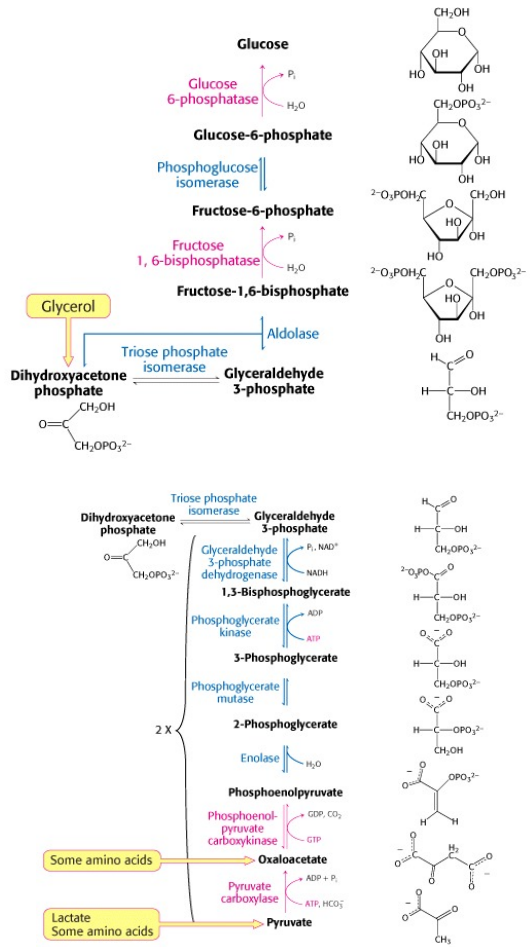
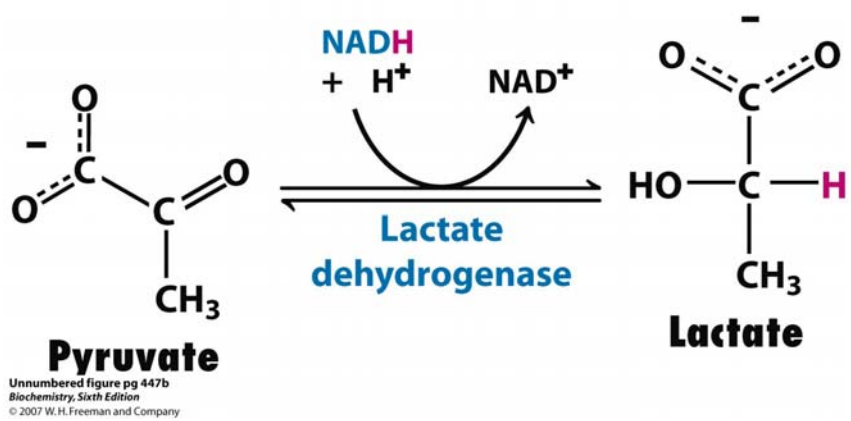
Gluconeogenesis = synthesis of glucose from non-carbohydrate

