White paper

Proteomic Exploration of Immune and Disease Pathways with Olink® Reveal

Introduction:

Proteins as functional mediators of disease biology

Proteins are the functional effectors of biology, driving enzymatic reactions, signaling cascades, immune responses, and structural integrity. While transcriptomics have transformed biomedical research by enabling comprehensive measurement of RNA abundance, mRNA levels frequently diverge from protein concentrations. This divergence arises from regulation at multiple stages of gene expression, including translation efficiency and protein turnover. As a result, protein measurements are often more directly linked to physiological state and clinical outcomes than their transcript counterparts.

In recent years, next-generation proteomics technologies, such as proximity extension assay (PEA) technology, have enabled the simultaneous quantification of thousands of proteins from minimal sample input, offering more comprehensive insight into disease biology than limited-scale panels. Olink Reveal applies this principle with a panel of ~1,000 proteins, measured through a simple workflow based on standard molecular biology methods and read out on widely available next-generation sequencing platforms. By making large-scale protein measurement broadly accessible, these approaches create new opportunities to investigate the biological pathways that underlie health and disease.

A central feature of disease biology is the immune system. Inflammation and immune responses drive, or at the very least influence, the majority of medical conditions, from cardiovascular disease and cancer to neurodegeneration and autoimmune disorders. These processes are inherently complex, involving hundreds of interacting proteins with synergistic, additive, or redundant roles. Processes such as metabolism, extracellular matrix organization, developmental biology, and cell cycle regulation also contribute fundamentally to health and disease. A proteomics solution that balances deep representation of immune pathways with broad coverage across diverse biological processes is therefore uniquely positioned to support disease research across therapeutic areas.

A carefully curated protein panel for exploratory research

Panel design is critical for proteomics studies. To be broadly useful, the protein content must cover pathways central to disease biology. Olink Reveal achieves this by offering deep representation of immune and inflammatory proteins—essential for understanding disease-driving processes—together with a wide range of non-immune proteins implicated in metabolism, development, signaling, and others (Figure 1).

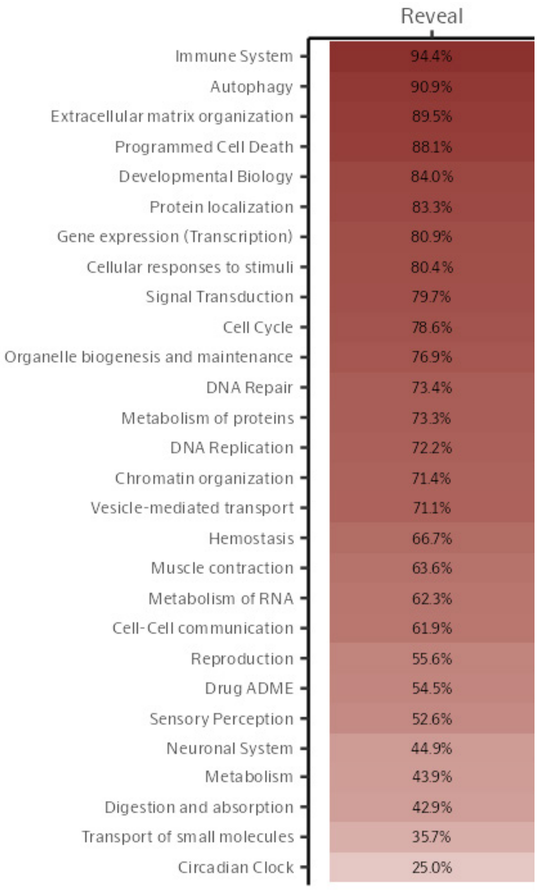


Figure 1. Biological pathway coverage of Olink Reveal. Proteins included in Olink Reveal mapped to Reactome pathways. The panel shows strong representation of immune and inflammation-related processes, alongside diverse pathways such as metabolism, cell cycle regulation, developmental biology, and signal transduction. This balanced coverage enables deep immune profiling and broad applicability across disease biology.

In total, 537 inflammation-related proteins are included, covering 96% of immune response pathways in Reactome, 100% of its top-level pathways, and 64% of all Reactome pathways. Importantly, more than 850 proteins included in the panel have been reported as associated with human disease, ensuring that the panel captures biomarkers with demonstrated clinical and biological relevance. In addition, over 700 proteins are associated with *cis* protein quantitative trait loci (*cis*-pQTLs), genetic variants near the encoding gene that regulate protein levels (Figure 2). These proteogenomic associations strengthen confidence in assay specificity and enable integration with genetic studies of disease.

