

Friday November 22, 2013

2:00 p.m.

Fourth Biochemistry Faculty Candidate

Room 158, Science Complex

Insights Into Lysosomal Storage Diseases, Circadian Rhythms, and Natural Product Biosynthesis From Protein Crystallography

Enzymology and X-ray crystallography are powerful tools for illuminating the molecular mechanisms of novel chemical transformations and how complex biological pathways emerge from coupled enzymatic reactions. Studies of several enzymes representing a diverse set of chemical reactions and biological functions will be described. Crystallographic analysis of protein palmitoyl thioesterase, a hydrolase mutated in the fatal lysosomal storage disorder Batten's disease, led to an understanding of the catalytic mechanism and provided a molecular basis for the difference in disease severity associated with different inherited mutations. Casein kinase 1, an enzyme that plays a role in the regulation of mammalian circadian rhythms, has been investigated using crystallography and chemical biology in an effort to understand mutations that impact human sleep disorders. Finally, preliminary characterization of enzymes in microbial biosynthetic pathways leading to a family of biologically active novel bisindole natural products will be discussed, including an unusual oxidative "ring flipping" reaction.