Hacking Protein-Protein Interaction Networks

Abstract: Protein-protein interactions are ubiquitous in biology and constitute a large number of potential drug targets. However, protein-protein interaction networks are also complicated and the protein surfaces themselves can be difficult to drug. To address the complexity, we aim to inhibit or stabilize a single protein-protein interaction, even for hub proteins with many interactors. We have used fragment-based drug discovery methods to systematically identify molecular-glue-type stabilizers of these complexes and protein allostery to inhibit a subset of hub-partner interactions. This talk will describe the 14-3-3/client protein-interaction network and our strategies to develop molecular glues for transcription factors and signal-transduction networks.