Analytical & Chemical Biology Seminar

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"A Proteomic Lens on the Molecular Biology of Bacterial Pathogens"

Mycobacteria, the causative agent of tuberculosis, like most organisms secretes proteins for biochemical functions. Secreted proteins are a proteome of 'target'-enriched material which contains virulence-factors, antigenic-determinants, and targets for treatment/detection. EsxA and EsxB (ESAT-6 and CFP10) are essential virulence factors exported by mycobacteria and other Gram positive pathogens. Identification of proteins that are required for effective synthesis and secretion of these crucial virulence determinants has been hindered by a lack of saturating genetic screens; high-throughput biochemical detection, and accurate quantification of disease phenotypes. We designed orthogonal antibody-free assays using a slew of proteogenetic approaches to comprehensively dissect the individual contribution of gene products towards a functioning disease secretion system (ESX-1) in pathogenic mycobacteria. This framework is highly extensible to the analysis of other pathogen and protein secretion systems, and has uncovered novel genes, pathways, and crosstalk among secretion systems. Most surprisingly; *in vitro* levels of proteome production by ESX secretion systems has poor correlation with quantities required for disease, giving rise to micro-phenotypes. Here we provide quantitative evidence for the basis micro-complementation and correlation of absolute protein values to those required for disease.

Thursday
February 5

12:15 pm
1315 Chemistry

Coffee & cookies at 12 p.m. outside 1315