Mass Spectrometry of Proteins and Protein Complexes as a Tool for Structural Biology

Ever since the development of electrospray ionization (ESI) and matrix-assisted laser desorption/ionization (MALDI) over 30-years ago, mass spectrometry (MS) has progressed as a defining analytical method for the detection and characterization of proteins. Native MS of proteins and protein assemblies reveals size and binding stoichiometry. ESI's gift for transforming solution-phase macromolecules into gas-phase ionized counterparts without disrupting weak non-covalent interactions is key for applying MS to study protein complexes. But elucidating the higher order structures of proteins to understand their function is more challenging. Combining native MS with top-down MS, i.e., the direct fragmentation of the gas-phase protein, yields an effective tool for deriving structural information for soluble and membrane protein complexes, and much of this information can be correlated to the solution-phase structure. Native top-down MS (nTDMS) generates information on the surface topology, ligand binding sites, and post-translational modifications (PTMs) and proteoforms of protein complexes. nTDMS endeavors to fragment covalent bonds in an intact biomolecule or complex in a conformation-sensitive manner, such that information about higher-order structure can be inferred from the fragmentation pattern. The investigation of the molecular action of compounds that prevent amyloid fibril formation in neurodegenerative diseases such as Alzheimer's and Parkinson's disease can be elucidated by nTDMS. Mass spectrometry is complementary to other biophysical methods used in structural biology; the integration of all of these methods form a powerful platform to address important questions in biology and medicine.

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Professor Loo is on the Editorial Boards of several scientific journals, and currently he is the Editor-in-Chief for the Journal of the American Society for Mass Spectrometry. He has held leadership and advisory positions with scientific organizations, including membership on the Board of Directors for the American Society for Mass Spectrometry (ASMS) and the US Human Proteome Organization (US HUPO). Before he joined UCLA in 2001, he was an Associate Research Fellow and Group Leader of the Biological Mass Spectrometry and Proteomics Teams at Parke-Davis Pharmaceutical (that later became Pfizer Global Research), Ann Arbor, MI.

Professor Loo received his Ph.D. in analytical chemistry from Cornell University with Professor Fred W. McLafferty, where he worked on the development of high resolution mass spectrometry for bioanalytical applications. He carried out research as a post-doctoral fellow, and later as a Senior Scientist, at Pacific Northwest National Laboratory (Richland, WA) with Dr. Richard Smith on the development of electrospray ionization mass spectrometry and capillary

electrophoresis for protein characterization.

His group uses and develops new mass spectrometry (MS) and proteomics strategies, including top-down MS (TDMS), native MS, ion mobility MS (IM-MS), and label-free quantification methods, to characterize proteins and protein complexes (and their proteoforms) and to develop new protein biomarkers to aid human health studies. The major current areas of emphasis include elucidating the importance of post-translational modifications, such as lysine acylation, to regulate enzymes and metabolic processes within microbial consortia. Native MS, TDMS, and IM-MS are being used to identify protein-protein/ligand interactions related to neurodegenerative diseases.