Glycolysis I

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الطب والجراحة لجنة

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Step 1 Hexokinases catalyze the ATP- dependent phosphorylation of glucose to produce glucose-6-phosphate (G6P)

- This first priming reaction is important to maintain the influx of glucose through glucose transporters (GLUTs) and at the same time to trap the transported glucose molecules inside the cell

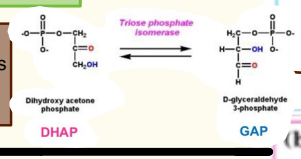
- **Step 2:** Phosphoglucose isomerase (PGI) interconverts G6P and F6P (reversible reaction)

- Indeed, Mannose and Fructose can enter the glycolysis pathway at this point

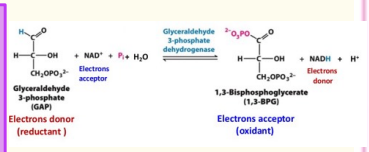
- **Step 3**: This is the rate limiting or key regulatory step. The activity of phosphofructokinase-1 (PFK-1) enzyme can be controlled.

- **Step 4:** Aldolase enzyme catalyzes the cleavage to two triose phosphates: DHAP (dihydroxyacetone phosphate) and GAP (glyceraldehyde-3-phosphate)
- The addition of the second phosphate group on C1 from the previous step destabilizes the hexose ring and facilitates the cleavage reaction

- **Step 5**: Isomerization of DHAP by triose phosphate isomerase (TPI) to GAP to proceed further in glycolysis as GAP is the substrate for the next reaction. This reaction is reversible



- **Step 6:** GAP dehydrogenase enzyme catalyzes the oxidative phosphorylation of GAP (electron donor) into super-high-energy compound (1,3-BPG) and the transfer of electrons into the coenzyme NAD+(electron acceptor) forming NADH



- **Step 7**:2 ATP molecules will be generated in this step

1. Substrate-level phosphorylation: it is a direct method of ATP synthesis by an enzyme which catalyzes the transfer of phosphate group from substrate to ADP

