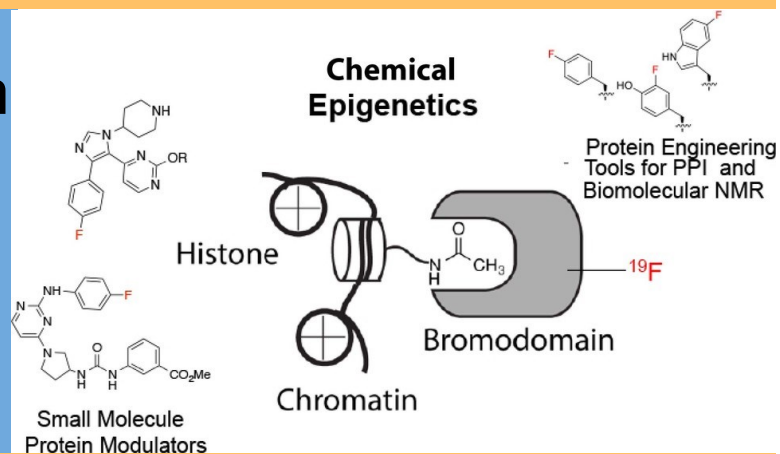


ORGANIC SEMINAR



Professor William Pomerantz
University of Minnesota
Department of Chemistry

Friday, January 18, 9:00 am
473 Hutchison Hall
University of Rochester
Department of Chemistry



Title: “Inspiration from Fluorination: Chemical Biology Approaches to Probe Molecular Recognition Events in Transcription”

Abstract: Protein-protein interaction inhibitor discovery has proven difficult due to the large surface area and dynamic interfaces of proteins. To facilitate the early lead discovery rate, I will first describe a rapid protein-based ^{19}F NMR method for detecting protein-ligand interactions by screening low complexity molecules (fragments), drug-like molecules, and peptidomimetics. We label the aromatic amino acids with the highly sensitive fluorine atom, due to the high conservation of aromatic residues at protein interfaces, and recently developed methods for simultaneous labeling with two different types of fluorinated aromatic amino acids. We have tested the sensitivity, accuracy, and speed of this method with the protein interaction through screening libraries of small molecule fragments. These studies have led to both new insights regarding allosteric regulation of protein-protein interactions, and the discovery of a new small molecule binding site. In the second part of the talk, I will describe improvements in our method for the field of epigenetics targeting bromodomain-containing proteins. These studies have led to the discovery of some of the first selective ligands for the bromodomain BPTF and new submicromolar ligands for N-terminal domain of BRD4. The speed, ease of interpretation, and low concentration of protein needed for binding experiments affords a new method to discover and characterize both native and new ligands for bromodomains and may find utility in the study of additional epigenetic “reader” domains.

Host: Professor Rudi Fasan • Email: fasan@chem.rochester.edu