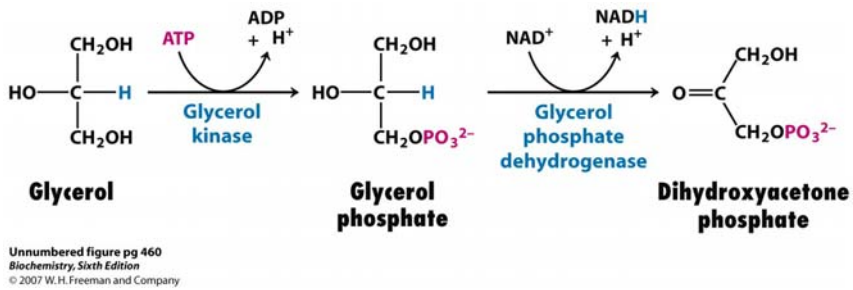
- Overview
- Pathway
- Regulation



Overview

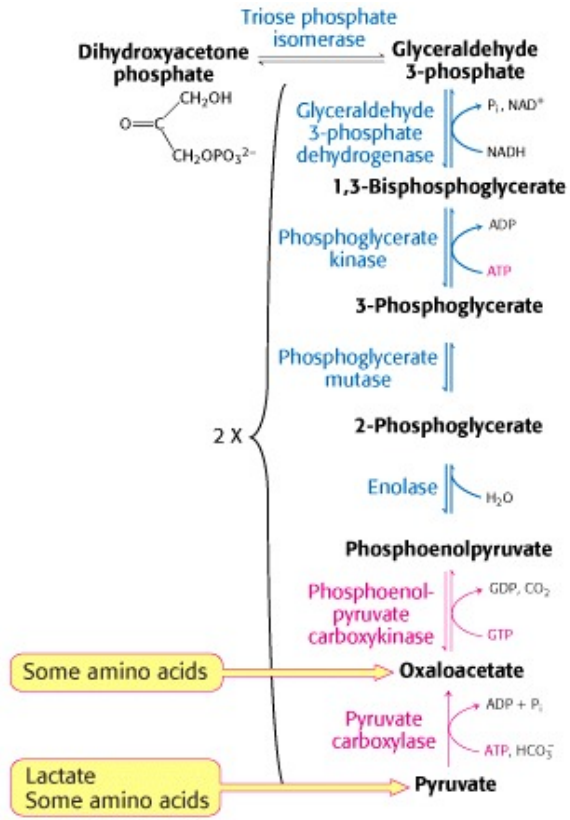
- degrade excess amino acids
- biosynthetic precursors
- acid/base balance
- Occurs mainly in liver and some in kidney
- provide glucose
  - brain, red blood cells, kidney medulla, testes, skin, nervous system
  - brain 120 g/day of glucose required, 20 g in bodily fluids, glycogen store = 190 g
- Cori cycle
- Sources:
  - amino acids: glucogenic/ketogenic
  - lactate (active skelatal muscle)
  - Glycerol (hydrolysis of triacylglycerol)





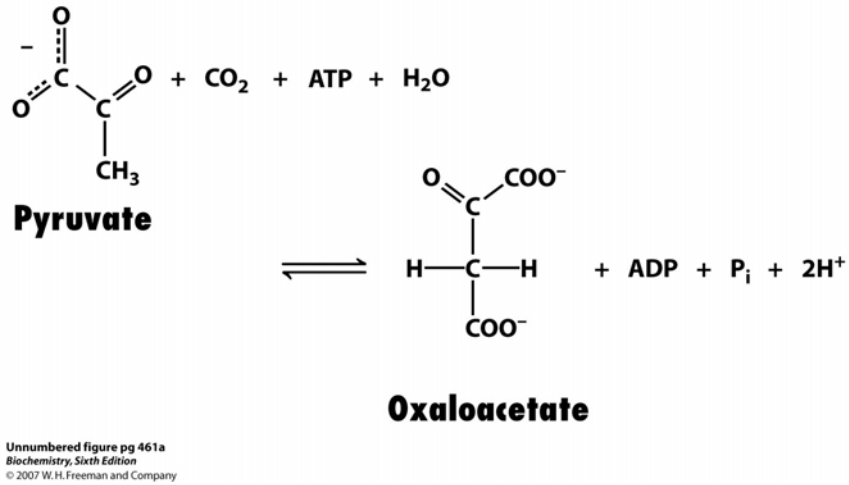
Pathway

- **Not just reverse of glycolysis**
- **Occurs in cytosol and mitochondria**
- **Four unique steps:**
  - **Pyruvate -----> PEP**
    - **Two enzymes**
    - **Pyruvate carboxylase**
    - **PEP carboxykinase**
    - **cytosolic/mitochondria**
    - **shuttle NADH depending on source of pyruvate**
    - **lactate or alanine**
  - **Fructose 1,6 P -----> Fru 6-P**
    - **Fructose 1,6 diphosphotase**
  - **Glucose 6-P ------> Glucose**
    - **located in SER**



Pyruvate Carboxylase

- Initial Conversion
- Three step process:



