

Quantum-Si's Next-Generation Protein Sequencer™ Enables Protein Detection and Peptide Characterization

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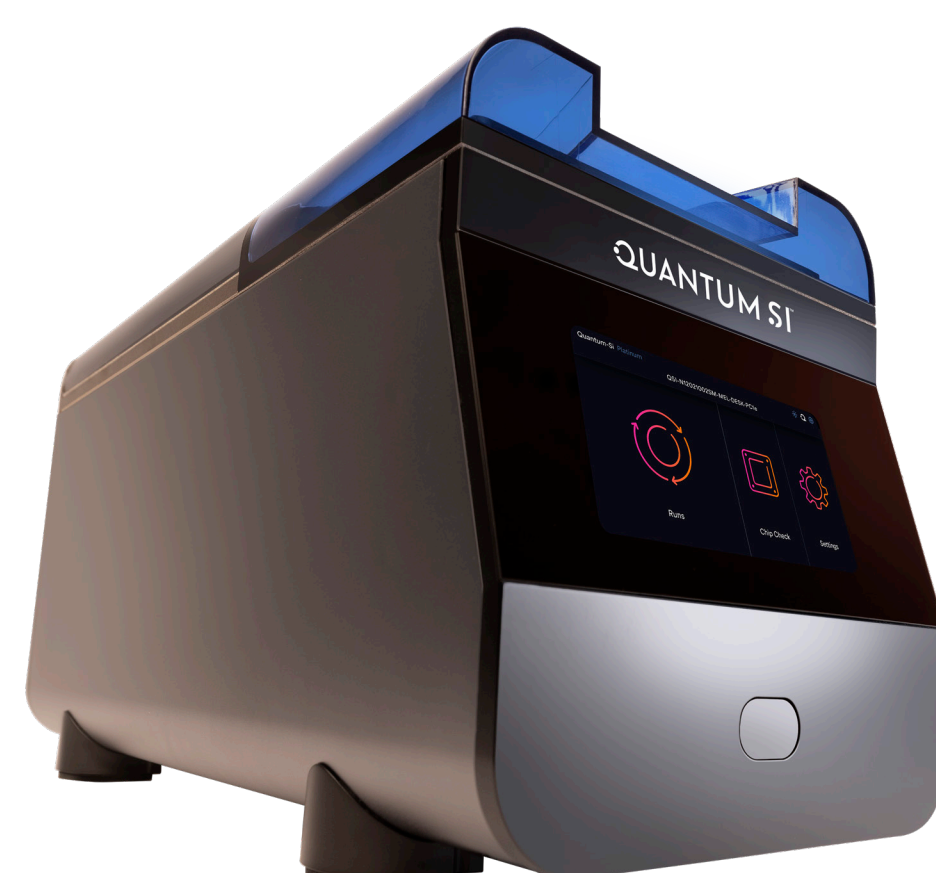
INTRODUCTION

Sequencing proteins and correlating amino acid changes to biological function is critical to advancing our understanding of human health and disease. Next-Generation Protein Sequencing™ (NGPS) on Platinum® enables researchers to identify and characterize proteins with single-molecule resolution in a simple workflow and on a benchtop instrument.

To demonstrate the versatility of Platinum and the use of Kinetic Signatures, we sequenced various types of samples, including recombinant proteins, protein mixtures, immunoprecipitated proteins, peptide barcodes, and peptides with PTMs. First, we sequenced a mixture of four proteins (CDNF, FGF2, IL4, and PDL1) and achieved comparable protein identification results to traditional LC-MS. Additionally, we demonstrated the platform's ability to sequence IL6 immunoprecipitated from human serum and correctly identified IL6 as the top protein against a reference panel of 7,921 proteins, highlighting its potential in analyzing complex biofluids.

