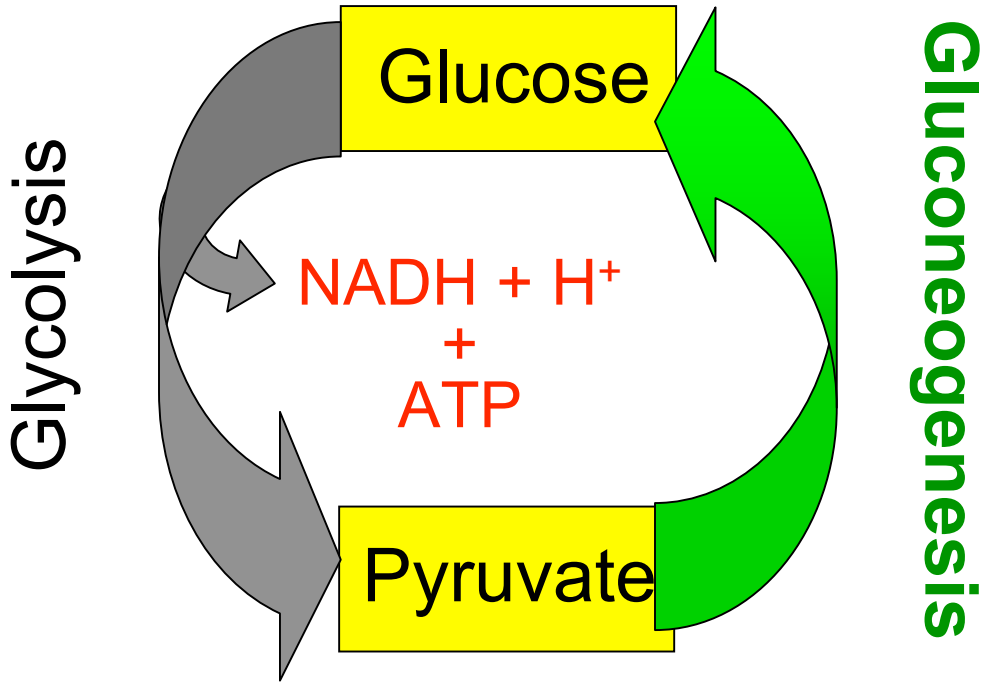
Key knowledge base & conceptual questions

- In what sense can gluconeogenesis be considered a reversal of the glycolytic pathway? Why can it be said that glycolysis gives energy which gluconeogenesis takes energy? Why is it important to prevent gluconeogenesis when the cell is low on ATP?
- Know the three steps of glycolysis which are bypassed by enzymes of gluconeogenesis. Know which of the glycolysis steps requires ATP, GTP, and/or NADH.
- Know the 4 reactions that 'reverse' the three steps above. Know which of these steps requires ATP, GTP, and/or NADH.
- Why can oxaloacetate be said to be 'starting material' for gluconeogenesis? How is oxaloacetate derived from lactate, amino acids, and glycerol?
- For pyruvate carboxylase, know the general features of its (a) location, (b) mechanism, and (3) regulation. Why is this enzyme the key to understanding regulation of gluconeogenesis? Know does this enzyme connect intermediates in glycolysis and in the CAC?

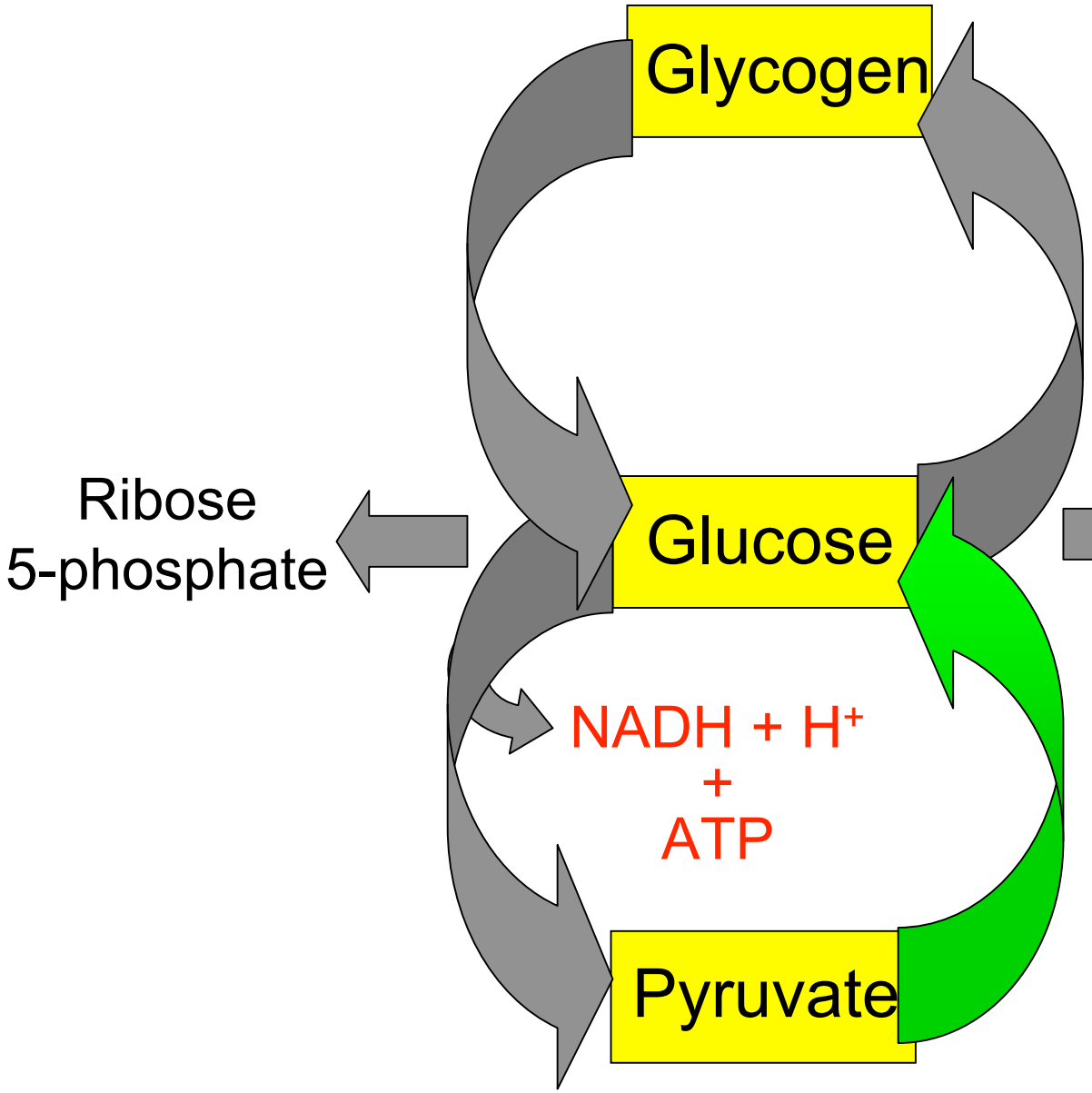
Overview: *Introduction*

Gluconeogenesis

- anabolic process by which glucose is synthesized from smaller molecules such as lactate and pyruvate
- important for maintenance of blood glucose levels within critical limits

