreatic: Having to do with the pancreas. [NIH]

Pancreatic cancer: Cancer of the pancreas, a salivary gland of the abdomen. [NIH]

Panic: A state of extreme acute, intense anxiety and unreasoning fear accompanied by disorganization of personality function. [NIH]

Papilloma: A benign epithelial neoplasm which may arise from the skin, mucous membranes or glandular ducts. [NIH]

Papillomavirus: A genus of Papovaviridae causing proliferation of the epithelium, which may lead to malignancy. A wide range of animals are infected including humans, chimpanzees, cattle, rabbits, dogs, and horses. [NIH]

Paraffin: A mixture of solid hydrocarbons obtained from petroleum. It has a wide range of uses including as a stiffening agent in ointments, as a lubricant, and as a topical anti-inflammatory. It is also commonly used as an embedding material in histology. [NIH]

Parasite: An animal or a plant that lives on or in an organism of another species and gets at least some of its nutrition from that other organism. [NIH]

Parasitic: Having to do with or being a parasite. A parasite is an animal or a plant that lives on or in an organism of another species and gets at least some of its nutrients from it. [NIH]

Parenteral: Not through the alimentary canal but rather by injection through some other route, as subcutaneous, intramuscular, intraorbital, intracapsular, intraspinal, intrasternal, intravenous, etc. [EU]

Parietal: 1. Of or pertaining to the walls of a cavity. 2. Pertaining to or located near the parietal bone, as the parietal lobe. [EU]

Paromomycin: An oligosaccharide antibiotic produced by various Streptomyces. [NIH]

Parotid: The space that contains the parotid gland, the facial nerve, the external carotid artery, and the retromandibular vein. [NIH]

Paroxysmal: Recurring in paroxysms (= spasms or seizures). [EU]

Patch: A piece of material used to cover or protect a wound, an injured part, etc.: a patch over the eye. [NIH]

Pathogen: Any disease-producing microorganism. [EU]

Pathogenesis: The cellular events and reactions that occur in the development of disease. [NIH]

Pathologic: 1. Indicative of or caused by a morbid condition. 2. Pertaining to pathology (= branch of medicine that treats the essential nature of the disease, especially the structural and functional changes in tissues and organs of the body caused by the disease). [EU]

Pathologic Processes: The abnormal mechanisms and forms involved in the dysfunctions of tissues and organs. [NIH]

Patient Education: The teaching or training of patients concerning their own health needs. [NIH]

PDQ: Physician Data Query. PDQ is an online database developed and maintained by the National Cancer Institute. Designed to make the most current, credible, and accurate cancer information available to health professionals and the public, PDQ contains peer-reviewed summaries on cancer treatment, screening, prevention, genetics, and supportive care; a registry of cancer clinical trials from around the world; and directories of physicians, professionals who provide genetics services, and organizations that provide cancer care. Most of this information is available on the CancerNet Web site, and more specific information about PDQ can be found at http://cancernet.nci.nih.gov/pdq.html. [NIH]

Pelvic: Pertaining to the pelvis. [EU]

Penicillamine: 3-Mercapto-D-valine. The most characteristic degradation product of the penicillin antibiotics. It is used as an antirheumatic and as a chelating agent in Wilson's disease. [NIH]

Penicillin: An antibiotic drug used to treat infection. [NIH]

Penis: The external reproductive organ of males. It is composed of a mass of erectile tissue enclosed in three cylindrical fibrous compartments. Two of the three compartments, the corpus cavernosa, are placed side-by-side along the upper part of the organ. The third compartment below, the corpus spongiosum, houses the urethra. [NIH]

Pentamidine: Antiprotozoal agent effective in trypanosomiasis, leishmaniasis, and some fungal infections; used in treatment of Pneumocystis carinii pneumonia in HIV-infected patients. It may cause diabetes mellitus, central nervous system damage, and other toxic effects. [NIH]

Peptide: Any compound consisting of two or more amino acids, the building blocks of proteins. Peptides are combined to make proteins. [NIH]

Peptide Fragments: Partial proteins formed by partial hydrolysis of complete proteins. [NIH]

Perception: The ability quickly and accurately to recognize similarities and differences among presented objects, whether these be pairs of words, pairs of number series, or multiple sets of these or other symbols such as geometric figures. [NIH]

Perfusion: Bathing an organ or tissue with a fluid. In regional perfusion, a specific area of the body (usually an arm or a leg) receives high doses of anticancer drugs through a blood vessel. Such a procedure is performed to treat cancer that has not spread. [NIH]

Pericardium: The fibroserous sac surrounding the heart and the roots of the great vessels. [NIH]

Perinatal: Pertaining to or occurring in the period shortly before and after birth; variously defined as beginning with completion of the twentieth to twenty-eighth week of gestation and ending 7 to 28 days after birth. [EU]

Periodontal disease: Disease involving the supporting structures of the teeth (as the gums and periodontal membranes). [NIH]

Periodontal disease: Disease involving the supporting structures of the teeth (as the gums and periodontal membranes). [NIH]

Periodontitis: Inflammation of the periodontal membrane; also called periodontitis simplex. [NIH]

Peripheral blood: Blood circulating throughout the body. [NIH]

Peripheral Neuropathy: Nerve damage, usually affecting the feet and legs; causing pain, numbness, or a tingling feeling. Also called "somatic neuropathy" or "distal sensory polyneuropathy." [NIH]

Perivascular: Situated around a vessel. [EU]

Petroleum: Naturally occurring complex liquid hydrocarbons which, after distillation, yield combustible fuels, petrochemicals, and lubricants. [NIH]

P-Glycoprotein: A 170 kD transmembrane glycoprotein from the superfamily of ABC transporters. It serves as an ATP-dependent efflux pump for a variety of chemicals, including many antineoplastic agents. Overexpression of this glycoprotein is associated with multidrug resistance. [NIH]

PH: The symbol relating the hydrogen ion (H+) concentration or activity of a solution to that of a given standard solution. Numerically the pH is approximately equal to the negative logarithm of H+ concentration expressed in molarity. pH 7 is neutral; above it alkalinity increases and below it acidity increases. [EU]

Phagocytosis: The engulfing of microorganisms, other cells, and foreign particles by phagocytic cells. [NIH]

Pharmaceutical Services: Total pharmaceutical services provided by a qualified pharmacist. In addition to the preparation and distribution of medical products, they may include consultative services provided to agencies and institutions which do not have a qualified pharmacist. [NIH]

Pharmacist: A person trained to prepare and distribute medicines and to give information about them. [NIH]

Pharmacokinetic: The mathematical analysis of the time courses of absorption, distribution, and elimination of drugs. [NIH]

Pharmacologic: Pertaining to pharmacology or to the properties and reactions of drugs. [EU]

Pharynx: The hollow tube about 5 inches long that starts behind the nose and ends at the top of the trachea (windpipe) and esophagus (the tube that goes to the stomach). [NIH]

Phenotype: The outward appearance of the individual. It is the product of interactions between genes and between the genotype and the environment. This includes the killer phenotype, characteristic of yeasts. [NIH]

Phenytoin: An anticonvulsant that is used in a wide variety of seizures. It is also an anti-arrhythmic and a muscle relaxant. The mechanism of therapeutic action is not clear, although several cellular actions have been described including effects on ion channels, active transport, and general membrane stabilization. The mechanism of its muscle relaxant effect appears to involve a reduction in the sensitivity of muscle spindles to stretch. Phenytoin has been proposed for several other therapeutic uses, but its use has been limited by its many adverse effects and interactions with other drugs. [NIH]

Phorbol: Class of chemicals that promotes the development of tumors. [NIH]

Phorbol Esters: Tumor-promoting compounds obtained from croton oil (Croton tiglium). Some of these are used in cell biological experiments as activators of protein kinase C. [NIH]

Phospholipases: A class of enzymes that catalyze the hydrolysis of phosphoglycerides or

glycerophosphatidates. EC 3.1.-. [NIH]

Phospholipids: Lipids containing one or more phosphate groups, particularly those derived from either glycerol (phosphoglycerides; glycerophospholipids) or sphingosine (sphingolipids). They are polar lipids that are of great importance for the structure and function of cell membranes and are the most abundant of membrane lipids, although not stored in large amounts in the system. [NIH]

Phosphorus: A non-metallic element that is found in the blood, muscles, nevers, bones, and teeth, and is a component of adenosine triphosphate (ATP; the primary energy source for the body's cells.) [NIH]

Phosphorylates: Attached to a phosphate group. [NIH]

Photocoagulation: Using a special strong beam of light (laser) to seal off bleeding blood vessels such as in the eye. The laser can also burn away blood vessels that should not have grown in the eye. This is the main treatment for diabetic retinopathy. [NIH]

Phototherapy: Treatment of disease by exposure to light, especially by variously concentrated light rays or specific wavelengths. [NIH]

Phylogeny: The relationships of groups of organisms as reflected by their evolutionary history. [NIH]

Physiologic: Having to do with the functions of the body. When used in the phrase "physiologic age," it refers to an age assigned by general health, as opposed to calendar age. [NIH]

Physiology: The science that deals with the life processes and functions of organismus, their cells, tissues, and organs. [NIH]

Phytotoxin: A substance which is toxic for plants. [NIH]

Pigments: Any normal or abnormal coloring matter in plants, animals, or micro-organisms. [NIH]

Pilot study: The initial study examining a new method or treatment. [NIH]

Placenta: A highly vascular fetal organ through which the fetus absorbs oxygen and other nutrients and excretes carbon dioxide and other wastes. It begins to form about the eighth day of gestation when the blastocyst adheres to the decidua. [NIH]

Plants: Multicellular, eukaryotic life forms of the kingdom Plantae. They are characterized by a mainly photosynthetic mode of nutrition; essentially unlimited growth at localized regions of cell divisions (meristems); cellulose within cells providing rigidity; the absence of organs of locomotion; absense of nervous and sensory systems; and an alteration of haploid and diploid generations. [NIH]

Plasma: The clear, yellowish, fluid part of the blood that carries the blood cells. The proteins that form blood clots are in plasma. [NIH]

Plasma cells: A type of white blood cell that produces antibodies. [NIH]

Plasma protein: One of the hundreds of different proteins present in blood plasma, including carrier proteins (such albumin, transferrin, and haptoglobin), fibrinogen and other coagulation factors, complement components, immunoglobulins, enzyme inhibitors, precursors of substances such as angiotension and bradykinin, and many other types of proteins. [EU]

