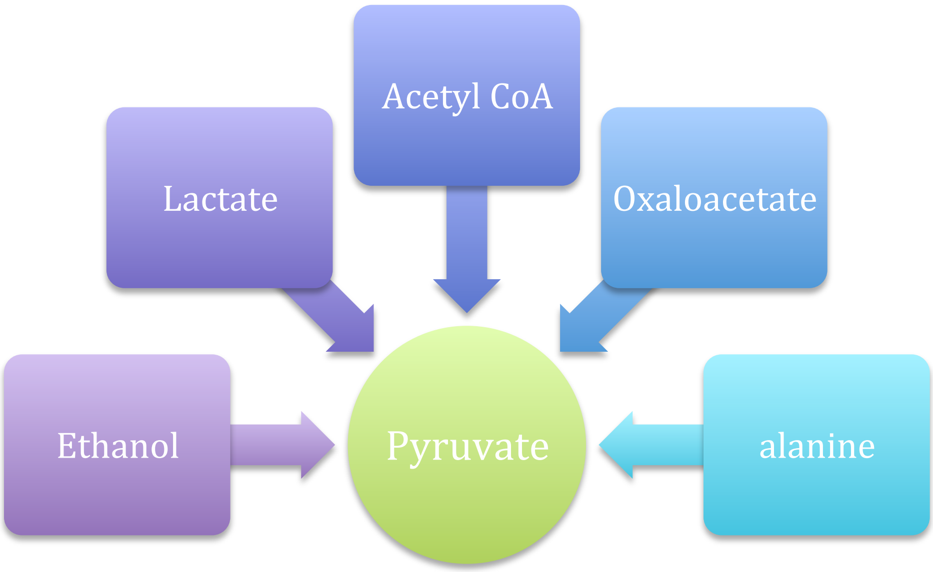
Krebs Cycle

Lecture 13

Biochemistry433@hotmail.com

433 Biochemistry Team

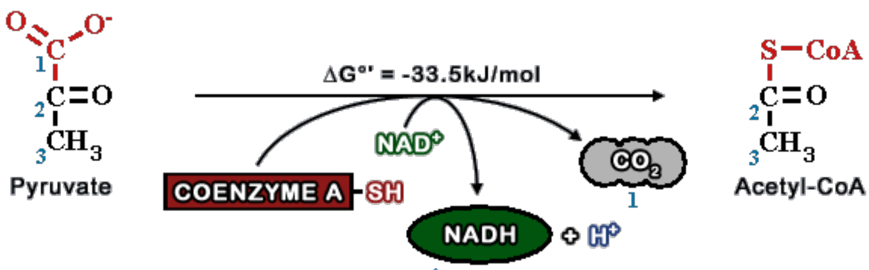
Pre-Krebs cycle:
Fate of Pyruvate:



1- **Ethanol**: it occurs in 2 steps: decarboxylation then reduction. Decarboxylation occurs in yeast and some micororganisms and in intestinal bacterial Flora. The enzyme requires thiamine pyrophohsphate (TPP) as a coenzyme.
2- **Lactate**: the enzyme is lactate dehydrogenase. (LDH). Important in anaerobic glycolysis and in gluconeogenesis. Reversible reaction.
3- Oxidative decarboxylation into **Acetyl CoA**: the enzyme is pyruvate dehydrogenase complex (PDH). It occurs in mitochondria. It is irreversible. Acetyl CoA can enter the Krebs cycle to produce energy, or acts as a building block for fatty acid synthesis. Inhibited by Acetyl CoA and NADH +H.
4- Carboxylation into **oxaloacetate** (OAA): the enzyme is pyruvate carboxylase. It occurs in mitochondria. It is irreversible. It needs biotin and ATP. OAA replenishes the Krebs cycle intermediate & provides substrate for gluconeogenesis.
5- Conversion to **Alanine** by alanine aminotransferase (ALT): an amino group is transferred from glutamate to pyruvate, resulting in the formation of alpha ketoglutarate (α KG) and alanine. The enzyme requires the coenzyme pyridoxal phosphate (PLP: vit B6 derivative) as a coenzyme. The reaction is reversible.

