

演題: Smart Cell Factory Design for Muconate and Shikimate in *Escherichia coli*

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要旨:

3-Dehydroshikimate (DHS) is a useful starting metabolite for the biosynthesis of muconic acid (MA) and shikimic acid (SA), which are precursors of various valuable polymers and drugs. Here, we created an engineered *Escherichia coli* cell factory to produce a high titer of DHS as well as an efficient system for the conversion DHS into MA. First, the genes showing negative effects on DHS accumulation in *E. coli* were disrupted. In addition, the genes involved in DHS biosynthesis were overexpressed to increase the glucose uptake and flux of intermediates. The redesigned DHS-overproducing *E. coli* strain grown in an optimized medium produced approximately 117 g/L DHS in 7-L fed-batch fermentation, which is the highest level of DHS production demonstrated in *E. coli*.

To accomplish the DHS-to-MA conversion, which is originally absent in *E. coli*, a codon-optimized heterologous gene cassette was expressed as a single operon under a strong promoter in a DHS-overproducing E. coli strain. This redesigned *E. coli* grown in an optimized medium produced about 64.5 g/L MA in 7-L fed-batch fermentation. Similarly, the rationally designed shikimate-overproducing *E. coli* strain grown in an optimized medium also produced approximately 101 g/L of shikimate in 7-L fed-batch fermentation, which is the highest level of shikimate production reported thus far. Overall, rational cell factory design and culture process optimization for microbial-based shikimate production will play a key role in complementing traditional plant-derived shikimate production processes.

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