Methanol biotransformation enables efficient production of fatty acid from yeast

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Fatty acids and their derivatives are promising raw materials for

manufacturing advanced biofuels, detergents, lubricants, surfactants and so on. The current supply of fatty acids is mainly through extraction from plants, which requires large amounts of arable land.

Methanol is an ideal and renewable feedstock for biomanufacturing. Methanol biotransformation might provide a sustainable route for fatty acid production with independence from arable land and fresh water.

Recently, a research group led by Prof. Zhou Yongjin from the Dalian Institute of Chemical Physics (DICP) of the Chinese Academy of Sciences (CAS) has engineered yeast Ogataea polymorpha for efficient production of free fatty acids (FFA) from sole methanol by rewiring cellular metabolism and relieving the methanol toxicity.

This study was published in *Nature Metabolism* on July 11.

Yeast is widely used for baking and brewing, and is an ideal host for methanol-based biomanufacturing. However, cellular methanol metabolism is highly regulated and methanol toxicity might limit the biosynthetic efficiency. In particular, there is limited information connecting methanol toxicity, methanol metabolism and product biosynthesis.

The researchers observed growth deficiency of engineered FFA producing Ogataea polymorpha in methanol, and this deficiency was restored by adaptive laboratory evolution. Multi-omics analysis (genomics, transcriptomics and lipidomics) showed that FFA overproduction perturbed phospholipid hemostasis.

A metabolic rewiring in this superior host achieved a high level of FFA accumulation (up to 15.9 g/L).

"This work reveals the mechanisms of methanol toxicity during bio-

productions, and achieves efficient methanol biotransformation to value-added products for industrial applications," Prof. Zhou said.

More information: Jiaoqi Gao et al, Rescuing yeast from cell death enables overproduction of fatty acids from sole methanol, *Nature Metabolism* (2022). DOI: 10.1038/s42255-022-00601-0

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