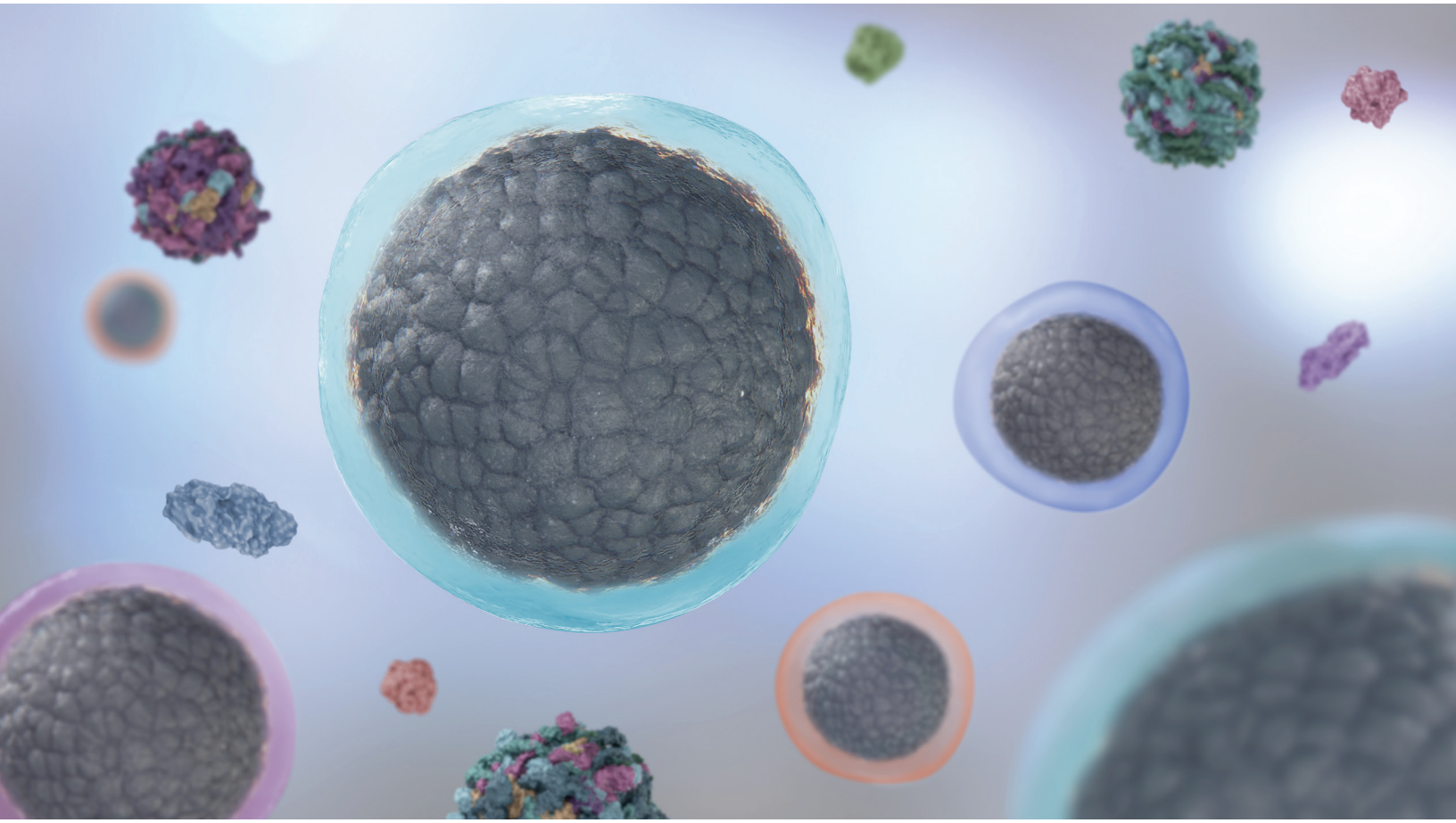
THE PROTEOGRAPH™ PRODUCT SUITE

See the proteome in a way that has never been possible before



Highlights

- Unbiased coverage: Discover new biology, not just what you can capture
- Deep access: Survey across the dynamic range of proteins in complex samples without depleting or fractionating
- Rapid workflow: Rely on an optimized, robust workflow to complete your projects with minimal hands-on time
- Scalable technology: Power longitudinal studies with scalable assay designs

seer

There is a big gap in our understanding of the proteome

In order to more fully understand the complexity of the proteome, we need to study the diversity of protein variants and the roles they play in biology and in health. The fundamental challenge with existing proteomics technologies is that they are not able to reach the depth, breadth, and scale to match biological complexity.

