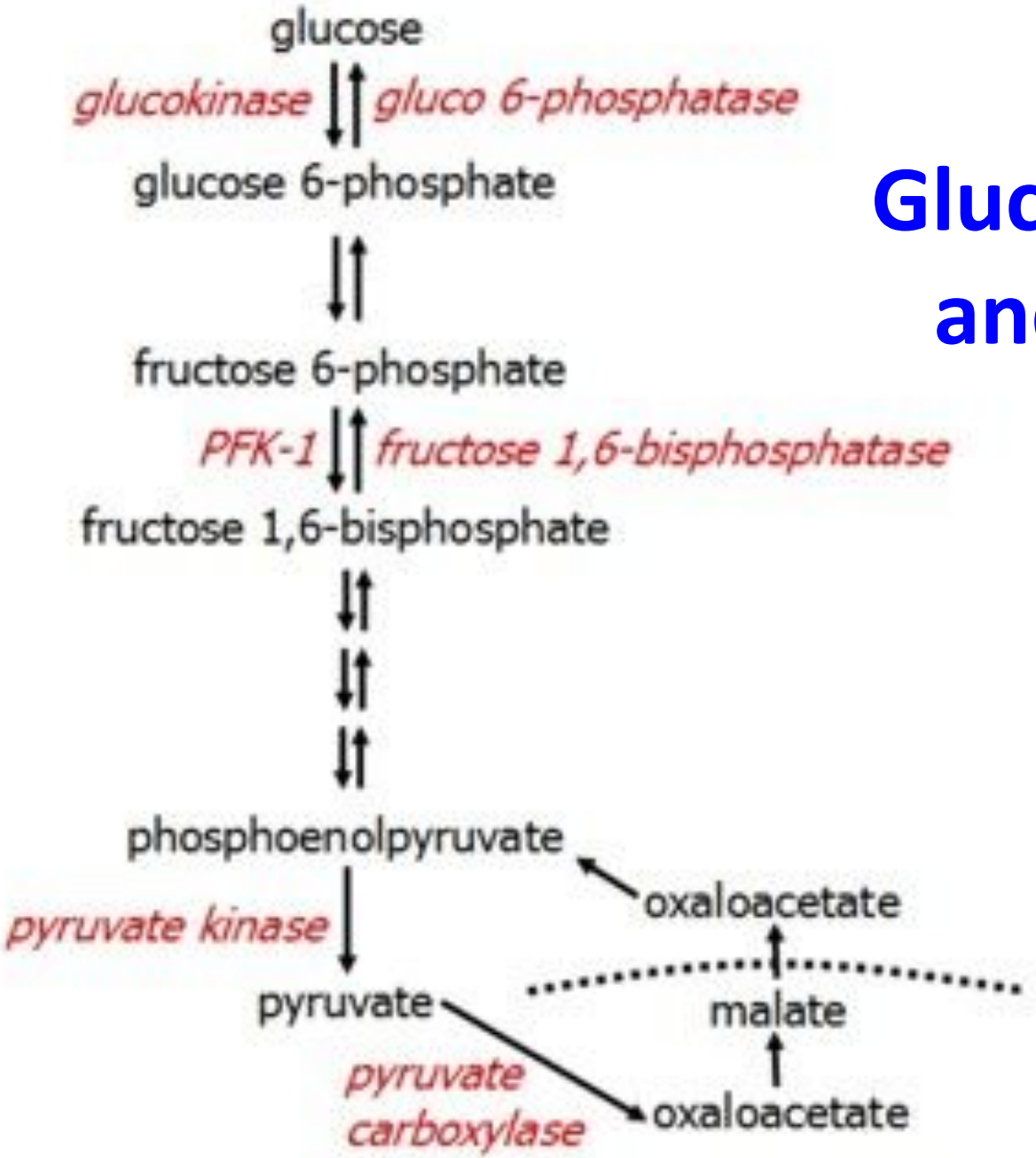
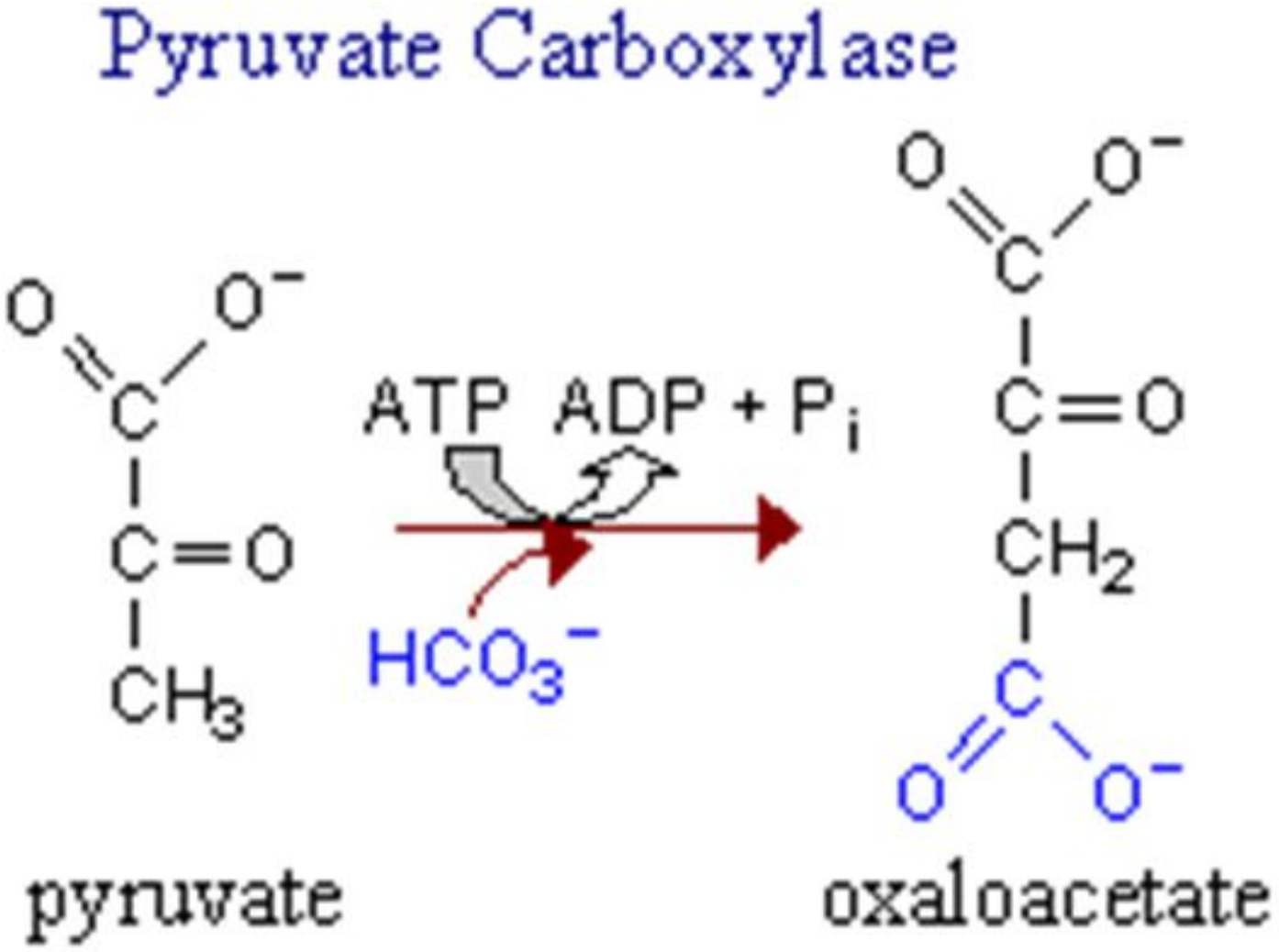
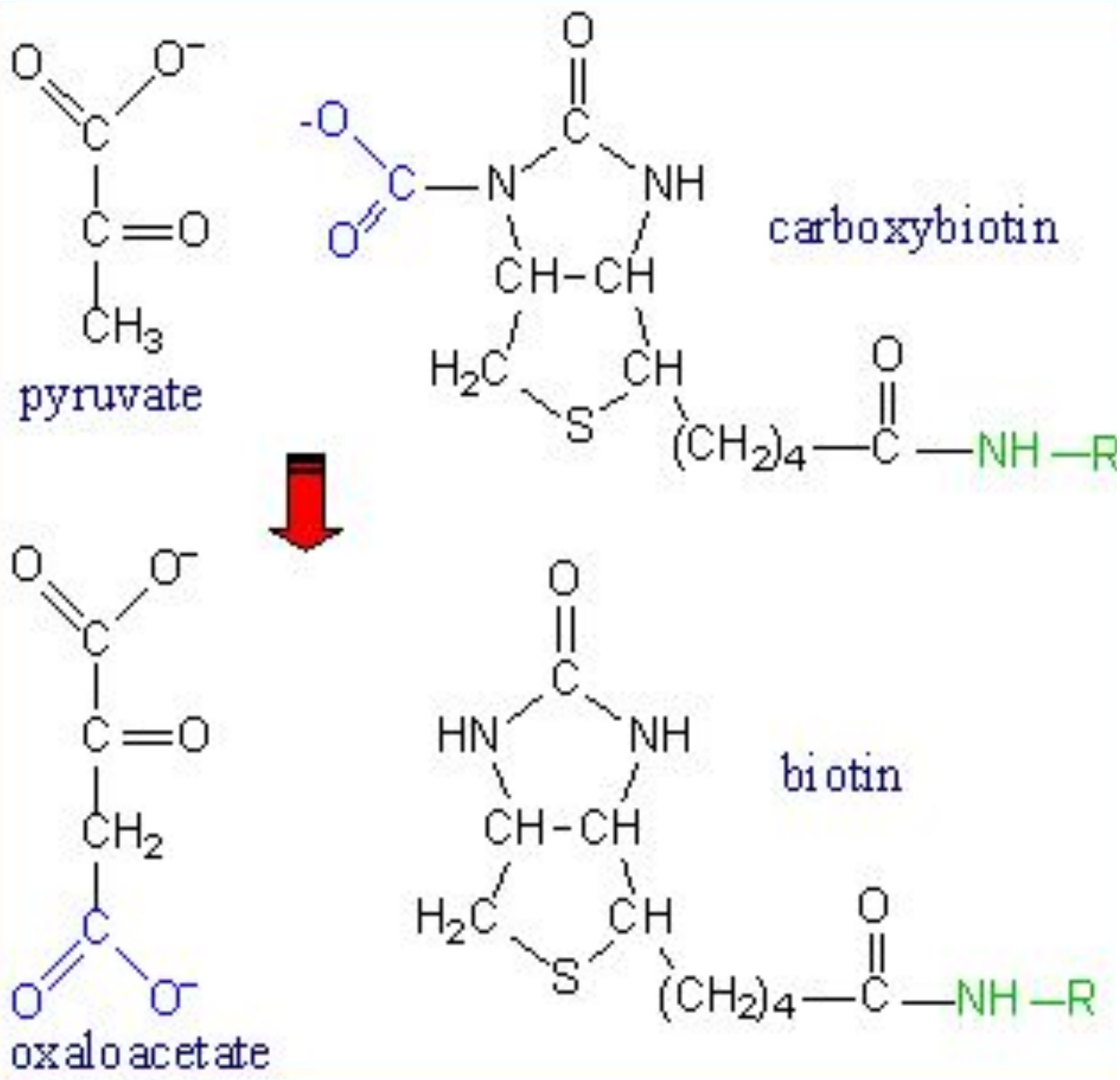
Carbohydrate metabolism

