GLUCONEOGENESIS, GLYCOGEN METABOLISM, STARCH/CELLULOSE METBOLISM, PENTOSE PHOSPHATE PATHWAY

Yoseph Cherinet (BSc, MSc; Assistant Professor)

DVM Year II

Learning objectives

- Describe gluconeogenesis
- Describe synthesis and break down of glycoge
- Describe starch/cellulose metabolism
- Explain pentose phosphate pathway and its role
- Recognize the key regulatory steps in above pathways

IMPORTANCE OF GLUCONEOGENESIS

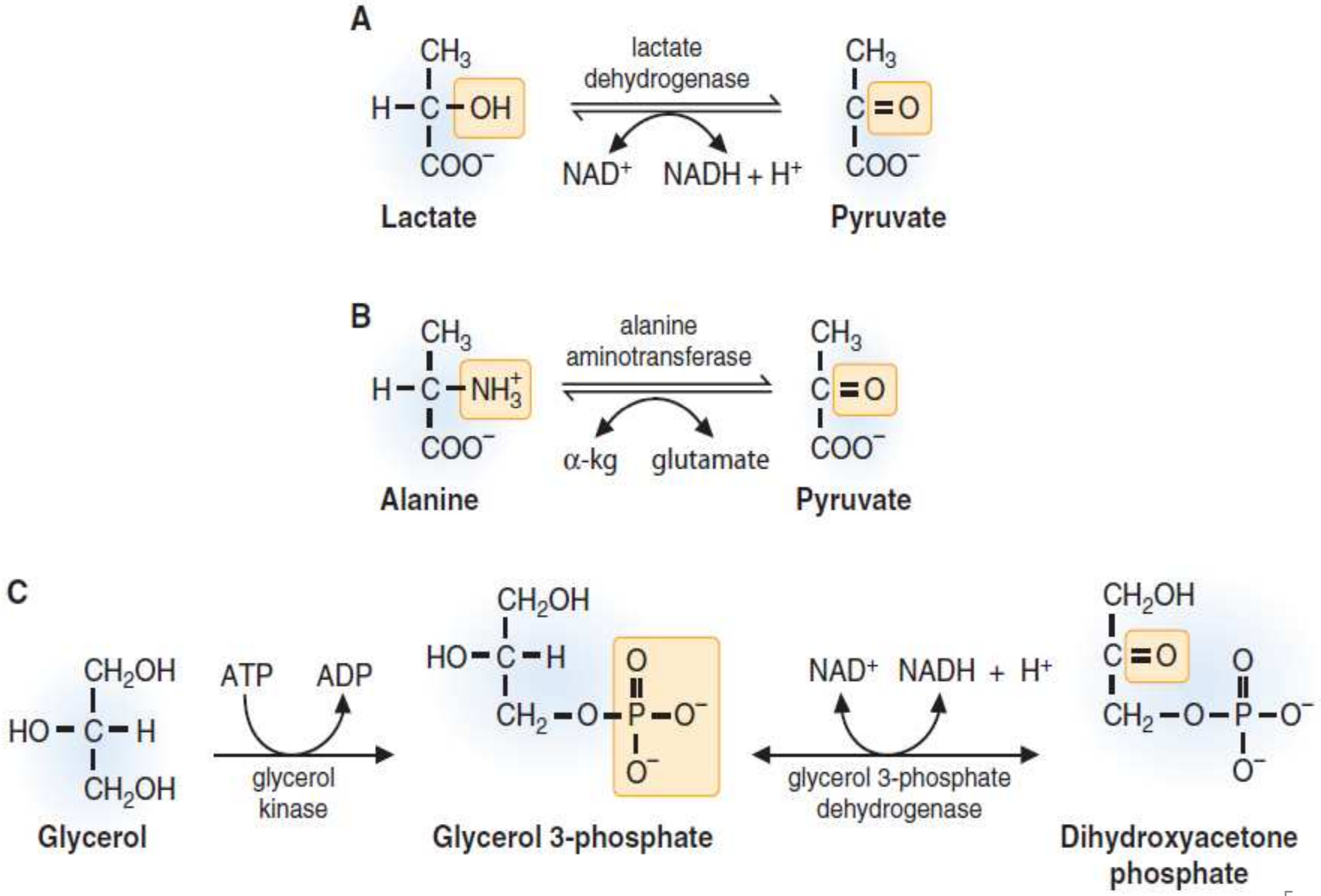
- Glucose occupies a key position in the metabolism and its continuous supply is absolutely essential to the body.

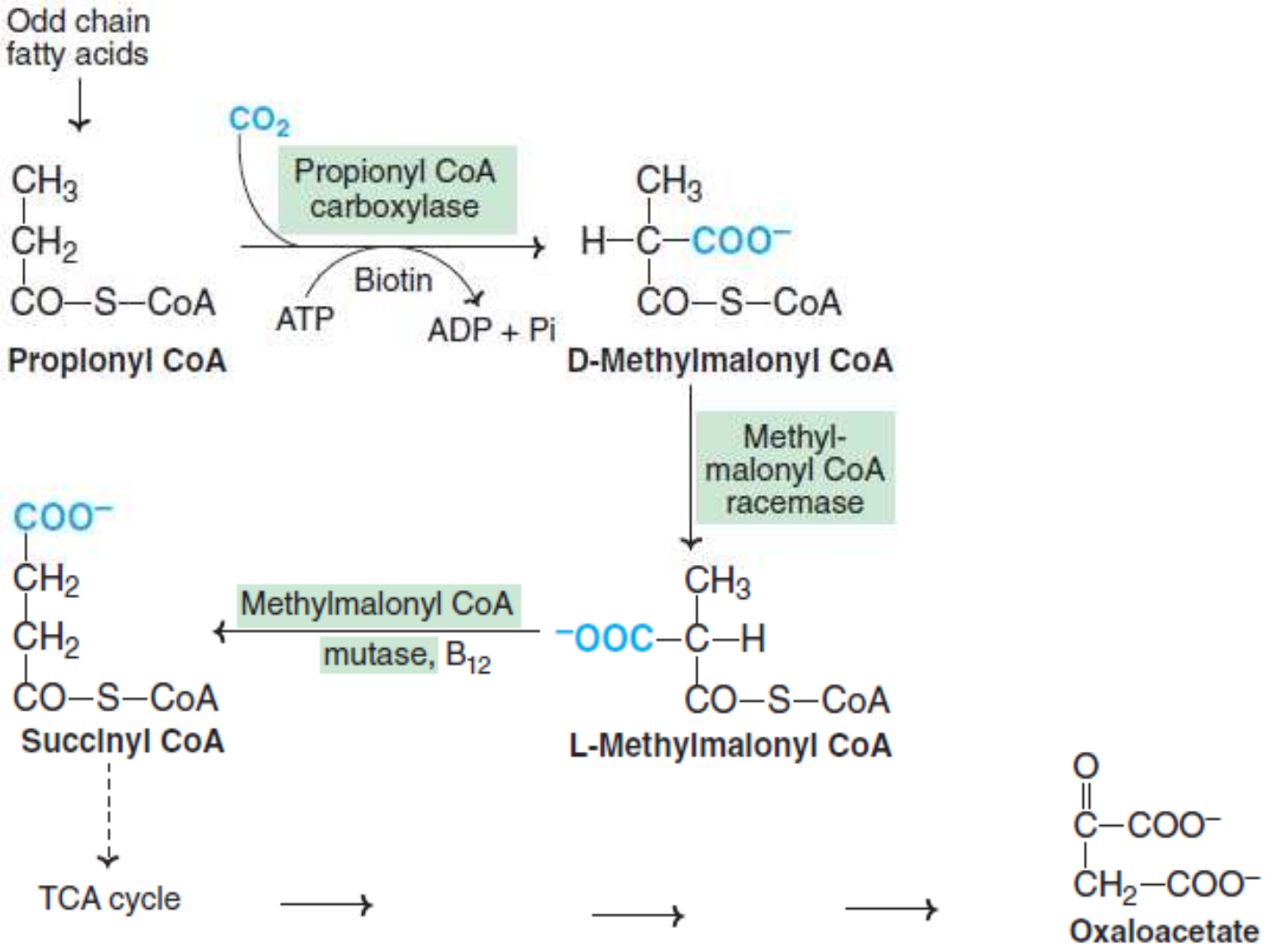
- Maintaining levels of glucose is important because the brain depends on glucose as its primary fuel and red blood cells use glucose as their only fuel.

GLUCONEOGENESIS

- Gluconeogenesis is the formation of glucose from non carbohydrate precursors, occurs primarily in the liver.
- Gluconeogenesis meets the need of the body for glucose when carbohydrate is not available in sufficient amount.
- Precursor molecules include:
  - Pyruvate
  - Lactate
  - Glycerol
  - Propionyl CoA
  - Glucogenic amino acids

Metabolism of Gluconeogenic Precursors





Conversion of propionyl CoA into succinyl CoA. Propionyl CoA, generated from fatty acids with an odd number of carbons, is converted into the citric acid cycle intermediate succinyl CoA; and later to oxaloacetate.

Reactions of Gluconeogenesis

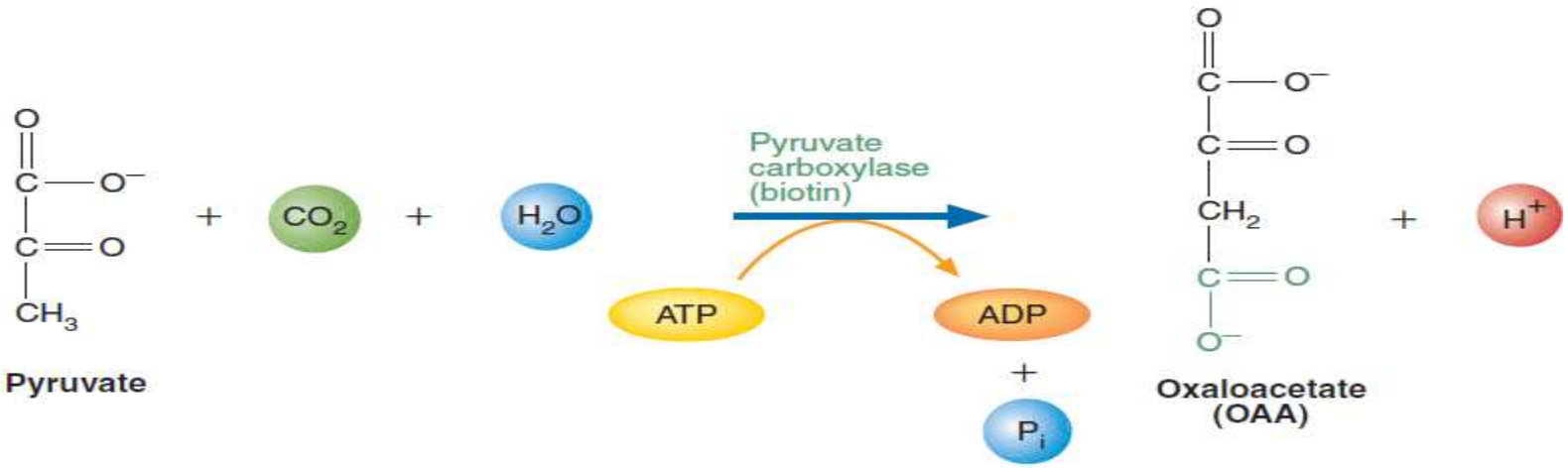
- The reaction sequence in gluconeogenesis is largely the reverse of glycolysis.
- In gluconeogenesis, alternate reactions catalyzed by different enzymes are used to bypass these obstacles.
- Recall three irreversible glycolytic reactions are catalyzed by:
  - **Hexokinase**
  - **PFK**
  - **Pyruvate kinase**

Enzymes of Gluconeogenesis

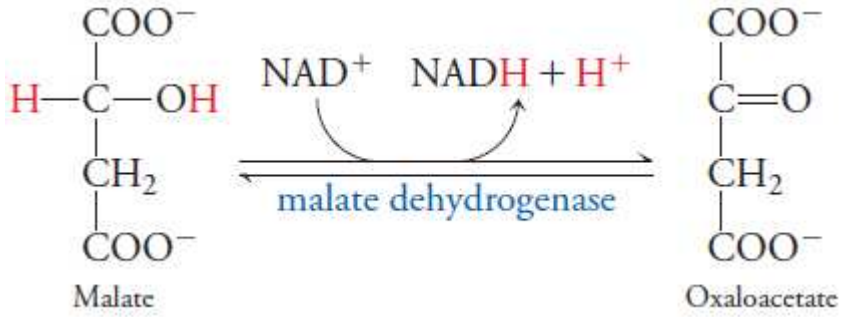
- Pyruvate carboxylase
- Malate dehydrogenase
  - Mitochondrial
  - Cytosolic
- Phosphoenolpyruvate carboxykinase
- Fructose-1,6-bisphosphatase
- Glucose-6-phosphatase

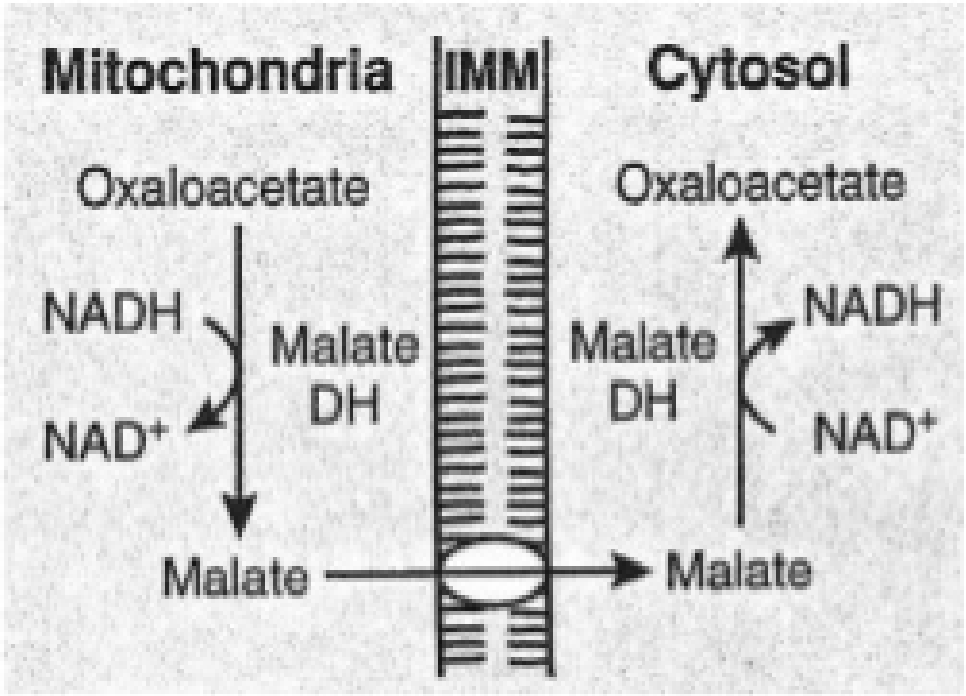
1.Synthesis of PEP

- Pyruvate for its conversion in to glucose should **enter to mitochondrial** matrix by a special carrier protein.
- PEP synthesis from pyruvate requires two enzymes: pyruvate carboxylase and PEP carboxykinase.
- Pyruvate carboxylase, found with in mitochondria, converts pyruvate to oxaloacetate (OAA).

