Exam III Review

11/19/2009

Exam 3 Review

Chapters:

12	*Enzyme Kinetic Mechanisms*
8	**Carbohydrates**
14	**Metabolism**
15	**Glucose Metabolism**
16	**Glycogen Metabolism and Gluconeogenesis**
17	***Primarily pyruvate dehydrogenase.***

The Citric acid cycle

It is called the Krebs cycle or the tricarboxylic and is the "hub" of the metabolic system. It accounts for the majority of carbohydrate, fatty acid and amino acid oxidation. It also accounts for a majority of the generation of these compounds and others as well.

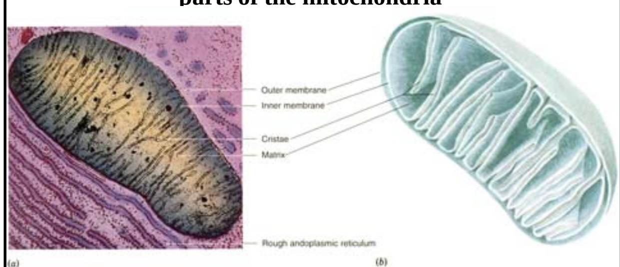
Amphibolic - acts both catabolically and anabolically

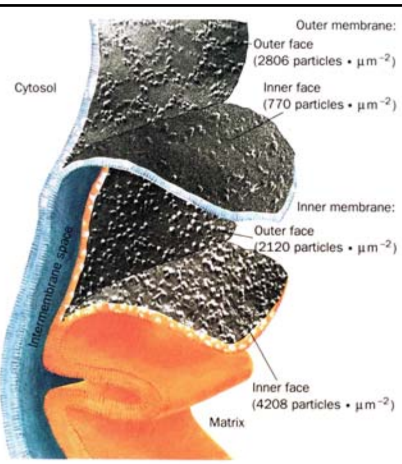
3NAD+ + FAD + GDP + Pi + acetyl-CoA ⟶

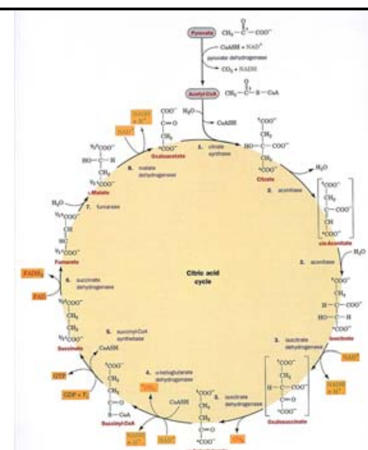
3NADH + $FADH_2$ + GTP + CoA + $2CO_2$

The citric acid cycle enzymes are found in the matrix of the mitochondria

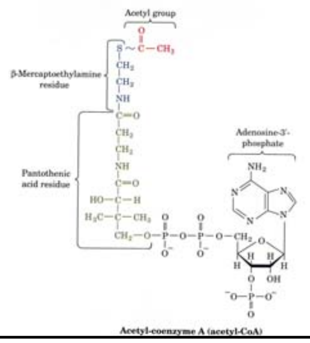
Substrates have to flow across the outer and inner parts of the mitochondria



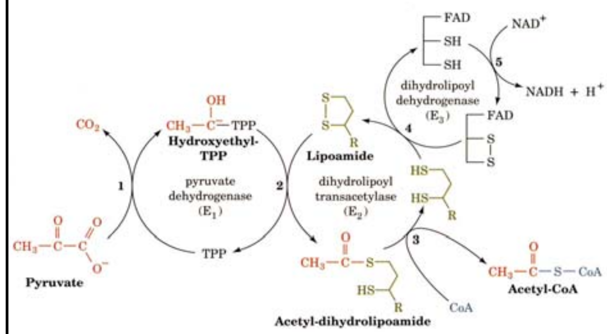




Nathan Kaplan and Fritz Lipmann discovered Coenzyme A and Ochoa and Lynen showed that acetyl-CoA was intermediate from pyruvate to citrate.



The five reactions of the pyruvate dehydrogenase multi enzyme complex



CoA acts as a carrier of acetyl groups

Acetyl-CoA is a "high energy" compound: The ΔG°' for the hydrolysis of its thioester is -31.5 kJ• mol^{-1} making it greater than the hydrolysis of ATP

Pyruvate dehydrogenase converts pyruvate to acetyl-CoA and CO_2

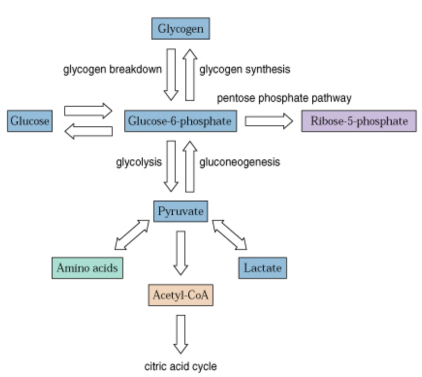
Pyruvate dehydrogenase

A multienzyme complexes are groups of non covalently associated enzymes that catalyze two or more sequential steps in a metabolic pathway.