This careful curation ensures applicability whether the research question centers on immune-mediated pathology or other disease-related mechanisms.

High performance	Broad coverage	Inflammation processes	Associated with disease	Associated with *cis* pQTLs
~1,000	**100%**	**537**	**>850**	**>700**
proteins detected in 86-100% of samples	top-level pathways	proteins	proteins	proteins

Figure 2. Overview of the protein content included in Olink Reveal, highlighting both performance and biological coverage. The panel quantifies ~1,000 proteins with high detection rates across samples. Content spans all major Reactome pathways, with strong representation of immune processes as well as proteins associated with human disease and genetic regulation. This design ensures broad biological coverage and clinical relevance for disease-focused proteomics. References: (1) Internal validation data; (2) Reactome; (3) Reactome, Open Targets, Gene Ontology; (4) Peer-reviewed literature and UK Biobank data; (5) UK Biobank *cis*-pQTL dataset (PMIDs: 37794188, 39316441, 37794186).

The largest population proteomics study as a resource for panel design

The UK Biobank Pharma Proteomics Project (UKB-PPP) represents the largest initiative to date linking circulating proteins to human disease. Using Olink® technology (Olink® Explore 3072), nearly 3,000 proteins were measured in plasma from more than 50,000 participants and integrated with longitudinal healthcare records to estimate the impact of protein levels on future disease risk. This large-scale study provided one of the foundations for designing Olink Reveal. Proteins showing robust associations with disease risk across multiple categories were prioritized for inclusion (Figure 3).

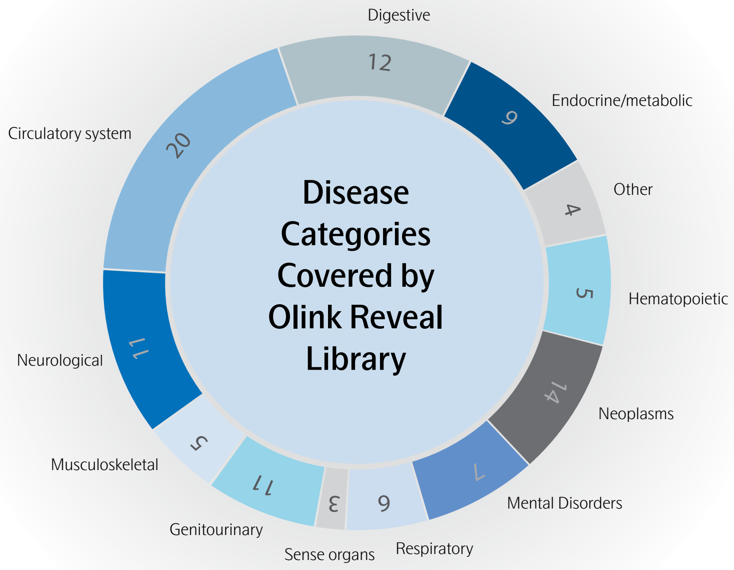


Figure 3. Diseases analyzed in the UK Biobank Pharma Proteomics Project (UKB-PPP) with at least one protein represented in Olink Reveal. Diseases were grouped into major categories according to the PheWAS (Phenome-Wide Association Study) ontology, spanning circulatory, digestive, endocrine/metabolic, genitourinary, hematopoietic, mental disorders, musculoskeletal, neoplasms, neurological, respiratory, sense organs, and other conditions. Each disease required ≥150 incident cases over a 10-year follow-up, with prevalent cases excluded. This classification provides a structured framework for evaluating protein–disease risk associations across diverse areas of human pathology.

UK BIOBANK

The UKB-PPP complete findings are openly accessible via the Olink® Insight platform

ACCESS NOW

High number of protein–disease associations enabling discovery across a wide range of diseases

The Olink Reveal library represents a carefully selected subset of the UKB-PPP proteomics data. It includes 29.4% of the 2,922 proteins measured in UKB-PPP and retains 35.7% of the statistically significant disease associations. Importantly, almost all (96.1%) diseases with significant protein association are covered by at least one protein in Olink Reveal. This demonstrates the panel's capacity to support research across a wide spectrum of diseases and biological processes.

