Chemical Engineering Doctoral Defense

Engineering Escherichia coli for the Novel and Enhanced Biosynthesis of Phenol, Catechol, and Muconic Acid

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abstract

The engineering of microbial cell factories capable of synthesizing industrially relevant chemical building blocks is an attractive alternative to conventional petrochemical-based production methods. This work focuses on the novel and enhanced biosynthesis of phenol, catechol, and muconic acid (MA). Although the complete biosynthesis from glucose has been previously demonstrated for all three compounds, established production routes suffer from notable inherent limitations. Here, multiple pathways to the same three products were engineered, each incorporating unique enzyme chemistries and/or stemming from different endogenous precursors. In the case of phenol, two novel pathways were constructed and comparatively evaluated, with titers reaching as high as 377 ± 14 mg/L at a glucose yield of 35.7 ± 0.8 mg/g. In the case of catechol, three novel pathways were engineered with titers reaching 100 ± 2 mg/L. Finally, in the case of MA, four novel pathways were engineered with titers reached 819 ± 44 mg/L at a glucose yield of 40.9 ± 2.2 mg/g. Furthermore, the unique flexibility with respect to engineering multiple pathways to the same product arises in part because these compounds are common intermediates in aromatic degradation pathways. Expanding on the novel pathway engineering efforts, a synthetic 'metabolic funnel' was subsequently constructed for phenol, catechol, and MA, wherein multiple pathways were expressed in parallel to maximize carbon flux toward the final product. Using this novel 'funneling' strategy, maximal phenol, catechol, and MA titers exceeding 500, 600, and 3000 mg/L, respectively, were achieved, representing the highest achievable production metrics for all three products reported to date.

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