SINERGY
MINI SYMPOSIUM



John A. Gerlt

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TOOLS AND STRATEGIES FOR DISCOVERING NOVEL ENZYMES IN NOVEL METABOLIC PATHWAYS

The number of proteins in the UniProt database (>89M sequences in Release 2017_08) is increasing with a doubling time of 2.5 yrs; however, ≥50% of the proteins have uncertain or unknown functions. Because sequence homology alone is not sufficient to assign *in vitro* activities and *in vivo* metabolic functions to uncharacterized enzymes, we are developing large-scale tools strategies to facilitate the prediction and subsequent experimental verification of their activities and functions. This lecture will highlight several examples of the use of these tools and strategies for discovery of novel enzymes and metabolic pathways: 1) a novel pathway for methionine salvage using metabolomics and transcriptomics, 2) a novel pathway for 4-hydroxyproline betaine catabolism using homology modeling and integrative pathway mapping, 3) large-scale assignment of functions to members of the proline racemase family guided by genome context, and 4) the use of solute binding proteins for microbial transport systems to guide the discovery of novel catabolic pathways. These approaches use sequence similarity networks (SSNs) for entire protein families and genome neighborhood networks (GNNs) for isofunctional groups in protein families to leverage the large amount of protein and nucleic sequence information now available; the lecture also will describe web servers for generation of SSNs (EFI-EST; efi.igb.illinois.edu/efi-est/) and GNNs (EFI-GNT; efi.igb.illinois.edu/efi-gnt/).

BIOGRAPHY

Professor Gerlt is the Program Director of the Enzyme Function Initiative (EFI) under the National Institute of General Medical Sciences involving 9 academic institutions in the US and Canada. He is a mechanistic enzymologist and an expert in structure-function studies of numerous metabolic enzymes. Prof Gerlt has made numerous significant contributions to the field of mechanistic enzymology and physical organic chemistry, and his seminal work on the enolase superfamily and the crotonase superfamily has established a new and important discipline of genomic enzymology. Prof Gerlt has won numerous awards and currently holds the Gutgsell Chair, a prestigious University Endowed Chair. He has published extensively in prestigious journals and is currently the Associate Editor for the ACS journal, Biochemistry, and is on the Editorial Board of several journals.

2 OCT 2017, MONDAY | 10AM TO 12PM

CLINICAL RESEARCH CENTRE, MD11 AUDITORIUM

HOSTED BY A/P YEW WEN SHAN

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Lunch reception to follow

For catering purposes, kindly register at contact@sinergy.sg by Friday 29 Sep, 12pm

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Steven C. Almo
Albert Einstein College of Medicine

ENZYME FUNCTIONAL ANNOTATION: FROM NEW MICROBIAL METABOLISM TO MAMMALIAN ANTIVIRAL DEFENSE MECHANISMS

The vast majority of proteins have not been subjected to experimental functional annotation, and a large proportion are misannotated. We describe an integrated pipeline that supports high-throughput cloning, expression, purification, structure determination and functional annotation. The utility of this pipeline is described for the discovery of new microbial metabolism, new metabolites and new chemistry. We have recently recapitulated our entire pipeline under anaerobic conditions, which provides a one-of-a-kind structural and functional genomics resource for oxygen-sensitive proteins. This anaerobic resource has allowed for the discovery of a new mammalian anti-flavivirus host defense mechanism. Future community-wide efforts and large-scale team-based consortia will be required to adequately address the "annotation vacuum".

BIOGRAPHY

Steven Almo is the Chairman of the Department of Biochemistry at Albert Einstein College of Medicine/ Montefiore Medical Center, where he is Professor of Biochemistry and Physiology & Biophysics. Dr. Almo holds the Wollowick Family Foundation Chair in Immunology and is Director of Einstein's Macromolecular Therapeutics Development Facility, a resource dedicated to the development and optimization of protein-based therapeutics. Dr. Almo is recognized for his broad contributions to structural biology and has published more than 300 papers. His laboratory has played key roles in the development and implementation of high-throughput approaches for protein production, structure determination and functional annotation. Dr. Almo received his Ph.D. in Biophysics from Harvard University, while working with Greg Petsko in the Chemistry Department at MIT, and is best known for his high resolution structural and biochemical characterization of the CTLA-4 and PD-1 immune checkpoint proteins and their respective ligands.

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