Gluconeogenesis

Editing File

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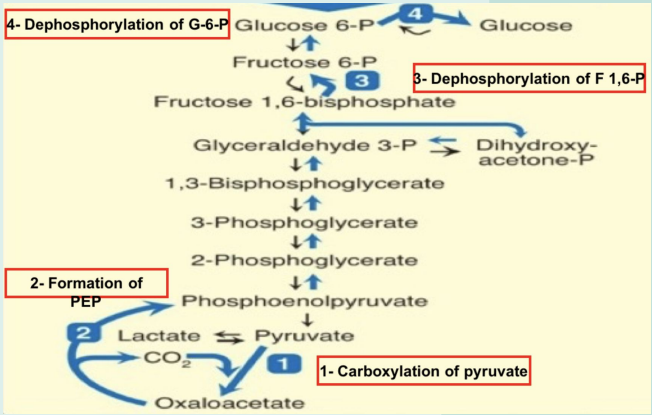
Objectives

- 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

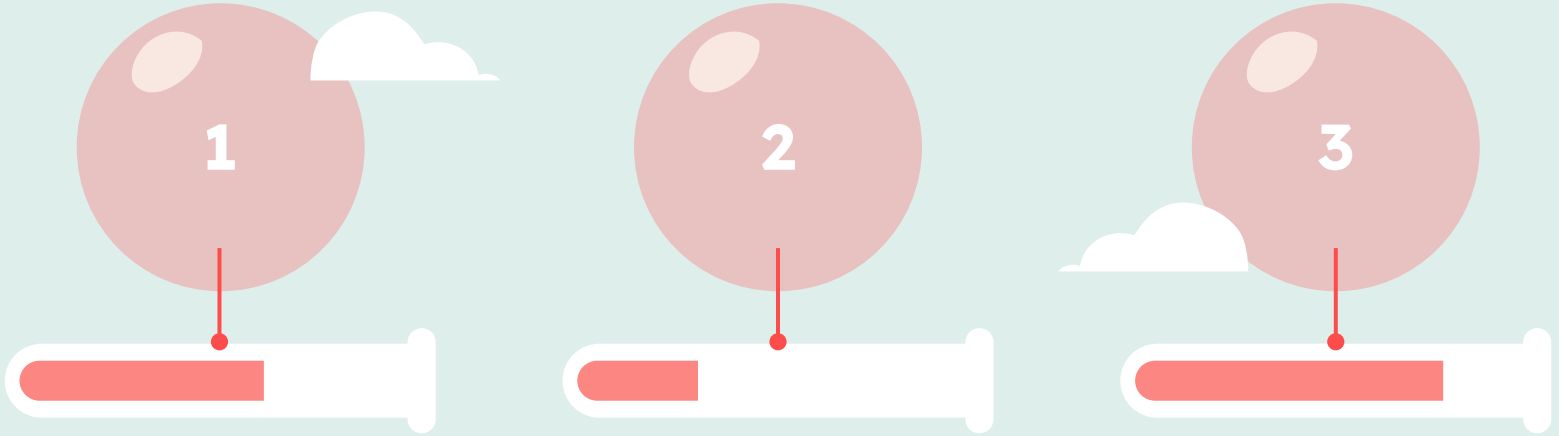
Gluconeogenesis in General Metabolism

- Gluconeogenesis (aka glucose metabolism): is the synthesis of glucose from non-carbohydrates source.
- It is one of the essential pathway for the energy metabolism.
- It works by Reciprocal control It doesn't happen at the same time with glycolysis.
- It has 3 irreversible steps.
- It happens mainly in the liver and later on in the kidney.
- It happens both in mitochondria and in the cytosol.