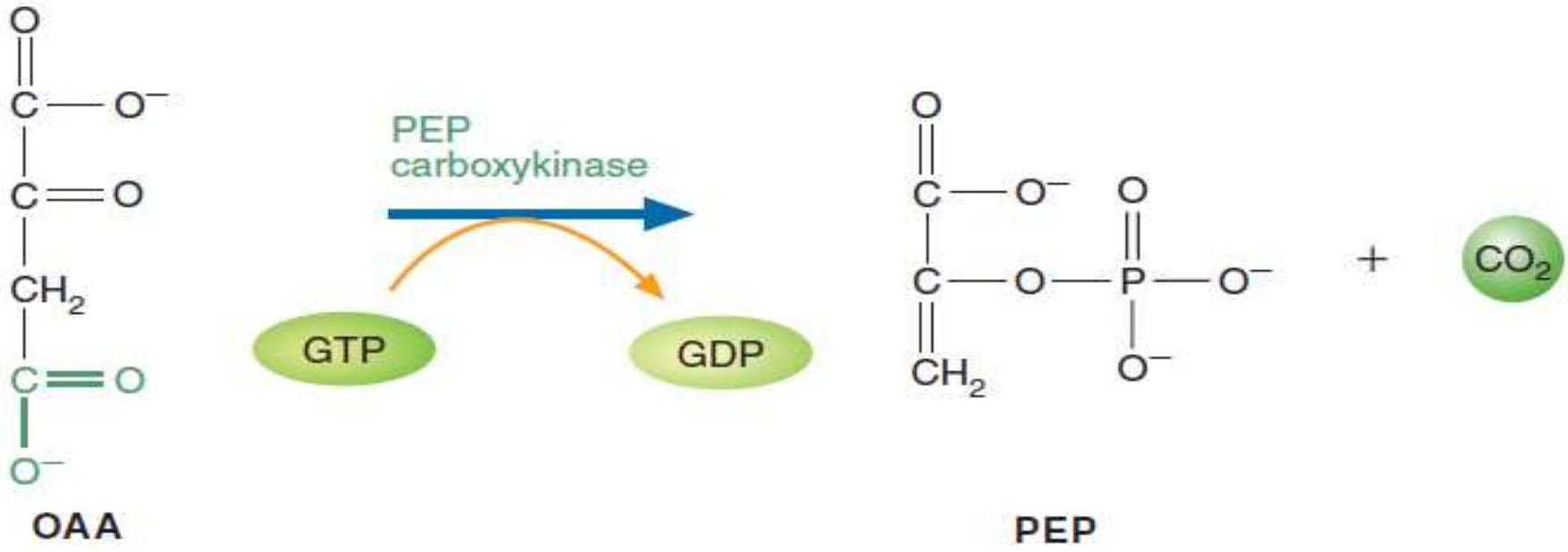


- OAA formed reversibly reduced to malate by <u>mitochondrial malate dehydrogenase</u>.
- Malate then leaves the mitochondria via special transport system to gain entry to cytosol where it is reoxidized to oxaloacetate by <u>cytosolic malate dehydrogenase</u>.



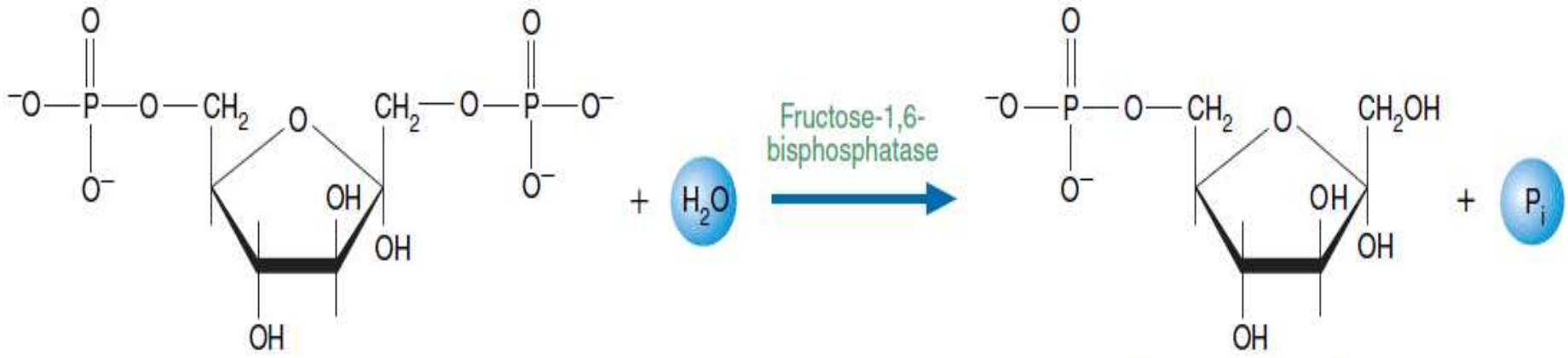


- Cytosolic OAA then decarboxylated and phosphorylated by PEP carboxykinase in a reaction driven by the hydrolysis of guanosine triphosphate (GTP) and form phosphoenolpyruvate (PEP).



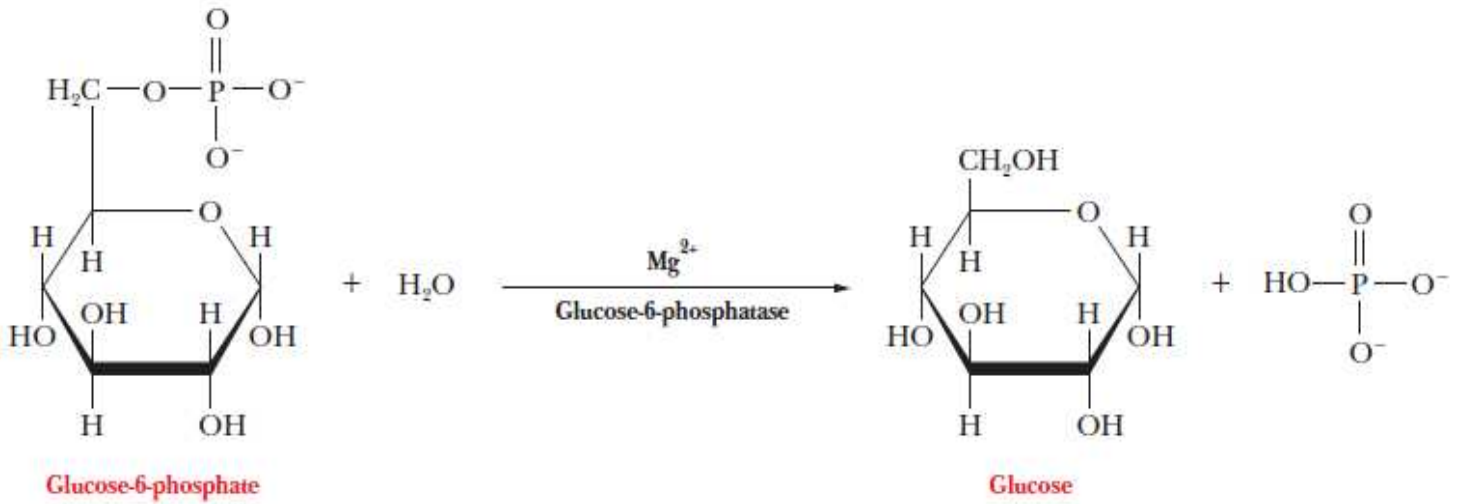
2. Conversion of fructose-1,6-bisphosphate to F-6-P

- The irreversible PFK catalyzed reaction in glycolysis is bypassed by fructose-1,6-bisphosphatase.



3. Formation of glucose from G-6-P

- Glucose-6-phosphatase catalyzes the irreversible hydrolysis of G-6-P to form glucose and P_i. Glucose is subsequently released into the blood.
- This final step in the generation of glucose does not take place in the cytoplasm. Rather, glucose6-phosphate is transported into the lumen of the endoplasmic reticulum, where it is hydrolyzed toglucose by glucose 6-phosphatase, which is bound to the membrane



Generation of glucose from glucose 6-phosphate

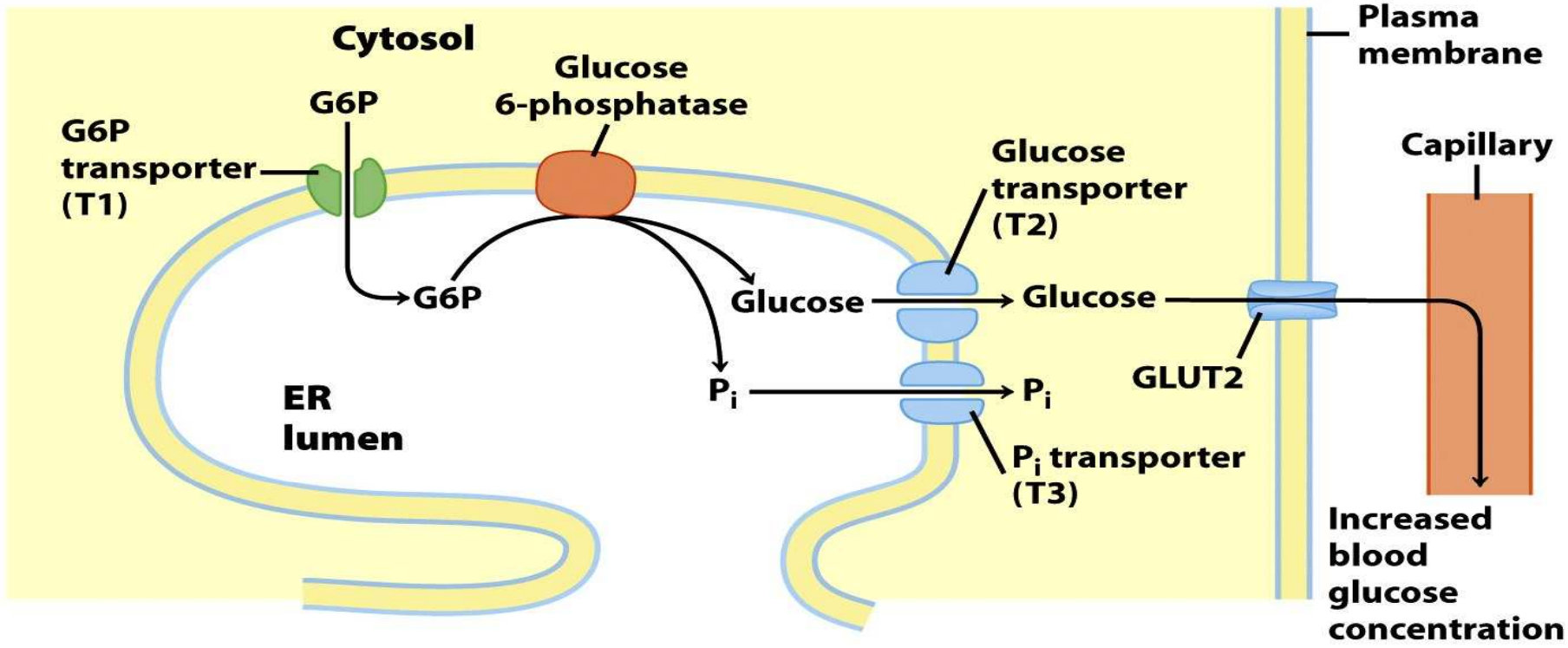
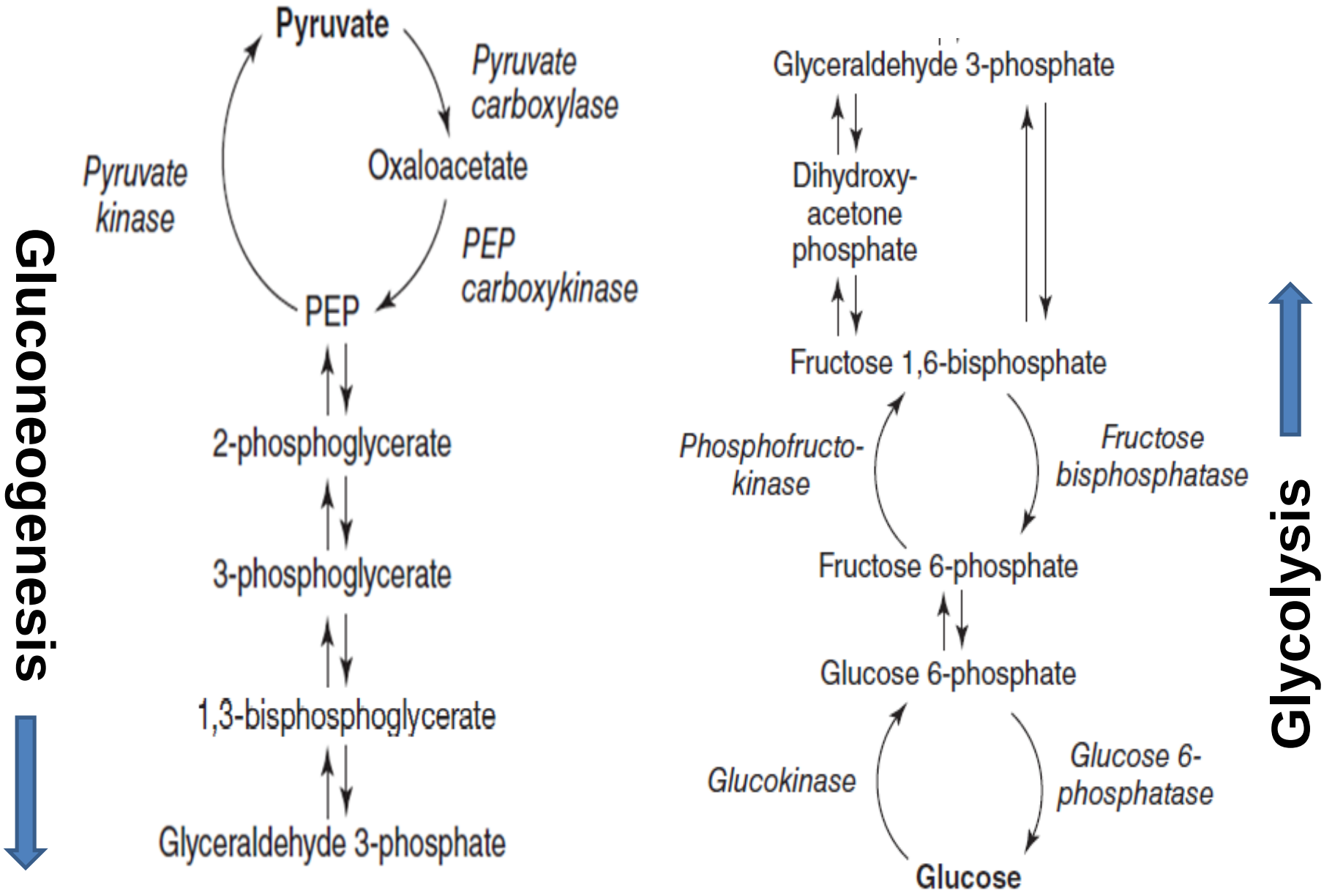


Figure 15-28
Lehninger Principles of Biochemistry, Fifth Edition

Hydrolysis of glucose 6-phosphate by glucose 6-phosphatase of the liver ER. The catalytic site of glucose 6-phosphatase faces the lumen of the ER. G-6-P transporter (**T1**) carries G-6-P from cytosol to the lumen, and by action of G-6-phosphatase glucose & P_i are formed. The products then pass to cytosol by specific transporters (**T2** & **T3**). Glucose leaves the cell via the **GLUT2** transporter in the plasma membrane.


Gluconeogenesis
Pyruvate
Pyruvate carboxylase
Oxaloacetate
PEP carboxykinase
PEP
Pyruvate kinase
2-phosphoglycerate
3-phosphoglycerate
1,3-bisphosphoglycerate
Glyceraldehyde 3-phosphate
Glyceraldehyde 3-phosphate
Dihydroxy-acetone phosphate
Fructose 1,6-bisphosphate
Phosphofructo-kinase
Fructose bisphosphatase
Fructose 6-phosphate
Glucose 6-phosphate
Glucokinase
Glucose 6-phosphatase
Glucose
Glycolysis

Step	Reaction
1	$\text{Pyruvate} + CO_2 + \text{ATP} + H_2O \longrightarrow \text{oxaloacetate} + \text{ADP} + P_i + 2H^+$
2	$\text{Oxaloacetate} + \text{GTP} \rightleftharpoons \text{phosphoenolpyruvate} + \text{GDP} + CO_2$
3	$\text{Phosphoenolpyruvate} + H_2O \rightleftharpoons \text{2-phosphoglycerate}$
4	$\text{2-Phosphoglycerate} \rightleftharpoons \text{3-phosphoglycerate}$
5	$\text{3-Phosphoglycerate} + \text{ATP} \rightleftharpoons \text{1,3-bisphosphoglycerate} + \text{ADP}$
6	$\text{1,3-Bisphosphoglycerate} + \text{NADH} + H^+ \rightleftharpoons \text{glyceraldehyde 3-phosphate} + NAD^+ + P_i$
7	$\text{Glyceraldehyde 3-phosphate} \rightleftharpoons \text{dihydroxyacetone phosphate}$
8	$\text{Glyceraldehyde 3-phosphate} + \text{dihydroxyacetone phosphate} \rightleftharpoons \text{fructose 1,6-bisphosphate}$
9	$\text{Fructose 1,6-bisphosphate} + H_2O \longrightarrow \text{fructose 6-phosphate} + P_i$
10	$\text{Fructose 6-phosphate} \rightleftharpoons \text{glucose 6-phosphate}$
11	$\text{Glucose 6-phosphate} + H_2O \longrightarrow + \text{glucose} + P_i$

Energy requirement of Gluconeogenesis

Reaction	ATP/GTP
2 Pyruvate to oxaloacetete	2 ATP
2 Oxaloacetete to Phosphoenolpyruvate	2 GTP
2 3-Phosphoglycerate to 1,3 biphosphoglycerate	2 ATP
Total	6

- Gluconeogenesis is energetically unfavorable if it occur by direct reversal of of glycolysis.

