Production of Carotenoids by Chassis Engineering and Modular Enzyme Assembly in Microbe

Tiangang Liu[a,b]

[a]Key Laboratory of Combinatorial Biosynthesis and Drug Discovery, Ministry of Education, Wuhan University School of Pharmaceutical Sciences, Wuhan 430071, P.R.China.
[b]Hubei Engineering Laboratory for Synthetic Microbiology, Wuhan Institute of Biotechnology, Wuhan 430075, P.R.China
Email: liutg@whu.edu.cn

Abstract

Saccharomyces cerevisiae is an efficient host for natural-compound production and preferentially employed in academic studies and bioindustries. However, restricted by the lipophilic and the cytotoxicity nature, high-yield production of carotenoids is restricted. To solve this problem, a nature-inspired strategy was employed to establish an effective platform to improve lipid oil–triacylglycerol (TAG) metabolism and enable increased lycopene accumulation. After the overexpression of fatty acid desaturase (OLE1) and deletion of Seipin (FLD1) in well-engineered high-yield lycopene overproduction strain, production of lycopene was further increased from 56.2 to 70.5 mg lycopene/g cdw, 2.37 g/L and 73.3 mg/g cdw in fed-batch fermentation, representing the reported highest lycopene yield in *S. cerevisiae*.[1]

In addition to increasing the productivity, modular enzyme assembly can facilitate the overproduction of carotenoids by enhancing cascade biocatalysis and metabolic flux. In our laboratory, a pair of short peptide tags (RIAD and RIDD) was utilized *in vitro* and *in vivo*. Upstream IDI and the first dedicated downstream enzyme CrtE of carotenoid biosynthetic pathway were assembled through the RIAD–RIDD pair to form a pathway node that physically links the two pathways. Markedly increases the metabolic flux, and results in 5.7-fold titer increase of carotenoids in laboratory-scale fermentation. This strategy is also successfully applied in *S. cerevisiae* and made 58% improvement of lycopene production, the highest record in literature.[2] Presents a new strategy to impose metabolic control in biosynthetic microbe factories – a method that is facile, efficient, orthogonal with other metabolic engineering methods, and universally applicable in both *E. coli* and *S. cerevisiae*.

References:

[1] Ma, T., Shi, B., Ye, Z., Li, X., Liu, M., Chen, Y., ... & Liu, T*. (2019). Lipid engineering combined with systematic metabolic engineering of *Saccharomyces cerevisiae* for high-yield production of lycopene. Metabolic Engineering, 52, 134-142.

[2] Kang, W., Ma, T., Qu, J., Zhang, H., Shi, B., Fu, S., & Deng, Z., Xia, J.,* Liu, T.*. 2019. Modular enzyme assembly for enhanced cascade biocatalysis and metabolic flux. Nature communication. Accepted.

Brief Biography

Tiangang Liu (Professor in the School of Pharmaceutical Sciences at Wuhan University) received his PhD in 2008 at Shanghai Jiao Tong University, China. After completing postdoctoral studies in the department of Chemical Engineering, he joined Wuhan University in 2010. He is selected into National Top-Notch Young Talents Program of National High-level Personnel of Special Support Program and National Natural Science Funds for Excellent Young Scholar. He is also one of project leaders for National Key R&D Program of China for Synthetic Biology. He is associate editor for Metabolic Engineering Communications, and serve as editorial board for ACS Synthetic Biology, Biotechnology Journal, etc. His research interest focused on overproduction of value-added chemicals by engineering of the interested pathways, overproduction of pharmaceuticals and its precursors by using synthetic biology strategies and high throughput genome mining of new compounds utilizing synthetic biology strategies.

Brief CV

Tiangang Liu, Ph.D.

Key Laboratory of Combinatorial Biosynthesis and Drug Discovery

(Wuhan University), Ministry of Education, Wuhan University

Education:

- B.S. Microbial engineering, School of Life Science (2002), Shandong University, China
- Exchange Ph.D student, Department of Chemistry(2006-2007), Brown University, USA
- Ph.D. Microbiology(2008), School of Life Science & Biotechnology, Shanghai Jiaotong University, China

Professional Career:

- Director, Hubei Engineering Laboratory for Synthetic Microbiology, China
  Deputy Chief Engineer, Wuhan Institute of Biotechnology, China (2012-)
- Professor, Wuhan University School of Pharmaceutical Sciences, Key Laboratory of Combinatorial Biosynthesis and Drug Discovery, Ministry of Education, China (2010.9-)

- Post-doc researcher, Department of Chemistry, Stanford University, USA (2008-2010)

Research Interests:

1. Synthetic biology
2. Metabolic Engineering

Selected publications

1. Kang W. et al. ***Nature Communications.***, 2019, Accepted.
2. Ma T. et al. ***Metabolic Engineering****,* 2019*,* 52: 134-142
3. Bian G. et al. ***Angew Chem Int Ed Engl****,* 2018, 57:15887-15890.
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10. Guo D. et al. ***Metabolic Engineering***, 2014, 22, 69-75.