A sense of balance: Development of metabolic pathway balancing approaches for the production of high value chemicals in recombinant E.coli

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. Finally, recent advances in engineering the development of a biotechnological production platform for the production of Glycosaminoglycans such as the anticoagulant drug heparin will also be presented.

Matthew Koffas
Dorothy and Fred Chau ’71 Biocatalysis Constellation Professor
Department of Chemical and Biological Engineering
Department of Biological Sciences
Rensselaer Polytechnic Institute, New York

Mattheos Koffas received his B.A. in Chemical Engineering from the National Technical University in Athens, Greece, in 1994 and his PhD in Biochemical Engineering from M.I.T. in 2000, working under the supervision of Gregory Stephanopoulos on metabolic engineering of Corynebacterium glutamicum for amino acid production. He was a Visiting Research Scientist at DuPont Central Research in Wilmington DE from 2001 to 2002 where he work on methanotrophic bacteria for the production of high value chemicals. He then joined the Department of Chemical and Biological Engineering at the University at Buffalo as an Assistant Professor in 2002 and promoted to Associate Professor with tenure in 2008. In 2011 he joined RPI as a Career Development Associate Professor; he was promoted to full Professor in 2015 and awarded the Dorothy and Fred Chau ’71 Professorship in the same year.

His research interests are in the area of metabolic engineering and synthetic biology with a special emphasis on tool and strain development for the efficient production of high value and commodity chemicals. Some of his most cited work includes the development of microbial production platforms for the biosynthesis of a variety of natural products derived from plants while recently, in collaboration with others, he has been working on developing production platforms for the biosynthesis of pharmaceutical polysaccharides. In addition, his group worked on engineering synthetic methylotrophy, where E.coli is used to convert methanol to biofuels. He is bringing his breakthrough research to market, by joining the Scientific Board of Chromadex, a chemical company that is currently scaling up the microbial production of anthocyanins. Professor Koffas and his research group have published 100 peer-reviewed journal publications in journals including PNAS, Nature Communications, Metabolic Engineering, Nucleic Acids Research and others. His work, presented in the form of more than 100 invited and contributed lectures, has been featured in the National Public Radio (NPR). He is fellow of the AIMBE and serves as Academic Editor for Biotechnology Advances, Metabolic Engineering Communications, BMC Plant Biology and editorial board member for Metabolic Engineering and Current Opinion in Biotechnology. He has chaired two international conferences in the area of Biomolecular Engineering. He is a member of the American Institute of Chemical Engineers, Americal Chemical Society and American Society for Microbiology.