Heterologous transporter expression for improved fatty alcohol secretion in yeast - DTU Orbit (01/12/2018)

**Heterologous transporter expression for improved fatty alcohol secretion in yeast**

The yeast Saccharomyces cerevisiae is an attractive host for industrial scale production of biofuels including fatty alcohols due to its robustness and tolerance towards harsh fermentation conditions. Many metabolic engineering strategies have been applied to generate high fatty alcohol production strains. However, impaired growth caused by fatty alcohol accumulation and high cost of extraction are factors limiting large-scale production. Here, we demonstrate that the use of heterologous transporters is a promising strategy to increase fatty alcohol production. Among several plant and mammalian transporters tested, human FATP1 was shown to mediate fatty alcohol export in a high fatty alcohol production yeast strain. An approximately five-fold increase of fatty alcohol secretion was achieved. The results indicate that the overall cell fitness benefited from fatty alcohol secretion and that the acyl-CoA synthase activity of FATP1 contributed to increased cell growth as well. This is the first study that enabled an increased cell fitness for fatty alcohol production by heterologous transporter expression in yeast, and this investigation indicates a new potential function of FATP1, which has been known as a free fatty acid importer to date. We furthermore successfully identified the functional domain of FATP1 involved in fatty alcohol export through domain exchange between FATP1 and another transporter, FATP4. This study may facilitate a successful commercialization of fatty alcohol production in yeast and inspire the design of novel cell factories.

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