Peptide Targeted Quantification by High Resolution Mass Spectrometry, a Paradigm Shift?

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Abstract: Traditionally, targeted peptide quantification studies use a triple quadrupole (QQQ) mass spectrometer because of the high throughput and high sensitivity, allowing for large numbers of proteins to be quantified in a single LC/MS experiment. However, several major challenges remain: (1) Low resolution of quadrupole limits its ability to achieve high selectivity on the targets from complex background. (2) The development of MRM-based assay for a given protein is still costly and slow. (3) Some peptide targets, especially those with higher charge states and/or higher mass, are difficult for SRM analysis. (4) The transition from discovery to target verification and quantification is cumbersome due to the different mass spectrometer platforms used for discovery and targeted quantification. In this presentation, new approaches to peptide targeted quantification using high-resolution and accurate mass (HR/AM) mass spectrometry are introduced, together with the new high-performance Orbitrap LC-MS/MS platforms. High resolution on the Orbitrap mass spectrometer allows separation of species as close as 5 ppm, which leads to high selectivity. The full MSMS spectrum of HCD provides additional opportunities to increase selectivity for targeted analysis in addition to confident identification / verification of targets in a complex mixture.