Oxidative Decarboxylation of Pyruvate: (Number 3 in fate of pyravute ↑)

Before the product enters Krebs cycle, it should be pass this stage in mitochondria:



Results:
1- NAD+ → NADH
2- the enzyme pyruvate dehydrogenase complex (PDH) converts one C to CO_2.

This stage is induced by insulin and inhabited by glacagon

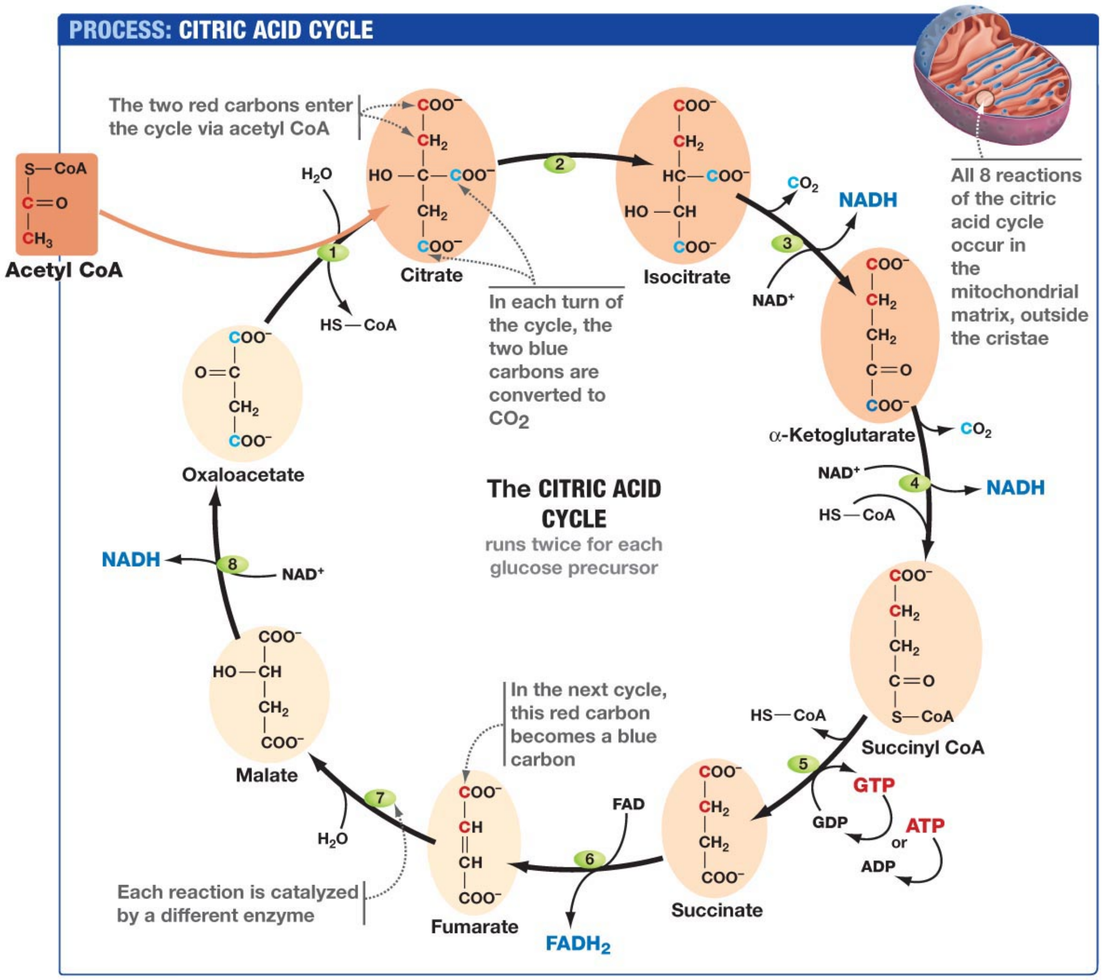
It can be controlled by the product (feed back inhabition) when product (Acetyl-coA & CO_2) increased the process will stop

Calcium ions activates the PDH complex, which is particularly important in skeletal muscle contraction.

