41. Regulatory Changes During Lipid Accumulation in Yarrowia lipolytica

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Project Goals: Our goal is to elucidate the regulation of lipid metabolism in Y. lipolytica to identify new targets to improve the TAG yield.

Oleaginous yeasts such as Yarrowia lipolytica are capable of accumulating lipids up to 70% of their biomass, predominantly in the form of triacylglycerols (TAGs), and this has fuelled interest in exploiting these fungi for the production of biodiesel. Y. lipolytica can use different carbon sources—including a genetic mutant that can grow on xylose—but TAG yields vary considerably under different growth conditions. To further optimise these yields, we are studying the metabolic fluxes and their regulation in Y. lipolytica in different growth conditions on a genomic scale.

A high lipid producing Y. lipolytica strain, with increased expression of diacylglycerol acyltransferase (DGA1), was compared during nitrogen and carbon restricted growth in chemostats at a constant dilution rate of 0.05 h-1. At steady state lipid and fatty acid compositions were determined, together with proteomics (performed under the Pan-omics Program at PNNL) and transcriptomics (RNAseq) measurements. All data were integrated using an updated genome-scale model of metabolism (GEM). Changes in internal fluxes were estimated by random sampling of the GEM solution space.

Regulation on the level of mRNA and protein abundances were primarily focused on reducing nitrogen requirements, while only limited regulation of lipid metabolism was observed. Correlation of changes in mRNA, protein and estimated flux levels were indicative of potentially transcriptionally regulated reactions.