

Molecular Snapshots of acetyl-CoA Metabolism

ABSTRACT: The metabolite acetyl-CoA is essential for life through participation in many biochemical reactions in protein, RNA carbohydrate, and lipid metabolism; and production of energy through the Krebs cycle. A major focus of the laboratory is to understand the molecular basis of acetyl-CoA metabolism. Two enzymes of recent interest in the laboratory are ATP-citrate Lyase (ACLY), which synthesizes most of the cytosolic acetyl-CoA; and fatty acid synthase (FASN), which uses acetyl-CoA for de novo lipogenesis. Both enzymes are therapeutic targets for various metabolic disorders and cancer. We determined the cryo-EM structures of ACLY in various substrate, product and intermediate -bound states. Together with biochemical and cellular studies, we are able to elucidate its mode of catalysis and inhibition. We also determined the cryo-EM structure of human FASN in a multitude of conformational states, including with the flexible acyl-carrier protein (ACP) stalled at several of the six catalytic domains. Together with biochemical and cellular studies, we derive new molecular insights into the dynamic nature of FASN and ACP shuttling.

Wednesday, March 26th

2:00 - 3:15 p.m.

Science Hall 126 & [Zoom](#)

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