

P450 Monooxygenases Mediated Artificial Biosynthetic Pathways Construction for Chemical Synthesis

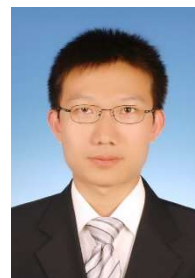
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Abstract

Cytochrome P450 monooxygenases can catalyze reactions including inert C-H bond hydroxylation, sulfoxidation, dealkylation and *etc.*, which has a wide range of applications in the fields of medicine, agriculture, environment and energy. Nowadays, the P450 enzyme related research has become a hot topic. In this study, we successfully engineered the P450BM3 monooxygenase derived from *Bacillus megaterium* by developing a new, rapid and efficient directed evolution strategy, which was then successfully used in artificial biosynthetic pathways construction for value-added chemical synthesis: 1. Firstly, a novel whole-cell catalyst was engineered by rational design based on P450BM3 mutants, which could transform the cyclohexane to produce corresponding chiral diols via a four-step cascade catalytic reaction; 2. Secondly, a P450BM3 mutant with high activity and regioselectivity was obtained by developing a rational enzyme directed strategy, and the mutant was able to catalyze the selective dihydroxylation of benzene to hydroquinone. Using the classical MD/QM-MM, the unique molecular catalytic mechanism of P450 mutant catalyzed benzene dihydroxylation was elucidated. Finally, the P450-catalyzed hydroquinone formation was further coupled with a glycosyltransferase, which enabled efficient biosynthesis of arbutin from benzene. The above studies provide an important idea for the efficient construction of non-natural biosynthetic pathways for the efficient synthesis of high value-added chemical products in a green manner.

Brief Biography

Prof. Aitao Li is now serving as vice director of State Key Laboratory of Biocatalysis and Enzyme Engineering in Hubei University. He received Ph.D. degree in fermentation engineering from East China University of Science and Technology in 2010. He joined National University of Singapore as a Research Fellow in 2011, and then Max-Planck Institute for Coal Research as a postdoctoral research fellow in 2014. He joined Hubei University as a professor at college of life sciences in 2017, and his research interest focuses on protein engineering, enzyme discovery, and biocatalysis and biotransformation. He has published more than 40 papers in prestigious journals including Nature Communications, Angewandte Chemie International Edition and ACS catalysis with a citation more than 800 and H-index of 23.

Brief CV

Aitao Li, Ph.D. Professor
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Education:

BS Bioengineering, Hebei University of Technology, China, 2001
Ph.D. Fermentation engineering, East China University of Science and Technology, China
2011

Professional Career:

2011-2014: National University of Singapore, Singapore, Research Fellow.
2014-2017: Max-Planck Institute for Coal Research, Postdoctoral Research Fellow.
2017-date: College of Life Sciences, Hubei University, Professor

Research Interests:

1. Enzyme Discovery
2. Protein Engineering
3. Biocatalysis and Biotransformation

Selected publications

1. Zhou, H. Li, A^{*} et al. *Angew. Chem. Int. Ed.* 2019, 58, 764–768.(Cover Story)
2. She, W. Li, A^{*} et al. *ACS Synthetic Biology*, 2018, 7, 2236-2244.(Cover Story)
3. He, Y. Li, A^{*} et al. *Green Chemistry*, 2017, 19, 3844-3850.
4. Li, A. et al. *Nature Communications*, 2017, 8, 14876.
5. Li, A. et al. *Angew. Chem. Int. Ed.* 2016, 128,12205-12208
6. Li, A.[#] Qu G.[#] et al. *ACS catalysis*, 2019 accepted
7. Qu G.[#] Li, A.[#] et al. *Angew. Chem. Int. Ed.* 2019 accepted.