The stoichiometry of gluconeogenesis is

$$2\,\text{Pyruvate} + 4\,\text{ATP} + 2\,\text{GTP} + 2\,\text{NADH} + 6\,\text{H}_2\text{O} \rightarrow \text{glucose} + 4\,\text{ADP} + 2\,\text{GDP} + 6\,\text{P}_\text{i} + 2\,\text{NAD}^+ + 2\,\text{H}^+$$

$$\Delta G^{\circ\prime} = -48\ \text{kJ mol}^{-1}\ (-11\ \text{kcal mol}^{-1})$$

In contrast, the stoichiometry for the reversal of glycolysis is

$$2\,\text{Pyruvate} + 2\,\text{ATP} + 2\text{NADH} + 2\,\text{H}_2\text{O} \rightarrow \text{glucose} + 2\,\text{ADP} + 2\,\text{P}_\text{i} + 2\,\text{NAD}^+ + 2\text{H}^+$$

$$\Delta G^{\circ\prime} = +90\ \text{kJ mol}^{-1}\ (+22\ \text{kcal mol}^{-1})$$

- Four additional molecules (2ATP & 2GTP) are needed to turn an energetically unfavorable process (the reversal of glycolysis) into a favorable one (gluconeogenesis).
- It is an example of the coupling of reactions: NTP hydrolysis is used to power an energetically unfavorable reaction.

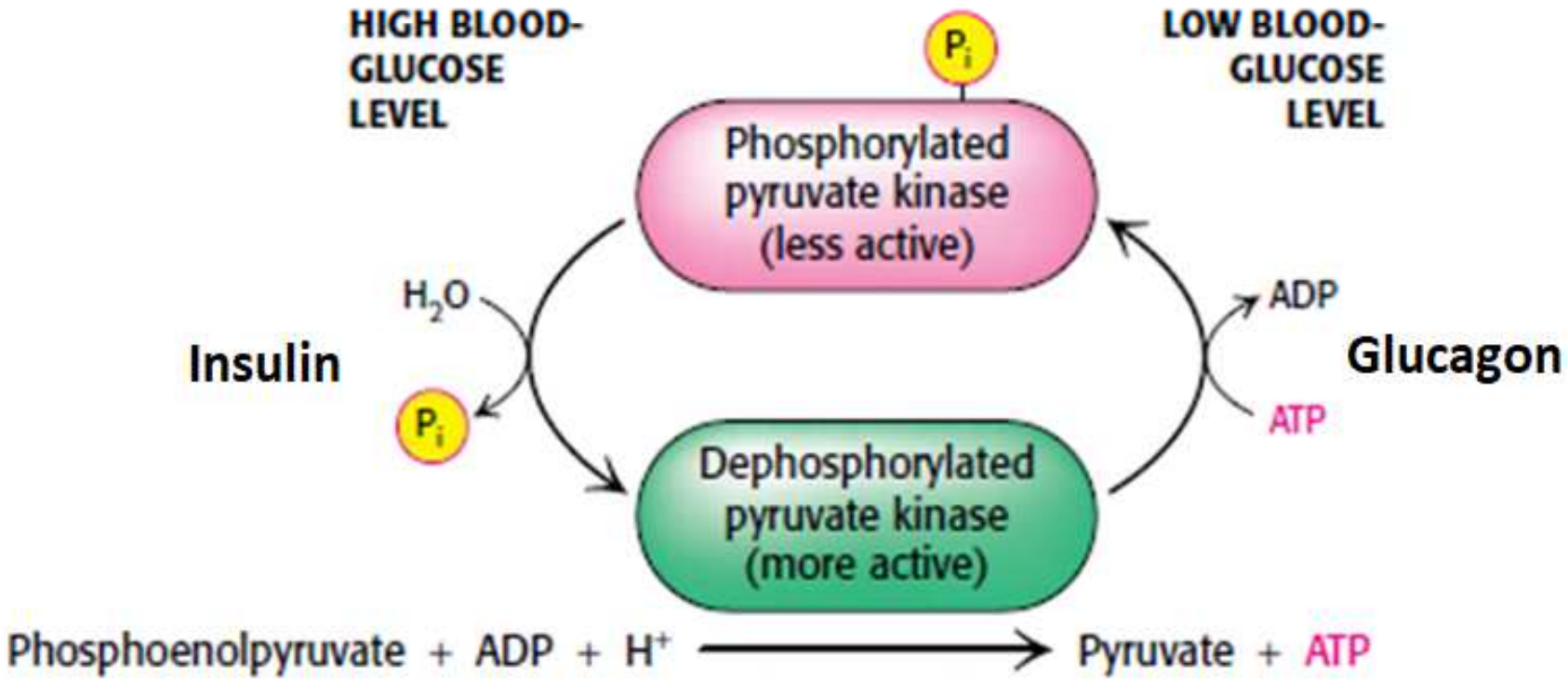
Gluconeogenesis Regulation

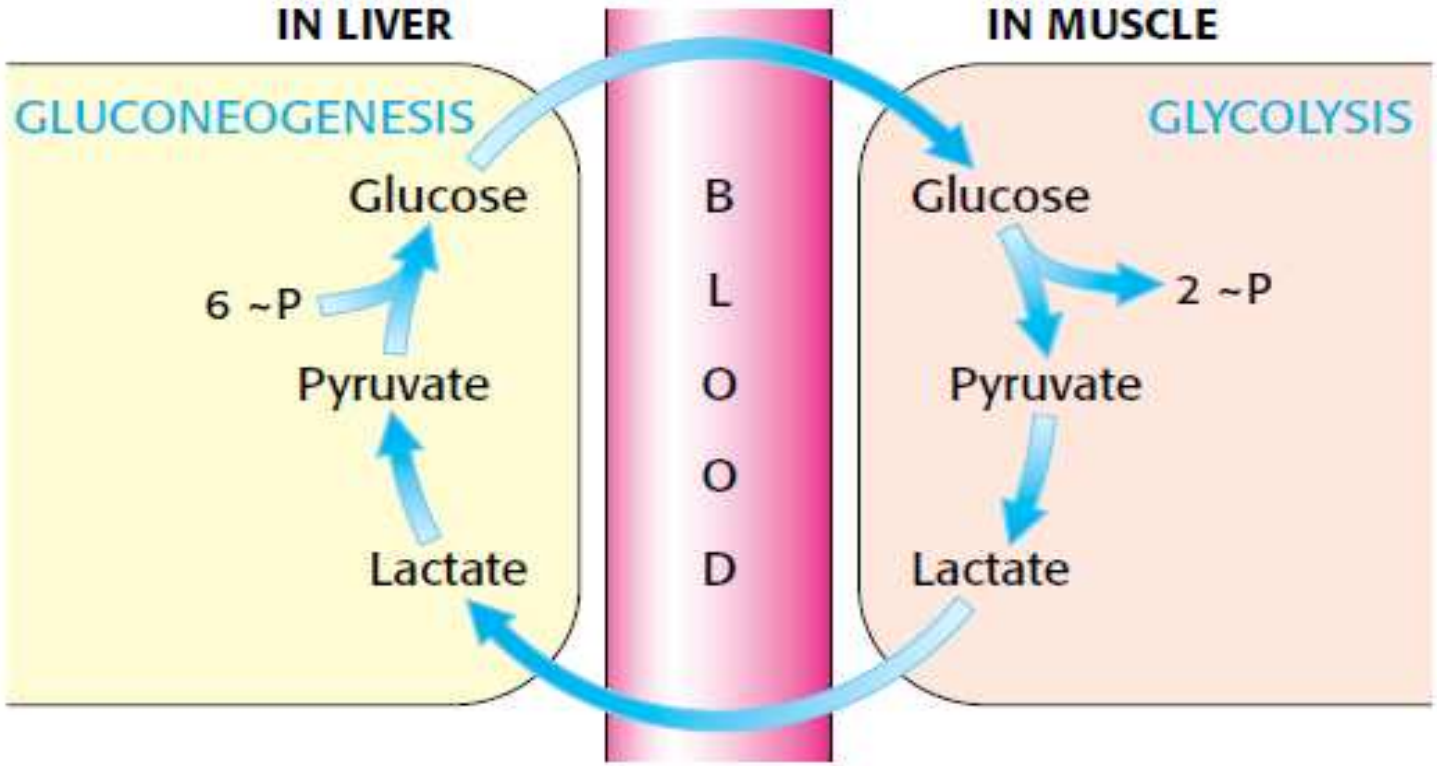
- Gluconeogenesis is affected primarily by substrate availability, allosteric effectors, and hormones.
- It is stimulated by high concentrations of lactate, glycerol and glucogenic amino acids.
- The enzymes are also affected to varying degrees by allosteric modulators.
  - Acetyl-CoA activates pyruvate carboxylase & inhibits pyruvate kinase.
  - ATP activates fructose-1,6-bisphosphatase while AMP inhibits fructose-1,6-bisphosphatase

– Hormones (glucagon& insulin) influence gluconeogenesis by altering enzyme synthesis.

- Glucagon induces synthesis of PEP carboxykinase, fructose-1,6-bisphosphatase & glucose-6-phosphatase.
- Insulin depresses the synthesis of PEP carboxykinase, fructose-1,6-bisphosphatase, & glucose-6-phosphatase.

- **Covalent Modification**
  - Glucagon inactivates pyruvate kinase through phosphorylation while insulin activates through dephosphorylation .
  - This decreases the conversion of PEP to pyruvate, which has the effect of <u>diverting PEP to the synthesis of glucose.</u>





THE CORI CYCLE: LINKING GLYCOLYSIS AND GLUCONEOGENESIS

Lactate formed by active muscle is converted into glucose by the liver. This cycle shifts part of the metabolic burden of active muscle to the liver. The symbol ,P represents nucleoside triphosphates.

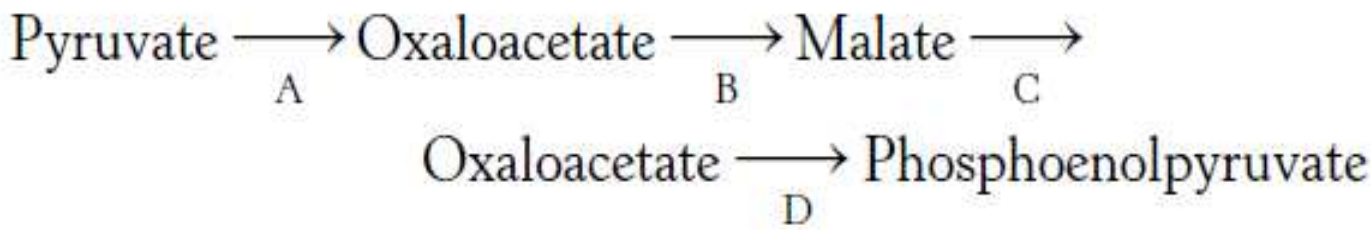
Gluconeogenesis: Summary

Where, When, What, ??

- Where does gluconeogenesis occur?
  - LIVER (Major)
  - Kidney (Minor)
- When does gluconeogenesis occur?
  - When dietary sources of glucose are not available
  - When liver has exhausted its glycogen stores
- What precursors does gluconeogenesis use?
  - Lactate, pyruvate, glycerol, propionyl CoA, glucogenic AAs (Leu & Lys cannot be used)

Learning Check

- The following sequence is a part of gluconeogenesis. Match the capital letters representing the rxn in gluconeogenic pathway with parts 1, 2, etc.



1. Takes place in mitochondria
2. Takes place in the cytoplasm
3. Produces CO_2
4. Consumes CO_2
5. Requires NADH
6. Produces NADH
7. Requires ATP
8. Requires GTP

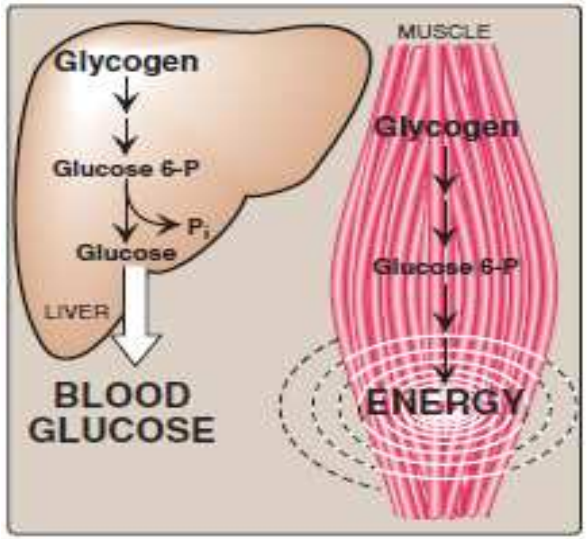
Answer:

A. 1, 4, 7

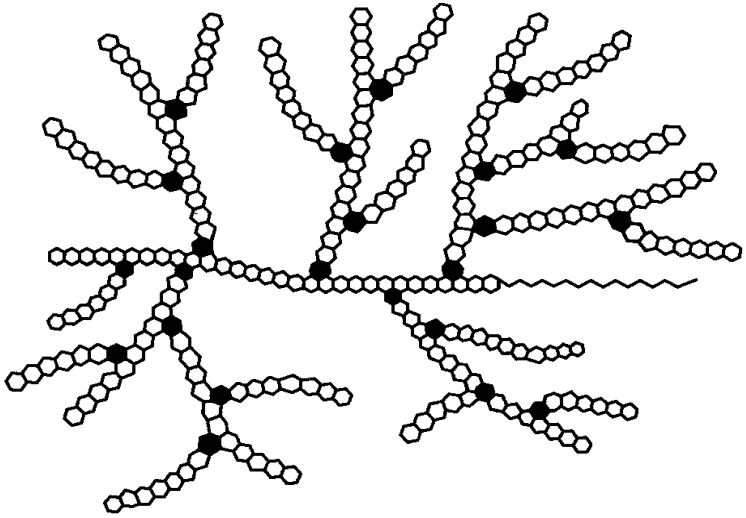
B. 1, 5

C. 2, 6

D. 2, 3, 8



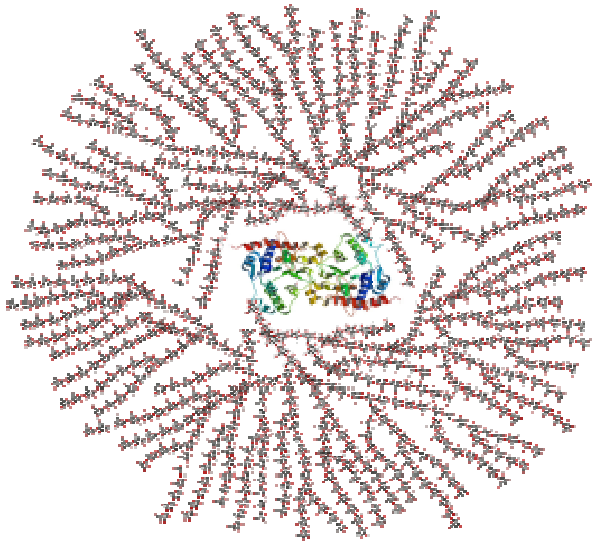
METABOLISM OF GLYCOGEN



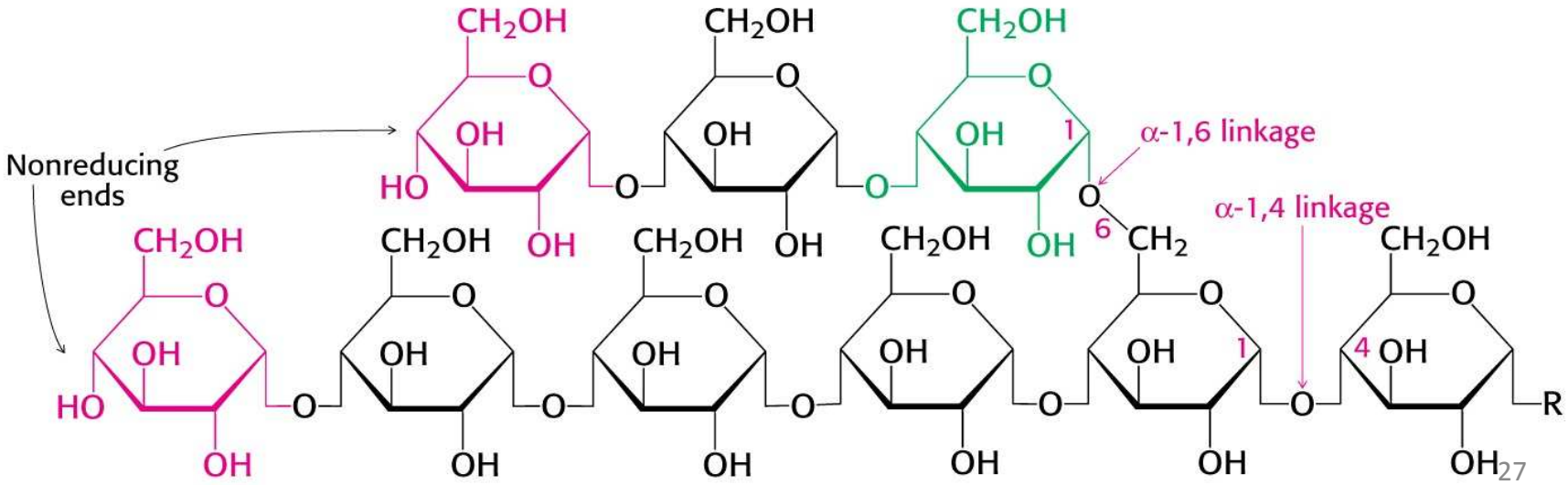
Glycogen Metabolism

- What is the importance of glycogen?
  - Glycogen can be rapidly metabolized
  - Glycogen can generate energy in absence of O_2
  - Brain/RBCs requires continuous supply of glucose
- Where is glycogen stored?
  - Liver = Maintain blood glucose levels
    - Up to 10% of weight of liver
  - Muscle = Fuel reserve for own ATP synthesis
    - 1-2% of weight of muscle

STRUCTURE OF GLYCOGEN



- Polymer held by glycosidic linkages
- Found in cytoplasm as granules
- Inner linear & outer branched
- Centrally it held glycogenin protein



Glycogen Degradation Pathways

- Cytosolic
  - Major
- Lysosomal
  - Minor

GLYCOGENOLYSIS

- Enzymes of glycogenolysis:
  - Glycogen phosphorylase
  - Debranching enzyme
  - Phosphoglucomutase
  - Glucose 6–phosphatase

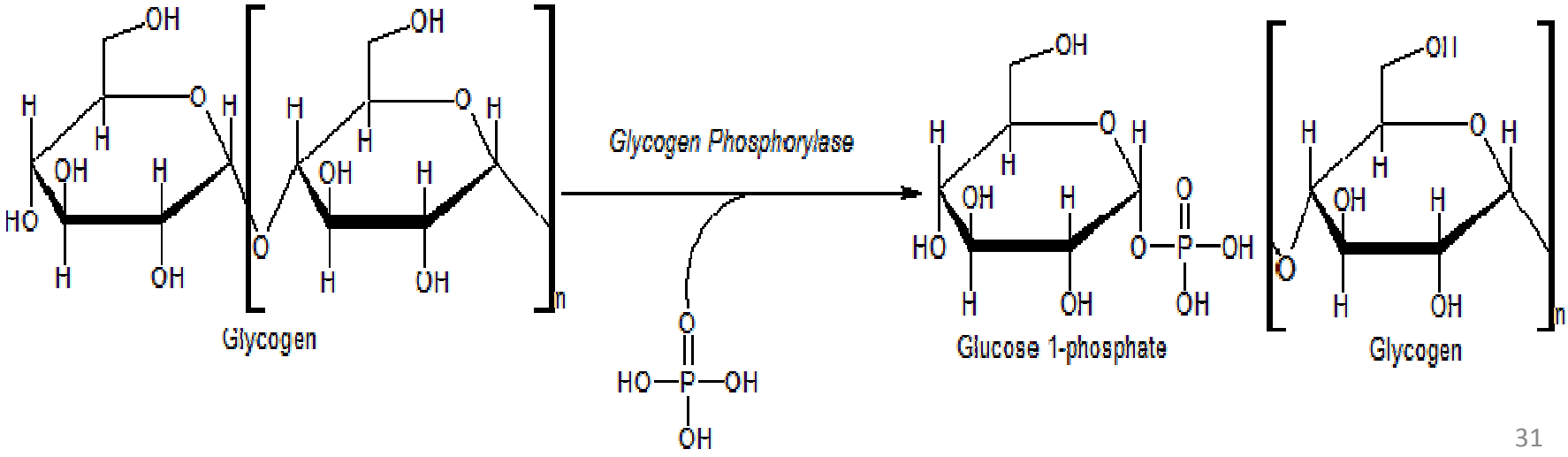
PHASES OF GLYCOGENOLYSIS

1. 1st Depolymerization
2. Debranching
3. 2nd Depolymerization
4. Conversion of Glu-1-P to Glu-6-P
5. Fate of Glu-6-P

Glu = Glucose

1. 1st Depolymerization

- The first step in glycogenolysis is catalyzed by **glycogen phosphorylase**, commonly called phosphorylase. It cleaves the *α*-1,4 glycosidic bonds of glycogen by adding phosphate & forms **glucose-1-phosphate**.
- The cleavage of a bond by the addition of phosphate is referred to as phosphorolysis.



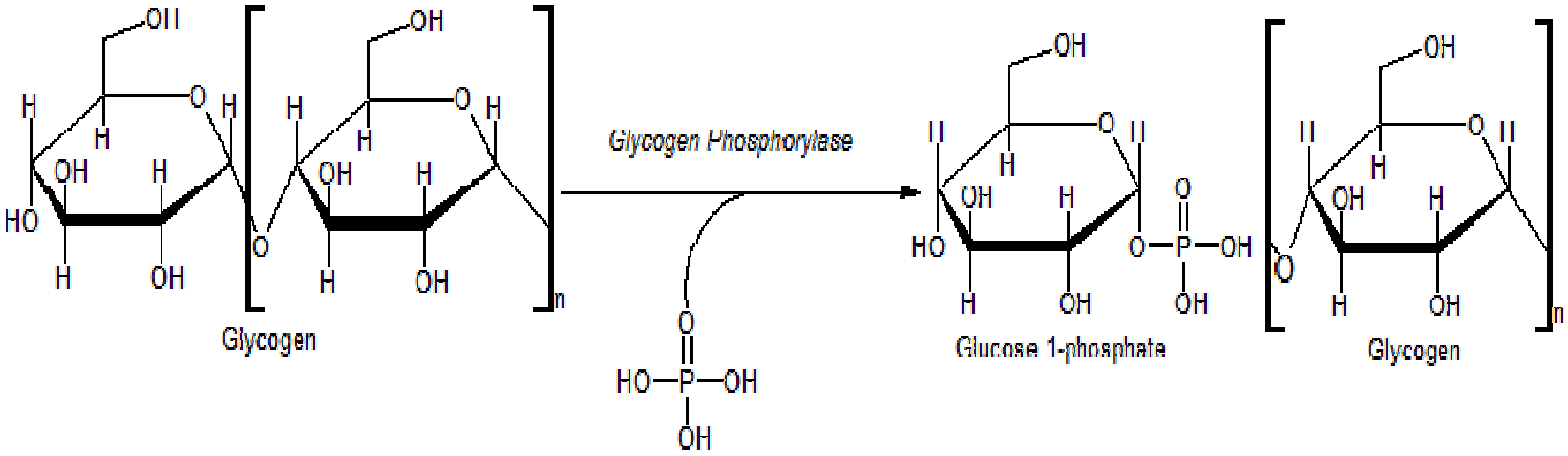
- Glycogen phosphorylase acts on repetitively on the non reducing ends of glycogen branches until it reaches a point **four glucose** residues away from an α-1,6 branch point, where its action stops.
- Further degradation by glycogen phosphorylase can occur only after the debranching enzyme catalyzes two successive reactions that transfer branches.

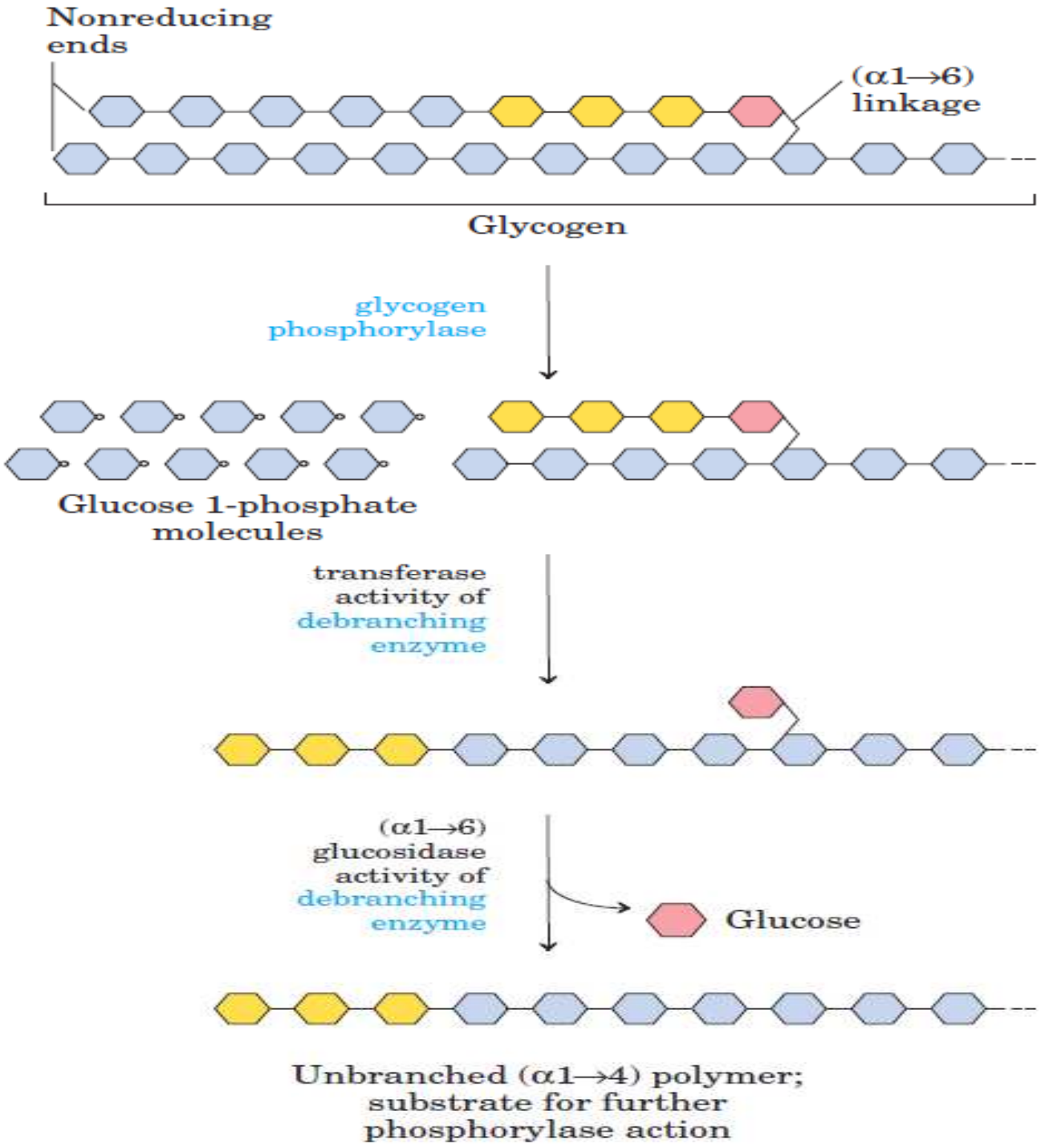
2. Debranching

- Debranching enzyme is multifunctional enzyme with single polypeptide protein that has two activities:
- **Transferase activity**
  - Debranching enzyme catalytic site transfers **three glucose residues** from the α-1,6 branch to an adjacent α-1,4 chain, leaving behind a single glucose unit in α-1,6 glycosidic linkage.
- **Glucosidase activity**
  - Debranching enzyme hydrolyzes the α-1,6 glycosidic bond of the remaining glucose unit, releasing free glucose & producing long, unbranched glycogen with α-1,4 glycosidic linkage.

3. 2nd Depolymerization

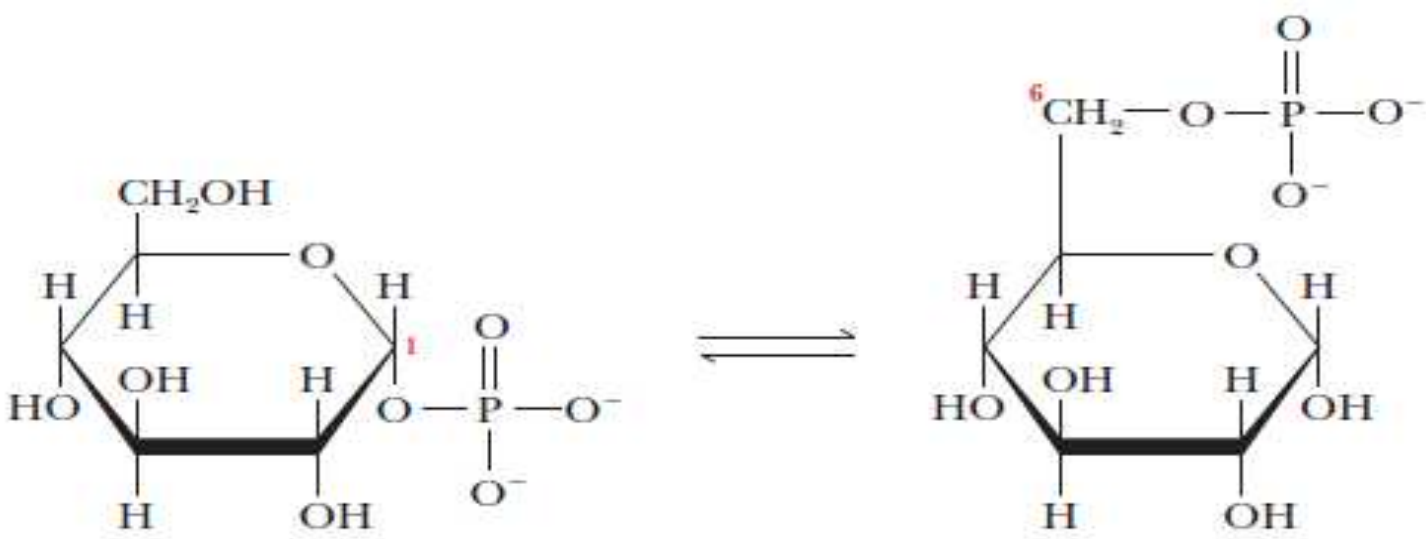
- The long unbranched α-1,4 glycosidic chain of glycogen then used by glycogen phosphorylase.
- It cleaves the *α*-1,4 glycosidic bonds of glycogen by adding phosphate & forms **<u>glucose-1-phosphate</u>**.