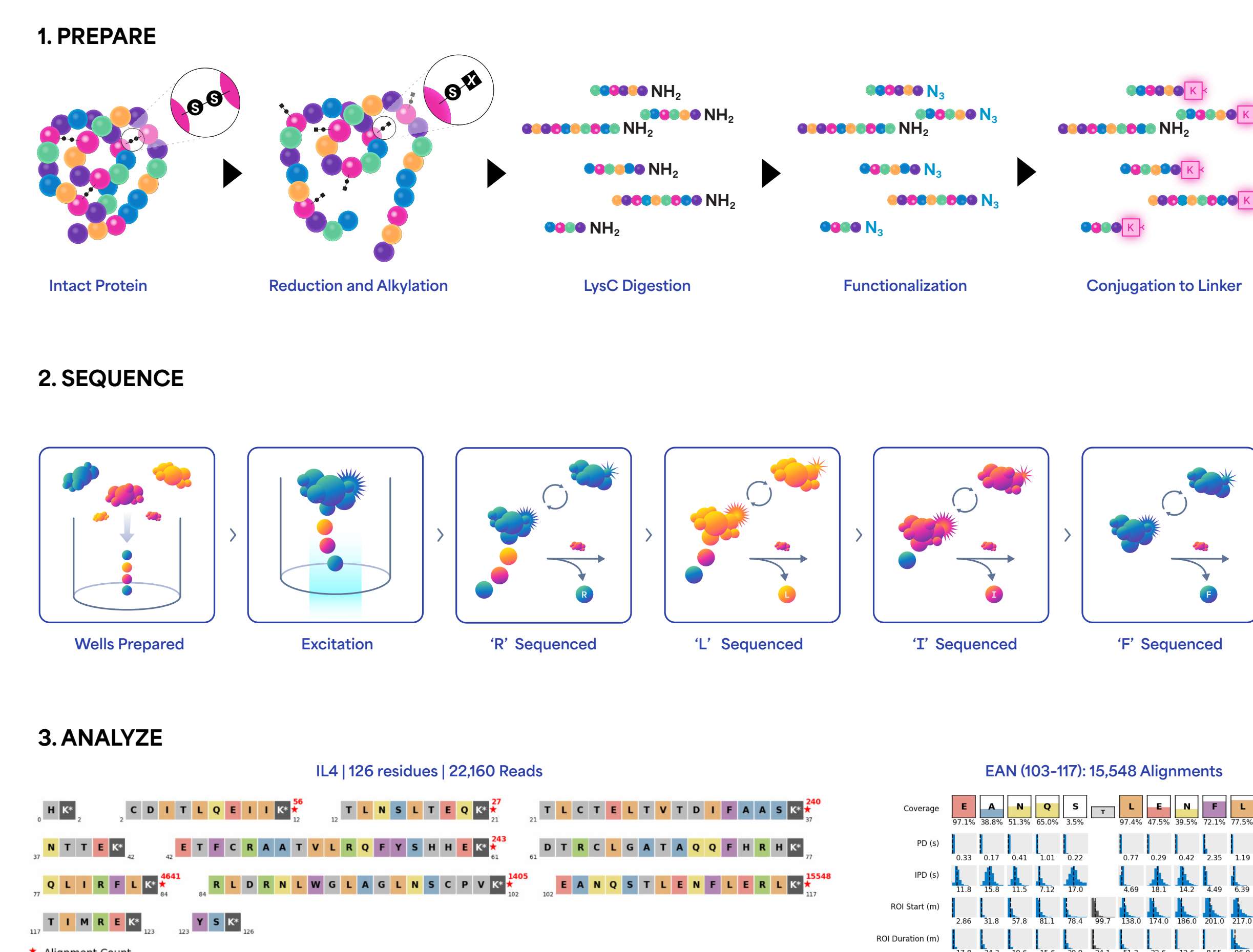
Furthermore, we showcased the detection of peptide barcodes along with the utilization of barcoding techniques to streamline protein engineering applications. Finally, we demonstrated the unique potential of Platinum to detect PTMs relevant to human disease using kinetic signatures by successfully identifying arginine citrullination in protein vimentin.

