

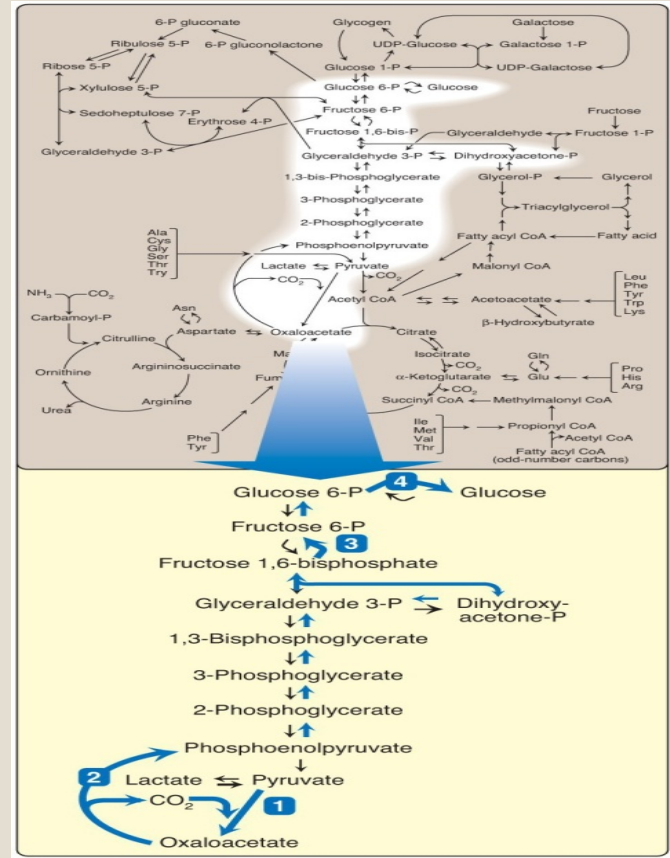
# Glucose Metabolism (Gluconeogenesis)

# Objectives

- The importance of gluconeogenesis as an important pathway for glucose production
- The main reactions of gluconeogenesis
- The rate-limiting enzymes of gluconeogenesis
- Gluconeogenesis is an energy-consuming, anabolic pathway

# Gluconeogenesis in general metabolism

The gluconeogenesis pathway shown as one of the essential pathways of energy metabolism.



