Metabolic engineering of *Clostridium tyrobutyricum* for enhanced butyric acid production from renewable biomass

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Butyric acid, as an important C4 platform chemical, was widely used in chemical, food, pharmaceutical and animal feed industries. Currently, industrial butyric acid production depends strongly on petroleum-based feedstocks and bioproduction of butyric acid is an inevitable trend from low-cost biomass feedstocks. Several strategies were provided to improve the industry application of butyric acid production from lignocellulosic biomass.

For enhanced xylose and glucose co-utilization, three heterologous xylose catabolism genes (*xylT*, *xylA* and *xlyB*) from *Clostridium acetobutylicum* were overexpressed in *Clostridium tyrobutyricum*. In glucose/xylose mixture, the xylose utilization rate of the engineered strain Ct-pTBA strain was significantly improved with 8 folds to compare with wild type strain (1.28 g/L·h vs. 0.16 g/L·h). By evaluating the performance of the Ct-pTBA strain in various lignocellulosic biomass hydrolysates, a high butyric acid titer, 42.6 g/L with a productivity of 0.56 g/L h and yield of 0.36 g/g, was obtained in batch fermentation from hydrolysates of sugarcane bagasse. For improving the strain tolerance of inhibiter, the native Class I heat shock protein (*groESL*) and short-chain dehydrogenase/reductase (*SDR)* from *Clostridium beijerinckii* NCIMB 8052 were identified for improving *C. tyrobutyricum* tolerance to lignocellulosic hydrolysate-derived inhibitors. The co-expressing strain of ATCC 25755/*sdr* + *groESL* was constructed and the ATCC 25755/*sdr* + *groESL* exhibited superior performance in butyric acid production with corncob acid hydrolysate as the substrate. Its titier of butyric acid was reached to 32.8 g/L, increased by 28.1% compared with the wild-type strain. For fermentation process development, a fibrous bed bioreactor (FBB) system was used to produce butyric acid and a much higher final butyric acid concentration of 86.9 g/L and productivity of 6.78 g/L·h was obtained in fed-batch fermentation with FBB. These studies can promote the development of an efficient and economical process for bio-butyric acid production from lignocellulosic biomass.

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Research Interests:

Lignocellulosic Fuel and Chemicals Production

Protein Engineering

Biomarker identification and Rapid detection of pathogens

Selected publications

1. Wang et al., *Biotechnology Advances,* 2018.
2. Wang et al., *Bioresource Technology*, 2019.
3. Wang et al., *Journal of the American Chemical Society*, 2018.
4. Wang et al., *Applied Microbiology and Biotechnology*, 2018
5. Wang et al., Biochemical Engineering Journal, 2017.