Molecular weight of 4,600,000 Da

		E. coli	yeast
Pyruvate dehydrogenase --	**E1**	**24**	**60**
dihydrolipoyl transacetylase --E2		**24**	**60**
dihydrolipoyl dehydrogenase--E3		**12**	**12**

Overview of Glucose Metabolism



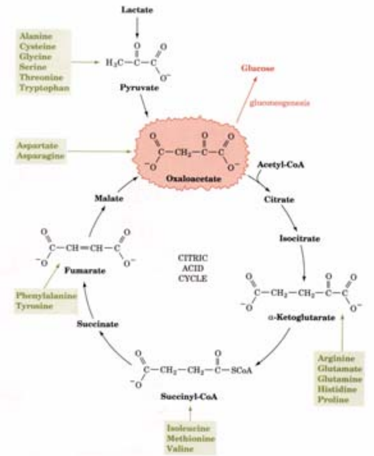
Gluconeogenesis

Gluconeogenesis is the process whereby precursors such as lactate, pyruvate, glycerol, and amino acids are converted to glucose.

Fasting requires all the glucose to be synthesized from these non-carbohydrate precursors.

Most precursors must enter the Krebs cycle at some point to be converted to oxaloacetate.

Oxaloacetate is the starting material for gluconeogenesis



Free energy changes in glycolysis

Reaction	enzyme	ΔG°´	ΔG°
1	Hexokinase	-20.9	-27.2
2	PGI	+2.2	-1.4
3	PFK	-17.2	-25.9
4	Aldolase	+22.8	-5.9
5	TIM	+7.9	+4.4
6+7	GAPDH+PGK	-16.7	-1.1
8	PGM	+4.7	-0.6
9	Enolase	-3.2	-2.4
10	PK	-23.3	-13.9

Gluconeogenesis is not just the reverse of glycolysis

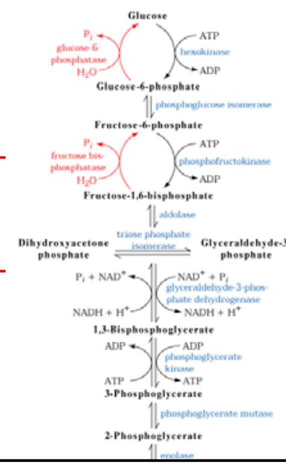
Several steps are different so that control of one pathway does not inactivate the other. However many steps are the same. Three steps are different from glycolysis.

1 Pyruvate to PEP

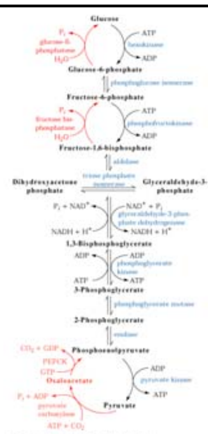
2 Fructose 1,6- bisphosphate to Fructose-6-phosphate

3 Glucose-6-Phosphate to Glucose

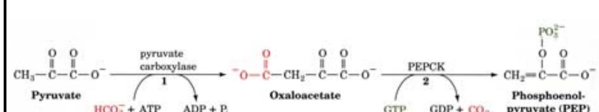
Gluconeogenesis versus Glycolysis



Gluconeogenesis versus Glycolysis



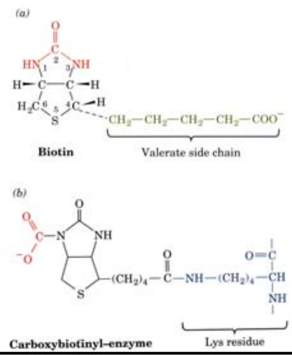
Pyruvate is converted to oxaloacetate before being changed to Phosphoenolpyruvate



1. Pyruvate carboxylase catalyses the ATP-driven formation of oxaloacetate from pyruvate and CO_2

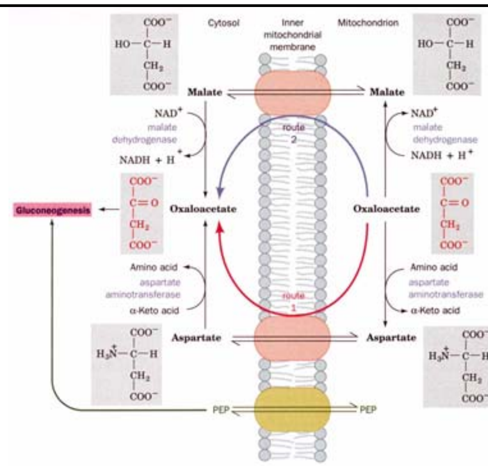
2. PEP carboxykinase (PEPCK) concerts oxaloacetate to PEP that uses GTP as a phosphorylating agent.