# Gluconeogenesis: An Overview

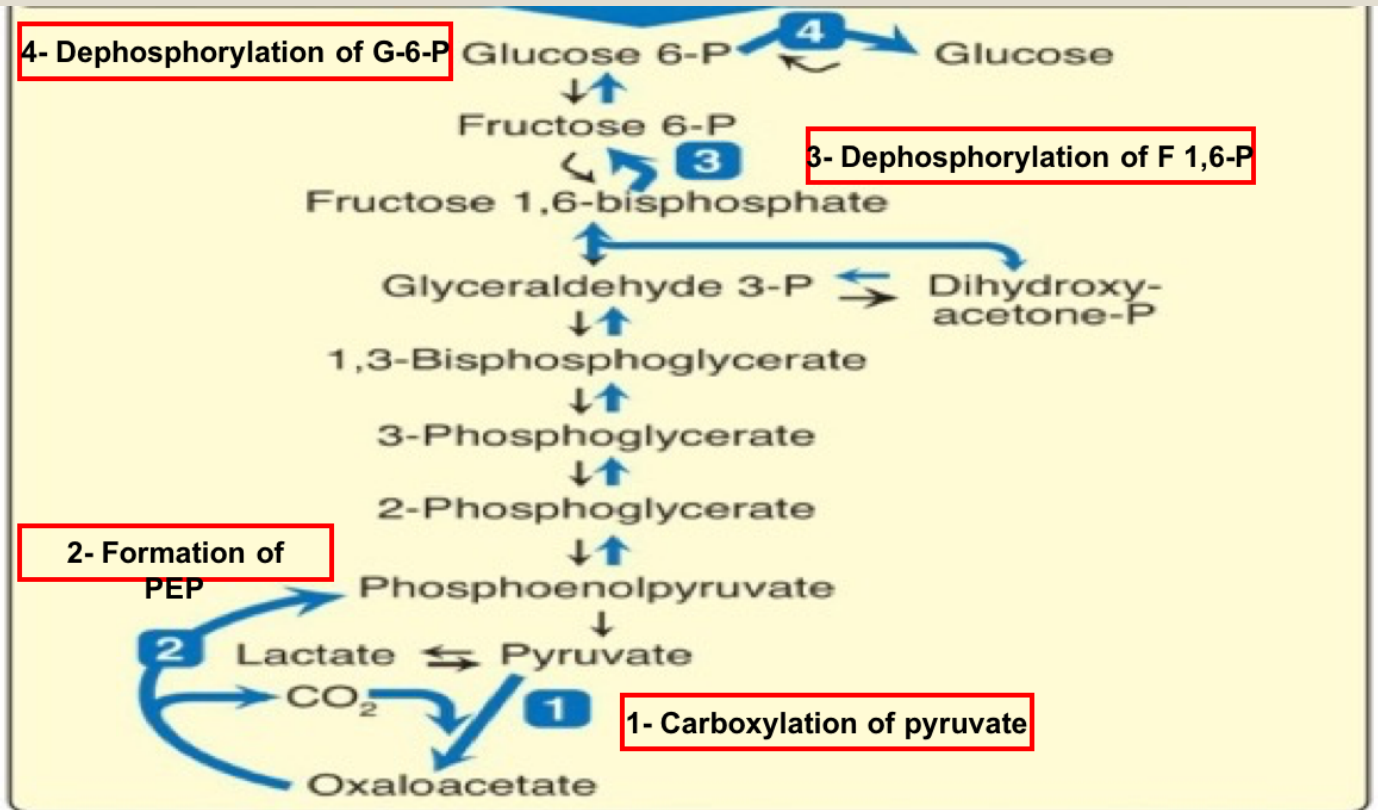
- Site: Liver (mainly) and Kidneys
- Both mitochondria and Cytosol are involved
- Exception: if the substrate is **Glycerol: only cytosol**
- Gluconeogenic substrates:

**Glycerol**

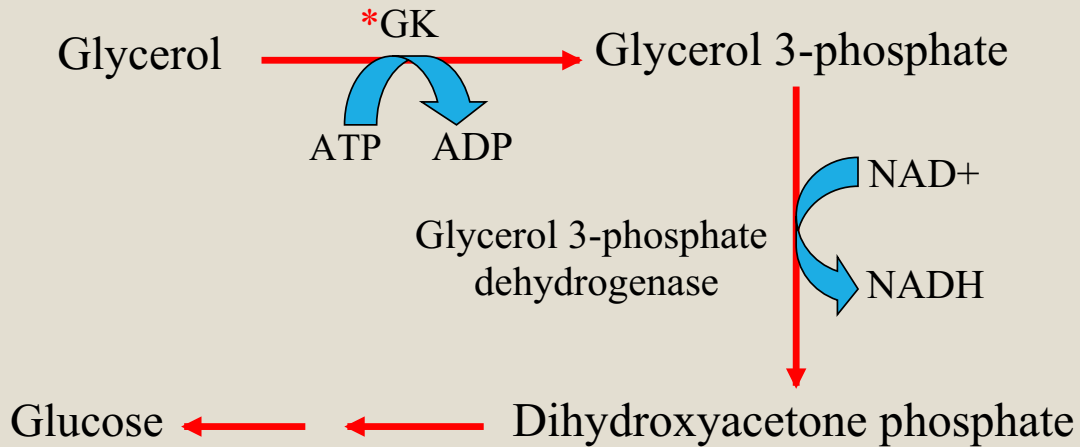
**Lactate and Pyruvate**

**Glucogenic amino acids**

# Gluconeogenesis Pathway

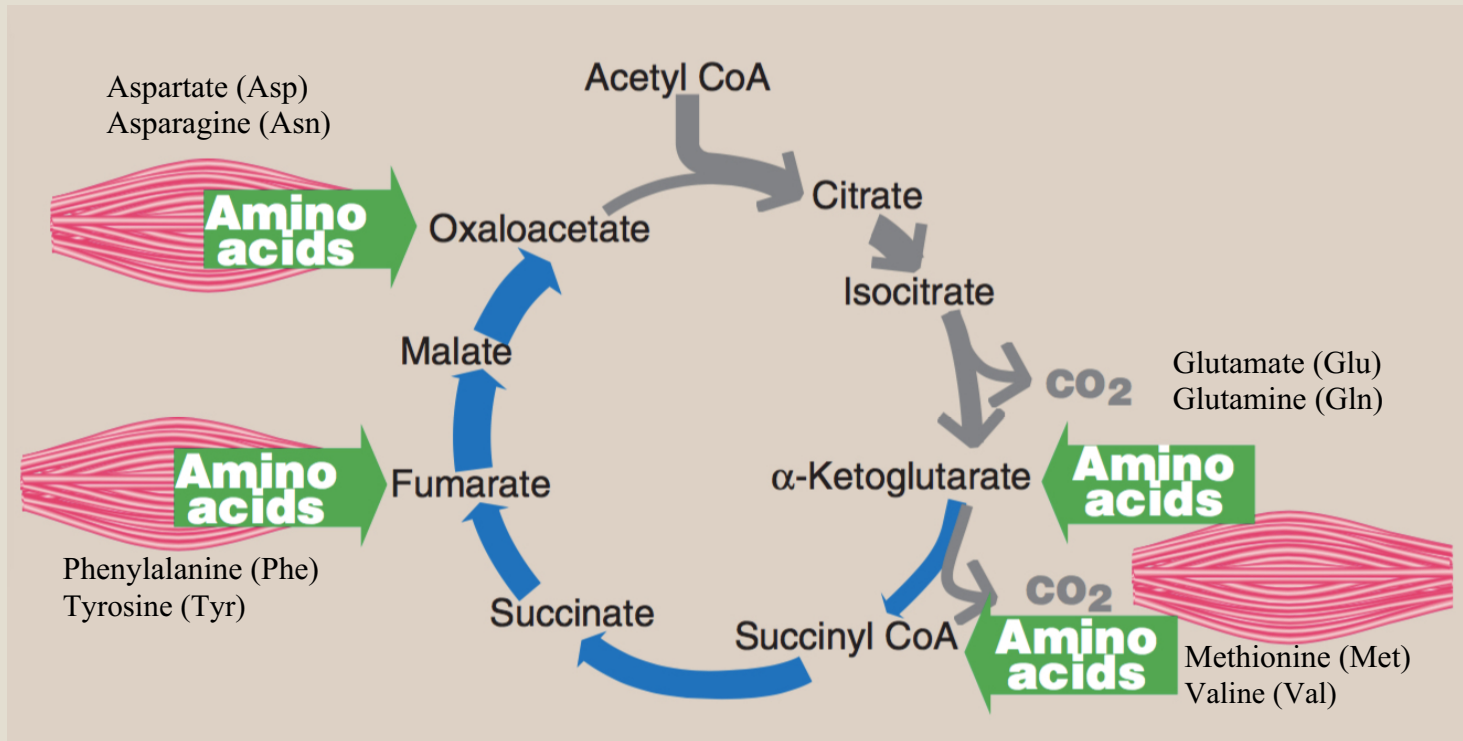