Nonreducing ends
(α1→6) linkage
Glycogen
glycogen phosphorylase
Glucose 1-phosphate molecules
transferase activity of debranching enzyme
(α1→6) glucosidase activity of debranching enzyme
Glucose
Unbranched (α1→4) polymer; substrate for further phosphorylase action

4. Conversion of Glucose-1-P to Glucose-6-P

- Glucose-1-phosphate, the end product of the glycogen phosphorylase reaction, is converted to glucose-6-phosphate by <u>phosphoglucomutase.</u>



Glucose-1-phosphate Glucose-6-phosphate

5. Fate of Glucose-6-phosphate

- In liver glucose-6-phosphate generated by glycogenolysis is not primarly catabolized within the hepatocyte but instead, released from cell as free glucose. This irreversible dephosphorylation step is catalyzed by glucose 6-phosphatase.

- In muscle, the resulting glucose-6-phosphate molecule then enters the glycolytic pathway to provide energy. This means that glycogen in muscle can not provide blood glucose as it lacks glucose 6-phosphatase.

Liver Vs Muscle Glycogenolysis

Liver glycogenolysis

1. Glycogen phosphorylase: Glycogen → Glucose-1-P
2. Phosphoglucomutase: Glucose-1-P → Glucose-6-P
3. Glucose -6- Phosphatase : Glucose-6-P → Glucose

Muscle glycogenolysis

1. Glycogen phosphorylase: Glycogen → Glucose 1-P
2. Phosphoglucomutase: Glucose-1-P → Glucose-6-P
3. Glycolysis : Glucose-6-P → Pyruvate → Lactate

- Muscle lacks enzyme → Glucose -6-phosphatase

How many ATP molecules are produced by glycolysis from glucose obtained after glycogenolysis in muscle?

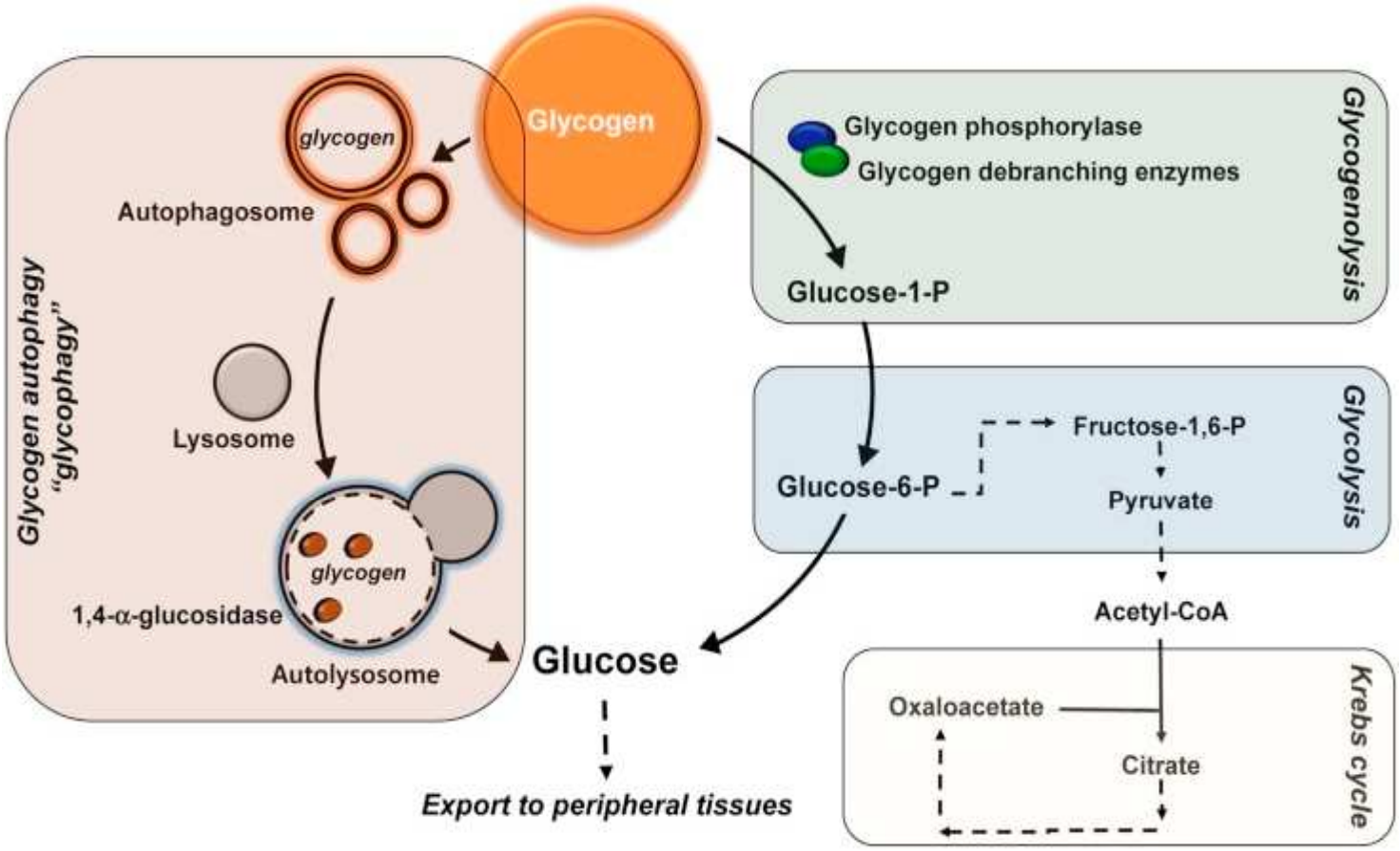
- **Hint** : The energy investment phase of glycolysis requires 2 ATP

The first step of glycolysis (Glucose to Glucose-6-phosphate) is passed as the product of glycogenolysis is Glucose-6-phosphate. So the net ATP becomes **three instead of two.**

Lysosomal Glycogen Degradation

- Glycophagy is the autophagic sequestration & degradation of glycogen to support glucose homeostasis.
- Minor fraction of glycogen degradation via the enzyme acid *α*-1,4 glucosidase (acid maltase) presumably used during normal turnover of cellular constituents.
- Glycogen autophagy is a very important process for the production of glucose of newborn animals & for disposal of structurally aberrant glycogen.
- Deficiency of acid maltase → accumulation of glycogen → Pompe's disease

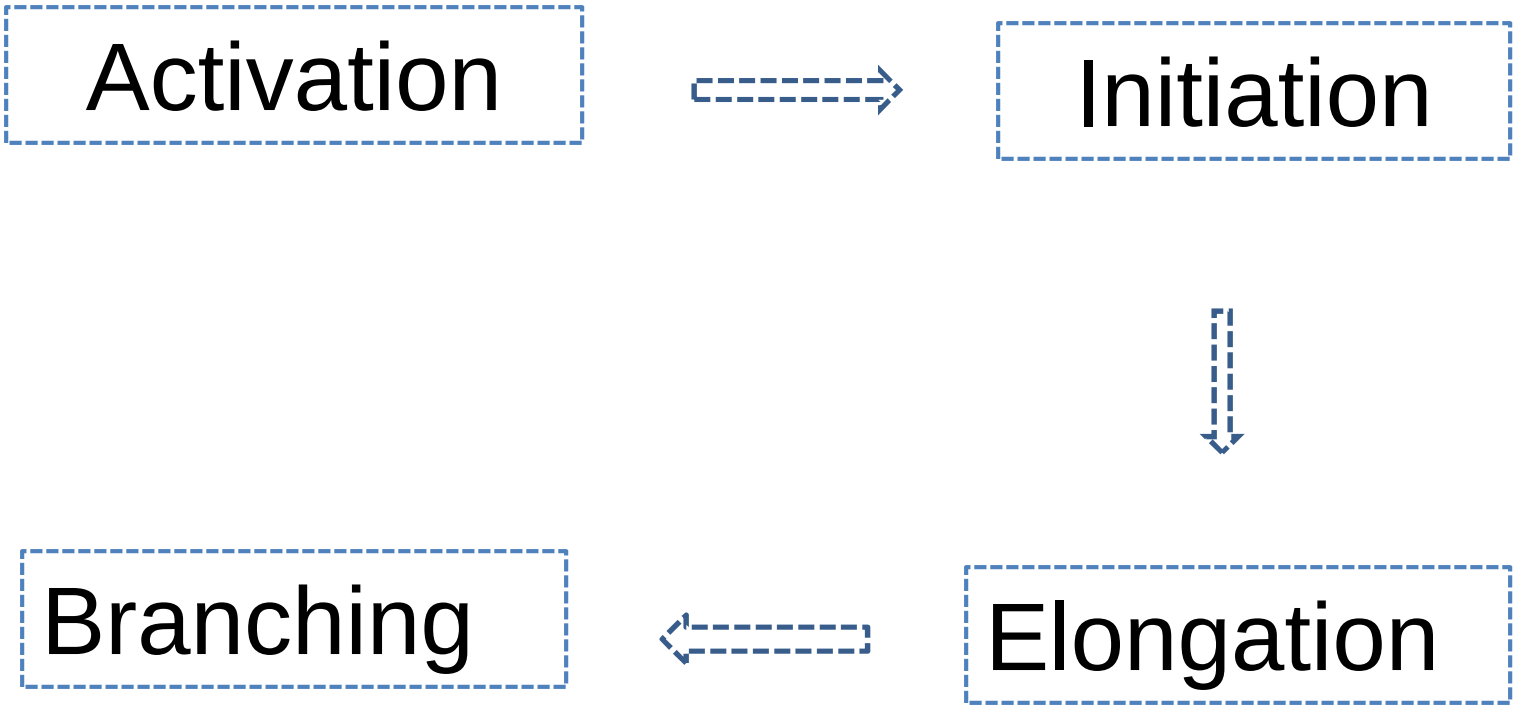
Glycogen Degradation Pathways



Joohun Ha, Kun-Liang Guan, Joungmok Kim: AMP-activated protein kinase & autophagy in glucose/glycogen metabolism : *Molecular Aspects of medicine 2015;46: 46-62*

GLYCOGENESIS

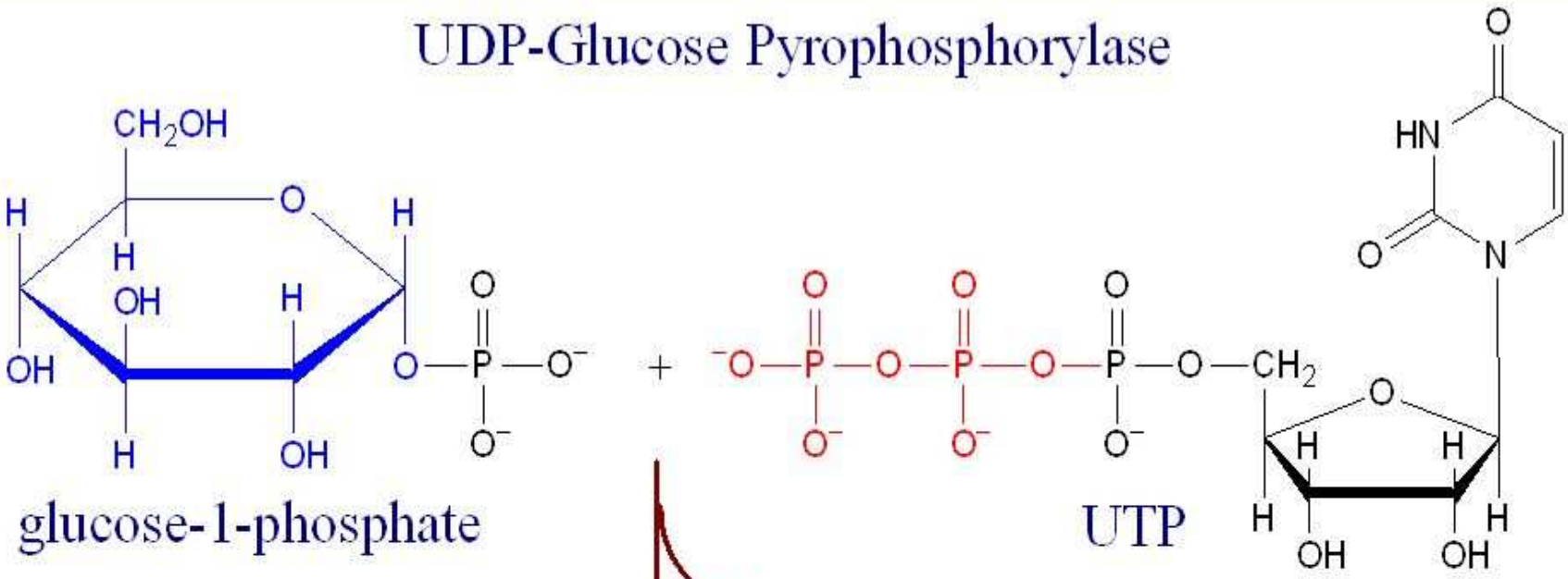
Phases of Glycogenesis

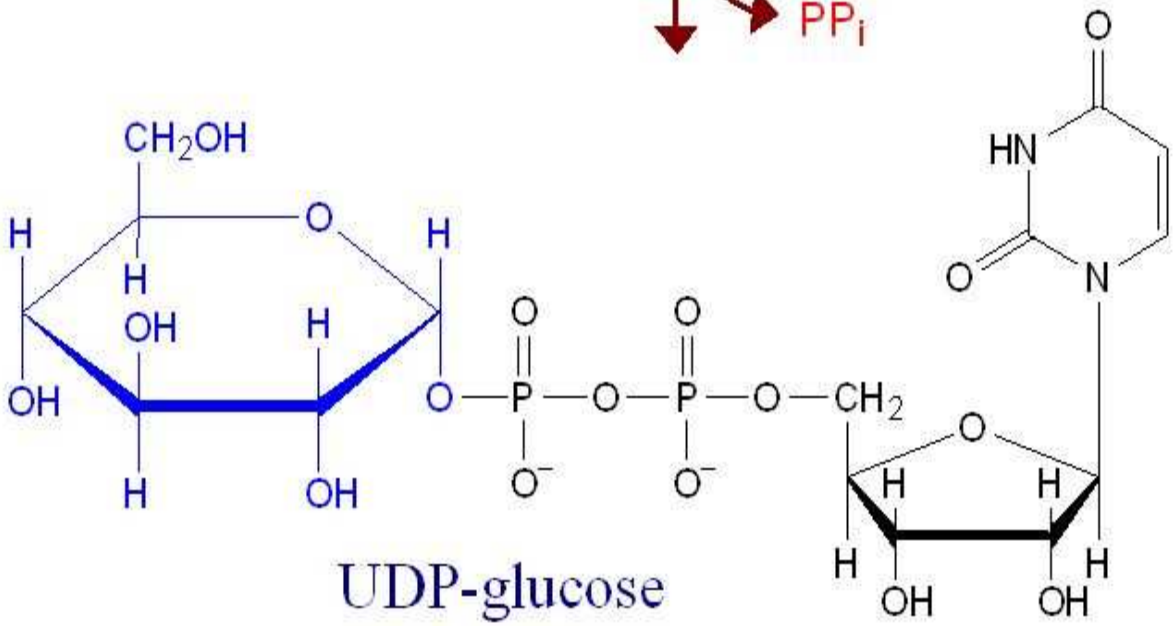


1. ACTIVATION

- Glycogenesis occurs primarily in muscle and liver.
- Following a meal, glucose is taken up by cells and phosphorylated to generate glucose-6-phosphate.
- Glucose-6-phosphate then converted to glucose-1-phosphate by phosphoglucomutase.
- Then uridine diphosphoglucose pyrophosphorylase catalyzes the synthesis of UDP-glucose from glucose-l-phosphate in the presence of UTP.

