Lipid Accumulation and its Impact on Amino Acid Metabolism in *Saccharomyces cerevisiae*

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Project Goals: Lipids are a group of highly diverse molecules with a multitude of biological functions such as formation of biological membranes, storage of energy, cell signaling, and apoptosis. Triacylglycerides (TAG) function as energy storage and source of membrane building blocks. *Saccharomyces cerevisiae* was metabolically engineered to accumulate increased levels of TAG. We observed that redirecting metabolic flux towards formation of TAG affected amino acid metabolism on the level of transcript and metabolite.

We have engineered *Saccharomyces cerevisiae* to accumulate increased levels of TAG by introducing a push and pull on TAG biosynthesis. A push was introduced by overexpression of acetyl-CoA carboxylase double mutant $ACC1^{S659A\ S1157A}$ (*ACC1***), while a pull was introduced by overexpression of phosphatidate phosphatase *PAH1* and diacylglycerol acyltransferase *DGA1*. The resulting strain was analyzed for changes in level of transcript and amino acids compared to a reference strain in batch cultivation during respiratory growth.

We observed a reduced abundance of total free amino acids in the engineered strain. This reduction was consistent with an observed downregulation of several amino acid biosynthetic genes. However, while all amino acids showed a lower absolute abundance (with the exception of aspartic acid), some amino acids showed a higher relative abundance in the total amino acid pool compared to the reference strain. Interestingly, a higher relative abundance was found for the branched-chain amino acids leucine, isoleucine and valine. Branched-chain amino acid metabolism in general, and leucine metabolism in particular, has been linked to lipid metabolism by several studies. A higher relative abundance was also found for the aromatic amino acids phenylalanine, tryptophan and tyrosine.

The interaction of lipid metabolism and amino acid metabolism highlights the complexity of the metabolic network in *Saccharomyces cerevisiae*. Studying this interaction in more detail will lead to more information about how these pathways relay information, and will lead to identification of metabolites and proteins involved in signaling.

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