# Gluconeogenic Substrates: Glycerol

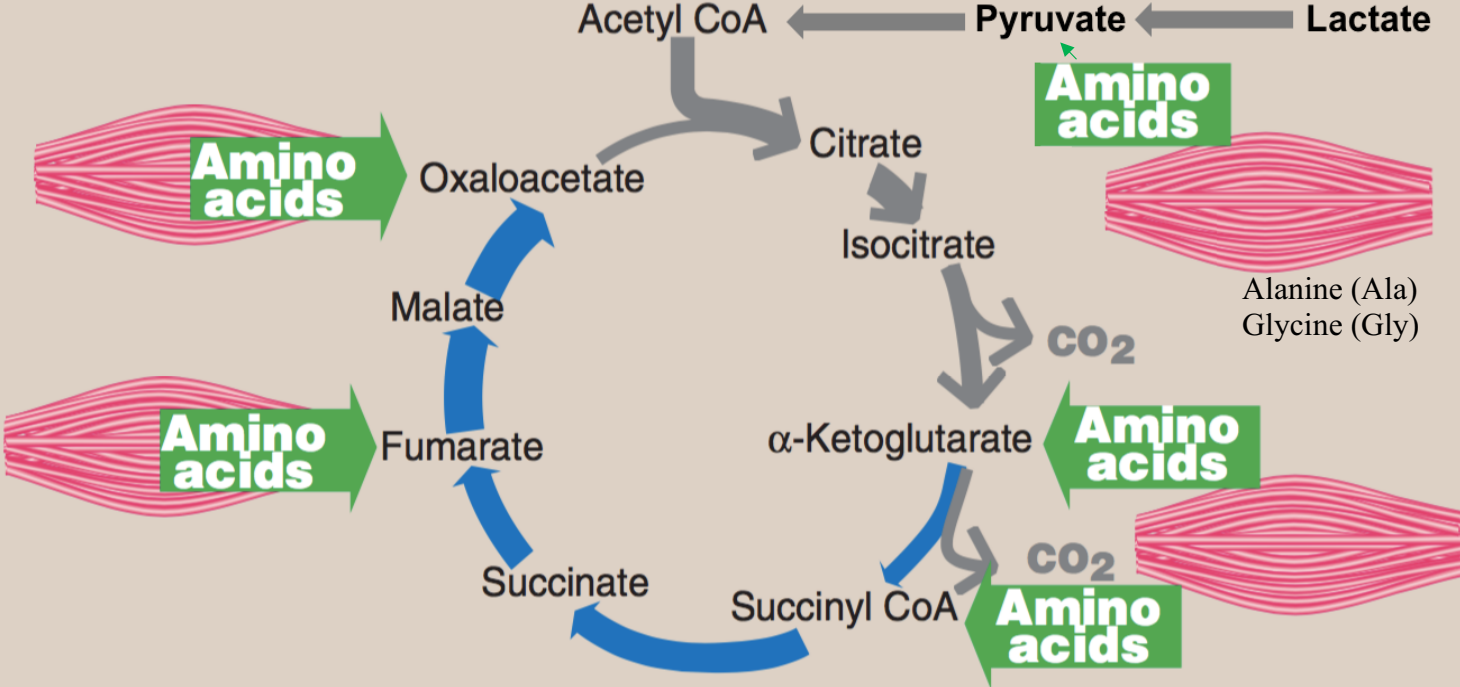


\*GK: Glycerol kinase (present only in liver & kidneys)

