

Strategies for construction of efficient microbial cell factories: enzyme, pathway and metabolic network

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Abstract

With the development of metabolic engineering and synthetic biology, biosynthesis of chemicals has become a promising alternative to chemical synthesis. To meet the requirement for commercial application, the performance of microbial cell factories need to be systematically optimized. Herein, we present several examples of improving production efficiency at the levels of enzyme, pathway and metabolic network. First, a diol dehydratase was engineered to catalyze non-natural substrate 1,2,4-butanetriol. Based on this enzyme, an artificial pathway was constructed to achieve 1,4-butanediol production via non-phosphorylated xylose metabolism. Second, glutarate production via lysine was significantly improved by creating multiple driving forces and preventing escape of pathway intermediates. The driving forces are generated by recycling glutamate and NADPH, releasing the feedback inhibition and boosting precursor supply. In addition, new activities of native transporters for intermediate influx are discovered, which results in glutarate production with both high titer and yield. Third, a synergetic carbon utilization mechanism (SynCar) was designed, in which glucose catabolism is inactivated and a second carbon source is employed to maintain cell growth. Glucose uptake and glycerol catabolism was coupled via the PTS system. Using the resultant platform strain, efficient production of trehalose and inositol was achieved. Our work provides a systematic and comprehensive research foundation for the large-scale synthesis of value-added products in microbial cell factories.

Speaker's biography

Dr. Qipeng Yuan is a Changjiang Distinguished professor at Beijing University of Chemical Technology and the associate director of State Key Laboratory of Chemical Resource Engineering. He received his Bachelor's degree in Chemical Engineering from Tsinghua University in 1992 and his Ph.D in Biochemical Engineering from Tianjin University in 2007. His research focuses on Isolation and extraction of bioactive compounds, Enzymatic bioconversion, Metabolic Engineering and synthetic biology. He has published over 200 peer-reviewed research and review papers on journals such as Nature Communications, Metabolic Engineering and ACS Synthetic Biology. He holds more than 50 patents, several of which have been commercialized.



Brief CV

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Education:

BS Chemical Engineering, Tsinghua University, China, 1992
MS Bioengineering, Tianjin University, China, 1994
Ph.D. Bioengineering, Tianjin University, China, 1997

Professional Career:

1997-1999: Beijing University of Chemical Technology, China, Postdoc.
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Research Interests:

1. Isolation and extraction of Bioactive compounds
2. Enzymatic bioconversion
3. Metabolic Engineering and Synthetic Biology

Selected publications

1. Wang, J., Yuan QP*. et al. ***Metabolic Engineering***, 2017, 40.
2. Li, W., Yuan QP*. et al. ***Nature Communications***, 2019, 10.
3. Wu, Y., Yuan QP*. et al. ***Metabolic Engineering***, 2017, 39.