Gluconeogenesis and glycolysis

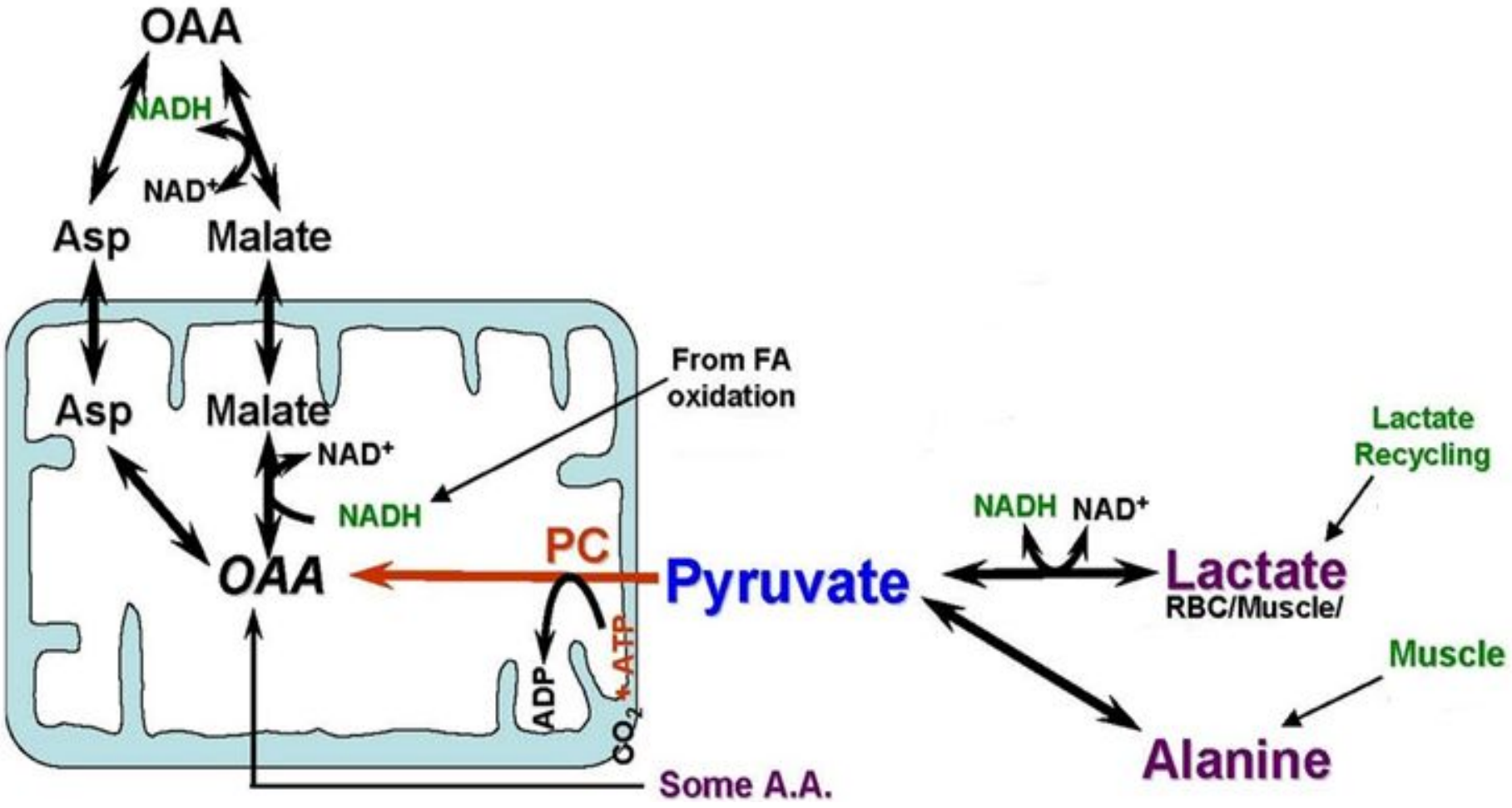


Gluconeogenesis

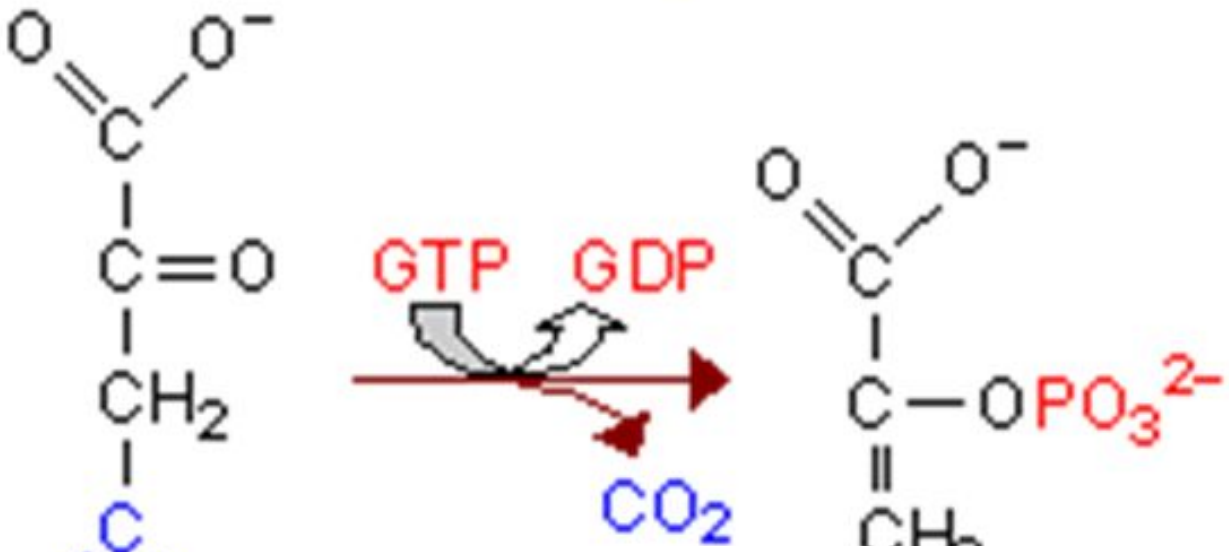



pyruvate
carboxybiotin
oxaloacetate
biotin

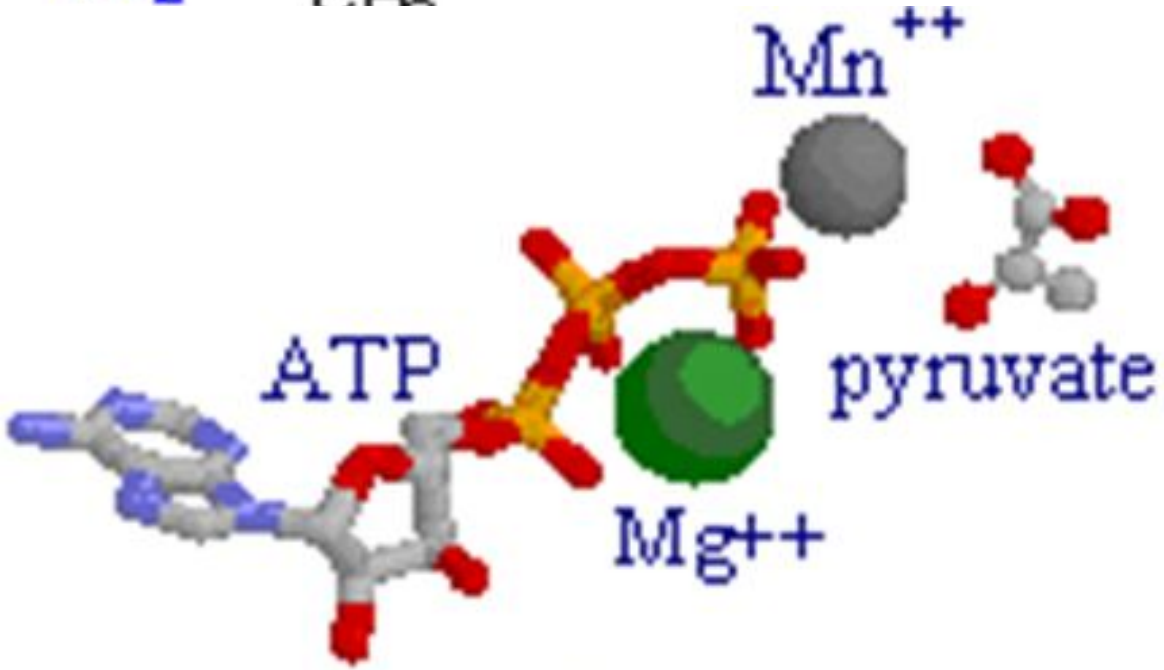
OAA transport

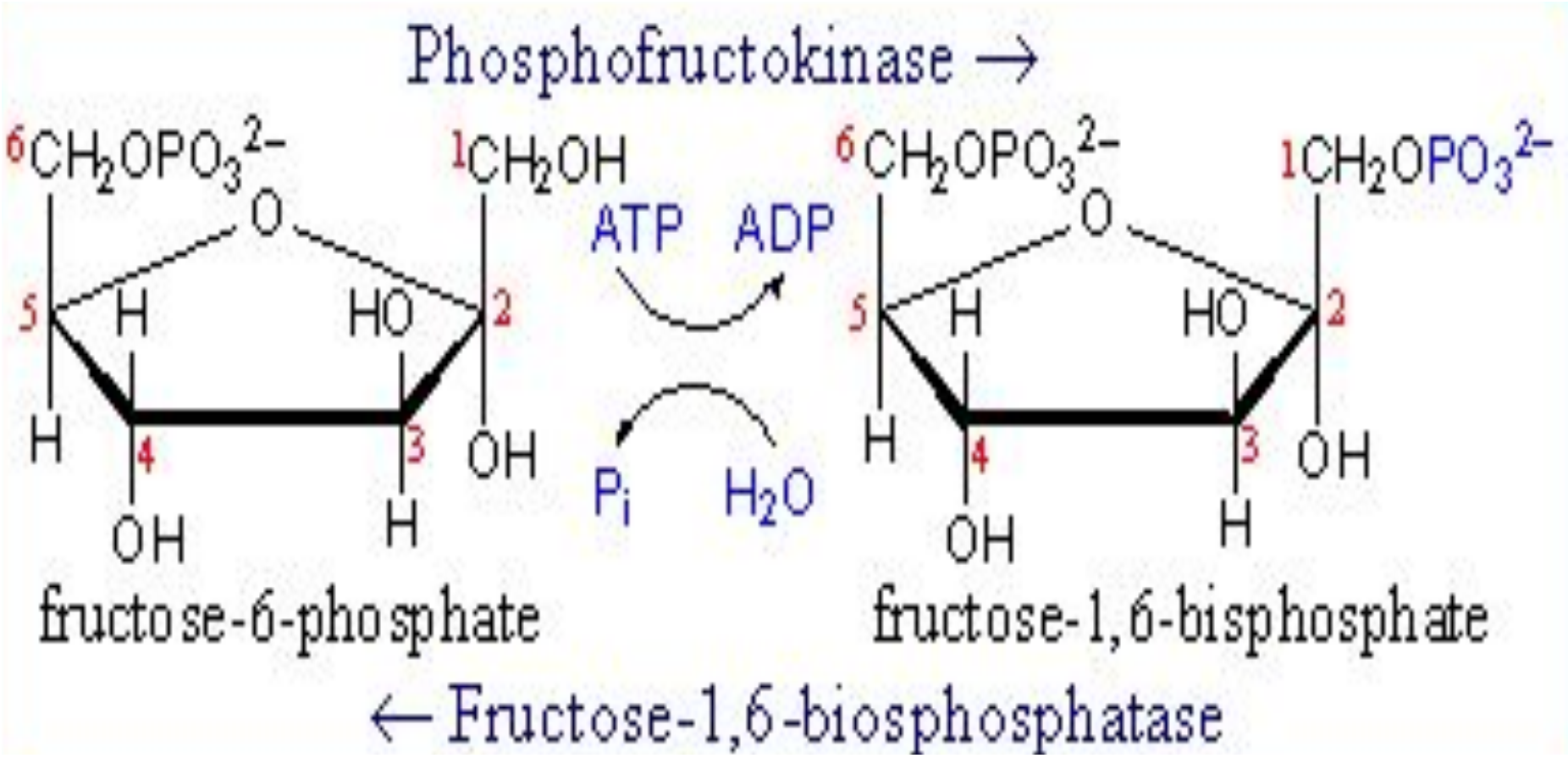


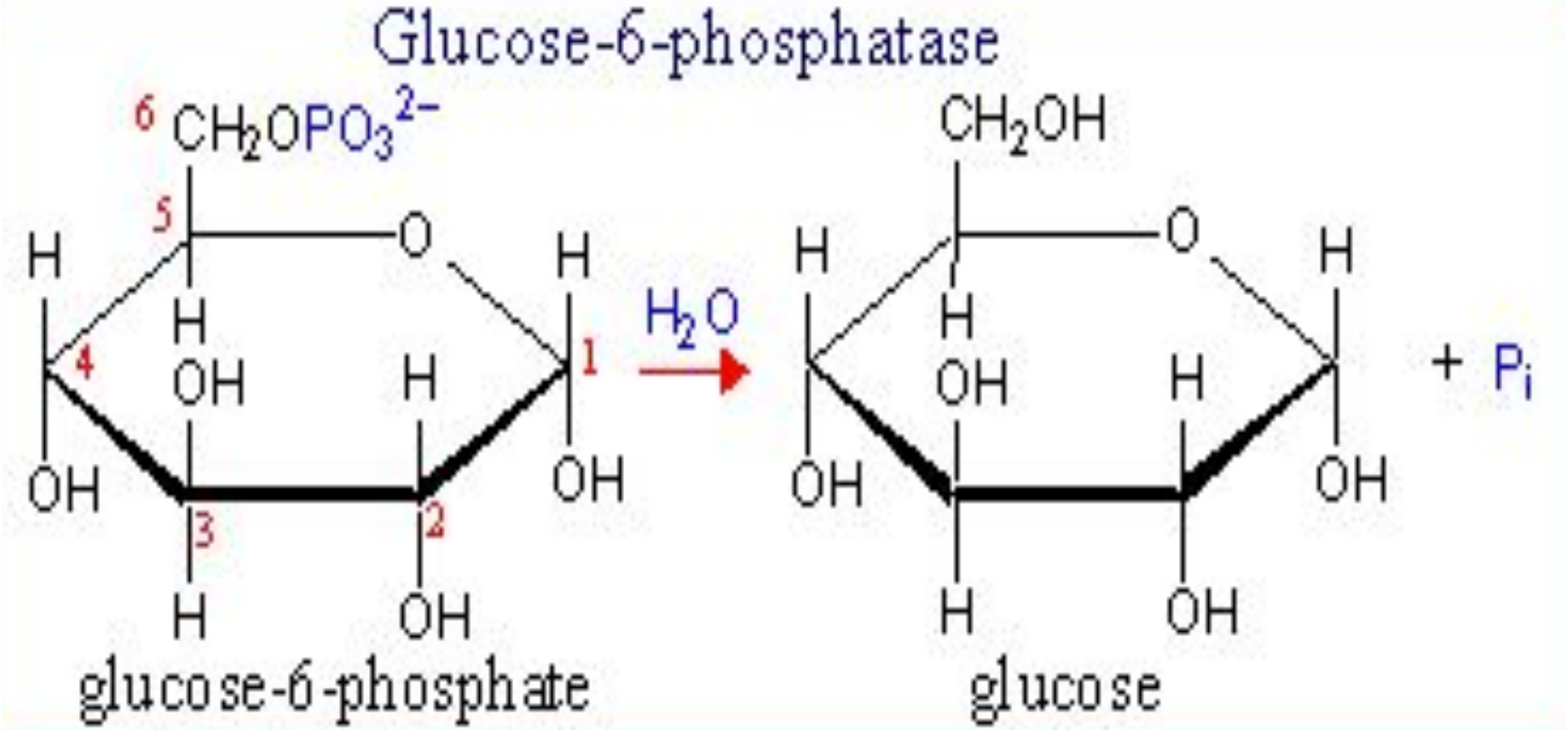
PEP Carboxykinase



oxaloacetate



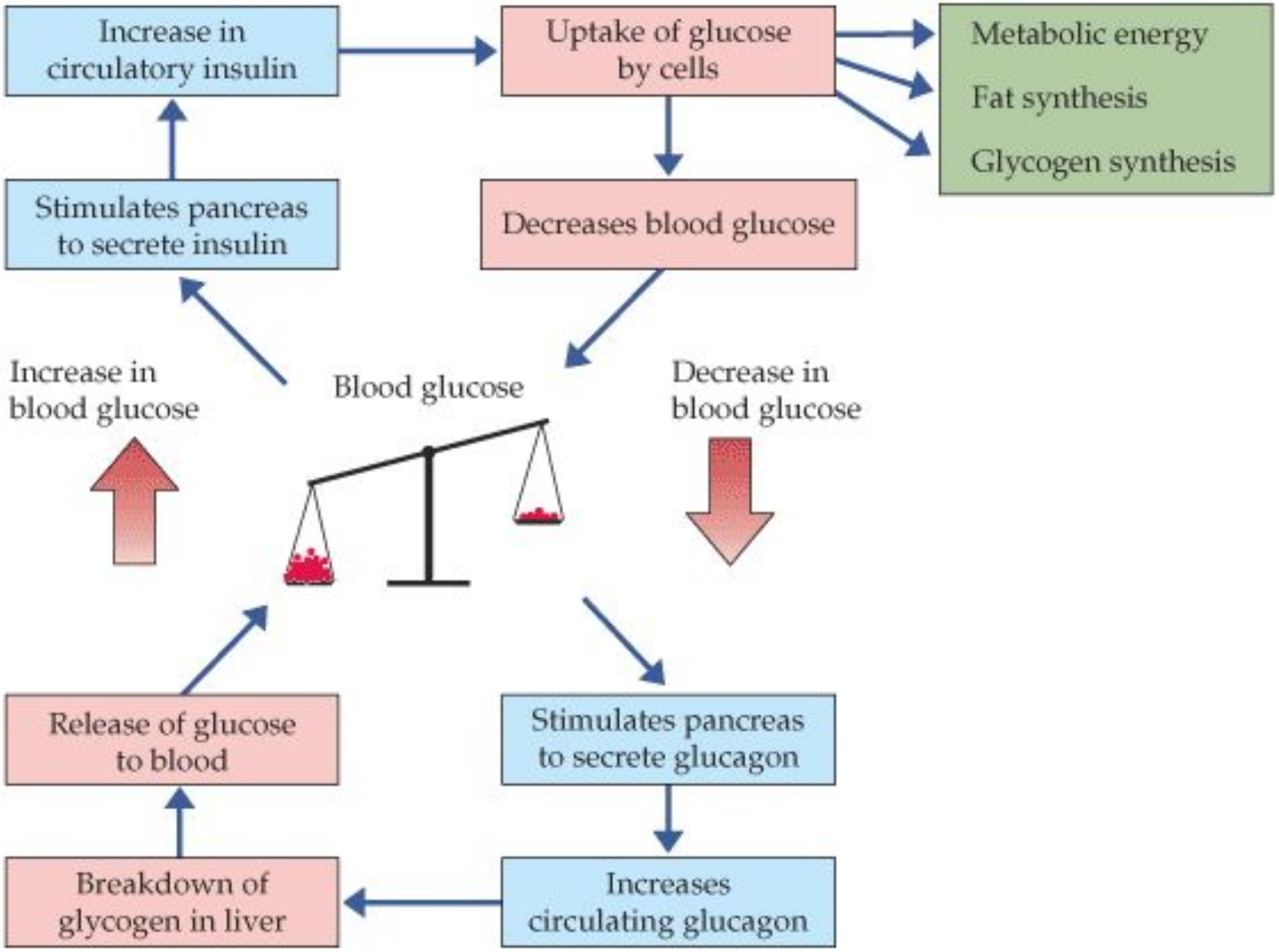

Phosphofructokinase →
6CH2OPO3 2–
1CH2OH
O
5
H
HO
2
H
4
3
OH
OH
H
ATP
ADP
Pi
H2O
6CH2OPO3 2–
1CH2OPO3 2–
O
5
H
HO
2
H
4
3
OH
OH
H
fructose-6-phosphate
fructose-1,6-bisphosphate
← Fructose-1,6-biosphosphatase


Glucose-6-phosphatase
6 CH2OPO3 2−
5
O
H
H
4
OH
H
1
OH
OH
3
2
H
OH
glucose-6-phosphate
H2O
CH2OH
O
H
H
OH
H
OH
OH
H
OH
glucose
+ Pi

The overall equation:

$$2\,\text{pyruvate} + 2\,\text{NADH} + H^+ + 4\,\text{ATP} + 2\,\text{GTP} \rightarrow$$

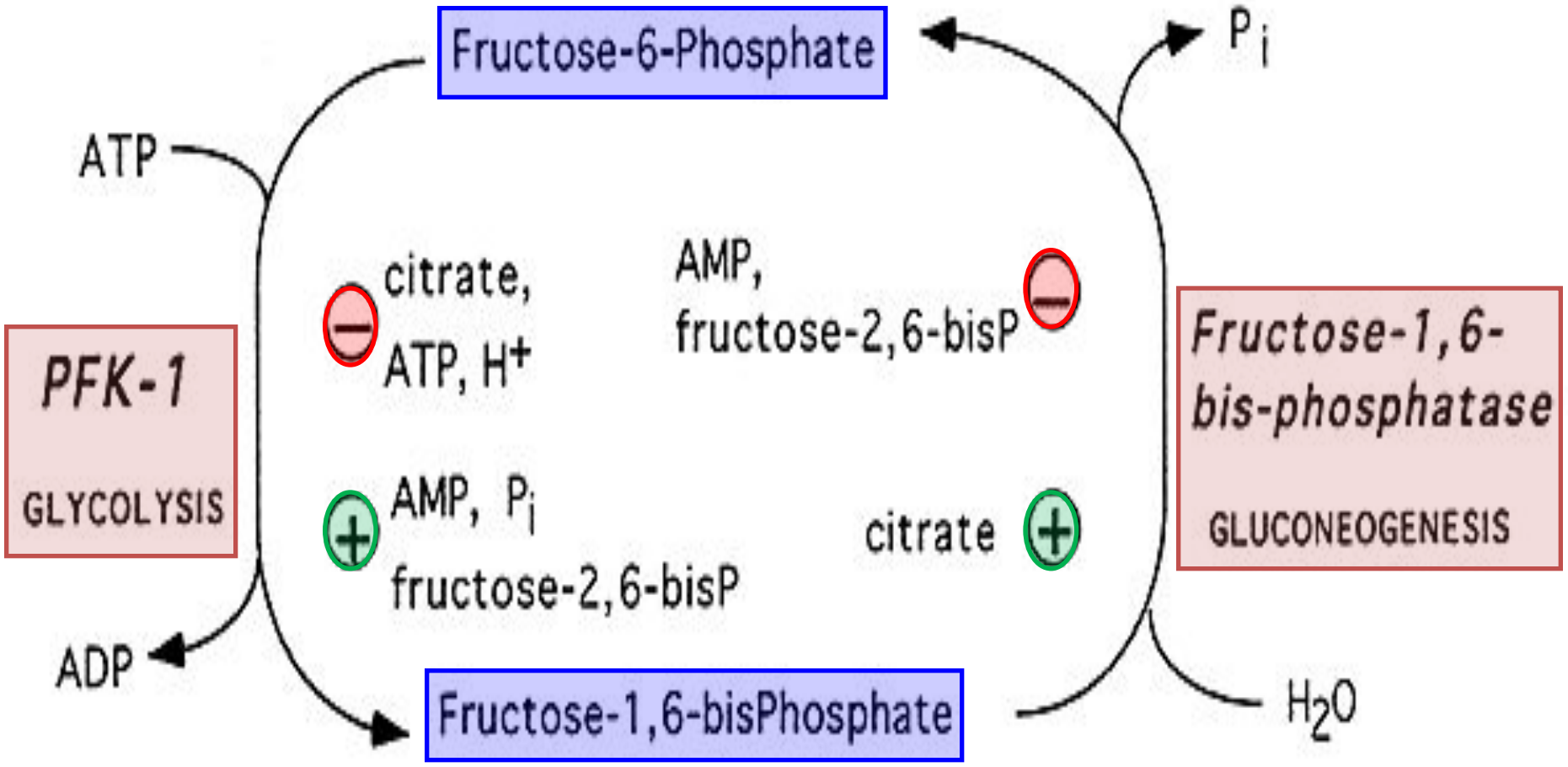
$$\rightarrow \text{glucose} + 2\,NAD^+ + 4\,\text{ADP} + 2\,\text{GDP} + 6\,P_i$$


Increase in circulatory insulin
Uptake of glucose by cells
Metabolic energy
Fat synthesis
Glycogen synthesis
Stimulates pancreas to secrete insulin
Decreases blood glucose
Increase in blood glucose
Blood glucose
Decrease in blood glucose
Release of glucose to blood
Stimulates pancreas to secrete glucagon
Breakdown of glycogen in liver
Increases circulating glucagon