UDP-Glucose Pyrophosphorylase





PP_i —(inorganic pyrophosphatase)→ 2 P_i

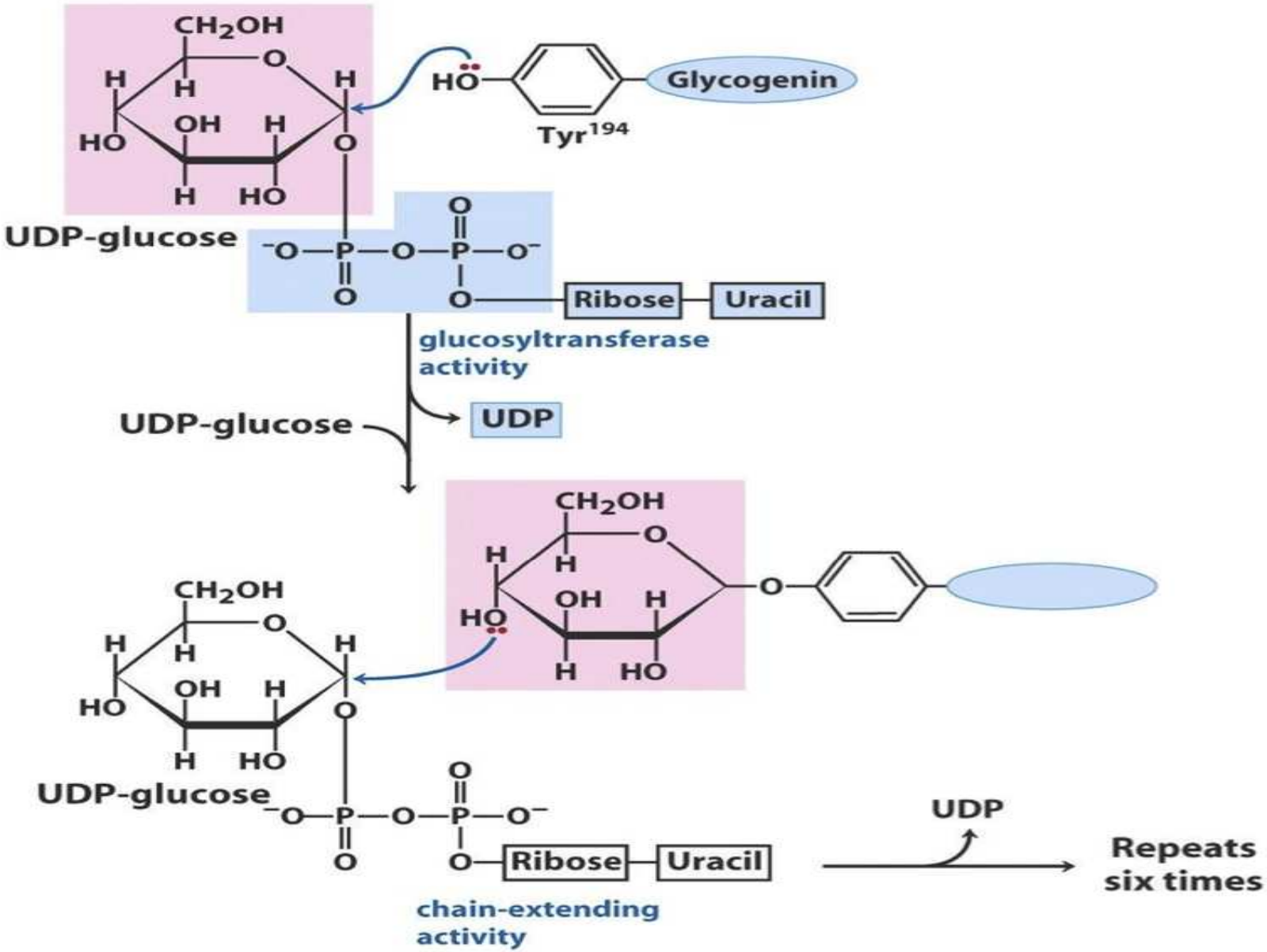
2. INITIATION

– Glycogenin

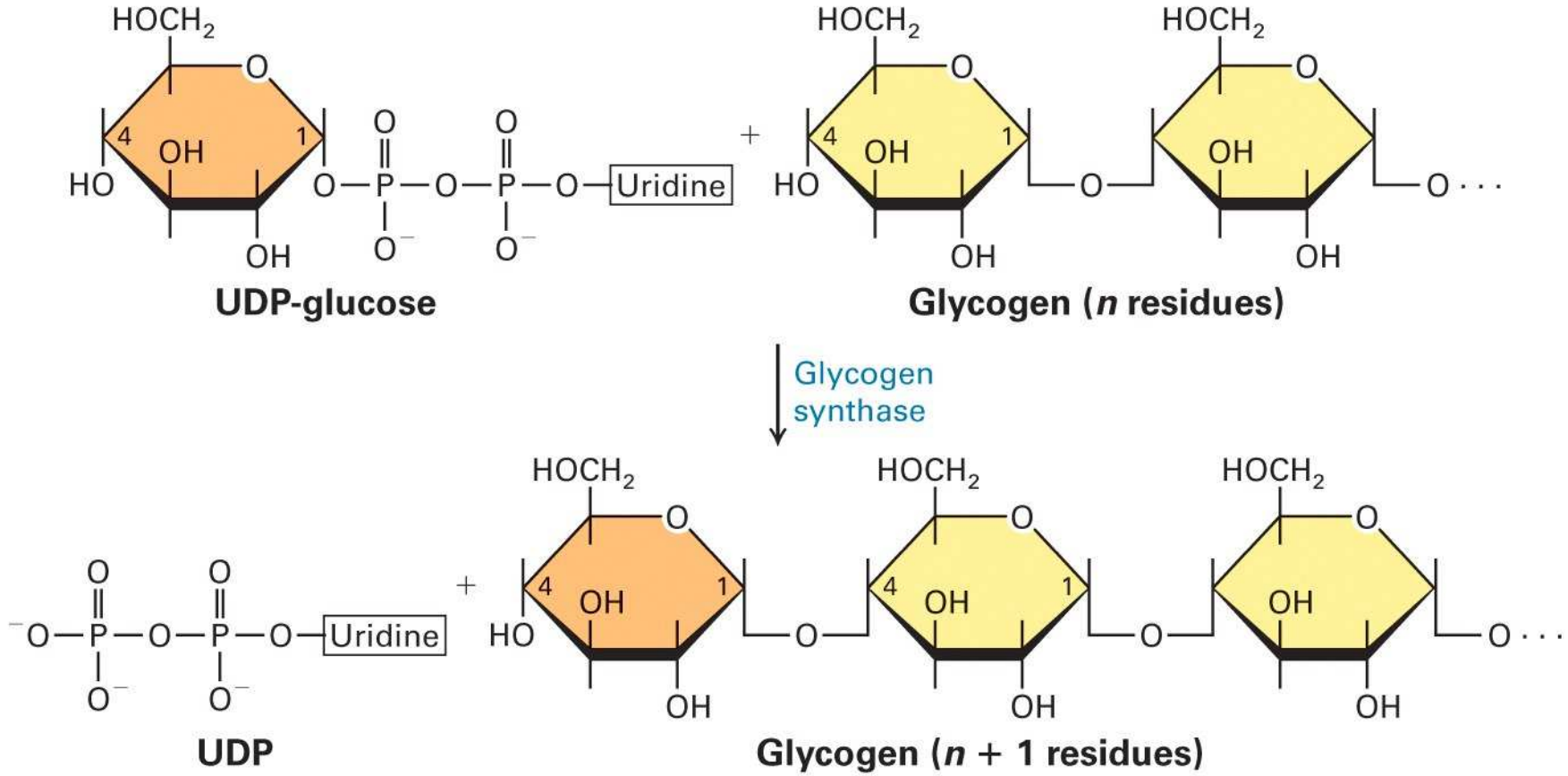
- A protein with intrinsic glucosyltransferase activity transfers UDP-glucose to glycogenin.

– Pre- existing glycogen residue

- Glycogen synthase transfers UDP-glucose to pre-existing glycogen.



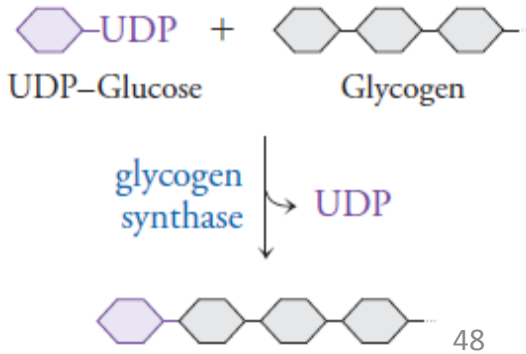
UDP + ATP $\rightleftharpoons$ UTP + ADP (Nucleoside diphosphate kinase)



Glycogen synthase transfers the activated glucose moiety of UDP-glucose to pre- existing glycogen residue

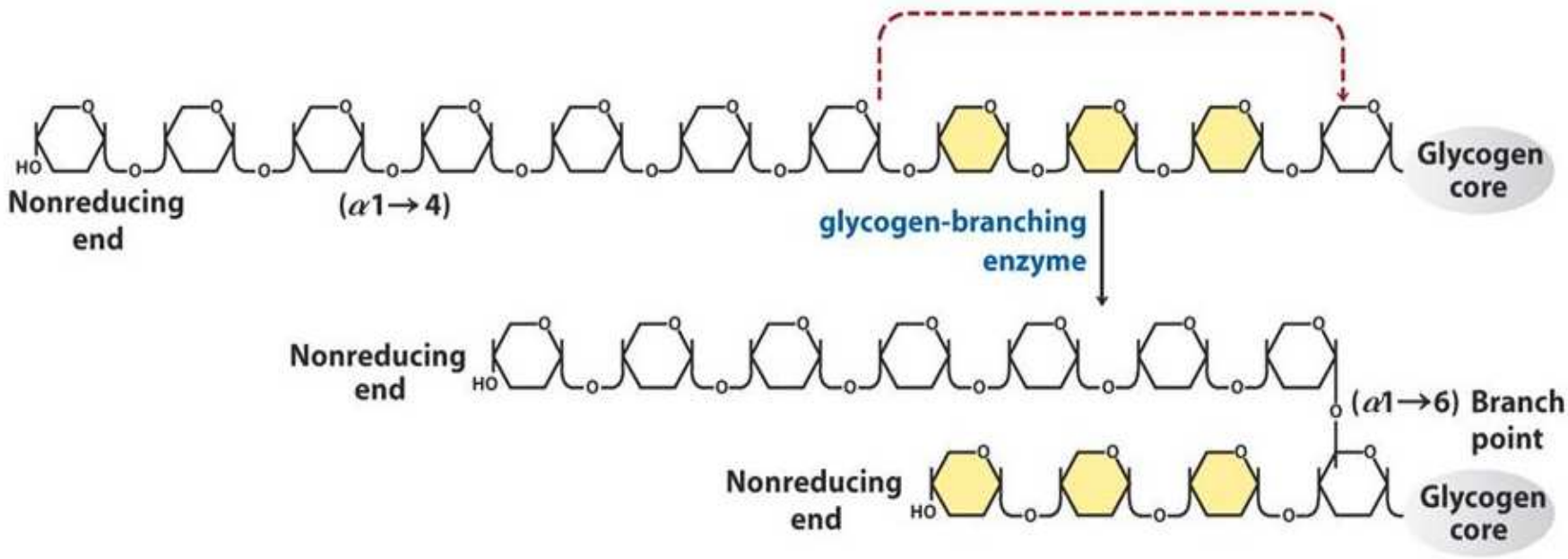
3. ELONGATION

- Sequential addition of seven more glucose residues, each derived from UDP-glucose; the reactions are catalyzed by the chain-extending activity of glycogenin.
- At this point, glycogen synthase takes over further extending the glycogen chain.
- Initiation & elongations occur by glycogen synthase if glycogen is made from pre-existing glycogen.



4. BRANCHING

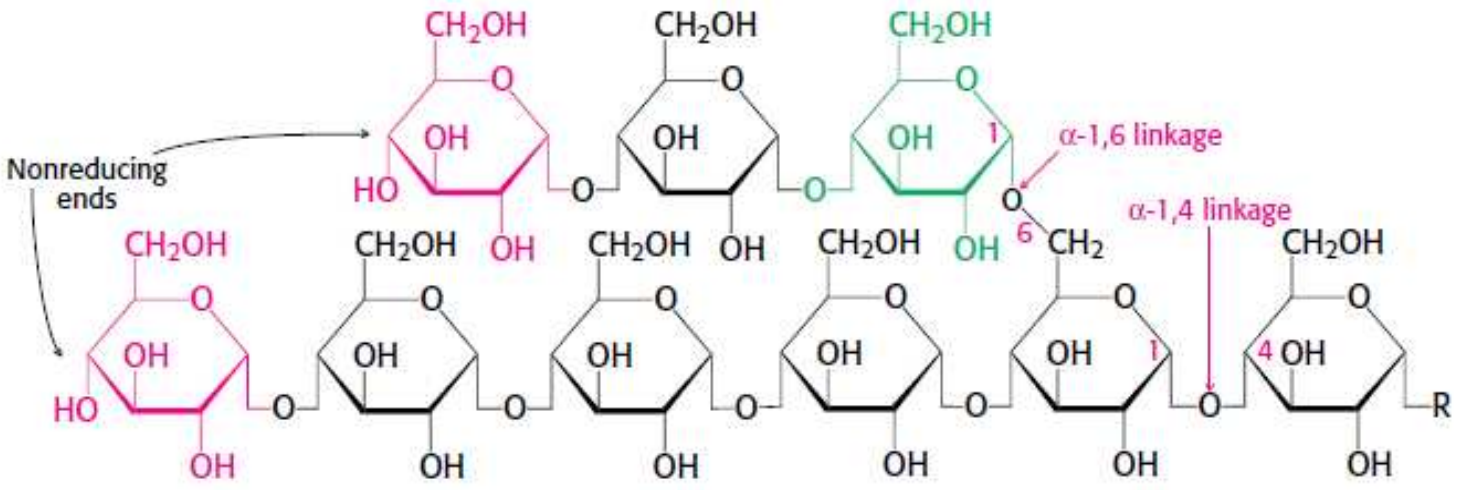
- When the chain has been lengthened to at least 11 glucose residues, glycogen branching enzyme transfers a part of the α-1,4 chain (at least six glucose) to a neighboring chain to form a α-1,6 linkage, establishing a branch point.



Significance of the branching of glycogen

- Branched glycogen molecule serves two major purposes

1. Provides numerous non reducing termini that serve as substrate for attack by phosphorylase & glycogen synthase.
2. Forms dense compact storage particle and increases its solubility in cell.

