### The Citric Acid Cycle

Created: Wednesday, 27 July 2011 10:25 | Published: Wednesday, 27 July 2011 10:25 | Written by <u>Super</u> <u>User</u> | <u>Print</u>

# Kreb's Cycle



The citric acid cycle is a series of reactions in which citrate is oxidized and oxaloacetate regenerated. This cycle is also called the Krebs Cycle or the tricarboxylic acid cycle (TCA cycle). It was discovered by Hans Kreb, so it is called the Krebs Cycle . The main intermediate substance is citric acid.

It takes place within the mitochondria of cells. The reaction begins and ends in the same molecule.

## Steps involved in Citric Acid Cycle:



Pyruvate is oxidized to acetate, with the formation

of NADH + H+ and the release of CO2; acetate is activated by combination with coenzyme A, yielding acetyl CoA

- · The two-carbon acetyl group and four-carbon oxaloacetate combine, forming six-carbon citrate
- Citrate is rearranged to form its isomer, isocitrate.
- Isocitrate is oxidized to ?-ketoglutarate, yielding NADH + H+ and CO2.

• ?-Ketoglutarate is oxidized to <u>Succinyl-CoA</u>, with the formation of NADH + H+ and CO2; this step is almost identical to pyruvate oxidation.

• Succinyl CoA releases coenzyme A, becoming succinate; the energy thus released converts GDP to GTP, which in turn converts ADP to ATP

- Succinate is oxidized to fumarate, with the formation of FADH2
- Fumarate and water react, forming malate

Malate is oxidized to oxaloacetate, with the formation of NADH + H+. Oxaloacetate can now react with acetyl CoA to reenter the cycle.

### **Cellular Respiration**



- All the fuel molecules are oxidized to generate a common two-carbon unit, acetyl-CoA.
- The <u>acetyl-CoA</u> is completely oxidized into CO2, with electrons collected by NAD+ and FAD via a cyclic pathway (the citric acid cycle, Krebs cycle, or tricarboxylic acid cycle).
- Electrons of <u>NADH and FADH2</u> are transferred to O2 via the respiratory chain (a series of electron carriers), producing H2O and a H+ gradient, which will promote ATP formation.
- Pyruvate produced from glycolysis must be decarboxylated to Acetyl-coA before it enters <u>TCA cycle</u>.

#### Kreb Cycle pathway:



• The first step in the Kreb Cycle is the condensation of 2 carbon

<u>acetyl-CoA</u> with water and 4 carbon oxaloacetic acid. The catalyzing enzyme is citrate synthetase.

• Citric acid by dehydrogenation loses water and is converted to cis-Aconitic acid. Again cis- Aconitic acid by hydration is converted to iso-citric acid. Both reactions are catalyzed by a single enzyme aconitase.

• In this stage isocitric acid is oxidized to oxalosuccnic acid. NAD acts as hydrogen carrier. The reaction is catalyzed by the enzyme isocitrate dehydrogenase. Oxalosuccinic acid looses carbon-dioxide and forms ?-ketoglutaric acid.

• This reaction is both decarboxylation and dehydration and is catalyzed by enzyme ?-keoglutarate dehydrogenase.

• In this stage succinyl CoA reacts with GDP and inorganic phosphate to form succinic acid and GTP and CoA is released in presence of Succinyl CoA synthetase enzyme.

- Succinic acid is dehydrogenated to Fumaric acid. The enzyme involved is succinate dehydrogenase.
- Fumaric acid under the influence of enzyme Fumerase is hydrated to malic acid.

• Malic acid is oxidized to 4-oxaloacetic acid, the coenzyme being NAD+. The reaction is catalyzed by the enzyme Malic dehydrgenase.

Krebs cycle - The quick Summary

- 1. Takes place within mitochondrian
- 2. The 3 carbons of the pyruate are released as CO2.
- 3. Five pairs of hydrogen become attached to hydrogen carriers (4 NADH & 1 FADH2).

4. One ATP is generated.

### What is formation of Acetyl CO A?

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#### **Reference Links:**

- http://en.wikipedia.org/wiki/Metabolic\_pathway
- <a href="http://en.wikipedia.org/wiki/Citric\_acid\_cycle">http://en.wikipedia.org/wiki/Citric\_acid\_cycle</a>
- http://en.wikipedia.org/wiki/Citric\_acid\_cycle#Major\_metabolic\_pathways\_converging\_on\_the\_TCA\_cycle
- http://en.wikipedia.org/wiki/Anaerobic\_respiration
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