

## **Reproducible Proteomic and Glycoproteomic Profiling for Better Biomarker Discovery.**

Dr. Yansheng Liu (Senior Postdoctoral Researcher, Department of Biology, Institute of Molecular Systems Biology, ETH Zurich, 8093 Zurich, Switzerland)

The reproducible proteomic profiling is crucial for protein biomarker discovery. We herein introduce SWATH MS, which is a variant of the emerging class of data-independent acquisition (DIA) methods that essentially converts the molecules in a physical sample into perpetually re-usable digital maps [1]. The thus generated SWATH maps are then mined using a targeted data extraction strategy, allowing us to profile disease-related proteomes at a high degree of reproducibility.

We demonstrate the application of our technique from two case studies. In the first study [2], to differentiate aggressive from non-aggressive prostate cancer (PCa) and to minimize the general over-treatment of patients with non-aggressive PCa, we isolated formerly *N*-linked glycopeptides from normal prostate, non-aggressive, aggressive and metastatic prostate tumor tissues by solid phase extraction and analyzed the samples by SWATH-MS. Further, we generated a spectral library covering a large part of the human N-glycoproteome, specifically optimized for SWATH-MS analysis. Promising PCa aggressive biomarkers were discovered. The second study is about quantification of the population level variability of human plasma protein abundances. Here, to determine the relative contributions of heritability, environmental and longitudinal factors to plasma proteome variability, we used SWATH-MS and systematically profiled 1904 peptides defining 342 unique plasma protein profiles from 232 plasma samples that were collected with 2-7 year intervals from monozygotic and dizygotic twins. This study therefore represents the first robust systematic dissection of generic and genetic variance in human plasma proteome enabled by the reproducible SWATH-MS.

## Reference

- [1] Gillet, L.C. *et al.* Targeted data extraction of the MS/MS spectra generated by data-independent acquisition: a new concept for consistent and accurate proteome analysis. *Mol Cell Proteomics* **11**, O111 016717 (2012).
- [2] Liu, Y. *et al.* Glycoproteomic analysis of prostate cancer tissues by SWATH mass spectrometry discovers N-acylethanolamine acid amidase and protein tyrosine kinase 7 as signatures for tumor aggressiveness. *Mol Cell Proteomics* (2014).