Unnumbered figure pg 461a
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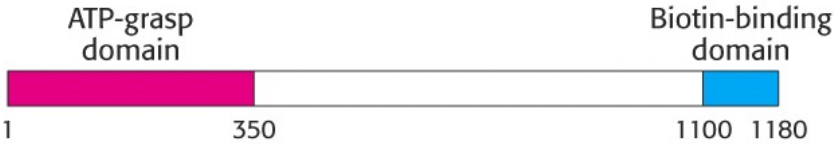
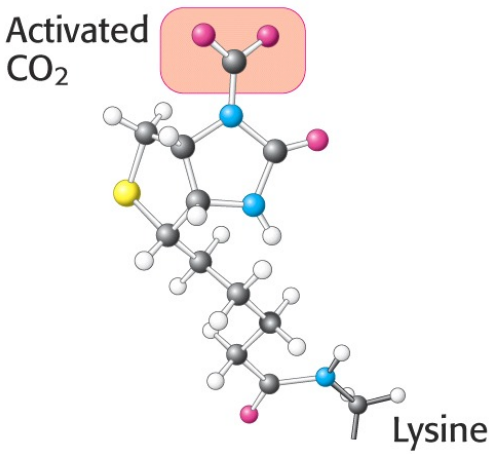
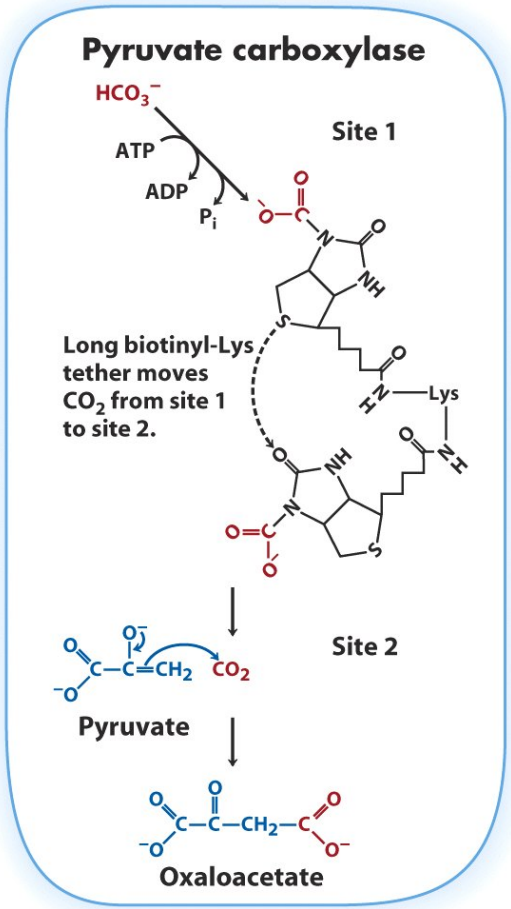
- HCO_3^- + ATP → $HOCO_{2-}$ PO_3^{2-} + ADP
- Biotin-enzyme + $HOCO_{2-}$ PO_3^{2-} → CO_2 –Biotin-enzyme + P_i
- CO_2 –Biotin-enzyme + Pyruvate → Biotin-enzyme + Oxaloacetate

Last step has a G of -20 kJ/mol
Dependent on Acetyl CoA bound to enzyme
Signifies need for OAA for either
-Glucose if energy charge high
-Citric acid cycle if energy charge low

Pyruvate Carboxylase

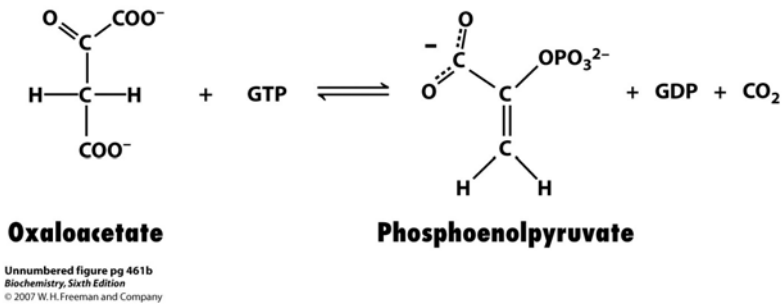






PEP carboxykinase

- **cytosolic/mitochondria**
- **shuttle NADH depending on source of Pyruvate**
- **Lactate or Alanine**



