High production of fatty alcohols in *Yarrowia lipolytica* by coordination with glycolysis

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Abstract

Fatty alcohol biosynthesis by oleaginous microbes was a promising alternative to the petroleum or other non-renewable resources-based process. However, low titer and yield hampers the further industrial and commercial applications. Here, we developed a novel and efficient strategy to coordinate fatty alcohol synthesis with glycolysis which achieved a 'pull-and-push' effect to improve fatty alcohol production. Transcript profiling indicated that genes in carbohydrate metabolism were up-regulated significantly in response to higher fatty alcohol production. Based on it, 11 glycolysis promoters were screened to express fatty acyl-CoA reductase (*FAR*) to corelate the fatty alcohol production with the up-regulated carbohydrate metabolism, and the fatty alcohol production reached to 557 mg/L when *FAR* was expressed by the promoter of P_{FBAin}. RNA-seq and qRT-PCR analysis demonstrated that a 'pull-and-push' effect caused by the coordination system dynamically enhanced the product synthesis flux from top to bottom, which was also testified and intensified by doubled glucose concentration. After manipulating structural and regulatory genes of lipid metabolism, the final strain achieved up to 5.75 g/L fatty alcohol production from modified YPD medium (containing 91 g/L glucose) in shake flasks, which represented the highest titer reported to date. This work not only offered a reference for dynamic coordination of biofuel synthesis, but also provided a feasible and effective platform of *Y. lipolytica* for fatty acid-derived chemicals production.

Brief Biography

Dr. Yingxiu Cao is a master supervisor in Tianjin University. Her researches mainly focus on the field of metabolic engineering and synthetic biology, including microbial biosynthesis of fuels and pharmaceutical chemicals and development of novel genomic regulation and engineering tools. She has created a serios of microbial cell factories to efficiently produce biofuels (fatty alkanes), antitumor drugs (betulinic acid), surfactants (fatty alcohols and surfactin), and degradable plastics (PHB) with novel strategies. Besides, she has developed a serious of toolkits or strategies for gene manipulation, such as a combined CRISPRi–sRNA transcriptional–translational regulation technology and a multiplex gRNAs strategy based on one-step Golden-brick assembly technology. She has published 26 SCI papers in reputational journal including *Metabolic Engineering*, *ACS Synthetic Biology*, *ACS Synthetic Biology* et al. She obtained Young Elite Scientists Sponsorship Program by Tianjin. She also won Third Class Prize for Science & Technology Progress of China Petroleum and Chemical Industry Association (CPCIA). She serves as a Review Editor on the Editorial Board of the journal Frontiers in Bioengineering and Biotechnology.

Brief CV

Yingxiu Cao, Ph.D.

School of Chemical Engineering and Technology (SCET), Tianjin University

Education:

B.S Dept. Biological Engineering, SCET, Tianjin University, China, 2008

Ph.D. Dept. Biochemical Engineering, SCET, Tianjin University, China, 2014

Professional Career:

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Research Interests:

1. Metabolic Engineering and Synthetic Biology
2. Microbial Biosynthesis of Fuels and Pharmaceutical Chemicals
3. Development of Novel Genomic Regulation and Engineering Tools

Selected publications

[1] **Cao YX,** Xiao WH, Liu D, Zhang JL, Ding MZ, Yuan YJ*. Biosynthesis of odd-chain fatty alcohols in *Escherichia coli*. ***Metab Eng***. 2015, 29:113-123.

[2] **Cao YX#,** Xiao WH#, Zhang JL, Xie ZX, Ding MZ, Yuan YJ*. Heterologous biosynthesis and manipulation of alkanes in Escherichia coli. ***Metab Eng***. 2016, 38:19-28.

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[6] **Cao YX#**, Li XF#, Li F, Song H*. CRISPRi-sRNA: transcriptional-translational regulation of extracellular electron transfer in *Shewanella oneidensis*. ***ACS Synth Biol***. 2017, 6:1679–1690.

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