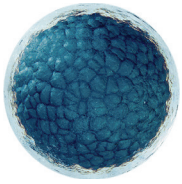
The Proteograph Product Suite changes that

To build a more transformative view of the proteome, we had to create a new technology. One that provides a new lens on the proteome, enabling researchers to see the breadth, depth and dynamic nature of protein diversity across populations and time. Seer developed a proprietary approach by engineering nanoparticles with unique physicochemical properties that enable deep and unbiased interrogation of the proteome in complex samples such as plasma, in a rapid and scalable workflow.

See more of the proteome

The Proteograph Product Suite is an automated solution that is comprised of consumables, a sample preparation automation instrument and software. It is designed to be detector agnostic, making it even easier to add unbiased, deep, rapid proteomics studies at scale to any lab.

The power of nanoparticles allows you to explore the proteome in new ways

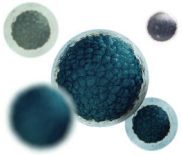


Broad affinity range

Seer's nanoparticles produce a reproducible and selective binding of proteins without prior knowledge of what is present in the sample. Our proprietary nanoparticles are engineered to allow unbiased interrogation of the proteome. Quantitative compression of the dynamic range renders low abundant proteins visible to detectors, enabling you to see across the range of proteins present in a plasma sample.

Tunable physicochemical properties

Our nanoparticles are configurable into a vast combination of distinct designs, using unique physicochemical properties. When combined, a set of nanoparticles can survey the full range of proteoform diversity in a sample.



Robust, simple and scalable

Seer's approach delivers reproducible performance across samples, labs, and experiments. The process is automated and easy to use, greatly simplifying workflow and reducing the complexity of a proteomics lab to a 96-well plate – essentially forming a lab on a nanoparticle.

Unbiased, deep, and rapid proteomics experiments that scale without sacrifice

The Proteograph Product Suite includes the SP100 Automation Instrument, a 5-nanoparticle panel with associated consumables, and the Proteograph Analysis Suite of software. It integrates seamlessly with existing lab equipment, working with nearly all existing mass spectrometers. The Proteograph Product Suite is designed to enable proteomics studies with an unprecedented combination of speed, efficiency, breadth and data output.

The automated Proteograph workflow is optimized for multiple samples in a single run and includes quality controls to ensure robust measurements. Survey thousands of proteins with precision – without sacrificing nuance – in hours. The Proteograph solution delivers the quantitation, precision, and reproducibility you need to tackle proteome studies of varying sizes with confidence (Figure 1).

Simple, elegant preparation

Put Seer's proprietary nanoparticles to work with an easy-to-use, fully automated protocol

A single, unified workflow

Go from sample to seeing more quickly

Seamless lab integration

Works with the LC-MS/MS your lab already uses

A clearer view of the proteome

Scalable analysis suite to QC, analyze, integrate data and generate reliable insights

Figure 1: Proteograph Product Suite

A workflow that scales with your studies

Simply load the SP100 instrument with consumables and your samples and press start, beginning the automated protocol (Figure 2). The instrument will divide each of the samples into five aliquots, adding one of five nanoparticles to each aliquot. Each distinctly functionalized nanoparticle will produce a specific and reproducible corona from the proteins contained within the sample, selected by that particle's properties (step one). The samples are then incubated, pulled down using the inherent magnetic properties of the nanoparticles, and washed (step two).

