A nature inspired route toward the synthesis of nonnatural straight-chain amino acids

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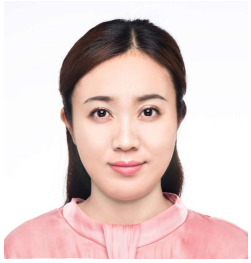

Abstract

Bioplastics produced from microbial source are promising green alternatives to traditional petrochemical-derived plastics. Nonnatural straight-chain amino acids, especially 5-aminovalerate, 6-aminocaproate and 7-aminoheptanoate are potential monomers for the synthesis of polymeric bioplastics as their primary amine and carboxylic acid are ideal functional groups for polymerization. Previous pathways for 5-aminovalerate and 6-aminocaproate biosynthesis in microorganisms are derived from L-lysine catabolism and the citric acid cycle, respectively. Here, we show the construction of a nature inspired carbon-chain-extension cycle in *Escherichia coli* for simultaneous production of a series of nonnatural amino acids with varying chain length. Overexpression of L-lysine α-oxidase in *E. coli* yields 2-keto-6-aminocaproate (2K6AC) as a non-native substrate for the artificial iterative carbon-chain-extension cycle. The chain-extended α-ketoacid products are decarboxylated and oxidized by an α-ketoacid decarboxylase and an aldehyde dehydrogenase, respectively, to yield their corresponding nonnatural straight-chain amino acids. The engineered system demonstrated simultaneous *in vitro* production of 99.16 mg/L of 5-aminovalerate, 46.96 mg/L of 6-aminocaproate and 4.78 mg/L of 7-aminoheptanoate after 8 hours of enzyme catalysis starting from 2K6AC as the substrate. Furthermore, simultaneous production of 2.15 g/L of 5-aminovalerate, 24.12 mg/L of 6-aminocaproate and 4.74 mg/L of 7-aminoheptanoate was achieved in engineered *E. coli*. This work illustrates a promising metabolic-engineering strategy to access other medium-chain organic acids with $-NH_2$, $-SCH_3$, $-SOCH_3$, -SH, -COOH, -COH, or -OH functional groups through carbon-chain-elongation chemistry.

Brief Biography

Dr. Dan Wang has worked as an Associate Professor in Chemical Engineering at Chongqing University since Sep. 2011. She obtained her Ph.D. in 2011 at Institute of Process Engineering, Chinese Academy of Sciences. She worked as a Research Associate at Rice University, USA, from 2013 to 2015. She was a visiting scholar in Massachusetts Institute of Technology and Institute of Whitehead, USA. Her research interests lies in Synthetic Biology and Bio-catalysis, Gene Regulation and Gene Circuits, Tumor Therapy and Separation and Purification to obtain the final product. She won the excellent award of the president award of the president of the Chinese Academy of Sciences. She was also selected as the Young Scientist by IUPAC. She has published more than 40 papers in Peer-Reviewed Journals including Metabolic Engineering, Biotechnology and Bioengineering, Bioresource Technology and Journal of Industrial Microbiology and Biotechnology.

Brief CV

Associate Professor, Ph.D.

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Education:

B.S Chemical Engineering, Sichuan University, Chengdu, China, 2005

Ph.D. Biochemical Engineering, Institute of Process Engineering, Chinese Academy of Sciences, Beijing, China, 2011

Professional Career:

2013-2015: Rice University, Houston, US, Postdoctoral Fellow.

2011-2013: Chongqing University, Chongqing, China, Assistant Professor.

2018-2018: Massachusetts Institute of Technology, Boston, US, Visiting Scholar.

2013-Present: Chongqing University, Chongqing, China, Associate Professor.

Research Interests:

1. Gene Regulation and Gene Circuits
2. Synthetic Biology and Bio-catalysis
3. Tumor Therapy

Selected publications

1. Cheng, J. et al. ***Metab. Eng.***, 2019, 55:23-32.
2. Huang, M. et al. ***J. Environ. Manag.***, 2019, 237:147-154.
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4. Cheng, J. et al. ***J. Ind. Microbiol. Biotechnol.***, 2018, 45:405-415.
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6. Qin, D. et al. ***Bioresour. Technol.***, 2016, 221:375-384.
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8. Wang, D. et al. ***Biotechnol. Bioeng.***, 2015, 112:2324-2333.
9. Wang, D. et al. ***Biotech. Prog.*** 2015, 31:686-694.
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