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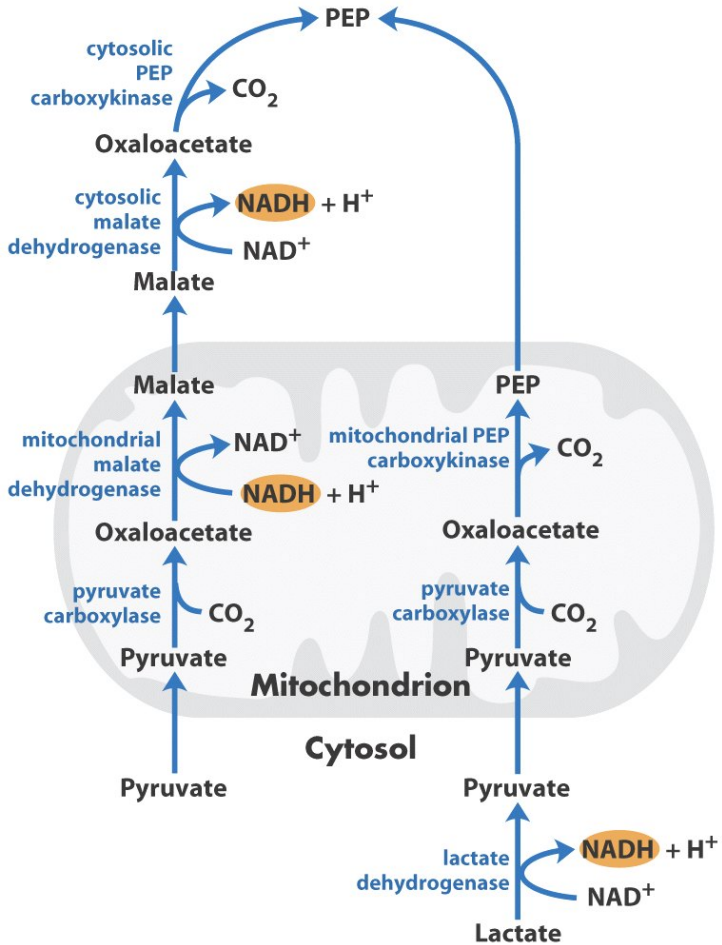
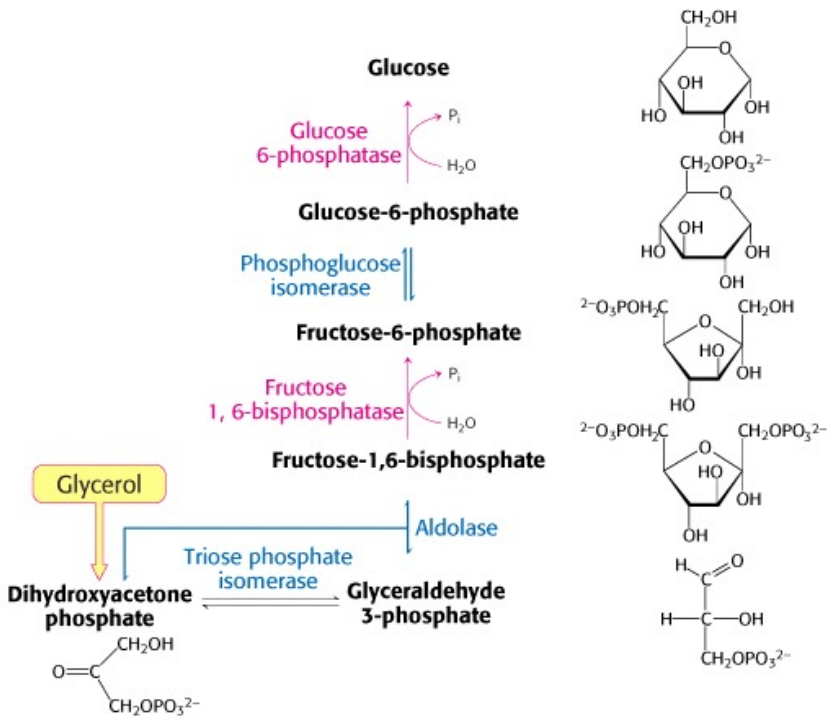