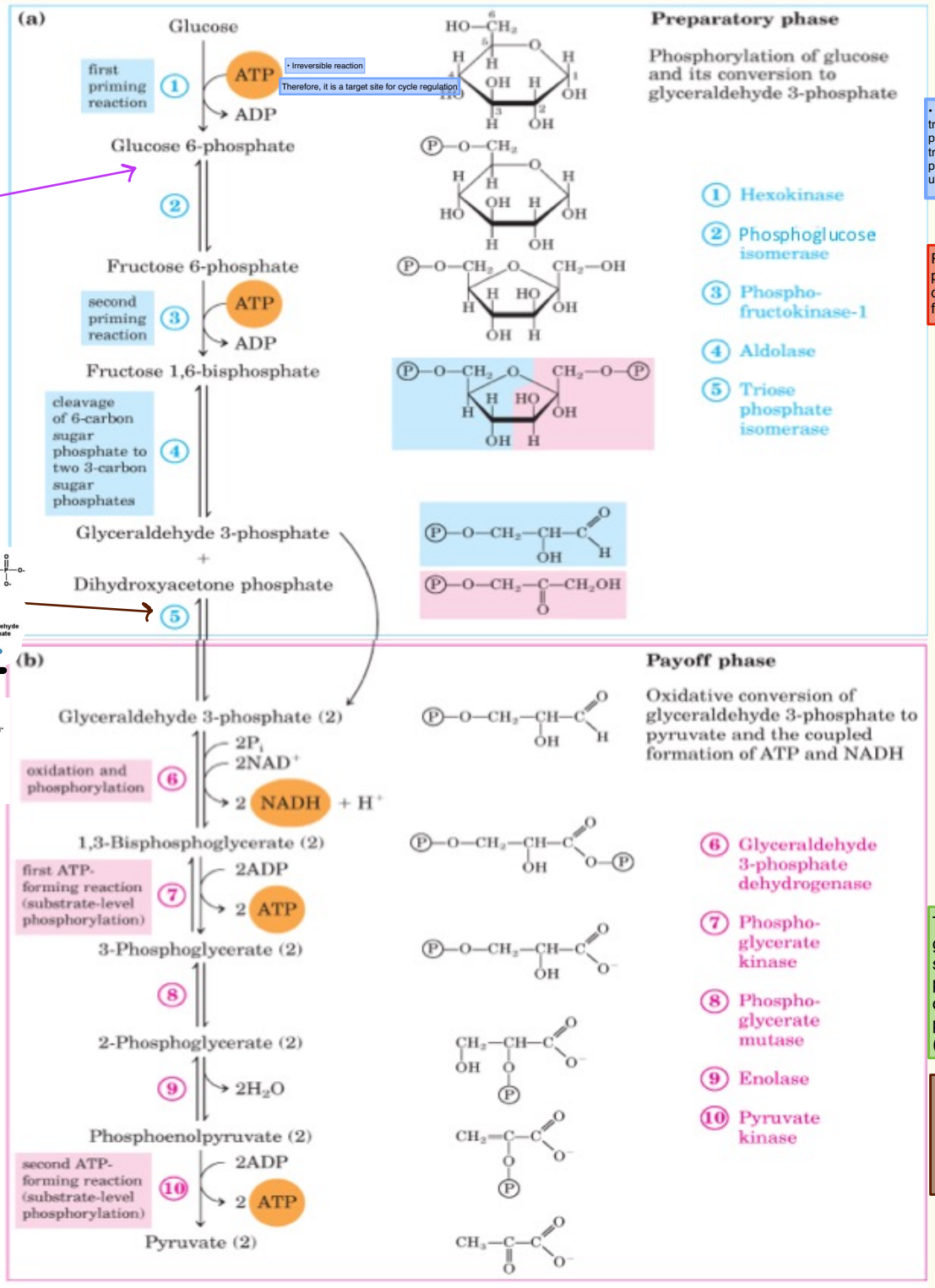
2. Oxidative phosphorylation: indirect method of ATP synthesis in which the oxidation of NADH/FADH2 and the subsequently transferred electrons indirectly drive ATP synthesis from ADP

- **Step 8**: Phosphoglycerate mutase (PGM) is an isomerase which catalyzes the isomerization of 3-phosphoglycerate to 2-phosphoglycerate
- It is actually an internal shifting of P group from C3 to C2 within the same molecule
- The main purpose of this step is the activation of the phosphate group to prepare for the generation of the second ATP in the next reactions

- **Step 9**: The synthesis of the second super-high-energy compound phosphoenolpyruvate (PEP) in a simple dehydration reaction catalyzed by enolase enzyme
- Thus, phosphate group on C2 is locked into unfavored (unstable) enol configuration. The aim of this step is to increase the energy stored in the phosphate bond

- **Step 10**: The second ATP molecule is generated by the substrate-level phosphorylation process catalyzed by pyruvate kinase (PK). Pyruvate is the final product of glycolysis

- The net result of glycolysis is the formation of:
2 pyruvate
2 ATP
2 NADH



- Hexokinase is a transferase enzyme which phosphorylates hexoses by transferring an inorganic phosphate from ATP usually to hydroxyl O at C6

PFK-1 catalyzes the phosphorylation of hydroxyl oxygen at C1 to produce fructose-1,6-bisphosphate

* step 6 = 2 NADH
step 9 = 2 H_2O
step 7,10 = 2 ATP

- Dehydrogenases are named as electrons donor substrate -dehydrogenase

The first ATP molecule is generated by the substrate-level phosphorylation process catalyzed by phosphoglycerate kinase (PGK)

- The activity of pyruvate kinase can be controlled (irreversible reaction) so this reaction is regulatory step