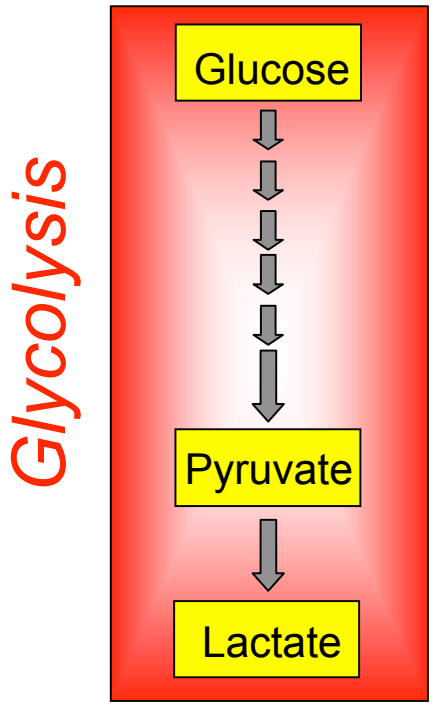


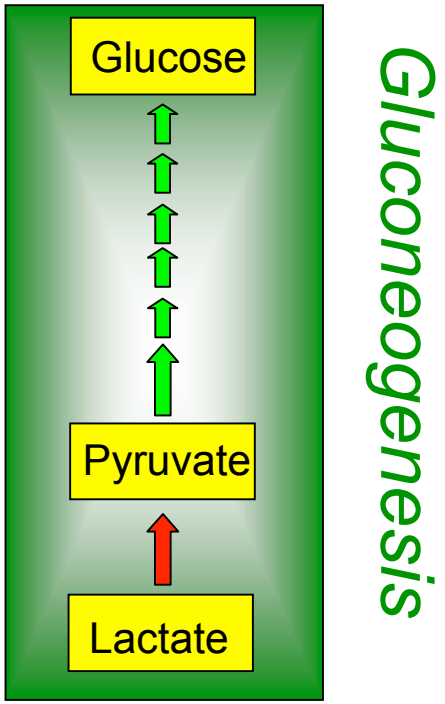
Overview: *Glucose Energy*



Glucose

- major energy source for most tissues
- brain alone uses more than 100 g/day
- can be stored as glycogen or used for biosynthesis.



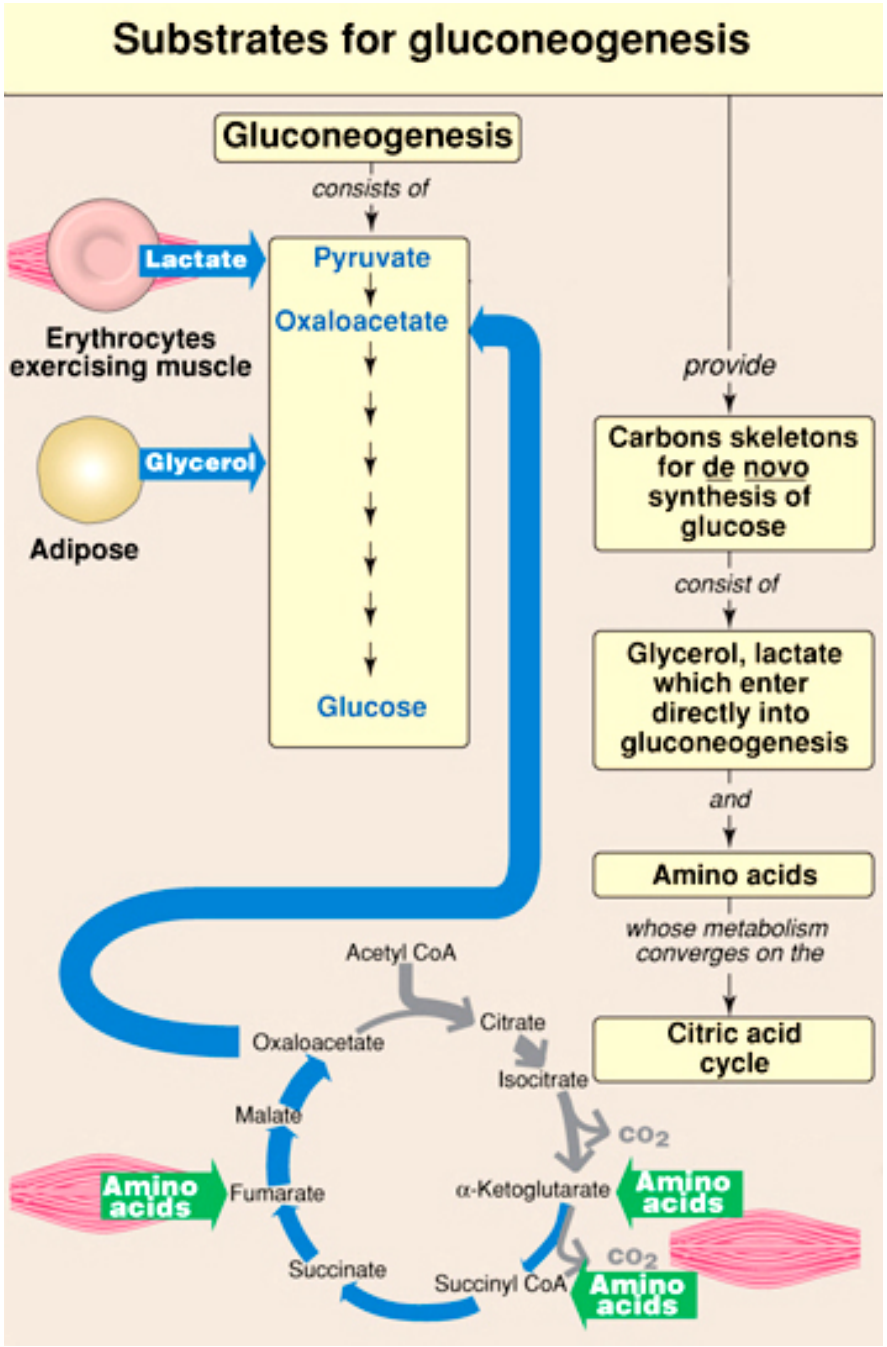


glucose + 2 ADP + 2 P_i + 2 NAD^+

2 pyr + 2 ATP + 2 NADH + $2H^+$ + 2 H_2O

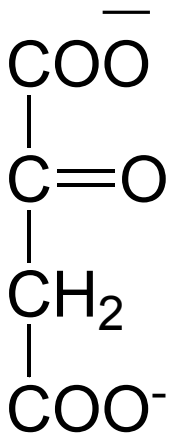
2 pyr + 4 ATP + 2 GTP + 2 NADH + $2H^+$ + 2 H_2O

glucose + 4 ADP + 2 GDP + 6 P_i + 2 NAD^+



Gluconeogenesis

- Key intermediate oxaloacetate, i.e. starting material for pathway



- Substrates are lactate, amino acids, or glycerol.

