CHEMICAL & BIOMOLECULAR ENGINEERING

SEMINAR SERIES

UNIVERSITY OF DELAWARE

CBE.UDEL.EDU

MARCH 29

10:00 - 11:00 AM
COLBURN LAB
ROOM 102

A SENSE OF BALANCE: DEVELOPMENT OF METABOLIC PATHWAY BALANCING APPROACHES FOR THE PRODUCTION OF HIGH VALUE CHEMICALS IN RECOMBINANT E.COLI

MATTHEOS KOFFAS

Rensselaer Polytechnic Institute

Dorothy and Fred Chau '71 Career Development Constellation Professor

ABSTRACT

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.

BIOGRAPHY

Mattheos Koffas, Ph.D., received his B.S. degree in Chemical Engineering from the National Technical University in Athens, Greece in 1994. He then joined the graduate program of the Department of Chemical Engineering at MIT where he worked on improving amino acid biosynthesis from Corynebacterium glutamicum. After completing his Ph.D. in 2000, he joined DuPont's Central Research and Development as a research scientist where he worked on engineering the carotenoid biosynthesis of an obligate methanotroph. In August of 2002 he joined the faculty of the Department of Chemical and Biological Engineering at SUNY Buffalo as a tenure-track Assistant Professor and was promoted to Associate Professor with tenure in the summer of 2008. In January of 2011 Prof. Koffas moved to his current position at RPI. In his research career, Dr. Koffas has worked with a variety of microorganisms and natural products including amino acids, polyphenols, fatty acids and terpenoids. He has published more than 40 peer-reviewed publications, more than 10 book chapters and holds 8 patents. He is a member of the Editorials Boards of various Journals in the area of Bioengineering. His research has been funded by Federal agencies (NIH and NSF), the State of New York (NYStem) and industrial partners (Evonik, Firstwave Technologies and Chromadex).

UNIVERSITY OF DELAWARE ENGINEERING