Fatty acid oxidation

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The mitochondrial fatty acid β-oxidation pathway has been characterised at the biochemical level as well as the molecular biological level. FAO plays a pivotal role in energy homoeostasis, but it competes with glucose as the primary oxidative substrate. The mechanisms behind this so-called glucose–fatty acid cycle operate at the hormonal, transcriptional and biochemical levels.

Glucose, fatty acids and amino acids are the three substrates an organism can use to maintain metabolic homoeostasis. They are required for the generation of energy, but also as building blocks for the biosynthesis of (macro) molecules. The prime pathway for the degradation of fatty acids is mitochondrial **fatty acid β-oxidation (FAO)**. FAO is a key metabolic pathway for energy homoeostasis in organs such as the liver, heart and skeletal muscle. During fasting, when glucose supply becomes limited, FAO is of particular importance. Under this condition, most tissues, except the brain, can use fatty acids directly to generate energy. Furthermore, the liver converts fatty acids into ketone bodies, a process for which FAO is indispensable. Ketone bodies serve as an additional energy source that is used by all tissues including the brain.

History

Georg Franz Knoop discovered fatty acid β-oxidation.

Occurrence and activation of fatty acid

Mitochondria, as well as peroxisomes, harbour all enzymes necessary for FAO. Mitochondria are the main site for the oxidation of plasma free fatty acids or lipoprotein-associated triglycerides. This implies that several transport steps are necessary before fatty acids are oxidised. Triglycerides are first hydrolysed by the action of endothelium-bound lipoprotein lipase. The uptake of fatty acids seems to be largely mediated by membrane proteins, although passive uptake probably also occurs.

Fatty acid transport proteins (FATPs) are integral trans membrane proteins that enhance the uptake of long chain and very long chain fatty acids into cells. In humans, FATPs comprise a family of six highly homologous proteins, FATP1–FATP6, which are found in all fatty acid-utilising tissues of the body

FATPs have acyl-CoA synthetase activity, suggesting that fatty acids are rapidly converted to acyl-CoAs after translocation across the plasma membrane, a process that may drive the transport.

1. Fatty acyl-CoA from the cytosol reacts with carnitine in the outer mitochondrial membrane, forming fatty acylcarnitine. The enzyme is carnitine acyltransferase I (CAT I), which is also called carnitine palmitoyltransferase I (CPT I). Fatty acylcarnitine passes to the inner membrane, where it re-forms to fatty acyl-CoA, which enters the matrix. The second enzyme is carnitine acyltransferase II (CAT II).
2. Carnitine acyltransferase I, which catalyzes the transfer of acyl groups from coenzyme A to carnitine, is inhibited by malonyl-CoA, an intermediate in fatty acid synthesis. Therefore, when fatty acids are being synthesized in the cytosol, malonyl-CoA inhibits their transport into mitochondria and, thus, prevents a futile cycle (synthesis followed by immediate degradation).

3. Inside the mitochondrion, the fatty acyl-CoA undergoes beta-oxidation.

Thank you