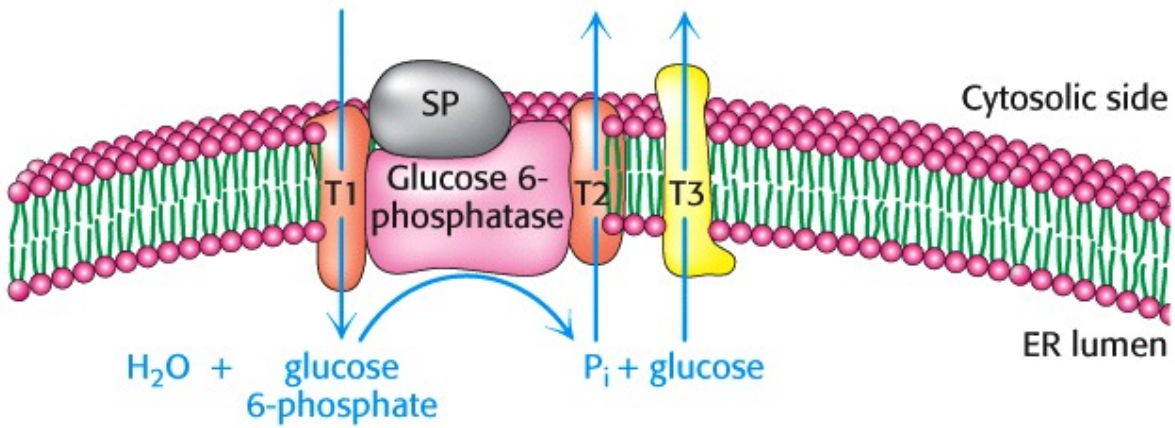
Fructose 6-P

- **Fructose 1,6 P -----> Fru 6-P**
  - **Fructose 1,6 bisphosphotase**



Glucose 6-P

- **Glucose 6-P ------> Glucose**
  - **Located in SER**
  - **Generates free glucose**
  - **Found in Liver and Kidney**
  - **Diffuse into Blood stream for Transport**



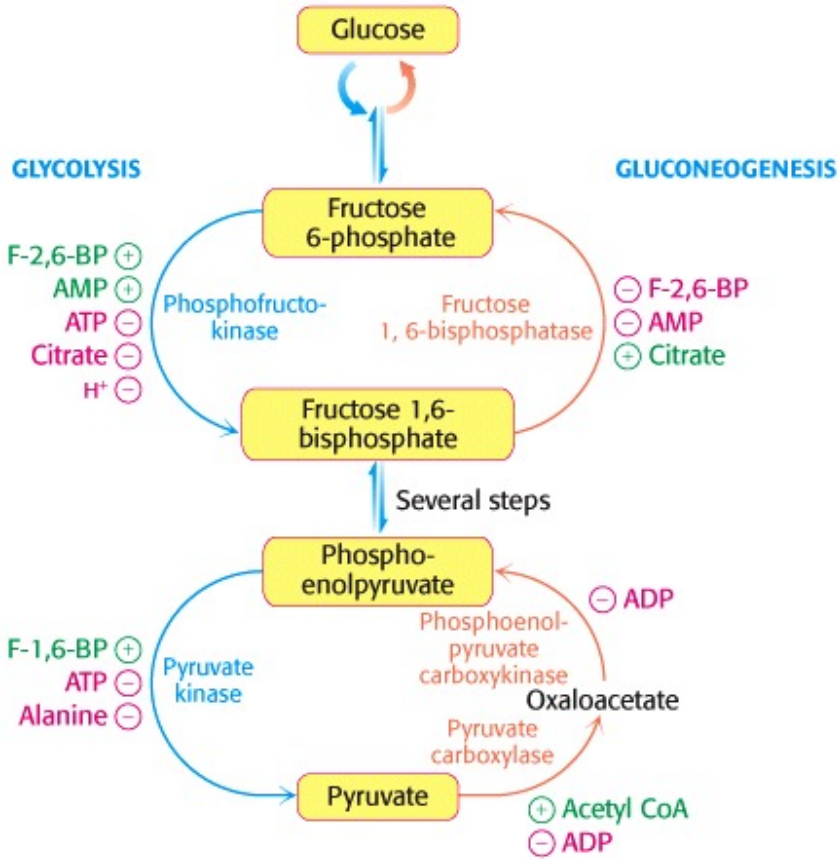
Energetics

- 2 pyruvate + 4 ATP + 2 GTP + 2NADH + 6 H_2O
- ----------→ Glucose + 4 ADP + 2 GDP + 6 P_i + 2 NAD^+ + 2 H^+

