

99. Regulation of lipid metabolism in *Yarrowia lipolytica*

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Project goals: This project aims to elucidate the regulation of lipid metabolism in *Y. lipolytica* under different growth conditions. This will allow us 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.

An updated genome-scale model of metabolism (GEM) was generated for *Y. lipolytica*, based on literature data and homology with related species. A set of possible flux distributions can be obtained by random sampling of the GEM solution space, constrained by a small set of measured metabolic fluxes. The obtained statistics allow estimation of the significance of changes in metabolic fluxes in different conditions, and this can be compared to observed changes in transcript levels.

To validate the model, a genetic mutant overexpressing the last enzyme of TAG synthesis was compared to wild-type *Y. lipolytica* during growth at high and low C/N-ratios.

Measurements were taken of metabolic fluxes, lipid composition and transcript levels. Integration of the experimental data with the *in silico* model gives insight on the regulation of *lipolytica* metabolism and how the TAG yield can be further improved.