Gluconeogenesis

is NOT a reversal of glycolysis

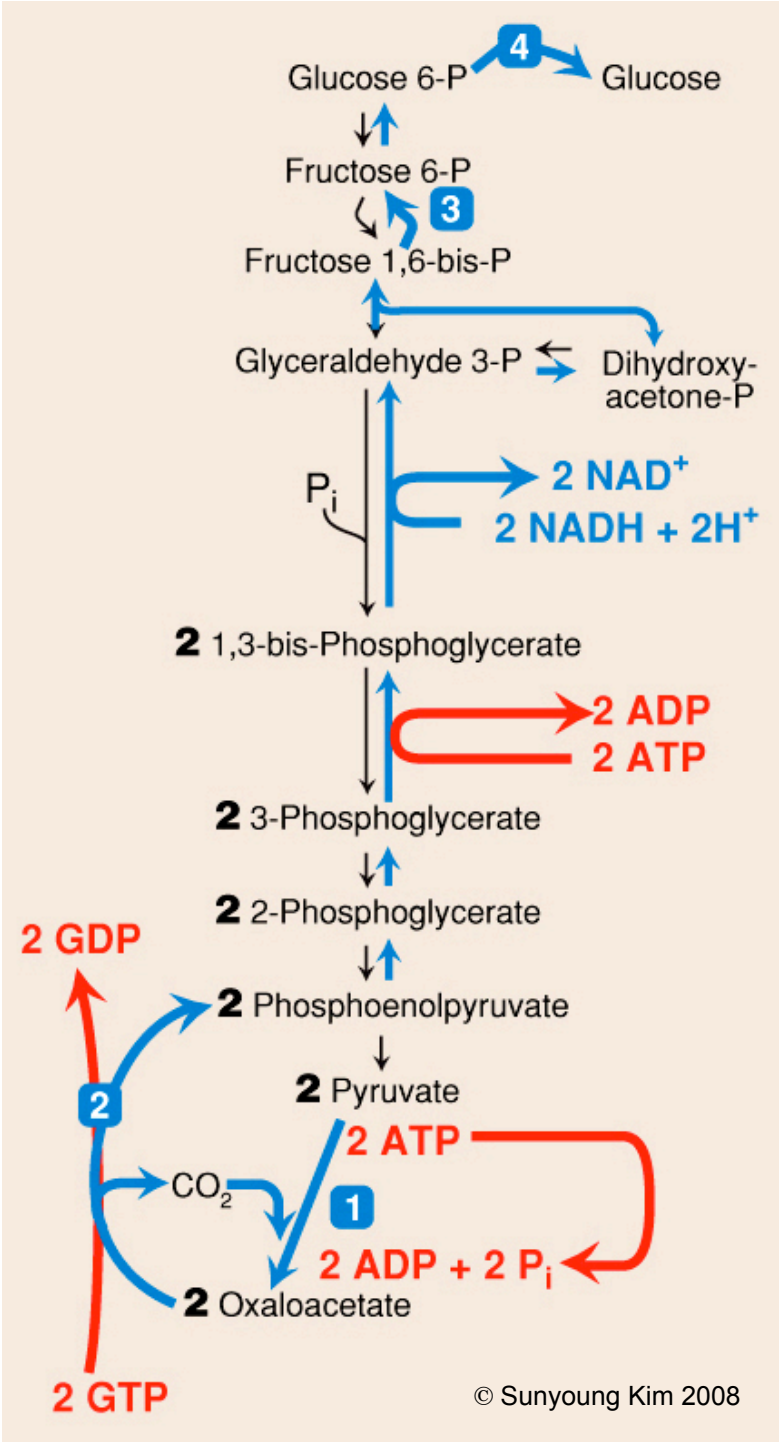
involves reversal of some glycolytic steps and some unique steps

Three steps in glycolysis are NOT reversible:

Glu + ATP → G-6-P + ADP

F-6-P + ATP → F-1,6-BP + ADP

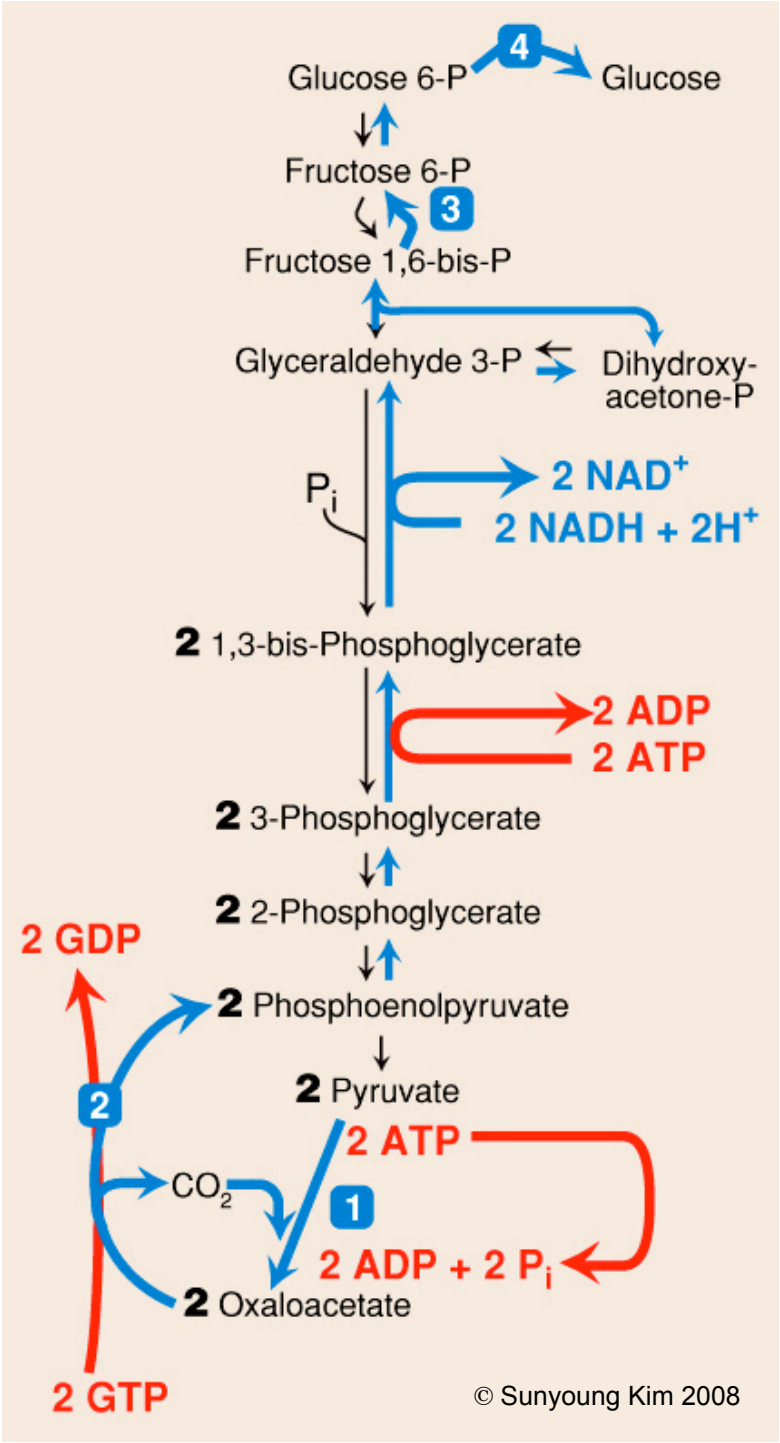
PEP + ADP → pyr + ATP



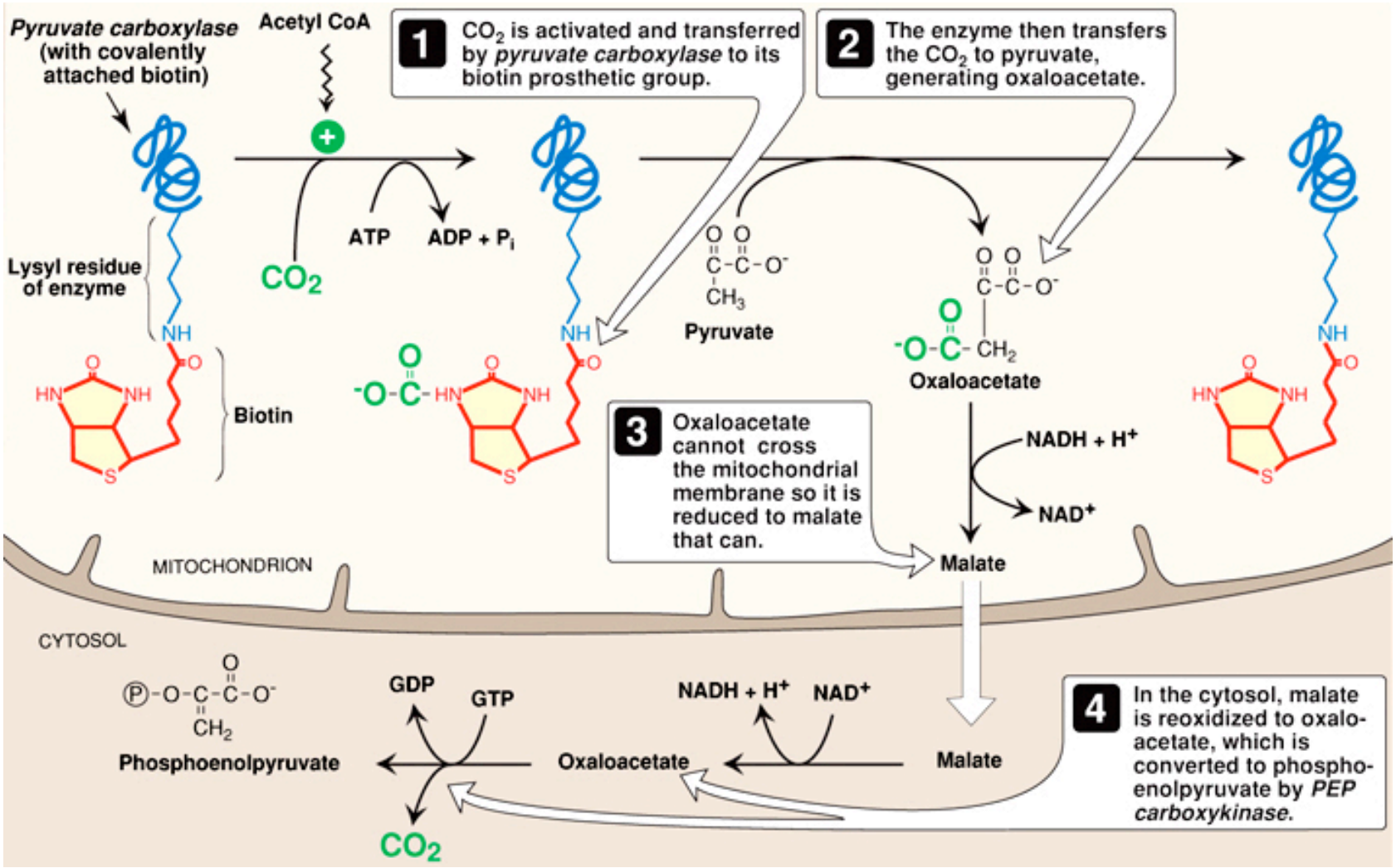
Gluconeogenesis

Four unique gluconeogenesis reactions are catalyzed by:

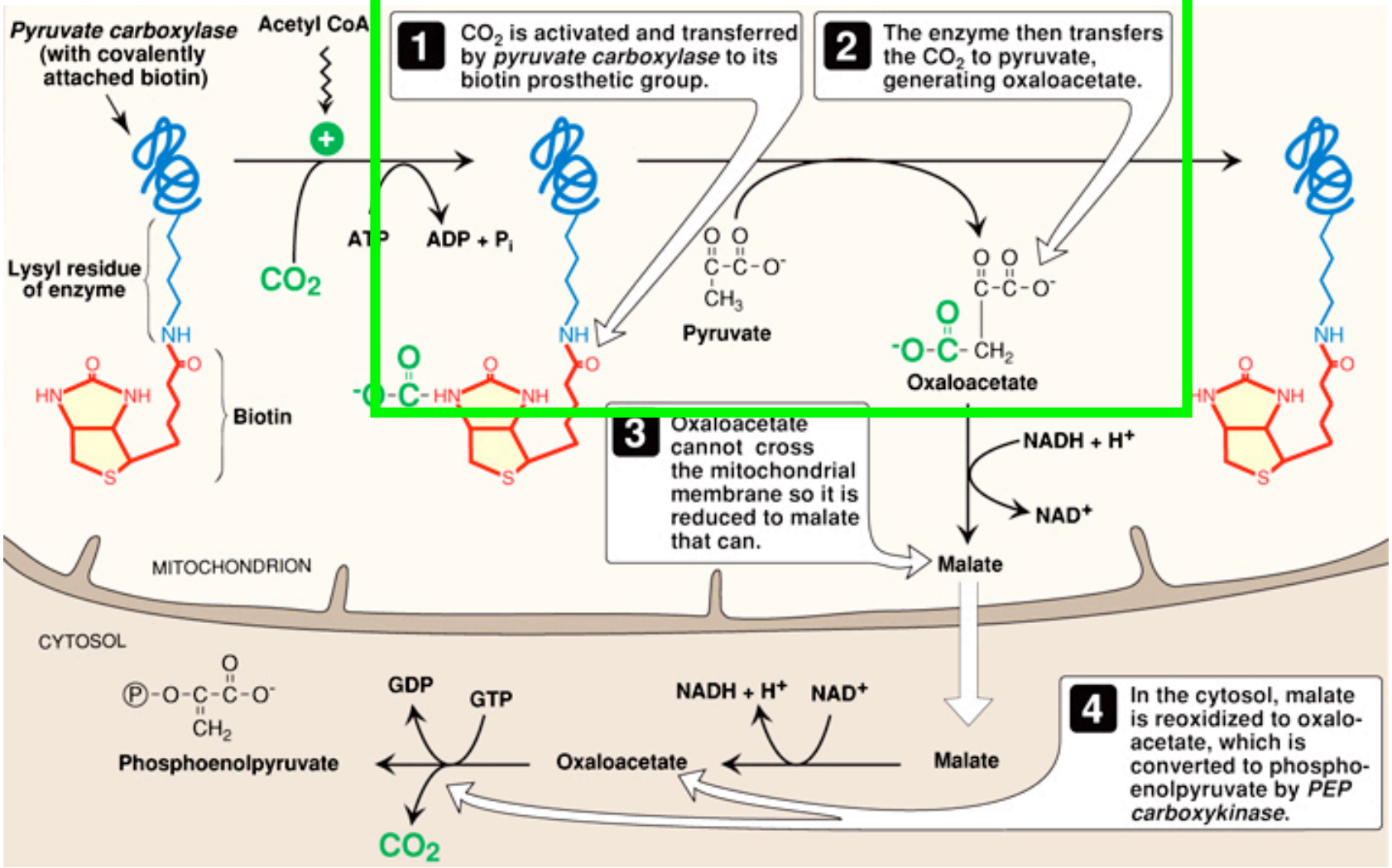
1. Pyruvate carboxylase
2. PEP carboxykinase
3. fructose 1,6-bisphosphatase
4. glucose 6-phosphatase



