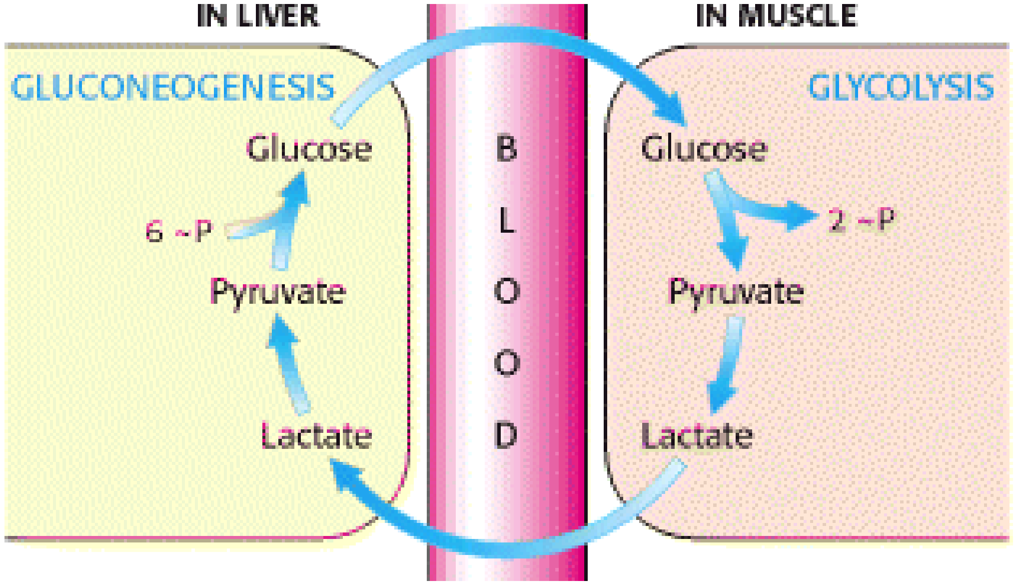
Gluconeogenesis

- **Mechanism to maintain adequate glucose levels in tissues, especially in brain (brain uses 120 g of the 160g of glucose needed daily). Erythrocytes also require glucose.**

- **Occurs exclusively in liver (90%) and kidney (10%)**

- **Glucose is synthesized from non-carbohydrate precursors derived from muscle, adipose tissue: pyruvate and lactate (60%), amino acids (20%), glycerol (20%)**