Plasmid: An autonomously replicating, extra-chromosomal DNA molecule found in many bacteria. Plasmids are widely used as carriers of cloned genes. [NIH]

Platelet Activation: A series of progressive, overlapping events triggered by exposure of the platelets to subendothelial tissue. These events include shape change, adhesiveness,

aggregation, and release reactions. When carried through to completion, these events lead to the formation of a stable hemostatic plug. [NIH]

Platinum: Platinum. A heavy, soft, whitish metal, resembling tin, atomic number 78, atomic weight 195.09, symbol Pt. (From Dorland, 28th ed) It is used in manufacturing equipment for laboratory and industrial use. It occurs as a black powder (platinum black) and as a spongy substance (spongy platinum) and may have been known in Pliny's time as "alutiae". [NIH]

Pleura: The thin serous membrane enveloping the lungs and lining the thoracic cavity. [NIH]

Pleural: A circumscribed area of hyaline whorled fibrous tissue which appears on the surface of the parietal pleura, on the fibrous part of the diaphragm or on the pleura in the interlobar fissures. [NIH]

Pleural cavity: A space enclosed by the pleura (thin tissue covering the lungs and lining the interior wall of the chest cavity). It is bound by thin membranes. [NIH]

Pleural Effusion: Presence of fluid in the pleural cavity resulting from excessive transudation or exudation from the pleural surfaces. It is a sign of disease and not a diagnosis in itself. [NIH]

Pneumonia: Inflammation of the lungs. [NIH]

Point Mutation: A mutation caused by the substitution of one nucleotide for another. This results in the DNA molecule having a change in a single base pair. [NIH]

Poison Control Centers: Facilities which provide information concerning poisons and treatment of poisoning in emergencies. [NIH]

Poisoning: A condition or physical state produced by the ingestion, injection or inhalation of, or exposure to a deleterious agent. [NIH]

Policy Making: The decision process by which individuals, groups or institutions establish policies pertaining to plans, programs or procedures. [NIH]

Polycystic: An inherited disorder characterized by many grape-like clusters of fluid-filled cysts that make both kidneys larger over time. These cysts take over and destroy working kidney tissue. PKD may cause chronic renal failure and end-stage renal disease. [NIH]

Polycystic Ovary Syndrome: Clinical symptom complex characterized by oligomenorrhea or amenorrhea, anovulation, and regularly associated with bilateral polycystic ovaries. [NIH]

Polyethylene: A vinyl polymer made from ethylene. It can be branched or linear. Branched or low-density polyethylene is tough and pliable but not to the same degree as linear polyethylene. Linear or high-density polyethylene has a greater hardness and tensile strength. Polyethylene is used in a variety of products, including implants and prostheses. [NIH]

Polyethylene Glycols: Alpha-Hydro-omega-hydroxypoly(oxy-1,2-ethanediyls). Additional polymers of ethylene oxide and water and their ethers. They vary in consistency from liquid to solid, depending on the molecular weight, indicated by a number following the name. Used as surfactants in industry, including foods, cosmetics and pharmaceutics; in biomedicine, as dispersing agents, solvents, ointment and suppository bases, vehicles, tablet excipients. Some specific groups are lauromagrogols, nonoxynols, octoxynols and poloxamers. [NIH]

Polymerase: An enzyme which catalyses the synthesis of DNA using a single DNA strand as a template. The polymerase copies the template in the 5'-3'direction provided that sufficient quantities of free nucleotides, dATP and dTTP are present. [NIH]

Polymerase Chain Reaction: In vitro method for producing large amounts of specific DNA or RNA fragments of defined length and sequence from small amounts of short

oligonucleotide flanking sequences (primers). The essential steps include thermal denaturation of the double-stranded target molecules, annealing of the primers to their complementary sequences, and extension of the annealed primers by enzymatic synthesis with DNA polymerase. The reaction is efficient, specific, and extremely sensitive. Uses for the reaction include disease diagnosis, detection of difficult-to-isolate pathogens, mutation analysis, genetic testing, DNA sequencing, and analyzing evolutionary relationships. [NIH]

Polymers: Compounds formed by the joining of smaller, usually repeating, units linked by covalent bonds. These compounds often form large macromolecules (e.g., polypeptides, proteins, plastics). [NIH]

Polymorphic: Occurring in several or many forms; appearing in different forms at different stages of development. [EU]

Polymorphism: The occurrence together of two or more distinct forms in the same population. [NIH]

Polyneuritis: Inflammation of several peripheral nerves at the same time. [NIH]

Polysaccharide: A type of carbohydrate. It contains sugar molecules that are linked together chemically. [NIH]

Porphyrins: A group of compounds containing the porphin structure, four pyrrole rings connected by methine bridges in a cyclic configuration to which a variety of side chains are attached. The nature of the side chain is indicated by a prefix, as uroporphyrin, hematoporphyrin, etc. The porphyrins, in combination with iron, form the heme component in biologically significant compounds such as hemoglobin and myoglobin. [NIH]

Posterior: Situated in back of, or in the back part of, or affecting the back or dorsal surface of the body. In lower animals, it refers to the caudal end of the body. [EU]

Postmenopausal: Refers to the time after menopause. Menopause is the time in a woman's life when menstrual periods stop permanently; also called "change of life." [NIH]

Postsynaptic: Nerve potential generated by an inhibitory hyperpolarizing stimulation. [NIH]

Potentiate: A degree of synergism which causes the exposure of the organism to a harmful substance to worsen a disease already contracted. [NIH]

Potentiation: An overall effect of two drugs taken together which is greater than the sum of the effects of each drug taken alone. [NIH]

Practicability: A non-standard characteristic of an analytical procedure. It is dependent on the scope of the method and is determined by requirements such as sample throughout and costs. [NIH]

Practice Guidelines: Directions or principles presenting current or future rules of policy for the health care practitioner to assist him in patient care decisions regarding diagnosis, therapy, or related clinical circumstances. The guidelines may be developed by government agencies at any level, institutions, professional societies, governing boards, or by the convening of expert panels. The guidelines form a basis for the evaluation of all aspects of health care and delivery. [NIH]

Precipitation: The act or process of precipitating. [EU]

Preclinical: Before a disease becomes clinically recognizable. [EU]

Precursor: Something that precedes. In biological processes, a substance from which another, usually more active or mature substance is formed. In clinical medicine, a sign or symptom that heralds another. [EU]

Prednisolone: A glucocorticoid with the general properties of the corticosteroids. It is the drug of choice for all conditions in which routine systemic corticosteroid therapy is

indicated, except adrenal deficiency states. [NIH]

Prednisone: A synthetic anti-inflammatory glucocorticoid derived from cortisone. It is biologically inert and converted to prednisolone in the liver. [NIH]

Prejudice: A preconceived judgment made without adequate evidence and not easily alterable by presentation of contrary evidence. [NIH]

Prenatal: Existing or occurring before birth, with reference to the fetus. [EU]

Prenatal Care: Care provided the pregnant woman in order to prevent complications, and decrease the incidence of maternal and prenatal mortality. [NIH]

Preoperative: Preceding an operation. [EU]

Prevalence: The total number of cases of a given disease in a specified population at a designated time. It is differentiated from incidence, which refers to the number of new cases in the population at a given time. [NIH]

Prickle: Several layers of the epidermis where the individual cells are connected by cell bridges. [NIH]

Probe: An instrument used in exploring cavities, or in the detection and dilatation of strictures, or in demonstrating the potency of channels; an elongated instrument for exploring or sounding body cavities. [NIH]

Progeny: The offspring produced in any generation. [NIH]

Progesterone: Pregn-4-ene-3,20-dione. The principal progestational hormone of the body, secreted by the corpus luteum, adrenal cortex, and placenta. Its chief function is to prepare the uterus for the reception and development of the fertilized ovum. It acts as an antiovulatory agent when administered on days 5-25 of the menstrual cycle. [NIH]

Program Evaluation: Studies designed to assess the efficacy of programs. They may include the evaluation of cost-effectiveness, the extent to which objectives are met, or impact. [NIH]

Progression: Increase in the size of a tumor or spread of cancer in the body. [NIH]

Progressive: Advancing; going forward; going from bad to worse; increasing in scope or severity. [EU]

Proline: A non-essential amino acid that is synthesized from glutamic acid. It is an essential component of collagen and is important for proper functioning of joints and tendons. [NIH]

Promoter: A chemical substance that increases the activity of a carcinogenic process. [NIH]

Pro-Opiomelanocortin: A precursor protein, MW 30,000, synthesized mainly in the anterior pituitary gland but also found in the hypothalamus, brain, and several peripheral tissues. It incorporates the amino acid sequences of ACTH and beta-lipotropin. These two hormones, in turn, contain the biologically active peptides MSH, corticotropin-like intermediate lobe peptide, alpha-lipotropin, endorphins, and methionine enkephalin. [NIH]

Prophase: The first phase of cell division, in which the chromosomes become visible, the nucleus starts to lose its identity, the spindle appears, and the centrioles migrate toward opposite poles. [NIH]

Prophylaxis: An attempt to prevent disease. [NIH]

Proportional: Being in proportion : corresponding in size, degree, or intensity, having the same or a constant ratio; of, relating to, or used in determining proportions. [EU]

Prospective study: An epidemiologic study in which a group of individuals (a cohort), all free of a particular disease and varying in their exposure to a possible risk factor, is followed over a specific amount of time to determine the incidence rates of the disease in the exposed and unexposed groups. [NIH]

Prostaglandins: A group of compounds derived from unsaturated 20-carbon fatty acids, primarily arachidonic acid, via the cyclooxygenase pathway. They are extremely potent mediators of a diverse group of physiological processes. [NIH]

Prostate: A gland in males that surrounds the neck of the bladder and the urethra. It secretes a substance that liquifies coagulated semen. It is situated in the pelvic cavity behind the lower part of the pubic symphysis, above the deep layer of the triangular ligament, and rests upon the rectum. [NIH]

Prostitution: The practice of indulging in promiscuous sexual relations for money. [NIH]

Protease: Proteinase (= any enzyme that catalyses the splitting of interior peptide bonds in a protein). [EU]

Protease Inhibitors: Compounds which inhibit or antagonize biosynthesis or actions of proteases (endopeptidases). [NIH]

Protein C: A vitamin-K dependent zymogen present in the blood, which, upon activation by thrombin and thrombomodulin exerts anticoagulant properties by inactivating factors Va and VIIIa at the rate-limiting steps of thrombin formation. [NIH]

