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COURSE TITLE: MEDICAL BIOCHEMISTRY

ASSIGNMENT: Describe the three (3) stages of beta oxidation. (Show pathways where necessary).

BETA OXIDATION

Beta oxidation is a metabolic process involving multiple steps by which fatty acid molecules are broken down to produce energy. More specifically, beta oxidation consists in breaking down long fatty acids that have been converted to acyl-CoA chains into progressively smaller fatty acyl-CoA chains. This reaction releases acetyl-CoA, FADH₂ and NADH, the three of which then enter another metabolic process called *citric acid cycle* or *Krebs cycle*, in which ATP is produced to be used as energy. Beta oxidation goes on until two acetyl-CoA molecules are produced and the acyl-CoA chain has been completely broken down. In eukaryotic cells, beta oxidation takes place in the mitochondria, whereas in prokaryotic cells, it happens in the cytosol.

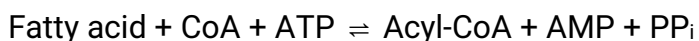
For beta oxidation to take place, fatty acids must first enter the cell through the cell membrane, then bind to coenzyme A (CoA), forming fatty acyl CoA and, in the case of eukaryotic cells, enter the mitochondria, where beta oxidation occurs.

The 3 stages of Beta Oxidation are

1. Activation of fatty acid to acyl- CoA
2. Transport of Acyl- CoA into Mitochondria by Carnitine Transport System
3. Reaction of Beta Oxidation in mitochondria.

1. Activation of fatty acid to acyl- CoA

The oxidative degradation of fatty acids is a two-step process, catalysed by acyl-CoA synthetase. First, the fatty acid reacts with ATP to form an acyl phosphate. This intermediate reacts subsequently to give acyl-CoA:



Fatty acids are activated in the cytosol, but oxidation occurs in the mitochondria. Because there is no transport protein for CoA adducts, acyl groups must enter the mitochondria via a shuttle system involving the small molecule carnitine. Acyl-CoA is made by an enzyme called Acyl-CoA synthase. There are three different types of acyl-CoA synthases which can help make 3 different lengths of acyl-CoA. For example, medium chain acyl-CoA synthase is made to work upon 4-11 carbon fatty acids to make 4-11 carbon acyl-CoA. A different type of Acyl-CoA synthase is used for a 11-20 carbon fatty acid to make it into a 11-20 Acyl-CoA. The reaction to make Acyl-CoA is also thermodynamically favoured because in this reaction ATP becomes AMP which is a two step reaction, and this is spontaneous. There is also an enzyme called Acyl-CoA thioesterase, and this enzyme does the opposite of Acyl-CoA synthase. This enzyme takes of the Acyl-CoA to form a free fatty acid and coenzyme A, in other words deactivates the fatty acid by breaking down Acyl-CoA.

2. Transport of Acyl- CoA into Mitochondria by Carnitine Transport System

Cytoplasmic fatty acyl CoA is converted to fatty acyl carnitine by carnitine acyl transferase (CAT I), an enzyme of the inner leaflet of the outer mitochondrial membrane. Fatty acyl carnitine is then transported by an antiport in exchange for free carnitine to the inner surface of the inner mitochondrial membrane. There carnitine acyl transferase II (CAT II) reverses the process, producing fatty acyl CoA and carnitine. This shuttle mechanism is required only for longer chain fatty acids. Medium- and short chain fatty acids are carnitine-independent. They cross the mitochondrial membranes, and are activated in the mitochondrion.

3. Reaction of Beta Oxidation in mitochondria.

In **biochemistry** and **metabolism**, **beta-oxidation** is the **catabolic process** by which **fatty acid** molecules are broken down[1] in the cytosol in prokaryotes and in the **mitochondria** in eukaryotes to generate **acetyl-CoA**, which enters the **citric acid**

cycle, and NADH and FADH₂, which are co-enzymes used in the electron transport chain. It is named as such because the beta carbon of the fatty acid undergoes oxidation to a carbonyl group. Beta-oxidation is primarily facilitated by the mitochondrial trifunctional protein, an enzyme complex associated with the inner mitochondrial membrane, although very long chain fatty acids are oxidized in peroxisomes.

The overall reaction for one cycle of beta oxidation is:

