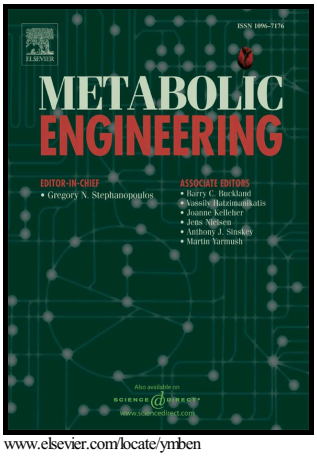

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Multi-omic elucidation of aromatic catabolism in adaptively evolved *Rhodococcus opacus*

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ABSTRACT

Lignin utilization has been identified as a key factor in biorefinery profitability. However, lignin depolymerization generates heterogeneous aromatic mixtures that inhibit microbial growth and conversion of lignocellulose to biochemicals. *Rhodococcus opacus* is a promising aromatic-catabolizing, oleaginous bacterium, but mechanisms for its aromatic tolerance and utilization remain undercharacterized. To better understand these mechanisms, we adaptively evolved *R. opacus* for improved utilization of 32 combinations of diverse aromatic compounds. Evolved *R. opacus* mutants showed up to 1900% growth improvement in the utilization of phenol, guaiacol, 4-hydroxybenzoate, vanillate, and benzoate compared to the wild-type strain. Whole genome sequencing revealed several redox-related genes with mutations shared across multiple adapted mutants. PVHG6, the mutant with the most improved growth on a mixture of multiple aromatic compounds, showed 56% lower superoxide dismutase activity than the wild-type strain, suggesting that redox reactions are important for aromatic tolerance and utilization. Comparative transcriptomics revealed by-product detoxification pathways and five aromatic funneling pathways that were upregulated in response to specific aromatic compounds. Gene knockout experiments confirmed the two degradation routes of the β-ketoadipate pathway for five aromatic compounds. These results provide an improved understanding of aromatic bioconversion and facilitate development of *R. opacus* as a biorefinery host.

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