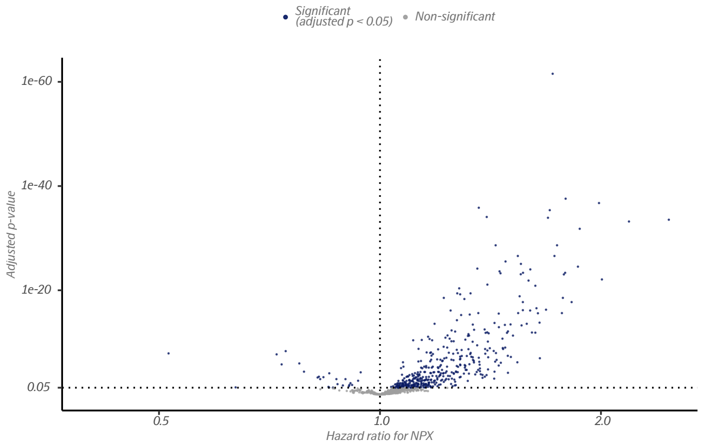
To facilitate detailed investigation of individual diseases, protein–disease risk associations can be visualized as volcano plots for each condition included in UKB-PPP. For interactive access to the complete set of volcano plots and significant protein–disease associations, visit https://insight.olink.com/olink-data/reveal-ukb

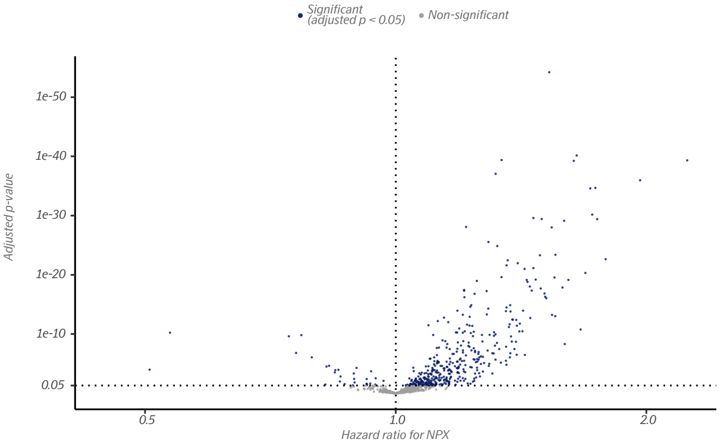
Selected volcano plots are highlighted in the next page, illustrating the number of proteins that show both strong effect sizes and robust statistical significance (Figure 4). These examples underscore the translational potential of such associations, whether for the identification of biomarker signatures, the stratification of patients, or the prioritization of therapeutic targets. Just a few of these plots already illustrate the breadth of Olink Reveal, highlighting its ability to capture clinically meaningful biology across major diseases.

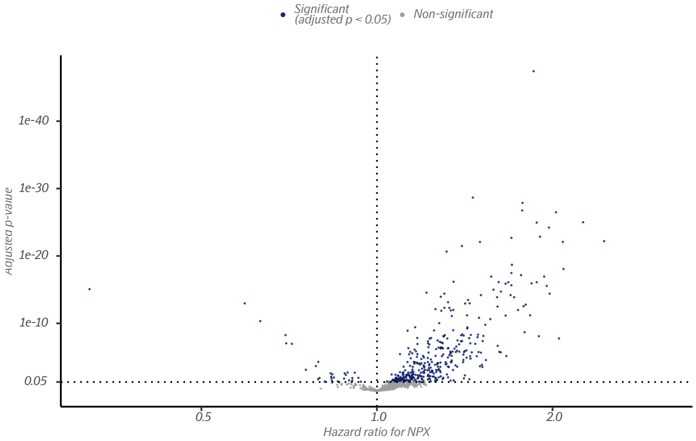
OLINK® INSIGHT

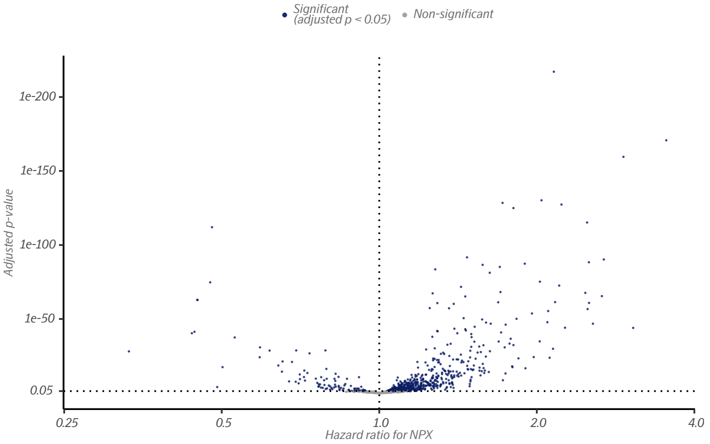
Researchers can interactively explore every protein association with future disease risk from Olink Reveal using Olink Insight.