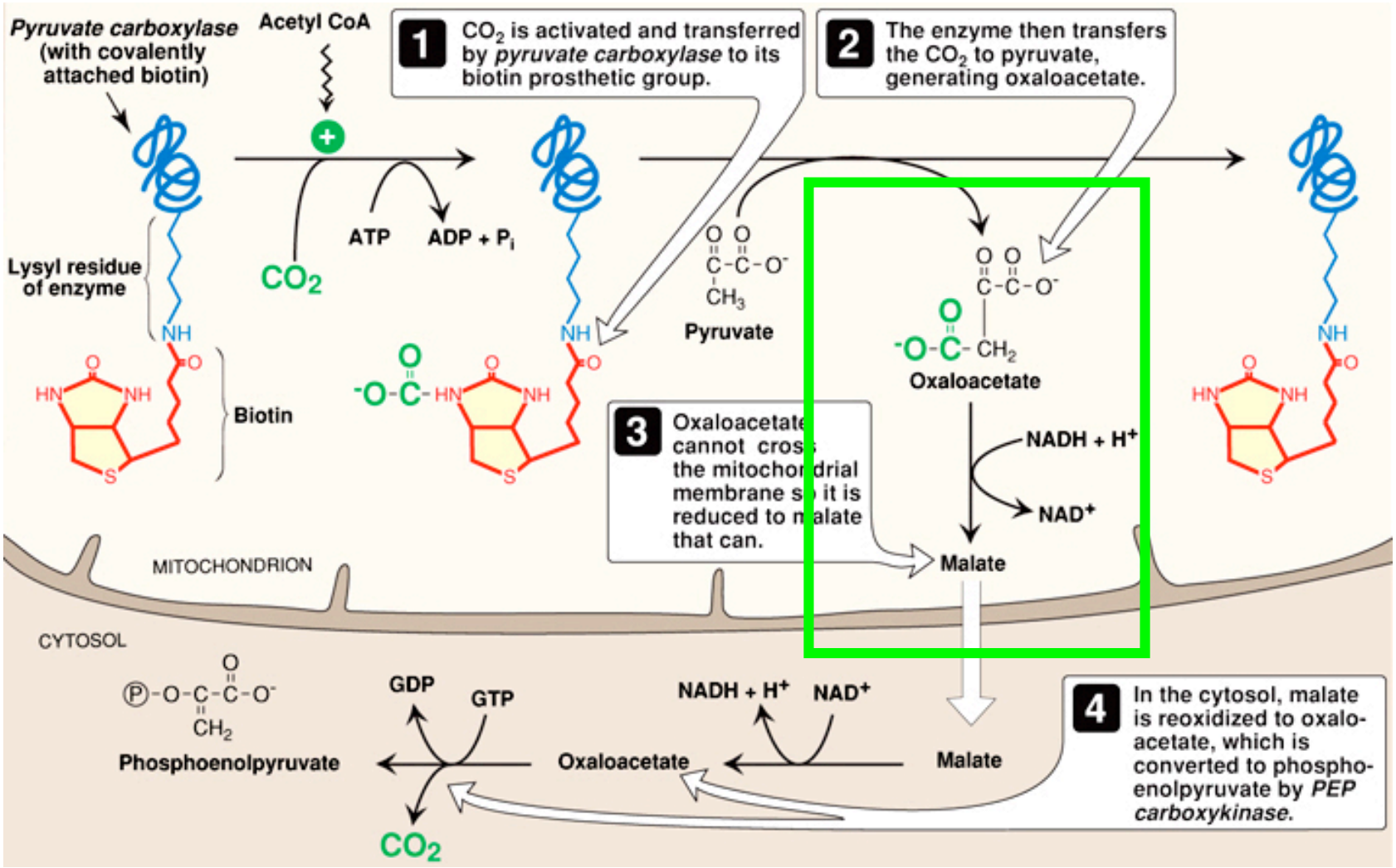
Pathway: *Location*



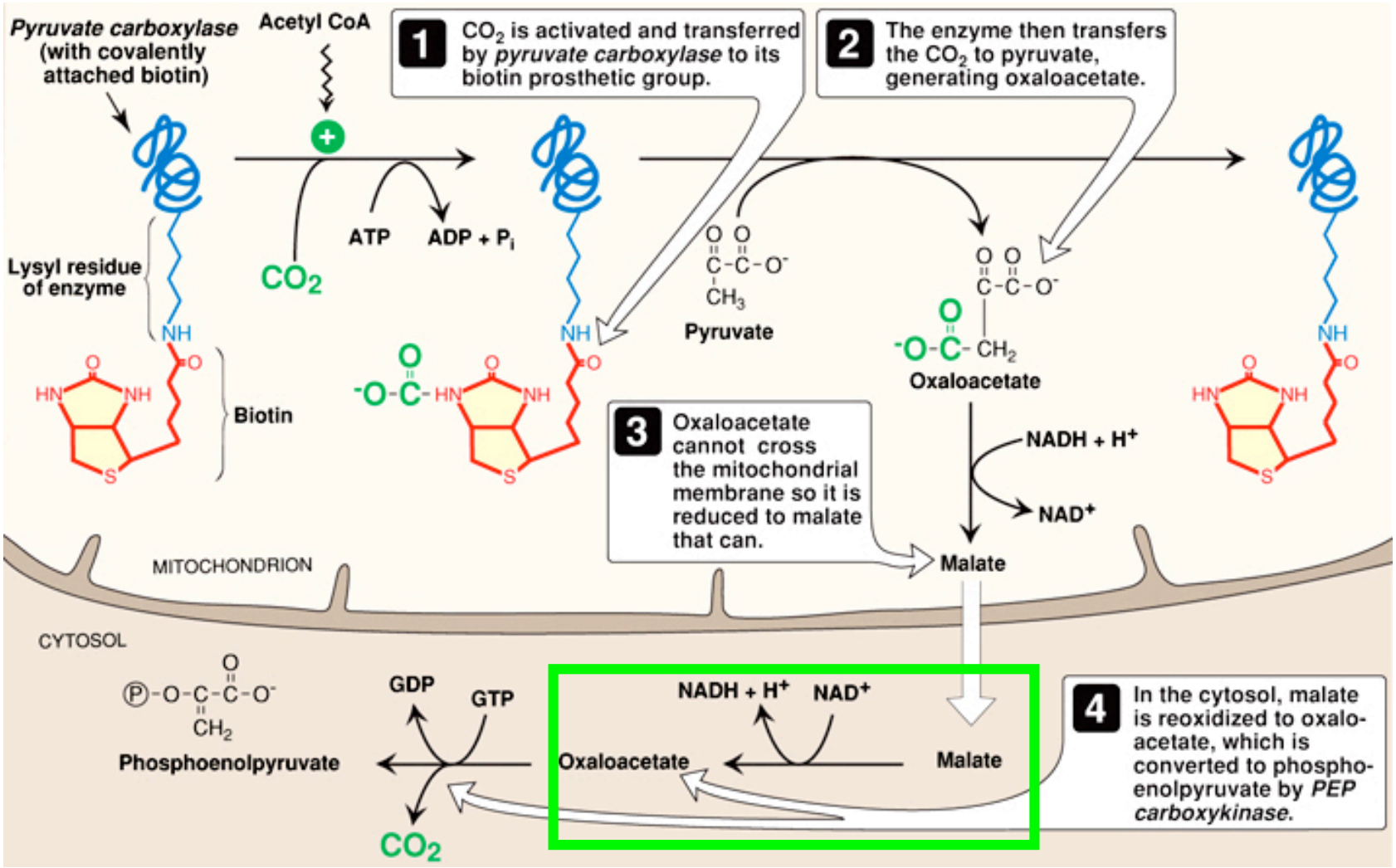
Pathway: *First Step*



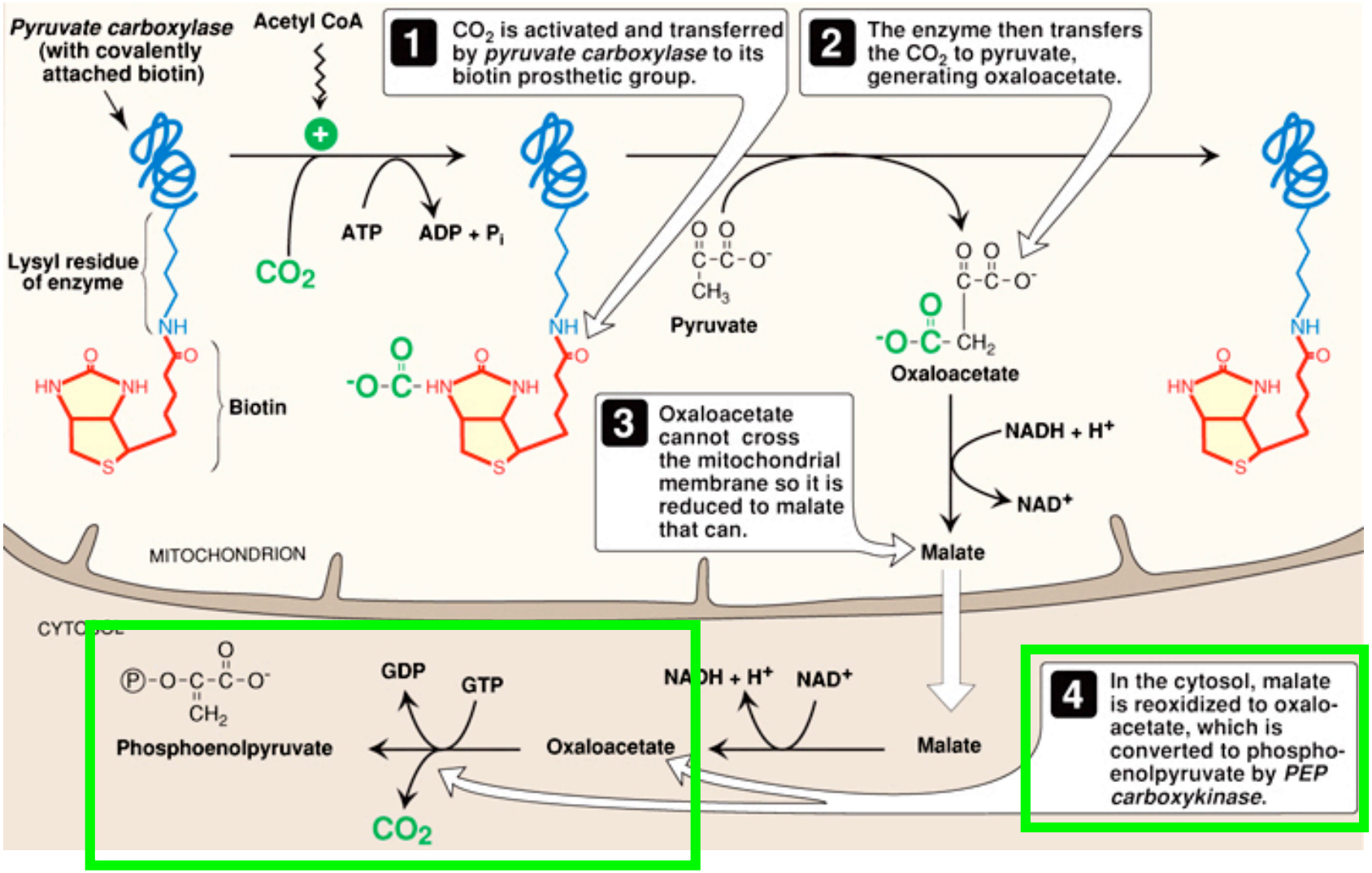
Pathway: *escape from mitochondria*



Pathway: *in the cytoplasm*