Hexokinases

- 4 isoforms (isozymes) of hexokinase (I, II, III & IV)

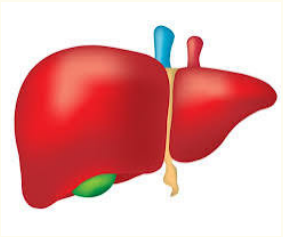
• Hexokinase I, II & III are nonspecific and can phosphorylate a variety of hexoses (e.g. glucose, fructose, mannose)

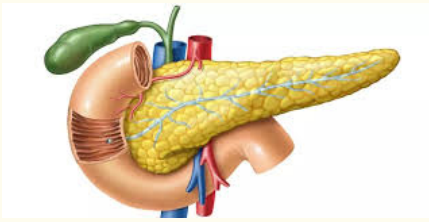
but type I is involved in catabolic pathways like glycolysis

whereas type II & III are involved in anabolic pathways like glycogenesis

• Hexokinase IV is called glucokinase expressed in liver and pancreatic β-cells. It is specific for D-glucose

• Glucokinase has low affinity for glucose (high Km value) compared to others (low Km value)

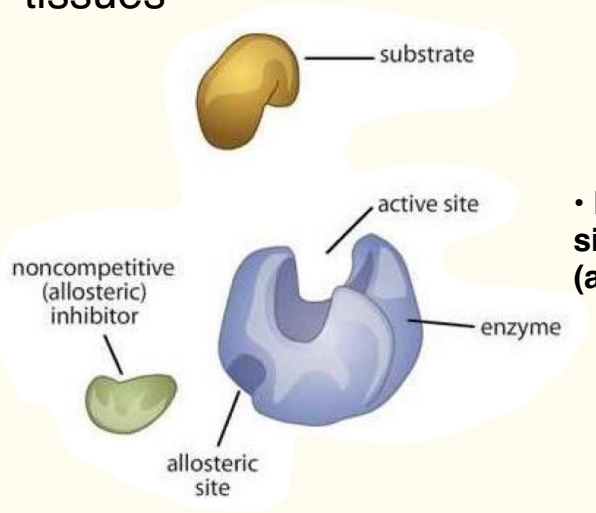




• Therefore, glucokinase in liver is active only at high blood glucose level to accumulate G6P for glycogen synthesis

pancreas it acts as glucose sensor to control insulin release from beta cells

which differ in their location, catalysis and regulation thereby, contributing to different pattern of glucose metabolism in different tissues



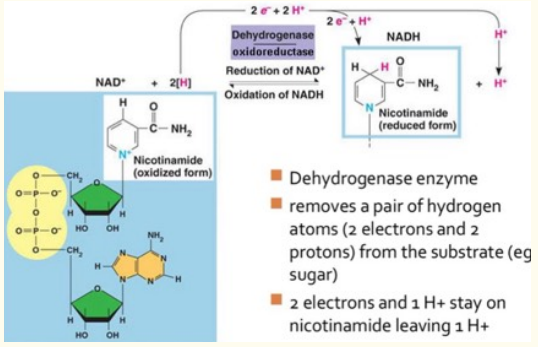
• Hexokinase is an allosteric enzyme with two binding sites: catalytic site (binds substrate) and regulatory site (allosteric site binds effectors)

• Hexokinase isoforms (except isoform IV) are allosterically inhibited by G6P only at high level

• NAD (Nicotinamide adenine dinucleotide) is a coenzyme which exists in two forms: NADH (the reduced form) and NAD+ (the oxidized form)

1 NADH = 2.5 ATP

• NAD (Nicotinamide adenine dinucleotide) is a coenzyme of dehydrogenases
• The reduced form NADH is electrons carrier and it is called energy rich molecule. It is an indirect form of energy



