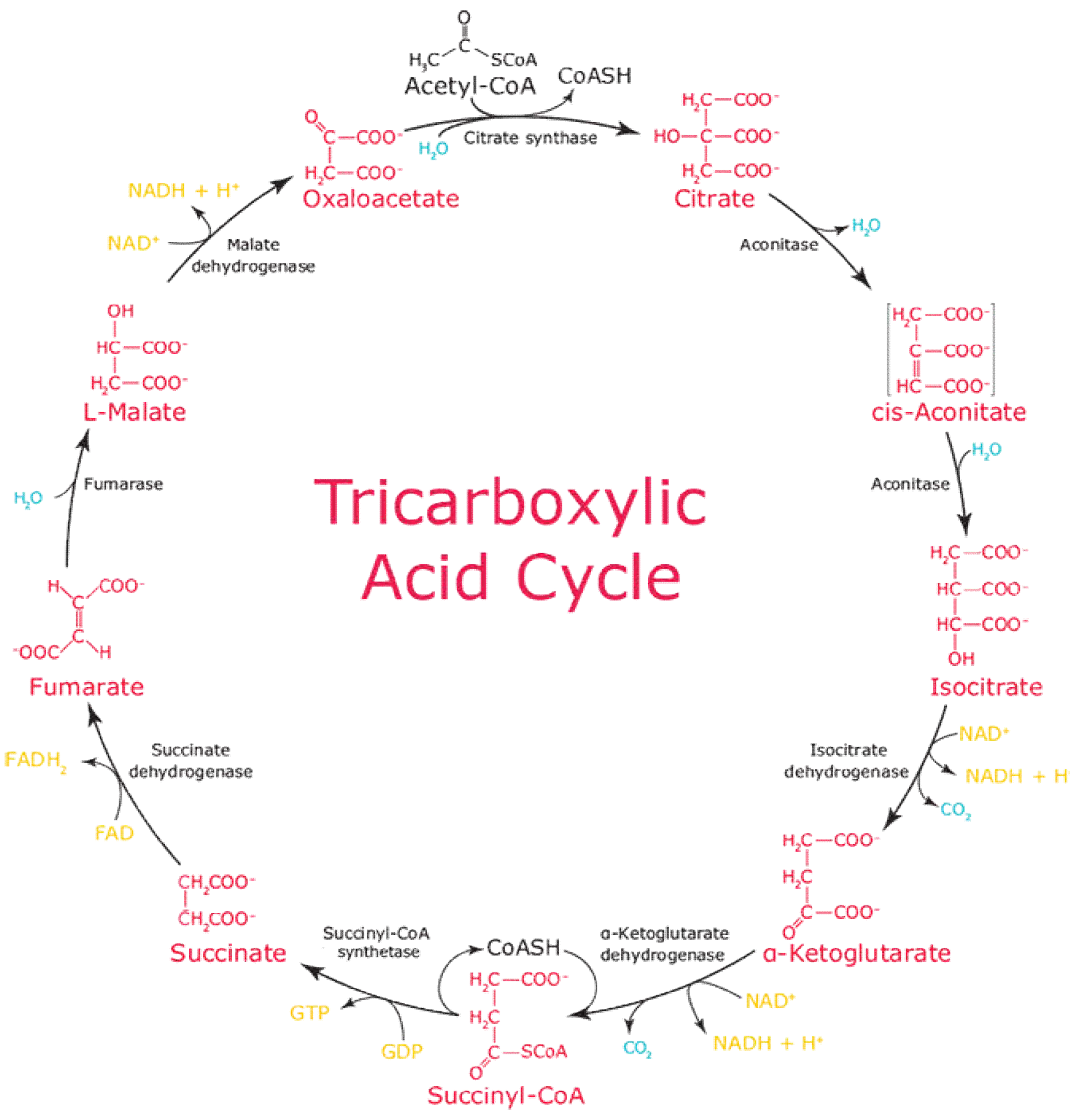
Citric acid Cycle

The citric acid cycle is the biochemical hub of the cell, oxidizing carbon fuels, usually in the form of acetyl CoA, as well as serving as a source of precursors for biosynthesis. glucose can be metabolized to pyruvate anaerobically to synthesize ATP through the glycolytic pathway. Glycolysis, however, harvests but a fraction of the ATP available from glucose.The aerobic processing of glucose, which is the source of most of the ATP generated in metabolism.