# Glucogenic Amino Acids

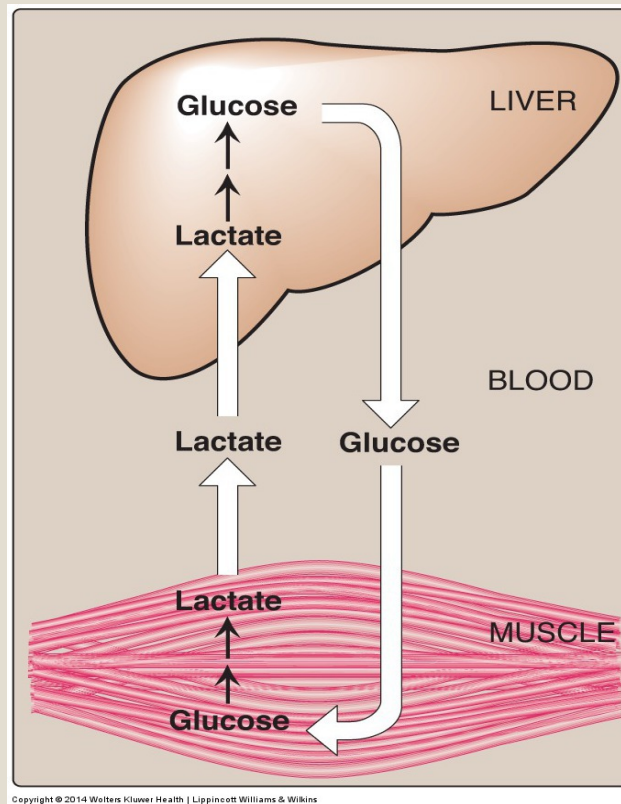


# Gluconeogenic Substrates

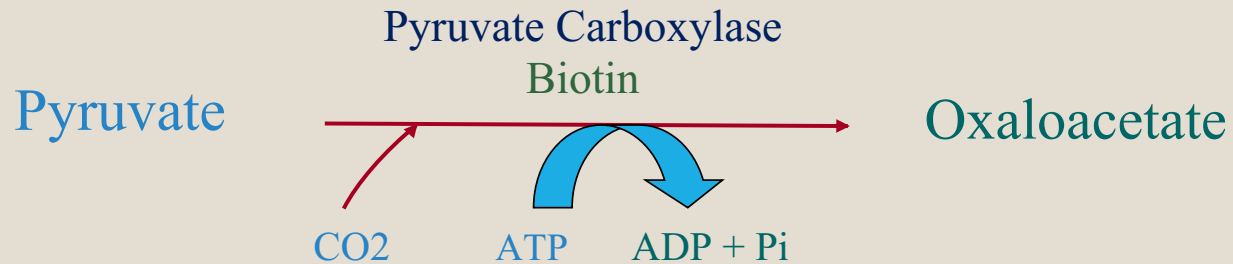