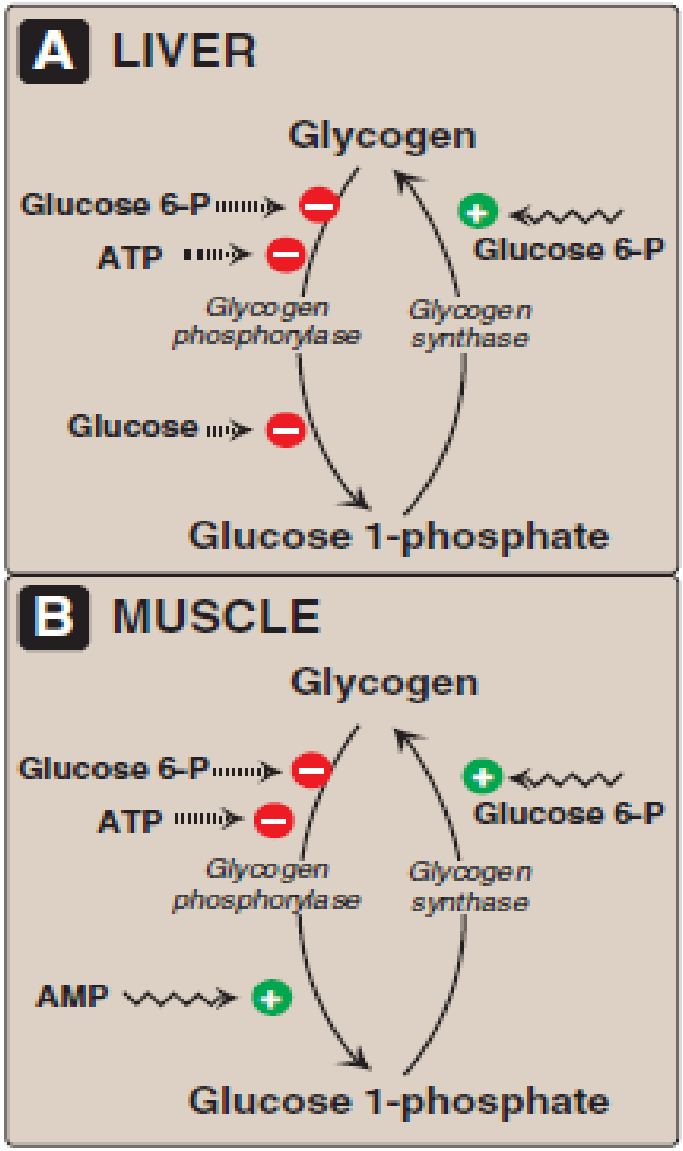


REGULATION OF GLYCOGEN METABOLISM

- Glycogenesis and glycogenolysis are reciprocally regulated so that both processes are not active at the same time.
- Glycogenesis occurs in the fed state, whereas glycogenolysis occurs both in the fasted state & in response to strenuous exercise.
- Regulation can also be allosteric or covalent modification

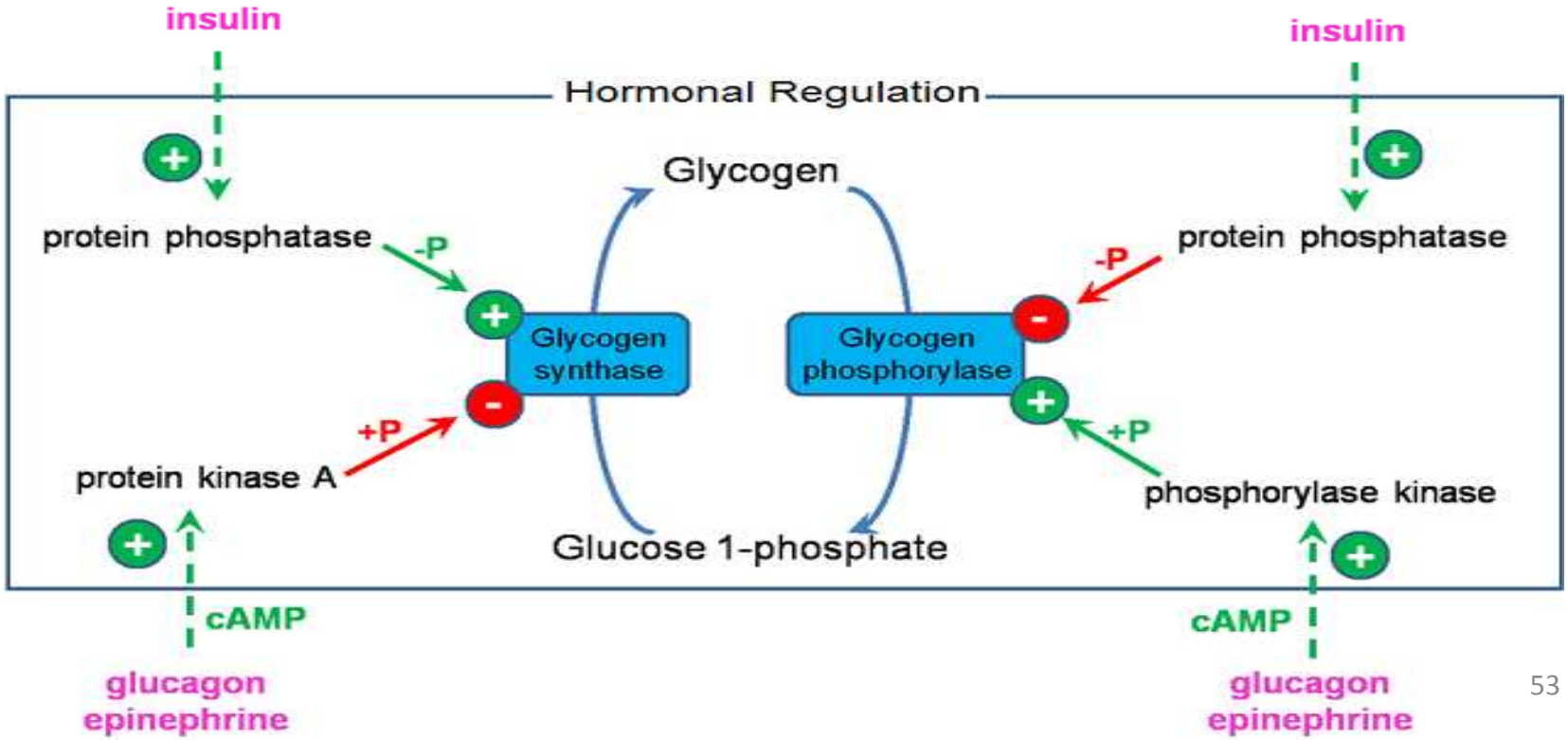
Allosteric Regulation of Glycogen Metabolism

- High G-6-P & ATP are inhibitors of glycogen phosphorylase.
- High G-6-P activates glycogen synthase
- In liver, but not in muscle, glucose is also an allosteric inhibitor of glycogen phosphorylase.
- In muscle glycogen phosphorylase is active in high AMP.
- Ca^{+2} causes activation of glycogen phosphorylase.



Covalent Modification

- Glucagon/Epinephrine: Phosphorylation activates glycogen phosphorylase & deactivates glycogen synthase.
- Insulin: Dephosphorylation activates glycogen synthase & deactivates glycogen phosphorylase.



53

Learning Check

- The role of insulin glycogeness

_____

_____

Ans:

- Increase intracellular concentrations of G-6-P
- Dephosphorylation and activation of glycogen synthase

STARCH AND CELLULOSE METABOLISM

- Starch is a polymer of glucose residues α(1,4) & cellulose consists of glucose units joined by β(1,4) linkages.
- The enzymes that break down starch into the constituent sugars are known as amylases.
  - Ruminants and carnivores do not secrete salivary α–amylase
- In ruminants microbes in rumen produce cellulase and ferment carbohydrates into VFA (acetic acid, propionc acid & butyrate). Microbes also ferment sugars to lactic acid.
- The main sources of glucose for ruminant is propionate.
- Monosaccharide released by amylase & hydrolytic enzymes of intestine are absorbed & funneled to glycolytic sequence.

PENTOSE PHOSPHATE PATHWAY

- The pentose phosphate pathway is an alternative metabolic pathway for glucose oxidation in which no ATP is consumed or generated. This pathway occurs entirely in the cytosol.

Functions

- To generate NADPH
  - ✓ NADPH is a cofactor for anabolic reactions. It also provides reducing power to redox reactions necessary for protecting cells against the reactive oxygen species (ROS).
- To provide the cell with ribose-5-phosphate (R-5-P)
- To provide glycolytic & gluconeogenic intermediates.

- The pentose phosphate pathway has two phases:
  - Oxidative
  - Non-Oxidative

PENTOSE PATHWAY IS A SHUNT

- The pathway begins with glycolytic intermediate glucose 6-P. It reconnects with glycolysis.
  - The end products of the pathway (G-3-P and F-6-P) further join the glycolytic pathway.
- It is for this reason that the pentose pathway is often referred to as a shunt; called hexoses monophosphate shunt.

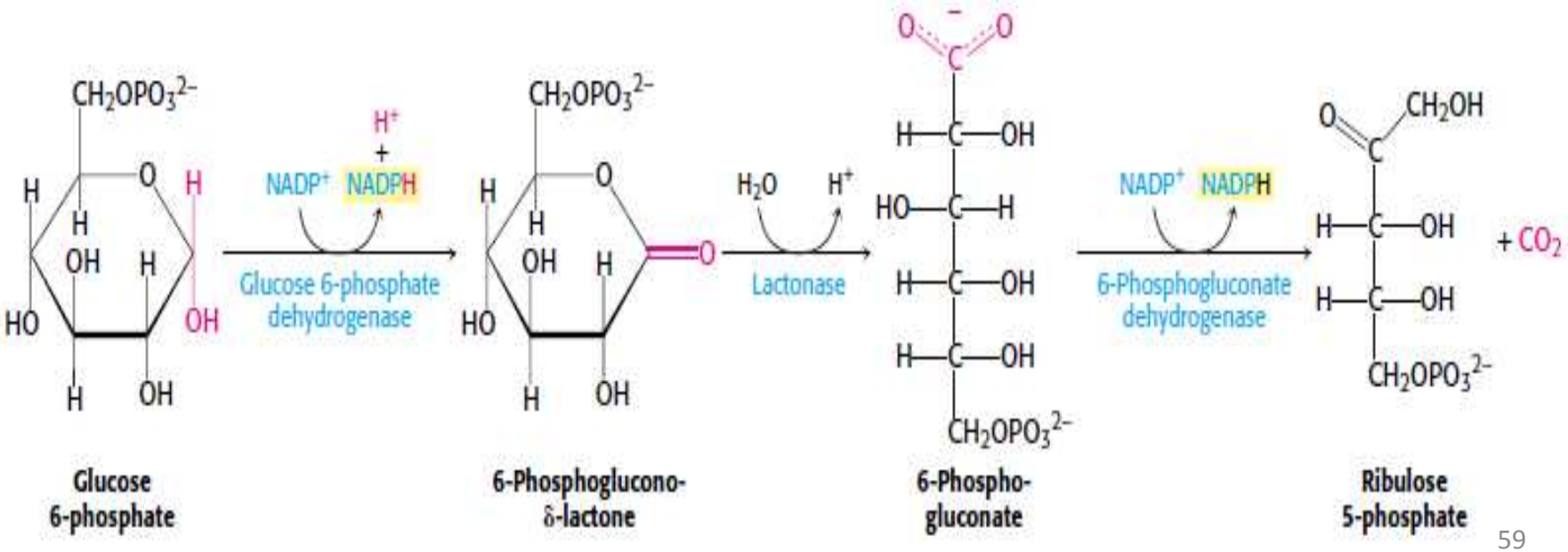
Occurrence of Pentose Phosphate Pathway

Tissues with active pentose phosphate pathways

Tissue	Function
Adrenal gland	Steroid synthesis
Liver	Fatty acid and cholesterol synthesis
Testes	Steroid synthesis
Adipose tissue	Fatty acid synthesis
Ovary	Steroid synthesis
Mammary gland	Fatty acid synthesis
Red blood cells	Maintenance of reduced glutathione

1. Oxidative Phase

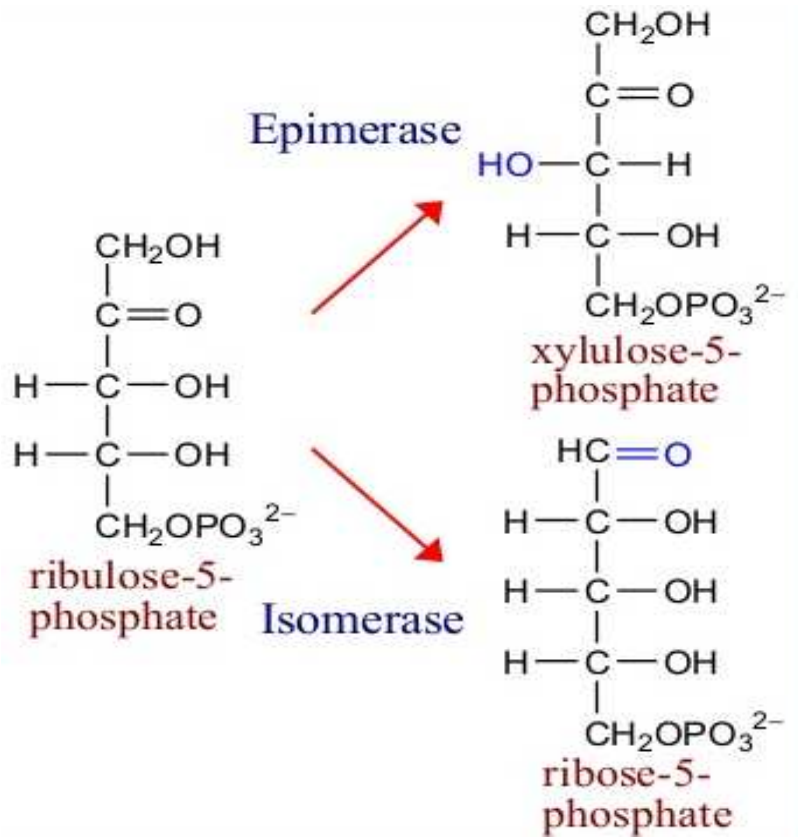
The oxidative phase of the pentose phosphate pathway starts with the dehydrogenation of glucose 6-phosphate at C1, by glucose 6-phosphate dehydrogenase followed by hydrolysis and oxidative decarboxylation of the intermediates. This yields formation of ribulose 5-phosphate, 2 NADPH & release CO_2.



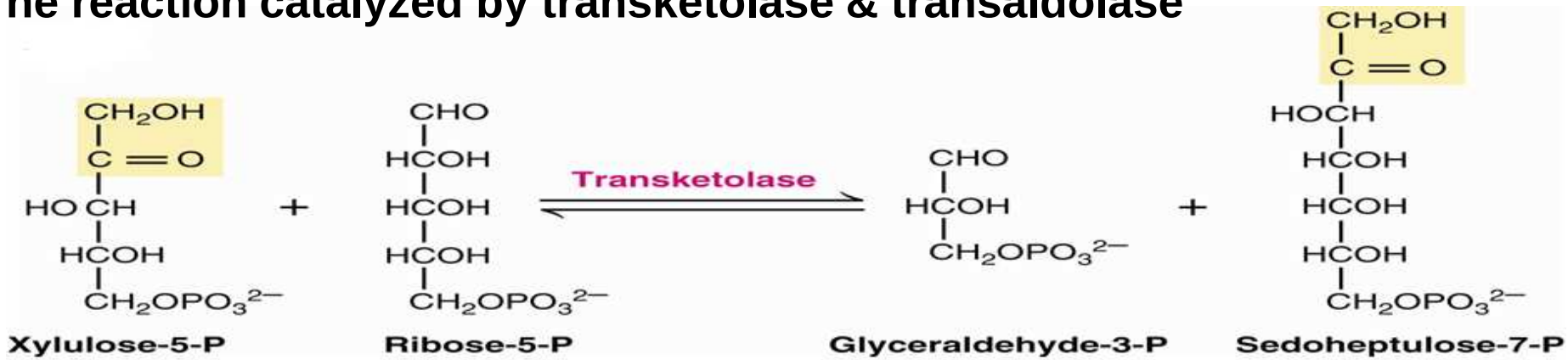
2. Non-Oxidative Phase

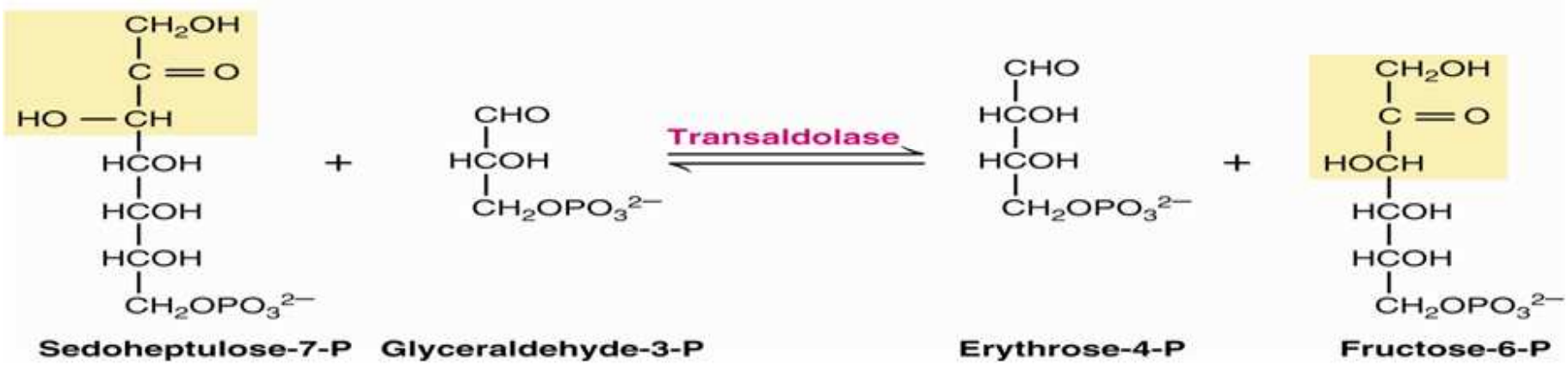
- Ribulose-5-phosphate can be converted into two different 5-carbon molecules (Ribose-5-phosphate and Xylulose-5-phospahte).
- The three pentose sugars Ribulose-5-P, Ribose-5-P and Xylulose-5-P are reshuffle to form two Fructose -6-Phosphate and one glyceraldehyde 3-Phosphate.
- The 5-carbon molecules combined one another to generate glycolytic intermediates via transketolase & transaldolase reactions.

