The natural product oxetanocin is a potent antiviral compound produced by *Bacillus megaterium* NK84-0128. The biosynthesis of oxetanocin has been linked to a plasmid-borne gene cluster that contains four genes involved in oxetanocin production (*oxsA* and *oxsB*) and oxetanocin resistance (*oxrA* and *oxrB*). In collaboration with the Liu Lab at the University of Texas, Austin, we now present detailed structural and biochemical analysis that confirms the involvement of the cobalamin (Cbl) dependent *S*-adenosylmethionine (AdoMet) radical enzyme, OxsB, and an HD-domain phosphohydrolase enzyme, OxsA, in oxetanocin production. These studies of OxsB provide a framework for understanding the coordination and interplay of AdoMet and Cbl cofactors in performing Nature’s chemistry. Additional X-ray crystal structures of the oxetanocin production partner protein, OxsA, reveal a phosphohydrolase enzyme with a restructured active site specific for a phosphorylated oxetanocin derivative. Our crystallographic endeavors and sequence-based comparisons have allowed for elucidation of a biochemical scheme for the challenging production of oxetanocin, expanded the catalytic repertoire of the HD-domain phosphohydrolase enzyme superfamily, and provided the first structural characterization of a Cbl-dependent AdoMet radical enzyme.

**Monday, January 9, 2017 at 11:00am**

**Room 209 Havemeyer**

Hosted by

**Tom Rovis**