Dr. Mattheos Koffas

“Engineering and Balancing Metabolic Fluxes in E.coli for the Biosynthesis of High Value Chemicals”

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A long theme in the field of metabolic engineering has been the identification of targets for genetic modifications in order to optimize cellular phenotypes, usually associated with the overproduction of a chemical of interest. In order to address this question and for the purpose of reprogramming the cellular network, we employ in silico model of the genome-wide metabolism in order to optimize the biosynthesis of high-value chemicals, such as phytochemicals, in *E.coli*. Such Systems Biology approaches, in combination with traditional genetic engineering have resulted in robust production levels that can result in the commercially viable processes for the synthesis of important molecules. However, often times, there is a need to further balance metabolic pathways in order to address the issue of metabolic burden, i.e. the draining of cellular resources in order to overexpress a recombinant pathway. Such metabolic pathway balancing has been achieved in our lab for the overproduction of chemicals that derive from long metabolic pathways, such as fatty acids, using episomal expression with vectors of different copy numbers, different strength promoters and different strength ribosome binding sites. It has also been achieved by engineering of feedback controls for dynamic tuning of metabolic fluxes around key intracellular metabolites, such as malonyl-CoA, using a dual transcriptional regulator. More recently, the use of synthetic microbial consortia has been employed to achieve metabolic balancing, opening up the possibility for the de novo production of a multitude of high-value chemicals.