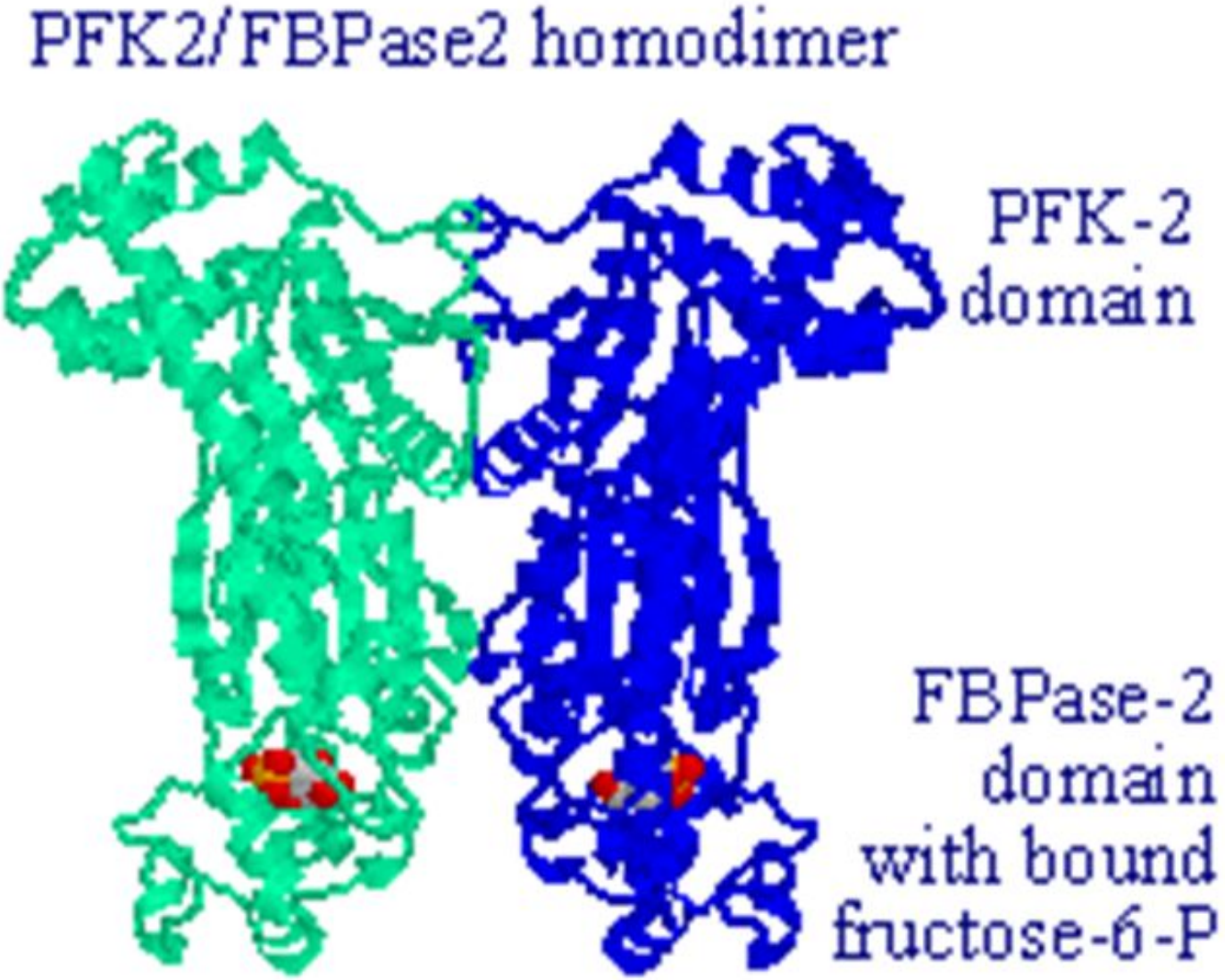
Insulin

- Stimulate glucose transport into cells
- Induses synthesis of glucokinase, phosphofructokinase, pyruvate kinase
- Activates protein phosphatase → pyruvate kinase

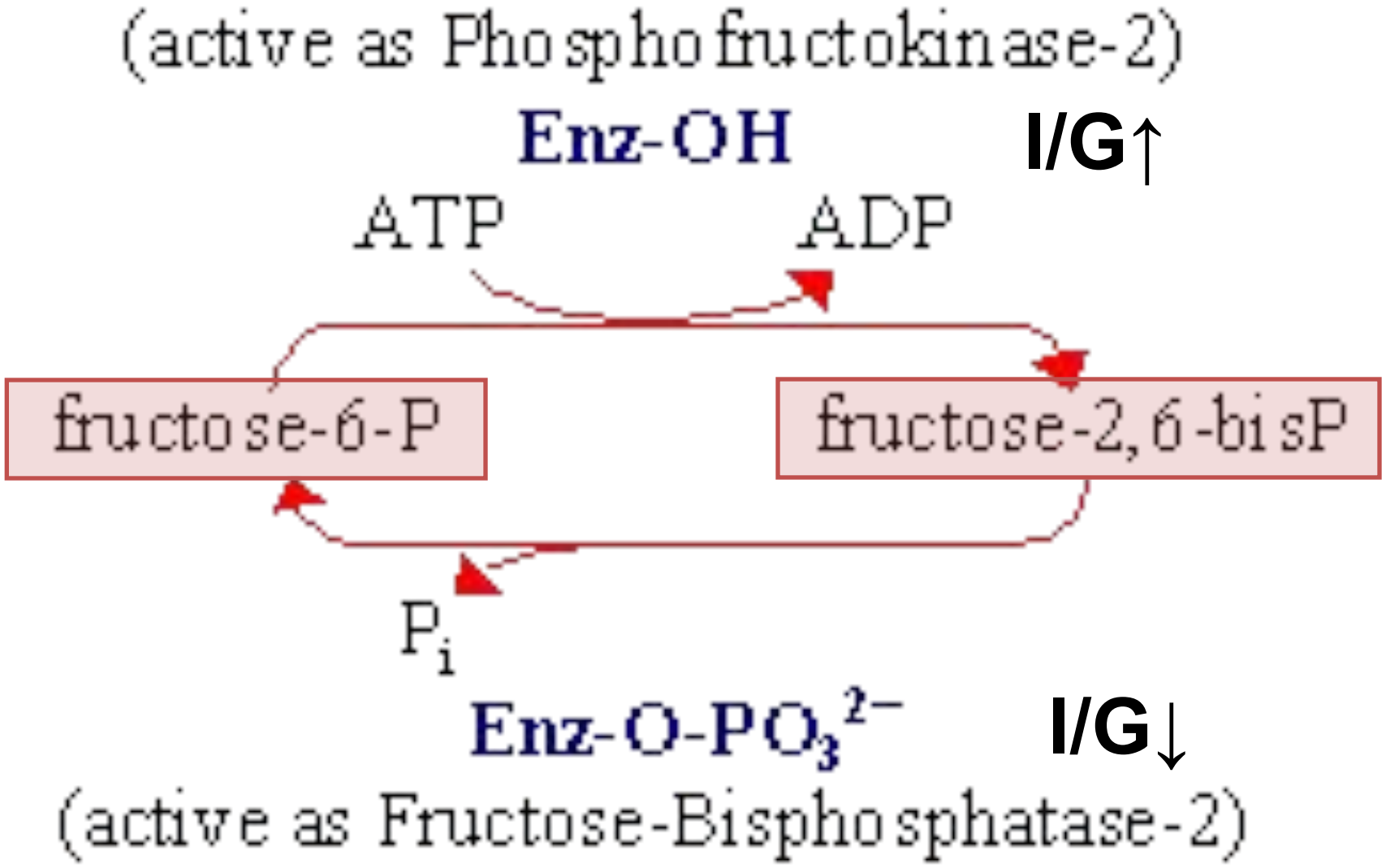
Glycolysis and gluconeogenesis regulation

