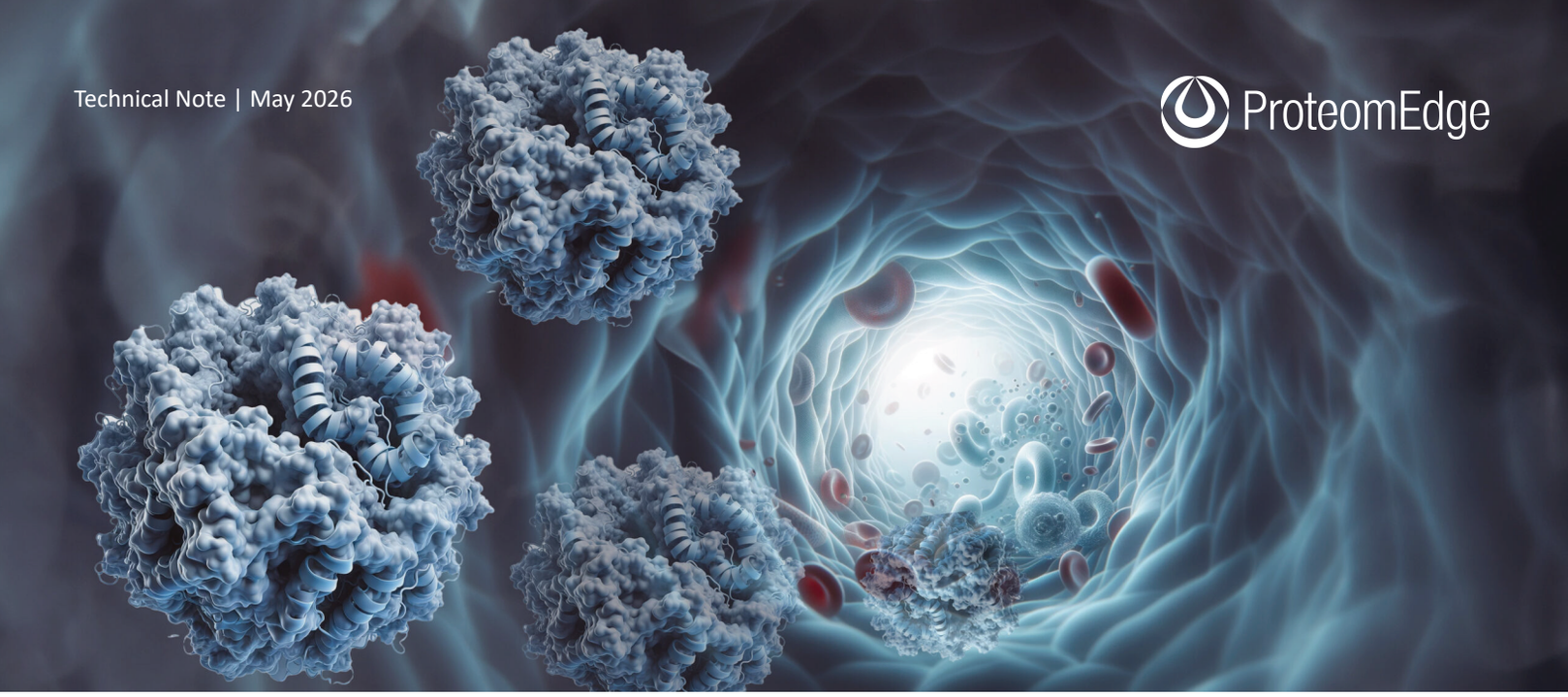

DiscoveryEdge600: High-throughput proteomics solution for scalable biomarker discovery

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Abstract

The DiscoveryEdge™600 is a high-throughput proteomics solution designed to enable rapid and reproducible biomarker discovery in complex biological samples. By integrating optimized sample preparation with robust LC-MS acquisition strategies, the system supports large cohort studies while maintaining data quality. This product is particularly well suited for plasma and serum proteomics, where sensitivity, reproducibility, and throughput are critical. Here, we outline the system architecture, workflow, and performance characteristics, and highlight its applicability in discovery-phase studies.

