Systems Approaches for Engineering Microbial Biocatalysts

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Microbes have been engineered to produce a variety of chemicals, including biofuels, commodity chemicals, specialty chemicals, and therapeutics. Chemical production can be enhanced by connecting synthesis pathways to host metabolism, re-wiring regulatory networks, improving precursor production, and optimizing gene expression. A number of computational systems biology approaches have been developed to facilitate metabolic engineering efforts by suggesting which combination of genetic changes would improve chemical production. Network analysis methods can be used to identify paths from renewable substrates to high-value chemical products and central metabolic precursors common to a variety of chemical products. Genome-scale metabolic models can be used to predict how gene deletions, gene additions, and gene expression changes would impact chemical product yields, growth rates, and/or productivities. Additionally, machine learning and active learning algorithms can be used to optimize gene expression constructs to efficiently convert metabolic precursors into desired products. Case studies will be presented that show how a variety of computational tools can guide development of strains with enhanced chemical production. This work will illustrate how integrating computational and experimental efforts can lead to the rapid development of microbial biocatalysts for renewable chemical production.