Ph.D. THESIS DEFENSE

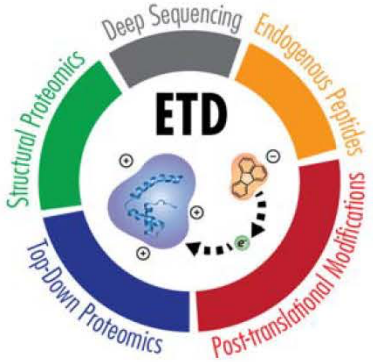
Nicholas M. Riley

Advancing electron transfer dissociation technologies for characterization of proteomes and post-translational modifications

Joshua J. Coon Group

Thursday April 12, 2018 at 2:00 pm in Genetics Room 1441

My graduate research has focused on the development of new instrumentation and methodology to leverage ion-ion reactions and other modes of tandem mass spectrometry (MS) for proteomic analyses. Electron transfer dissociation (ETD) technologies have proven a valuable alternative to collision-based fragmentation methods for sequencing peptides and proteins to advance global proteome characterization. Low dissociation efficiencies in ETD reactions can limit their effectiveness, however, so a significant focus of my graduate work has been on improving the efficacy of ETD fragmentation via concurrent infrared photoactivation, a process termed activated ion ETD (AI-ETD). Here I describe implementation of AI-ETD on the newest generation of quadrupole-Orbitrap-linear ion trap hybrid MS systems and discuss how AI-ETD improves proteome characterization via analysis of both peptides and intact proteins. Furthermore, I demonstrate the utility AI-ETD brings to characterization of post-translational modifications, including protein phosphorylation and glycosylation. AI-ETD technologies have enabled the largest glycoproteomic study to date via interrogation of intact N-glycopeptides, and I discuss both AI-ETD performance for intact glycopeptide fragmentation as well as strategies we can use to understand layers of complexities in glycoproteomic data. I will also discuss future directions of AI-ETD work, including how this technology can be used to enable proteomic analyses in the negative mode and how we can apply AI-ETD to other classes of challenging biomolecules.



Department of Chemistry
UNIVERSITY OF WISCONSIN-MADISON