- $\Delta G^{o'}$ = -38 kJ/mol
- Cost 6 ATP versus 2 produced in Glycolysis

Regulation

- **Hormones: Glucagon and epinephrine**
  - **Via cAMP signal pathway**
  - **inhibit glycolysis**
- **Starvation**
  - **upregulates kidney to produce more glucose, up to 50%**
  - **Breakdown of proteins**
- **Cost 6 ATP**
- **150 g protein produces 75 g glucose**



Regulation between glycolysis and gluconeogenesis

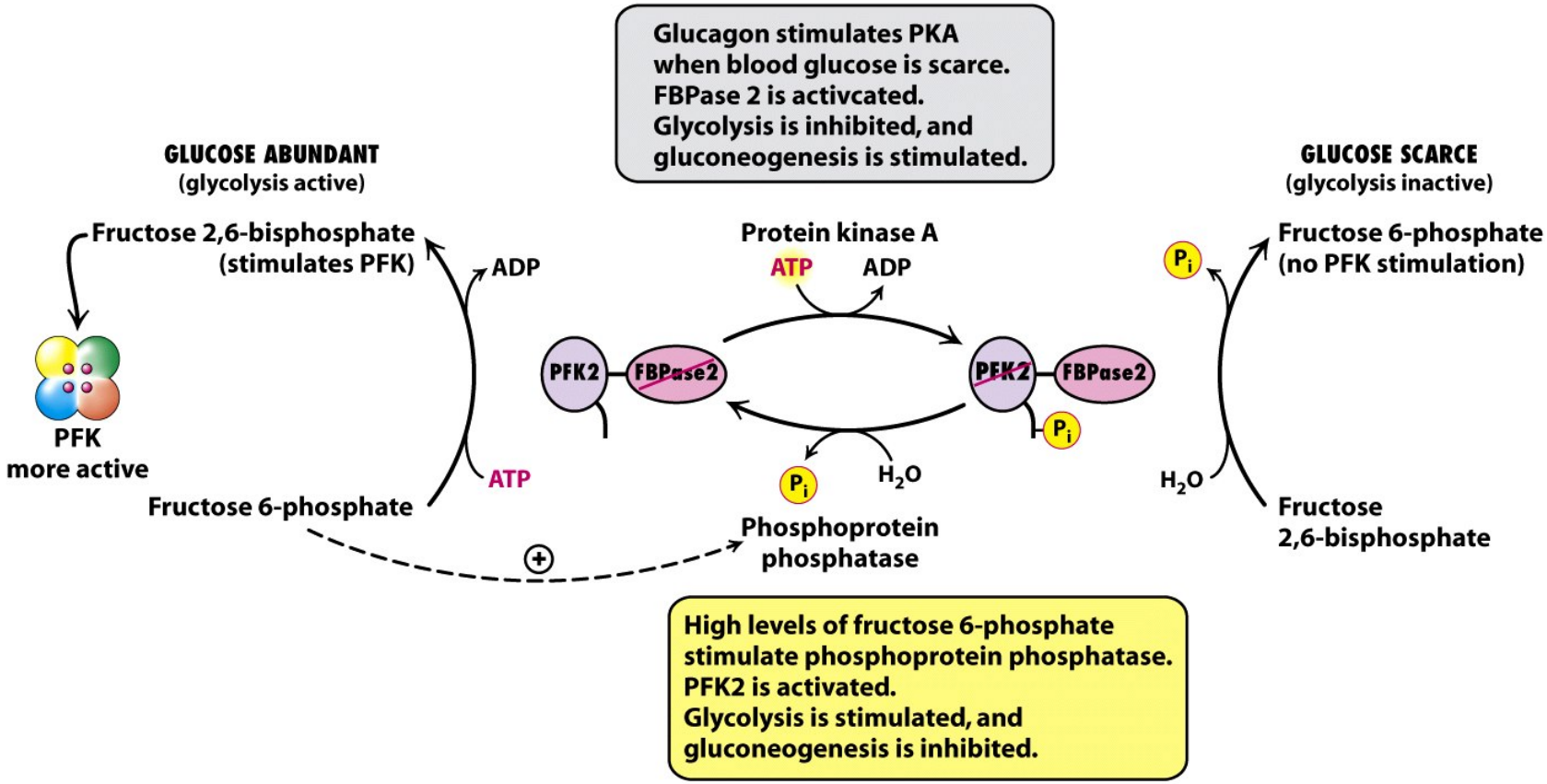


Figure 16-30
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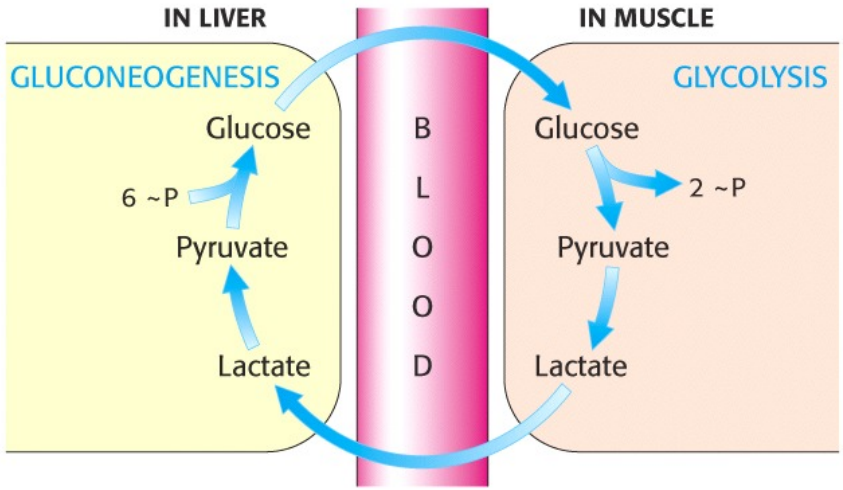
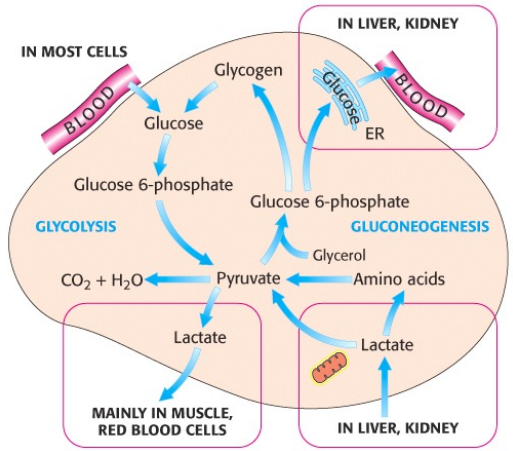
