In silico identification of gene targets to enhance C12 fatty acid production in Escherichia coli

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Abstract

The global interest in fatty acids is steadily rising due to their wealth of industrial potential ranging from cosmetics to biofuels. Unfortunately, certain fatty acids, such as monounsaturated C12, cannot be produced cost and energy-efficiently using conventional methods. Biosynthesis of fatty acids using microorganisms can overcome this drawback. However, rewiring a microbe's metabolome for increased production remains challenging. To overcome this, sophisticated genome-wide metabolic network models have become available. These models predict the effect of genetic perturbations on the metabolism, thereby serving as a guide for metabolic pathways optimization. In this work, we used constraint-based modeling in combination with the algorithm Optknock to identify gene deletions in *Escherichia coli* that improve the C12 fatty acid production. Nine gene targets were identified that, when deleted, were predicted to increase C12 titers. Targets play a role in anaplerotic reactions, amino acid synthesis, carbon metabolism and cofactor-balancing. Subsequently, we constructed the corresponding (combinatorial) deletion mutants to validate the *in silico* predictions *in vivo*. Our highest producer (Δ *maeB* Δ *ndk* Δ *pykA*) reaches a titer of 6.7 mg/L, corresponding to a 7.5-fold increase in C12 fatty acid production. This study demonstrates that model-guided metabolic engineering is a useful tool to improve C12 fatty acid production.

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