Establishing a synthetic pathway for high-level production of 3-hydroxypropionic acid in Saccharomyces cerevisiae via β-alanine

Microbial fermentation of renewable feedstocks into plastic monomers can decrease our fossil dependence and reduce global CO2 emissions. 3-Hydroxypropionic acid (3HP) is a potential chemical building block for sustainable production of superabsorbent polymers and acrylic plastics. With the objective of developing Saccharomyces cerevisiae as an efficient cell factory for high-level production of 3HP, we identified the β-alanine biosynthetic route as the most economically attractive according to the metabolic modeling. We engineered and optimized a synthetic pathway for \textit{de novo} biosynthesis of β-alanine and its subsequent conversion into 3HP using a novel β-alanine-pyruvate aminotransferase discovered in Bacillus cereus. The final strain produced 3HP at a titer of $13.7\pm0.3 \text{ g} \cdot \text{L}^{-1}$ with a $0.14\pm0.0 \text{ C-mol} \cdot \text{C-mol}^{-1}$ yield on glucose in 80 hours in controlled fed-batch fermentation in mineral medium at pH 5, and this work therefore lays the basis for developing a process for biological 3HP production.

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