Session I: Poster Abstract

Mode of Action Studies of the S-linked Glycopeptide Sublancin

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Infectious diseases are a continuous threat to human health and the rapid development of bacterial antibiotic resistance not only decreases the effectiveness of known antibiotics but also increases the need for the discovery of novel drugs. A rapidly expanding class of such compounds is the ribosomally synthesized and post-translationally modified peptide (RiPP) natural products. Sublancin 168, produced by *Bacillus subtilis* 168, contains a glucose moiety linked to a cysteine residue, an unprecedented post-translational modification assembled by a glycosyltransferase (SunS). In addition, sublancin 168 has been shown to be extremely stable and has a narrow spectrum of activity with an unknown mode of action. Its extreme stability and unique structure have led us to hypothesize that sublancin has a novel antimicrobial mechanism of action. We have employed the use of various biochemical, microbiological, and genomic tools to characterize sublancin's activity. Data obtained from comparative genomic analysis and global gene expression using DNA microarrays has identified the PTS-glucose specific transport system as a possible mechanism by which sublancin could affect the cell. Current efforts include investigating sublancin's localization in the cell by creating fluorescent sublancin analogues. In addition, we synthetized a sublancin analogue lacking the glycan to investigate the role of the sugar and have solved the solution NMR structure of sublancin for clues regarding it's mechanism of action. A clear understanding of how this unique antibiotic exerts its antimicrobial activity may facilitate the development of new antibiotics.

Catalyst-Controlled Aliphatic C—H Oxidations with a Predictive Model for Site-Selectivity

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Selective methods for aliphatic C–H bond oxidation stand to have a profound impact on chemical synthesis because these bonds exist across all classes of organic molecules. Central to realizing this goal is development of catalysts with broad substrate scope (small molecule-like) that predictably enhance or overturn the substrate's inherent reactivity preference for oxidation (enzyme-like). Herein we report a simple small molecule iron catalyst that achieves predictable catalyst-controlled site-selectivity in preparative yields over a range of topologically diverse substrates. A structure-based catalyst reactivity model is disclosed that quantitatively correlates the innate physical properties of the substrate to the site-selectivities observed as a function of the catalyst.