Krebs cycle (Tricarboxylic Acid Cycle):

- It is the final common pathway for oxidation of carbohydrates, amino acids, and fatty acids.
- It occurs exclusively in mitochondria.
- It is Aerobic pathway.
- It is a major source for ATP.
- It is mainly catabolic with some anabolic features.
- Synthetic reactions (anabolic features):
    - ✓ Glucose from amino acids (gluconeogenesis)
    - ✓ Nonessential amino acids
    - ✓ Fatty acids
    - ✓ Heme (the part of hemoglobin)

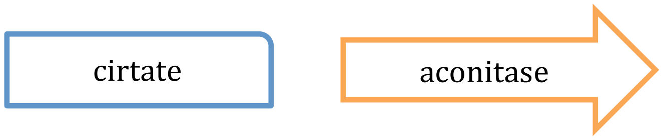
Steps of Krebs cycle:



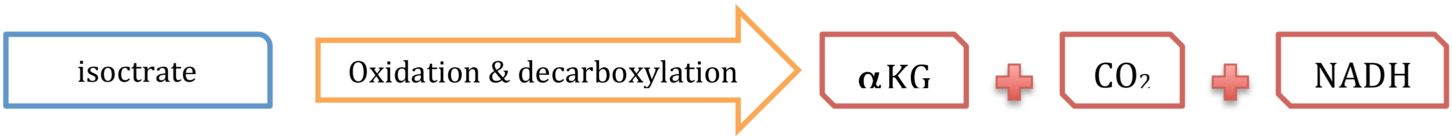
1) Synthesis of <u>citrate</u> (from acetyl CoA + OAA): the enzyme is citrate synthase. Citrate inhibits PFK-1 (The rate limiting step in glycolysis) Isomerization of citrate to isocitrate by aconitase enzyme.

Acetyle coA + Oxaloactate → Citrate synthase → Ciratate

2) Isomerization of citrate to isocitrate by aconitase enzyme.



3) Oxidation & decarboxylation of Isocitrate to αKG by isocitrate dehydrogenase. The reaction releases CO2 and NADH.



4) Oxidation & decarboxylation of αKG to succinyl CoA by αKG dehydrogenase complex. The reaction releases CO2 and NADH.

5) Cleavage of succinyl CoA by succinate thiokinase into succinate. The reaction produces GTP (which can be converted to 1 ATP). This is substrate-level phosphorylation.

6) Oxidation of succinate to fumarate by succinate dehydrogenase. The reaction produces FADH2.

7) Hydration of fumarate by fumarase to L-malate.

8) Oxidation of L-malate to OAA by malate dehydrogenase. The reaction releases NADH.

L-malate → Oxidation → Oxaloacetate + NADH

Energy yielded from Krebs cycle:

Quantity	Reaction in Electron Transport Chain	Number of ATP produced
3	$NADH \rightarrow NAD^+$	9 ATP
1	$FADH_2 \rightarrow FAD$	2 ATP
1	$GDP + P_i \rightarrow GTP$	1 ATP
Net		**12 ATP**

Always remember:
NADH produces 3 ATP
$FADH_2$ produces 2 ATP
GTP produces 1 ATP

Net ATP Production by Complete Glucose Oxidation:

	Anarobic glycolysis	8 ATP
2 pyravate	Oxidative decarbocylation	6 ATP
2 acetyle CoA	Krebs cycle	24 ATP
Net		38 ATP

- Video about Krebs cycle from KhanAcademy :

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