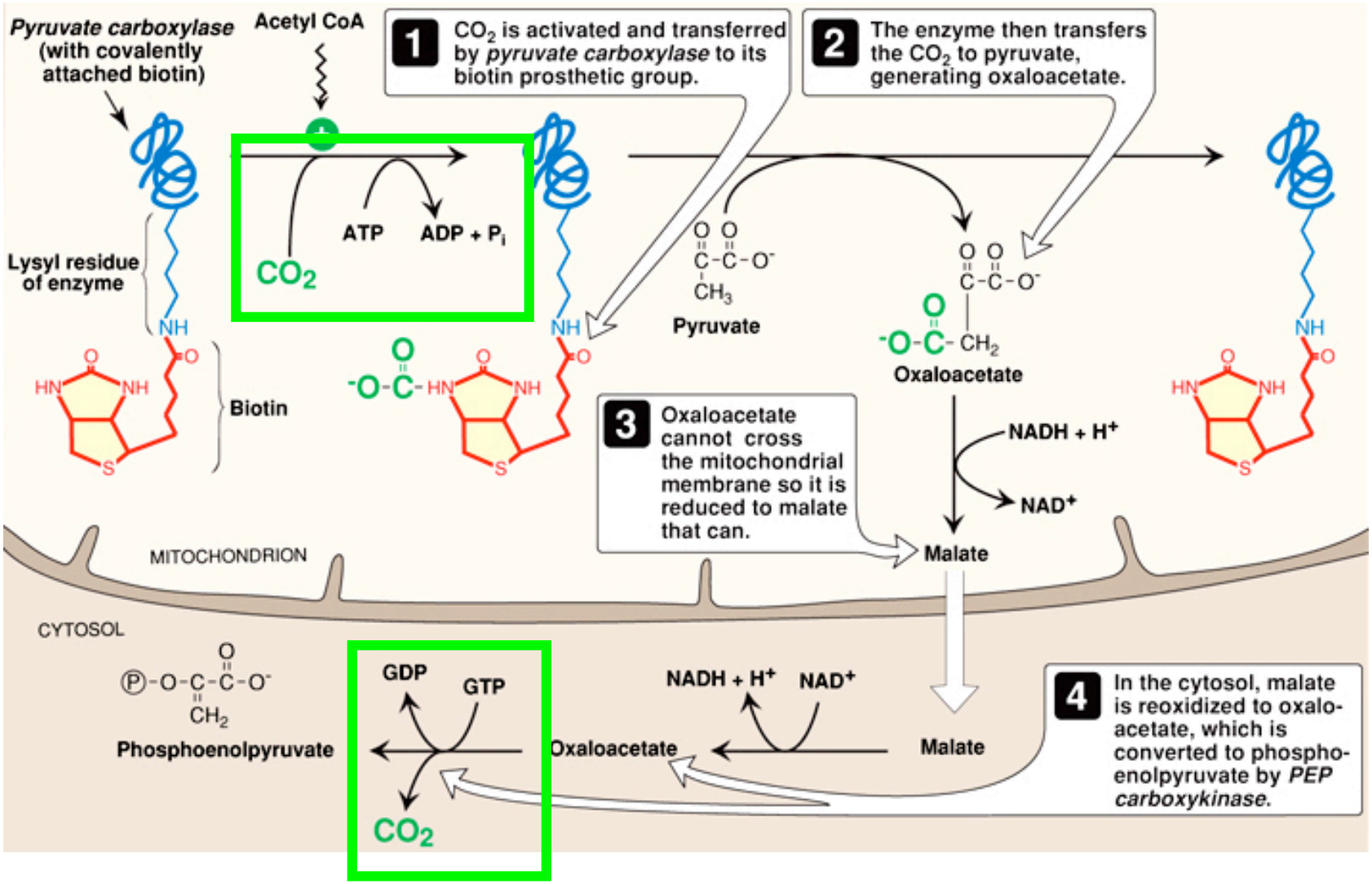


Pathway: *PEP*



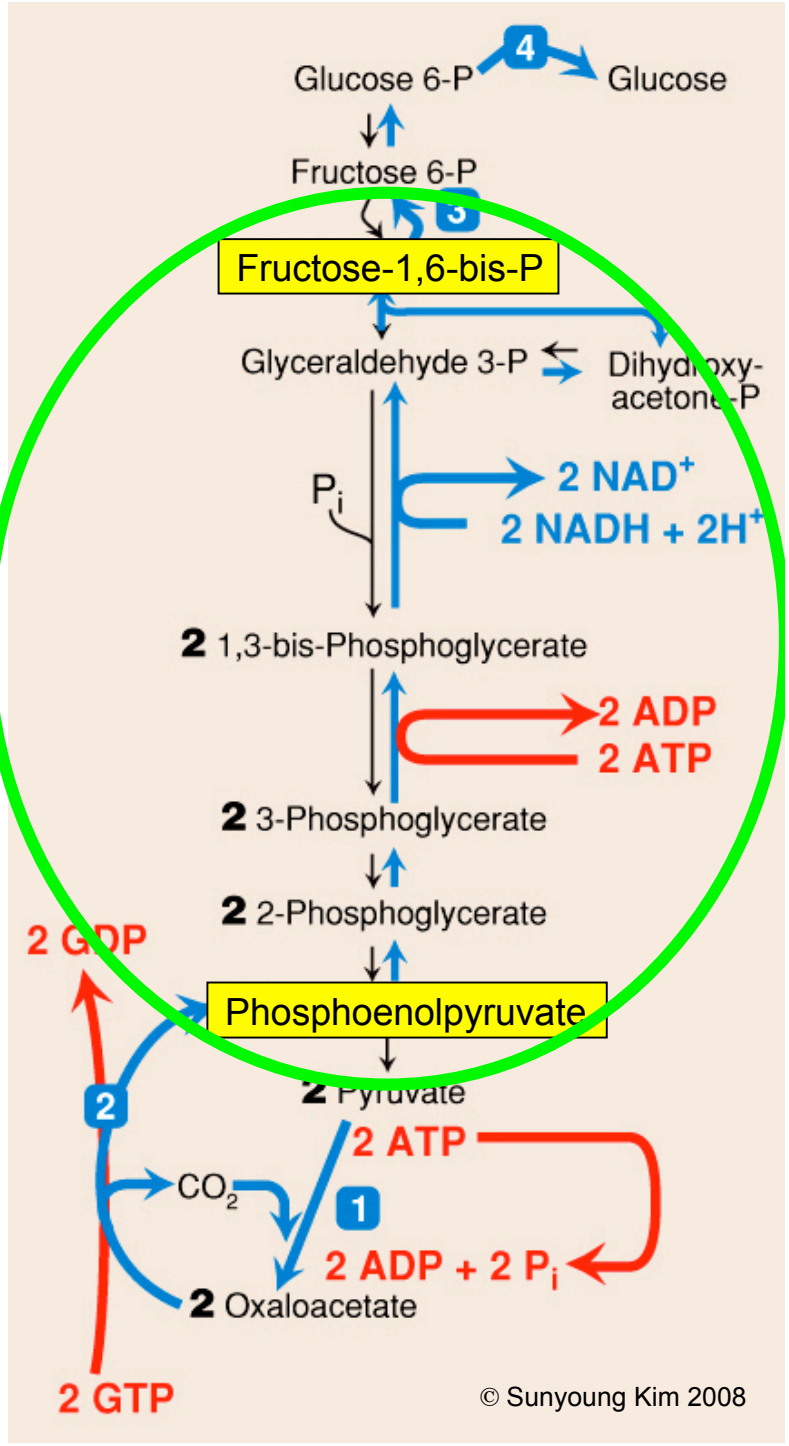
The **second unique enzyme** of gluconeogenesis, phosphoenolpyruvate (PEP) carboxykinase, converts oxaloacetate to PEP.

