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ACCEPTED MANUSCRIPT

Engineering a short, aldolase-based pathway for (R)-1,3-butanediol production in *Escherichia coli*

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Abstract

Microbial processes can produce a wide range of compounds; however, producing complex and long chain hydrocarbons remains a challenge. Aldol condensation offers a direct route to synthesize these challenging chemistries and can be catalyzed by microbes using aldolases. Deoxyribose-5-phosphate aldolase (DERA) condenses aldehydes and/or ketones to β -hydroxyaldehydes, which can be further converted to value-added chemicals such as a precursor to cholesterol-lowering drugs. Here, we implement a short, aldolase-based pathway in *Escherichia coli* to produce (R)-1,3-BDO from glucose, an essential component of pharmaceutical products and cosmetics. First, we expressed a three step heterologous pathway from pyruvate to produce 0.3 g/L of (R)-1,3-BDO with a yield of 11.2 mg/g of glucose in wild-type E.

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