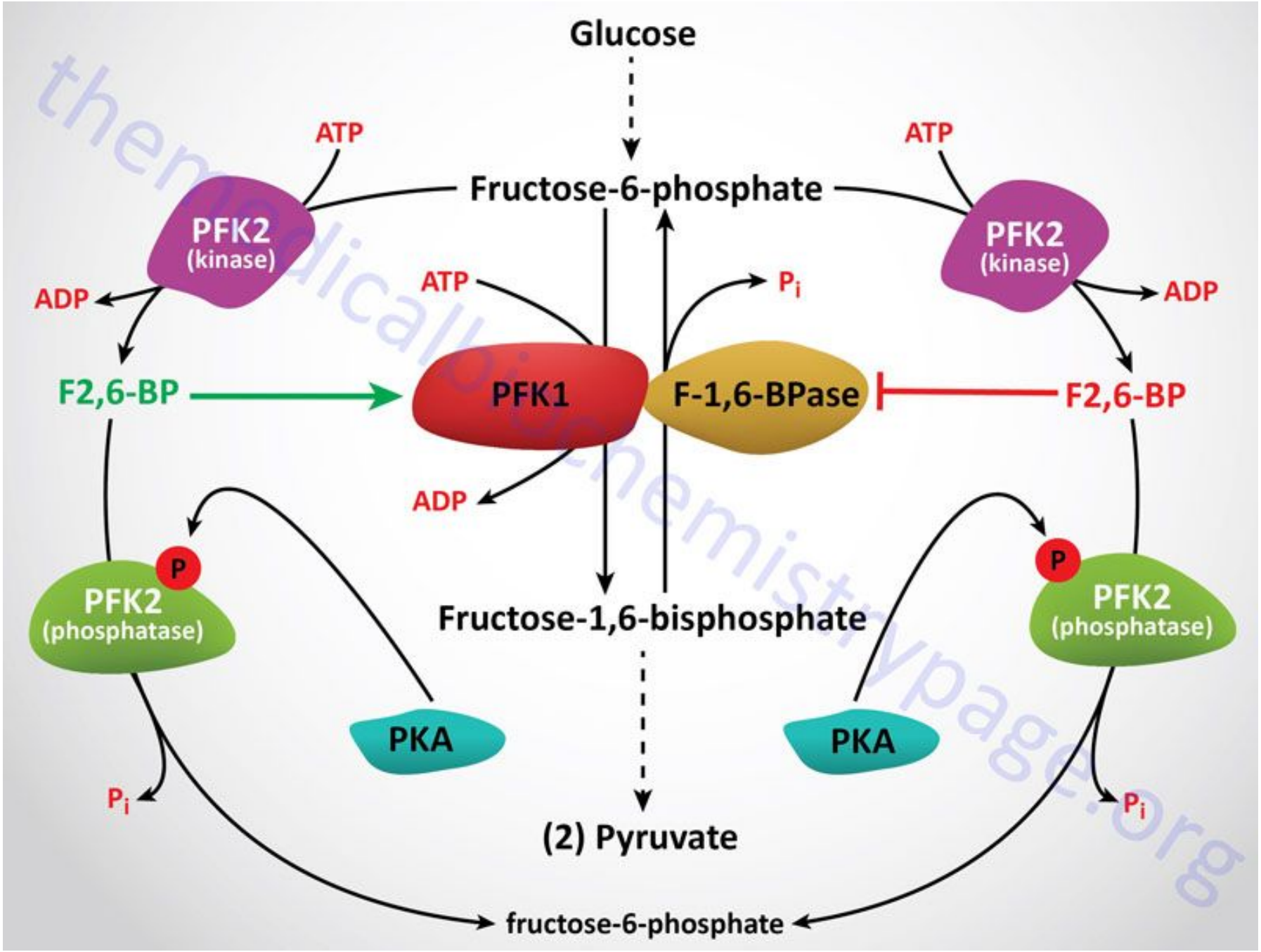


Bi-functional enzyme

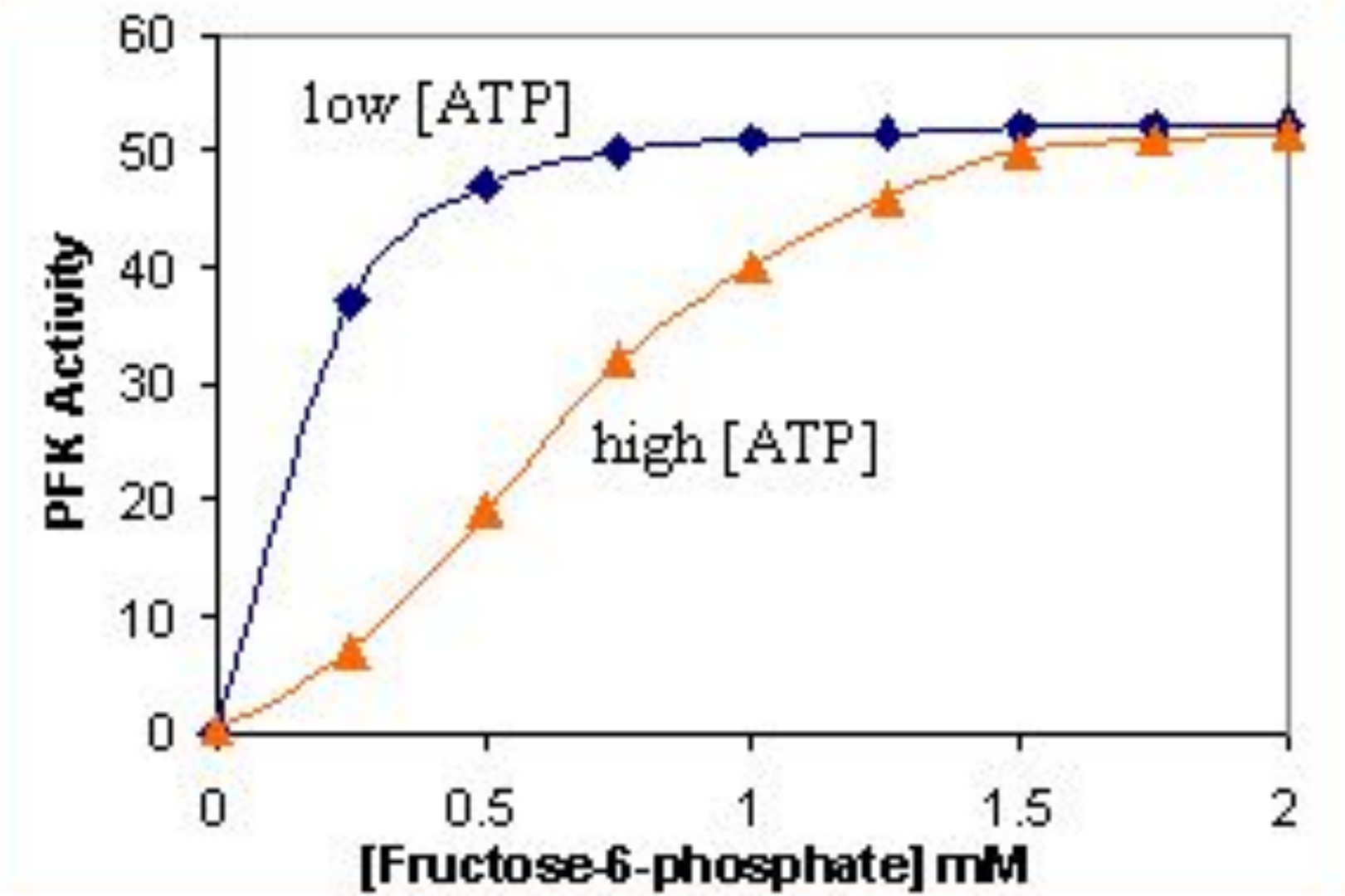


Bi-functional enzyme

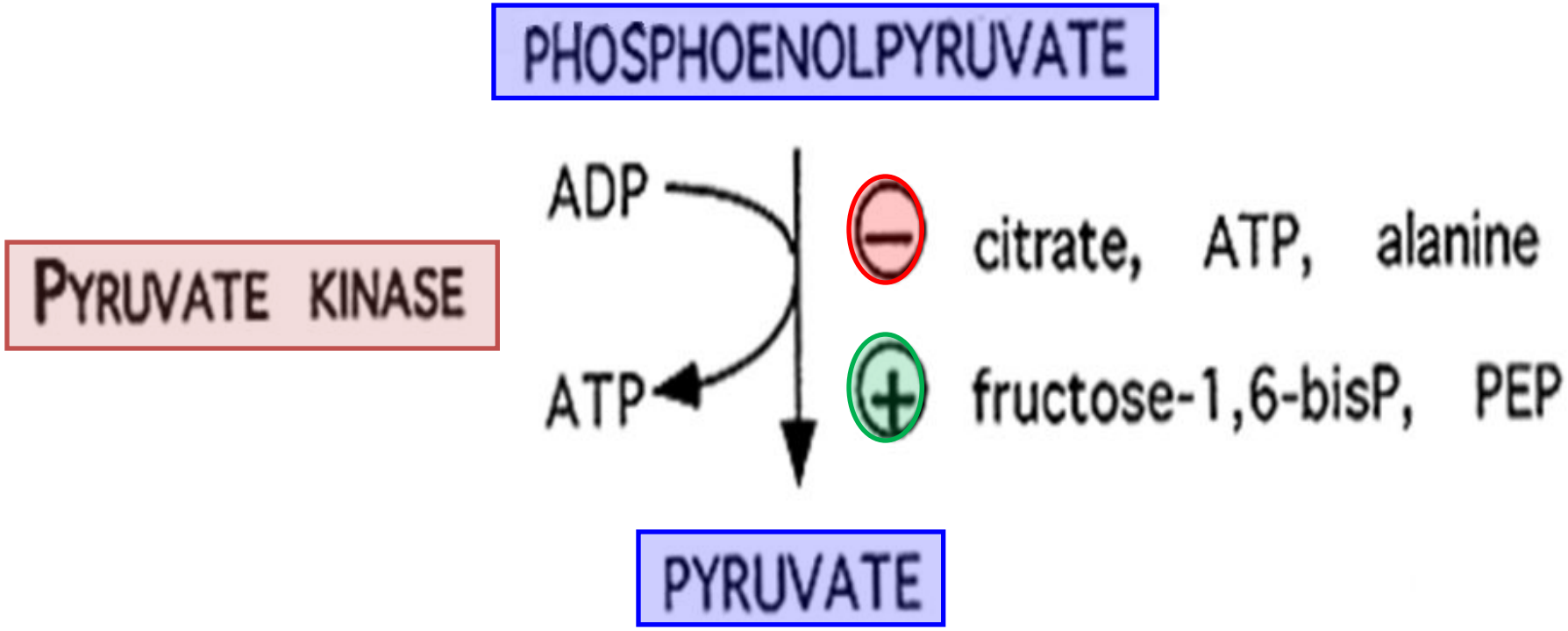




Regulation of phosphofructokinase activity

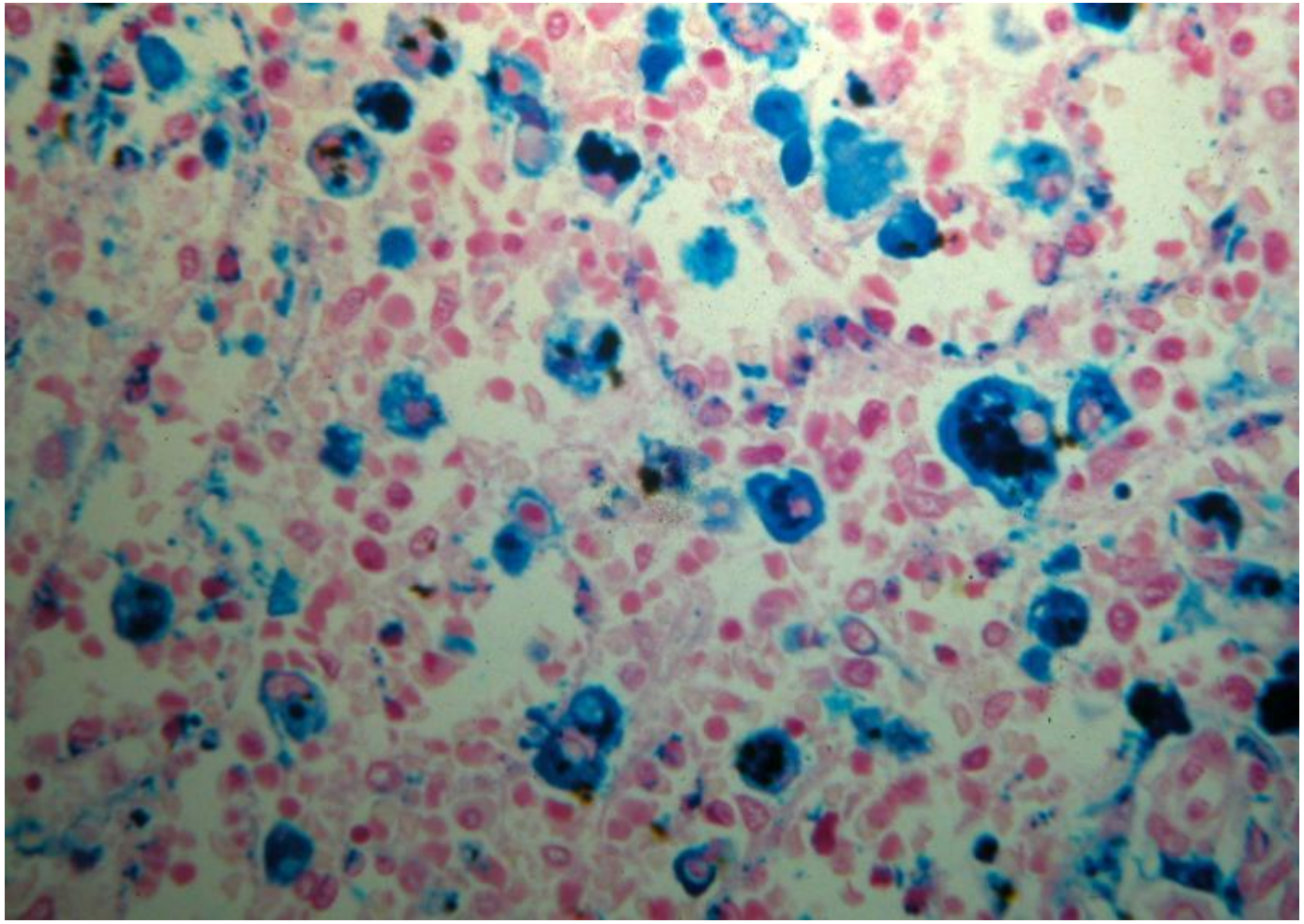


Regulation of pyruvate kinase activity

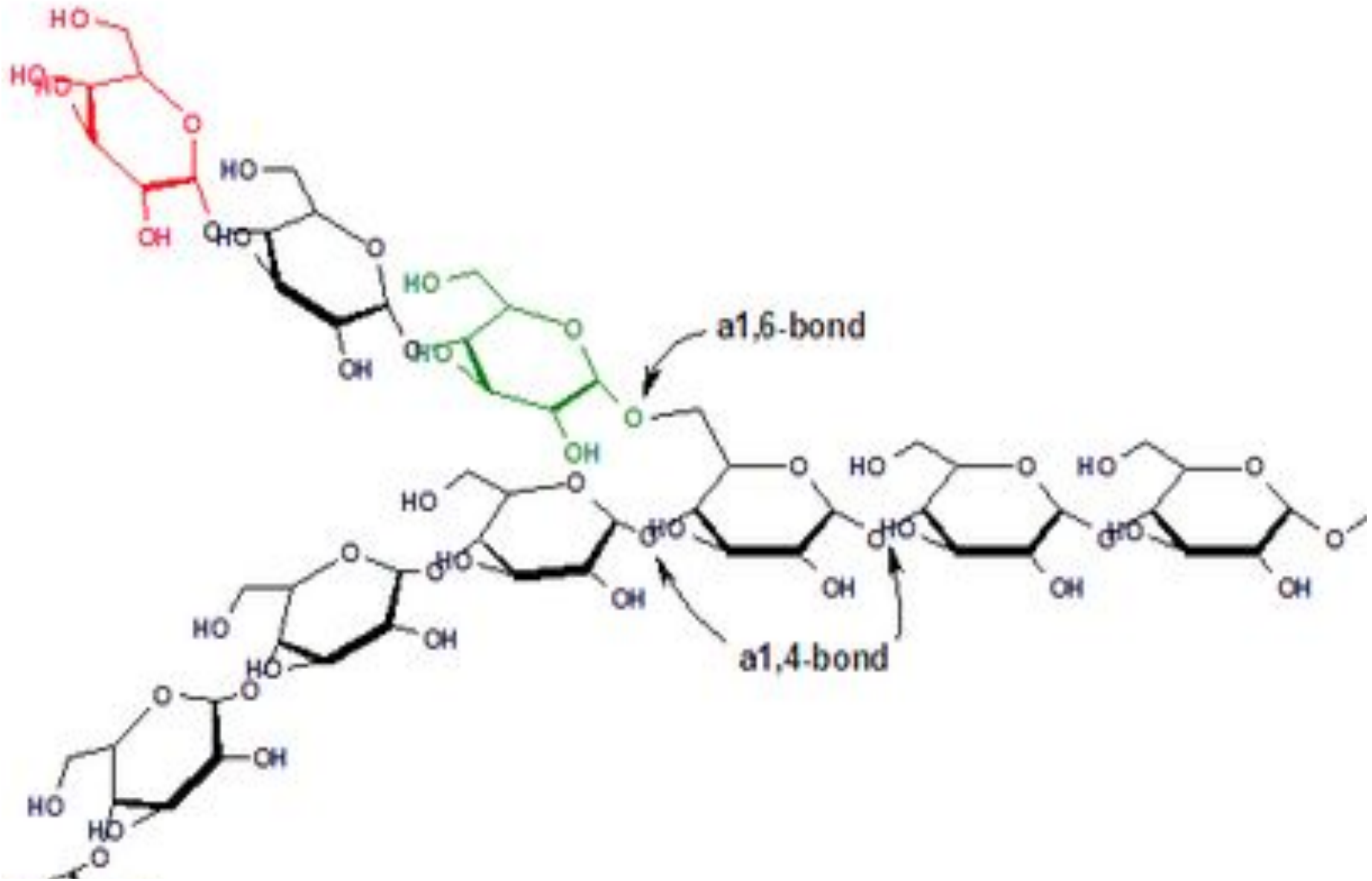


Glycogen Metabolism

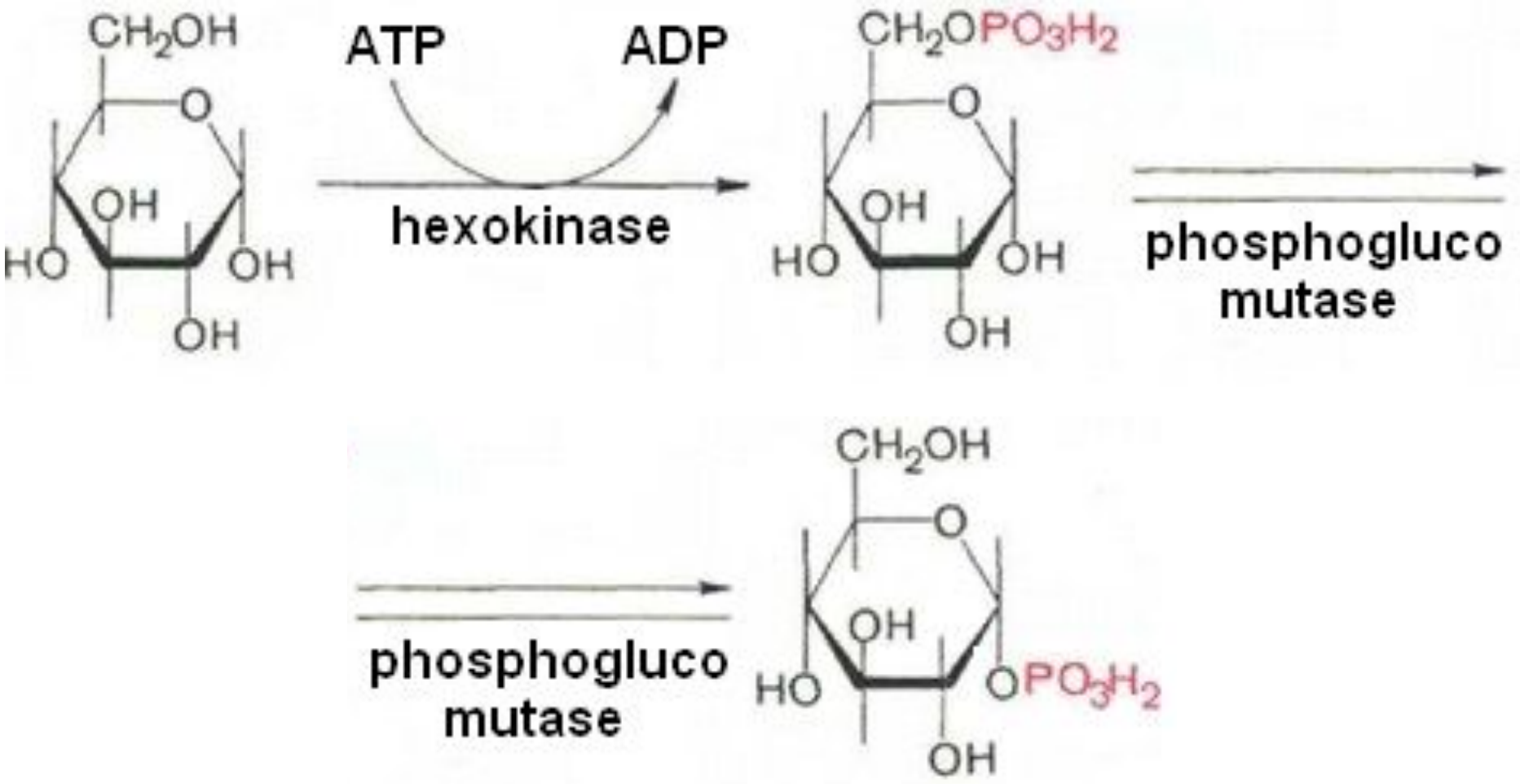
Glycogen in the cell



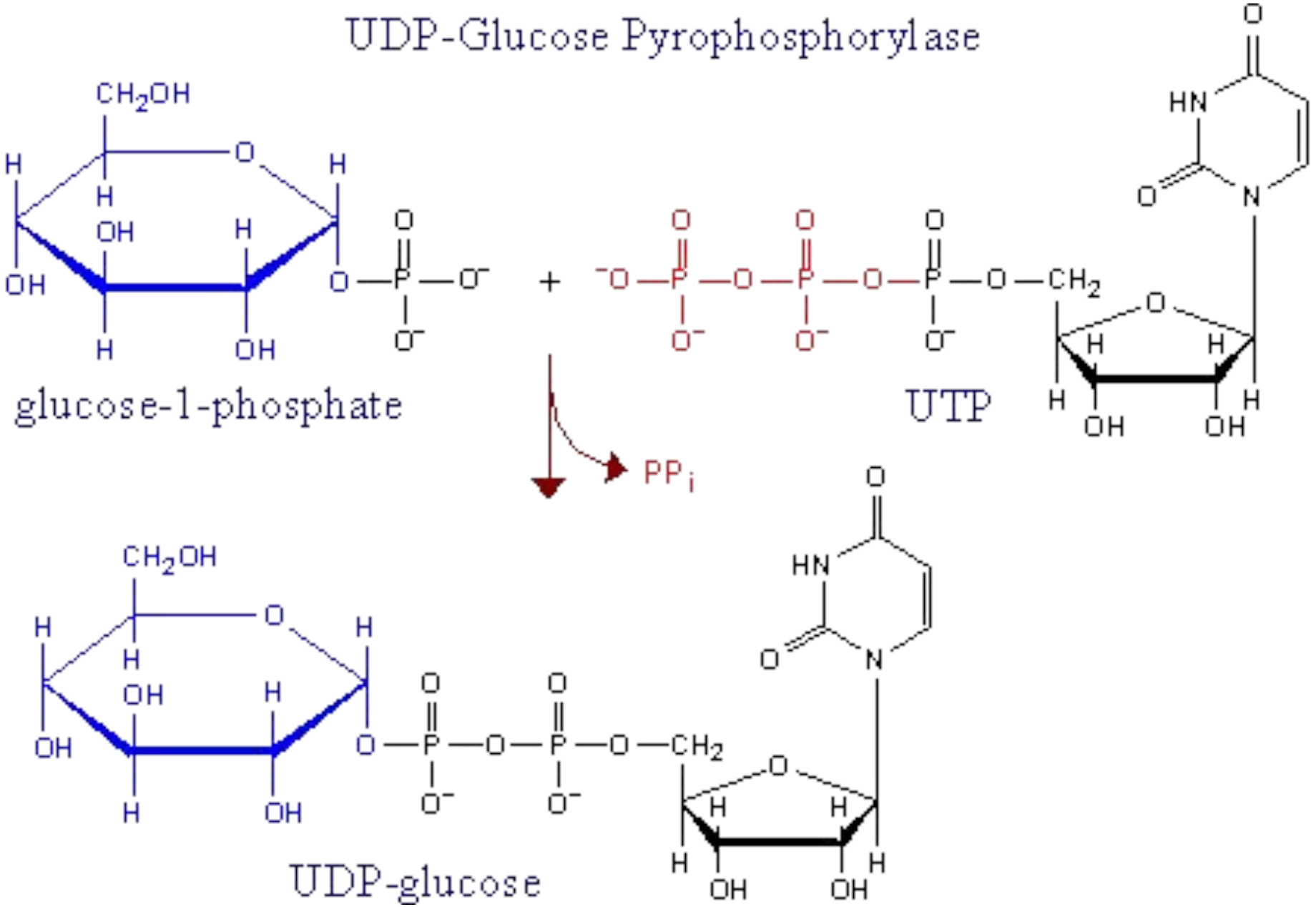
Glycogen structure



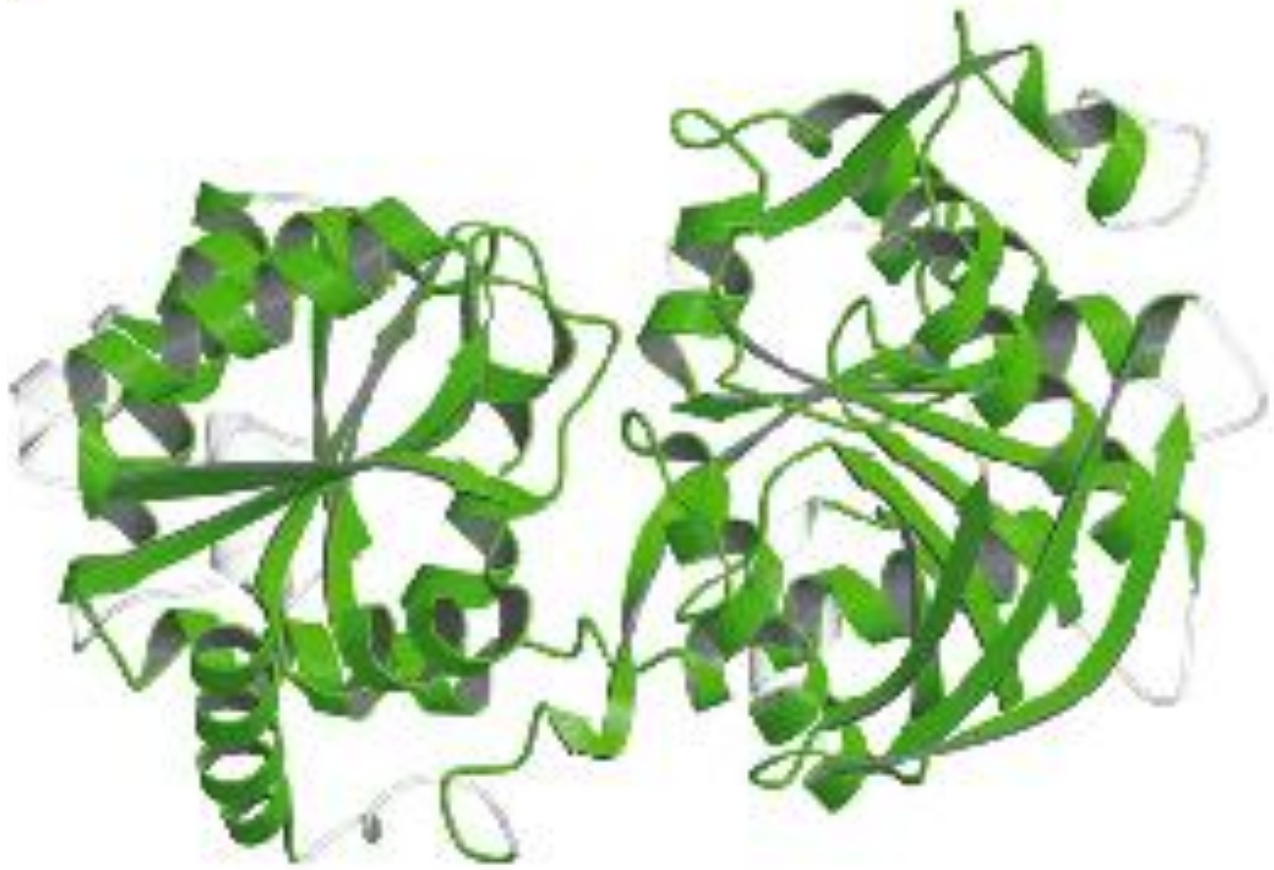
Glycogenesis (glycogen synthesis)