Recent product enhancements to the platform include new sequencing kit and chip chemistry as well as advanced analytical software tools. These enhancements unlock new applications such as the use of protein inference to study unknown protein samples. In the future, we expect NGPS to further enable the detection of protein variant and modifications



METHODS

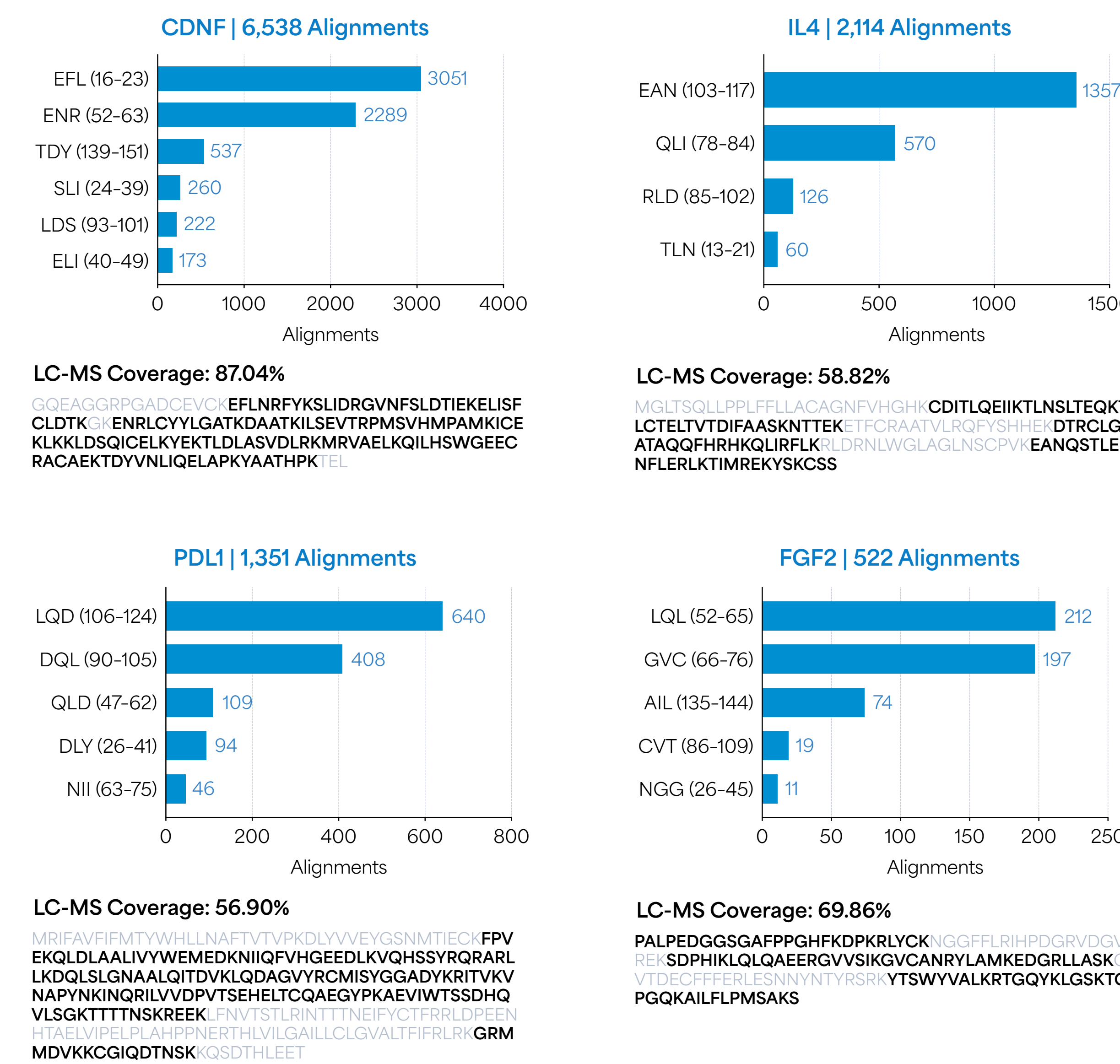
- Proteins are reduced, alkylated, and digested with LysC.
- Peptides are functionalized, conjugated, and immobilized on the surface of Quantum-Si's semiconductor chip.
- Fluorescently labeled N-terminal amino acid (NAA) recognizers and aminopeptidases are added to the semiconductor chip.
- Fluorescence lifetime, intensity, and kinetic properties of NAA binding events generate a unique kinetic signature.
- Kinetic signatures are converted into amino acid calls to identify peptides and proteins.