Protein Conformation: The characteristic 3-dimensional shape of a protein, including the secondary, supersecondary (motifs), tertiary (domains) and quaternary structure of the peptide chain. Quaternary protein structure describes the conformation assumed by multimeric proteins (aggregates of more than one polypeptide chain). [NIH]

Protein Kinase C: An enzyme that phosphorylates proteins on serine or threonine residues in the presence of physiological concentrations of calcium and membrane phospholipids. The additional presence of diacylglycerols markedly increases its sensitivity to both calcium and phospholipids. The sensitivity of the enzyme can also be increased by phorbol esters and it is believed that protein kinase C is the receptor protein of tumor-promoting phorbol esters. EC 2.7.1.-. [NIH]

Protein S: The vitamin K-dependent cofactor of activated protein C. Together with protein C, it inhibits the action of factors VIIIa and Va. A deficiency in protein S can lead to recurrent venous and arterial thrombosis. [NIH]

Protein Subunits: Single chains of amino acids that are the units of a multimeric protein. They can be identical or non-identical subunits. [NIH]

Protein-Energy Malnutrition: The lack of sufficient energy or protein to meet the body's metabolic demands, as a result of either an inadequate dietary intake of protein, intake of poor quality dietary protein, increased demands due to disease, or increased nutrient losses. [NIH]

Proteins: Polymers of amino acids linked by peptide bonds. The specific sequence of amino acids determines the shape and function of the protein. [NIH]

Protein-Tyrosine Kinase: An enzyme that catalyzes the phosphorylation of tyrosine residues in proteins with ATP or other nucleotides as phosphate donors. EC 2.7.1.112. [NIH]

Proteolytic: 1. Pertaining to, characterized by, or promoting proteolysis. 2. An enzyme that promotes proteolysis (= the splitting of proteins by hydrolysis of the peptide bonds with formation of smaller polypeptides). [EU]

Protocol: The detailed plan for a clinical trial that states the trial's rationale, purpose, drug or vaccine dosages, length of study, routes of administration, who may participate, and other aspects of trial design. [NIH]

Protons: Stable elementary particles having the smallest known positive charge, found in the nuclei of all elements. The proton mass is less than that of a neutron. A proton is the nucleus of the light hydrogen atom, i.e., the hydrogen ion. [NIH]

Proto-Oncogene Proteins: Products of proto-oncogenes. Normally they do not have oncogenic or transforming properties, but are involved in the regulation or differentiation of cell growth. They often have protein kinase activity. [NIH]

Proto-Oncogene Proteins c-mos: Cellular proteins encoded by the c-mos genes. They function in the cell cycle to maintain maturation promoting factor in the active state and have protein-serine/threonine kinase activity. Oncogenic transformation can take place when c-mos proteins are expressed at the wrong time. [NIH]

Protozoa: A subkingdom consisting of unicellular organisms that are the simplest in the animal kingdom. Most are free living. They range in size from submicroscopic to macroscopic. Protozoa are divided into seven phyla: Sarcomastigophora, Labyrinthomorpha, Apicomplexa, Microspora, Ascetospora, Myxozoa, and Ciliophora. [NIH]

Protozoan: 1. Any individual of the protozoa; protozoon. 2. Of or pertaining to the protozoa; protozoal. [EU]

Provirus: Virus that is integrated into the chromosome of a host cell and is transmitted in that form from one host cell generation to another without leading to the lysis of the host cells. [NIH]

Proximal: Nearest; closer to any point of reference; opposed to distal. [EU]

Psychiatric: Pertaining to or within the purview of psychiatry. [EU]

Psychiatry: The medical science that deals with the origin, diagnosis, prevention, and treatment of mental disorders. [NIH]

Psychic: Pertaining to the psyche or to the mind; mental. [EU]

Psychoactive: Those drugs which alter sensation, mood, consciousness or other psychological or behavioral functions. [NIH]

Psychology: The science dealing with the study of mental processes and behavior in man and animals. [NIH]

Psychomotor: Pertaining to motor effects of cerebral or psychic activity. [EU]

Psychosis: A mental disorder characterized by gross impairment in reality testing as evidenced by delusions, hallucinations, markedly incoherent speech, or disorganized and agitated behaviour without apparent awareness on the part of the patient of the incomprehensibility of his behaviour; the term is also used in a more general sense to refer to mental disorders in which mental functioning is sufficiently impaired as to interfere grossly with the patient's capacity to meet the ordinary demands of life. Historically, the term has been applied to many conditions, e.g. manic-depressive psychosis, that were first described in psychotic patients, although many patients with the disorder are not judged psychotic. [EU]

Psychotherapy: A generic term for the treatment of mental illness or emotional disturbances primarily by verbal or nonverbal communication. [NIH]

Public Health: Branch of medicine concerned with the prevention and control of disease and disability, and the promotion of physical and mental health of the population on the international, national, state, or municipal level. [NIH]

Public Policy: A course or method of action selected, usually by a government, from among alternatives to guide and determine present and future decisions. [NIH]

Pulmonary: Relating to the lungs. [NIH]

Pulmonary Artery: The short wide vessel arising from the conus arteriosus of the right ventricle and conveying unaerated blood to the lungs. [NIH]

Pulmonary hypertension: Abnormally high blood pressure in the arteries of the lungs. [NIH]

Pulse: The rhythmical expansion and contraction of an artery produced by waves of pressure caused by the ejection of blood from the left ventricle of the heart as it contracts. [NIH]

Purines: A series of heterocyclic compounds that are variously substituted in nature and are known also as purine bases. They include adenine and guanine, constituents of nucleic acids, as well as many alkaloids such as caffeine and theophylline. Uric acid is the metabolic end product of purine metabolism. [NIH]

Purpura: Purplish or brownish red discoloration, easily visible through the epidermis, caused by hemorrhage into the tissues. [NIH]

Purulent: Consisting of or containing pus; associated with the formation of or caused by pus. [EU]

Pyogenic: Producing pus; pyopoietic (= liquid inflammation product made up of cells and a thin fluid called liquor puris). [EU]

Pyrazinamide: A pyrazine that is used therapeutically as an antitubercular agent. [NIH]

Pyridoxal: 3-Hydroxy-5-(hydroxymethyl)-2-methyl-4- pyridinecarboxaldehyde. [NIH]

Pyrimidines: A family of 6-membered heterocyclic compounds occurring in nature in a wide variety of forms. They include several nucleic acid constituents (cytosine, thymine, and uracil) and form the basic structure of the barbiturates. [NIH]

Quality of Life: A generic concept reflecting concern with the modification and enhancement of life attributes, e.g., physical, political, moral and social environment. [NIH]

Rabies: A highly fatal viral infection of the nervous system which affects all warm-blooded animal species. It is one of the most important of the zoonoses because of the inevitably fatal outcome for the infected human. [NIH]

Race: A population within a species which exhibits general similarities within itself, but is both discontinuous and distinct from other populations of that species, though not sufficiently so as to achieve the status of a taxon. [NIH]

Radiation: Emission or propagation of electromagnetic energy (waves/rays), or the waves/rays themselves; a stream of electromagnetic particles (electrons, neutrons, protons, alpha particles) or a mixture of these. The most common source is the sun. [NIH]

Radiation therapy: The use of high-energy radiation from x-rays, gamma rays, neutrons, and other sources to kill cancer cells and shrink tumors. Radiation may come from a machine outside the body (external-beam radiation therapy), or it may come from radioactive material placed in the body in the area near cancer cells (internal radiation therapy, implant radiation, or brachytherapy). Systemic radiation therapy uses a radioactive substance, such as a radiolabeled monoclonal antibody, that circulates throughout the body. Also called radiotherapy. [NIH]

Radioactive: Giving off radiation. [NIH]

Radioisotope: An unstable element that releases radiation as it breaks down. Radioisotopes can be used in imaging tests or as a treatment for cancer. [NIH]

Radiopharmaceutical: Any medicinal product which, when ready for use, contains one or more radionuclides (radioactive isotopes) included for a medicinal purpose. [NIH]

Randomized: Describes an experiment or clinical trial in which animal or human subjects are assigned by chance to separate groups that compare different treatments. [NIH]

Randomized clinical trial: A study in which the participants are assigned by chance to separate groups that compare different treatments; neither the researchers nor the participants can choose which group. Using chance to assign people to groups means that

the groups will be similar and that the treatments they receive can be compared objectively. At the time of the trial, it is not known which treatment is best. It is the patient's choice to be in a randomized trial. [NIH]

Reactivation: The restoration of activity to something that has been inactivated. [EU]

Reagent: A substance employed to produce a chemical reaction so as to detect, measure, produce, etc., other substances. [EU]

Reality Testing: The individual's objective evaluation of the external world and the ability to differentiate adequately between it and the internal world; considered to be a primary ego function. [NIH]

Receptor: A molecule inside or on the surface of a cell that binds to a specific substance and causes a specific physiologic effect in the cell. [NIH]

Recombinant: A cell or an individual with a new combination of genes not found together in either parent; usually applied to linked genes. [EU]

Recombinant Proteins: Proteins prepared by recombinant DNA technology. [NIH]

Recombination: The formation of new combinations of genes as a result of segregation in crosses between genetically different parents; also the rearrangement of linked genes due to crossing-over. [NIH]

Reconstitution: 1. A type of regeneration in which a new organ forms by the rearrangement of tissues rather than from new formation at an injured surface. 2. The restoration to original form of a substance previously altered for preservation and storage, as the restoration to a liquid state of blood serum or plasma that has been dried and stored. [EU]

Rectal: By or having to do with the rectum. The rectum is the last 8 to 10 inches of the large intestine and ends at the anus. [NIH]

Rectum: The last 8 to 10 inches of the large intestine. [NIH]

Recurrence: The return of a sign, symptom, or disease after a remission. [NIH]

Red blood cells: RBCs. Cells that carry oxygen to all parts of the body. Also called erythrocytes. [NIH]

Red Nucleus: A pinkish-yellow portion of the midbrain situated in the rostral mesencephalic tegmentum. It receives a large projection from the contralateral half of the cerebellum via the superior cerebellar peduncle and a projection from the ipsilateral motor cortex. [NIH]

Reductase: Enzyme converting testosterone to dihydrotestosterone. [NIH]

Refer: To send or direct for treatment, aid, information, de decision. [NIH]

