

BRUCE BOWLER

Professor

University of Montana



Wednesday, September 10th

10:30 AM – 11:30AM

Steele 006

"Peroxidase Activity of Cytochrome c: Non-synonymous SNPs versus Evolutionary Changes"

Abstract: Cytochrome c is a protein that is important both for electron transport and apoptotic pathways. In the latter pathway, cytochrome c acts as a peroxidase that oxygenates the mitochondrial membrane lipid cardiolipin. Oxygenation of cardiolipin is believed to help initiate apoptosis. Studies on the effects of evolutionary changes of residues in W-loops C (residues 40 – 57) and D (residues 70 – 85) of cytochrome c on the stability, dynamics and peroxidase activity of the protein will be described. These studies will be compared with results obtained with variants of human cytochrome c that result from non-synonymous single-nucleotide polymorphisms (SNPs) and cause mild thrombocytopenia 4. The largest effects on dynamics and peroxidase activity are observed for variants in W-loop D at positions 81 and 83 that have evolved from small to large amino acid side chains and for the SNPs that cause THC4. Differential effects on the acid dissociation constant (pK_H) of the ionizable group that triggers the alkaline conformational transition of cytochrome c and the conformational equilibrium constant (pK_C) for this transition appear to control the dynamics that modulate peroxidase activity.

Bio: Bruce Bowler is Professor of Chemistry and Biochemistry at the University of Montana in Missoula. He also directs the Center for Biomolecular Structure and Dynamics, which is funded by a phase 3 NIH CoBRE grant. Recently, he was appointed interim dean of the newly formed College of Science at the University of Montana. His research interests include the structure and dynamics of heme proteins and the process of protein folding, particularly the properties of protein denatured states. Most recently his lab has been developing rational methods to stabilize proteins using stereochemical data available in the Protein Data Bank.