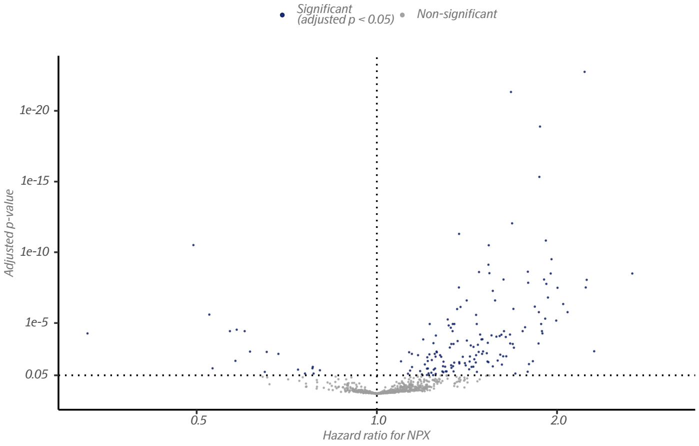
ACCESS NOW

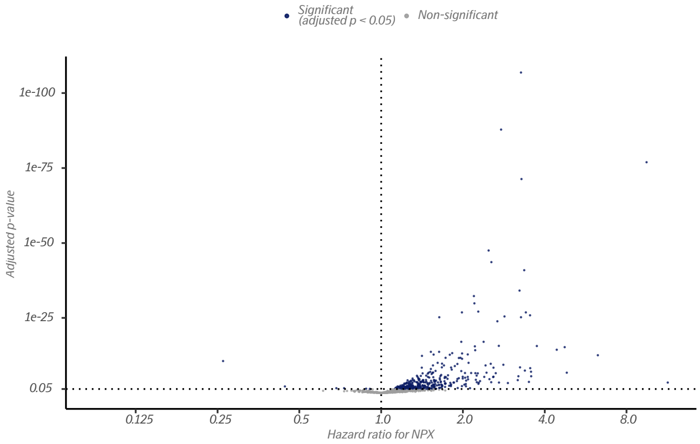

Coronary atherosclerosis

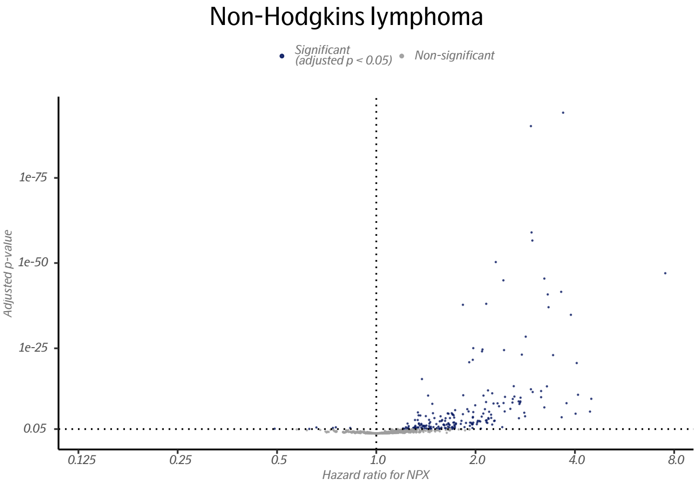

Ischemic Heart Disease

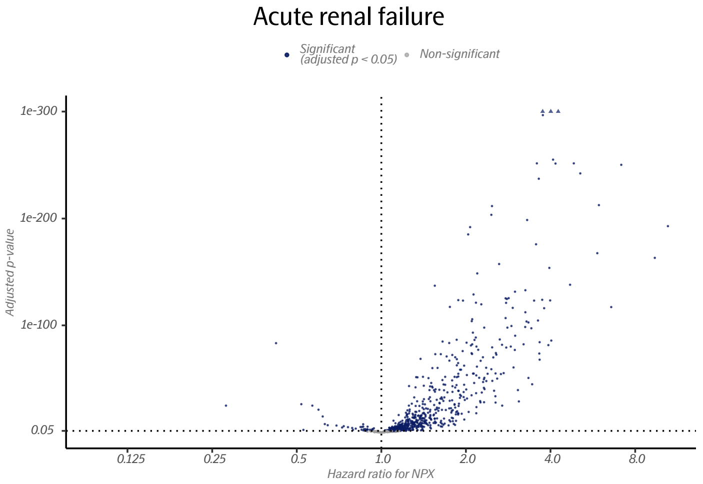

Cerebrovascular disease

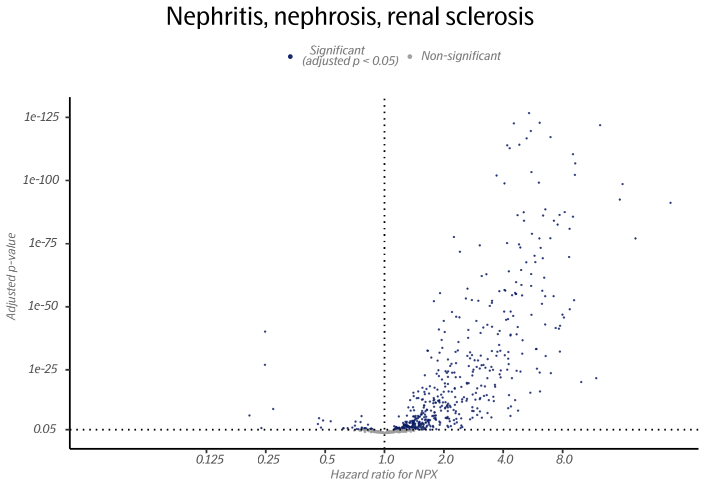

Type 2 diabetes

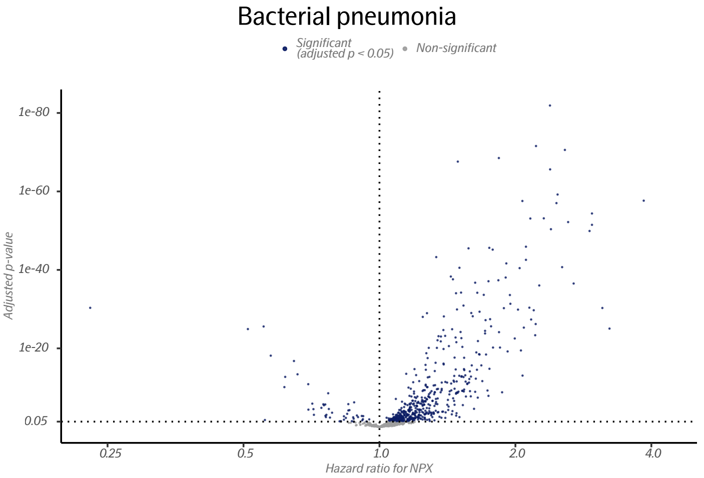

Cancer of bronchus, lung

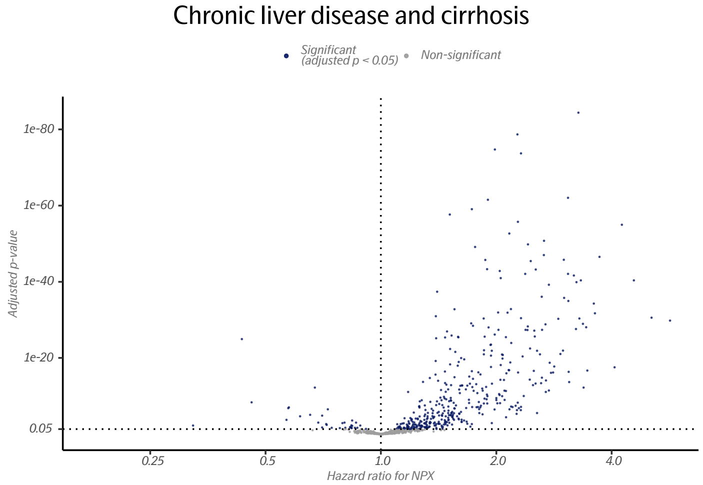

Leukemia

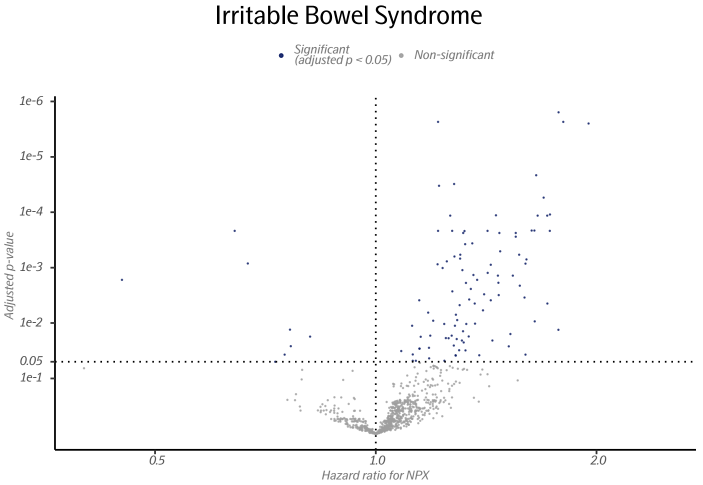

