Rapid and Robust Plasma Proteomics Platform for Clinical Settings

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The blood plasma proteome is thought to be a unique reflection of individual physiology, as it integrates genetic background and environmental factors. Mass spectrometry (MS)-based proteomics should in principle be an ideal technology to discover and quantify disease indicators in this clinically accessible and relevant body fluid. Moreover, plasma is the most important body fluid for medical diagnosis. The complex sample composition and the enormous dynamic range of protein abundances made MS-based plasma proteomics extremely challenging (1). However, advances in liquid chromatography, mass spectrometry, and computational analysis have dramatically increased the capacity for peptide identification, accuracy of protein quantification, and comprehensiveness of analysis over the last 10 years (2).

Technological developments in our group enable fast and multiplexed sample processing with very high reproducibility (3). The combination of our 'in StageTip' (iST)-preparation workflow with optimized high-throughput LC-MS measurement technologies enables the identification and quantification of more than 40 FDA-approved biomarkers, including a large number of potential biomarkers of metabolic disease states, in very short (< 30 min) mass spectrometry measurements.

We can obtain blood proteomes in as little as 3 h after taking a small blood droplet (5 µl). This workflow is highly reproducible ($R^2 \geq 0.99$) and results in low coefficients of variation (CV < 20 %) for the majority (81 %) of the top 200 quantified proteins. In particular, our high-throughput sample preparation and the use of short gradients will simplify the measurement of large patient cohorts. We anticipate that these developments will facilitate MS-based blood plasma proteomics for routine, quantitative analysis of patient samples in clinical settings.

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