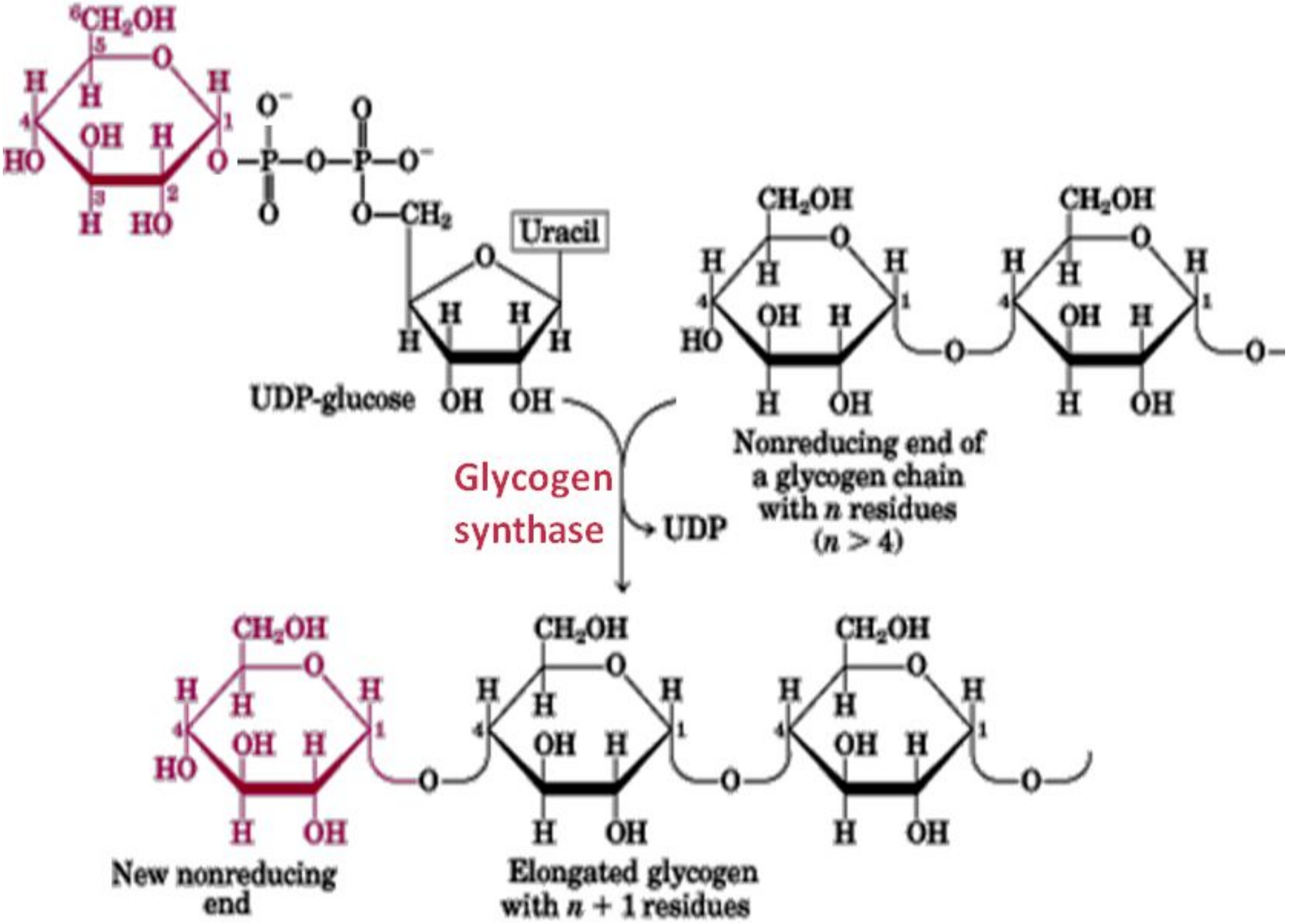


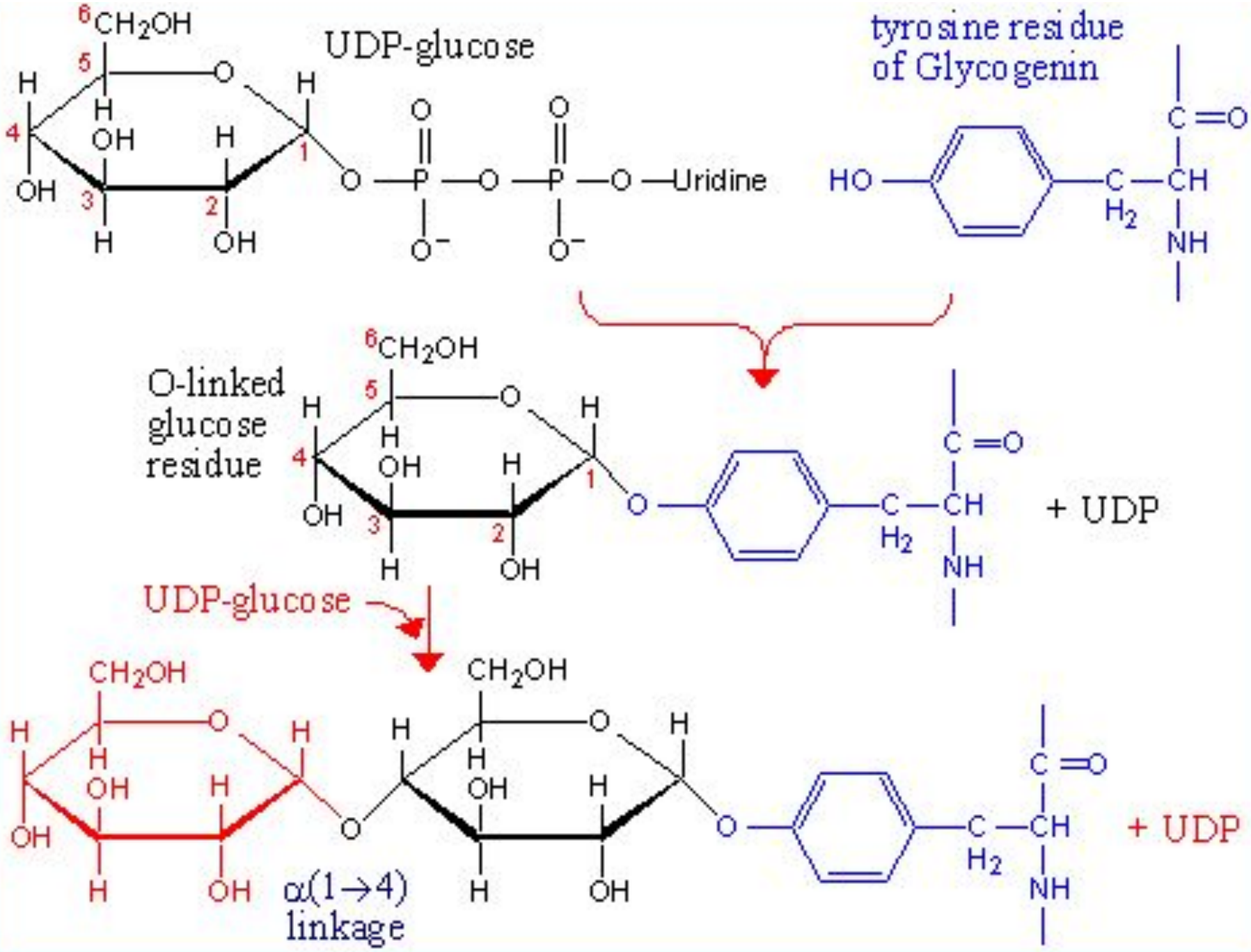
UDP-Glucose Pyrophosphorylase

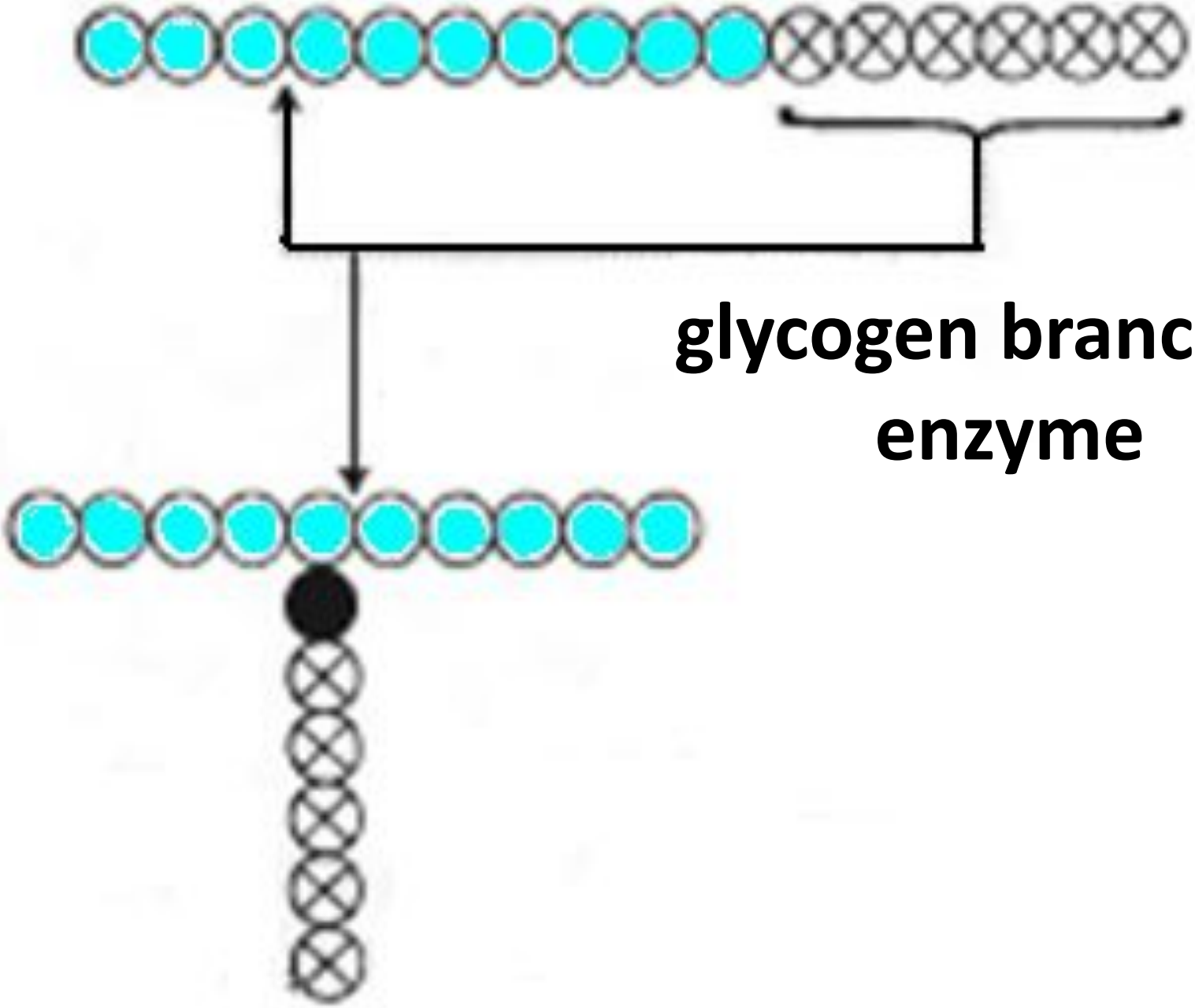


Glycogen syntase



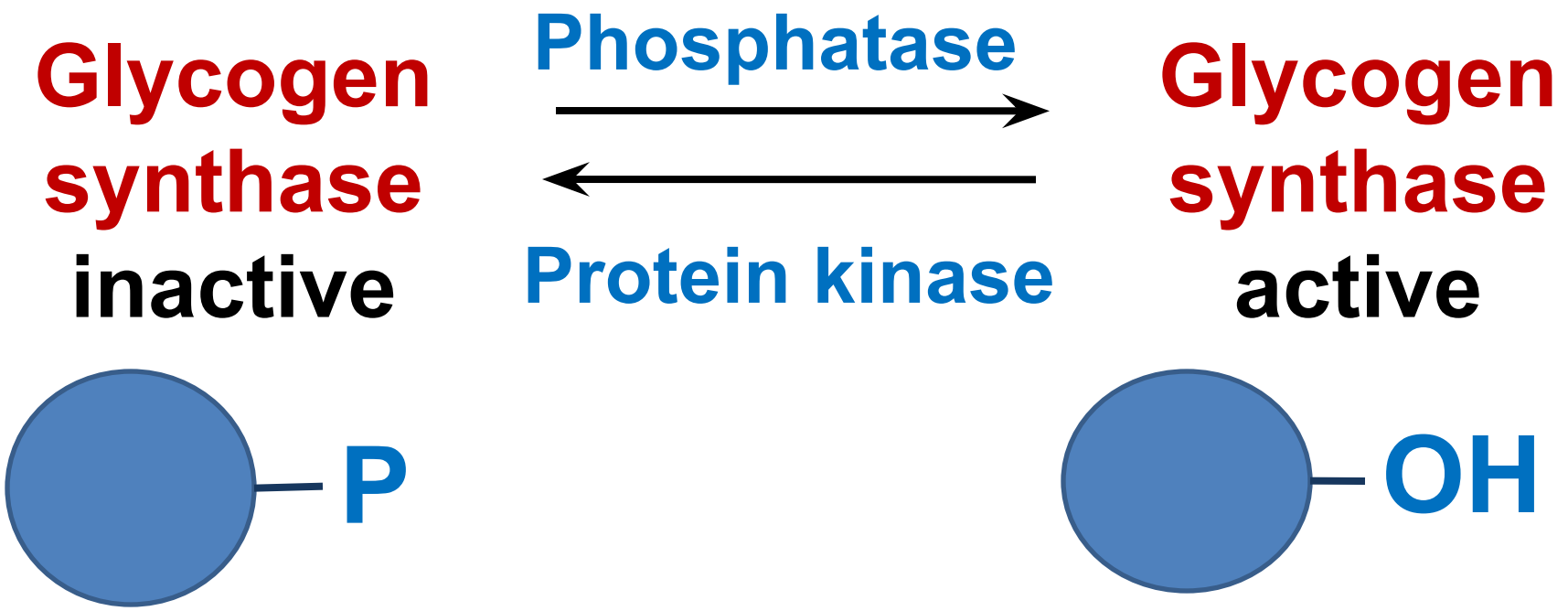

Uracil
UDP-glucose
Glycogen synthase
UDP
Nonreducing end of a glycogen chain with n residues (n > 4)
New nonreducing end
Elongated glycogen with n + 1 residues


UDP-glucose
tyrosine residue of Glycogenin
Uridine
O-linked glucose residue
+ UDP
UDP-glucose
+ UDP
α(1→4) linkage