We need three enzymes here

Substrates for gluconeogenesis



Glycerol

the only one that happens in cytosol only

Amino acids

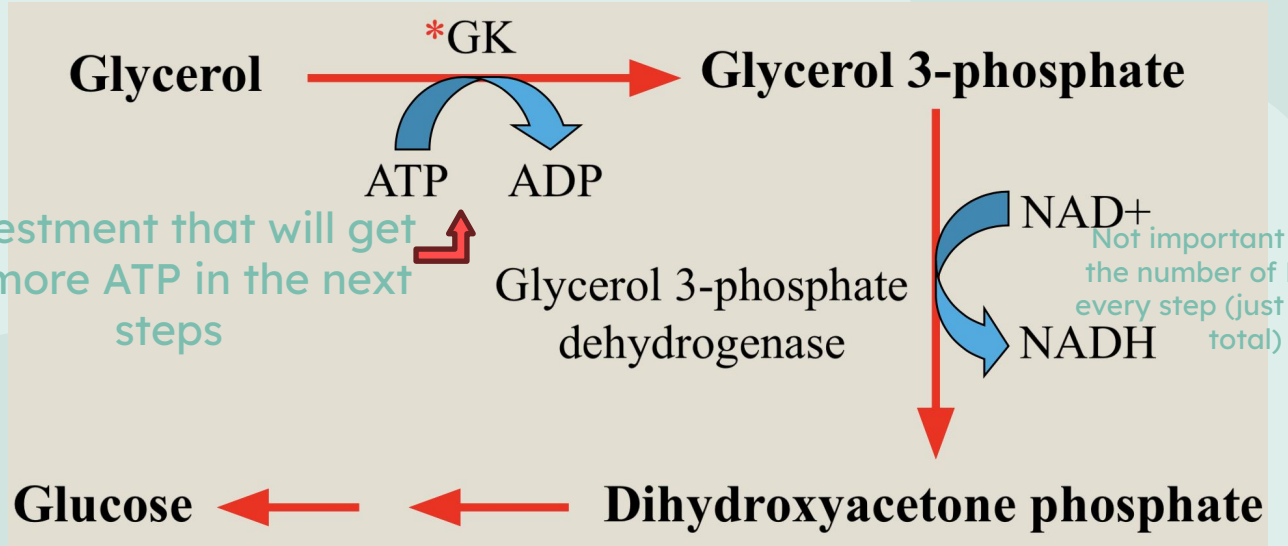
Only some Amino acids can enter this cycle

Lactate (Cori cycle)

convert into oxaloacetate in the mitochondria and then phosphoenolpyruvate

Glycerol

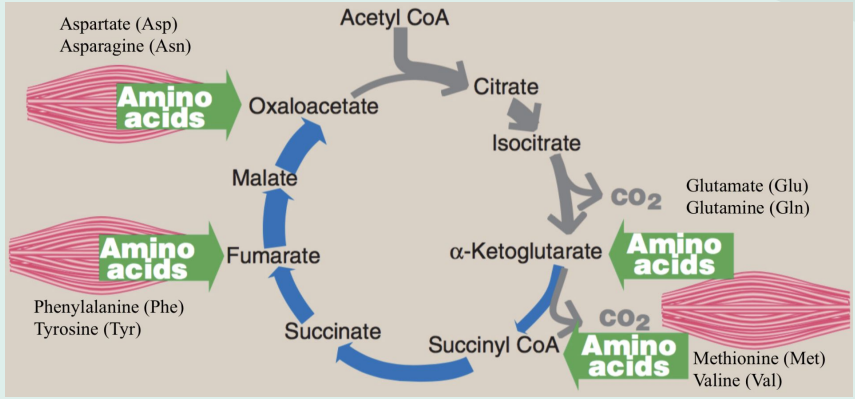
Glycerol kinase(present only in liver & kidneys)



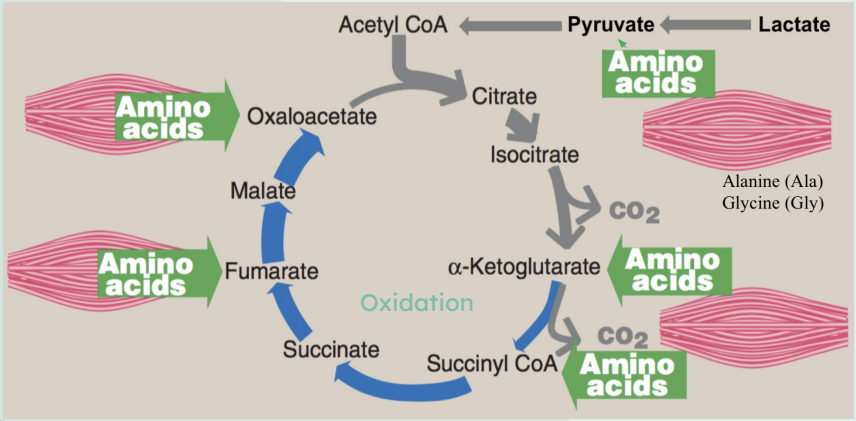
Investment that will get us more ATP in the next steps

