

Lipolysis

The body preferentially uses up its fat stores during fasts and in low-energy states. Triglycerides, stored in adipose tissue, are converted into NADH, FADH₂, and acetyl-CoA molecules. This process begins when hormone sensitive lipase breaks down triglycerides, releasing glycerol and fatty acids. Glycerol can be directly used in glycolysis, but the fatty acids require transport and further processing via beta-oxidation. Beta-oxidation occurs in the inner mitochondrial membrane, which is impermeable to long-chain fatty acids. These molecules must be transported across the membrane via the carnitine shuttle. However medium-chain and short-chain fatty acids can diffuse freely. Once inside the inner mitochondrial membrane, beta oxidation can begin. This process breaks down fatty acids, two carbons at a time, with each round releasing acetyl-CoA. Odd chain fatty acids require additional steps, as their final product is propionyl-CoA. This molecule is acted upon by propionyl-CoA carboxylase, which requires biotin as a cofactor, to produce methylmalonyl-CoA. Methylmalonyl-CoA is then acted upon by methylmalonyl-CoA mutase, which requires vitamin B12 as a cofactor, to finally form succinyl-CoA. This final molecule of succinyl-CoA can then enter the Krebs cycle directly.



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Triglyceride Breakdown

Triglycerides

[TAG-triceratops](#)

The process of transforming stored fat into energy begins with triglycerides. These molecules are largely stored within adipose tissue and are used preferentially in fasting or low-energy states.

Hormone Sensitive Lipase

[Harmonica on Lips-ace](#)

The enzyme hormone-sensitive lipase begins this process by hydrolyzing triglycerides. Hormone-sensitive lipase frees the fatty acids from their glycerol backbone. This enzyme is activated by catecholamines and inhibited by insulin.

Glycerol

[Glitter-roll](#)

Glycerol is one of the two main products of triglyceride breakdown. This molecule is easily utilized by the body. It can be phosphorylated into glycerol-3-phosphate or formed into dihydroxyacetone. Both of these molecules may enter glycolysis after being converted into dihydroxyacetone phosphate.

Fatty Acids

[Bacon Acid-lemon](#)

Fatty acids are the other main product of triglyceride breakdown. Following their release, they can be transported to the mitochondria for beta-oxidation.

Fatty Acid Transport

Long-chain Fatty Acids

[Long-chain Bacon Acid-lemon](#)

Long-chain fatty acids are not capable of entering the mitochondria on their own. These molecules require specialized transport in order to cross the lipid bilayer of the organelle.

Carnitine Shuttle

Car-teen Shuttle

Long-chain fatty acids are transported into the mitochondria via the carnitine shuttle. This process begins with the transformation of the long-chain fatty acid into acyl-CoA via the enzyme fatty acyl-CoA synthetase. Acyl-CoA and carnitine are then combined to form acylcarnitine via the enzyme carnitine palmitoyltransferase-1 (CPT-1, CAT-1). This is the rate-limiting step in fatty acid oxidation. The newly formed acylcarnitine molecule can diffuse freely into the inner mitochondrial membrane, where it is broken down by CPT-2 into acyl-CoA and carnitine.

Medium-chain and Short-chain Fatty Acids Diffuse Freely

Medium/Short-chain Bacon Acidic-lemon D-fusing Freely

Medium and short-chain fatty acids are capable of diffusing freely into the inner mitochondrial membrane and do not require carrier molecules. Once inside the mitochondria, they are immediately converted into acyl-CoA molecules.

Fatty Acid Breakdown

Beta Oxidation

Beta-fish Ox

Beta-oxidation is a biochemical process that occurs within the mitochondria of cells responsible for turning long acyl-CoA molecules into two-carbon acetyl-CoA molecules. These are then capable of entering the Krebs cycle, subsequently providing substrates for cellular respiration and providing energy in the form of ATP.

Acetyl-CoA if Even Number of Carbon Atoms

Seagull-Coin-A-purse with Even Number of Car-bombs

Fatty acids with an even number of carbons are cleaved, two carbons at a time, into acetyl-CoA molecules, NADH, and FADH₂.

Propionyl-CoA if Odd Number of Carbon Atoms

Purple-eel Coin-A-purse with Odd Number of Car-bombs

If a fatty acid has an odd number of carbons, the end result of beta-oxidation is propionyl-CoA, a three-carbon molecule. This molecule can be converted into succinyl-CoA for use in the Krebs cycle.

Propionyl-CoA Carboxylase

Purple-eel Coin-A-purse Cardboard-lace

The process of converting propionyl-CoA into succinyl-CoA begins with the formation of methylmalonyl-CoA from propionyl-CoA via the enzyme propionyl-CoA carboxylase.

Biotin Cofactor

Bionic-tin-man Crow-flagger

The formation of methylmalonyl-CoA from propionyl-CoA requires biotin as a cofactor.

Methylmalonyl-CoA

Methyl-melon Coin-A-purse

Methylmalonyl-CoA is produced from propionyl-CoA through carboxylation. It can be converted into succinyl-CoA via the enzyme methylmalonyl-CoA mutase. This molecule can also serve as a marker of sorts for patients with suspected vitamin B12 (cobalamin) deficiency. Since these patients cannot convert methylmalonyl-CoA into succinyl-CoA, they will have elevated levels of methylmalonyl-CoA.

Methylmalonyl-CoA Mutase

Methyl-melon Coin-A-purse Mutant-ace

The enzyme methylmalonyl-CoA mutase is responsible for the conversion of methylmalonyl-CoA into succinyl-CoA. This enzyme represents the final step of the beta-oxidation of odd-chain fatty acids, as the succinyl-CoA resulting from this step can enter the Krebs cycle directly.

Vitamin B12 Cofactor

[\(12\) Dozen Viking \(B\) Bees and Crow-flagger](#)

The enzyme methylmalonyl-CoA mutase requires vitamin B12 (cobalamin) as a cofactor. As such, the observation that this biochemical pathway is not progressing as it should (evidenced by increased levels of methylmalonyl-CoA) can be helpful in diagnosing vitamin B12 deficiency. It is especially useful for differentiating B12 deficiency from other causes of megaloblastic anemia, such as vitamin B9 (folate) deficiency.

Succinyl-CoA

[Suckers Coin-A-purse](#)

Succinyl-CoA is the end product of odd-chain fatty acid oxidation. It is formed via the enzyme methylmalonyl-CoA mutase and is capable of directly entering the Krebs cycle.