"Discovery of Functional Ligands from Genetically-Encoded Libraries of Peptide Derivatives"

ORGANIC SEMINAR

Friday, December 11, 2015
9:00 a.m.
Hutchison Hall 473
University of Rochester
Department of Chemistry

Guest Speaker:
Professor Ratmir Derda
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Department of Chemistry and
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Abstract: Phage display has unlocked the potential of peptide-based therapeutics and diagnostics. It accelerates the discovery of peptide-derived drugs, some of which have been FDA-approved, and many are progressing through the clinical pipeline. However, the building blocks and diversity of phage libraries is limited to amino acids. Our group uses phage display as a foundation for multi-step organic synthesis to produce libraries of peptide derivatives displayed on phage. We developed the methodology for quantification of yield and purity of reactions on phage-displayed peptide libraries; examples are N-terminal conjugation[1] and cyclization of linear peptides.[2] Chemical modification of libraries allowed us to develop Genetically-Encoded Fragment-Based Discovery (GE-FBD) platform,[3] which combines non-peptide ligands with $>10^8$ variable peptide fragments. For example, GE-FBD can be used to select phage-displayed glycopeptides to dock a glycan fragment at the carbohydrate-binding site and guide selection of synergistic peptide motifs adjacent to the pocket.[3] We believe that display of peptide derivatives on phage can be developed into an efficient platform for discovery of biological probes and drug leads that combine advantages of small-molecule and "biological" classes of drugs.

Host: Professor Rudi Fasan, email: fasan@chem.rochester.edu