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Describe the three stages of beta oxidation (show pathways where necessary)

Beta oxidation is a metabolic process involving multiple steps by which fatty acid molecules are broken down to produce energy. It 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 the Krebs’ cycle or citric acid 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 while it occurs in the cytosol in prokaryotic cells.

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. Beta oxidation takes place in four steps: dehydrogenation, hydration, oxidation and thyolisis. Each step is catalyzed by a distinct enzyme. Each cycle of this process begins with an acyl-CoA chain and ends with one acetyl-CoA, one FADH2, one NADH and water, and the acyl-CoA chain becomes two carbons shorter. The total energy yield per cycle is 17 ATP molecules (see below for details on the breakdown). This cycle is repeated until two acetyl-CoA molecules are formed as opposed to one acyl-CoA and one acetyl-CoA.

The first is dehydrogenation and in this first step, acyl-CoA is oxidized by the enzyme acyl CoA dehydrogenase. A double bond is formed between the second and third carbons (C2 and C3) of the acyl-CoA chain entering the beta oxidation cycle; the end product of this reaction is trans-Δ2-enoyl-CoA (trans-delta 2-enoyl CoA). This step uses FAD and produces FADH2, which will enter the citric acid cycle and form ATP to be used as energy.

 

The second is hydration and here, the double bond between C2 and C3 of trans-Δ2-enoyl-CoA is hydrated, forming the end product L-β-hydroxyacyl CoA, which has a hydroxyl group (OH) in C2, in place of the double bond. This reaction is catalyzed by another enzyme: enoyl CoA hydratase. This step requires water.



The third is oxidation and in this stage, the hydroxyl group in C2 of L-β-hydroxyacyl CoA is oxidized by NAD+ in a reaction that is catalyzed by 3-hydroxyacyl-CoA dehydrogenase. The end products are β-ketoacyl CoA and NADH + H. NADH will enter the citric acid cycle and produce ATP that will be used as energy.



The last stage is thiolysis and in the last step, β-ketoacyl CoA is cleaved by a thiol group (SH) of another CoA molecule (CoA-SH). The enzyme that catalyzes this reaction is β-ketothiolase. The cleavage takes place between C2 and C3; therefore, the end products are an acetyl-CoA molecule with the original two first carbons (C1 and C2), and an acyl-CoA chain two carbons shorter than the original acyl-CoA chain that entered the beta oxidation cycle.

