**A new method for qualitative and quantitative protein profiling and biomarker discovery using accurate mass LC-MS**

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Current methodologies for protein quantification include 2DE Gel Electrophoresis, stable isotope coded affinity tags (ICAT, GIST), metabolic labelling (15N), and stable isotope labelling with amino acids in cell culture (SILAC) to name only a few. Perusal of the current literature clearly illustrates both pros and cons for each of the previously mentioned methodologies. In this presentation we will present a new concept for qualitative and quantitative protein profiling. This is based upon a simple LC-MS based methodology that will allow for determining the relative change in abundance of proteins in highly complex mixtures. Utilizing a reproducible chromatographic separations system along with the high mass resolution and mass accuracy of an orthogonal time-of-flight mass spectrometer. This allows for the identification of tens of thousands of ions emanating from identically prepared control and experimental samples. Using this configuration, we can determine the change in relative abundance of a small number of ions between the two conditions solely by accurate mass and retention time. Our data clearly shows that with respect to digestion, ionization, and chromatographic reproducibility as well as high mass precision we are capable of generating the appropriate levels of reproducibility and mass precision to provide such conclusions and in addition that the associated algorithms are capable of extracting the data and calculating the appropriate responses with careful attention to proper error modelling.

In addition this technology provides a powerful MS based peptide identification alternative to conventional LC-MS/MS strategies. In the course of an LC-MS acquisition the collision energy is continuously switching from low to high energy throughout the entire LCMS acquisition. The resulting high-energy data provides extensive fragmentation information across the entire mass range, including the low mass region, across the entire peak width for every precursor ion detected in the low energy function of the chromatogram. The fragment ions (high energy function) are aligned to their related precursor ions in chromatographic space by retention time and chromatographic peak shape. The results clearly demonstrate the ability to confidently identify proteins with higher sequence coverage than traditional approaches as well as the identification of minor peptide components within a complex peptide mixture. Results from the study of various biological samples such as *E. coli* and Human plasma and serum will be presented.