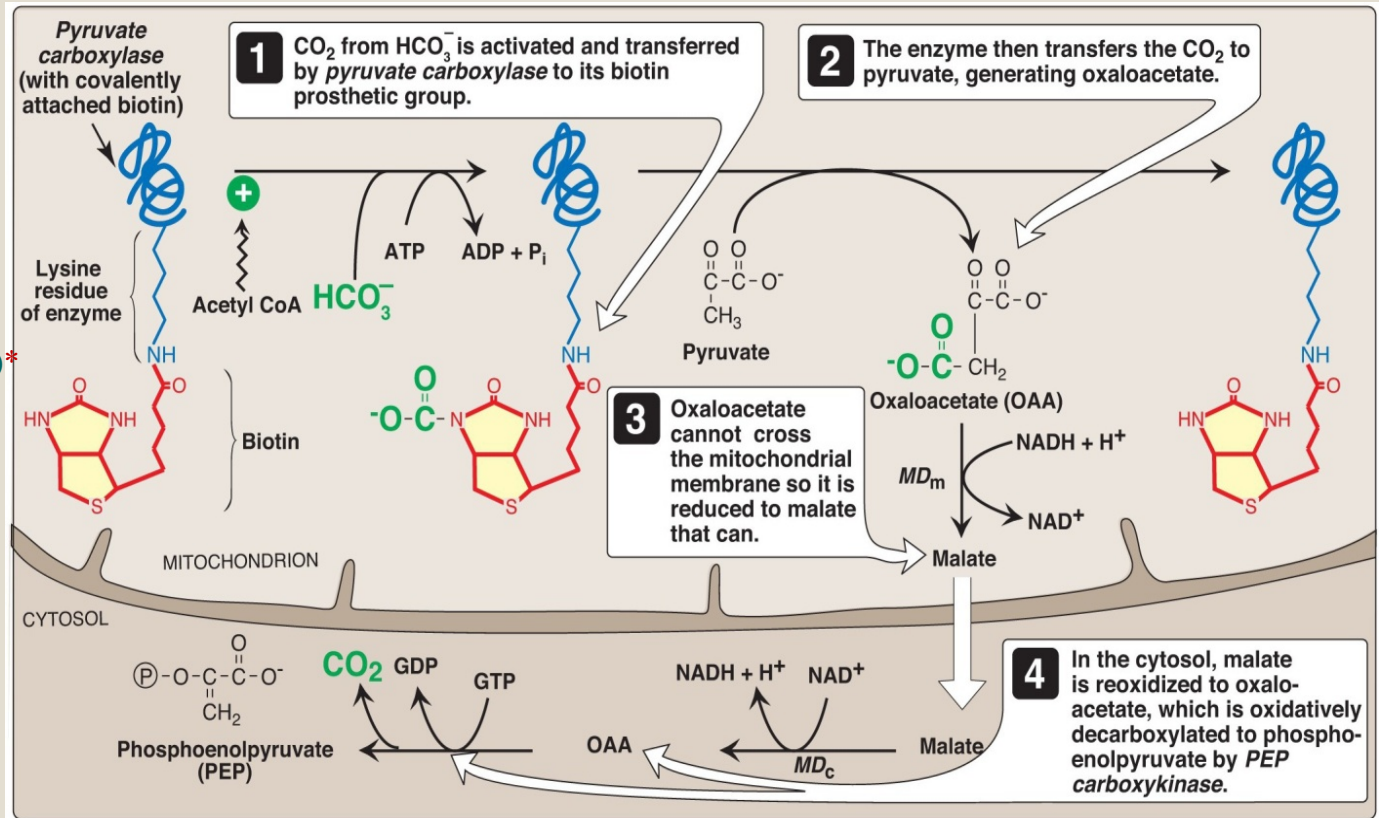
# Gluconeogenic Substrates: Lactate (Cori Cycle)