Following the washes, the proteins are denatured and digested directly on the particles to yield tryptic peptides (step three), which are then purified using solid-phase extraction on the instrument. At the end of the run, these peptides are ready to be dried and injected onto a mass spectrometer (step four). The reproducible compression of the dynamic range facilitates quantification of more proteins in a shorter time. Next, upload run data to the Proteograph QC software tool to check the run, and proceed to data analysis and insights using the Proteograph Analysis Suite (step five).

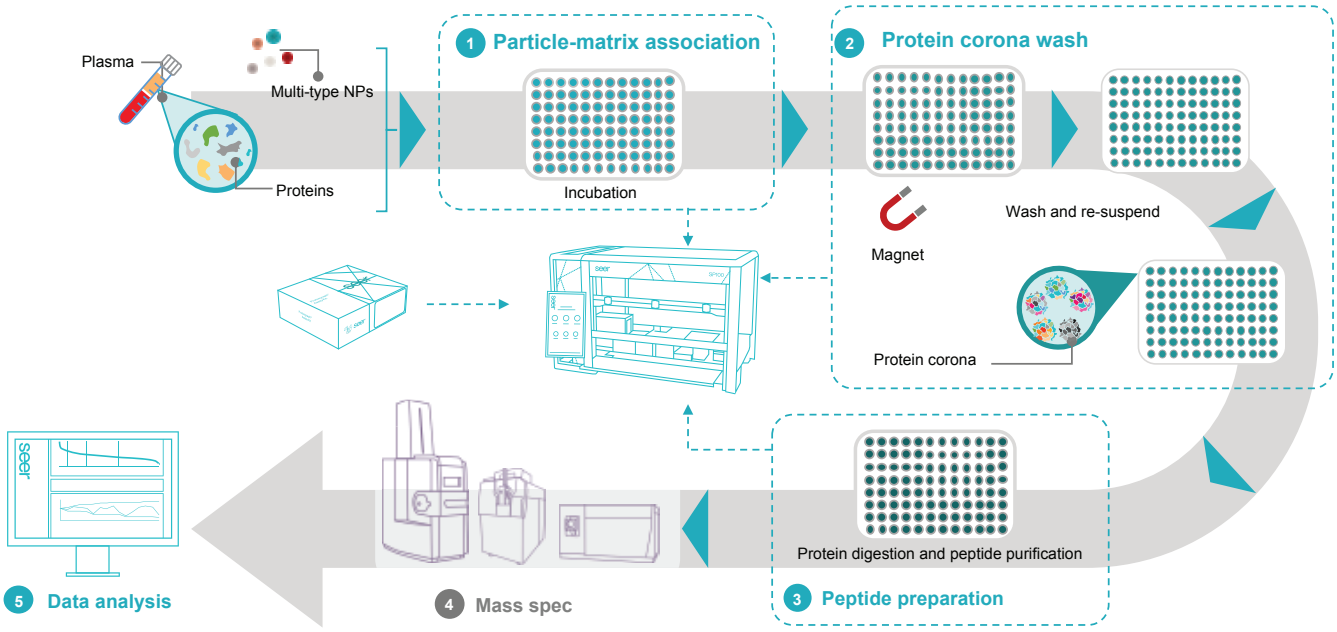


Figure 2: Proteograph workflow

See more of the proteome with the Proteograph Product Suite

Go deeper than traditional methods for unbiased proteomics

The Proteograph Product Suite was designed to make unbiased, deep proteomics scalable. To compare performance, we used a single plasma pool and compared a five nanoparticle panel vs neat, depleted, and fractionated plasma.The Proteograph Product Suite's five nanoparticle panel yielded significantly more protein groups covering low abundance proteins at a higher precision than a depleted and deep fractionated workflow (Figure 3).[1-3]