Non-Hodgkins lymphoma

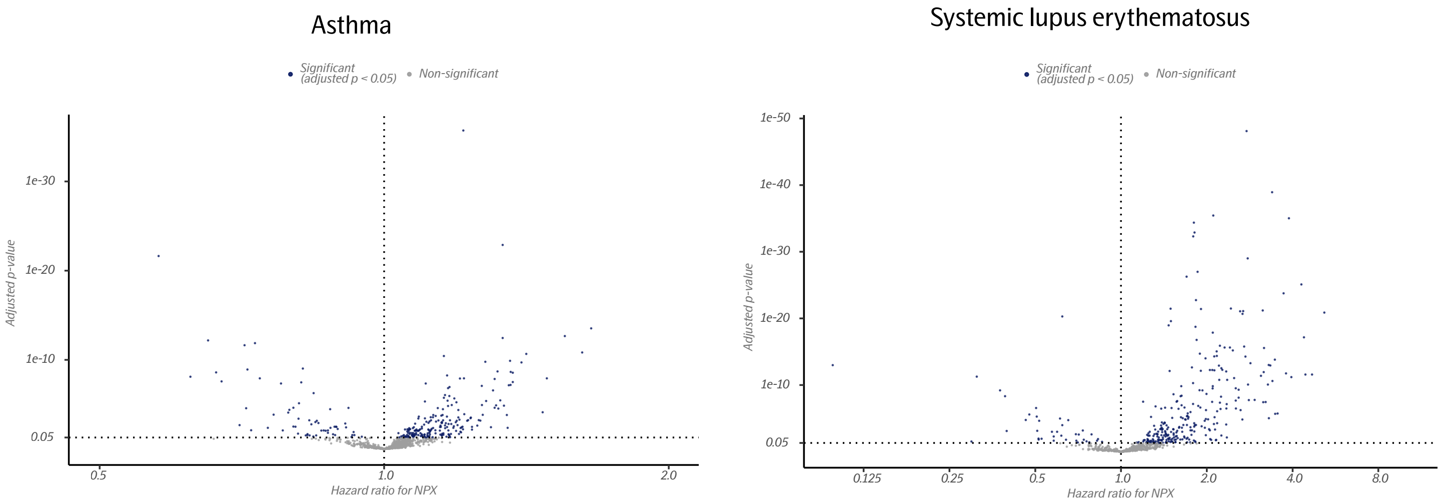

Acute renal failure


Nephritis, nephrosis, renal sclerosis


Bacterial pneumonia


Chronic liver disease and cirrhosis


Irritable Bowel Syndrome



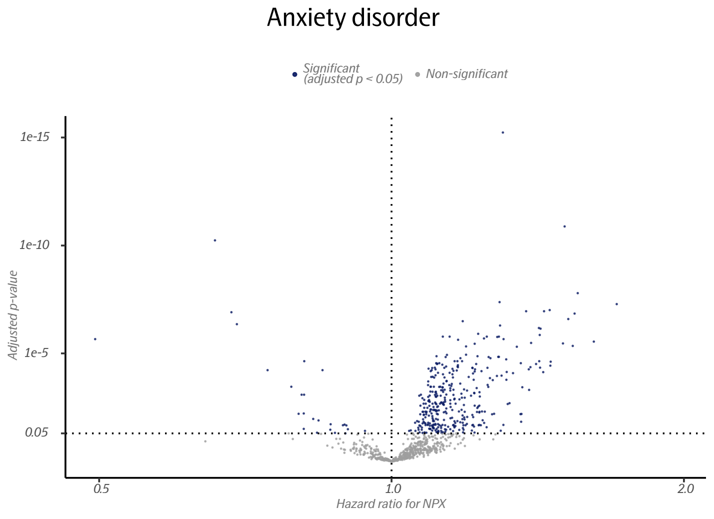


Figure 4. Selected volcano plots of protein–disease risk associations across major disease areas (e.g., cardiovascular disease, type 2 diabetes, lung cancer, systemic lupus erythematosus). Each plot illustrates both effect size (hazard ratio) and statistical significance, highlighting the translational relevance of proteins included in Olink Reveal. In these plots, the x-axis represents the effect size of associations, measured as hazard ratios (HRs). For example, an HR of 2 or 0.5 indicates a doubling or halving of disease incidence rate, respectively, per unit increase in normalized protein expression (NPX). The y-axis depicts the statistical significance of each association after multiple testing correction.

