

Implementing a new synthetic pathway by coordinating intracellular redox balance for butyric acid production in *Escherichia coli*

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Biorefinery, as the future-oriented technology, is leading to a new manufacturing paradigm for the industrial synthesis of chemicals from renewable biomass. However, one of the challenges in the biorefinery is a low-yield conversion process limited by efficiency of the biocatalysts. In this study, the native redox cofactor regeneration system in *Escherichia coli* was engineered to implement non-native synthetic pathway for production of butyric acid. The engineered strain JHL26, which regenerate  $\text{NAD}^+$  from NADH using butyrate as the only final electron acceptor enabled high-yield production of butyric acid from glucose (83.4% of the molar theoretical yield). The high selectivity for butyrate, with a butyrate/acetate ratio of 41, suggests dramatically improved industrial potential for the production of butyric acid from nonnative hosts compared to the native producers (*Clostridium* species). Furthermore, this strategy could be broadly utilized for the production of various other useful chemicals in the fields of metabolic engineering and synthetic biology.