SWATH-MS: A NEW DATA INDEPENDENT ACQUISITION LC-MS METHODOLOGY FOR QUANTITATIVE COMPLETE PROTEOME ANALYSIS

P. Navarro [(1)], L. Gillet [(1)], C. Carapito [(2)], H. Röst [(1)], L. Reiter [(3)], O. Rinner [(3)], S. Tate[(4)], R. Bonner [(4)], L. Malmström [(1)], R. Aebersold [(1)].

[(1)] Institute of Molecular Systems Biology, ETH Zürich, [(2)] CNRS, Université de Strasbourg, [(3)] Biognosys AG, [(4)] ABSciex.

The analysis of biomolecules in complex sample mixtures has relied for many years on LC-MS. In proteomics selected reaction monitoring (SRM) is a particularly attractive technique in cases in which reproducible data sets with high quantitative accuracy and wide dynamic range are required [1,2]. Despite the advances of SRM, the method presents certain limitations: the method requires a preliminary selection of reactions, and allows monitoring of a limited number of analytes per run.

To overcome these limitations we introduce a new strategy to acquire fragment ion spectra on all the analytes in a sample, by cycling a sequence of precursor ion selection windows in the mass analyzer that collectively cover the whole targeted mass range during the entire chromatography. These windows may be seen as an analogy of the swath acquisitions in Earth satellite scans. The collected fragment ion spectra are recorded to generate a map with the dimensions retention time - fragment ion m/z - and intensity, for each precursor ion selection window. The data analysis is then performed in the translation of the product ion spectra acquired for each isolation window into separate LC-MS2 maps, from where the fragments, derived from a spectral library and defining any precursor of interest can be extracted and analyzed to unambiguously detect and quantify the targeted analytes in the injected sample. The confidence in the peptide identification is scored based on the mass accuracy and the relative intensities of the acquired product ion fragments compared to that of the reference spectrum and on the co-elution of the extracted ion chromatograms of these fragments. Altogether, this methodology is expected outperform former LC-MS methods in terms of identification rates, quantification speed and accuracy, reproducibility of data collection, and should therefore be of large interest for performing LC-MS analyses of samples of high complexity.

[1] Lange, V.; Picotti, P.; Domon, B.; Aebersold, R. *Mol Syst Biol*. 2008, *4*, 222.
[2] Picotti, P.; Bodenmiller, B.; Mueller, L. N.; Domon, B.; Aebersold, R. *Cell*. 2009, *138*, 795-806.