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Studying Protein Structure and Function by Mass Spectrometry

Proteins act as biological nano-machines that carry out a myriad of functions inside living organisms. In order to perform these tasks, the linear amino acid chain of each protein has to fold into a highly specific three-dimensional structure. Once a protein has reached this native state, conformational dynamics play a key role for energy transduction, signaling, enzyme catalysis and many other processes. Electrospray ionization (ESI) mass spectrometry (MS) provides a number of exquisitely sensitive strategies for exploring protein structure and dynamics. Our laboratory employs a combination of "native" ESI-MS, on-line rapid mixing, H/D exchange (HDX), as well as covalent labeling for studies in this area. This presentation will discuss novel approaches for detecting interactions of proteins with noncovalent binding partners such as metal ions. Bottom-up HDX provides detailed insights into the mechanism of bacterial signal transduction, whereas top-down HDX with electron capture dissociation (ECD) represents an entirely new approach for exploring protein structures. Exciting new developments in microsecond hydroxyl radical labeling provide insights into the folding mechanisms of water-soluble and membrane proteins. The information gained using these techniques is complementary to that obtainable with traditional structural biology tools such as NMR and X-ray crystallography.

Representative publications:

"Solution-Phase Chelators for Suppressing Nonspecific Protein-Metal Interactions in Electrospray Mass Spectrometry" J. Pan, K. Xu, X. Yang, W.-Y. Choy, and L. Konermann *Anal. Chem.* ASAP (2009).

"Protein Oxidative Modifications During Electrospray Ionization: Solution Phase Electrochemistry or Corona Discharge-Induced Radical Attack?" B. L. Boys, M. C. Kuprowski, J. J. Noël, and L. Konermann *Anal. Chem.* *81*, 4027-4034 (2009).

"Molecular Dynamics Simulations of Electrosprayed Water Nanodroplets: Internal Potential Gradients, Location of Excess Charge Centers, and 'Hopping' Protons" E. Ahadi and L. Konermann *J. Phys. Chem. B* *113*, 7071-7080 (2009).

"Structural Characterization of an Integral Membrane Protein in its Natural Lipid Environment by Oxidative Methionine Labeling and Mass Spectrometry" Y. Pan, B. B. Stocks, L. Brown, and L. Konermann *Anal. Chem.* *81*, 28-35 (2009).

"Structural Characterization of Short-Lived Protein Unfolding Intermediates by Laser-Induced Oxidative Labeling and Mass Spectrometry" B. B. Stocks and L. Konermann *Anal. Chem.* *81*, 20-27 (2009).

"Electron Capture Dissociation of Electrosprayed Protein Ions for Spatially-Resolved Hydrogen Exchange Measurements" J. Pan, J. Han, C. H. Borchers, and L. Konermann *J. Am. Chem. Soc.* *130*, 11574-11575 (2008).

"Protein structure and dynamics studied by mass spectrometry: H/D exchange, hydroxyl radical labeling, and related approaches" L. Konermann, X. Tong, and Y. Pan *J. Mass Spectrom.* *43*, 1021-1036 (2008).

"Conformational Dynamics of Free and Catalytically Active Thermolysin Are Indistinguishable by H/D Exchange Mass Spectrometry" Y.-H. Liu and L. Konermann, *Biochemistry* *47*, 6342-6351 (2008).