Refraction: A test to determine the best eyeglasses or contact lenses to correct a refractive error (myopia, hyperopia, or astigmatism). [NIH]

Regeneration: The natural renewal of a structure, as of a lost tissue or part. [EU]

Regimen: A treatment plan that specifies the dosage, the schedule, and the duration of treatment. [NIH]

Reinfection: A second infection by the same pathogenic agent, or a second infection of an organ such as the kidney by a different pathogenic agent. [EU]

Relapse: The return of signs and symptoms of cancer after a period of improvement. [NIH]

Relaxation Techniques: The use of muscular relaxation techniques in treatment. [NIH]

Reliability: Used technically, in a statistical sense, of consistency of a test with itself, i. e. the extent to which we can assume that it will yield the same result if repeated a second time. [NIH]

Remission: A decrease in or disappearance of signs and symptoms of cancer. In partial remission, some, but not all, signs and symptoms of cancer have disappeared. In complete remission, all signs and symptoms of cancer have disappeared, although there still may be cancer in the body. [NIH]

Renal failure: Progressive renal insufficiency and uremia, due to irreversible and progressive renal glomerular tubular or interstitial disease. [NIH]

Replicon: In order to be replicated, DNA molecules must contain an origin of duplication and in bacteria and viruses there is usually only one per genome. Such molecules are called replicons. [NIH]

Repressor: Any of the specific allosteric protein molecules, products of regulator genes, which bind to the operator of operons and prevent RNA polymerase from proceeding into the operon to transcribe messenger RNA. [NIH]

Research Design: A plan for collecting and utilizing data so that desired information can be obtained with sufficient precision or so that an hypothesis can be tested properly. [NIH]

Research Support: Financial support of research activities. [NIH]

Resident physician: A physician who lives in a hospital and is constantly available, as an intern. [NIH]

Respiration: The act of breathing with the lungs, consisting of inspiration, or the taking into the lungs of the ambient air, and of expiration, or the expelling of the modified air which contains more carbon dioxide than the air taken in (Blakiston's Gould Medical Dictionary, 4th ed.). This does not include tissue respiration (= oxygen consumption) or cell respiration (= cell respiration). [NIH]

Restoration: Broad term applied to any inlay, crown, bridge or complete denture which restores or replaces loss of teeth or oral tissues. [NIH]

Retina: The ten-layered nervous tissue membrane of the eye. It is continuous with the optic nerve and receives images of external objects and transmits visual impulses to the brain. Its outer surface is in contact with the choroid and the inner surface with the vitreous body. The outer-most layer is pigmented, whereas the inner nine layers are transparent. [NIH]

Retinal: 1. Pertaining to the retina. 2. The aldehyde of retinol, derived by the oxidative enzymatic splitting of absorbed dietary carotene, and having vitamin A activity. In the retina, retinal combines with opsins to form visual pigments. One isomer, 11-cis retinal combines with opsin in the rods (scotopsin) to form rhodopsin, or visual purple. Another, all-trans retinal (trans-r.); visual yellow; xanthopsin) results from the bleaching of rhodopsin by light, in which the 11-cis form is converted to the all-trans form. Retinal also combines with opsins in the cones (photopsins) to form the three pigments responsible for colour vision. Called also retinal, and retinene1. [EU]

Retinal Neovascularization: Formation of new blood vessels originating from the retinal veins and extending along the inner (vitreal) surface of the retina. [NIH]

Retinal Vein: Central retinal vein and its tributaries. It runs a short course within the optic nerve and then leaves and empties into the superior ophthalmic vein or cavernous sinus. [NIH]

Retinitis: Inflammation of the retina. It is rarely limited to the retina, but is commonly associated with diseases of the choroid (chorioretinitis) and of the optic nerve (neuroretinitis). The disease may be confined to one eye, but since it is generally dependent on a constitutional factor, it is almost always bilateral. It may be acute in course, but as a rule it lasts many weeks or even several months. [NIH]

Retinoblastoma: An eye cancer that most often occurs in children younger than 5 years. It

occurs in hereditary and nonhereditary (sporadic) forms. [NIH]

Retinoids: Derivatives of vitamin A. Used clinically in the treatment of severe cystic acne, psoriasis, and other disorders of keratinization. Their possible use in the prophylaxis and treatment of cancer is being actively explored. [NIH]

Retinol: Vitamin A. It is essential for proper vision and healthy skin and mucous membranes. Retinol is being studied for cancer prevention; it belongs to the family of drugs called retinoids. [NIH]

Retroviral vector: RNA from a virus that is used to insert genetic material into cells. [NIH]

Retrovirus: A member of a group of RNA viruses, the RNA of which is copied during viral replication into DNA by reverse transcriptase. The viral DNA is then able to be integrated into the host chromosomal DNA. [NIH]

Reverse Transcriptase Inhibitors: Inhibitors of reverse transcriptase (RNA-directed DNA polymerase), an enzyme that synthesizes DNA on an RNA template. [NIH]

Rhinitis: Inflammation of the mucous membrane of the nose. [NIH]

Rhodopsin: A photoreceptor protein found in retinal rods. It is a complex formed by the binding of retinal, the oxidized form of retinol, to the protein opsin and undergoes a series of complex reactions in response to visible light resulting in the transmission of nerve impulses to the brain. [NIH]

Ribavirin: 1-beta-D-Ribofuranosyl-1H-1,2,4-triazole-3-carboxamide. A nucleoside antimetabolite antiviral agent that blocks nucleic acid synthesis and is used against both RNA and DNA viruses. [NIH]

Ribonuclease: RNA-digesting enzyme. [NIH]

Ribonucleic acid: RNA. One of the two nucleic acids found in all cells. The other is deoxyribonucleic acid (DNA). Ribonucleic acid transfers genetic information from DNA to proteins produced by the cell. [NIH]

Ribonucleoside Diphosphate Reductase: An enzyme of the oxidoreductase class that catalyzes the formation of 2'-deoxyribonucleotides from the corresponding ribonucleotides using NADPH as the ultimate electron donor. The deoxyribonucleoside diphosphates are used in DNA synthesis. (From Dorland, 27th ed) EC 1.17.4.1. [NIH]

Ribosome: A granule of protein and RNA, synthesized in the nucleolus and found in the cytoplasm of cells. Ribosomes are the main sites of protein synthesis. Messenger RNA attaches to them and there receives molecules of transfer RNA bearing amino acids. [NIH]

Ricin: A protein phytotoxin from the seeds of Ricinus communis, the castor oil plant. It agglutinates cells, is proteolytic, and causes lethal inflammation and hemorrhage if taken internally. [NIH]

Rigidity: Stiffness or inflexibility, chiefly that which is abnormal or morbid; rigor. [EU]

Risk factor: A habit, trait, condition, or genetic alteration that increases a person's chance of developing a disease. [NIH]

Risk patient: Patient who is at risk, because of his/her behaviour or because of the type of person he/she is. [EU]

Risk-Taking: Undertaking a task involving a challenge for achievement or a desirable goal in which there is a lack of certainty or a fear of failure. It may also include the exhibiting of certain behaviors whose outcomes may present a risk to the individual or to those associated with him or her. [NIH]

Ritonavir: An HIV protease inhibitor that works by interfering with the reproductive cycle of HIV. [NIH]

Rituximab: A type of monoclonal antibody used in cancer detection or therapy. Monoclonal antibodies are laboratory-produced substances that can locate and bind to cancer cells. [NIH]

Rod: A reception for vision, located in the retina. [NIH]

Role-play: In this method, a conflict is artificially constructed, and the trainee is given a strategic position in it. [NIH]

Rural Health: The status of health in rural populations. [NIH]

Rural Population: The inhabitants of rural areas or of small towns classified as rural. [NIH]

Saliva: The clear, viscous fluid secreted by the salivary glands and mucous glands of the mouth. It contains mucins, water, organic salts, and ptylin. [NIH]

Salivary: The duct that convey saliva to the mouth. [NIH]

Salivary glands: Glands in the mouth that produce saliva. [NIH]

Salmonella: A genus of gram-negative, facultatively anaerobic, rod-shaped bacteria that utilizes citrate as a sole carbon source. It is pathogenic for humans, causing enteric fevers, gastroenteritis, and bacteremia. Food poisoning is the most common clinical manifestation. Organisms within this genus are separated on the basis of antigenic characteristics, sugar fermentation patterns, and bacteriophage susceptibility. [NIH]

Salvage Therapy: A therapeutic approach, involving chemotherapy, radiation therapy, or surgery, after initial regimens have failed to lead to improvement in a patient's condition. Salvage therapy is most often used for neoplastic diseases. [NIH]

Sanitation: The development and establishment of environmental conditions favorable to the health of the public. [NIH]

Saponin: A substance found in soybeans and many other plants. Saponins may help lower cholesterol and may have anticancer effects. [NIH]

Sarcoma: A connective tissue neoplasm formed by proliferation of mesodermal cells; it is usually highly malignant. [NIH]

Schizoid: Having qualities resembling those found in greater degree in schizophrenics; a person of schizoid personality. [NIH]

Schizophrenia: A mental disorder characterized by a special type of disintegration of the personality. [NIH]

Schizotypal Personality Disorder: A personality disorder in which there are oddities of thought (magical thinking, paranoid ideation, suspiciousness), perception (illusions, depersonalization), speech (digressive, vague, overelaborate), and behavior (inappropriate affect in social interactions, frequently social isolation) that are not severe enough to characterize schizophrenia. [NIH]

Sclera: The tough white outer coat of the eyeball, covering approximately the posterior five-sixths of its surface, and continuous anteriorly with the cornea and posteriorly with the external sheath of the optic nerve. [EU]

Sclerosis: A pathological process consisting of hardening or fibrosis of an anatomical structure, often a vessel or a nerve. [NIH]

Scrapie: A fatal disease of the nervous system in sheep and goats, characterized by pruritus, debility, and locomotor incoordination. It is caused by proteinaceous infectious particles called prions. [NIH]

Screening: Checking for disease when there are no symptoms. [NIH]

Scrub Typhus: An acute infectious disease caused by Orientia tsutsugamushi. It is limited to eastern and southeastern Asia, India, northern Australia, and the adjacent islands.

