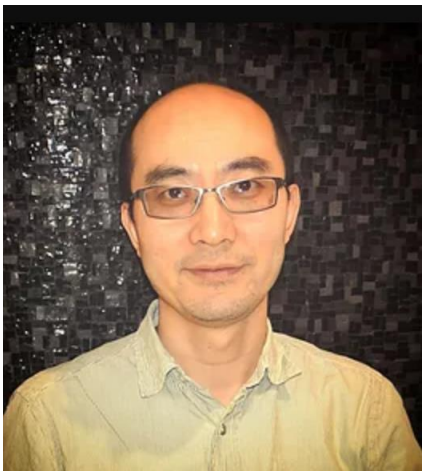
Donnelly Center
PDF and RA Seminar Series



Dr. Hongbo Guo

Emili Lab

When Small Molecule Met Big Molecule

I will present two case studies about using mass spectrometry to address small molecule (drugs, ligands, and metabolites) and protein interactions.

First Case: Label-free Chemical Proteomics approach to detect drug-protein interaction

Detection of drug-protein interactions is important for characterizing the mechanism of action of bioactive small molecules, but unbiased screening approaches remain elusive. Here, we report a high-throughput experimental platform for systematic target identification that combines complimentary protein thermal stabilization and affinity pull down assays to monitor the physical association of collections of bioactive small molecules with cellular proteins. We demonstrate the effectiveness of this hybrid approach by detecting both known and unexpected targets of diverse compounds including anti-cancer drugs and antibiotics. Several protein targets of brominated natural products were identified, and FabI protein was validated as the primary pathway for OH-BDE47 to inhibit growth of E. coli.

Second Case: global metabolome-proteome "interactome"

To understand and manipulate biochemical processes and signaling pathways, the knowledge of endogenous protein-metabolite interactions would be extremely helpful. However, measuring the association of chemically diverse bioactive small compounds with the myriad of possible protein binding partners present in a complex cellular context remains extremely challenging in practice. Recent developments in precision mass spectrometry, high-throughput proteomics and sensitive metabolomic profiling are now beginning to converge on a possible solution, heralding a new era of global metabolome-proteome "interactome" studies that promise to change biomedical research and drug discovery. To investigate the protein-metabolites interactions at proteome-wide level, we developed an affinity pull down platform with high sensitivity and specificity. A library of overexpressed His-tagged E. coli proteins were constructed. Then affinity pulldown was conducted for each of the proteins. The interacted metabolites were analyzed and identified by untargeted metabolomics workflow.

DATE: Monday January 8th, 2018
TIME: 12:00 – 1:00 pm
LOCATION: Red Room

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