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SEMINAR ANNOUNCEMENT

Design, Evolution, and Ensemble Modeling of High Flux Microbial Synthesis Networks

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Date: Wednesday, February 23, 2011
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ABSTRACT

Higher alcohols possess several characteristics that make them attractive as biofuels and chemical feedstock. We have designed a metabolic network to synthesize these molecules in high yield. We further developed various strategies for improving the throughput of these products to industrially relevant levels from CO_2. In addition, we have utilized an evolutionary strategy for isolating strains of *Escherichia coli* for high-flux production of or increased tolerance to isobutanol. The genomes of the mutants were sequenced and essential mutations giving rise to those phenotypes are identified. Strains were reconstructed to avoid unnecessary and deleterious mutations.

Using this strategy, E. coli mutants have been isolated to produce isobutanol, with titers reaching greater than the toxicity level and comparable to that reached by rational design. In addition, we identify genotype–phenotype relationships in isobutanol tolerance. Five mutations (acrA, gatY, tnaA, yhbJ, and marCRAB) were found to be primarily responsible for the increased isobutanol tolerance. We successfully reconstructed the tolerance phenotype by combining deletions of these five loci, and identified glucosamine-6-phosphate as an important metabolite for isobutanol tolerance, which presumably enhanced membrane synthesis. In addition, we used an Ensemble Modeling strategy to reconstruct production phenotypes, which allows further improvement of the strain.