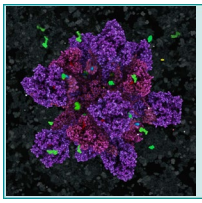

Citric Acid Cycle

hhmi | BioInteractive

Animation
Transcript

The origin of energy production and biosynthesis inside your living cells is the dynamic mitochondria organelle. Mitochondria are filled with metabolic enzymes that catalyze a loop of chemical reactions called the citric acid cycle.

The eight steps of the citric acid cycle gradually break apart two carbon atoms from glycolysis, capturing liberated electrons for the electron transport chain, while generating carbon dioxide as waste.

The citric acid cycle starts with the end product of a previous cycle, the 4-carbon molecule oxaloacetate. New carbon enters from glycolysis in the form of acetyl-CoA, a 2-carbon acetyl group attached to coenzyme A.

Step 1 is the catalytic transfer of a 2-carbon acetyl group from coenzyme A to 4-carbon oxaloacetate, creating 6-carbon citric acid, the molecule that gives the cycle its name.

Citric acid is used by your cells for the biosynthesis of fatty acids, lipids, and cholesterol, and is also the substrate for Step 2 of the citric acid cycle. The enzyme reaction of Step 2 makes a small change to the citric acid molecule, moving the position of an oxygen atom, converting citrate into isocitrate.

Step 3 of the cycle removes a carbon atom, forming carbon dioxide as waste, while converting 6-carbon isocitrate to 5-carbon ketoglutarate. During this process, chemical energy is harvested when two electrons are transferred to coenzyme NADH, which delivers them to nearby enzymes of the electron transport chain.

Step 4 of the citric acid cycle is performed by a huge multienzyme complex, connecting multiple chemical reactions with flexible tethers, efficiently moving reactants between active sites and diverting electrons between pathways.

The large complex is made with a repeating unit of three core enzymes, working in sequence to remove a carbon atom from ketoglutarate, generating carbon dioxide waste, then attaching 4-carbon succinyl to coenzyme A. The electron from ketoglutarate oxidation is retained by the tethered enzyme, before passing it to coenzyme NADH, which delivers electrons to the electron transport chain.

Enzymes of Step 5 separate succinyl from coenzyme A by breaking an energetic bond, providing enough energy to create GTP. GTP is a building block of RNA and an energy source for protein synthesis. In the most direct path to ATP from the citric acid cycle, other enzymes in the matrix can use GTP to make the chemical fuel ATP.

Step 6 is performed by an enzyme embedded in the inner mitochondrial membrane. This enzyme is also known as Complex II of the electron transport chain. The enzyme catalyzes the oxidation of succinate to create fumarate, releasing two electrons that hop through the interior to coenzyme Q,

which is reduced. Coenzyme Q travels in the membrane, carrying the electrons to nearby enzymes of the electron transport chain.

Step 7 takes fumarate generated by Step 6 and reacts it with water to create 4-carbon malate.

The final step of the citric acid cycle uses malate to regenerate oxaloacetate, transferring electrons to coenzyme NADH, which supplies the electron transport chain. Oxaloacetate can return to Step 1 for another loop of the cycle and is also an essential building block for making amino acids and the genetic code of DNA and RNA.

At the center of cellular metabolism, the citric acid cycle generates both chemical energy and material for biosynthesis of the entire diversity of molecules found inside a living cell.