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COURSE: MEDICAL BIOCHEMISTRY **COURSE CODE:** BCH 204

DEPT: ANATOMY

Q: *Describe the three stages of beta-oxidation (show pathways where necessary)*

A:

Beta- Oxidation Stages

This involves multiple steps by which fatty acid molecules are broken down. The oxidation and splitting of two-carbon units occur at the beta carbon atom. The oxidation of the hydrocarbon chain occurs by a sequential cleavage of two carbon atoms. Breakdown of fatty acid to acetyl CoA

Preparatory Stage 1and2

1) Activation of fatty acids

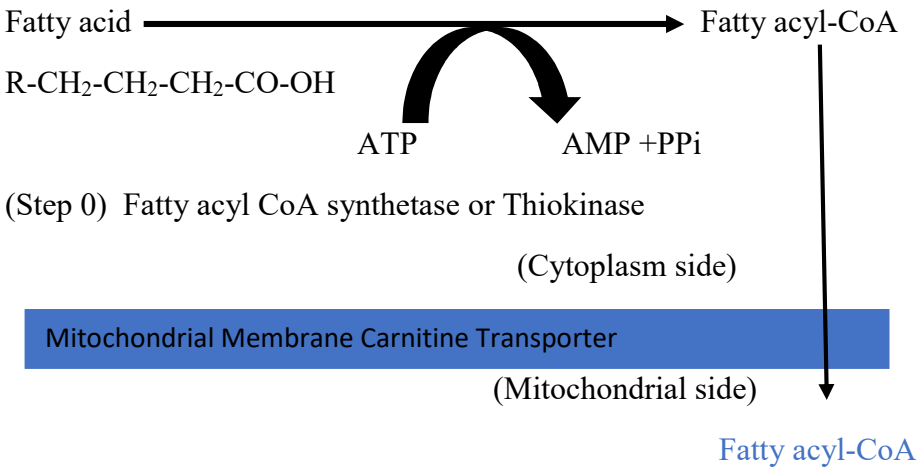
Fatty acids are activated to their coenzyme (CoA) derivative. This activation takes place in cytoplasm. ATP is hydrolysed to AMP and PPi and the energy from the hydrolysis of PPi drives the reaction forward. Thus two high energy bonds are utilized in this reaction. The enzyme is thiokinase or fatty acyl CoA synthetase.

2) Transport of Fatty acyl CoA cytosol into mitochondria

Beta oxidation occurs in the mitochondrial, so transport of fatty acid through the mitochondrial is essential. Long Chain Fatty acyl CoA cannot pass through the inner mitochondrial membrane. Therefore a transporter, Carnitine is used. Carnitine is beta-hydroxyl-gamma-trimethyl ammonium butyrate (**$(CH3)_3$-N^+-CH_2-CHOH- CH_2-COOH**

The enzyme Carnitine Acyl Transferase–I (CAT-I) transfers fatty acyl group to the hydroxyl group of Carnitine to form acyl Carnitine which occurs at the cytosolic side of mitochondrial membrane.

The protein translocase will carry acyl carnitine across the membrane to the matrix of mitochondria. On the matrix of mitochondria another enzyme, Carnitine Acyl Transferase (CAT II) transfers the acyl group back to coenzyme A molecule. Carnitine is then returned to the cytosolic side by translocase.

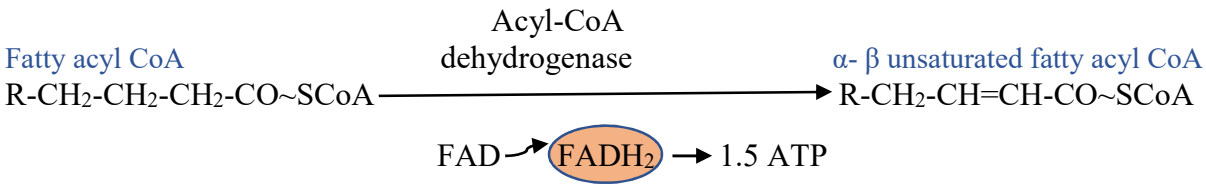


3) Beta-Oxidation in the Mitochondrial Matrix

There are four steps which are sequentially repeated for complete oxidation of fatty acids

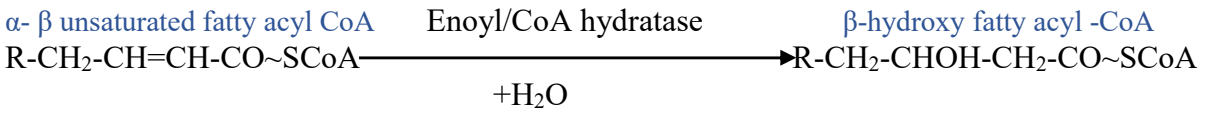
Step 1: Oxidation by FAD Linked Dehydrogenase

The fatty acyl-CoA is dehydrogenated to a transenoyl CoA with FAD accepting the hydrogen atoms. **$FADH_2$** when oxidised in electron transport chain will produce **1.5 ATP** molecules.



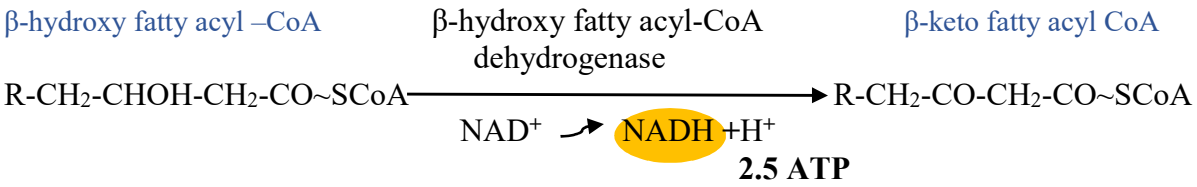
Step 2: Hydration

This is catalysed by an enoyl-CoA hydratase. This step forms a beta-hydroxy fatty acyl CoA. The L isomer alone is formed during the hydration of the trans double bond.



Step 3: NAD+ Dependent Dehydrogenase

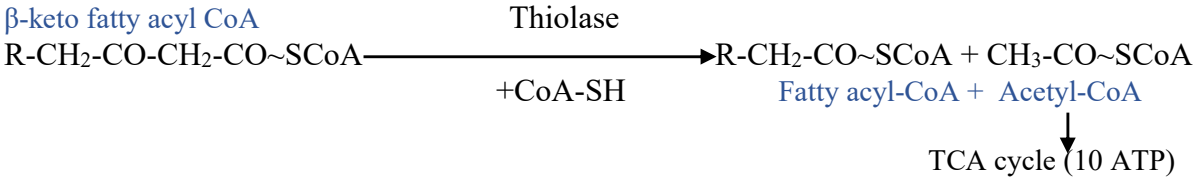
The beta-hydroxy fatty acyl-CoA is again oxidised to form beta-keto fatty acyl-CoA. This dehydrogenase acts only on L isomer. The **NADH** when oxidized in electron transport chain will generate **2.5 ATPs**.



Step 4: Cleavage

The fourth reaction is cleavage of the two carbon fragment by splitting the bond between alpha and beta carbons, using a thiolase enzyme

The beta-keto fatty acyl-CoA now undergoes thiolytic cleavage, splitting of a molecule of acetyl-CoA and leaving behind a fatty acyl-CoA with 2 carbon atoms less



Further Cycles

This fatty acyl-CoA will sequentially undergo beta-oxidation steps 1-4 until the fatty acid is completely converted to acetyl-CoA