

One-pot cascade preparation of dicarboxylic acids using engineered *Acetobacter malorum*

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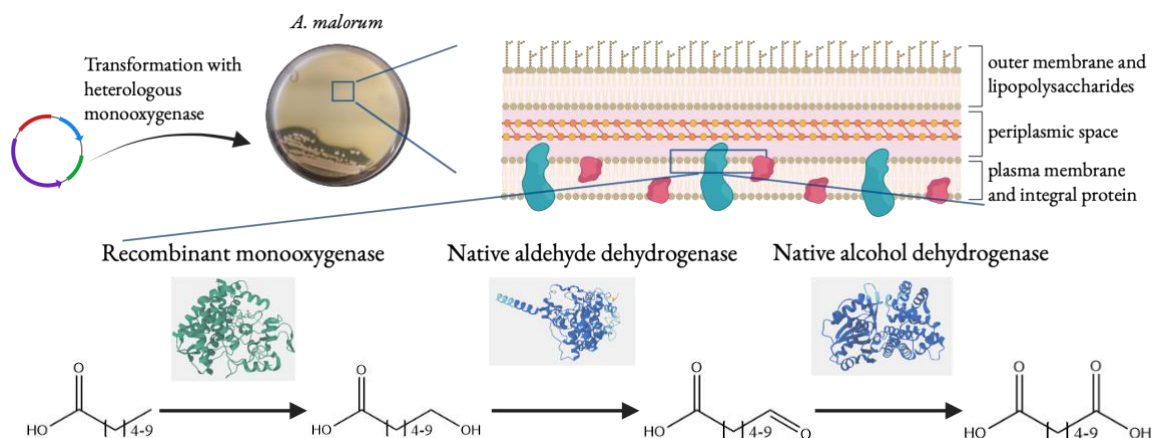
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This study addresses the growing demand for sustainable chemical production by exploiting acetic acid bacteria (AAB) as a biocatalytic platform for the development of building blocks for sustainable biopolymers. AAB are Gram-negative, strictly aerobic bacteria with a remarkable capacity to oxidize a broad range of sugars, alcohols and polyols [1]. This metabolic versatility is driven by membrane-bound and periplasmic dehydrogenases, which ensure high stereo- and regioselectivity in oxidation reactions. In this study, *Acetobacter malorum* DSM 112354 [2] demonstrated high conversion rates (ranging from 42 to 97%) in the oxidation of ω -hydroxycarboxylic acids to their corresponding C7–C12 dicarboxylic acids. Similar results were obtained using *A. malorum* cells immobilized within barium alginate beads.

A triple mutant of cytochrome P450 CYP153A_{M.aq} from *Marinobacter aquaeolei* (M.aqRLT) capable of catalyzing the selective hydroxylation of the terminal methyl group of different fatty acids [3] has been introduced into *A. malorum* to expand its biocatalytic potential. This strategy enables a multi-step, one-pot oxidation cascade that converts fatty carboxylic acids into the corresponding dicarboxylic acids. These compounds are useful building blocks for the synthesis of bio-based polymers, addressing the growing demand for sustainable plastic materials.



[1] He Y, Xie Z, Zhang H, Liebl W, Toyama H and Chen F (2022) Oxidative Fermentation of Acetic Acid Bacteria and Its Products. *Front. Microbiol.* 13:879246. doi: 10.3389/fmicb.2022.879246.

[2] Nespoli, L., Donzella, S., Moro, E. R., Mafezoli, J., Contente, M. L., Romano, D., & Molinari, F. (2025). Oxidation of benzyl alcohol derivatives into carboxylic acids with a new *Acetobacter malorum* strain: boosting the productivity in a continuous flow system. *Molecular Catalysis*, 571, 114698.

[3] Rapp, L. R., Marques, S. M., Zukic, E., Rowlinson, B., Sharma, M., Grogan, G., ... & Hauer, B. (2021). Substrate anchoring and flexibility reduction in CYP153A M. aq leads to highly improved efficiency toward octanoic acid. *ACS Catalysis*, 11(5), 3182-3189.