

## **NEW MS TECHNOLOGIES FOR INVESTIGATING PROTEIN-PROTEIN INTERACTIONS : THE NEXT FRONTIER IN PROTEOMICS**

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Protein-protein interactions play a central role in many cellular processes and thus a complete description of the proteome relies on the characterization of these complexes. In particular, many human diseases including cancers, autoimmune disorders and viral infections occur as a result of failures or aberrations in protein-protein interactions. Elucidating the complete series of associations of proteins involved with human disease is an important step in the development of targeted new drugs and therapeutics.

Although mass spectrometry now plays an essential role in the characterization of protein structures, its use in the study of protein-protein interactions is less advanced. We have developed new mass spectrometry based technologies for studying protein-protein interactions that offer a number of advantages over current approaches and afford optimal sensitivities with high sample throughput. These include the development of matrix-assisted laser desorption ionization mass spectrometry for the study of non-covalent immune complexes<sup>1,2</sup> associated with viral and bacterial infection. Samples are isolated and prepared using advanced gel extraction techniques and robotic loading procedures. Mass spectrometric analysis from preformed surfaces is performed in an automated fashion without human intervention.

A second approach has been developed to study protein complexes through electrospray-assisted oxidation.<sup>3</sup> Amino acid residues are covalently modified through reaction with oxygen radicals dependent upon their accessibility to solvent. When protein surfaces interact, the reactivity of residues in the binding domain is perturbed allowing these regions to be characterized. The advantages of each of these two technologies will be presented and illustrated for several protein-protein complexes.

1. J.G. Kiselar, K.M. Downard (2000) *J. Am.Soc Mass Spectrom.*, 11 (8), 746-750.

2. J.G. Kiselar, K.M. Downard (1999) *Biochemistry* 43, 14185-14191.

3. S.D. Maleknia, M.R. Chance, K.M. Downard (1999) *Rapid Commun. Mass Spectrom.* 13, 2352-2358.

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