47. Improving de novo lipids production through engineering the availability of cytosolic NADPH in Yarrowia lipolytica

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Project Goals: We focused on achieving a fundamental understanding of the metabolism of the oleaginous yeast Yarrowia lipolytica and developing tools to characterize and engineer it towards cost-effective lipids production. More specifically, we aimed to improve its fermentation characteristics towards the development of a cost-effective process which converts renewable resources to lipids for biodiesel production. The conversion yield and volumetric productivity on various carbon sources are the key metrics for optimization.

Fatty acids are an important product that can be used for the production of biofuels such as biodiesel. Living organisms share the enzymatic machinery to biosynthesize fatty acids. De novo biosynthesis of fatty acid is an energy-intensive process, requiring two NADPH and one ATP to install one two-carbon brick-acetyl-CoA onto fatty acid chain. Oxidative pentose phosphate pathway was found to provide majority of the intracellular NADPH supporting lipogensis in most of the organisms, in particular, oleaginous yeast Yarrowia lipolytica in light of recent performed flux analysis of lipid hyper-producing strain ACCDGA. Engineering NADPH availability could potentially improve the yield and productivity of lipids. Toward this end, six different strategies have been tested to enrich the cytosolic NADPH in Y. lipolytica and three of them were demonstrated to be effective. In the 2 liter bioreactor experiments, the engineered strain exhibited an improved lipid productivity and yield comparing to the control strain ACCDGA. Our investigation here has sucessfully demonstrated that increasing the engineering NADPH availability is an effective strategy towards cost-effective productions of lipids from glucose using oleaginous yeast.