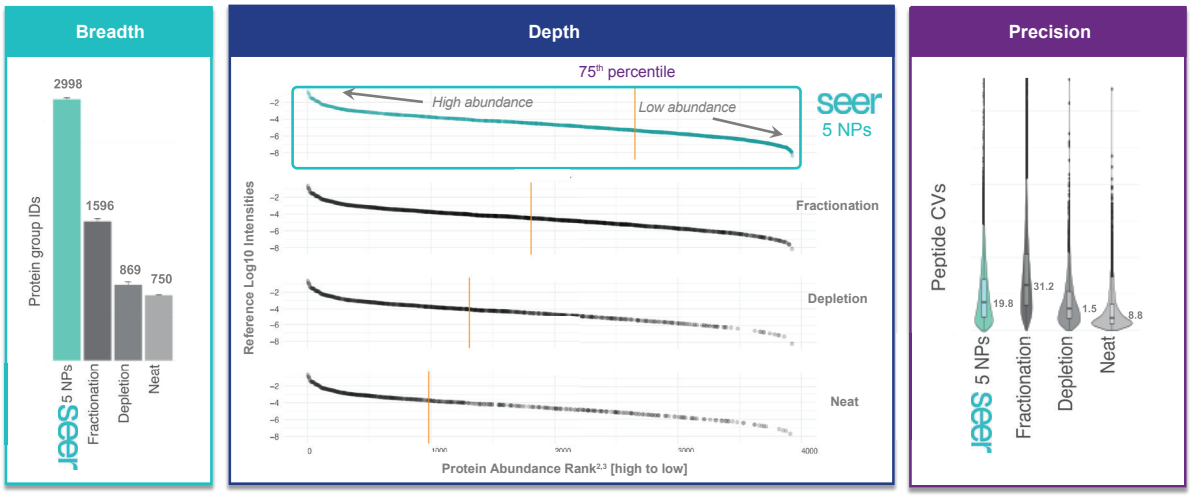


Figure 3: The Proteograph Product Suite yields more low abundant proteins with higher precision. Fractionation of 19 high pH fractions of digested, depleted plasma concatenated to 9 injections. All samples were run with a 30-minute gradient and processed using DIA-NN software in library-free mode.

Detect more common and rare variants than targeted approaches

Using the Proteograph Product Suite, you can detect rare protein variants, or variants that have never seen before. The fraction of variants of any given allele frequency detected matches their fraction in the population (Figure 4).[4,5] The ability to detect both common and rare variants distinguishes the Proteograph Product Suite from targeted approaches, which require known, catalogued common variants with target-specific analytes.

Rare protein variants are important. In a population, rare genetic variants vastly outnumber common variants. As a result, in each personalized proteome a large fraction of variants are rare. Importantly, rare variants are highly enriched for pathogenicity. Common variants are known to usually be either benign, or to have a small effect in disease. Rare variants are much more likely to be deleterious and to have a large effect in common and rare disease.

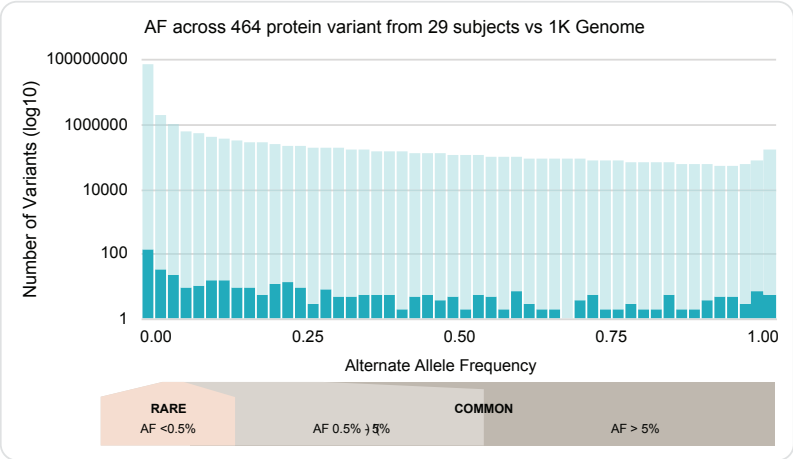


Figure 4: 1000 Genomes Consortium 2015 - Allele frequencies across 464 protein variants from 29 subjects.

Targeted approaches are unable to detect rare and personalized protein variants. Aptamer- or antibody-based methods rely on the design of a unique probe for each target. Each target protein variant has to have been observed before, and the pool of targets has to be of limited size.