Characteristics include the formation of a primary cutaneous lesion at the site of the bite of an infected mite, fever lasting about two weeks, and a maculopapular rash. [NIH]

Secretion: 1. The process of elaborating a specific product as a result of the activity of a gland; this activity may range from separating a specific substance of the blood to the elaboration of a new chemical substance. 2. Any substance produced by secretion. [EU]

Secretory: Secreting; relating to or influencing secretion or the secretions. [NIH]

Segregation: The separation in meiotic cell division of homologous chromosome pairs and their contained allelomorphic gene pairs. [NIH]

Seizures: Clinical or subclinical disturbances of cortical function due to a sudden, abnormal, excessive, and disorganized discharge of brain cells. Clinical manifestations include abnormal motor, sensory and psychic phenomena. Recurrent seizures are usually referred to as epilepsy or "seizure disorder." [NIH]

Selenium: An element with the atomic symbol Se, atomic number 34, and atomic weight 78.96. It is an essential micronutrient for mammals and other animals but is toxic in large amounts. Selenium protects intracellular structures against oxidative damage. It is an essential component of glutathione peroxidase. [NIH]

Self-Help Groups: Organizations which provide an environment encouraging social interactions through group activities or individual relationships especially for the purpose of rehabilitating or supporting patients, individuals with common health problems, or the elderly. They include therapeutic social clubs. [NIH]

Semen: The thick, yellowish-white, viscid fluid secretion of male reproductive organs discharged upon ejaculation. In addition to reproductive organ secretions, it contains spermatozoa and their nutrient plasma. [NIH]

Senile: Relating or belonging to old age; characteristic of old age; resulting from infirmity of old age. [NIH]

Septicaemia: A term originally used to denote a putrefactive process in the body, but now usually referring to infection with pyogenic micro-organisms; a genus of Diptera; the severe type of infection in which the blood stream is invaded by large numbers of the causal. [NIH]

Sequence Analysis: A multistage process that includes the determination of a sequence (protein, carbohydrate, etc.), its fragmentation and analysis, and the interpretation of the resulting sequence information. [NIH]

Sequence Homology: The degree of similarity between sequences. Studies of amino acid and nucleotide sequences provide useful information about the genetic relatedness of certain species. [NIH]

Sequencing: The determination of the order of nucleotides in a DNA or RNA chain. [NIH]

Serine: A non-essential amino acid occurring in natural form as the L-isomer. It is synthesized from glycine or threonine. It is involved in the biosynthesis of purines, pyrimidines, and other amino acids. [NIH]

Seroconversion: The change of a serologic test from negative to positive, indicating the development of antibodies in response to infection or immunization. [EU]

Serologic: Analysis of a person's serum, especially specific immune or lytic serums. [NIH]

Serotypes: A cause of haemorrhagic septicaemia (in cattle, sheep and pigs), fowl cholera of birds, pasteurellosis of rabbits, and gangrenous mastitis of ewes. It is also commonly found in atrophic rhinitis of pigs. [NIH]

Serum: The clear liquid part of the blood that remains after blood cells and clotting proteins have been removed. [NIH]

Sex Behavior: Sexual activities of humans. [NIH]

Sex Characteristics: Those characteristics that distinguish one sex from the other. The primary sex characteristics are the ovaries and testes and their related hormones. Secondary sex characteristics are those which are masculine or feminine but not directly related to reproduction. [NIH]

Sex Determination: The biological characteristics which distinguish human beings as female or male. [NIH]

Sex Education: Education which increases the knowledge of the functional, structural, and behavioral aspects of human reproduction. [NIH]

Sexual Abstinence: Refraining from sexual intercourse. [NIH]

Sexual Partners: Married or single individuals who share sexual relations. [NIH]

Sexually Transmitted Diseases: Diseases due to or propagated by sexual contact. [NIH]

Shame: An emotional attitude excited by realization of a shortcoming or impropriety. [NIH]

Shedding: Release of infectious particles (e. g., bacteria, viruses) into the environment, for example by sneezing, by fecal excretion, or from an open lesion. [NIH]

Shock: The general bodily disturbance following a severe injury; an emotional or moral upset occasioned by some disturbing or unexpected experience; disruption of the circulation, which can upset all body functions: sometimes referred to as circulatory shock. [NIH]

Side effect: A consequence other than the one(s) for which an agent or measure is used, as the adverse effects produced by a drug, especially on a tissue or organ system other than the one sought to be benefited by its administration. [EU]

Signal Transduction: The intercellular or intracellular transfer of information (biological activation/inhibition) through a signal pathway. In each signal transduction system, an activation/inhibition signal from a biologically active molecule (hormone, neurotransmitter) is mediated via the coupling of a receptor/enzyme to a second messenger system or to an ion channel. Signal transduction plays an important role in activating cellular functions, cell differentiation, and cell proliferation. Examples of signal transduction systems are the GABA-postsynaptic receptor-calcium ion channel system, the receptor-mediated T-cell activation pathway, and the receptor-mediated activation of phospholipases. Those coupled to membrane depolarization or intracellular release of calcium include the receptor-mediated activation of cytotoxic functions in granulocytes and the synaptic potentiation of protein kinase activation. Some signal transduction pathways may be part of larger signal transduction pathways; for example, protein kinase activation is part of the platelet activation signal pathway. [NIH]

Signs and Symptoms: Clinical manifestations that can be either objective when observed by a physician, or subjective when perceived by the patient. [NIH]

Sindbis Virus: The type species of alphavirus normally transmitted to birds by Culex mosquitoes in Egypt, South Africa, India, Malaya, the Philippines, and Australia. It may be associated with fever in humans. [NIH]

SIV: Species of the genus Lentivirus, subgenus primate immunodeficiency viruses, that induces acquired immunodeficiency syndrome in monkeys and apes (SAIDS). The genetic organization of SIV is virtually identical to HIV. SIV is 50% homologous in nucleotide sequence to HIV-1. SIV and HIV-2 exhibit close structural and immunologic properties and are 75% homologous. SIV does not cause immune deficiency in its natural host, the African green monkey, but does produce SAIDS in the rhesus macaque. Subgroups of SIV include SIV-1 and SIV-2. [NIH]

Skeletal: Having to do with the skeleton (boney part of the body). [NIH]

Skeleton: The framework that supports the soft tissues of vertebrate animals and protects many of their internal organs. The skeletons of vertebrates are made of bone and/or cartilage. [NIH]

Skin test: A test for an immune response to a compound by placing it on or under the skin. [NIH]

Skin Transplantation: The grafting of skin in humans or animals from one site to another to replace a lost portion of the body surface skin. [NIH]

Skull: The skeleton of the head including the bones of the face and the bones enclosing the brain. [NIH]

Small intestine: The part of the digestive tract that is located between the stomach and the large intestine. [NIH]

Smallpox: A generalized virus infection with a vesicular rash. [NIH]

Smooth muscle: Muscle that performs automatic tasks, such as constricting blood vessels. [NIH]

Sneezing: Sudden, forceful, involuntary expulsion of air from the nose and mouth caused by irritation to the mucous membranes of the upper respiratory tract. [NIH]

Social Behavior: Any behavior caused by or affecting another individual, usually of the same species. [NIH]

Social Environment: The aggregate of social and cultural institutions, forms, patterns, and processes that influence the life of an individual or community. [NIH]

Social pressure: A strategy used in behavior therapy in which individuals are told that they possess the basic self-control ability to lose weight, but that coming to group meetings will strengthen their abilities. The group is asked to listen and give advice, similar to the way many self-help groups, based on social support, operate. [NIH]

Social Support: Support systems that provide assistance and encouragement to individuals with physical or emotional disabilities in order that they may better cope. Informal social support is usually provided by friends, relatives, or peers, while formal assistance is provided by churches, groups, etc. [NIH]

Social Welfare: Organized institutions which provide services to ameliorate conditions of need or social pathology in the community. [NIH]

Social Work: The use of community resources, individual case work, or group work to promote the adaptive capacities of individuals in relation to their social and economic environments. It includes social service agencies. [NIH]

Sodium: An element that is a member of the alkali group of metals. It has the atomic symbol Na, atomic number 11, and atomic weight 23. With a valence of 1, it has a strong affinity for oxygen and other nonmetallic elements. Sodium provides the chief cation of the extracellular body fluids. Its salts are the most widely used in medicine. (From Dorland, 27th ed) Physiologically the sodium ion plays a major role in blood pressure regulation, maintenance of fluid volume, and electrolyte balance. [NIH]

Sodium Channels: Cell membrane glycoproteins selective for sodium ions. Fast sodium current is associated with the action potential in neural membranes. [NIH]

Soft tissue: Refers to muscle, fat, fibrous tissue, blood vessels, or other supporting tissue of the body. [NIH]

Solvent: 1. Dissolving; effecting a solution. 2. A liquid that dissolves or that is capable of dissolving; the component of a solution that is present in greater amount. [EU]

Soma: The body as distinct from the mind; all the body tissue except the germ cells; all the axial body. [NIH]

Somatic: 1. Pertaining to or characteristic of the soma or body. 2. Pertaining to the body wall in contrast to the viscera. [EU]

Somatic cells: All the body cells except the reproductive (germ) cells. [NIH]

Specialist: In medicine, one who concentrates on 1 special branch of medical science. [NIH]

Species: A taxonomic category subordinate to a genus (or subgenus) and superior to a subspecies or variety, composed of individuals possessing common characters distinguishing them from other categories of individuals of the same taxonomic level. In taxonomic nomenclature, species are designated by the genus name followed by a Latin or Latinized adjective or noun. [EU]

Specificity: Degree of selectivity shown by an antibody with respect to the number and types of antigens with which the antibody combines, as well as with respect to the rates and the extents of these reactions. [NIH]

Spectrum: A charted band of wavelengths of electromagnetic vibrations obtained by refraction and diffraction. By extension, a measurable range of activity, such as the range of bacteria affected by an antibiotic (antibacterial s.) or the complete range of manifestations of a disease. [EU]

Sperm: The fecundating fluid of the male. [NIH]

Spinal cord: The main trunk or bundle of nerves running down the spine through holes in the spinal bone (the vertebrae) from the brain to the level of the lower back. [NIH]

Spinous: Like a spine or thorn in shape; having spines. [NIH]

Spirochete: Lyme disease. [NIH]

Spleen: An organ that is part of the lymphatic system. The spleen produces lymphocytes, filters the blood, stores blood cells, and destroys old blood cells. It is located on the left side of the abdomen near the stomach. [NIH]

Sporadic: Neither endemic nor epidemic; occurring occasionally in a random or isolated manner. [EU]

Squamous: Scaly, or platelike. [EU]

