Seer Proteograph
Maximizing Protein Identification in Plasma Samples

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Plasma proteomics is challenging due to the dominance of high-abundance proteins like albumins and globulins, which overshadow low-abundance proteins crucial for biomarker discovery. Traditional methods, such as trypsin digestion or depletion of abundant proteins, often fail to fully access the hidden proteome. Here, we show how Seer's Proteograph technology outperforms these approaches, identifying significantly more proteins in plasma samples. Using engineered nanoparticles, the Proteograph workflow enriches low-abundance proteins without the need for depletion steps, enabling comprehensive proteomic analysis with exceptional sensitivity and efficiency. Our study highlights the Proteograph Product Suite's ability to detect nearly five times more proteins, demonstrating its potential to transform plasma proteomics and advance biomarker research.

Technology and Method

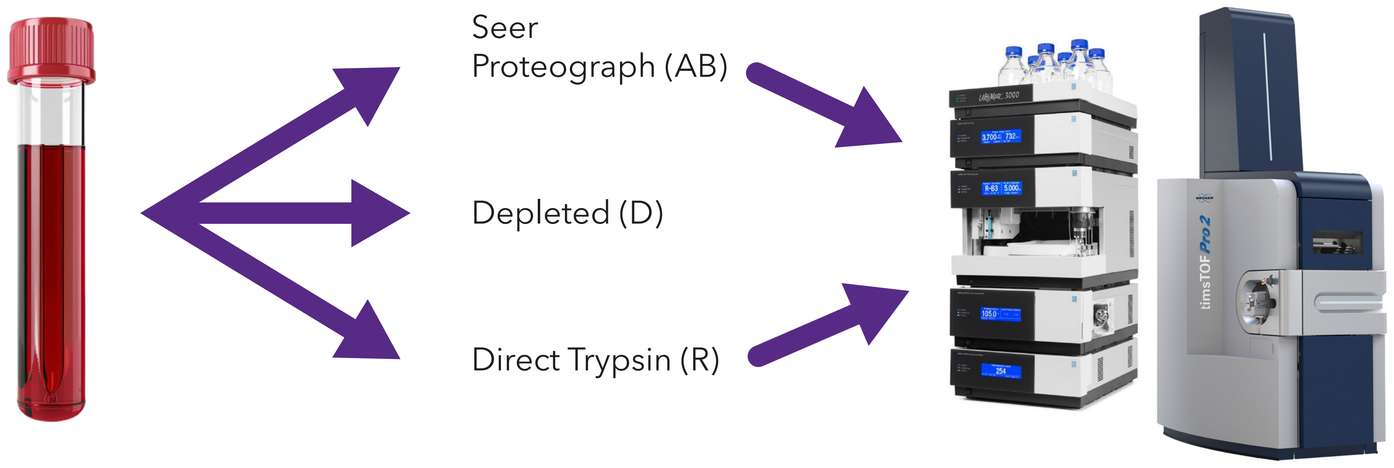
In this study, six human bone marrow plasma samples were analyzed to compare Seer's Proteograph technology with conventional proteomic approaches. Samples were processed using three methods: Direct trypsin digestion (R), Depletion of 14 high-abundance proteins followed by trypsin digestion (D), and Seer Proteograph processing with two fractions per sample (AB). Mass spectrometry analysis was performed using the timsTOF Pro 2 system coupled with an Ultimate 3000 RSLCnano, employing a 60-minute separation gradient and diaPASEF method (m/z 400–1000). For data acquisition, 200 ng of protein per sample was injected, and raw MS/MS data were processed in DIA-NN in library-free mode. Proteograph fractions were combined at the precursor level, and protein quantification was achieved using the top1 algorithm, ensuring robust identification of proteotypic peptides. This streamlined workflow enabled high-resolution analysis, delivering a superior depth of proteome coverage.

Workflow

1) 6 bone marrow plasma samples

2) Processed by disctinc methods

3) UHPLC separation and Mass-spec analysis



4) Data analysis

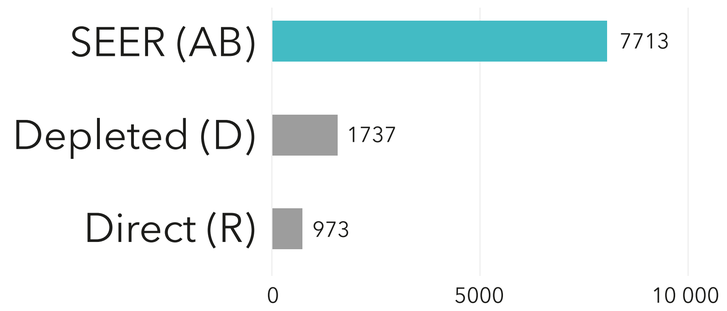


Fig.1. Seer workflow yielded significantly more indentified proteins then conventional methods.

Results

The analysis highlights the superior performance of Seer's Proteograph workflow in protein identification from plasma samples. Proteograph-processed samples (AB) yielded an average of 7,713 identified proteins, compared to 973 proteins detected in samples digested with trypsin alone (R) and 1,737 proteins identified after abundant protein depletion and trypsin digestion (D) (Fig. 1). Importantly, 3,401 proteins were uniquely identified in the Proteograph workflow and were not detected in the other two methods, indicating its enhanced sensitivity and ability to enrich low-abundance proteins (Fig. 2). This significant increase in protein identification shows that the nanoparticle-based enrichment strategy employed by the Seer Proteograph provides a more comprehensive proteomic profile than conventional sample preparation methods.

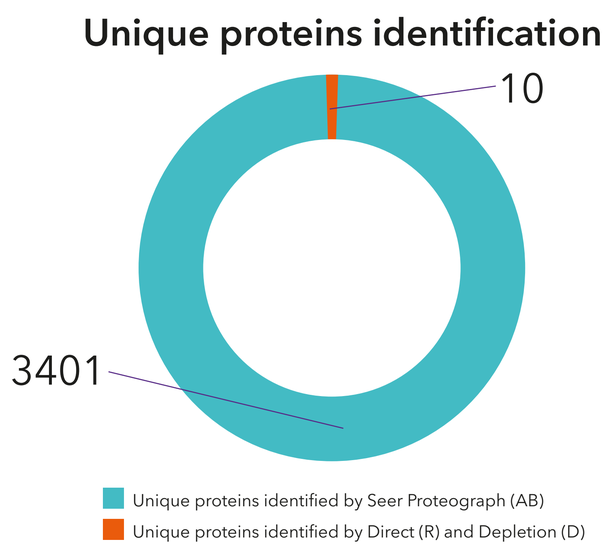


Fig. 2. Seer Proteograph workflow identifies group of 3,401 unique proteins in the plasma samples. Direct and Depletion method identified 10 unique proteins.

Conclusion

The comparative analysis underscores the superior performance of Seer's Proteograph technology in plasma proteomics, demonstrating its capability to identify a significantly greater number of proteins compared to conventional approaches. By leveraging nanoparticle-based enrichment, the Proteograph excels in detecting low-abundance proteins, providing a more comprehensive proteomic profile and uncovering critical molecular insights. This fully automated system not only enhances reproducibility and throughput but also reduces human intervention, ensuring consistency across experiments. The study validates Seer's Proteograph as a cutting-edge solution for complex proteomic analyses, offering unparalleled sensitivity and versatility. At GeneTiCA Experience Centre, we are fully equipped with Seer's technology to provide end-to-end sample processing, enabling researchers to harness the full potential of this innovative workflow for their scientific endeavors.