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18/MHS07/014

MEDICAL BIOCHEMISTRY

BCH 204

THREE STAGES OF BETA OXIDATION

BETA OXIDATON is a process in which two carbon units sequentially removed beginning from the carboxyl end of the fatty acid in the form of acetyl-coA. It is called beta oxidation because oxidation of fatty acids take place at the B carbon atom. It consists of three steps which occur in the mitochondria:

In the first stage-β oxidation-the fatty acids undergo oxidative removal of successive two-carbon units in the form of acetyl-CoA, starting from the carboxyl end of the fatty acyl chain. For example, the 16-carbon fatty acid palmitic acid (palmitate at pH 7) undergoes seven passes through this oxidative sequence, in each pass losing two carbons as acetyl-CoA. At the end of seven cycles the last two carbons of palmitate (originally C-15 and C-16) are left as acetyl-CoA. The overall result is the conversion of the 16-carbon chain of palmitate to eight two-carbon acetyl-CoA molecules. Formation of each molecule of acetyl-CoA requires removal of four hydrogen atoms (two pairs of electrons and four H+) from the fatty acyl moiety by the action of dehydrogenases.

In the second stage of fatty acid oxidation the acetyl residues of acetyl-CoA are oxidized to CO2 via the citric acid cycle, which also takes place in the mitochondrial matrix. Acetyl-CoA derived from fatty acid oxidation thus enters a final common pathway of oxidation along with acetyl-CoA derived from glucose via glycolysis and pyruvate oxidation .

The first two stages of fatty acid oxidation produce the reduced electron carriers NADH and FADH2, which in the third stage donate electrons to the mitochondrial respiratory chain, through which the electrons are carried to oxygen . Coupled to this flow of electrons is the phosphorylation of ADP to ATP. Thus energy released by fatty acid oxidation is conserved as ATP.

our enzyme-catalyzed reactions are involved in the first stage of fatty acid oxidation . First, dehydrogenation produces a double bond between the α and β carbon atoms (C-2 and C-3), yielding a **trans-Δ2-enoyl-CoA**. The symbol Δ2 designates the position of the double bond. The new double bond has the trans configuration; recall that naturally occurring unsaturated fatty acids normally have their double bonds in the cis configuration. We shall consider the significance of this difference later.

The enzyme responsible for this first step, **acyl-CoA dehydrogenase**, includes FAD as a prosthetic group. The electrons removed from the fatty acyl-CoA are transferred to the FAD, and the reduced form of the dehydrogenase then immediately donates its electrons to an electron carrier, the **electron-transferring** flavoprotein (ETFP). ETFP, an integral protein of the inner mitochondrial membrane, is one of the electron carriers of the mitochondrial respiratory chain . The transfer of a pair of electrons from the FADH2 of acyl-CoA dehydrogenase to O2 via the respiratory chain provides the energy for the synthesis of two ATP molecules.

The oxidation catalyzed by acyl-CoA dehydrogenase is analogous to succinate dehydrogenation in the citric acid cycle.