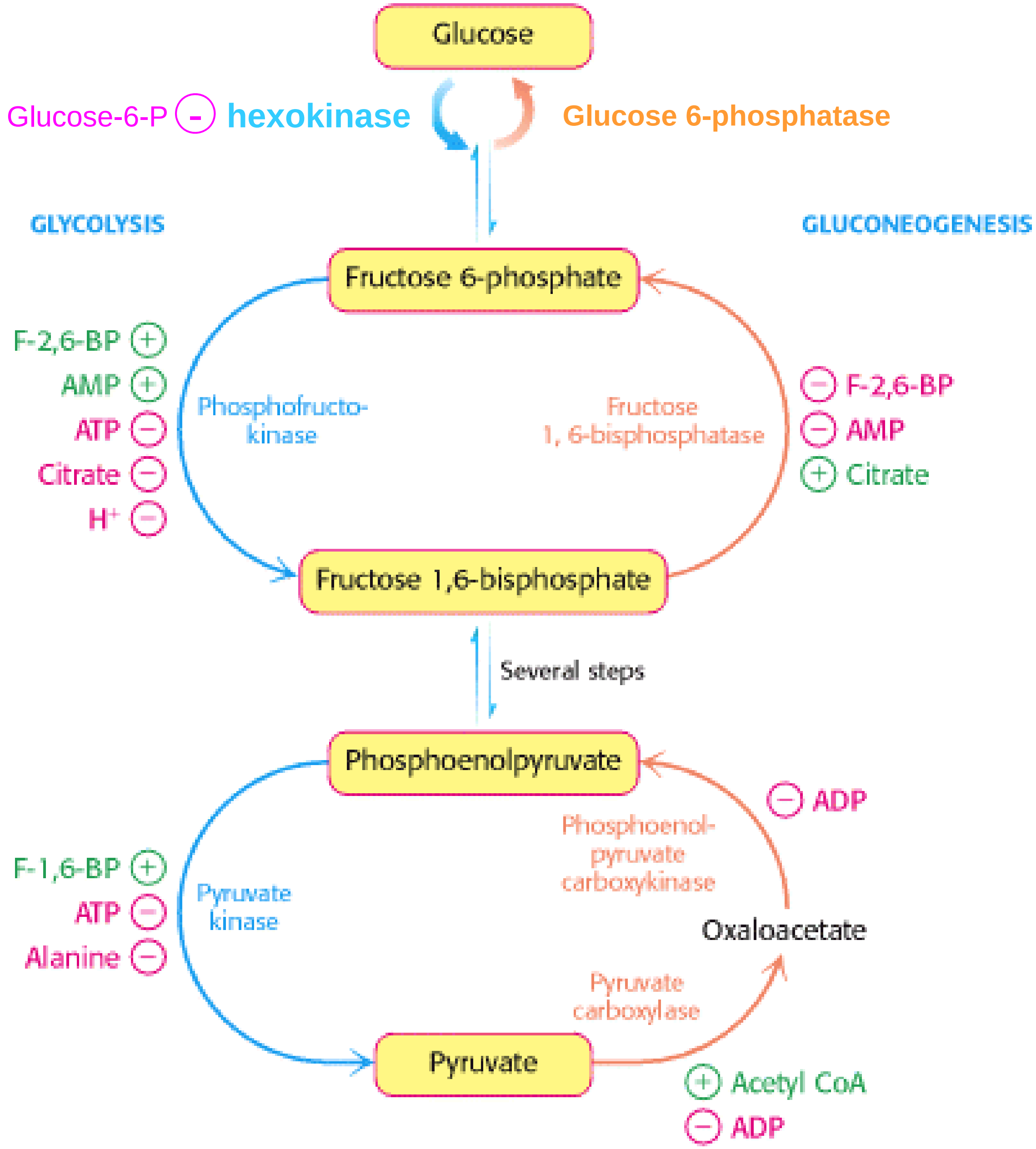


Gluconeogenesis takes energy and is regulated

Converts pyruvate to glucose

Gluconeogenesis is not simply the reverse of glycolysis; it utilizes unique enzymes (pyruvate carboxylase, PEPCK, fructose-1,6-bisphosphatase, and glucose-6-phosphatase) for irreversible reactions.

6 ATP equivalents are consumed in synthesizing 1 glucose from pyruvate in this pathway



Irreversible steps in gluconeogenesis

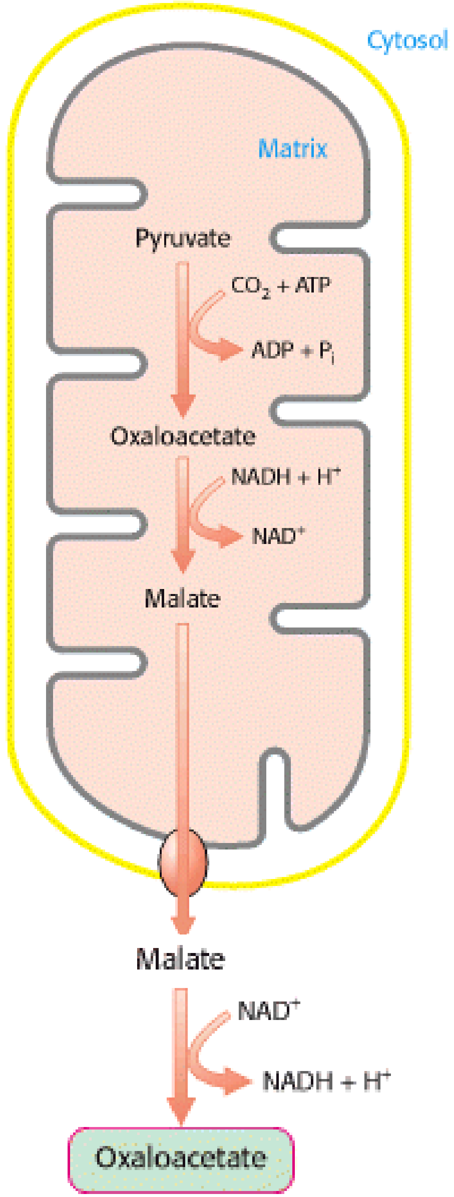
• First step by a gluconeogenic-specific enzyme occurs in the mitochondria