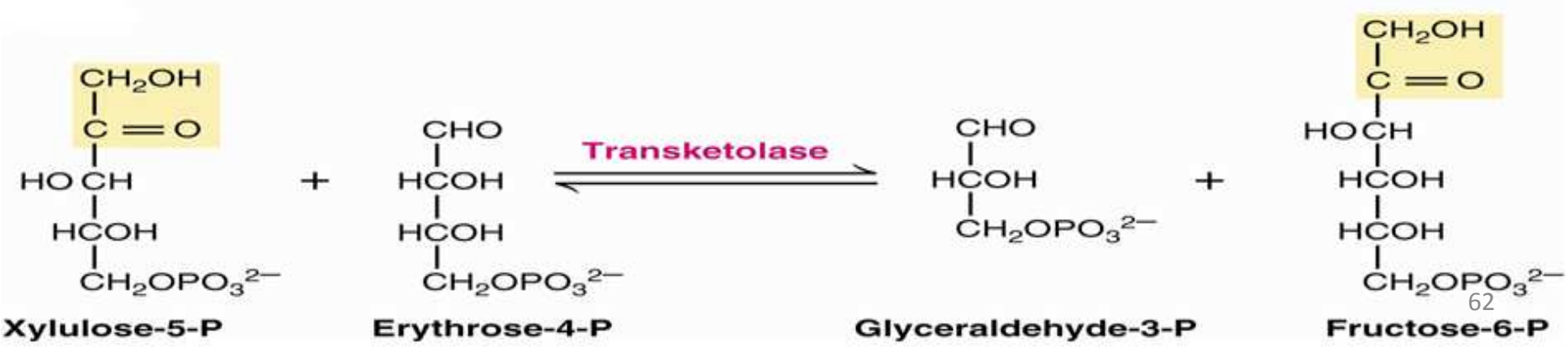
- Phosphopentose Isomerase
  - Converts ketose to aldose
- Phosphopentose Epimerase
  - Epimerizes at C-3
- Transketolase
  - Transfers 2-Carbon units
- Transaldolase
  - Transfers 3-Carbon units
- Carbon donor is ketose and acceptor is aldose



The reaction catalyzed by transketolase & transaldolase





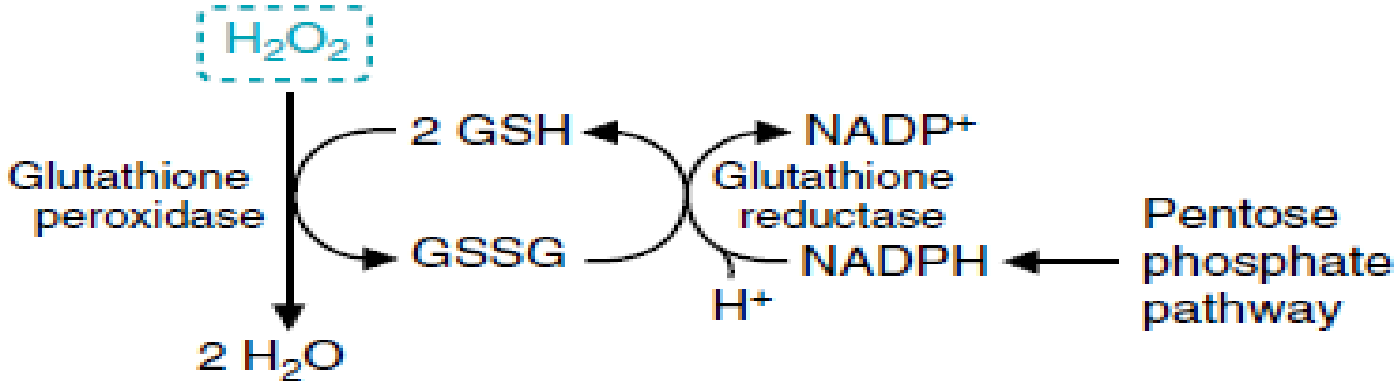


Pentose phosphate pathway

Reaction	Enzyme
Oxidative phase	
Glucose 6-phosphate + $NADP^+$ $\longrightarrow$ 6-phosphoglucono-δ-lactone + NADPH + H^+	Glucose 6-phosphate dehydrogenase
6-Phosphoglucono-δ-lactone + H_2O $\longrightarrow$ 6-phosphogluconate + H^+	Lactonase
6-Phosphogluconate + $NADP^+$ $\longrightarrow$ ribulose 5-phosphate + CO_2 + NADPH	6-Phosphogluconate dehydrogenase
Nonoxidative Phase	
Ribulose 5-phosphate $\rightleftharpoons$ ribose 5-phosphate	Phosphopentose isomerase
Ribulose 5-phosphate $\rightleftharpoons$ xylulose 5-phosphate	Phosphopentose epimerase
Xylulose 5-phosphate + ribose 5-phosphate $\rightleftharpoons$ sedoheptulose 7-phosphate + glyceraldehyde 3-phosphate	Transketolase
Sedoheptulose 7-phosphate + glyceraldehyde 3-phosphate $\rightleftharpoons$ fructose 6-phosphate + erythrose 4-phosphate	Transaldolase
Xylulose 5-phosphate + erythrose 4-phosphate $\rightleftharpoons$ fructose 6-phosphate + glyceraldehyde 3-phosphate	Transketolase

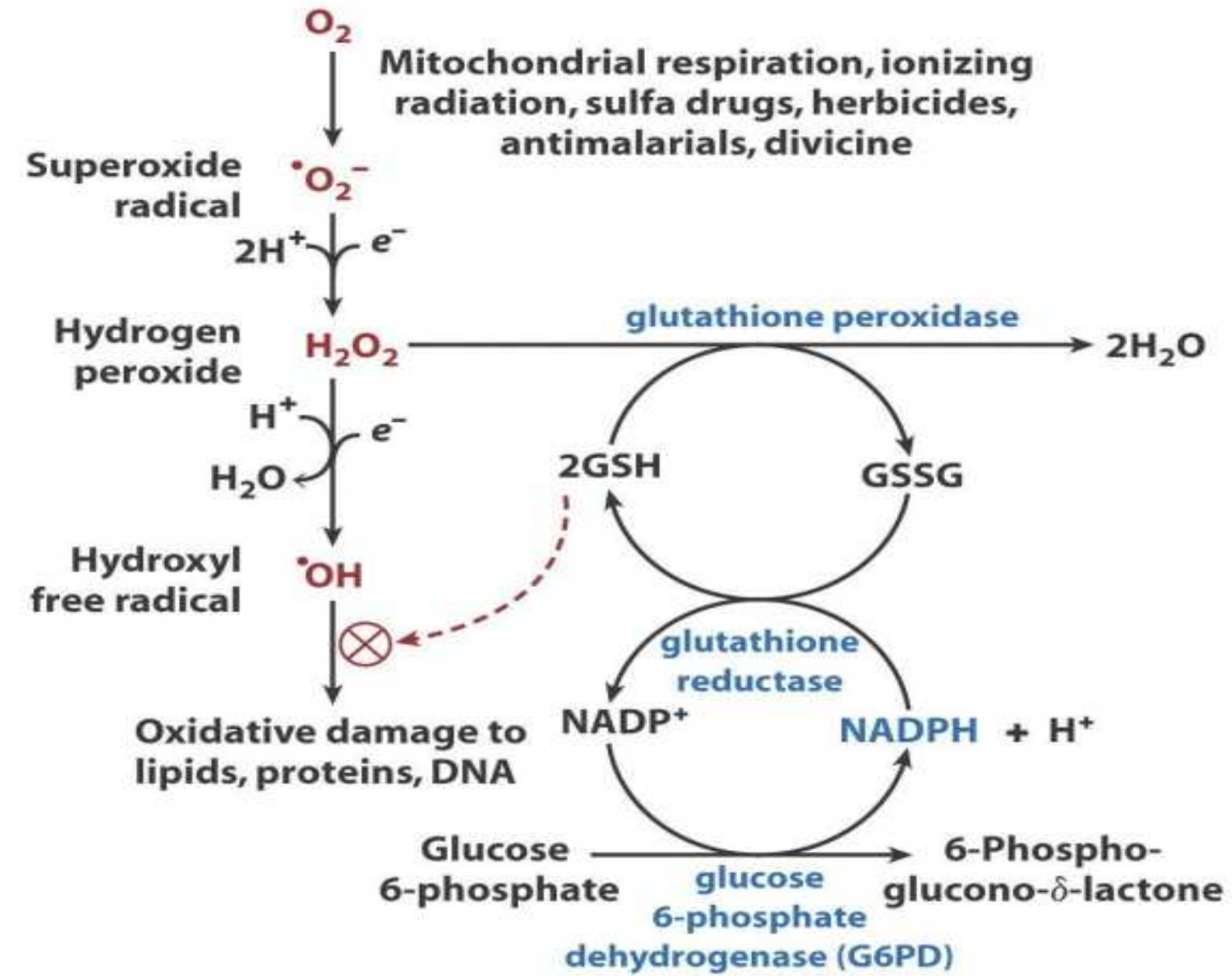
The role of NADPH in RBCs

- Removal of H_2O_2 is achieved in a reaction with reduced glutathione (GSH) , catalysed by glutathionine peroxidase.
- Since this reaction is required continuously, the oxidised glutathione (GSSG) must be reduced continuously and this is achieved with NADPH, catalysed by glutathione reductase as follows:



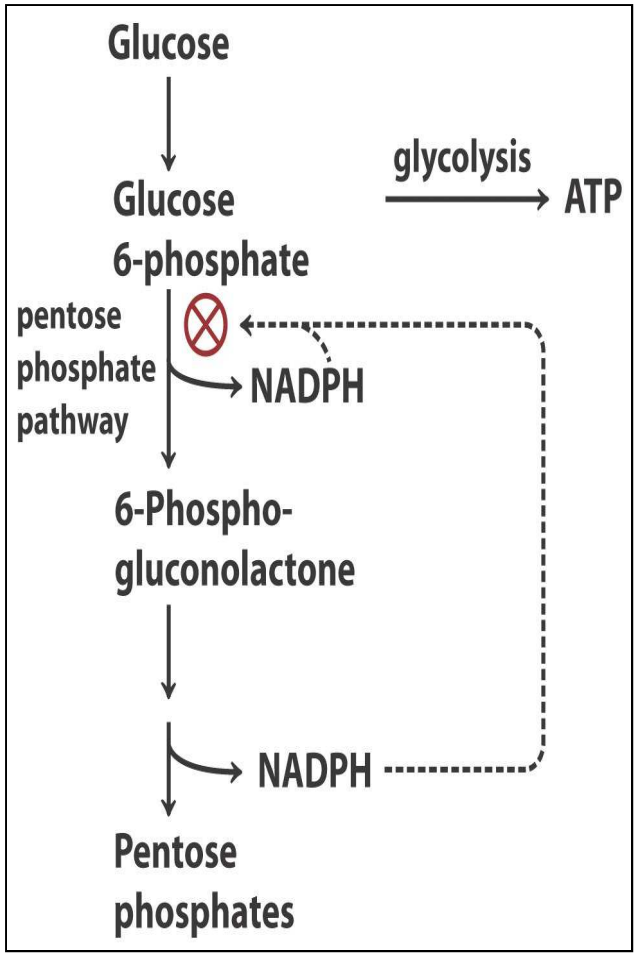
- Lack of GSH means GSH cannot protect the cell from the reactive oxygen species, which damage the cell membrane: Cell membrane integrity & flexibility (It is most important in RBCs).

Protection from Radical Damage

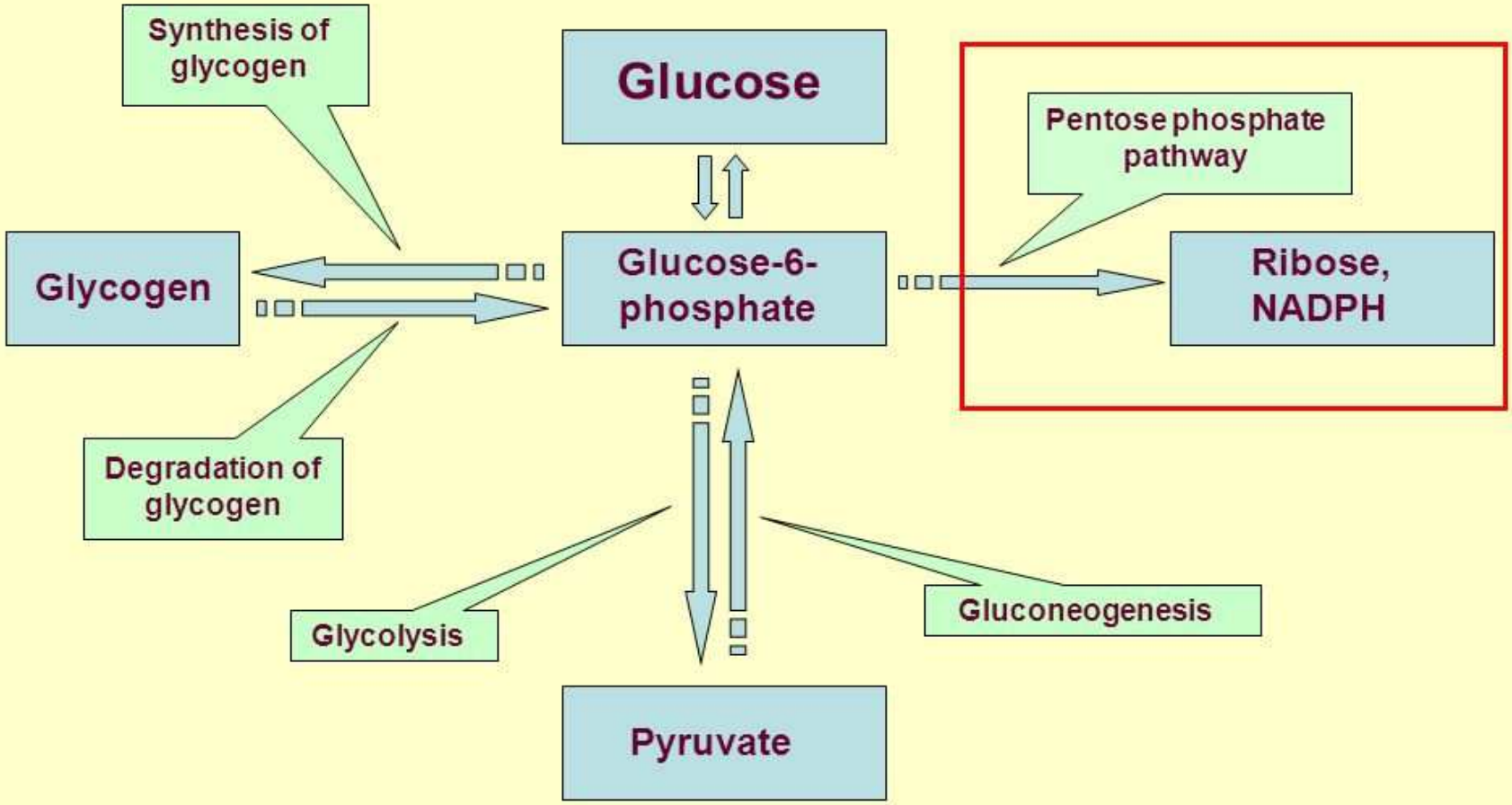


REGULATION OF THE PENTOSE PHOSPHATE PATHWAY

- ✓ Glucose-6-P-dehydrogenase (rate limiting reaction) is controlled by:
  - Stimulated by Glucose-6-P
  - Inhibited by NADPH
  - Insulin induce its synthesis.
  - Stimulated by GSSG



The fate of glucose molecule in the cell



Learning Check

- Red blood cells lack mitochondria. These cells process glucose to lactate, but they also generate CO_2.
- What is the purpose of producing lactate?
  - **LACTATE IS USED BY CORI CYCLE & PRODUCES GLUCOSE**
- How can red blood cells generate CO_2 if they lack mitochondria?
  - **PENTOSE PHOSPHATE PATHWAY**