DEPARTMENT OF
Chemistry
UNIVERSITY OF WISCONSIN–MADISON

Ph.D. Dissertation Defense

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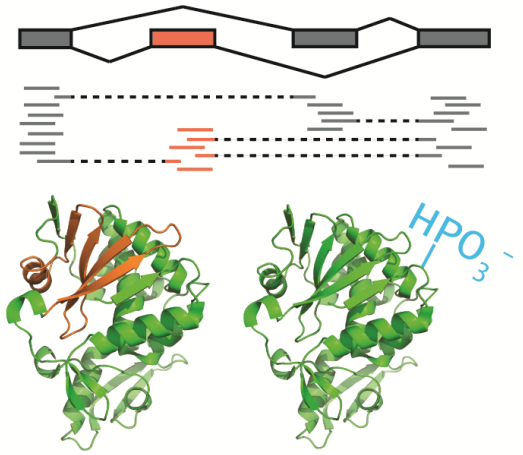
Smith Research Group

Thursday, December 13 - 3 pm in room 1360 Biotech Center

"Computational Tools for Discovering Proteoforms in Complex Systems"

The desire to understand the molecular nature of biology and disease can reveal a need for new analytical tools. Proteins perform many biological functions, and they can be adorned with posttranslational modifications (PTMs) that alter these functions. Curiosity about how ensembles of PTMs and amino acid sequence variations change protein function has led to the analysis of intact proteoforms, proteins with PTMs at specific positions along their sequences. In this work, I built new computational tools for analyzing proteoforms in complex systems and communicating the results of those analyses. Central to this effort was the development of Proteoform Suite, which uses measurements of intact proteoform masses to identify and quantify thousands of proteoforms. Proteoform Suite also facilitates data visualization for these results. Comparing and integrating proteoform results from multiple tools is made difficult by the wide variety of formats used to describe proteoforms. This problem was addressed by developing ProForma, a notation for proteoform sequences.

Proteoform diversity derives from PTMs, as well as from amino acid sequence variations that stem from alternative splicing of RNAs and missense mutations in the genome. RNA sequencing (RNA-Seq) analysis was used to detect these variations and amend protein databases to enable detection of these protein sequence variations in proteomic data. Tools for RNA-Seq analysis were also applied to discover long noncoding RNAs (lncRNAs) distinct to aggressive or indolent prostate cancers in a final study.



Contributing tools for analyzing intact proteoforms has spurred studies of mammalian systems that will hopefully shed light on proteoform function and roles in human disease.