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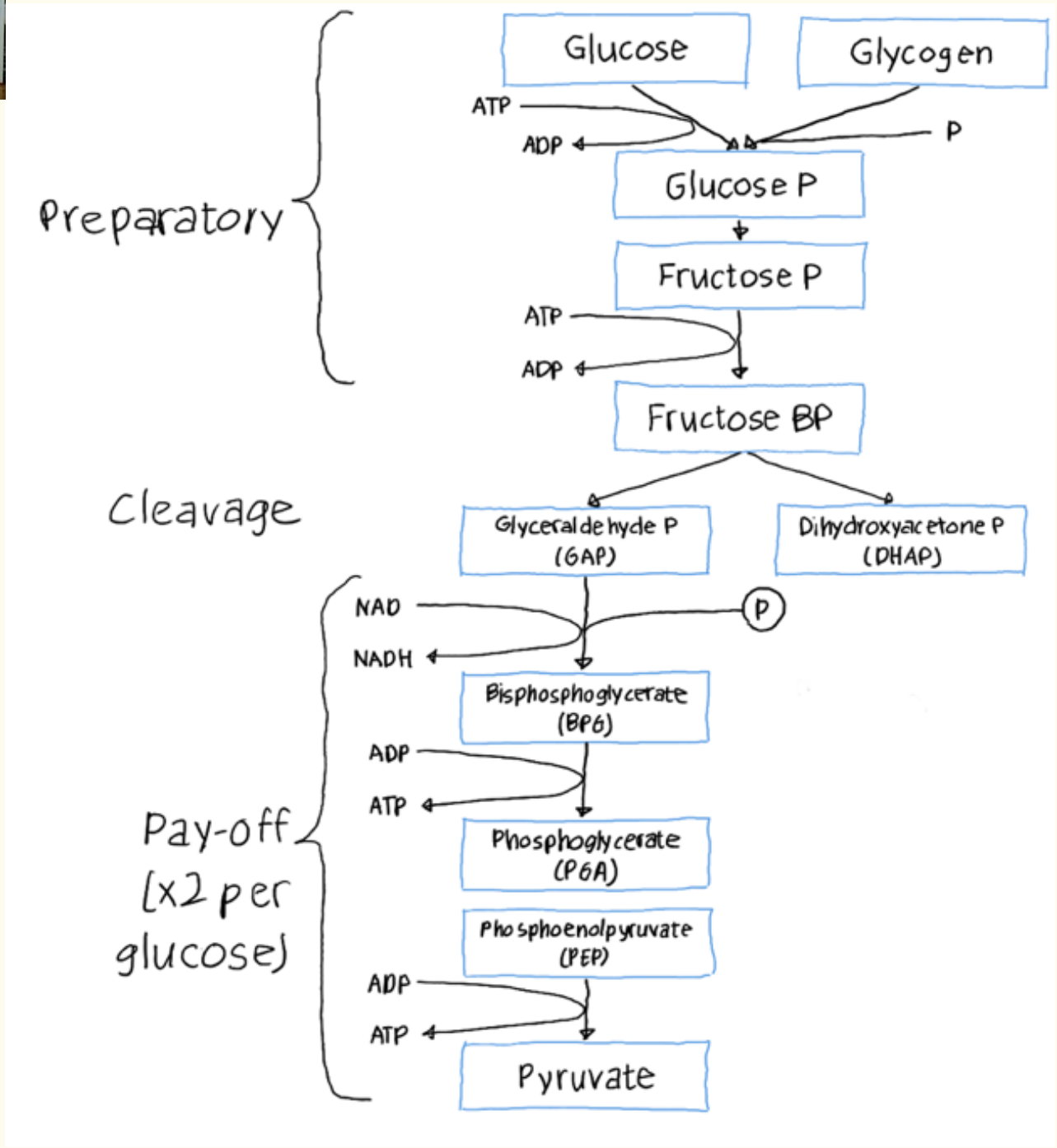

