Fluoroacetate often used as a rodenticide inhibits the aconitase enzyme activity. Naturally it is non-toxic, but in the body, it is metabolized to fluoroacetyl-CoA, which gives rise to fluorocitrate after condensing with oxaloacetate. The aconitase is strongly inhibited by fluorocitrate. This is a form of metabolic lethal synthesis.

STEP3: Oxidation of Isocitrate to $\alpha$-ketoglutarate and CO$_2$: at this stage, the enzyme “isocitrate dehydrogenase” catalyzes the oxidative decarboxylation of isocitrate to $\alpha$-ketoglutarate. This reaction involves a carbonyl intermediate (oxalosuccinate). Also, manganese ion is a required cofactor, while either NAD$^+$ or NADP function as a coenzyme in the reaction (depending on the form of isocitrate dehydrogenase present); reducing C$_2$–OH group to a keto group.

STEP4: Oxidation of $\alpha$-ketoglutarate to succinylCoA and CO$_2$: this step is another oxidative decarboxylation in which $\alpha$-ketoglutarate is converted to succinylCoA and CO$_2$ by the enzyme “$\alpha$-ketoglutarate dehydrogenase complex”. In this reaction, NAD$^+$ is the electron acceptor and CoA-SH functions as the carrier of the succinyl group.

It is worthy of note that the enzyme involved; $\alpha$-ketoglutarate dehydrogenase closely resembles the PDH complex in structure and function, having three domain homologous to the E1, E2, & E3 of PDH complex, as well as enzyme bound TPP, lipoate, NAD and CoA-SH, the main difference between the two homologous enzyme is their substrate specificities at their E1 domain.
In conclusion, it is imperative that we learn the co-ordinate regulation between the glyoxylate cycle and the citric acid cycle.

Between the glyoxylate cycle and the citric acid cycle, four distinct pathways participate in the conversion:

- **a. Fatty acid catabolism into acetylCoA (in the glyoxysome)**
- **b. The glyoxylate cycle (in the glyoxysome)**
- **c. The citric acid cycle (in the mitochondria)**
- **d. Gluconeogenesis (in the cytosol)**

Isocitrate is a crucial intermediate at the branch point between glyoxylate and the citric acid cycle. Isocitrate dehydrogenase is regulated by covalent modification: through a specific Protein kinase which phosphorylates and inactivates the dehydrogenase and shunts isocitrate (the substrate) into the glyoxylate cycle.

Another enzyme Phosphoprotein-phosphatase removes the phosphoryl group from the isocitrate dehydrogenase; activating it and signaling the proceeding of the citric acid cycle.
References

This study guide is a simplified and compressive presentation of the topic compiled from Success biochemistry academy lecture note and some other trusted biochemistry authority and classical textbook. All pieced together in a simplified easily digestible form for all and sundry.

Classical textbooks whose phrases and picture reflect in this writeup are:

1. Lehningher principles of biochemistry, 6th edition, David Nelson & Micheal Cox
2. Medical Biochemistry by N. Mallikarjuna Rao
4. Textbook of medical biochemistry. MN Chatterjea, Rana shinde
5. Biochemistry: the chemical reactions of living cell . David Metzler
6. Fundamentals of biochemistry, life at molecular level. Donald & Judith Voet, Charlotte Pratt