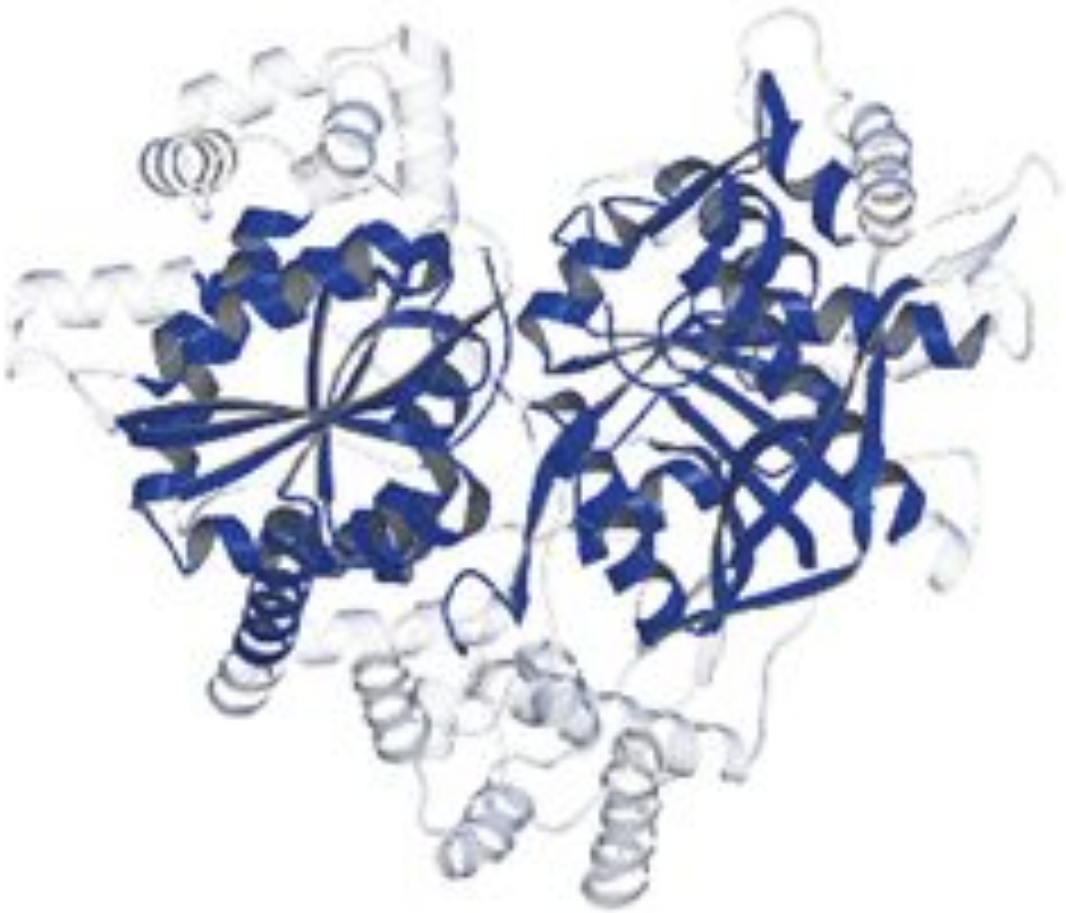
glycogen branching enzyme

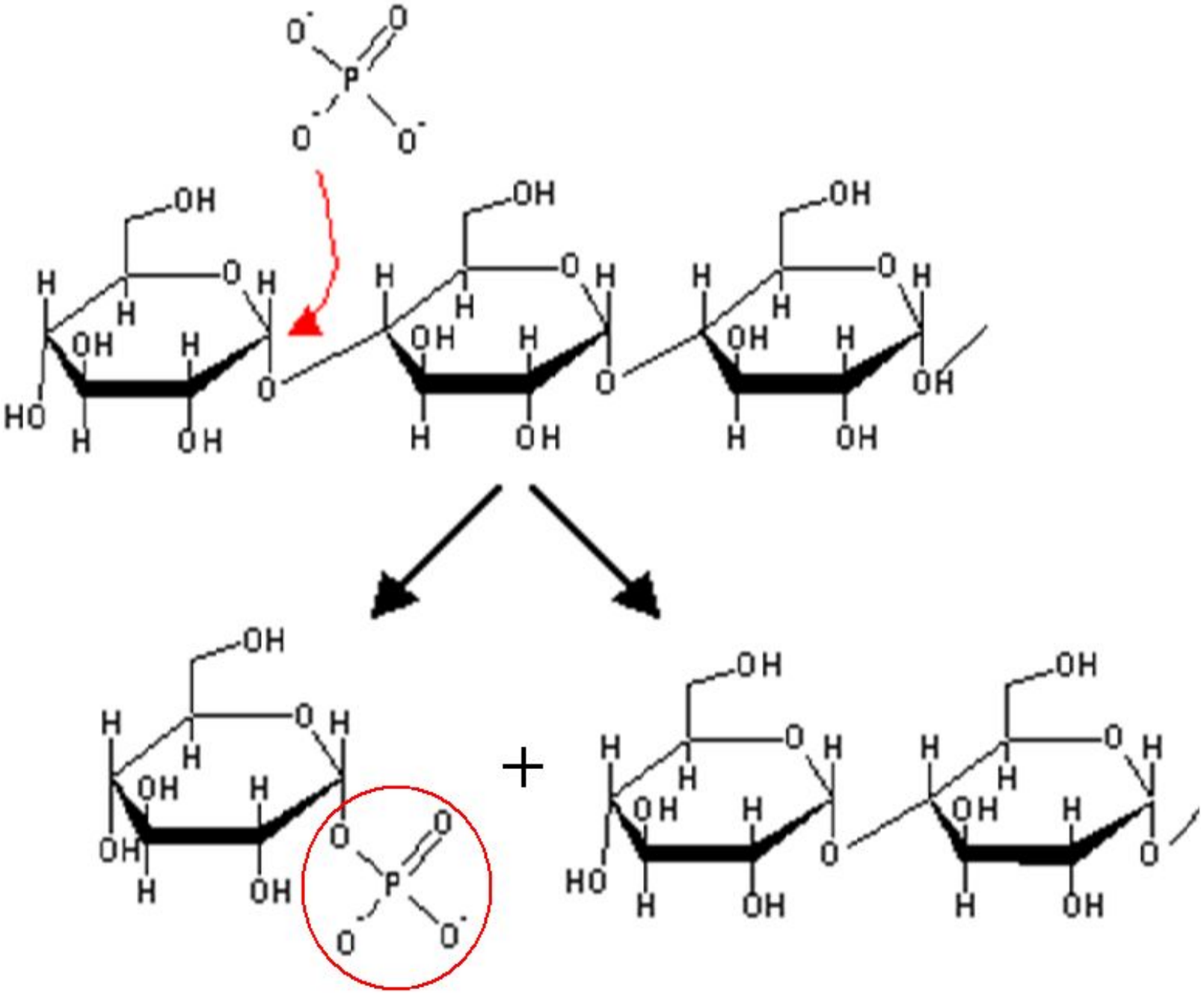
Regulation of glycogen synthase activity