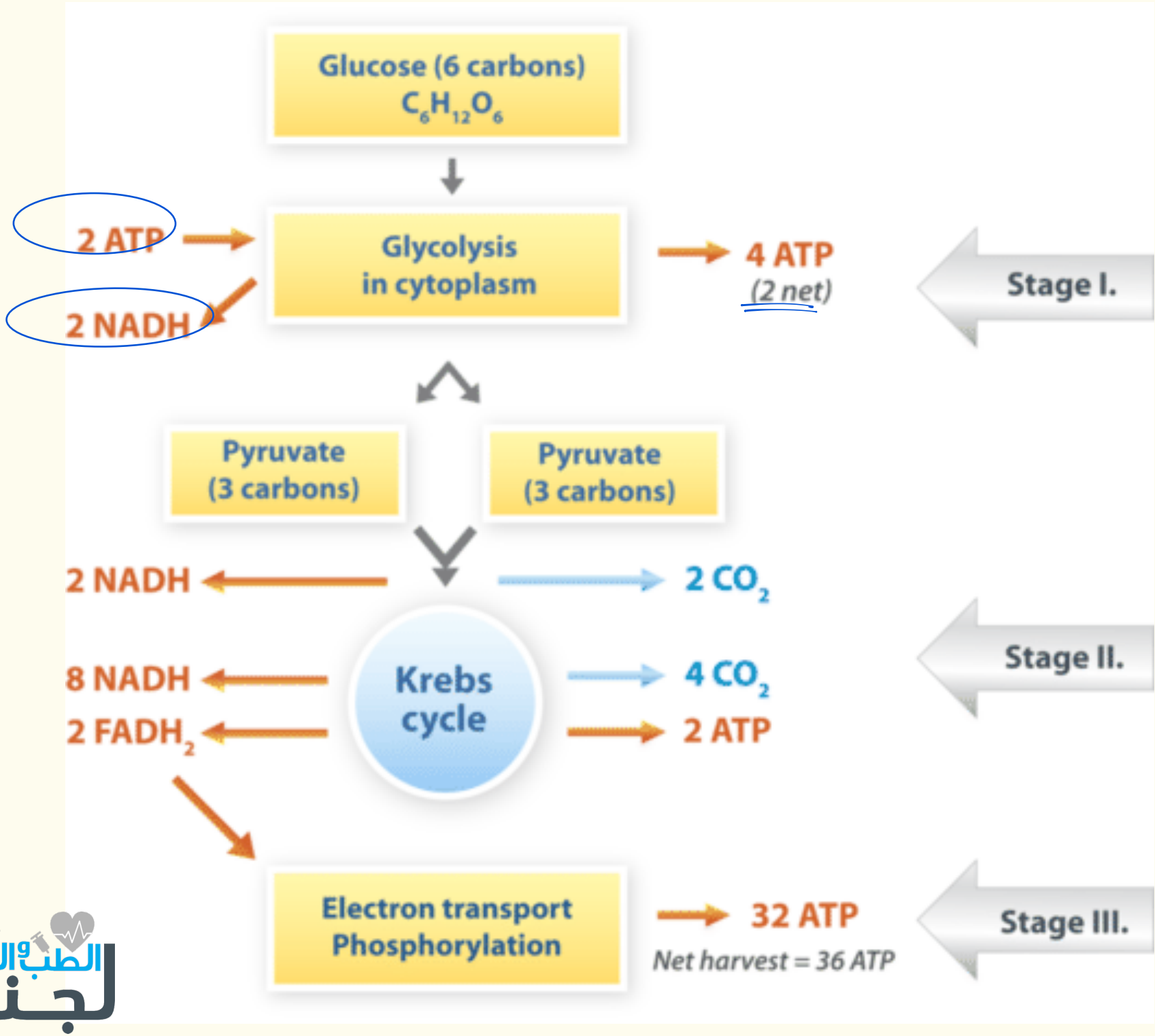

Cellular Respiration

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