CONCEPT: GLUCONEOGENESIS AND METABOLIC REGULATION

Gluconeogenesis

● **Gluconeogenesis** is the process of synthesizing glucose from pyruvate

□ When stores of glucose are depleted, the body needs to synthesize it

□ Synthesis (anabolic reactions) require ______________________________

- Uses 4 ATPs and 2 GTPs

□ Runs almost in reverse of glycolysis (but not exactly in reverse – three steps are different)

- Steps 1, 3, and 10 of glycolysis are so exergonic (energetically favorable) they cannot be reversed

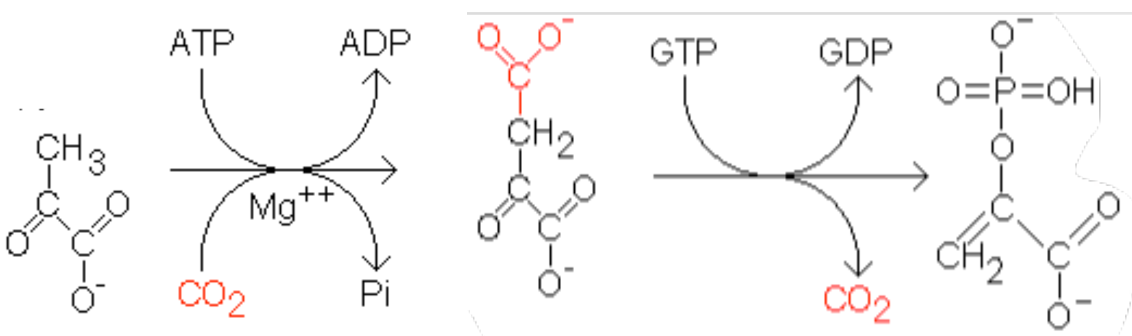
- Step 10: CO_2 and a carboxyl group are added to pyruvate to form *phosphoenolpyruvate* (PEP)

- Steps 3 and 1: Enzymes remove inorganic phosphates

- Enzymes specific to gluconeogenesis work in these steps to bypass the huge energy requirement

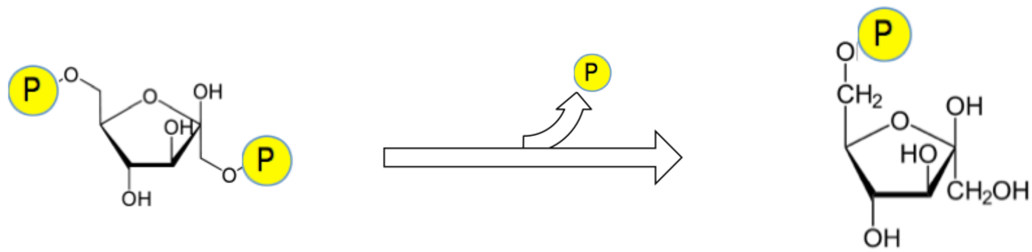
EXAMPLE: Three irreversible glycolysis steps

1. **Addition of CO_2 and phosphate to pyruvate** (Step 10 of glycolysis)



Pyruvate oxaloacetate Phosphoenolpyruvate (PEP)

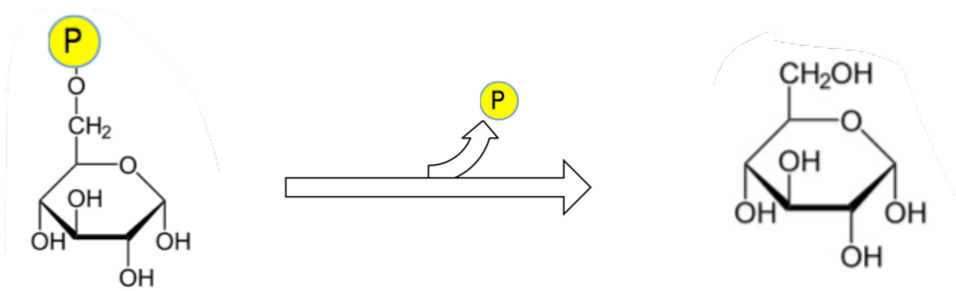
7. **Removal of a phosphate** (Step 3 of glycolysis)



Fructose 1,6-bisphosphate

Fructose 6-phosphate

10. **Removal of a phosphate #2** (Step 1 of glycolysis)



