# OXIDATION OF FATTY ACIDS

## EXPERIMENT TO DEMONSTRATE B OXIDATION OF FATTY ACID

Franz Knoop in his classical experiment indicated that fatty acids are metabolized at beta position of carbon atom.

He fed dogs with benzene ring labelled fatty acids at their Omega carbon atom.

Dogs excreted hippuric acid and phenylaceturic acid, when fed with labelled odd chain fatty acids and even chain fatty acid, respectively.

He concluded that carbon atom B to the the carboxyl group in fatty acid is involved in its breakdown by its oxidation.

Knoop experiment was confirmed with the help of biochemical techniques and radioactive tracing methods.

## STEPS IN FATTY ACID OXIDATION

Activation of fatty acid

Activation of fatty acid is catalysed by acyl -CoA synthetases. At Least 3 types of acyl-CoA synthetases function depending upon the length of chain. It is an energy requiring step and require one molecule of ATP.

Activation occurs in the cytoplasm

Transport across the mitochondrial membrane

Fatty acyl-CoA cannot cross the inner mitochondrial membrane hence, its acyl part is transferred to carnitine.

Enzyme involved in transfer of acyl portion on to carnitine is catalyzed by Carnitine palmitoyl transferase. There are two such enzymes called Carnitine palmitoyl transferase I and Carnitine palmitoyl transferase II located on the external and internal surface of the inner mitochondrial membrane, respectively.These two enzymes transfer a variety of acyl group.

Translocation of acyl-carnitine from cytosol to inner membrane of mitochondria and free Carnitine back into the cytosol is mediated by a specific carrier protein. The chronology of transport across mitochondrial membrane is as follows

The acyl group of acyl-CoA is transferred from cytosol by loading acyl on to carnitine. In this way coenzyme a remains in the cytosol.

Acyl-carnitine is transported into the mitochondria matrix by a carrier protein.

The acyl group is again attached with CoA molecule present in the mitochondria.

Carnitine is transferred back to the cytosol from mitochondrial matrix with the help of carrier protein.

Beta oxidation

Degradation of fatty acids through beta oxidation of fatty acyl-CoA occurs in 4 steps

Formation of a trans alpha beta double bond with the help of acyl-CoA dehydrogenase enzyme. The product formed is corresponding trans Lambda Enoyl-CoA.

Hydration of double bond by the enzyme enoyl-CoA hydratase to form 3-L-hydroxyacyl-CoA.

Hydrogenation of 3-L-hydroxyacyl-CoA by the enzyme 3-L-hydroxyacyl-CoA dehydrogenase to form beta-ketoacyl-CoA. This step require NAD+.

Cleavage of Alpha Beta bond with the help of enzyme beta-ketoacyl-CoA thiolase to form acetyl-CoA and a new acyl-CoA having two less carbon atoms than the original fatty acid molecule. This reaction requires CoA.

The final round of B oxidation of even chain fatty acid yields 2 molecules of acetyl-CoA. Hence,oxidation of even chain fatty acids yields only acetyl -CoA.

## OXIDATION OF ODD CHAIN FATTY ACIDS

The final round of Beta oxidation of odd chain fatty acids form propionyl-CoA and acetyl-CoA.

Propionyl-A is converted into succinyl-CoA by three steps.

Propionyl-CoA is converted into (S)- methylmalonyl-CoA by the enzyme Propionyl-CoA carboxylic. 1 molecule ATP is required in this reaction.

(S)-methylmalonyl-CoA is converted into (R )-methylmalonyl-CoA by the enzyme methylmalonyl-CoA racemase.

(R)-methylmalonyl-CoA is converted into succinyl-CoA by the enzyme methylmalonyl-CoA mutase.

Thus, B oxidation of odd chain fatty acid yields acetyl-CoA and succinyl-CoA.

FATE OF ACETYĹ CoA and SUCCINYL CoA

Acetyl CoA enters citric acid cycle to generate energy while succinyl CoA is either converted into pyruvate or directly to acetyl CoA.

Succinyl-CoA is converted into malate through citric acid cycle. Malate is transported to cytosol when present in high concentration inside the mitochondria with the help of transporter protein. In the cytosol, Male is converted into pyruvate with the help of malate dehydrogenase. Pyruvate is then oxidized via pyruvate dehydrogenase and citric acid cycle to generate energy.

SITE OF B OXIDATION OF FATTY ACIDS

In mammalian cells, mitochondria is the important site of B fatty acid oxidation, however, B oxidation of very long chain fatty acids, and branched chain fatty acids occur in peroxisome. Peroxisome produce shorter fatty acid chains that are further metabolized in mitochondria.

B OXIDATION OF FATTY ACIDS IN PEROXISOME

Fatty acyl-CoA in presence of enzyme acyl-CoA oxidase produces trans-delta2-enoyl-CoA and hydrogen peroxide. FAD cofactor is present in both mitochondrial and peroxiso

Transport of fatty acyl-CoA from cytoplasm to mitochondrial matrix is a rate limiting step for beta oxidation of fatty acid.

Ratio of NADH/NAD+ also regulates b oxidation of fatty acids.

High ratio inhibit the activity of beta hydroxyacetyl CoA dehydrogenase.

Concentration of acetyl-CoA inhibit thiolase.