

228. A nature inspired platform for production of acetyl-CoA derived mevalonate pathway products in *S. cerevisiae*

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Project Goals:

We aim to develop a robust *S. cerevisiae* system to drive the production of isoprenoids and other industrial products derived from acetyl-CoA. Our strategy to increase the abundance of cytosolic acetyl-coA is modeled after the well-studied, endogenous mechanisms of oleaginous, lipid accumulating yeast. Enzymes responsible for oleagenicity divert excess acetyl-coA from the mitochondria while providing a sufficient supply of redox potential and ATP units required for lipid biosynthesis. Specifically, cytoplasmic acetyl-CoA is generated through the activity of ATP:citrate lyase (ACL), which cleaves citrate to form acetyl-CoA and oxaloacetate. The combination of expression of mevalonate producing enzymes, a heterologous ACL from the oleaginous yeast, *Aspergillus nidulans*, and modifications to increase precursor supply, have demonstrated the utility of a robust host engineered with strong acetyl-CoA production for improved flux through the mevalonate pathway.

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