Conclusion:

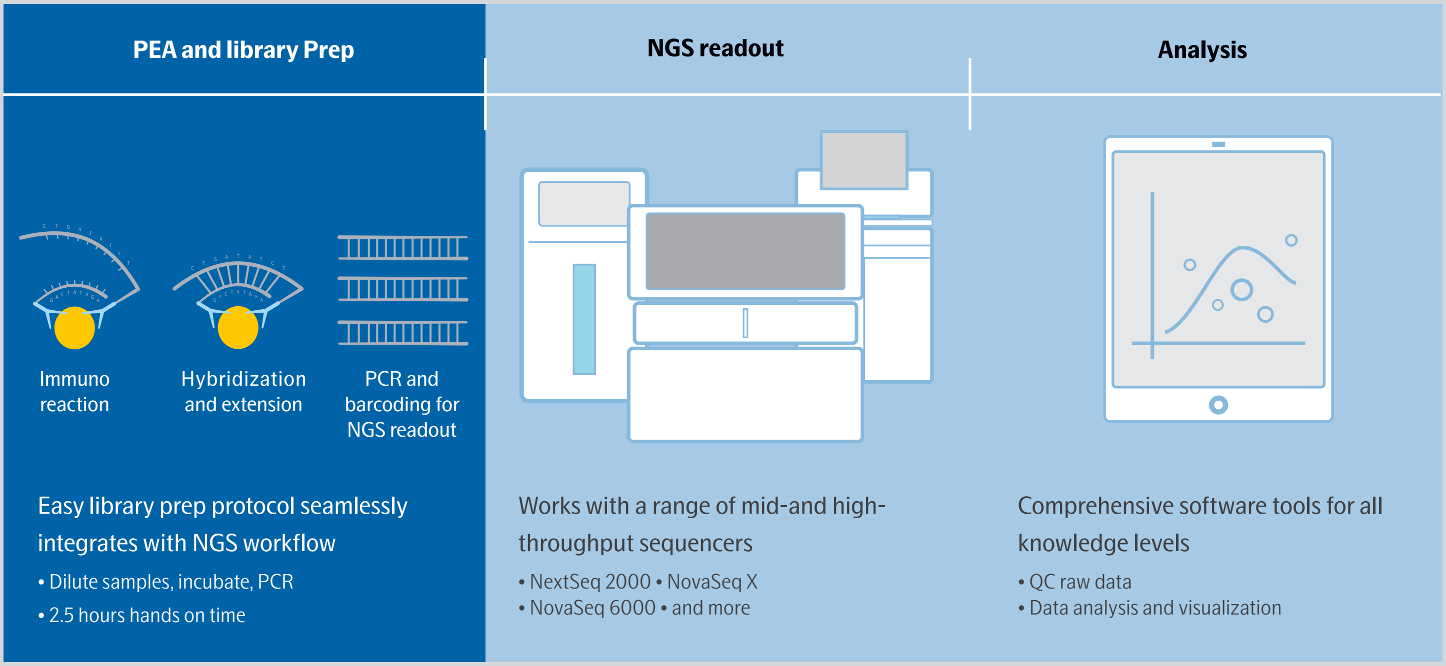
Olink Reveal provides a proteomic panel designed to understand the immunological complexity that drives much of human disease while also representing diverse biological pathways. This ensures broad applicability across research areas, from immune-mediated conditions to oncology, cardiovascular, neurological, and metabolic diseases.

The panel was informed by population-scale data from the UK Biobank Pharma Proteomics Project, ensuring that proteins included are biologically relevant and statistically associated with future disease risk.

By uniting comprehensive pathway coverage with robust disease-association evidence and a streamlined PEA–NGS workflow, Olink Reveal empowers researchers to investigate immune complexity and broader disease biology at scale. This positions the panel as a versatile tool for exploratory studies, biomarker discovery, and the prioritization of therapeutic targets across nearly all research areas.

Beyond the content of the panel itself, it is important to note that Olink provides researchers with a choice of discovery depth. Olink Reveal enables discovery at the scale of ~1,000 carefully selected proteins, optimized for immune and disease-relevant pathways, whereas Olink Explore HT expands coverage to more than 5,400 proteins for broader, proteome-wide discovery. This flexibility allows investigators to select the level of depth most appropriate to their research question. In addition, the Olink platform is highly scalable, offering a portfolio that includes targeted panels with absolute quantification capabilities. Assays are highly concordant across panels, facilitating smooth translation from discovery to clinical utility.