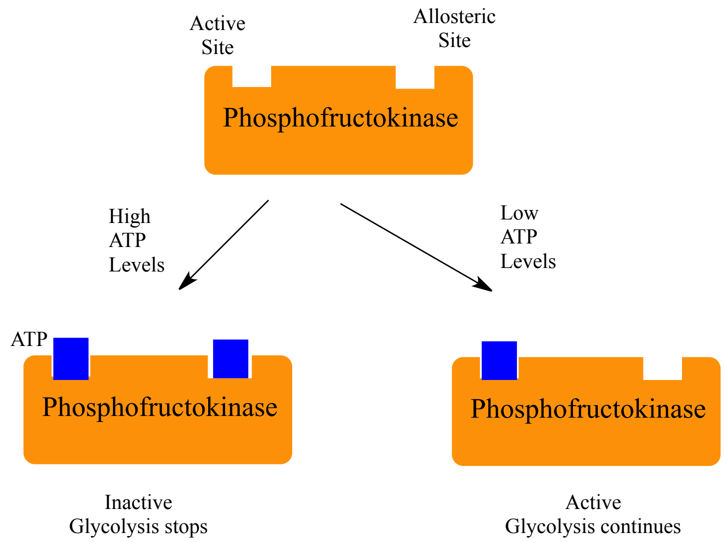
Glucose 6-phosphate

Glucose

<u>Feedback Regulation</u>

- Cells regulate whether to perform glycolysis or gluconeogenesis through two main ________________________
  - □ Activated **phosphofructokinase 1** promotes glycolysis and is controlled through allosteric ATP regulation
    - When ATP is low, the allosteric site remains unbound – and it remains on and promotes glycolysis
    - When ATP is high, the allosteric site is bound – and it turns off which stops glycolysis
  - □ **Fructose 2,6-bisphosphate** activates phosphofructokinase 1 and inhibits gluconeogenesis enzyme FBPase
    - Allosteric activator of phosphofructokinase 1 (PFK1) and allosteric inhibitor of F1,6BPase
  - □ Metabolic enzymes are regulated via phosphorylation, allosteric modulations, and feedback inhibition

EXAMPLE: Allosteric Regulation of Phosphofructokinase 1



<u>Energy Storage in Other Macromolecules</u>

● Cells do not only consume glucose, but also fats and larger polysaccharides that can be broken down to release energy

□ Fats are typically broken down into glycerol and free ________________________________

- Fatty acids are used to make acetyl CoA, NADH, and $FADH_2$

- 16 carbon fatty acid (palmiate) = 7 NADH, 7 $FADH_2$ and 8 acetyl CoA (eventually leading to 131 ATPs)

- For comparison the energy from 1 glucose makes 38 ATPs

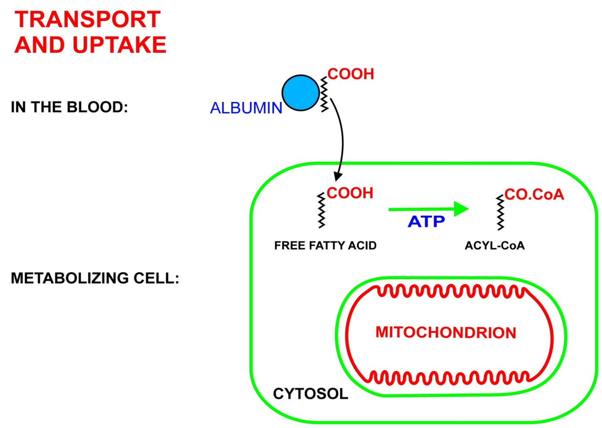
□ Glycogen and starch __________________ glucose as large, branched polysaccharides

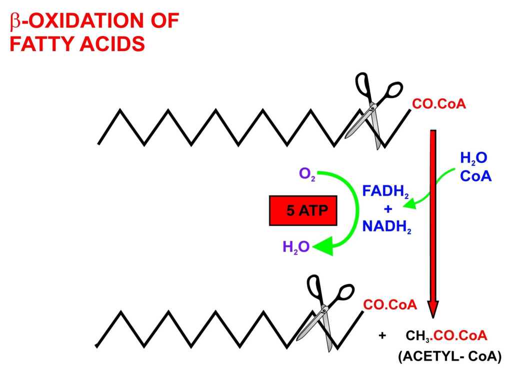
- Can be broken down and used in glycolysis

- *Glycogen phosphorylase* converts glycogen into glucose 6-phosphate (step __ of glycolysis)

- **Phosphorolysis:** separation of glucose units by adding a P_i instead of a water (hydrolysis)

EXAMPLE: Breakdown of fatty acids to acetyl CoA, ATP, NADH, and $FADH_2$





PRACTICE

1. Which of the following is not true regarding gluconeogenesis?
   a. It requires energy from ATP
   b. It generates glucose
   c. It is the exact reverse of glycolysis
   d. It requires energy from GTP

2. True or False: Gluconeogenesis occurs in the exact reverse as glycolysis.
    a. True
    b. False

3. What happens to the glycolysis and gluconeogenesis when ATP levels are high and glucose is low?
    a. Glycolysis and gluconeogenesis are activated
    b. Glycolysis is activated and gluconeogenesis is suppressed
    c. Glycolysis is suppressed and gluconeogenesis is activated
    d. Nothing, the rates of glycolysis and gluconeogenesis stay the same

4. When phosphofructokinase-1 is active, what happens to gluconeogenesis?
    a. It is also activated
    b. It is repressed
    c. Nothing