Leucine Biosynthesis is Involved in Regulating High Lipid Accumulation in \textit{Yarrowia lipolytica}

Eduard J. Kerkhoven$^1$ (eduardk@chalmers.se), Young-Mo Kim$^2$, Siwei Wei$^2$, Carrie D. Nicora$^2$, Thomas L. Fillmore$^2$, Samuel O. Purvine$^2$, Bobbie-Jo Webb-Robertson$^3$, Richard D. Smith$^2$, Scott E. Baker$^2$, Thomas O. Metz$^2$, \textbf{Jens Nielsen}$^1$

$^1$ Chalmers University of Technology, Gothenburg, Sweden; $^2$ Earth and Biological Sciences Directorate, Pacific Northwest National Laboratory, Richland, WA; $^3$ National Security Directorate, Pacific Northwest National Laboratory, Richland, WA

Project Goals: Our goal is to elucidate the regulation of lipid metabolism in \textit{Yarrowia lipolytica} to identify new targets to improve the TAG yield.

The yeast \textit{Yarrowia lipolytica} is a potent accumulator of lipids and lipogenesis in this organism can be influenced by a variety of factors, such as genetics and environmental conditions. We have previously identified the involvement of the regulation of amino-acid metabolism to redirect flux to lipid accumulation [1]. We have followed up on this using a multifactorial study, thereby elucidating the effects of both genetic and environmental factors on regulation of lipogenesis in \textit{Y. lipolytica} and identifying how two opposite regulatory states both result in lipid accumulation.

The study involved the comparison of a strain overexpressing diacylglycerol acyltransferase (\textit{DGA1}) with a control strain grown under either nitrogen or carbon limited conditions. A strong correlation was observed between the responses on the levels of transcript and protein. Combination of \textit{DGA1} overexpression with nitrogen limitation resulted in high-level of lipid accumulation accompanied by downregulation of various amino acid biosynthetic pathways, with leucine in particular, and these changes were further correlated with a decrease in metabolic fluxes.

The downregulation in leucine biosynthetic pathway genes was supported by a measured decrease in the level of 2-isopropylmalate, an intermediate of leucine biosynthesis. Combining the multi-omics data with putative transcription factor binding motifs uncovered a contradictory role for TORC1 in controlling lipid accumulation, likely mediated through 2-isopropylmalate and a Leu3-like transcription factor.

\textbf{References}


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