6.6: Glyoxylate Pathway

A pathway related to the Citric Acid Cycle (CAC) is the glyoxylate pathway (Figure 6.6.1). This pathway, which overlaps all of the non-decarboxylation reactions of the CAC does not operate in animals, because they lack two enzymes necessary for the pathway – isocitrate lyase and malate synthase. Isocitrate lyase catalyzes the conversion of isocitrate into succinate and glyoxylate. Because of this, all six carbons of the CAC survive and do not end up as carbon dioxide.
Succinate continues through the remaining reactions of the CAC to produce oxaloacetate. Glyoxylate combines with another acetyl-CoA (one acetyl-CoA was used to start the cycle) to create malate (catalyzed by malate synthase). Malate can, in turn, be oxidized to oxaloacetate.

It is at this point that the pathway’s contrast with the CAC is apparent. After one turn of the CAC, a single oxaloacetate is produced and it balances the single one used in the first reaction of the cycle. Thus, in the CAC, no net production of oxaloacetate is realized. By contrast, at the end of a turn of the glyoxylate cycle, two oxaloacetates are produced, starting with one. The extra oxaloacetate can then be used to make other molecules, including glucose in gluconeogenesis.

Because animals do not run the glyoxylate cycle, they cannot produce glucose from acetyl-CoA in net amounts, but plants and bacteria can. As a result, these organisms can turn acetyl-CoA from fat into glucose, while animals can’t. Bypassing the decarboxylations (and substrate level phosphorylation) has its costs, however. Each turn of the glyoxylate cycle produces one FADH and one NADH instead of the three NADHs, one \( \text{FADH}_2 \), and one GTP made in each turn of the CAC.

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