Introduction

Proteomics-based biomarker discovery requires the analysis of large sample cohorts while maintaining high analytical depth and quantitative reproducibility. Traditional workflows often struggle to balance throughput and data quality, particularly in complex matrices such as blood plasma. ProteomEdge panels, including DiscoveryEdge600, use Quantitative Recombinant Protein Standards (qRePS™) technology to address these challenges. qRePS are recombinant human protein fragments incorporating heavy isotope labeled ($^{13}C/^{15}N$) lysine and arginine residues. Each qRePS covers 50-150 amino acids of a single endogenous protein, where each sequence carefully selected to achieve the best performance during MS analysis (Figure 1).

Figure 1: *qRePS (Quantitative Recombinant Protein Standards) undergo identical processing as endogenous proteins, providing a strategy to control analytical variability and enable absolute protein quantification.*

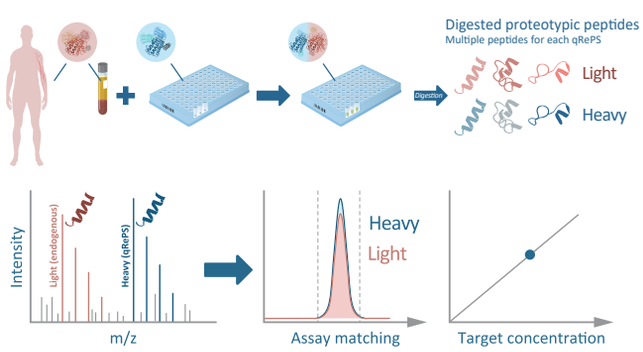


Figure 2: *In the qRePS workflow, one microliter of blood plasma is added to the panel, which is pre-aliquoted and dried in each well of the 96-well plate. Using any bottom-up proteomics workflow to generate heavy/light peptide pairs for LC-MS/MS absolute quantification.*

Panels of qRePS are supplied pre-aliquoted and dried in 96-well plates, designed for the addition of one microliter diluted blood plasma as a first step of sample preparation. The qRePS are processed together with the sample throughout the proteomics workflow, and digested to generate heavy (qRePS) and light (endogenous) peptide pairs enabling absolute quantification. DiscoveryEdge600 is suitable for automated sample preparation protocols and adapted LC-MS methods to deliver consistent performance across large, complex sample sets. The product is designed for scalability, supporting hundreds of samples per batch with minimal manual intervention. Key components include standardized preparation protocols, high-resolution mass spectrometry acquisition, and data processing pipelines tailored for discovery (Figure 2).

Methods

The DiscoveryEdge600 panel includes 620 qRePS targeting 619 different proteins. It was spiked-in to a blood plasma pool and processed in 24 biological replicates accross three different product plates. Digested samples were analysed using Stellar (Thermo Fisher Scientific) mass spectrometer coupled to the Evosep One (Evosep) liquid chromatography system. A targeted LC-MS/MS method (Table 1) was used with 1 minute isolation windows targeting 1,178 peptides.

Table 1: *Setup parameters for LC-MS analysis of DiscoveryEdge600.*

Mass Spectrometer	**Stellar MS**
Fragmentation	HCD, 30 NCE
Scan Rate	125 kDa/s
Isolation Window	1 m/z
RF Lens (%)	30
Liquid chromatograpy	**Evosep One**
Analytical column	15 cm x 75 µm, 1.9 µm
Emitter	Fused silica, ID 10µm
LC Method	40SPD, Whisper Zoom

Results

DiscoveryEdge600 demonstrates high reproducibility across large sample sets, with consistent protein identification and quantitative precision. The workflow enables deep proteome coverage while maintaining throughput suitable for discovery-phase studies. The system is optimized for challenging matrices, such as blood plasma, where dynamic range and complexity are significant constraints. The mass spectrometry read-out allows for qRePS and endogenous peptides to generate heavy and light chromatograms. Extracted chromatograms are overlaid, and ratios calculated for determination of concentration with a one-point calibration strategy (Figure 2). DiscoveryEdge600 qRePS are designed to be present at higher levels than low abundant proteins, thereby increasing reliability of peptide identification, quantification and sensitivity (Figure 3).