The aerobic processing of glucose starts with the complete oxidation of glucose derivatives to carbon dioxide. This oxidation takes place in the *citric acid cycle,* a series of reactions also known as the *tricarboxylic acid (TCA) cycle* or the *Krebs cycle.* The citric acid cycle is the *final common pathway for the oxidation of fuel molecules*—amino acids, fatty acids, and carbohydrates. Most fuel molecules enter the cycle as acetyl coenzyme A. Under aerobic conditions, the pyruvate generated from glucose is oxidatively decarboxylated to form acetyl CoA. **In eukaryotes, the reactions of the citric acid cycle take place inside mitochondria**, in contrast with those of glycolysis, which take place in the cytosol. the gateway to the aerobic metabolism of any molecule that can be transformed into an acetyl group or dicarboxylic acid. **The cycle is also an important source of precursors, not only for the storage forms of fuels, but also for the building blocks of many other molecules** such as amino acids, nucleotide bases, cholesterol, and porphyrin (the organic component of heme). **The citric acid cycle includes a series of oxidation-reduction reactions that result in the oxidation of an acetyl group to two molecules of carbon dioxide.**

A four- carbon compound (oxaloacetate) condenses with a two-carbon acetyl unit to yield a six-carbon tricarboxylic acid (citrate). An isomer of citrate is then oxidatively decarboxylated. The resulting five-carbon compound (α-ketoglutarate) also is oxidatively decarboxylated to yield a four-carbon compound (succinate). Oxaloacetate is then regenerated from succinate. Two carbon atoms enter the cycle as an acetyl unit and two carbon atoms leave the cycle in the form of two molecules of carbon dioxide. Three hydride ions (hence, six electrons) are transferred to three molecules of nicotinamide adenine dinucleotide (NAD^+), whereas one pair of hydrogen atoms (hence, two electrons) is transferred to one molecule of flavin adenine dinucleotide (FAD). *The function of the citric acid cycle is the harvesting of high-energy electrons from carbon fuels.* Note that the citric acid cycle itself neither generates a large amount of ATP nor includes oxygen as a reactant (Figure 17.3). Instead, **the citric acid cycle removes electrons from acetyl CoA and uses these electrons to form NADH and $FADH_2$**. In *oxidative phosphorylation* . Electrons released in the reoxidation of NADH and $FADH_2$ flow through a series of membrane proteins (referred to as the *electron-transport chain*) to generate a proton gradient across the membrane. These protons then flow through ATP synthase to generate ATP from ADP and inorganic phosphate. Oxygen is required for the citric acid cycle indirectly as much as it is the electron acceptor at the end of the electron-transport chain, necessary to regenerate NAD^+ and FAD.



Overview of the Citric Acid Cycle. The citric acid cycle oxidizes two-carbon units, producing two molecules of CO_2, one molecule of GTP, and high-energy electrons in the form of NADH and $FADH_2$.

The citric acid cycle, in conjunction with oxidative phosphorylation, provides the vast majority of energy used by aerobic cells—in human beings, greater than 95%. It is highly efficient because a limited number of molecules can generate large amounts of NADH and $FADH_2$. The four-carbon molecule, oxaloacetate,that initiates the first step in the citric acid cycle is regenerated at the end of one passage through the cycle. The oxaloacetate acts catalytically: it participates in the oxidation of the acetyl group but is itself regenerated. Thus, one molecule of oxaloacetate is capable of participating in the oxidation of many acetyl molecules.