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* Stages of Beta oxidation of Fatty Acids.

Fatty acids in the body are mostly oxidized by beta oxidation. Beta oxidation may be defined as the oxidation of Fatty acids on the beta carbon atom. This results in the sequential removal of a two carbon fragment, acetyl-coA.

Fatty acid oxidation occurs in three stages.

- I. Activation of fatty acids occurring in the cytosol
- II. Transport of fatty acids into mitochondria
- III. Beta oxidation proper in the mitochondrial matrix.
- A. Fatty acid activation.

Fatty acids are activated to acyl coA by thiokinases or acyl coA sunthetases. The reaction occurs in two steps and required energy(ATP), coenzyme A and magnesium. Fatty acid reacts with ATP to form acyladenylate which then combines with coenzyme A to produce acyl coA. In the activation, two high energy phosphates are utilized since ATP is converted to pyrophosphate. The immediate elimination of pyrophosphate makes this reaction totally irreversible.

B. Transport of acyl coA into mitochondria.

The inner mitochondrial membrane is impermeable to fatty acids. A specialized carnitine carrier system functions to transport activated fatty acids from cytosol to the mitochondria. This occurs in four steps.

- 1. Acyl group of coA is transferred to carnitine, catalysed by carnitine acyltransferase I(present on the outer surface of inner mitochondrial membrane).
- 2. The acyl-carnitine is transported across the membrane to the mitochondrial matrix by a specific protein.
- 3. Carnitine acyltransferase II(found on the inner surface of inner mitochondrial membrane) converts acyl carnitine to acyl-coA.
- 4. The carnitine released returns to cytosol for reuse.

The coenzyme A used for activation is different from the one that finally combines with fatty acid in the mitochondria to form acyl-coA. Therefore, the cell has separate pools of cytosolic and

mitochondrial coenzyme A.

C. Beta oxidation proper.

Each cycle of beta oxidation, liberating a two carbon unit acetyl-coA occurs in a sequence of four reactions.

1. Oxidation.

Acyl coA undergoes dehydrogenation by an FAD-dependent flavoenzyme, acyl coA dehydrogenase.

2. Hydration

Enoyl coA hydratase brings about the hydration of the double bond to form beta hydroxyacyl coA.

3. Oxidation

Beta hydroxyacyl coA dehydrogenase catalyses the second oxidation and generates NADH. The product formed is beta ketoacylcoA

4. Cleavage

The final reaction in beta oxidation is the liberation of a two carbon fragment, acetyl coA from acyl coA. This occurs by a thiolytic cleavage catalysed by beta ketoacylcoA thiolase.

The new acyl coA, containing two carbon less than the original, reenters the beta oxidation cycle. This process continues till the fatty acid is completely oxidized.

Reference.

Biochemistry_Satyanarayana_Chakapani textbook