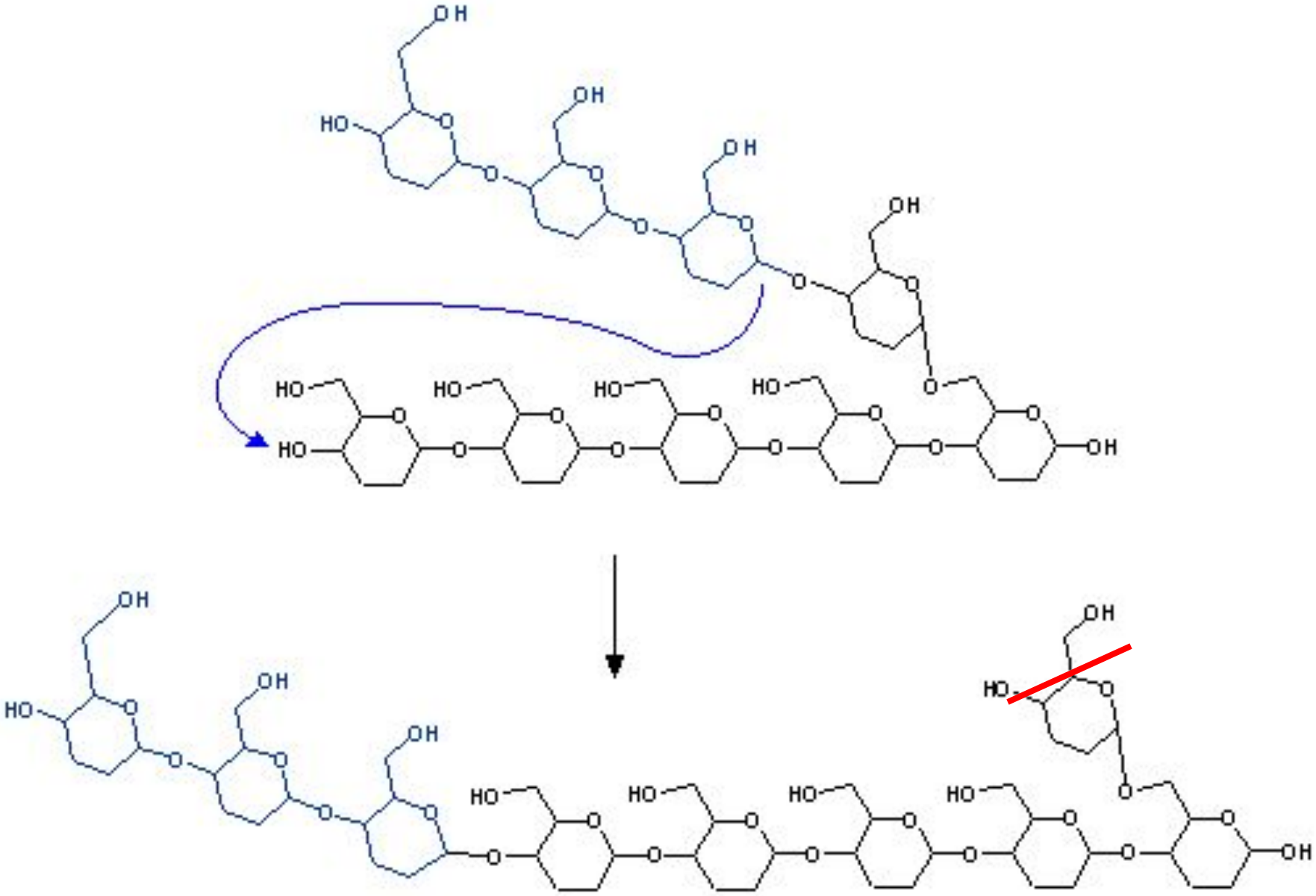
Degradation of glycogen

Glycogen phosphorylase

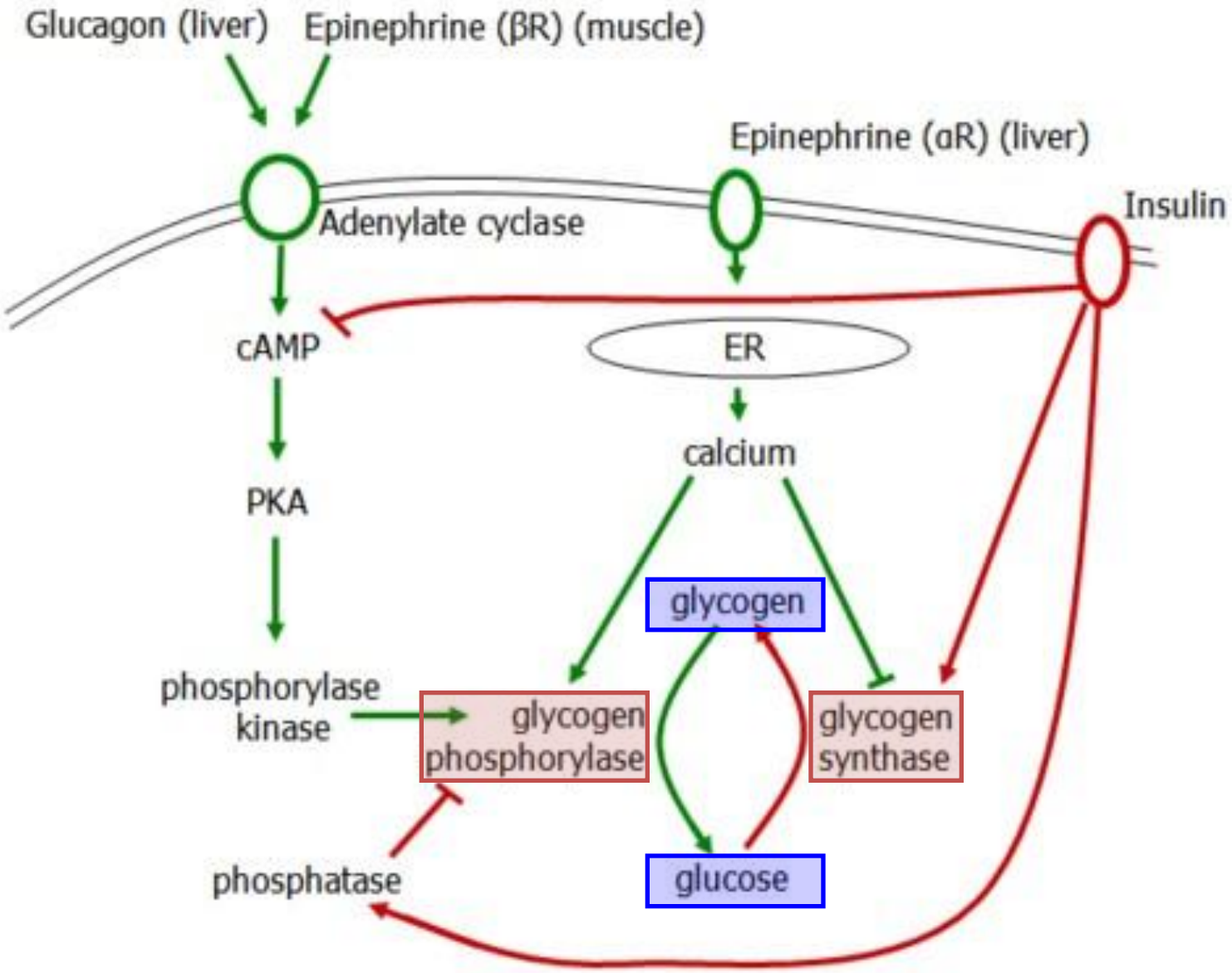



O
O
P
O
O
OH
H
O
HO
+

Action of debranching enzyme

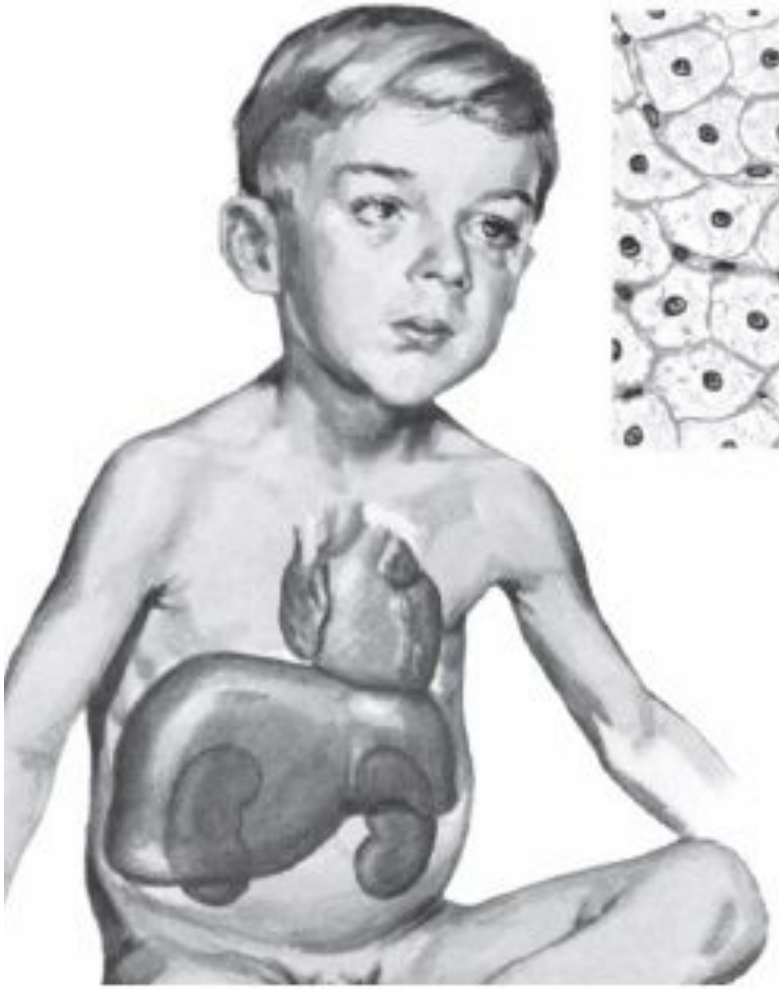


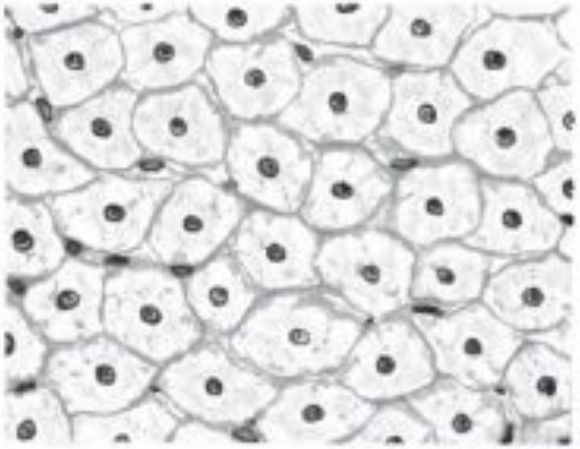
Glycogen metabolism regulation



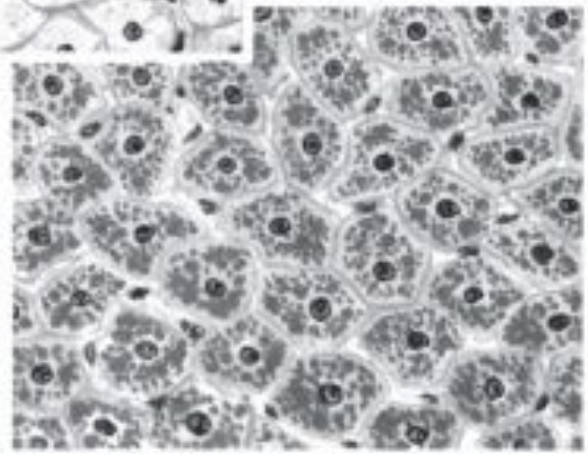
Glycogenosis

Gierke's disease, glycogenosis type I





Hepatocytes with large vacuoles

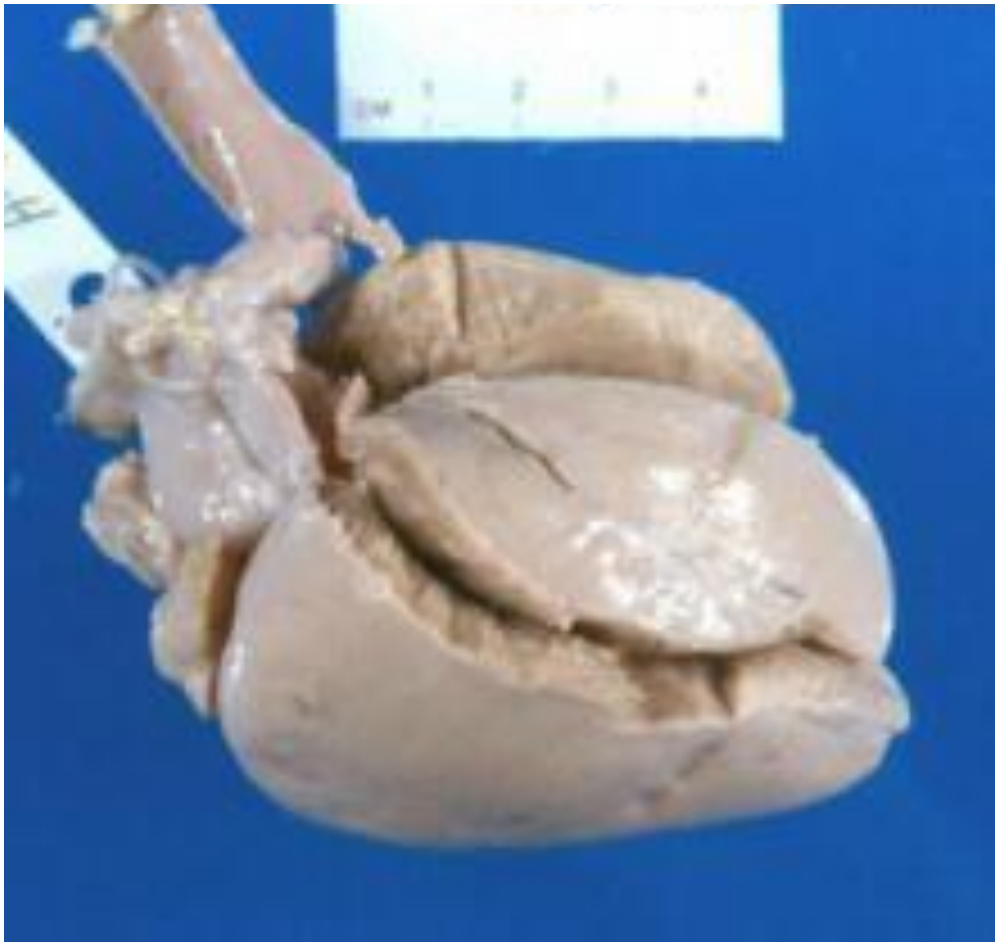


Intracellular glycogen

Glycogenosis type I

Glucose-6-phosp hatase deficiency

Pompe's disease, glycogenosis type II

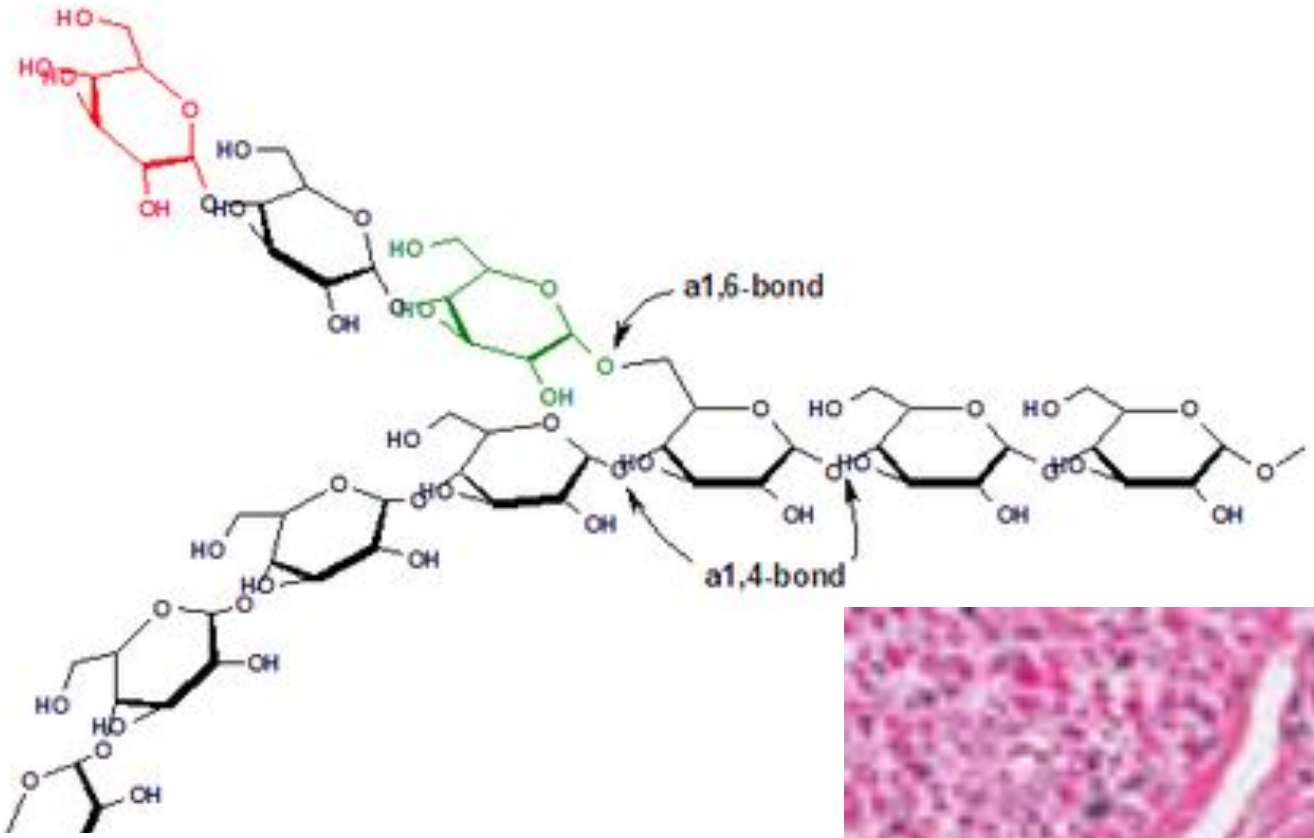


α-1,4-glucosidase deficiency

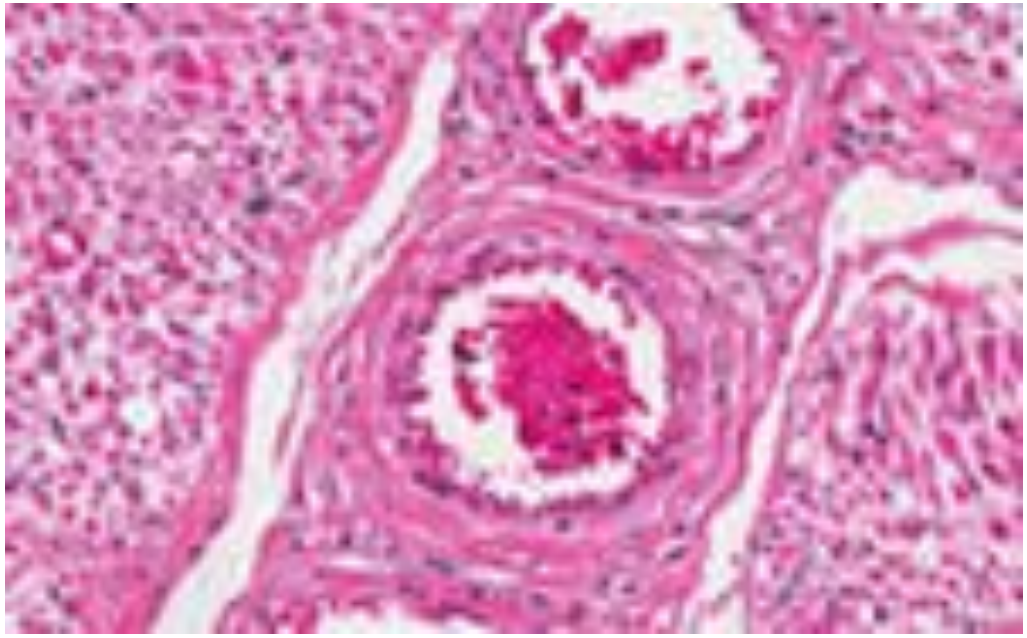
Corey's disease, glycogenosis type III

Amilo-(1-6)-glycosidase and (or) glycogen branching enzyme deficiency

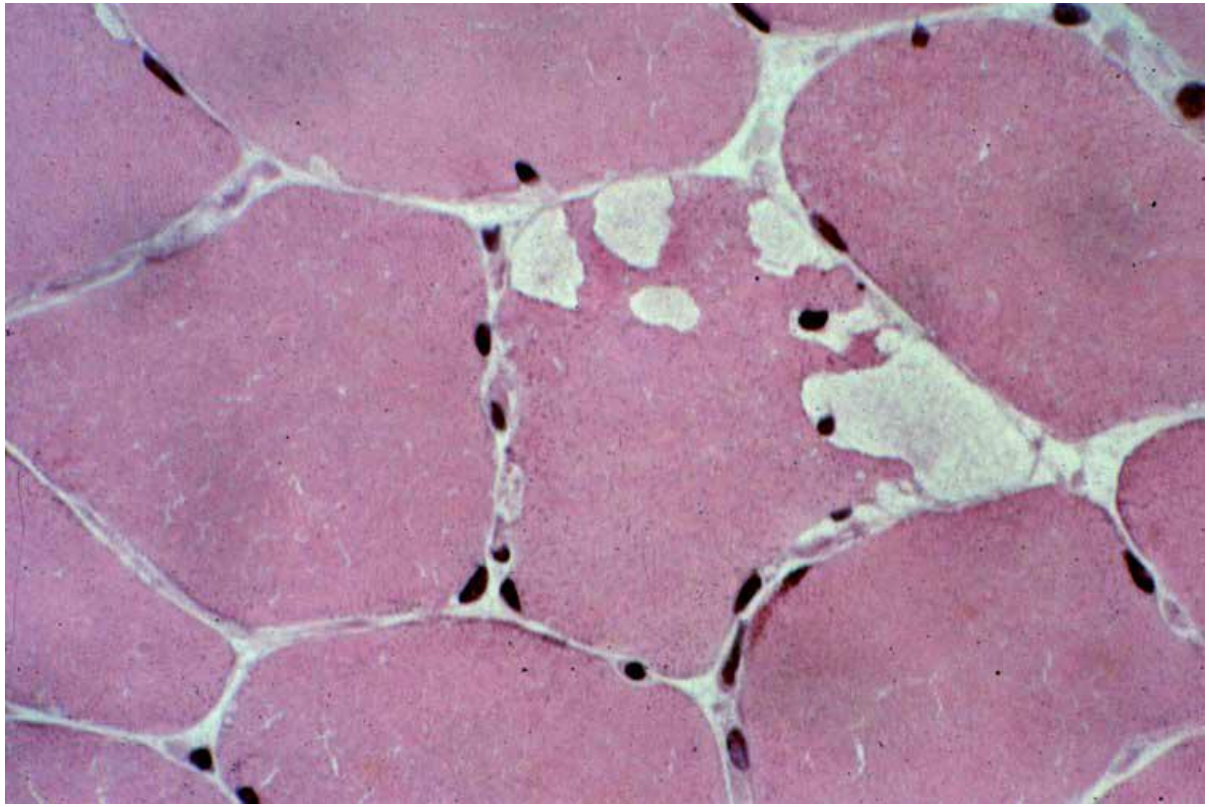
Andersen's disease, glycogenosis type IV



glycogen branching enzyme deficiency



McArdle's disease, glycogenosis type V

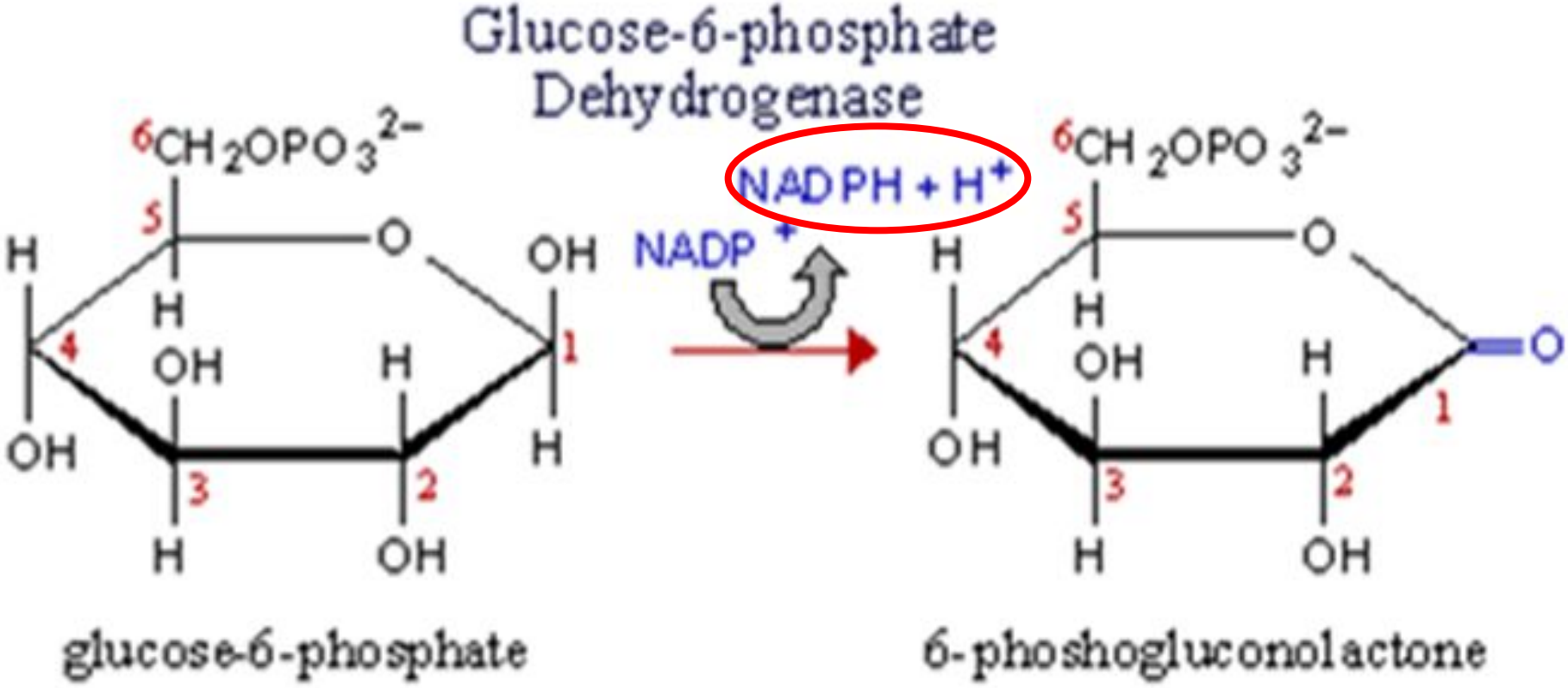


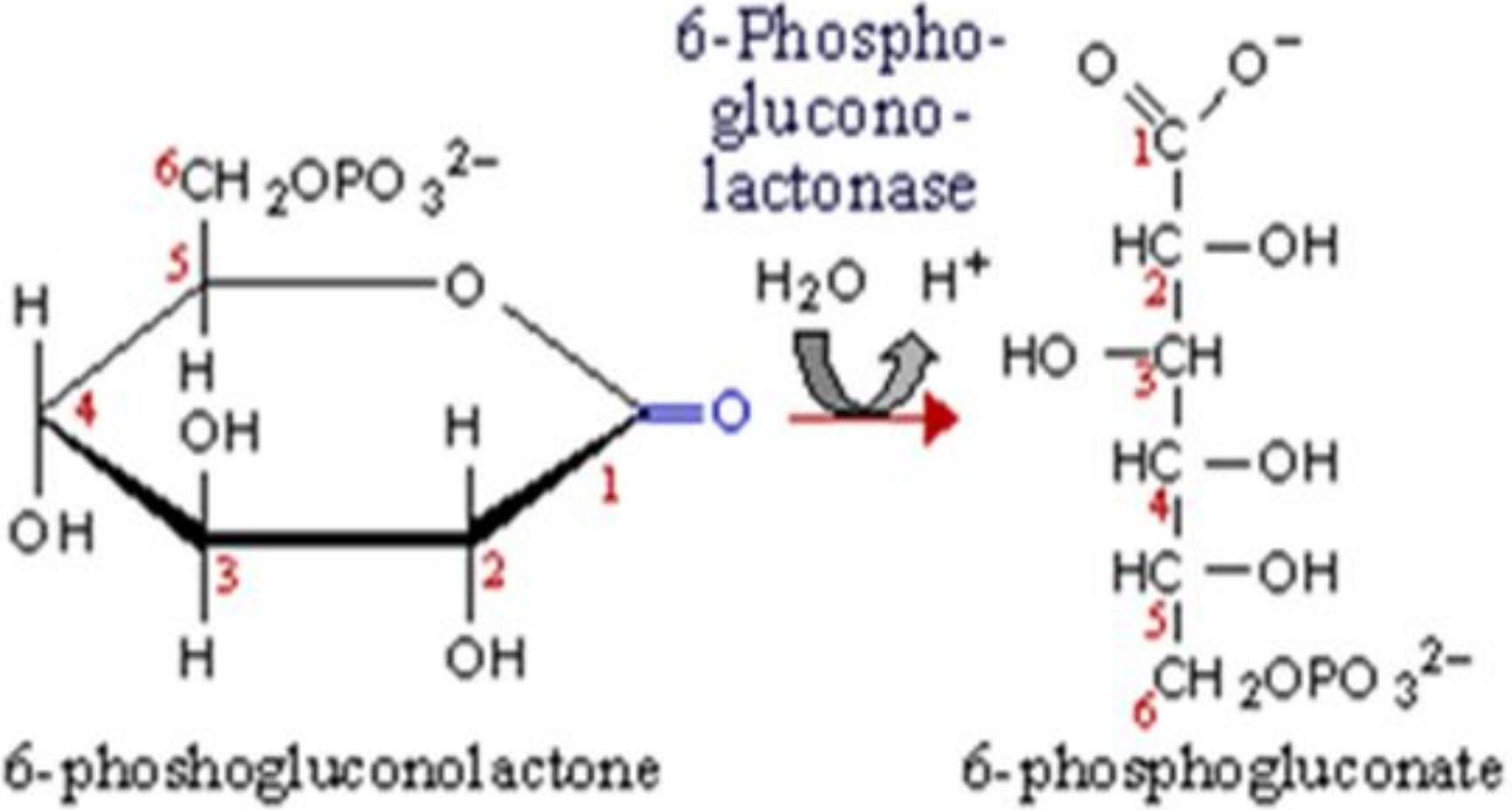
Muscle phosphorylase deficiency

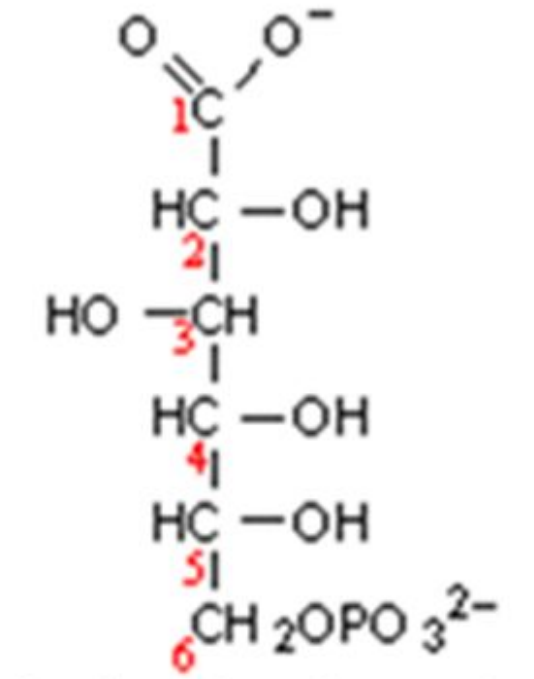
PENTOSE PHOSPHATE PATHWAY

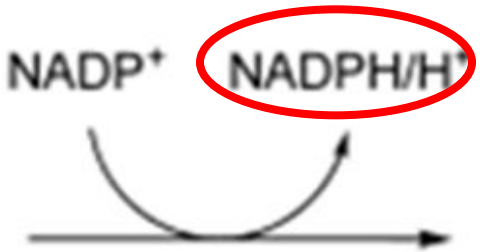
(HEXOSE MONOPHOSPHATE SHUNT)

