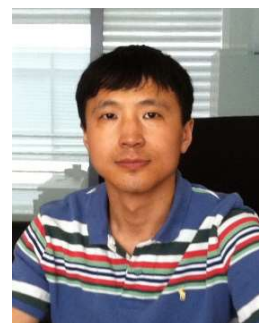


De novo biosynthesis of vitamin B₁₂ in *E. coli*

Name

Professor of Biotechnology and Bioengineering;
Tianjin Institute of Industrial Biotechnology,
Chinese Academy of Sciences, 300308 Tianjin, China
Email: zhangdawei@tib.cas.cn



Abstract

The only known source of vitamin B₁₂ (adenosylcobalamin) is from bacteria and archaea, and the only unknown step in its biosynthesis is the production of the intermediate adenosylcobinamide phosphate. Here, using genetic and metabolic engineering, we generated an *Escherichia coli* strain that produces vitamin B₁₂ via an engineered *de novo* aerobic biosynthetic pathway. Excitingly, the BluE and CobC enzymes from *Rhodobacter capsulatus* transform L-threonine into (R)-1-Amino-2-propanol O-2-Phosphate, which is then condensed with adenosylcobyrinic acid to yield adenosylcobinamide phosphate by either CobD from the aerobic *R. capsulatus* or CbiB from the anaerobic *Salmonella typhimurium*. These findings suggest that the biosynthetic steps from co(II)byrinic acid a,c-diamide to adocobalamin are the same in both the aerobic and anaerobic pathways. Finally, we increased the vitamin B₁₂ yield of a recombinant *E. coli* strain by more than ~250-fold to 307.00 µg/g DCW via metabolic engineering and optimization of fermentation conditions. Beyond our scientific insights about the aerobic and anaerobic pathways and our demonstration of *E. coli* as a microbial biosynthetic platform for vitamin B₁₂ production, our study offers an encouraging example of how the several dozen proteins of a complex biosynthetic pathway can be transferred between organisms to facilitate industrial production.

Brief Biography

Prof. Dawei Zhang received his PhD from Beijing University of Chemical Technology in 2007. After performing his postdoctoral research at University of Wisconsin Milwaukee and California Institute of Technology from 2007 to 2012, he joined Tianjin Institute of Industrial Biotechnology, Chinese Academy of Sciences. He is currently the leader of Protein Expression and Microbial Metabolic Engineering Group. His group integrates genetic engineering, synthetic biology and systematic biology tools to (1) construct microbial cell factory to produce amino acids, vitamins and other valuable natural products; (2) construct and optimize the protein secretion pathway in *Bacillus* species for industrial enzyme production. He has published more than 30 peer reviewed research and review articles on prestigious journals, such as Nature Communications, J Biol Chem, JACS, ACS Synthetic Biology, Scientific Reports and Microbial Cell Factories.

Brief CV

Dawei Zhang, Ph.D.

Tianjin Institute of Industrial Biotechnology, Chinese Academy of Sciences, Professor, PI

Education:

BS Bioengineering, Dalian Polytech University, China, 2001

MS Plant protection and plant virus, Anhui Agriculture University, China, 2004

Ph.D. Bioengineering, Beijing University of Chemical technology, China, 2007

Professional Career:

2007-2008: University of Wisconsin, Milwaukee, Postdoc.

2008-2012: California Institute of Technology, Postdoc.

2012-date: Tianjin Institute of Industrial Biotechnology, Chinese Academy of Sciences,
Professor

Research Interests:

1. Metabolic engineering
2. Microbial Systems and Synthetic Biology
3. Protein expression system construction

Selected publications

1. Metabolic engineering of *Escherichia coli* for de novo biosynthesis of vitamin B12. Nature Communications. (2018) volume 9, Article number: 4917
2. Engineering a vitamin B12 high-throughput screening system by riboswitch sensor in *Sinorhizobium meliloti*. BMC Biotechnol. 2018 May 11;18(1):27
3. Biosensor-based evolution and elucidation of a biosynthetic pathway in *Escherichia coli*. ACS Synthetic Biology. 2017 May 19;6(5):837-848.
4. Microbial production of vitamin B12: A review and future perspectives. Microbial Cell Factories. 2017 Jan 30;16(1):15