Rational design of microbial chemical factories

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The growing interest in a "biomass-based" economy has led to new efforts to construct and improve microorganisms capable of producing chemicals. The current focus is largely on liquid biofuels; however, a successful "biorefinery" is likely to be a mixed-product facility, with many compounds produced from one or more biomass-derived feeds. Identifying methods for the production of both novel biofuels and "value-added" compounds is both a challenge and an opportunity. The potential for biological conversion of feedstocks to bulk chemicals is enhanced by the availability of tools and techniques from the established discipline of Metabolic Engineering, which has enjoyed tremendous successes in the development of highly productive microorganisms for a variety of products of interest. We can also gain insights from Biocatalysis, where the choice of enzymes to mediate biotransformation of chemical substrates is based largely on consideration of the required functional group conversion without being limited by prior evidence of transformation of the full structure. The focus of Synthetic Biology on the application of engineering principles to the design and re-design of biological systems to perform prescribed tasks, and to do in a predictive, robust, and more reliable manner, has led to the development of new tools and methodologies for both design and assembly that further enhance our ability to engineer microbial chemical factories. Our group is interested in applying principles from each of these intellectual arenas towards the design and construction of novel biosynthetic pathways for specified target compounds. In particular, we will present our work on the microbial synthesis of glucaric acid (a dicarboxylic acid) and hydroxyvaleric acids as value-added compounds from biomass. We will also discuss the challenges of constructing productive organisms in a predictive manner through the use of well-characterized biological parts.