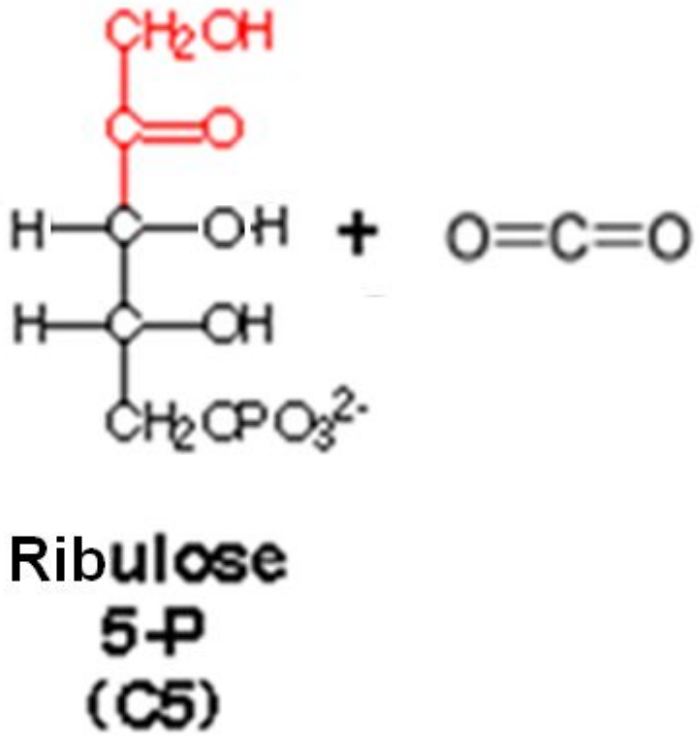
Oxidative phase

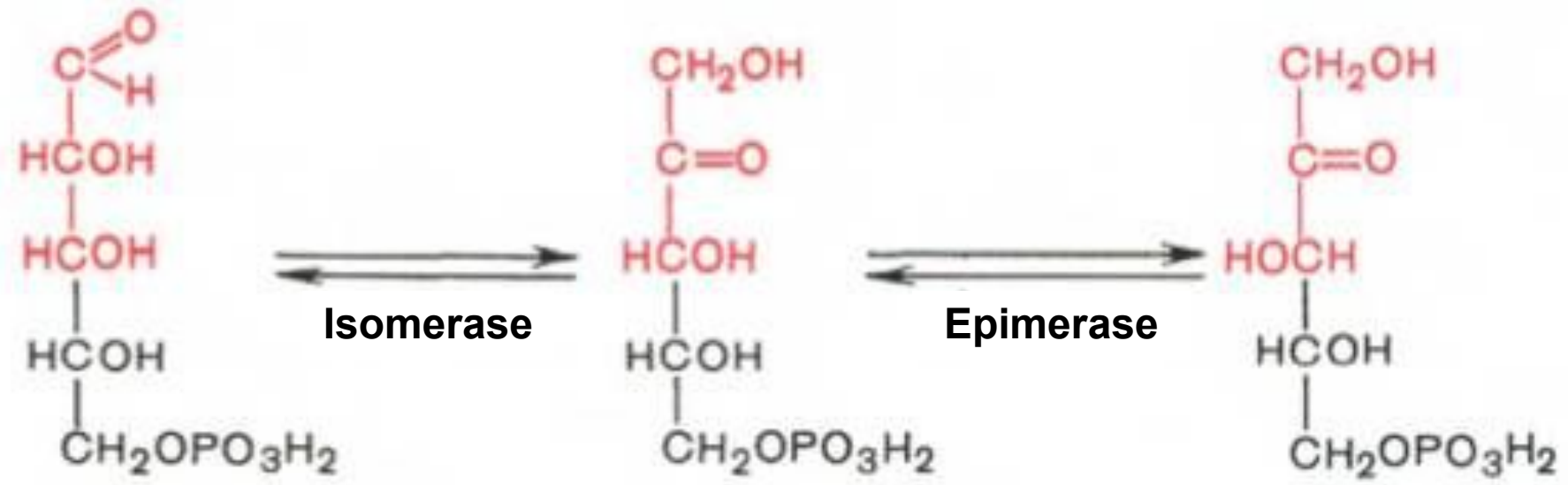


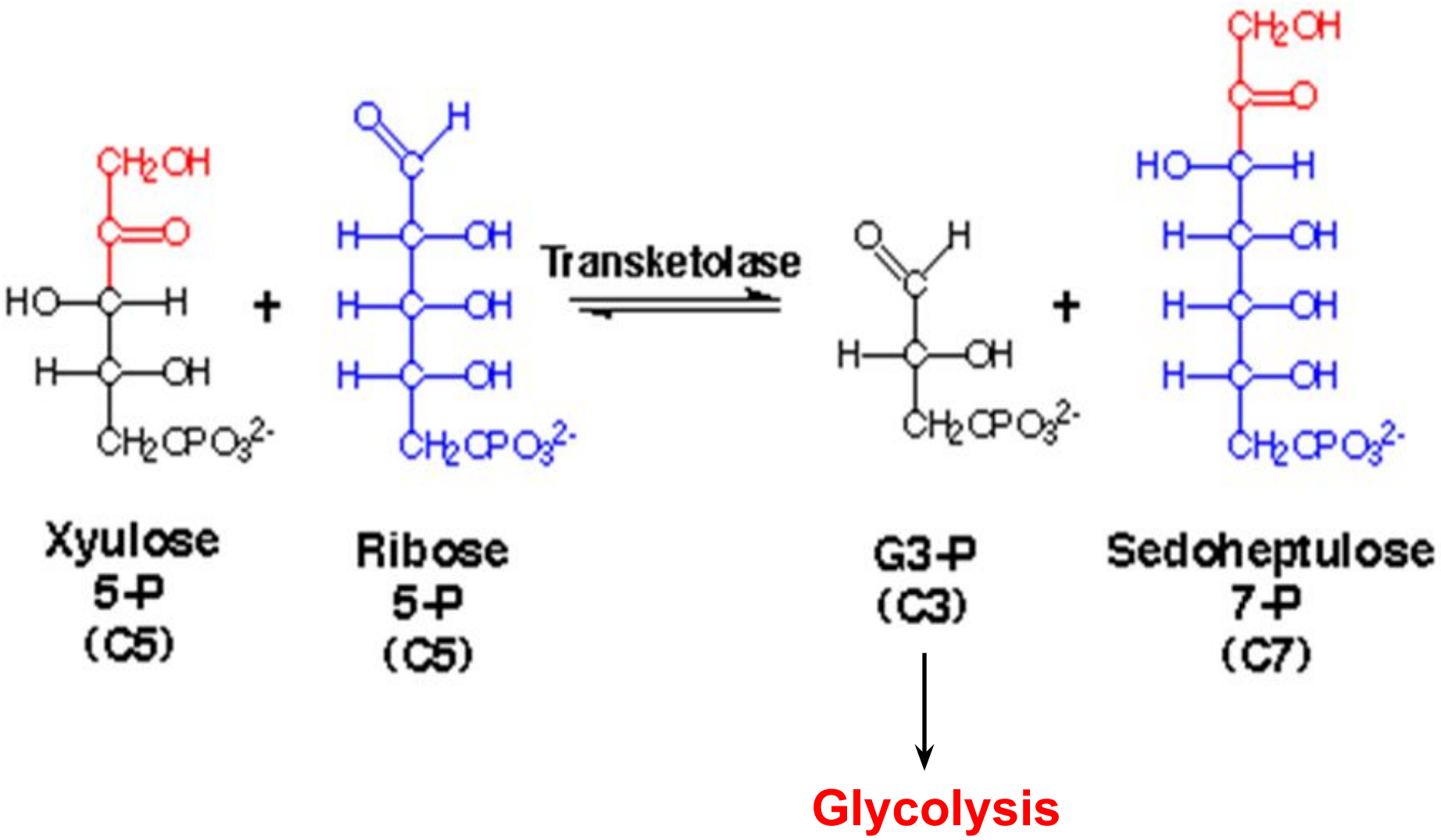

6-Phospho-
glucono-
lactonase
H2O H+
6CH2OPO3 2−
5
O
H
H
4
OH
H
1
O
OH
3
2
H
OH
O
O−
1C
HC —OH
2
HO —CH
3
HC —OH
4
HC —OH
5
6CH2OPO3 2−
6-phoshogluconolactone
6-phosphogluconate

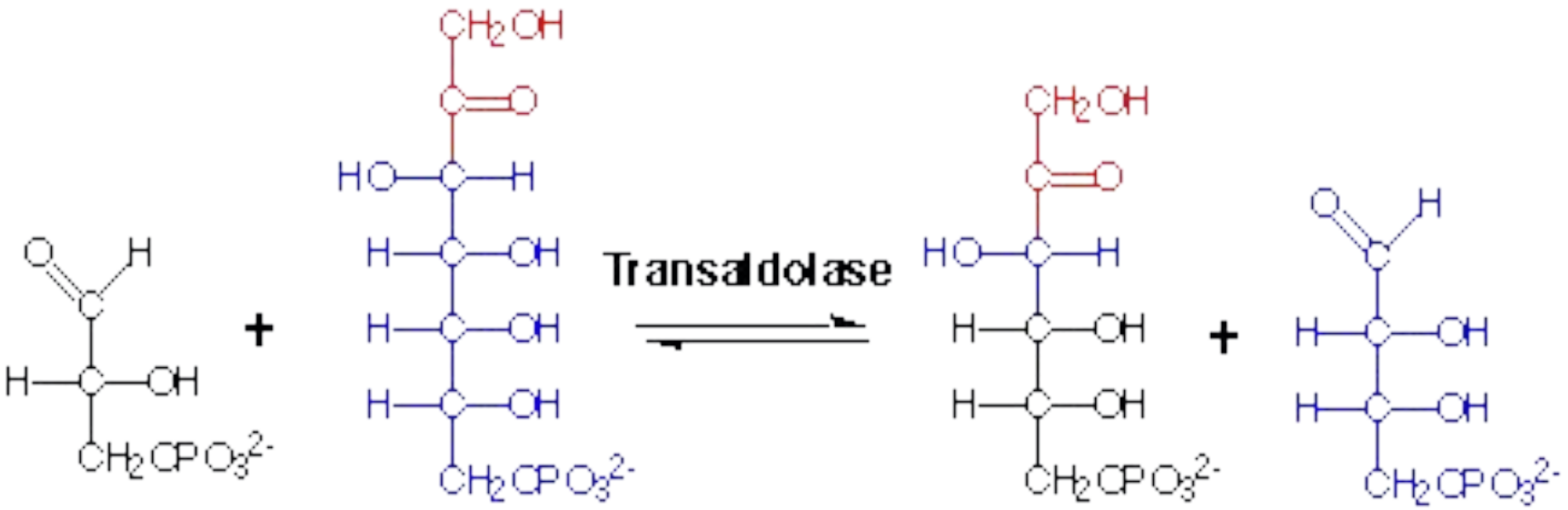

6-phosphogluconate


NADP+
NADPH/H+
decarboxylating
6-phospho-gluconate
dehydrogenase


Ribulose
5-P
(C5)


Isomerase
Epimerase
Ribose-5 phospate
Ribulose-5 phospate
Xylulose-5 phospate
Nucleotides
Nucleic Acids
Nonoxidative phase


Transketolase
Xyulose 5-P (C5)
Ribose 5-P (C5)
G3-P (C3)
Sedoheptulose 7-P (C7)
Glycolysis

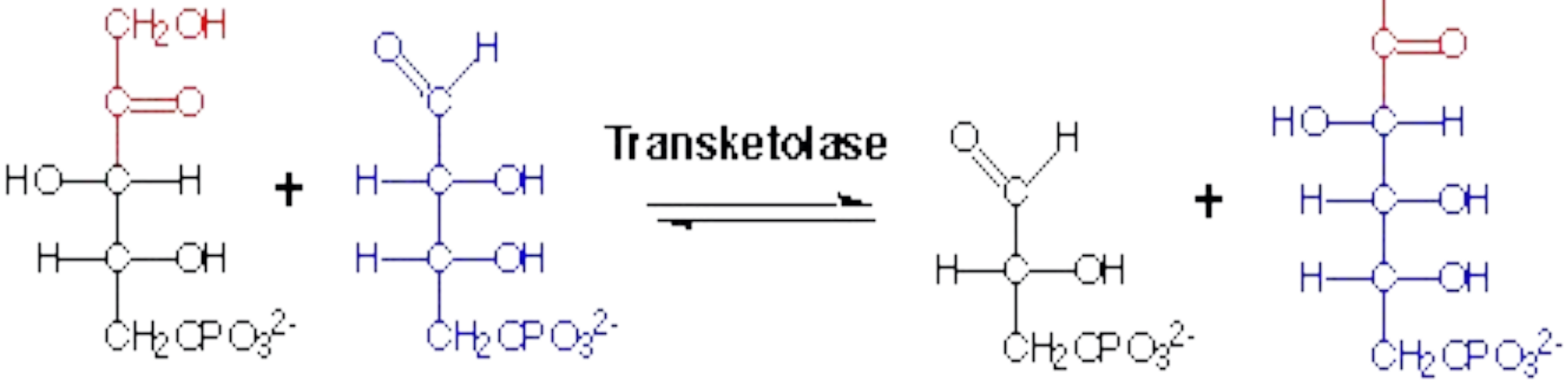


G3-P
(C3)

Sedoheptulose
7-P
(C7)

Fructose
6-P
(C6)

Erythrose
4-P
(C4)



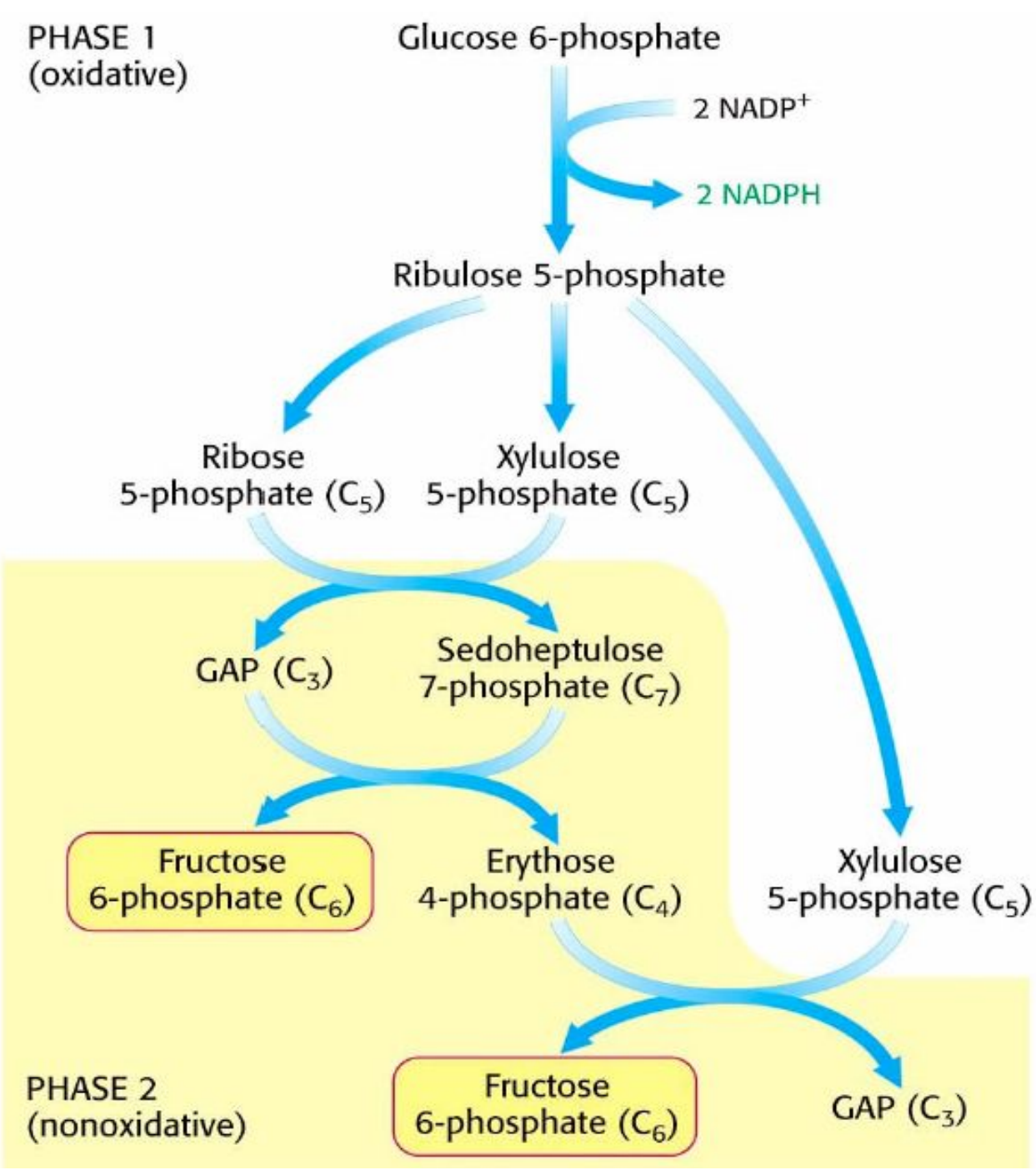
Xyulose 5-P (C5)

Erythrose 4-P (C4)

G3-P (C3)

Fructose 6-P (C6)

Glycolysis


PHASE 1
(oxidative)
Glucose 6-phosphate
2 NADP+
2 NADPH
Ribulose 5-phosphate
Ribose
5-phosphate (C5)
Xylulose
5-phosphate (C5)
GAP (C3)
Sedoheptulose
7-phosphate (C7)
Fructose
6-phosphate (C6)
Erythose
4-phosphate (C4)
Xylulose
5-phosphate (C5)
PHASE 2
(nonoxidative)
Fructose
6-phosphate (C6)
GAP (C3)

The overall equation:

$$6\ \text{G-6-P} + 12\ NADP^{+} + 7\ H_2O \rightarrow$$

$$\rightarrow 5\ \text{G-6-P} + 12\ NADPH + 12H^{+} + 6\ CO_2$$

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

Violation of pentose phosphate pathway