Not important to know the number of NADH at every step (just know the total)

Amino acids



Both of the two carbon in Acetyl CoA are going to be removed



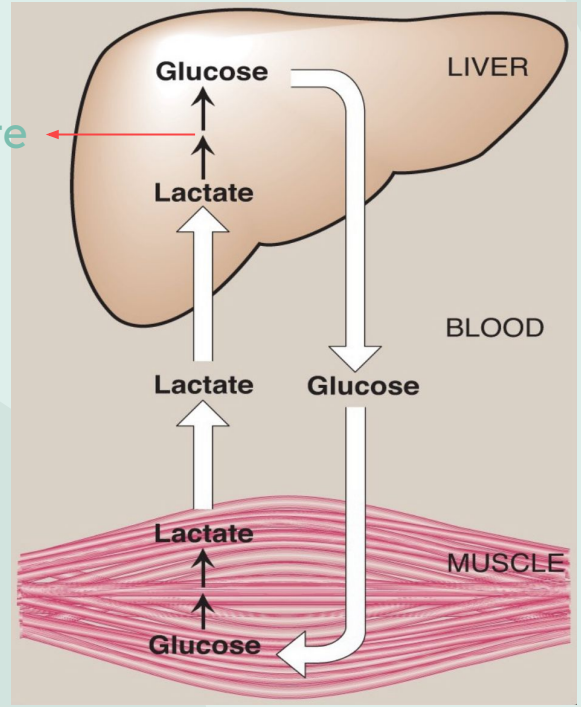
The blue arrows are the only one that are glucogenic

Reducing

Lactate (Cori Cycle)

When there's no oxygen (only in cytosol)

