Protein Structure and Function Studied by Mass Spectrometry

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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, folding, and dynamics [1]. 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 [2]. We will discuss how "bottom-up" HDX can provide detailed insights into the mechanism of bacterial signal transduction. Another focus are "top-down" HDX measurements with electron capture dissociation (ECD), an approach that represents a novel strategy for probing protein H-bonding networks [3]. Exciting new developments in microsecond hydroxyl radical labeling provide information on the folding mechanisms of water-soluble and membrane proteins [4, 5]. The information gained using these techniques is complementary to that obtainable by traditional structural biology tools such as NMR spectroscopy and X-ray crystallography.

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