Guest Speaker:
Professor William M. Wuest
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ORGANIC SEMINAR

Friday, April 8, 2016
9:00 a.m.
Hutchison Hall 473
University of Rochester
Department of Chemistry

"Draining the Moat: A Natural Product-Inspired Approach to Combat Bacterial Biofilms"

Abstract: The importance of natural products as anticancer and antibiotic compounds is undisputed due to their wide application as potent and effective pharmaceuticals. In contrast, the investigation of natural products toward biofilm-implicated bacterial infections, a rising concern among scientists and medical professionals, has been significantly understudied. Biofilm formation is the first line of defense for many bacteria similarly to how a moat protects a castle, and it is this defense that makes them so hard to combat. Bacterial biofilms have been estimated to cost society in excess of $200 billion/yr, affecting everything from human health to water purification. Furthermore, biofilms are increasingly resistant to antibiotic treatment and are responsible for persistent infections. Over the past four years our group has looked to Nature for inspiring chemical scaffolds and have leveraged diverted total synthesis (DTS) to develop inhibitors and probe molecules to study bacterial biofilms.

In contrast to broad-spectrum agents, the development of species-specific, "narrow-spectrum" antibiotics would be of interest to the medical community serving as novel therapeutics and also to microbiologists as chemical probes to deconvolute complex biofilm communities. Our group has investigated two such molecules, promysalin and carolacton, which specifically target *P. aeruginosa* (indwelling devices, multi-drug resistant) and *S. mutans* (dental caries, endocarditis), respectively. We have recently synthesized both natural products, confirmed their structure and biological activity, and identified novel phenotypes. More recently, we have utilized DTS to develop rational libraries through which the structure-activity relationships have shed light on the mechanism of action. In addition, this endeavor has provided analogs with unprecedented anti-virulence activity. The talk will highlight the conceptualization of the research hypotheses of both projects, the synthesis and evaluation of each class of analogs, and the current progress toward utilizing each set of molecules as chemical probes to better understand the chemical biology of bacterial biofilms.

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