Pathway: *Review*

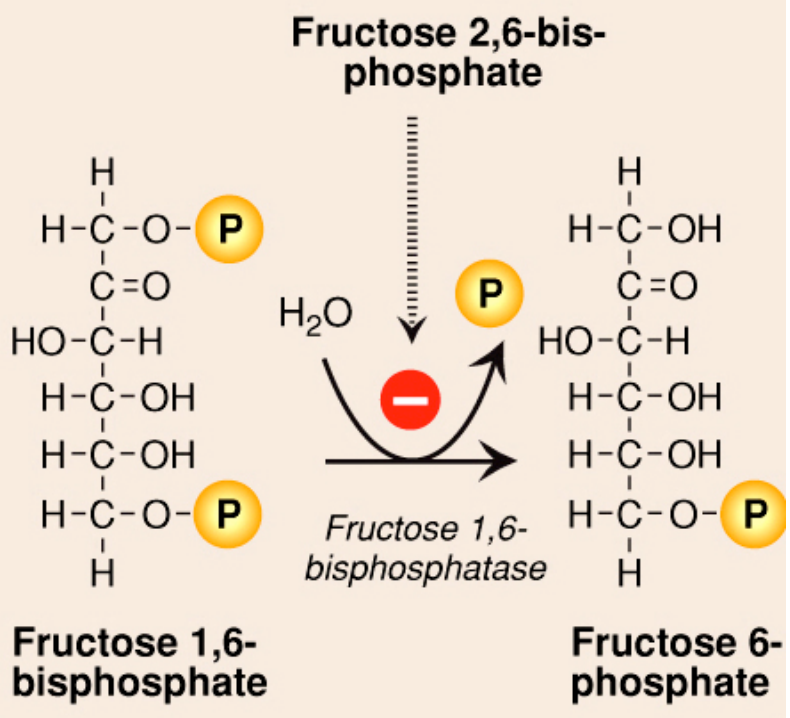


Pathway: *reversal*

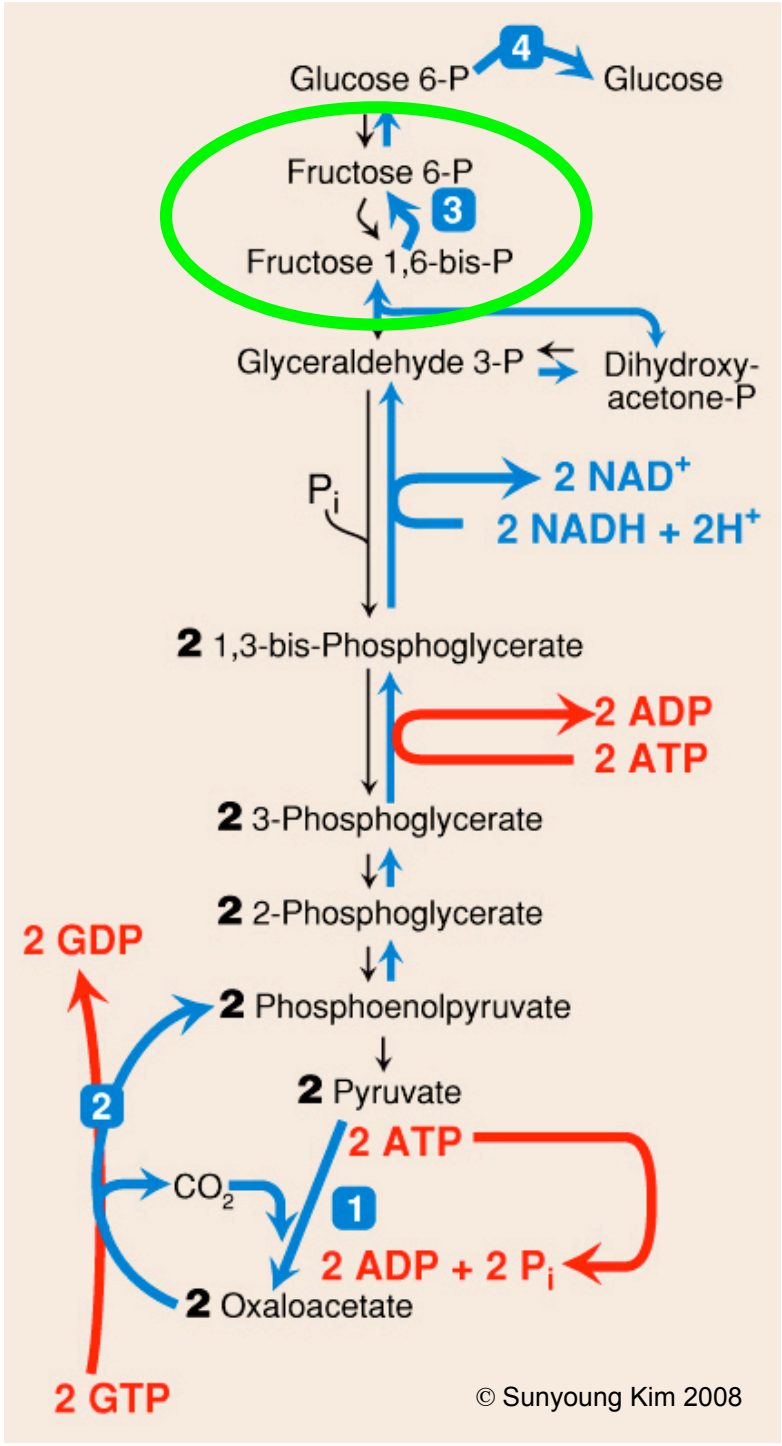
Gluconeogenesis steps up to generation of fructose-1,6-bisphosphate uses same enzymes as glycolysis.