Squamous cell carcinoma: Cancer that begins in squamous cells, which are thin, flat cells resembling fish scales. Squamous cells are found in the tissue that forms the surface of the skin, the lining of the hollow organs of the body, and the passages of the respiratory and digestive tracts. Also called epidermoid carcinoma. [NIH]

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Squamous cells: Flat cells that look like fish scales under a microscope. These cells cover internal and external surfaces of the body. [NIH]

Squamous intraepithelial lesion: SIL. A general term for the abnormal growth of squamous cells on the surface of the cervix. The changes in the cells are described as low grade or high grade, depending on how much of the cervix is affected and how abnormal the cells appear. [NIH]

Stabilization: The creation of a stable state. [EU]

Stavudine: A dideoxynucleoside analog that inhibits reverse transcriptase and has in vitro activity against HIV. [NIH]

Steady state: Dynamic equilibrium. [EU]

Stem cell transplantation: A method of replacing immature blood-forming cells that were destroyed by cancer treatment. The stem cells are given to the person after treatment to help the bone marrow recover and continue producing healthy blood cells. [NIH]

Stem Cells: Relatively undifferentiated cells of the same lineage (family type) that retain the ability to divide and cycle throughout postnatal life to provide cells that can become specialized and take the place of those that die or are lost. [NIH]

Sterile: Unable to produce children. [NIH]

Sterility: 1. The inability to produce offspring, i.e., the inability to conceive (female s.) or to induce conception (male s.). 2. The state of being aseptic, or free from microorganisms. [EU]

Sterilization: The destroying of all forms of life, especially microorganisms, by heat, chemical, or other means. [NIH]

Steroid: A group name for lipids that contain a hydrogenated cyclopentanoperhydrophenanthrene ring system. Some of the substances included in this group are progesterone, adrenocortical hormones, the gonadal hormones, cardiac aglycones, bile acids, sterols (such as cholesterol), toad poisons, saponins, and some of the carcinogenic hydrocarbons. [EU]

Stimulant: 1. Producing stimulation; especially producing stimulation by causing tension on muscle fibre through the nervous tissue. 2. An agent or remedy that produces stimulation. [EU]

Stimulus: That which can elicit or evoke action (response) in a muscle, nerve, gland or other excitable issue, or cause an augmenting action upon any function or metabolic process. [NIH]

Stomach: An organ of digestion situated in the left upper quadrant of the abdomen between the termination of the esophagus and the beginning of the duodenum. [NIH]

Stomatitis: Inflammation of the oral mucosa, due to local or systemic factors which may involve the buccal and labial mucosa, palate, tongue, floor of the mouth, and the gingivae. [EU]

Stool: The waste matter discharged in a bowel movement; feces. [NIH]

Strand: DNA normally exists in the bacterial nucleus in a helix, in which two strands are coiled together. [NIH]

Streptavidin: A 60kD extracellular protein of Streptomyces avidinii with four high-affinity biotin binding sites. Unlike AVIDIN, streptavidin has a near neutral isoelectric point and is free of carbohydrate side chains. [NIH]

Stress: Forcibly exerted influence; pressure. Any condition or situation that causes strain or tension. Stress may be either physical or psychologic, or both. [NIH]

Stroke: Sudden loss of function of part of the brain because of loss of blood flow. Stroke may be caused by a clot (thrombosis) or rupture (hemorrhage) of a blood vessel to the brain. [NIH]

Stromal: Large, veil-like cell in the bone marrow. [NIH]

Subacute: Somewhat acute; between acute and chronic. [EU]

Subarachnoid: Situated or occurring between the arachnoid and the pia mater. [EU]

Subclinical: Without clinical manifestations; said of the early stage(s) of an infection or other disease or abnormality before symptoms and signs become apparent or detectable by clinical examination or laboratory tests, or of a very mild form of an infection or other disease or abnormality. [EU]

Subculture: A culture derived from another culture or the aseptic division and transfer of a culture or a portion of that culture (inoculum) to fresh nutrient medium. [NIH]

Subcutaneous: Beneath the skin. [NIH]

Submandibular: Four to six lymph glands, located between the lower jaw and the submandibular salivary gland. [NIH]

Subspecies: A category intermediate in rank between species and variety, based on a smaller number of correlated characters than are used to differentiate species and generally conditioned by geographical and/or ecological occurrence. [NIH]

Substance P: An eleven-amino acid neurotransmitter that appears in both the central and peripheral nervous systems. It is involved in transmission of pain, causes rapid contractions of the gastrointestinal smooth muscle, and modulates inflammatory and immune responses. [NIH]

Substrate: A substance upon which an enzyme acts. [EU]

Substrate Specificity: A characteristic feature of enzyme activity in relation to the kind of substrate on which the enzyme or catalytic molecule reacts. [NIH]

Sulfur: An element that is a member of the chalcogen family. It has an atomic symbol S, atomic number 16, and atomic weight 32.066. It is found in the amino acids cysteine and methionine. [NIH]

Superantigens: Microbial antigens that have in common an extremely potent activating effect on T-cells that bear a specific variable region. Superantigens cross-link the variable region with class II MHC proteins regardless of the peptide binding in the T-cell receptor's pocket. The result is a transient expansion and subsequent death and anergy of the T-cells with the appropriate variable regions. [NIH]

Superinfection: A frequent complication of drug therapy for microbial infection. It may result from opportunistic colonization following immunosuppression by the primary pathogen and can be influenced by the time interval between infections, microbial physiology, or host resistance. Experimental challenge and in vitro models are sometimes used in virulence and infectivity studies. [NIH]

Supplementation: Adding nutrients to the diet. [NIH]

Support group: A group of people with similar disease who meet to discuss how better to cope with their cancer and treatment. [NIH]

Supportive care: Treatment given to prevent, control, or relieve complications and side effects and to improve the comfort and quality of life of people who have cancer. [NIH]

Suppositories: A small cone-shaped medicament having cocoa butter or gelatin at its basis and usually intended for the treatment of local conditions in the rectum. [NIH]

Suppository: A medicated mass adapted for introduction into the rectal, vaginal, or urethral orifice of the body, suppository bases are solid at room temperature but melt or dissolve at body temperature. Commonly used bases are cocoa butter, glycerinated gelatin, hydrogenated vegetable oils, polyethylene glycols of various molecular weights, and fatty acid esters of polyethylene glycol. [EU]

Suppression: A conscious exclusion of disapproved desire contrary with repression, in which the process of exclusion is not conscious. [NIH]

Suppressive: Tending to suppress : effecting suppression; specifically : serving to suppress activity, function, symptoms. [EU]

Sympathomimetic: 1. Mimicking the effects of impulses conveyed by adrenergic postganglionic fibres of the sympathetic nervous system. 2. An agent that produces effects similar to those of impulses conveyed by adrenergic postganglionic fibres of the sympathetic nervous system. Called also adrenergic. [EU]

Symphysis: A secondary cartilaginous joint. [NIH]

Symptomatic: Having to do with symptoms, which are signs of a condition or disease. [NIH]

Synapse: The region where the processes of two neurons come into close contiguity, and the nervous impulse passes from one to the other; the fibers of the two are intermeshed, but, according to the general view, there is no direct contiguity. [NIH]

Synapsis: The pairing between homologous chromosomes of maternal and paternal origin during the prophase of meiosis, leading to the formation of gametes. [NIH]

Synaptic: Pertaining to or affecting a synapse (= site of functional apposition between neurons, at which an impulse is transmitted from one neuron to another by electrical or chemical means); pertaining to synapsis (= pairing off in point-for-point association of homologous chromosomes from the male and female pronuclei during the early prophase of meiosis). [EU]

Syncytium: A living nucleated tissue without apparent cellular structure; a tissue composed of a mass of nucleated protoplasm without cell boundaries. [NIH]

Syphilis: A contagious venereal disease caused by the spirochete Treponema pallidum. [NIH]

Systemic: Affecting the entire body. [NIH]

Systemic lupus erythematosus: SLE. A chronic inflammatory connective tissue disease marked by skin rashes, joint pain and swelling, inflammation of the kidneys, inflammation of the fibrous tissue surrounding the heart (i.e., the pericardium), as well as other problems. Not all affected individuals display all of these problems. May be referred to as lupus. [NIH]

Taboo: Any negative tradition or behavior that is generally regarded as harmful to social welfare and forbidden within a cultural or social group. [NIH]

Tachycardia: Excessive rapidity in the action of the heart, usually with a heart rate above 100 beats per minute. [NIH]

Tachypnea: Rapid breathing. [NIH]

Tacrolimus: A macrolide isolated from the culture broth of a strain of Streptomyces tsukubaensis that has strong immunosuppressive activity in vivo and prevents the activation of T-lymphocytes in response to antigenic or mitogenic stimulation in vitro. [NIH]

Tailing: The modification of some forms of HnRNA following transcription by the addition of between 10 and 20 adenosine residues to the 3'-end. [NIH]

Tamponade: The inserting of a tampon; a dressing is inserted firmly into a wound or body cavity, as the nose, uterus or vagina, principally for stopping hemorrhage. [NIH]

Telangiectasia: The permanent enlargement of blood vessels, causing redness in the skin or mucous membranes. [NIH]

Telomerase: Essential ribonucleoprotein reverse transcriptase that adds telomeric DNA to the ends of eukaryotic chromosomes. Telomerase appears to be repressed in normal human somatic tissues but reactivated in cancer, and thus may be necessary for malignant transformation. EC 2.7.7.-. [NIH]

Temporal: One of the two irregular bones forming part of the lateral surfaces and base of the skull, and containing the organs of hearing. [NIH]

Terminator: A DNA sequence sited at the end of a transcriptional unit that signals the end of transcription. [NIH]

Testis: Either of the paired male reproductive glands that produce the male germ cells and the male hormones. [NIH]

Testosterone: A hormone that promotes the development and maintenance of male sex characteristics. [NIH]

Thalamic: Cell that reaches the lateral nucleus of amygdala. [NIH]

Thalamic Diseases: Disorders of the centrally located thalamus, which integrates a wide range of cortical and subcortical information. Manifestations include sensory loss, movement disorders; ataxia, pain syndromes, visual disorders, a variety of neuropsychological conditions, and coma. Relatively common etiologies include cerebrovascular disorders; craniocerebral trauma; brain neoplasms; brain hypoxia; intracranial hemorrhages; and infectious processes. [NIH]

Therapeutics: The branch of medicine which is concerned with the treatment of diseases, palliative or curative. [NIH]

Thermal: Pertaining to or characterized by heat. [EU]