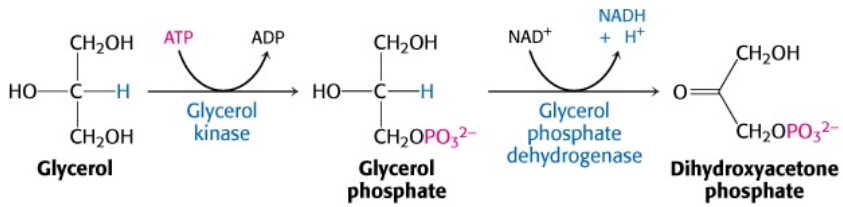
Cycles


IN LIVER
GLUCONEOGENESIS
Glucose
6 ~P
Pyruvate
Lactate
BLOOD
IN MUSCLE
GLYCOLYSIS
Glucose
2 ~P
Pyruvate
Lactate


IN MOST CELLS
IN LIVER, KIDNEY
BLOOD
Glycogen
Glucose
Glucose
ER
BLOOD
Glucose 6-phosphate
Glucose 6-phosphate
GLYCOLYSIS
GLUCONEOGENESIS
Glycerol
$CO_2 + H_2O$
Pyruvate
Amino acids
Lactate
Lactate
MAINLY IN MUSCLE, RED BLOOD CELLS
IN LIVER, KIDNEY


CH_2OH
HO—C—H
CH_2OH
Glycerol
ATP
ADP
Glycerol kinase
CH_2OH
HO—C—H
$CH_2OPO_3^{2-}$
Glycerol phosphate
NAD^+
NADH + H^+
Glycerol phosphate dehydrogenase
CH_2OH
O
$CH_2OPO_3^{2-}$
Dihydroxyacetone phosphate