RESULTS

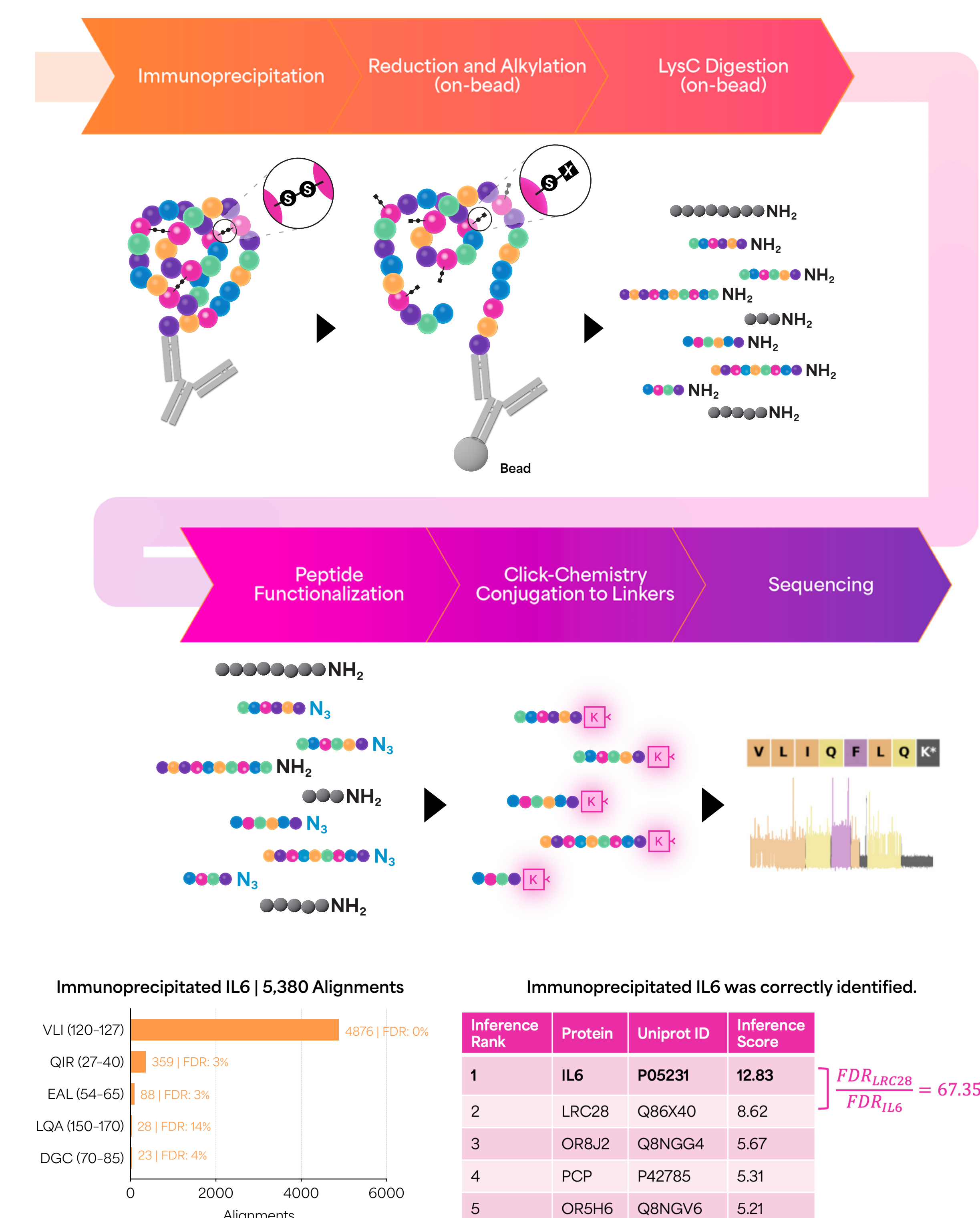
Accurate Identification of All Proteins in a Mixture