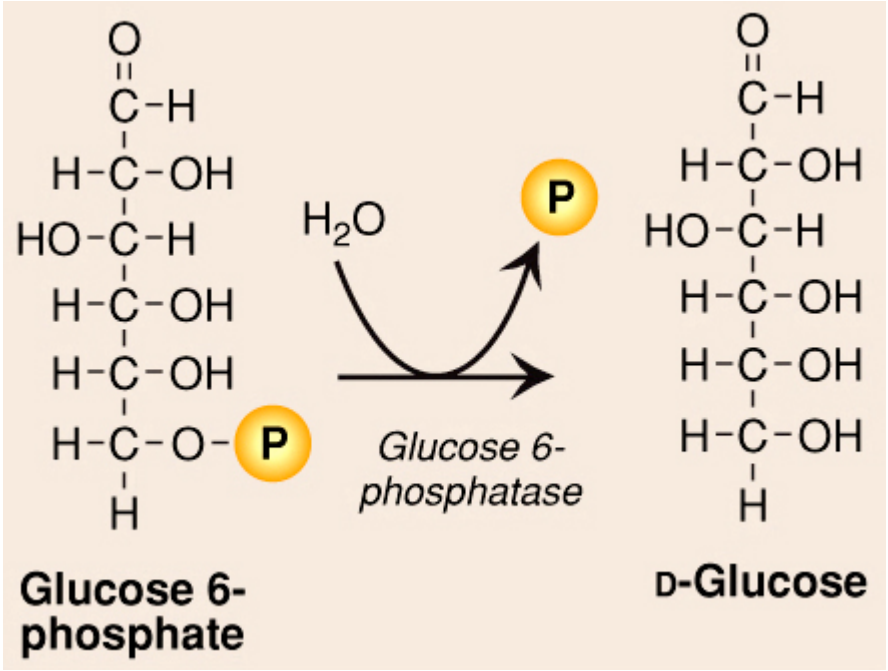
Pathway: *phosphate cleavage*

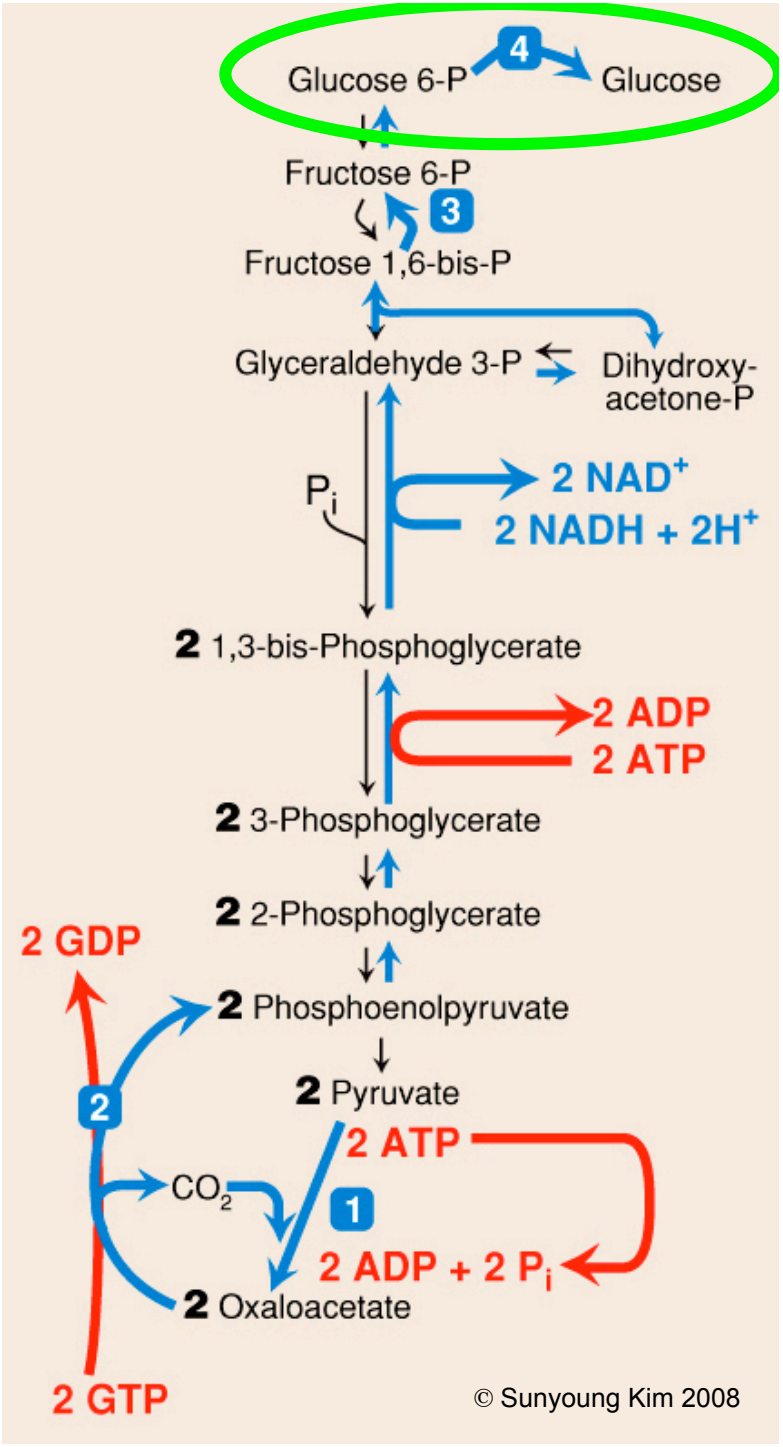


Reversal of the phosphofructokinase step is provided by fructose 1,6-bisphosphatase.



Pathway: *finish line*





Gluconeogenesis

Recognize enzymes that use up 4 ATP and 2 GTP in this pathway

1. Pyruvate carboxylase
2. PEP carboxykinase
3. Phosphoglycerate kinase