Understand more diversity in the proteome

Discover novel protein biomarkers

Using Seer's powerful and unbiased approach, identification of unknown protein targets is now possible. Unbiased proteomic profiling of 141 samples from patients with non-small cell lung cancer (NSCLC) was compared to healthy and comorbid controls.[6] Early stage (stages 1-3) NSCLC were classified compared to healthy controls, showing greater power than a number of other studies that have used genomics-driven approaches.

This illustrates the value of unbiased proteomic data, and suggests greater predictive power from combining proteomic and genomic information.

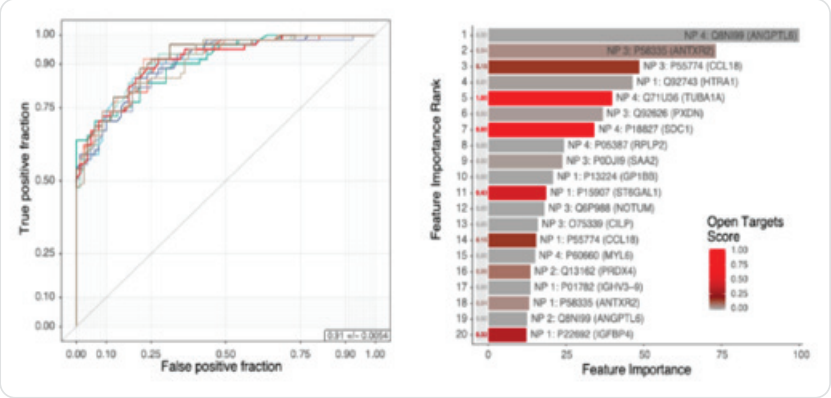


Figure 5: Classifier performance (left) AUC 0.91, 58% sensitivity/98% specificity, multiple cross-validation. Classifier top features (right) majority not known for NSCLC utility, includes tubulin, paclitaxel target.

Characterize genomic variants with proteomic insights

Combining genomics at scale with deep, unbiased proteomics has the potential to detect changes in proteins at the amino acid level that are induced by single nucleotide variants. To demonstrate this, whole exome sequencing across 30 subjects was performed to create personalized libraries and then matched with proteomic signatures to genomic information.

The results show an average of 69 protein variants in the plasma of each subject, with a range from the high 120's to low 50's of protein variants (figure 6). In the plot on the right, the allele is very rare in the population, with a minor allele frequency of 0.01%. This subject is heterozygous for this allele which means they have one copy of this rare allele from one parent and another copy of the normal reference allele from the other parent. The Proteograph Product Suite detects both protein variants.

By studying the functional impact of genetic changes across different disease states, the relationship between allele specific expression and disease status can be revealed, accelerating the synergistic value that genomics and proteomics bring together in understanding health and disease.

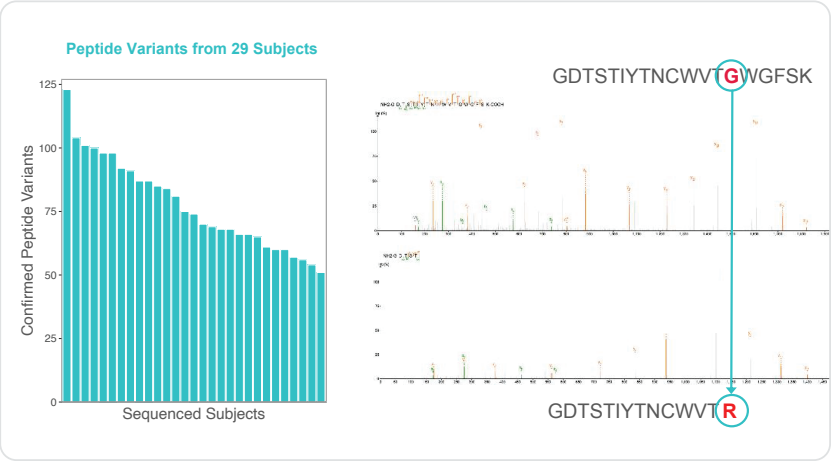


Figure 6: Peptide variants from 29 subjects analyzed via exome sequencing, amino acid substitution, SNV (at right, 0.01% population frequency) detected by the Proteograph Product Suite.

