

Cryo-EM structure of *E. coli* acetyl-CoA carboxylase complex

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The first step of fatty acid biosynthesis is the carboxylation of acetyl-CoA to malonyl-CoA performed by an acetyl-CoA carboxylase (ACC) enzyme complex. Since this reaction is powered by ATP it is highly regulated, yet how the various regulators work is unknown. In addition, the organization of many bacterial and plant enzymes remains unknown. We have determined the Cryo-EM structure of the *E. coli* ACC, which forms unprecedented tube-like complexes with a diameter of ~300 nm. The organization of the biotin carboxylase (BC) domain and carboxyltransferase (CT) domain leads to active sites that are packed near each other allowing for regulatory interactions. Furthermore, the structure points all of the active sites toward the interior of the filament. While crystal structures of the BC and CT domains were known, the N- and C- termini were disordered. These disordered regions make contacts that are responsible for holding together the complex and are somewhat variable between bacterial strains. Our structure will provide information necessary to dissect various modes of allosteric regulation to support biofuel biosynthesis and provide novel sites to inhibit the ACC of specific bacteria.