Thigh: A leg; in anatomy, any elongated process or part of a structure more or less comparable to a leg. [NIH]

Thiourea: A photographic fixative used also in the manufacture of resins. According to the Fourth Annual Report on Carcinogens (NTP 85-002, 1985), this substance may reasonably be anticipated to be a carcinogen (Merck Index, 9th ed). Many of its derivatives are antithryoid agents and/or free radical scavengers. [NIH]

Threonine: An essential amino acid occurring naturally in the L-form, which is the active form. It is found in eggs, milk, gelatin, and other proteins. [NIH]

Thrombin: An enzyme formed from prothrombin that converts fibrinogen to fibrin. (Dorland, 27th ed) EC 3.4.21.5. [NIH]

Thrombocytopenia: A decrease in the number of blood platelets. [NIH]

Thrombomodulin: A cell surface glycoprotein of endothelial cells that binds thrombin and serves as a cofactor in the activation of protein C and its regulation of blood coagulation. [NIH]

Thrombopenia: Reduction in the number of platelets in the blood. [NIH]

Thromboses: The formation or presence of a blood clot within a blood vessel during life. [NIH]

Thrombosis: The formation or presence of a blood clot inside a blood vessel. [NIH]

Thromboxanes: Physiologically active compounds found in many organs of the body. They are formed in vivo from the prostaglandin endoperoxides and cause platelet aggregation, contraction of arteries, and other biological effects. Thromboxanes are important mediators of the actions of polyunsaturated fatty acids transformed by cyclooxygenase. [NIH]

Thrombus: An aggregation of blood factors, primarily platelets and fibrin with entrapment of cellular elements, frequently causing vascular obstruction at the point of its formation. Some authorities thus differentiate thrombus formation from simple coagulation or clot formation. [EU]

Thrush: A disease due to infection with species of fungi of the genus Candida. [NIH]

Thymidine: A chemical compound found in DNA. Also used as treatment for mucositis. [NIH]

Thymidine Kinase: An enzyme that catalyzes the conversion of ATP and thymidine to ADP and thymidine 5'-phosphate. Deoxyuridine can also act as an acceptor and dGTP as a donor. (From Enzyme Nomenclature, 1992) EC 2.7.1.21. [NIH]

Thymosin: A family of heat-stable, polypeptide hormones secreted by the thymus gland. Their biological activities include lymphocytopoiesis, restoration of immunological

competence and enhancement of expression of T-cell characteristics and function. They have therapeutic potential in patients having primary or secondary immunodeficiency diseases, cancer or diseases related to aging. [NIH]

Thymus: An organ that is part of the lymphatic system, in which T lymphocytes grow and multiply. The thymus is in the chest behind the breastbone. [NIH]

Thymus Extracts: Extracts of the thymus that contain specific, but uncharacterized factors or proteins with specific activities; three distinct substances are already known: thymotoxin, thymin and thymosin. [NIH]

Thyroid: A gland located near the windpipe (trachea) that produces thyroid hormone, which helps regulate growth and metabolism. [NIH]

Thyrotropin: A peptide hormone secreted by the anterior pituitary. It promotes the growth of the thyroid gland and stimulates the synthesis of thyroid hormones and the release of thyroxine by the thyroid gland. [NIH]

Ticks: Blood-sucking arachnids of the order Acarina. [NIH]

Tinnitus: Sounds that are perceived in the absence of any external noise source which may take the form of buzzing, ringing, clicking, pulsations, and other noises. Objective tinnitus refers to noises generated from within the ear or adjacent structures that can be heard by other individuals. The term subjective tinnitus is used when the sound is audible only to the affected individual. Tinnitus may occur as a manifestation of cochlear diseases; vestibulocochlear nerve diseases; intracranial hypertension; craniocerebral trauma; and other conditions. [NIH]

Tissue: A group or layer of cells that are alike in type and work together to perform a specific function. [NIH]

Tissue Culture: Maintaining or growing of tissue, organ primordia, or the whole or part of an organ in vitro so as to preserve its architecture and/or function (Dorland, 28th ed). Tissue culture includes both organ culture and cell culture. [NIH]

Tolerance: 1. The ability to endure unusually large doses of a drug or toxin. 2. Acquired drug tolerance; a decreasing response to repeated constant doses of a drug or the need for increasing doses to maintain a constant response. [EU]

Topical: On the surface of the body. [NIH]

Toxic: Having to do with poison or something harmful to the body. Toxic substances usually cause unwanted side effects. [NIH]

Toxicity: The quality of being poisonous, especially the degree of virulence of a toxic microbe or of a poison. [EU]

Toxicology: The science concerned with the detection, chemical composition, and pharmacologic action of toxic substances or poisons and the treatment and prevention of toxic manifestations. [NIH]

Toxin: A poison; frequently used to refer specifically to a protein produced by some higher plants, certain animals, and pathogenic bacteria, which is highly toxic for other living organisms. Such substances are differentiated from the simple chemical poisons and the vegetable alkaloids by their high molecular weight and antigenicity. [EU]

Toxoplasmosis: The acquired form of infection by Toxoplasma gondii in animals and man. [NIH]

Trachea: The cartilaginous and membranous tube descending from the larynx and branching into the right and left main bronchi. [NIH]

Transaminase: Aminotransferase (= a subclass of enzymes of the transferase class that

catalyse the transfer of an amino group from a donor (generally an amino acid) to an acceptor (generally 2-keto acid). Most of these enzymes are pyridoxal-phosphate-proteins. [EU]

Transcriptase: An enzyme which catalyses the synthesis of a complementary mRNA molecule from a DNA template in the presence of a mixture of the four ribonucleotides (ATP, UTP, GTP and CTP). [NIH]

Transcription Factors: Endogenous substances, usually proteins, which are effective in the initiation, stimulation, or termination of the genetic transcription process. [NIH]

Transduction: The transfer of genes from one cell to another by means of a viral (in the case of bacteria, a bacteriophage) vector or a vector which is similar to a virus particle (pseudovirion). [NIH]

Transfection: The uptake of naked or purified DNA into cells, usually eukaryotic. It is analogous to bacterial transformation. [NIH]

Transfer Factor: Factor derived from leukocyte lysates of immune donors which can transfer both local and systemic cellular immunity to nonimmune recipients. [NIH]

Transferases: Transferases are enzymes transferring a group, for example, the methyl group or a glycosyl group, from one compound (generally regarded as donor) to another compound (generally regarded as acceptor). The classification is based on the scheme "donor:acceptor group transferase". (Enzyme Nomenclature, 1992) EC 2. [NIH]

Transfusion: The infusion of components of blood or whole blood into the bloodstream. The blood may be donated from another person, or it may have been taken from the person earlier and stored until needed. [NIH]

Translation: The process whereby the genetic information present in the linear sequence of ribonucleotides in mRNA is converted into a corresponding sequence of amino acids in a protein. It occurs on the ribosome and is unidirectional. [NIH]

Translational: The cleavage of signal sequence that directs the passage of the protein through a cell or organelle membrane. [NIH]

Translocation: The movement of material in solution inside the body of the plant. [NIH]

Transmitter: A chemical substance which effects the passage of nerve impulses from one cell to the other at the synapse. [NIH]

Transplantation: Transference of a tissue or organ, alive or dead, within an individual, between individuals of the same species, or between individuals of different species. [NIH]

Trauma: Any injury, wound, or shock, must frequently physical or structural shock, producing a disturbance. [NIH]

Treatment Failure: A measure of the quality of health care by assessment of unsuccessful results of management and procedures used in combating disease, in individual cases or series. [NIH]

Treatment Outcome: Evaluation undertaken to assess the results or consequences of management and procedures used in combating disease in order to determine the efficacy, effectiveness, safety, practicability, etc., of these interventions in individual cases or series. [NIH]

Trichomoniasis: An infection with the protozoan parasite Trichomonas vaginalis. [NIH]

Triglyceride: A lipid carried through the blood stream to tissues. Most of the body's fat tissue is in the form of triglycerides, stored for use as energy. Triglycerides are obtained primarily from fat in foods. [NIH]

Trimethoprim-sulfamethoxazole: An antibiotic drug used to treat infection and prevent

pneumocystis carinii pneumonia. [NIH]

Tropism: Directed movements and orientations found in plants, such as the turning of the sunflower to face the sun. [NIH]

Trypanosomiasis: Infection with protozoa of the genus Trypanosoma. [NIH]

Trypsin: A serine endopeptidase that is formed from trypsinogen in the pancreas. It is converted into its active form by enteropeptidase in the small intestine. It catalyzes hydrolysis of the carboxyl group of either arginine or lysine. EC 3.4.21.4. [NIH]

Trypsin Inhibitors: Serine proteinase inhibitors which inhibit trypsin. They may be endogenous or exogenous compounds. [NIH]

Tubercle: A rounded elevation on a bone or other structure. [NIH]

Tuberculin: A sterile liquid containing the growth products of, or specific substances extracted from, the tubercle bacillus; used in various forms in the diagnosis of tuberculosis. [NIH]

Tuberculostatic: Inhibiting the growth of Mycobacterium tuberculosis. [EU]

Tuberous Sclerosis: A rare congenital disease in which the essential pathology is the appearance of multiple tumors in the cerebrum and in other organs, such as the heart or kidneys. [NIH]

Tumor marker: A substance sometimes found in an increased amount in the blood, other body fluids, or tissues and which may mean that a certain type of cancer is in the body. Examples of tumor markers include CA 125 (ovarian cancer), CA 15-3 (breast cancer), CEA (ovarian, lung, breast, pancreas, and gastrointestinal tract cancers), and PSA (prostate cancer). Also called biomarker. [NIH]

Tumor Necrosis Factor: Serum glycoprotein produced by activated macrophages and other mammalian mononuclear leukocytes which has necrotizing activity against tumor cell lines and increases ability to reject tumor transplants. It mimics the action of endotoxin but differs from it. It has a molecular weight of less than 70,000 kDa. [NIH]

Tunica: A rather vague term to denote the lining coat of hollow organs, tubes, or cavities. [NIH]

Ulcer: A localized necrotic lesion of the skin or a mucous surface. [NIH]

Unconscious: Experience which was once conscious, but was subsequently rejected, as the "personal unconscious". [NIH]

Universal Precautions: Prudent standard preventive measures to be taken by professional and other health personnel in contact with persons afflicted with a communicable disease, to avoid contracting the disease by contagion or infection. Precautions are especially applicable in the diagnosis and care of AIDS patients. [NIH]