Resolve biology at the peptide level

Large scale proteomics studies are key to understanding the biology underlying disease, linking protein variants produced to alternative RNA splicing, alternative transcription and post translational modifications.

The Bone Morphogenic Protein 1 (BMP1) gene is known to have seven variants at the RNA level from alternative splicing, and four variants at the protein level. Of these four variants, two are the long form and two represent the short form of the BMP1 protein. Among the peptides detected in this study, six specific peptides came from various parts of BMP1. Interestingly, the short form of the BMP1 protein was expressed predominantly in cancer patients, whereas the long forms of the protein were seen more often or at a higher level among the healthy controls (Figure 7). This observation has not been previously reported in the literature and may merit further investigation for the potential role of different BMP1 protein variants in health and cancer.

The Proteograph Product Suite is designed to allow exploration of proteome complexity and diversity at the peptide and amino acid levels, and to discover many distinct protein variants.

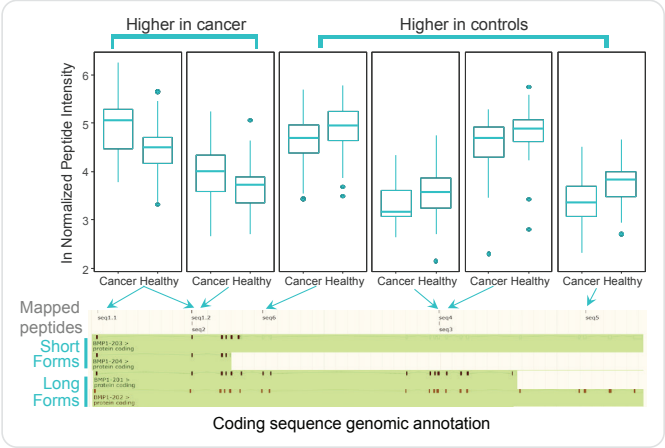


Figure 7: Bone Morphogenic Protein 1 (BMP1) analysis of protein variants long and short form.

Ask deeper biological questions

The nodes formed by proteins interacting with other proteins provides a framework for understanding the underlying biology of disease and health. A comparison of healthy individuals to those in early or late lung cancer shows how expression in clusters of putatively interacting proteins change.[7]

Mapping the protein groups found in this study to high-quality protein-protein Interactions (PPI) derived from the STRING database resulted in 13,966 PPIs covering 1,061 proteins.[8] A network algorithm to partition the resulting PPI graph is shown in Figure 8. Colors represent the partition of the map into clusters of proteins that are highly linked. After normalization of the protein expression inside the same group, expression levels are overlaid on the PPI maps with green indicating high expression and red indicating low expression. Changes were observed in expression of PPI clusters from healthy controls to NSCLC. For example, cluster 46 has the lowest expression in healthy and comorbid pulmonary controls and progressively higher expression in early-stage and late-stage NSCLC which may have relevance to disease progression.

The totality of proteomics information, from amino acid variants to pathway analysis is made tangible and measurable with the Proteograph Product Suite.

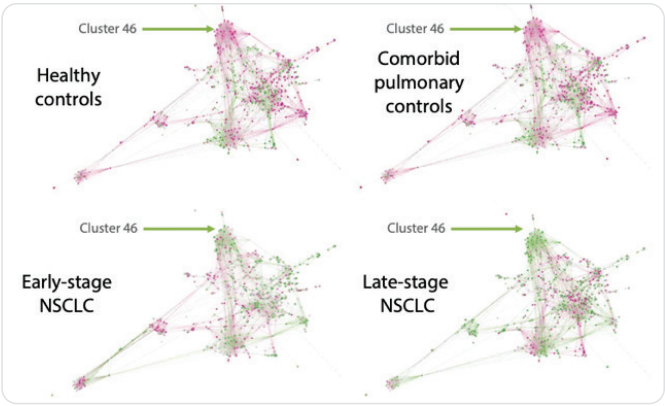


Figure 8: Overlaying Proteograph data on PPI maps allows investigation of functional modules in NSCLC subjects.

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