Pyruvate carboxylase requires biotin as a cofactor



Acetyl-CoA regulates pyruvate carboxylase

Increases in oxaloacetate concentrations increase the activity of the Krebs cycle and acetyl-CoA is a allosteric activator of the carboxylase. However when ATP and NADH concentrations are high and the Krebs cycle is inhibited, oxaloacetate goes to glucose.

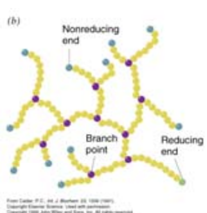


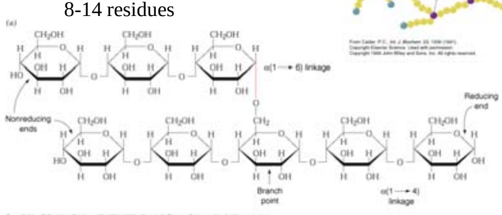
Regulators of gluconeogenic enzyme activity

Enzyme	Allosteric Inhibitors	Allosteric Activators	Enzyme Phosphorylation	Protein Synthesis
PFK	ATP, citrate	AMP, F2-6P		
FBPase	AMP, F2-6P			
PK	Alanine	F1-6P	Inactivates	
Pyr. Carb.		AcetylCoA		
PEPCK				Glucogon
PFK-2	Citrate	AMP, F6P, Pi	Inactivates	
FBPase-2	F6P	Glycerol-3-P	Activates	

Glycogen Storage

- Glycogen is a D-glucose polymer
- α(1→4) linkages
- α(1→6) linked branches every
  8-14 residues





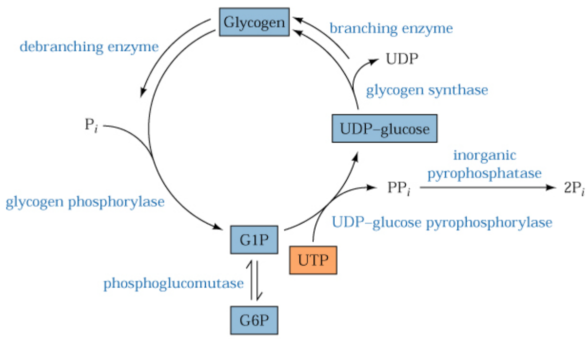
Glycogen Breakdown or Glycogenolysis

- Three steps
  - Glycogen phosphorylase

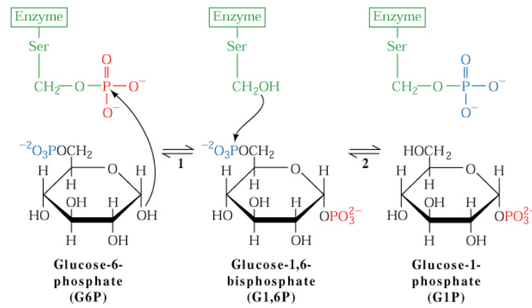
    Glycogen + Pi <-> glycogen + G1P
    (n residues) (n-1 residues)

  - Glycogen debranching
  - Phosphofructomutase

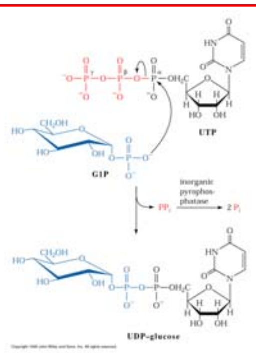
Glycogen Synthesis



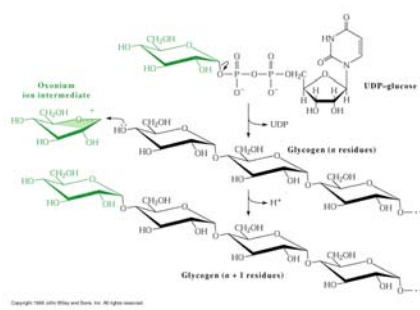
Phosphoglucomutase

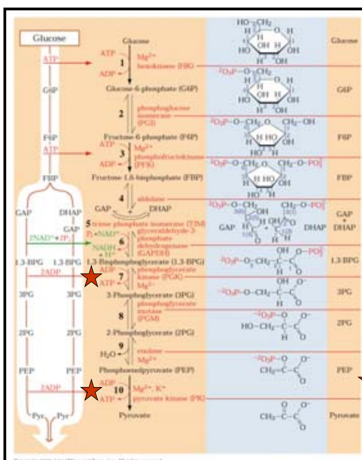


UDP-glucose Pyrophorylase



Glycogen Synthase





Glycolysis Review

- Stage I: Energy investment (rxns. 1-5), glucose phosphorylated and cleaved to yield 2 G3P and consumes 2 ATP
- State II: Energy recovery (rxns. 6-10), G3P converted to pyruvate with generation of 4 ATP
- Net profit of 2 ATP per glucose

Glucose + 2NAD$^+$ + 2ADP +2P*i* → 2NADH + 2pyruvate + 2ATP + 2H$_2$O + 4H$^+$

Next Lecture
Thursday 11/24/09
Exam III

After Thanksgiving
Lecture 28
Pentose Phosphate Pathway
12/01/09