Olink Reveal: workflow and assay list



PEA and library Prep

Easy library prep protocol seamlessly integrates with NGS workflow

- Dilute samples, incubate, PCR
- 2.5 hours hands on time

NGS readout

Works with a range of mid-and high-throughput sequencers

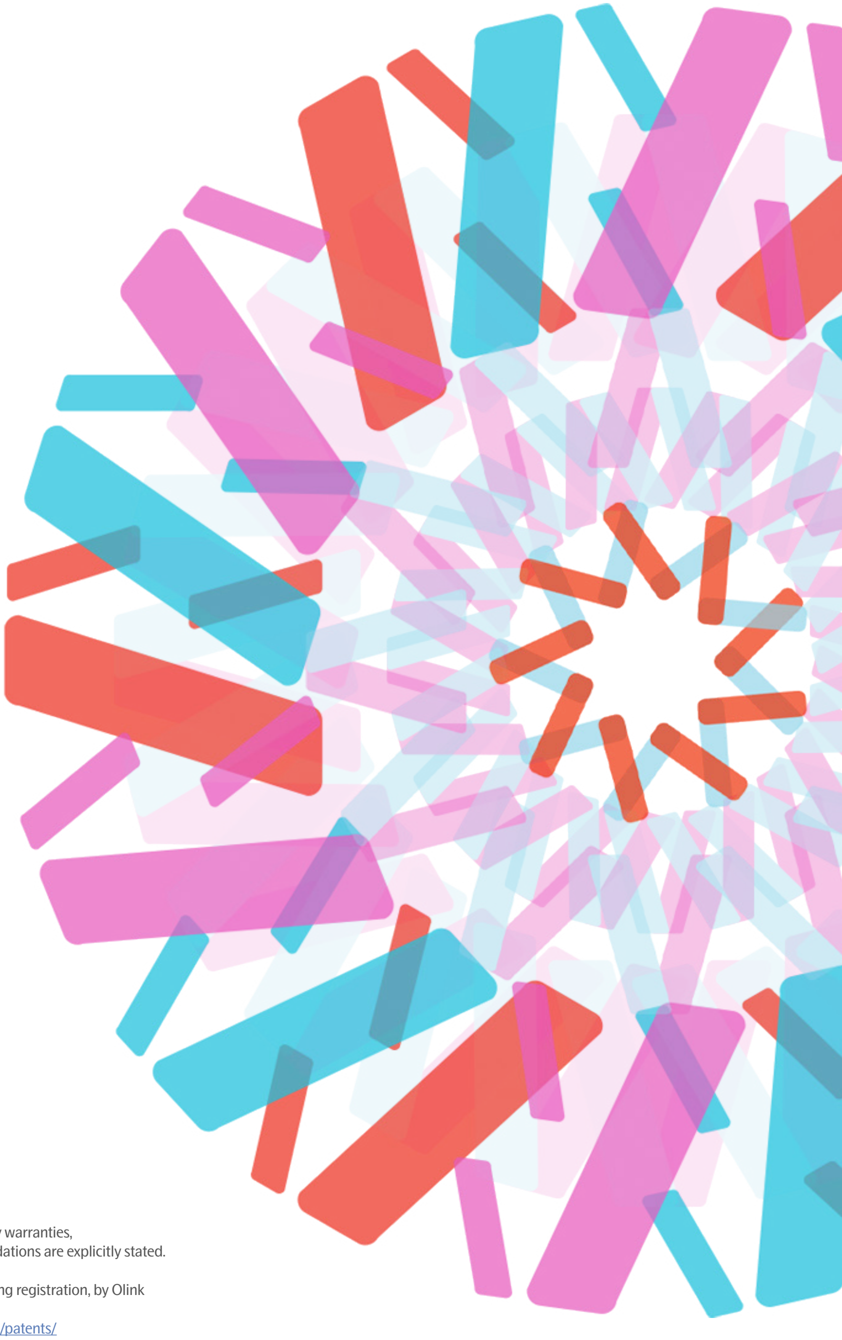
- NextSeq 2000 • NovaSeq X
- NovaSeq 6000 • and more

Analysis

Comprehensive software tools for all knowledge levels

- QC raw data
- Data analysis and visualization

ASSAY LIST



www.olink.com

Olink Proteomics, Salagatan 16F , SE-753 30 Uppsala, Sweden
1662, v1.0, 2025-09-25