
Rosetta Briegel Barton Lecture

CHEMISTRY AND BIOCHEMISTRY DEPARTMENT, THE UNIVERSITY OF OKLAHOMA NORMAN, OK 73019-3051 (405) 325-4811

We Are Pleased to Announce A Seminar
Presented By

Neil Kelleher
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Friday, March 24, 2023
4:15 pm
NWC 1313

**Measuring proteoform signatures in human disease: Leveling up proteomics to
bridge the gap from genotype to phenotype**

Since the completion of the Human Genome Project, much has been made of the need to bridge the gap from genes and traits. As a key nexus for the many interacting '-omes' (genome, transcriptome, proteome, metabolome, exposome, interactome, etc.), the proteome should offer a tight link between genotype and phenotype. Why then is proteomics challenged in this connection after 20 years of intense development? The proteoform concept offers a potential solution by considering protein composition with complete molecular specificity. Proteoforms, or all of the precise molecular forms of a protein, capture all sources of variability in protein composition (i.e., SNPs, isoforms, post-translational modifications, etc.), and thus provide crucial insights into biological function of a protein by integrating primary sequence and post-translational modifications (e.g., enabling discovery of allele- or isoform-specific PTM patterns). This level of characterization is not possible at the peptide level, the unit of measurement of traditional 'bottom-up' proteomics, or the epitope level, the target of antibody-based techniques. Our group's studies of disease-related genes have demonstrated the importance of proteoform measurement in clinically relevant protein targets such as KRAS (Adams et al., JBC, 2023), ApoA-1 (Wilkins et al., JAMA, 2021), and immunoproteoforms (Melani et al., Science, 2022). Now, "single molecule" mass spectrometry is poised to convert genes to proteoform signatures at a far faster rate. The latest technologies for scalable and systematic mapping of proteoforms to promote human health will be described in this seminar.

Refreshments will be served.