

Metabolic engineered microorganisms producing methyl anthranilate, a grape flavoring compound

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Methyl anthranilate (MANT) is a chemical that gives off grape scent and flavor widely used compound in flavoring foods and drugs, but it is currently produced by petroleum-based processes. Here, we report the fermentative production of MANT from glucose by metabolically engineered bacteria harboring a synthetic plant-derived metabolic pathway. Optimizing the key enzyme anthranilic acid (ANT) methyltransferase1 (AAMT1) expression, increasing direct precursor ANT supply, and enhancing intracellular availability and salvage of cofactor S-adenosyl-L-methionine required by AAMT1, results in improved MANT production in both engineered microorganisms. Furthermore, in situ two-phase extractive fermentation using tributyrin as an extractant is developed to overcome MANT toxicity. The metabolic engineering strategies developed here will be useful for the production of volatile aromatic esters including MANT. [This work was supported by the Technology Development Program to Solve Climate Changes on Systems Metabolic Engineering for Biorefineries from the Ministry of Science and ICT through the National Research Foundation (NRF) of Korea (Grants NRF-2012M1A2A2026556 and NRF-2012M1A2A2026557).]