# Pyruvate Carboxylation



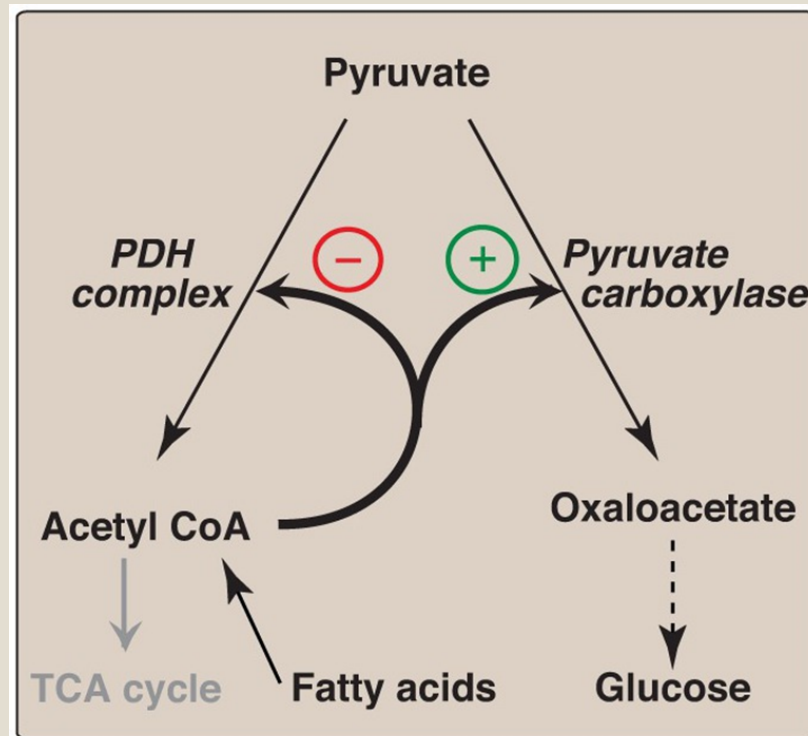
# Pyruvate Carboxylase and PEP-CK



Copyright © 2014 Wolters Kluwer Health | Lippincott Williams & Wilkins

Pyruvate carboxylase + PEP-CK ≠ Pyruvate kinase

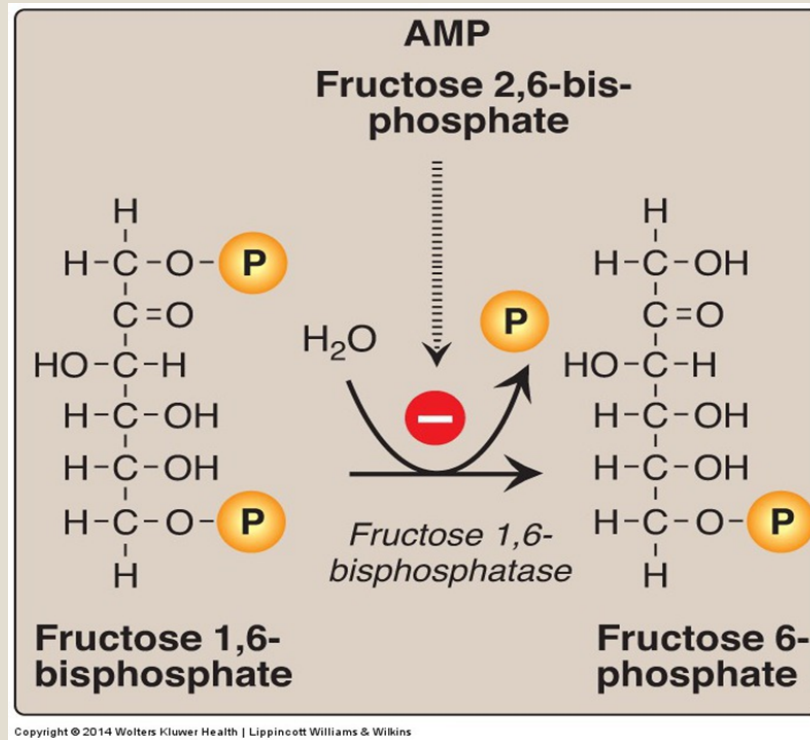
# Regulation of Pyruvate Carboxylase reaction