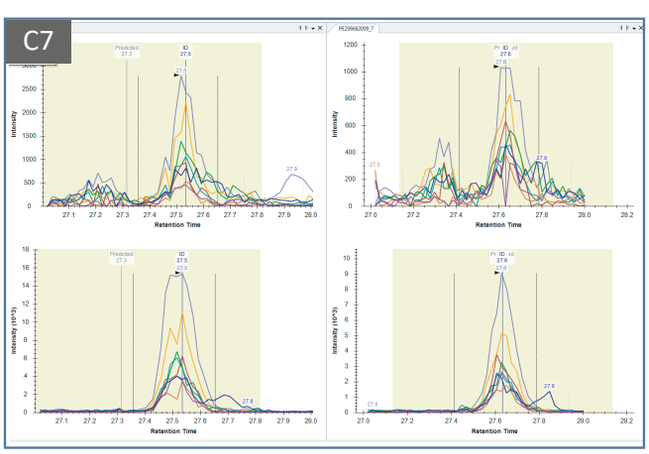


Figure 3: *Extracted peptide ion chromatograms originating from protein C7 in two biological replicates. The top pane shows signal of the endogenous peptide and bottom pane signal from the corresponding qRePS peptide.*

The capacity of DiscoveryEdge600 does not compromise the detection of endogenous signals or sensitivity. We investigated the effect of spiking the panel side-by-side a neat blood plasma digest without any added qRePS (Figure 4). We could verify that high multiplexing is achieved without loss of endogenous peptide detection.

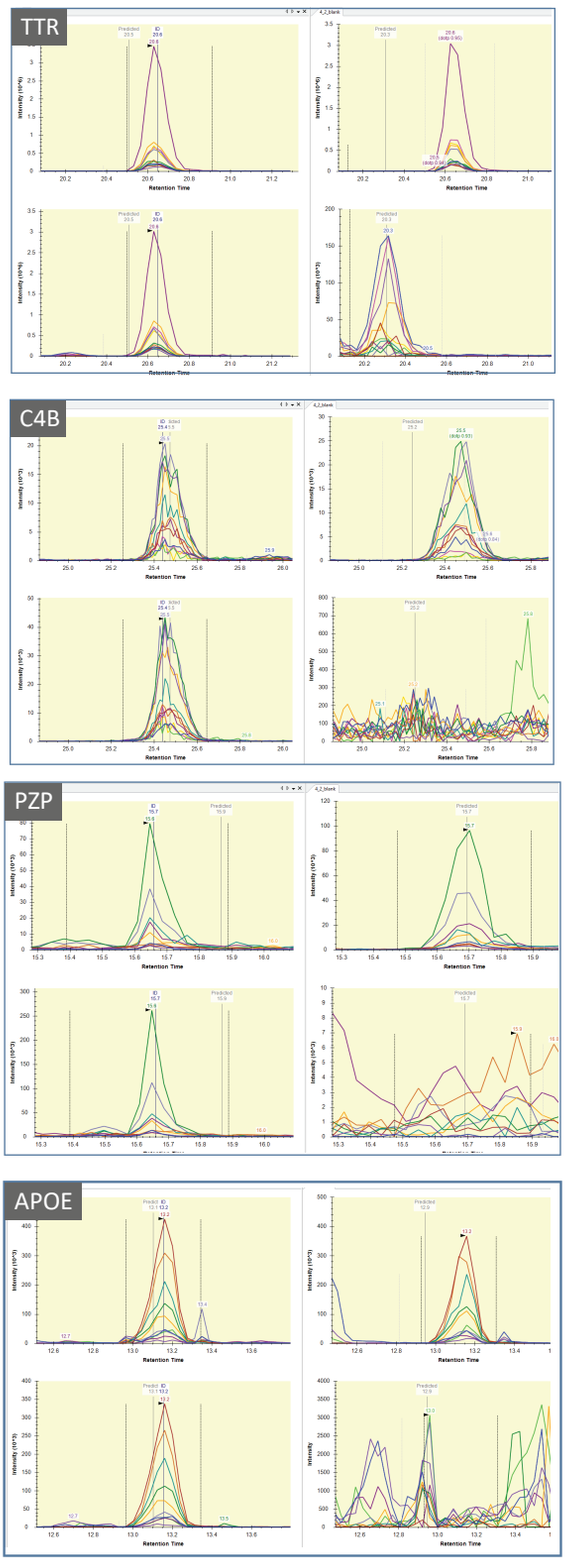


Figure 4: *Extracted peptide ion chromatograms originating from proteins PZP, TTR, APOE and C4B. The left pane shows results of plasma sample spiked with DiscoveryEdge600, the right one of neat blood plasma only. The top pane shows signal of the endogenous peptide and bottom pane signal from digested qRePS.*

Co-digestion of qRePS with endogenous proteins generates multiple quantitative peptides, strengthening the accuracy of measurement. The qRePS are spiked in to increase sensitivity, provide built-in quality control and deliver clinical-grade precision. Reproducible quantification is key, and qRePS enables translation of methods across different MS instruments and platforms while ensuring consistent results between all ProteomEdge products over extended time periods. We acquired the same results across different products, LC-MS configurations and biological replicates prepared two years apart (Figure 5).

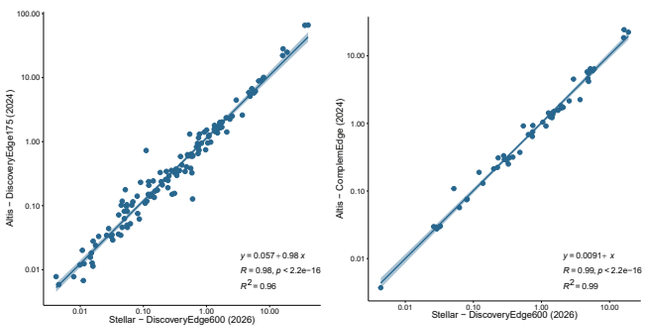


Figure 5: *Comparison of blood plasma protein concentrations based on quantification using DiscoveryEdge175 (left) and ComplemEdge (right) with DiscoveryEdge600. DiscoveryEdge175 and ComplemEdge results were acquired in 2024 using Thermo Fisher Scientific's MS Altis while the Stellar platform was used for quantification with DiscoveryEdge600 in 2026. The results demonstrate the robustness and stability of the qRePS panels.*

The qRePS technology is highly suited for implementation on the Stellar platform, and the combination enables state-of-the-art accuracy and quantification of blood plasma proteins across a broad dynamic range. High precision, with a median CV of 7.4% across 24 biological replicates, was achieved over five orders of magnitude of plasma protein concentrations (Figure 6).

Conclusions

The DiscoveryEdge600 provides a highly scalable and analytically robust solution for targeted plasma proteomics and biomarker discovery across large clinical and translational research cohorts. By combining high-throughput LC-MS workflows with qRePS™ technology, the platform enables reproducible absolute quantification of hundreds of proteins while maintaining the sensitivity and precision required for complex biological matrices such as blood plasma.

The data presented demonstrate that the extensive multiplexing capacity of the DiscoveryEdge600 does not compromise endogenous peptide detection or quantitative performance, even in highly complex samples. Instead, the inclusion of heavy isotope labeled recombinant protein standards enhances peptide identification confidence, improves quantification reliability, and supports consistent performance across biological replicates, product batches, and instrument configurations. The strong correlation observed between measurements generated years apart and on different mass spectrometry platforms further highlights the long-term stability and transferability of the qRePS-based workflow.

The combination of broad proteome coverage, clinical-grade quantitative precision, and compatibility with automated workflows positions DiscoveryEdge600 as a next-generation solution for proteomics-driven research. Together with the Stellar MS platform, the technology enables accurate measurement of proteins across a wide dynamic range while maintaining low variability, supporting both discovery-phase investigations and future clinical research applications. Ultimately, DiscoveryEdge600 represents a powerful platform for accelerating the identification, validation, and translation of protein biomarkers into meaningful biological and clinical insights.

