

# **System metabolic and process engineering of a yeast-like fungus for polymalic acid and malic acid production**

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Polymalic acid (PMA) is a novel polyester polymer that has been broadly used in the medical and food industries. Its monomer, L-malic acid (MA), is also a potential C4 platform chemical. Recently, great researches have been attempted to develop biotechnological process for PMA and MA production. MA can be simply generated from PMA through acid hydrolysis, which become an alternative routine for MA production. In this study, we integrated multi-omics, genome-scale metabolic model and genome-editing technique to engineer the signaling pathway or key metabolic nodes for efficient PMA production. TOR signaling pathway was emphasized and found a potential switch *sch9* to regulate the flux of PMA and polysaccharide biosynthesis. Glyoxylate shunt were verified and redesigned to strengthen carbon flux for PMA synthesis. Subsequently, some nodes, including pyruvate carboxylase gene (*pyc*), malate synthase gene (*mls*), isocitrate lyase gene (*icl*), and carbon response transcription factor *cat8* gene, were overexpressed, respectively. Moreover, CRISPR/Cas9 system was successfully developed for knocking-out the *idh* gene in *A. pullulans*. Among of them, the OE:: *mls-icl-cat8* strain was showed the greatest PMA titer and yield (155 g/L and 0.70 g/g) with sucrose as the carbon source in 5-L fermentor. Some renewable biomass feedstocks, i.e. sugarcane molasses and xylose mother liquor, were well utilized for PMA biosynthesis.

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### **Education:**

PhD, 2006 – 2009 Biochemical Engineering, East China of Science and Technology

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### **Professional Career:**

2010 – 2012 Visiting scholar, Department of Chemical and Biomolecular Engineering, The University of Ohio State, USA

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### **Research Interests:**

Biopolymers and Chemicals Production

Biochemical Engineering

Biohealth and Biomedical Engineering

### **Selected publications**

- 1.Zou et al., *Critical Reviews in Biotechnology*, 2019, 39(3): 408-421
- 2.Zou et al., *Journal of Cleaner Production*, 2019, 230: 1074-1084.
- 3.Zou et al., *Applied Microbiology Biotechnology*, 2019, 103 (16): 6519-6527
- 4.Zou et al., *Biotechnology for Biofuels*, 2018,11: 94
5. Zou et al., *Journal of Biotechnology*, 2018, 275: 24-30.
6. Zou et al., *Microbial Cell Factories*, 2016, 15: 146.
7. Zou et al. *Biotechnology and Bioengineering*, 2013,110(8):2105-2113.