

Computational Design of Novel one-carbon assimilation pathways

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Abstract

The utilization of one-carbon (C₁) assimilation pathways to produce chemicals and fuels from low-cost C₁ compounds could greatly reduce the substrate-related production costs, and would also alleviate the pressure of the resource supply for bio-manufacturing. However, the natural C₁ assimilation pathways normally involve ATP consumption or the loss of carbon resources as CO₂, resulting in low product yields, making the design of novel pathways highly pertinent. Here we present several new ATP-independent and carbon-conserving C₁ assimilation cycles with 100% theoretical carbon yield, which were discovered by computational analysis of metabolic reaction set with 6,578 natural reactions from MetaCyc database and 73 computationally predicted aldolase reactions from ATLAS database. Then, kinetic evaluation of these cycles was conducted and the cycles without kinetic traps were chosen for further experimental verification. Finally, we used the two engineered enzymes Gals and TalB^{F178Y} for the artificial reactions to construct a novel C₁ assimilation pathway *in vitro* and optimized the pathway to achieve 88% carbon yield. These results demonstrate the usefulness of computational design in finding novel metabolic pathways for the efficient utilization of C₁ compounds and shedding light on other promising pathways.

Brief Biography

Dr Hongwu Ma got his Ph.D from Tianjin University, China in 2001. He then worked in German Research Centre for Biotechnology (GBF) as a postdoc and moved to the University of Edinburgh at the end of 2005 as a senior research fellow. He was appointed as a professor at Tianjin Institute of Industrial Biotechnology, Chinese Academy of Sciences at Dec 2011. He has been working on various research fields in Systems Biology, Bioinformatics and Synthetic Biology. Major research topics include: the reconstruction and analysis of large scale biological networks, modelling analysis of metabolic pathways and gene circuits, development of methods and tools for analysis and design of biological systems. He has published over 30 papers in international journals. He was awarded “Highly Cited Researchers” by Thomson Reuters in 2014 due to his highly cited papers on Bioinformatics.

Brief CV

Hongwu Ma, Ph.D.

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Education:

B.S Chemistry, Tianjin University, China, 1993

Ph.D. Biochemical Engineering, Tianjin University, China, 2001

Professional Career:

2001-2005: Germany Research Centre for Biotechnology, Postdoctoral Fellow.

2005-2011: School of Informatics, University of Edinburgh, UK, Senior Research Fellow.

2011-Present: Tianjin Institute of Industrial Biotechnology, Chinese Academy of Sciences, Professor.

Research Interests:

1. Computational biology
2. Microbial Systems and Synthetic Biology
3. Metabolic Engineering

Selected publications

1. Yang, X. et al. *Metabolic Engineering*, 2019, in revision.
2. Wang, Y. et al. *Biotech. Bioeng.*, 2019, Epub
3. Liu, D. et al. *Front Microbiol.* 2019, 10:1350.
4. Li, F. et al. *AMB Express*, 2018, 8:106.