Hello students, today we are going to study breakdown of lipids by beta oxidation pathway from Unit 3 that is chemoheterotrophic lipid metabolism. In this module we are going to study the beta oxidation pathway and its bioenergetics. After studying this module, students will be able to describe breakdown of saturated fatty acids by beta oxidation pathway and explain bioenergetics of the same.

Now first of all, let us understand what lipids are. Lipids are organic compounds which are insoluble in water and they have various roles to play in living organisms. They act as storage of energy in the form of fats and oils. They are structural elements of biological membranes as phospholipids and sterols, and they have various other roles to play in a cell: as enzyme cofactors, electron carriers, light absorbing pigments, hormones, etc. Fats and oils are primarily made of fatty acids. Fatty acids are carboxylic acids with hydrocarbon chains ranging from 4 to 36 carbons long.

Fatty acids may either be saturated or unsaturated. Unsaturated are further categorized as monounsaturated if they have single, double bond or polyunsaturated if they have more than one double bond. Now, what is beta oxidation? Fatty acids with even numbers of carbon atoms are degraded by successive removal of two carbon fragments in the form of acetyl group by the beta oxidation pathway. This takes place in the mitochondrial matrix. However, the fatty acids are found in the cell cytosol. They can freely enter into mitochondria only if the chain length is 12 carbons or lesser. Those fatty acids which have more than 14 carbons cannot pass through the mitochondrial membrane, so they undergo a series of four reactions which we are going to see now.

The first reaction is the activation of fatty acid. The enzyme Acyl CoA Synthetase which is present in the outer mitochondrial membrane, activates fatty acid to acyl CoA ester. So a thioester link is formed between the carboxyl group of fatty acid, and thiol group of coenzyme A. In this reaction, two high energy phosphate bonds from ATP are used.

Step 2 is transfer of these fatty esters to carnitine. Since Fatty ester cannot cross the inner mitochondrial membrane, the entry is stimulated by carnitine and the enzyme carnitine acyl transferase I, which is present on the outer mitochondrial membrane. It transfers acyl group from CoA to carnitine. Fatty acyl carnitine, which is now formed, crosses the inner membrane with the help of co-transport proteins and enters the matrix. Fatty acyl group is then transferred from carnitine to intramitochondrial CoA by the enzyme carnitine acyl Transferase II. And the carnitine which is released, returns to intermembrane space. Fatty acyl CoA, which is present in the mitochondrial matrix, can now be used as substrate for the beta oxidation cycle. So we can see this is the outer mitochondrial membrane, wherein the fatty acid is bound to carnitine to form carnitine acyl transferase. Carnitine is transported into the inner mitochondrial membrane and acyl will now bind to CoA, forming acyl CoA which is released into the mitochondrial matrix, and carnitine is now free to take or transport another molecule of acyl.

Coming to the steps of fatty acid oxidation. Beta oxidation is the oxidative removal of two carbon units as acetyl CoA. Later on, this acetyl groups can enter in Krebs cycle and are oxidized to carbon dioxide. NADH and $FADH_2$ produced in stage one and two donate electrons to ETC,which is linked to phosphorylation of ADP to ATP. So the energy that is released by Fatty oxidation is conserved as ATP.

In beta oxidation step one is dehydrogenation wherein a double bond is formed between Alpha and beta carbon, that is carbon number two and three to form trans-Δ^2-enoyl-CoA. This is catalyzed by the enzyme acyl CoA dehydrogenase, which requires FAD as a prosthetic group. Electrons are removed from fatty acyl CoA and transferred to FAD. So in this reaction we see a palmitoyl Co A which is converted to trans Δ^2 enoyl CoA by the action of acyl CoA dehydrogenase and a double bond has been introduced between Alpha and beta carbon, which we can see in this structure.

Second step in beta oxidation is hydration reaction. In this step in which water is added to the double bond of trans-Δ^2-enoyl CoA to form L stereoisomer of beta hydroxy acyl CoA. And this particular reaction is catalyzed by enoyl CoA hydratase. So this structure is beta hydroxy acyl CoA.

The third step is the second dehydrogenation step, in which beta hydroxy acyl CoA is dehydrogenated to form beta ketoacyl CoA and this is catalyzed by the enzyme beta hydroxy acyl CoA Dehydrogenase. The fourth step is the thiolytic cleavage in which acetyl CoA acetyl transferase or thiolase enzyme cleaves off two carbon unit from the carboxy terminus of beta keto acyl CoA. So, this forms an acetyl CoA and leaves behind the CoA ester of fatty acid which is shortened by two carbon atoms. So if we start with a 16 carbon compound then we are left with 14 carbon compound after removal of two carbons as Acetyl CoA.

So the overall equation for one turn of fatty acid is this in which Palmitoyl CoA converted to Myristoyl CoA. And if we consider 7 turns, then after breakdown of Palmitoyl CoA we have 8 acetyl CoA which are released. If we consider the energetics,then oxidation of palmitoyl Co A to acetyl CoA generates 28 ATPs. Which then enters into a citric acid cycle and yields 80 ATP. So if we combine both the equations, we get 108 ATPs. But since 2 ATPs are used in activation of fatty acids, the net gain is 106 ATPs.

So in this module we have seen how beta oxidation plays a role in catabolism of lipids. And these are the references for this module.

Thank you.