A mixture of four proteins was successfully sequenced with Platinum with achievable results compared to traditional LC-MS.



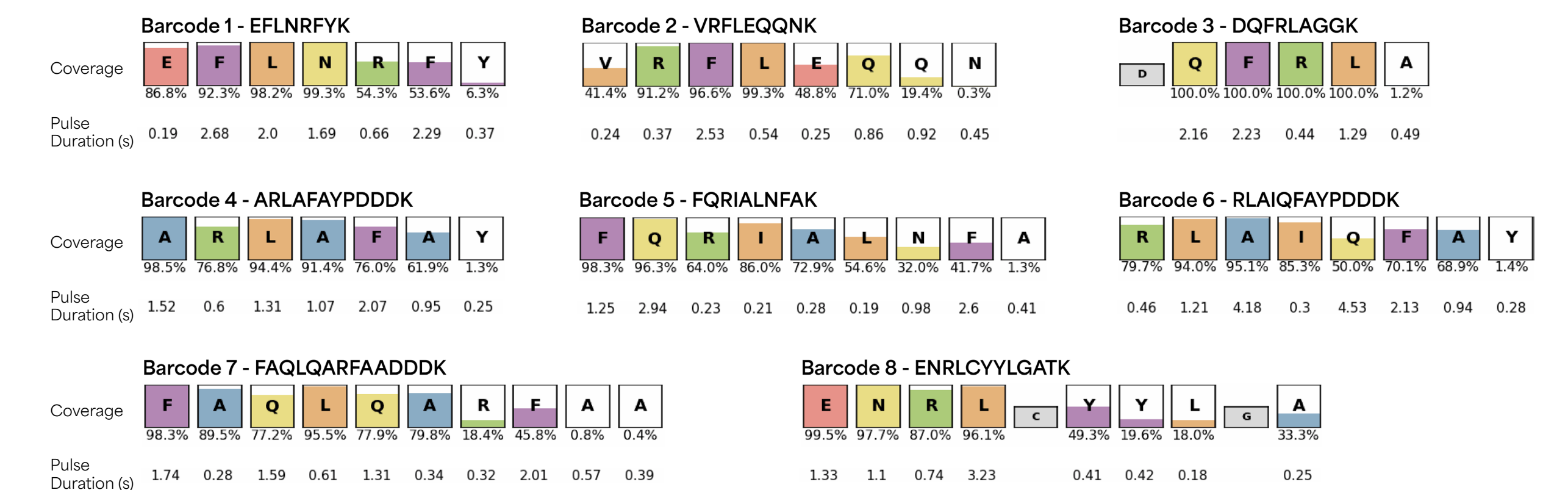
Accurate Identification of IL6 Immunoprecipitated from Human Serum

IL6 immunoprecipitated from human serum was correctly identified as the top protein against an 8K-protein reference panel.



Using Peptide Barcodes to Screen for Proteins with Select Properties

This set of peptide barcodes displays unique recognition patterns and on-chip pulse durations, enabling accurate identification with Platinum.