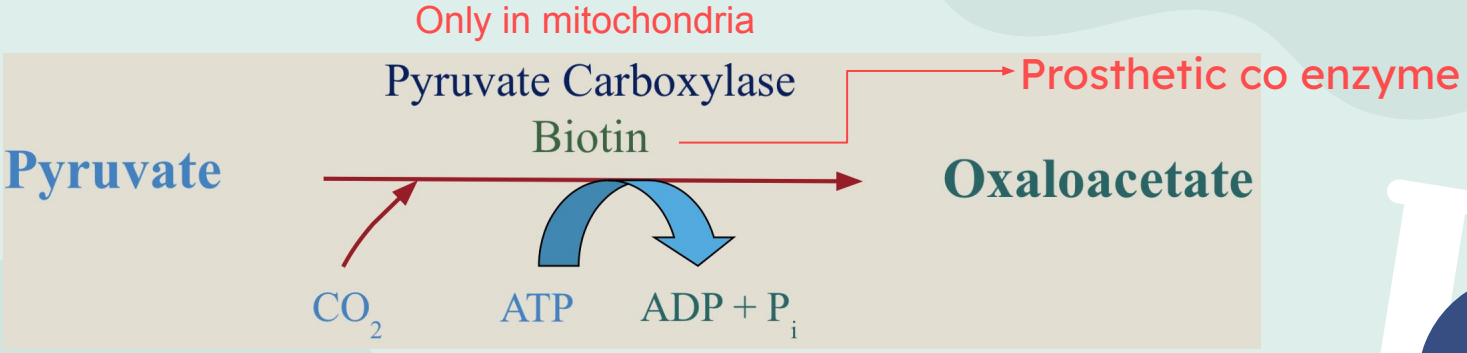
Pyruvate



This can come in SAQ

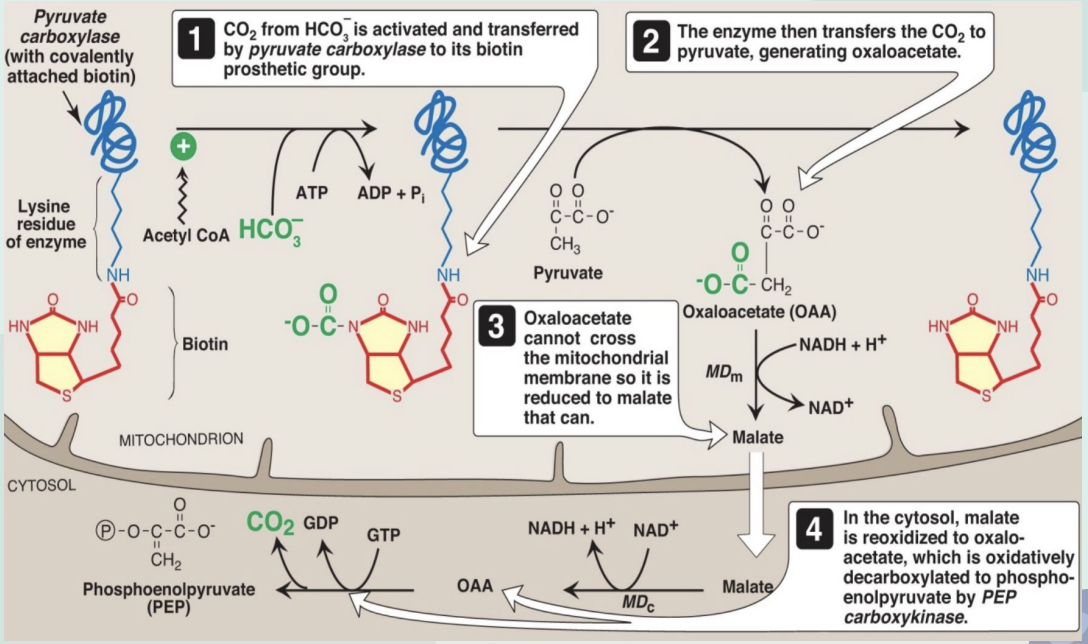
Pyruvate Carboxylation

Adding carbon and then removing it



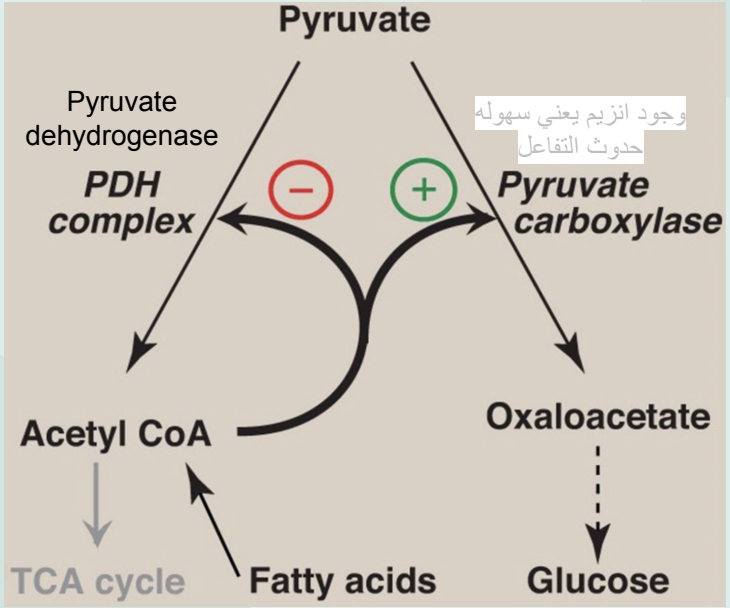
Pyruvate Carboxylase and PEP-CK

Fasting: ↑ Acetyl CoA from Fatty Acid Oxidation



Pyruvate carboxylase + PEP-CK = pyruvate kinase

Regulation of Pyruvate Carboxylase

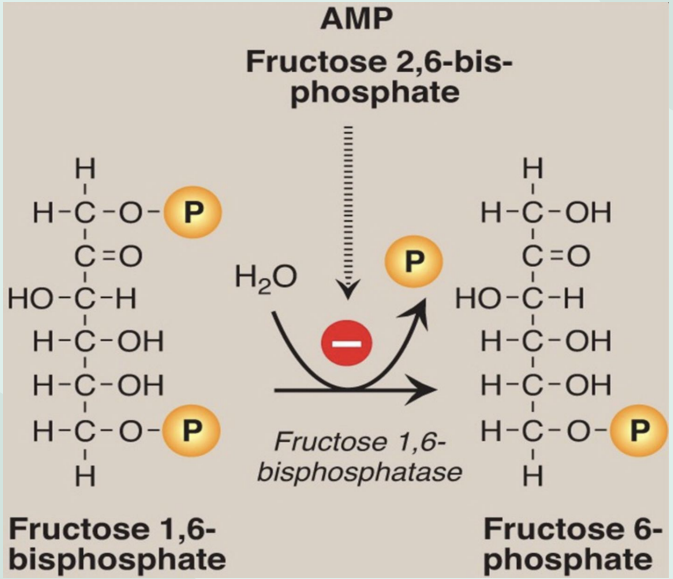


Krebs cycle

Acetyl CoA diverts pyruvate away from oxidation and toward gluconeogenesis

Fructose 1,6-Bisphosphatase

Activated by ATP



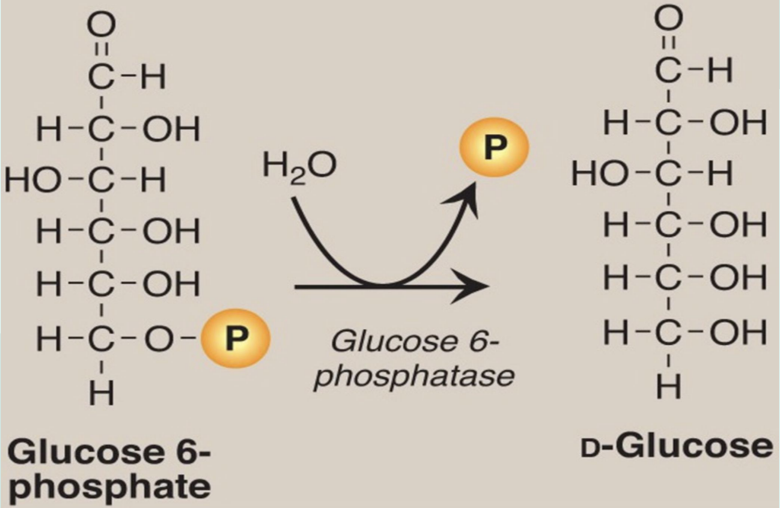
Dephosphorylation of fructose 1,6-Bisphosphate (opposite direction)

Fructose 1,6-Bisphosphate = PFK-1

Glucose 6-phosphatase

Out of the cell

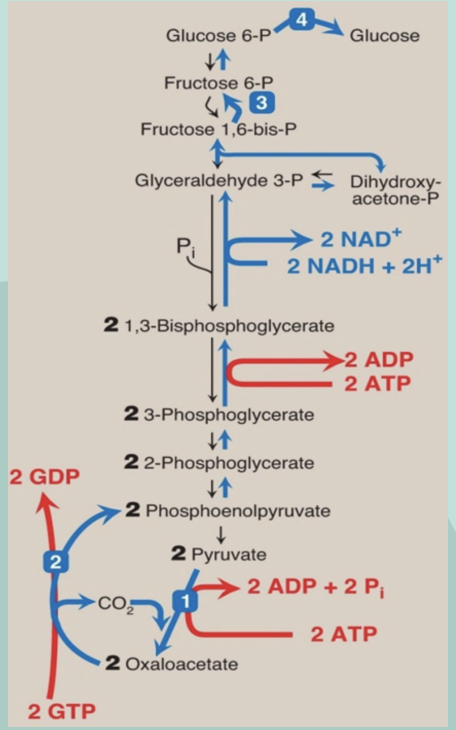
Glucokinase is only in the liver
Hexokinase is in all body tissue



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

Glucose 6-phosphatase = glucokinase

Gluconeogenesis: Energy-Consumed



4 ATP and 2GTP are utilized

6 high-energy phosphate bonds from pyruvate to glucose

Allosteric Regulation

Inhibit

- AMP
- F 2,6-Bisphosphate
- I/G ratio

Activate

- Acetyl CoA (Pyruvate carboxylase)
- F 1,6-Bisphosphatase
- 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

MCQs

1. Which of these is allosteric inhibitor of gluconeogenesis?			
A)ATP	B)AMP	C)F 2,6-Bisphosphate	D)Acetyl CoA
2. How many high energy bond are there from pyruvate to glucose?			
A) six	B)four	C)three	D)five
3. Which of these gluconeogenesis substrate happens only in cytosol?			
A)Lactate	B)Amino acids	C)Glycerol	D)Cori cycle
4. What is the main site of gluconeogenesis?			
A)Bone marrow	B)brain	C)heart	D)Liver
5. How many irreversible steps are there in gluconeogenesis?			
A)three	B)four	C)Only one	D)six

Answers:
1-B
2-A
3-C
4-D
5-A

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