Project proposal template – Faculty studentships Summer 2014

Project title	Mass Spectrometry-based Proteomics: Development of negative ion mode mass spectrometry for analysis of	*Director of Study*	James Barker
Second Supervisor	Dr Marina Edelson-Averb	*School*	Pharmacy and Chem
Other members of supervisory team		*Any requirements from applicant (eg degree in specific subject area)*	physical and life sciences

Project summary

(max 1,000 characters)

Post-translational modifications (PTMs) of proteins play a key role in many cellular processes including the maintenance of protein structure and integrity, regulation of metabolism, cellular recognition events, signaling etc. Protein PTMs are implicated in a broad spectrum of human diseases such as cancer, diabetes and others. Understanding biological functions of protein PTMs and drug development requires a reliable detection and localisation of the modifying groups in the amino acid sequences of proteins. Mass spectrometry has established itself as a premier method for analysis of protein PTMs. Nevertheless, since commonly occurring protein modifying groups exhibit strong acidic properties (e.g. phosphorylation) application of the standard positive ion – based MS methods leads to missing of multiple protein PTMs by the analysis. Edelson-Averbukh et al have recently demonstrated that negative ion mode collision-induced dissociation is a very powerful approach for analysis of acidic protein PTMs.[1-4] The proposed PhD project aims at further advancement of this promising direction of mass spectrometry, both on methodological and on technical sides. The planned research will target several biologically relevant protein PTMs and will run in close collaboration with Dr Edelson-Averbukh (Imperial College London). The candidate will make use of a wide range of chromatographic and mass spectrometry-based proteomic technologies at Kingston and in Imperial College.

References:

1. Edelson-Averbukh M, Pipkorn R, Lehmann WD.: Phosphate group-driven fragmentation of multiply charged phosphopeptide anions. Improved recognition of peptides phosphorylated at serine, threonine, or tyrosine by negative ion electrospray tandem mass spectrometry. *Anal Chem*. **78**, 1249-56 (2006).
2. Edelson-Averbukh M, Pipkorn R, Lehmann WD.: Analysis of protein phosphorylation in the regions of consecutive serine/threonine residues by negative ion electrospray collision-induced dissociation. Approach to pinpointing of phosphorylation sites. *Anal Chem*. **79**, 3476-86 (2007).
3. Edelson-Averbukh M, Shevchenko A, Pipkorn R, Lehmann WD.: Gas-phase intramolecular phosphate shift in phosphotyrosine-containing peptide monoanions. Anal Chem. **81**, 4369-81 (2009).
4. Edelson-Averbukh M, Shevchenko A, Pipkorn R, Lehmann WD.: Discrimination between peptide O-sulfo- and O-phosphotyrosine residues by negative ion mode electrospray tandem mass spectrometry. *J Am Soc Mass Spectrom*. **22**, 2256-68 (2011).