Pyruvate carboxylase

pyruvate ——→ oxaloacetate

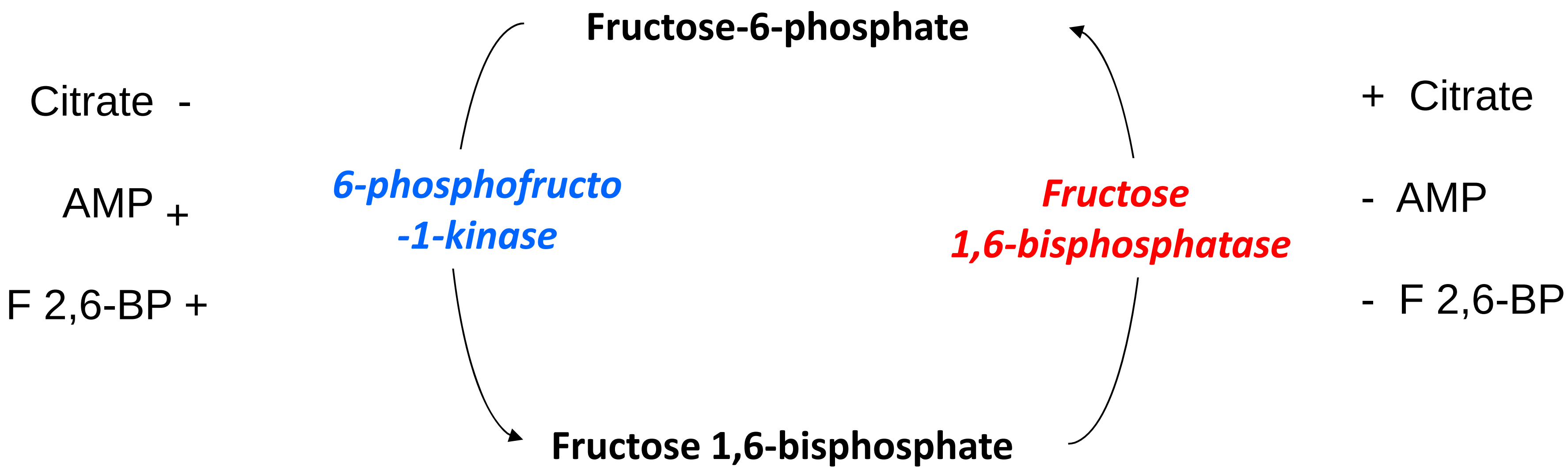
• Once oxaloacetate is produced, it is reduced to malate so that it can be transported to the cytosol. In the cytosol, oxaloacetate is subsequently dexcarboxylated/phosphorylated by PEPCK (phosphoenolpyruvate carboxykinase), a second enzyme unique to gluconeogenesis.

The resulting phosphoenol pyruvate is metabolized by glycolysis enzymes in reverse, until the next irreversible step



Gluconeogenesis and Glycolysis are reciprocally regulated

- Fructose 1,6-bisphosphatase is main regulatory step in gluconeogenesis.
- Corresponding step in glycolysis is 6-phosphofructo-1-kinase (PFK-1).
- These two enzymes are regulated in a reciprocal manner by several metabolites.



Reciprocal control—prevents simultaneous reactions in same cell.