Copyright © 2014 Wolters Kluwer Health | Lippincott Williams & Wilkins

Acetyl CoA diverts pyruvate away from oxidation and toward gluconeogenesis

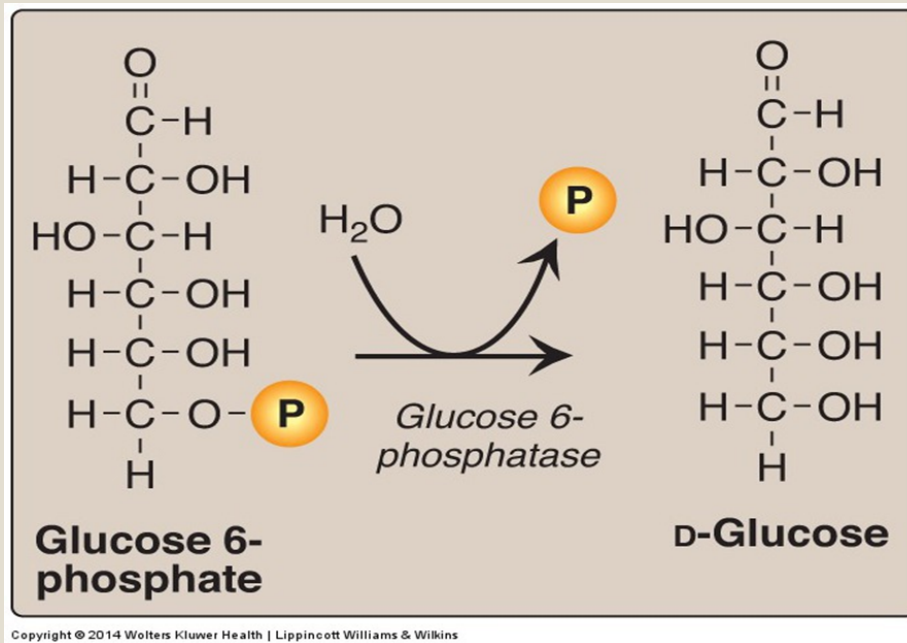
# Fructose 1,6-Bisphosphatase



Dephosphorylation of fructose 1,6-bisphosphate

Fructose 1,6-bisphosphatase  $\neq$  PFK-1

# Glucose 6-Phosphatase

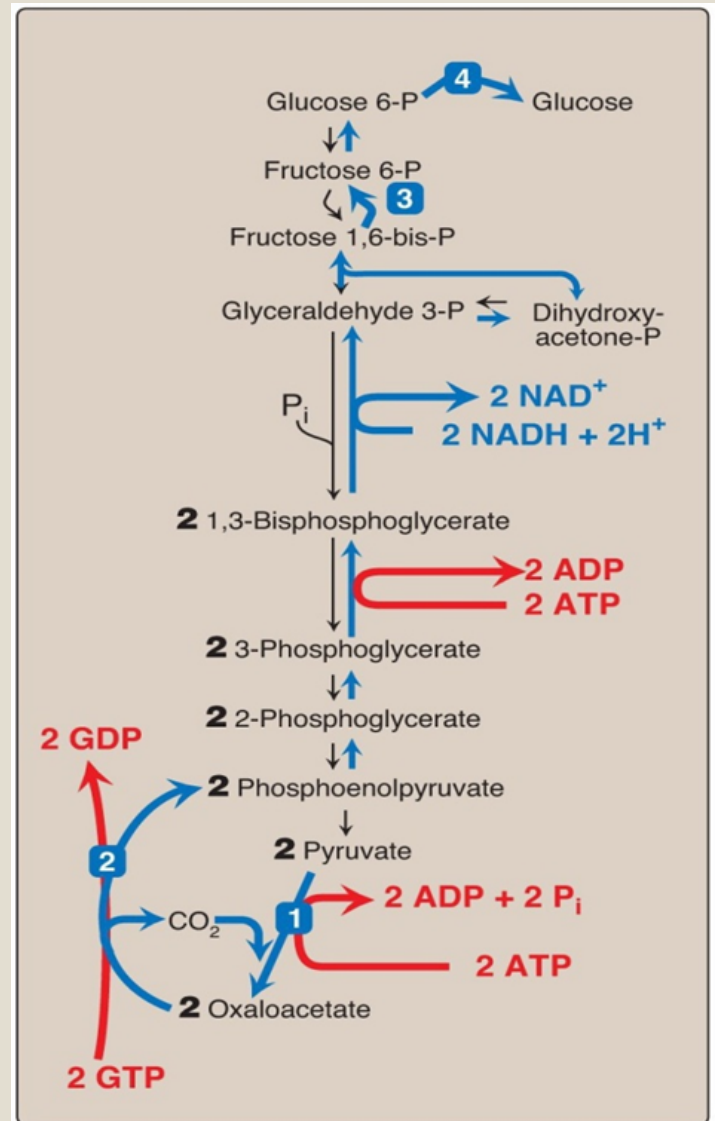


Dephosphorylation of glucose 6-phosphate allows release of free glucose from the liver and kidney into blood

Glucose 6-phosphatase  $\neq$  Glucokinase

# Gluconeogenesis: Energy- Consumed

Six High-Energy Phosphate Bonds  
From Pyruvate to Glucose



# Gluconeogenesis: Regulation

- Reciprocal control  
Gluconeogenesis & Glycolysis
- Allosteric:  
Acetyl CoA (Pyruvate carboxylase)

AMP or ATP  
F 2,6-Bisphosphate } F 1,6-bisphosphatase  
+  
-

- Glucagon ( I/G ratio) stimulates gluconeogenesis

- ↑ - Allosteric ( F 2,6-Bisphosphate)
- Induction (PEP-CK)





# Take Home Messages

- Gluconeogenesis is an important pathway for glucose production from non-carbohydrate sources during prolonged fasting.
- Lactate, glycerol and glucogenic amino acids are the major gluconeogenic substrates.
- Gluconeogenesis is not a simple reversal of glycolysis. In fact, gluconeogenesis requires 4 unique reactions to circumvent the 3 irreversible reactions of glycolysis.
- Gluconeogenesis and glycolysis are reciprocally controlled, allowing efficient glucose metabolism.
- It is mainly anabolic pathway that consumes ATP for the synthesis of glucose.

# Reference

Lippincott Illustrated Review of Biochemistry, 6th edition, 2014,  
Unit 2, Chapter 10, Pages 117-124.