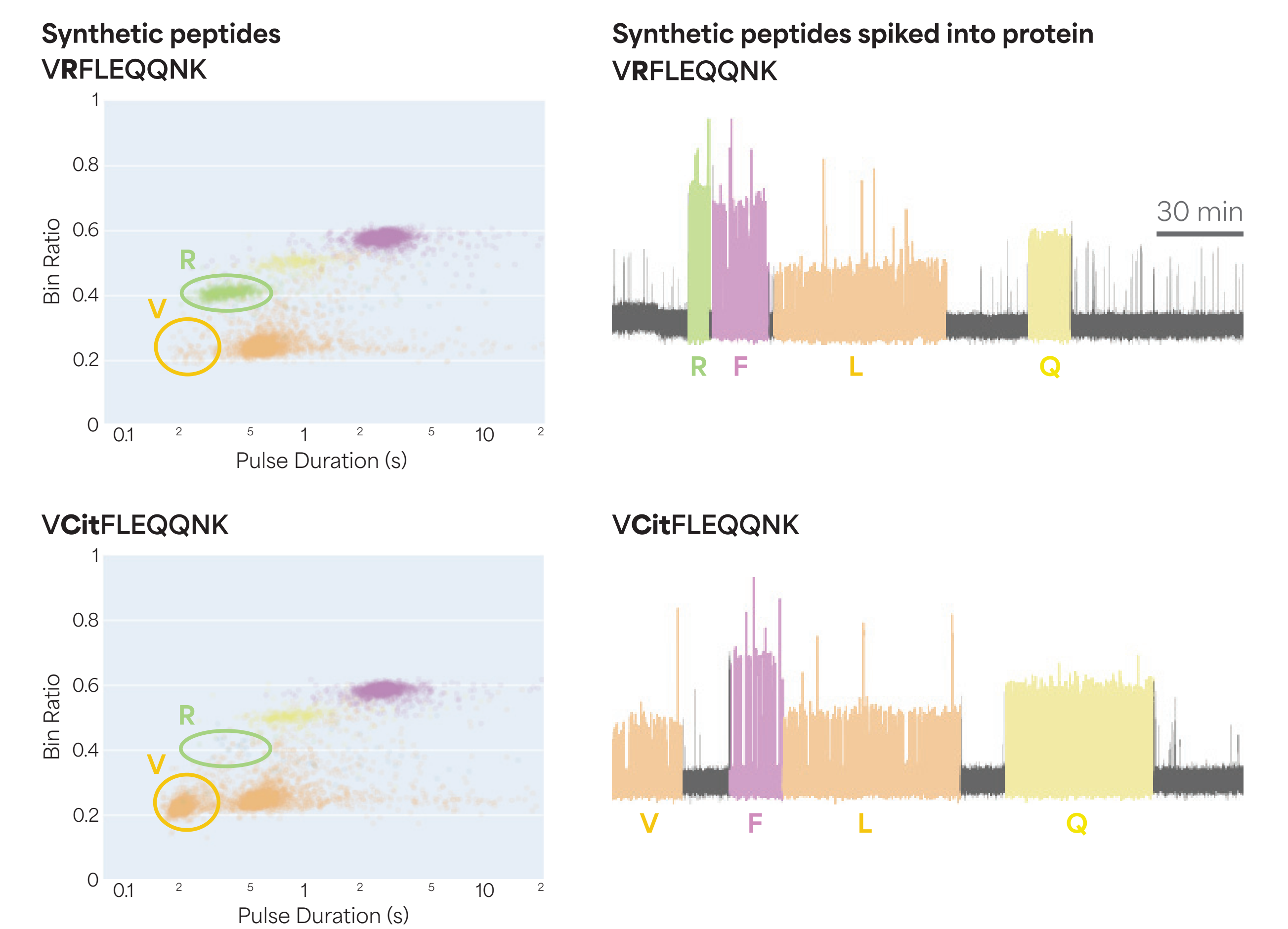


Workflow for enrichment and sequencing of barcoded nanobodies.



Detection of Arginine Citrullination from Peptides Derived from Vimentin

Citrullination led to the recognition of the first V residue, while the recognition of the second R residue was eliminated.



REFERENCE

Brian D. Reed et al, Science 2022, 378 (6166) 186-192.

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