

Strategies to Improve Resistance and Production Phenotypes of *E. coli*

Adrienne E. McKee, John Haliburton, Helcio Burd, **Jay Keasling** and Swapnil Chhabra*

Presenting author: *Swapnil Chhabra – SRChhabra@lbl.gov

Fuels Synthesis Division, Joint BioEnergy Institute

Many of the microbial phenotypes of interest to metabolic engineers are complex in that multiple genes, pathways, and regulatory networks are involved in generating the targeted behavior. *A priori* prediction of additional changes that will further improve phenotypes can therefore prove difficult due to our incomplete understanding of the functions and connectivity of gene products far removed from the pathway of interest. One complement to rational approaches is to exploit the strength of mutation and selection or screening to obtain strains capable of improved resistance to pretreatment growth improved production titers in the case of production phenotypes. Towards these goals, we are employing and refining methods that rely on natural or augmented mutation rates or on directed protein evolution to improve *E. coli* phenotypes. Our three major avenues of investigation include selection for inhibitor resistance by continuous culture in chemostats, development of inducible and temperature sensitive mutator plasmids, and generation and screening plasmid libraries of mutated gene regulators for enhanced phenotypic behavior. We are interested in both the genetic and regulatory alterations that underlie phenotypic improvements.

This work was part of the DOE Joint BioEnergy Institute (<http://www.jbei.org>) supported by the U.S. Department of Energy, Office of Science, Office of Biological and Environmental Research, through contract DE-AC02-05CH11231 between Lawrence Berkeley National Laboratory and the U.S. Department of Energy.

DISCLAIMER

This document was prepared as an account of work sponsored by the United States Government. While this document is believed to contain correct information, neither the United States Government nor any agency thereof, nor the Regents of the University of California, nor any of their employees, makes any warranty, express or implied, or assumes any legal responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product, or process disclosed, or represents that its use would not infringe privately owned rights. Reference herein to any specific commercial product, process, or service by its trade name, trademark, manufacturer, or otherwise, does not necessarily constitute or imply its endorsement, recommendation, or favoring by the United States Government or any agency thereof, or the Regents of the University of California. The views and opinions of authors expressed herein do not necessarily state or reflect those of the United States Government or any agency thereof or the Regents of the University of California.