Uracil: An anticancer drug that belongs to the family of drugs called alkylating agents. [NIH]

Urban Population: The inhabitants of a city or town, including metropolitan areas and suburban areas. [NIH]

Urea: A compound (CO(NH2)2), formed in the liver from ammonia produced by the deamination of amino acids. It is the principal end product of protein catabolism and constitutes about one half of the total urinary solids. [NIH]

Ureters: Tubes that carry urine from the kidneys to the bladder. [NIH]

Urethra: The tube through which urine leaves the body. It empties urine from the bladder. [NIH]

Urinary: Having to do with urine or the organs of the body that produce and get rid of urine. [NIH]

Urinary tract: The organs of the body that produce and discharge urine. These include the kidneys, ureters, bladder, and urethra. [NIH]

Urinary tract infection: An illness caused by harmful bacteria growing in the urinary tract. [NIH]

Urine: Fluid containing water and waste products. Urine is made by the kidneys, stored in the bladder, and leaves the body through the urethra. [NIH]

Urogenital: Pertaining to the urinary and genital apparatus; genitourinary. [EU]

Uterine Contraction: Contraction of the uterine muscle. [NIH]

Uterus: The small, hollow, pear-shaped organ in a woman's pelvis. This is the organ in which a fetus develops. Also called the womb. [NIH]

Uvea: The middle coat of the eyeball, consisting of the choroid in the back of the eye and the ciliary body and iris in the front of the eye. [NIH]

Uveitis: An inflammation of part or all of the uvea, the middle (vascular) tunic of the eye, and commonly involving the other tunics (the sclera and cornea, and the retina). [EU]

Vaccination: Administration of vaccines to stimulate the host's immune response. This includes any preparation intended for active immunological prophylaxis. [NIH]

Vaccine: A substance or group of substances meant to cause the immune system to respond to a tumor or to microorganisms, such as bacteria or viruses. [NIH]

Vaccinia: The cutaneous and occasional systemic reactions associated with vaccination using smallpox (variola) vaccine. [NIH]

Vaccinia Virus: The type species of Orthopoxvirus, related to cowpox virus, but whose true origin is unknown. It has been used as a live vaccine against smallpox. It is also used as a vector for inserting foreign DNA into animals. Rabbitpox virus is a subspecies of vaccinia virus. [NIH]

Vacuoles: Any spaces or cavities within a cell. They may function in digestion, storage, secretion, or excretion. [NIH]

Vagina: The muscular canal extending from the uterus to the exterior of the body. Also called the birth canal. [NIH]

Vaginal: Of or having to do with the vagina, the birth canal. [NIH]

Vaginitis: Inflammation of the vagina characterized by pain and a purulent discharge. [NIH]

Valine: A branched-chain essential amino acid that has stimulant activity. It promotes muscle growth and tissue repair. It is a precursor in the penicillin biosynthetic pathway. [NIH]

Valproic Acid: A fatty acid with anticonvulsant properties used in the treatment of epilepsy. The mechanisms of its therapeutic actions are not well understood. It may act by increasing GABA levels in the brain or by altering the properties of voltage dependent sodium channels. [NIH]

Variola: A generalized virus infection with a vesicular rash. [NIH]

Vascular: Pertaining to blood vessels or indicative of a copious blood supply. [EU]

VE: The total volume of gas either inspired or expired in one minute. [NIH]

Vector: Plasmid or other self-replicating DNA molecule that transfers DNA between cells in nature or in recombinant DNA technology. [NIH]

Vein: Vessel-carrying blood from various parts of the body to the heart. [NIH]

Venereal: Pertaining or related to or transmitted by sexual contact. [EU]

Venous: Of or pertaining to the veins. [EU]

Ventricles: Fluid-filled cavities in the heart or brain. [NIH]

Vertigo: An illusion of movement; a sensation as if the external world were revolving around the patient (objective vertigo) or as if he himself were revolving in space (subjective vertigo). The term is sometimes erroneously used to mean any form of dizziness. [EU]

Very low-calorie diet: Very low-calorie diet. The VLCD of 800 (approximately 6-10 kcal/kg body weight) or fewer calories per day is conducted under physician supervision and monitoring and is restricted to severely obese persons. [NIH]

Vesicular: 1. Composed of or relating to small, saclike bodies. 2. Pertaining to or made up of vesicles on the skin. [EU]

Veterinary Medicine: The medical science concerned with the prevention, diagnosis, and treatment of diseases in animals. [NIH]

Video Recording: The storing or preserving of video signals for television to be played back later via a transmitter or receiver. Recordings may be made on magnetic tape or discs (videodisc recording). [NIH]

Videodisc Recording: The storing of visual and usually sound signals on discs for later reproduction on a television screen or monitor. [NIH]

Viral: Pertaining to, caused by, or of the nature of virus. [EU]

Viral Hepatitis: Hepatitis caused by a virus. Five different viruses (A, B, C, D, and E) most commonly cause this form of hepatitis. Other rare viruses may also cause hepatitis. [NIH]

Viral Load: The quantity of measurable virus in the blood. Change in viral load, measured in plasma, is used as a surrogate marker in HIV disease progression. [NIH]

Viral Proteins: Proteins found in any species of virus. [NIH]

Viral Regulatory Proteins: Proteins which regulate the rate of transcription of viral structural genes. [NIH]

Viral Structural Proteins: Viral proteins that do not regulate transcription. They are coded by viral structural genes and include nucleocapsid core proteins (gag proteins), enzymes (pol proteins), and membrane components (env proteins). Transcription of viral structural genes is regulated by viral regulatory proteins. [NIH]

Viremia: The presence of viruses in the blood. [NIH]

Virion: The infective system of a virus, composed of the viral genome, a protein core, and a protein coat called a capsid, which may be naked or enclosed in a lipoprotein envelope called the peplos. [NIH]

Virulence: The degree of pathogenicity within a group or species of microorganisms or viruses as indicated by case fatality rates and/or the ability of the organism to invade the tissues of the host. [NIH]

Virus: Submicroscopic organism that causes infectious disease. In cancer therapy, some viruses may be made into vaccines that help the body build an immune response to, and kill, tumor cells. [NIH]

Virus Diseases: A general term for diseases produced by viruses. [NIH]

Virus Latency: The ability of a pathogenic virus to lie dormant within a cell (latent infection). In eukaryotes, subsequent activation and viral replication is thought to be caused by extracellular stimulation of cellular transcription factors. Latency in bacteriophage is maintained by the expression of virally encoded repressors. [NIH]

Virus Replication: The process of intracellular viral multiplication, consisting of the

synthesis of proteins, nucleic acids, and sometimes lipids, and their assembly into a new infectious particle. [NIH]

Virus Shedding: The expelling of virus particles from the body. Important routes include the respiratory tract, genital tract, and intestinal tract. Virus shedding is an important means of vertical transmission (disease transmission, vertical). [NIH]

Viscera: Any of the large interior organs in any one of the three great cavities of the body, especially in the abdomen. [NIH]

Visceral: , from viscus a viscus) pertaining to a viscus. [EU]

Visna: Demyelinating leukoencephalomyelitis of sheep caused by the Visna-Maedi virus. It is similiar to but not the same as scrapie. [NIH]

Vitamin A: A substance used in cancer prevention; it belongs to the family of drugs called retinoids. [NIH]

Vitreous: Glasslike or hyaline; often used alone to designate the vitreous body of the eye (corpus vitreum). [EU]

Vitro: Descriptive of an event or enzyme reaction under experimental investigation occurring outside a living organism. Parts of an organism or microorganism are used together with artificial substrates and/or conditions. [NIH]

Vivo: Outside of or removed from the body of a living organism. [NIH]

War: Hostile conflict between organized groups of people. [NIH]

Warts: Benign epidermal proliferations or tumors; some are viral in origin. [NIH]

Weight Gain: Increase in body weight over existing weight. [NIH]

White blood cell: A type of cell in the immune system that helps the body fight infection and disease. White blood cells include lymphocytes, granulocytes, macrophages, and others. [NIH]

Windpipe: A rigid tube, 10 cm long, extending from the cricoid cartilage to the upper border of the fifth thoracic vertebra. [NIH]

Withdrawal: 1. A pathological retreat from interpersonal contact and social involvement, as may occur in schizophrenia, depression, or schizoid avoidant and schizotypal personality disorders. 2. (DSM III-R) A substance-specific organic brain syndrome that follows the cessation of use or reduction in intake of a psychoactive substance that had been regularly used to induce a state of intoxication. [EU]

Xenograft: The cells of one species transplanted to another species. [NIH]

X-ray: High-energy radiation used in low doses to diagnose diseases and in high doses to treat cancer. [NIH]

Yeasts: A general term for single-celled rounded fungi that reproduce by budding. Brewers' and bakers' yeasts are Saccharomyces cerevisiae; therapeutic dried yeast is dried yeast. [NIH]

Zalcitabine: A dideoxynucleoside compound in which the 3'-hydroxy group on the sugar moiety has been replaced by a hydrogen. This modification prevents the formation of phosphodiester linkages which are needed for the completion of nucleic acid chains. The compound is a potent inhibitor of HIV replication at low concentrations, acting as a chain-terminator of viral DNA by binding to reverse transcriptase. Its principal toxic side effect is axonal degeneration resulting in peripheral neuropathy. [NIH]

Zidovudine: A dideoxynucleoside compound in which the 3'-hydroxy group on the sugar moiety has been replaced by an azido group. This modification prevents the formation of phosphodiester linkages which are needed for the completion of nucleic acid chains. The compound is a potent inhibitor of HIV replication, acting as a chain-terminator of viral DNA

during reverse transcription. It improves immunologic function, partially reverses the HIV-induced neurological dysfunction, and improves certain other clinical abnormalities associated with AIDS. Its principal toxic effect is dose-dependent suppression of bone marrow, resulting in anemia and leukopenia. [NIH]

Zoonoses: Diseases of non-human animals that may be transmitted to man or may be transmitted from man to non-human animals. [NIH]

Zoster: A virus infection of the Gasserian ganglion and its nerve branches, characterized by discrete areas of vesiculation of the epithelium of the forehead, the nose, the eyelids, and the cornea together with subepithelial infiltration. [NIH]

Zymogen: Inactive form of an enzyme which can then be converted to the active form, usually by excision of a polypeptide, e. g. trypsinogen is the zymogen of trypsin. [NIH]

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