Effects of overexpression of STB5 in Saccharomyces cerevisiae on fatty acid biosynthesis, physiology and transcriptome - DTU Orbit (04/11/2019)

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Microbial conversion of biomass to fatty acids (FA) and products derived thereof is an attractive alternative to the traditional oleochemical production route from animal and plant lipids. This study examined if NADPH-costly FA biosynthesis could be enhanced by overexpressing the transcription factor Stb5 in Saccharomyces cerevisiae. Stb5 activates expression of multiple genes encoding enzymes within the pentose phosphate pathway (PPP) and other NADPH-producing reactions. Overexpression of STB5 led to a decreased growth rate and an increased free fatty acid (FFA) production during growth on glucose. The improved FFA synthetic ability in the glucose phase was shown to be independent of flux through the oxidative PPP. RNAseq analysis revealed that STB5 overexpression had wide-ranging effects on the transcriptome in the batch phase, and appeared to cause a counterintuitive phenotype with reduced flux through the oxidative PPP. During glucose limitation, when an increased NADPH supply is likely less harmful, an overall induction of the proposed target genes of Stb5 (eg. GND1/2, TAL1, ALD6, YEF1) was observed. Taken together, the strategy of utilizing STB5 overexpression to increase NADPH supply for reductive biosynthesis is suggested to have potential in strains engineered to have strong ability to consume excess NADPH, alleviating a potential redox imbalance.

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