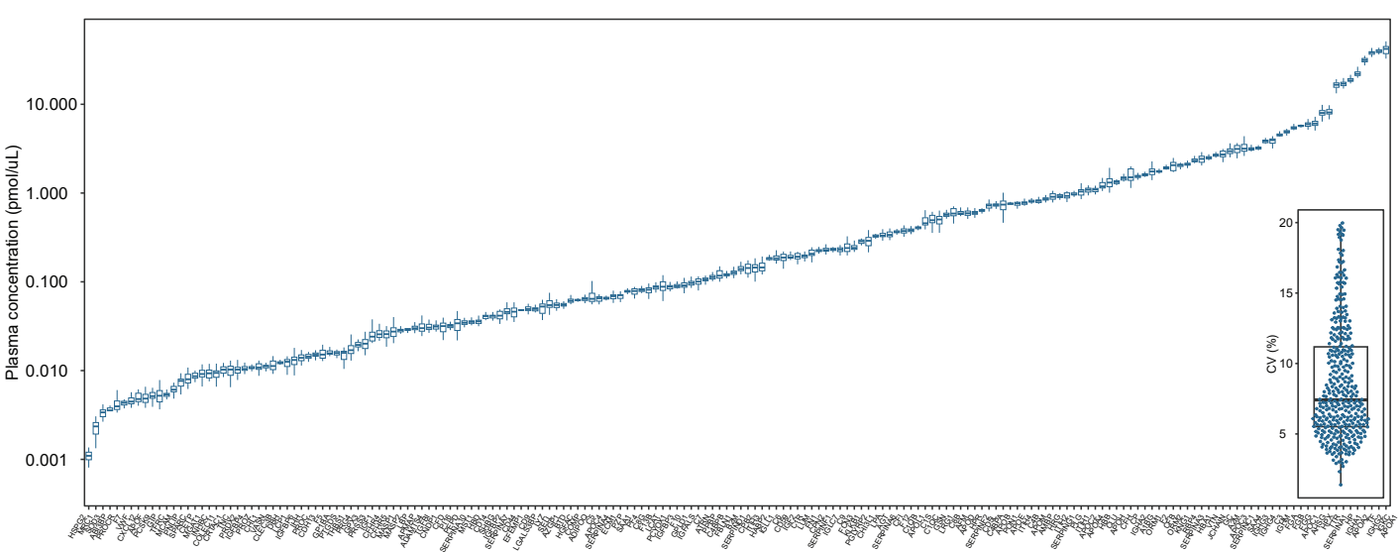
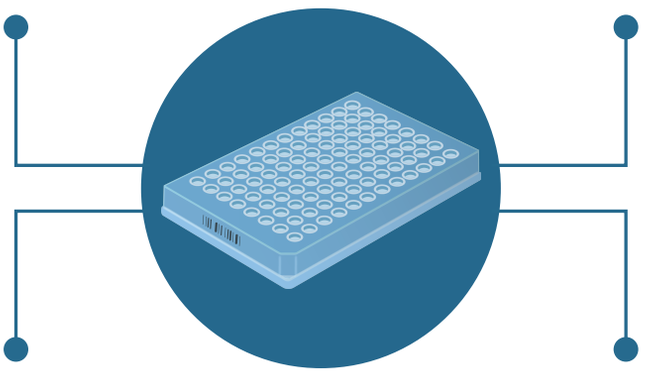


Figure 6: *Dynamic range of concentrations for proteins quantified with Stellar MS using a cutoff of CV < 20% (median CV = 7.4%) across 24 biological replicates and 3 different DiscoveryEdge600 product plates.*

The power of 620-plex absolute quantification in the palm of your hand

Cleavage-dependent Standards
Multipeptide quantification
Unmet precision and accuracy

Protein Panel in Every Well
Designed for plasma analysis
Multiplex absolute quantification



Standardized Plate Format
Easy to automate
Highly scalable

Pre-aliquoted and Dried
Stable at room temperature
Seamless sample processing

Drug Targets
Proteins used as focal points in drug or therapy development to modify disease progression or alleviate symptoms.

Cancer Markers
Biomarkers that reflect cancer severity, progression or stage, supporting disease monitoring and prognosis over time.

Renal Function
Proteins indicative of kidney function and pathology, enabling early detection, monitoring and clinical insight to disease.

Inflammation & Immune Response
Proteins involved in the defense mechanisms, often relevant in autoimmune diseases, infections, and inflammation.

Clinical Diagnostics
Proteins used to detect or monitor diseases and medical conditions.

Metabolic Diseases
Proteins reflecting metabolic health, nutritional state, or liver function.

Coagulation
Proteins essential for blood clotting and regulation of thrombosis or bleeding disorders.

Cardiovascular Health
Proteins involved in cardiovascular disease, cholesterol transport, lipid metabolism.

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