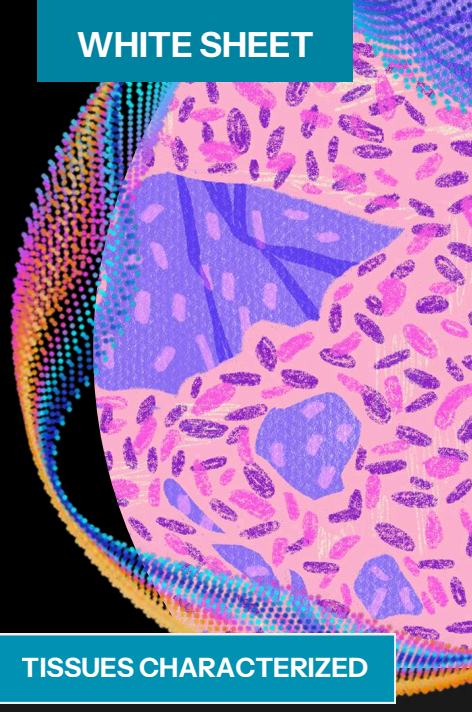
WHITE SHEET

SAPIENT

DynamiQ™ Normal Human Tissue Proteomics Atlas



Reference Map of Human Protein Expression Across Normal Tissues

TISSUES CHARACTERIZED

- Liver
- Lung
- Heart
- Large Intestine
- Pancreas
- Skeletal Muscle
- Skin
- Kidney
- PBMC
- Vascular Tissue
- Small Intestine
- Stomach
- Exocrine Gland
- Uterine Tube
- Serous Membrane

The DynamiQ Normal Human Tissue Proteomics Atlas **combines direct measures of protein expression, signaling activity, cell surface accessibility, immune biology, and resistance pathways across 15+ normal human tissues,** enabling drug developers to identify novel therapeutic targets and evaluate on-target, off-tissue safety liabilities before reaching the clinic.

Mapping Normal Human Tissue Biology at Unprecedented Depth

The atlas covers the **primary organs associated with dose-limiting toxicities** across ADC, T-cell engager, radioligand, and CAR-T therapies, cancer vaccines, and targeted biologic programs, with the following data captured using Sapient's mass spectrometry-based proteomics platform:

- **Global expression** across 12,000+ protein groups
- **Cell surface** protein expression
- **Phosphorylation-driven** signaling activity
- **Immune cell** states and pathway activity
- **Resistance-associated** protein networks

Why Normal Tissue Biology Is a Critical Blind Spot

Most modern oncology therapeutics, from ADCs to targeted biologics, are designed to engage specific protein targets on tumor cells. However, these targets are **rarely exclusive to tumors.** When a drug engages its intended target in normal tissues such as heart, lung, liver, or kidney, the **consequence is on-target, off-tissue toxicity** – one of the leading causes of dose limitation, clinical holds, and program failure.

Most development programs lack reliable, protein-level data on target expression in normal human tissues and **instead rely on indirect proxies:**

Common Approach	Key Limitation
RNA expression databases (GTEx, HPA)	mRNA does not reliably predict protein abundance, surface accessibility, or post-translational state
Immunohistochemistry (IHC)	Semi-quantitative, single or low multiplex, and dependent on antibody quality
Single-cell RNA sequencing	Does not measure protein expression, cell surface presentation, or pathway activation
Preclinical models	Species differences in tissue protein expression confound translation to human biology

As a result:

- On-target, off-tissue toxicity is **discovered late,** often in Phase I or beyond
- Target selection is based on **incomplete expression data** biased toward tumor-centric measures
- Safety liabilities in specific organs **are missed or underestimated**
- Novel targets with favorable therapeutic index profiles **are overlooked**

De-Risking Drug Development with the DynamiQ Normal Human Tissue Proteomics Atlas

Shift evaluation of normal tissue biology from inference to direct protein measurement, for whole-body biological context to mitigate on-target, off-tissue liabilities.

RNA sequencing → **Direct** protein measurement in human normal tissues

Single-marker IHC → **Multi-dimensional** proteomic characterization

Animal model extrapolation → **Human** tissue measures

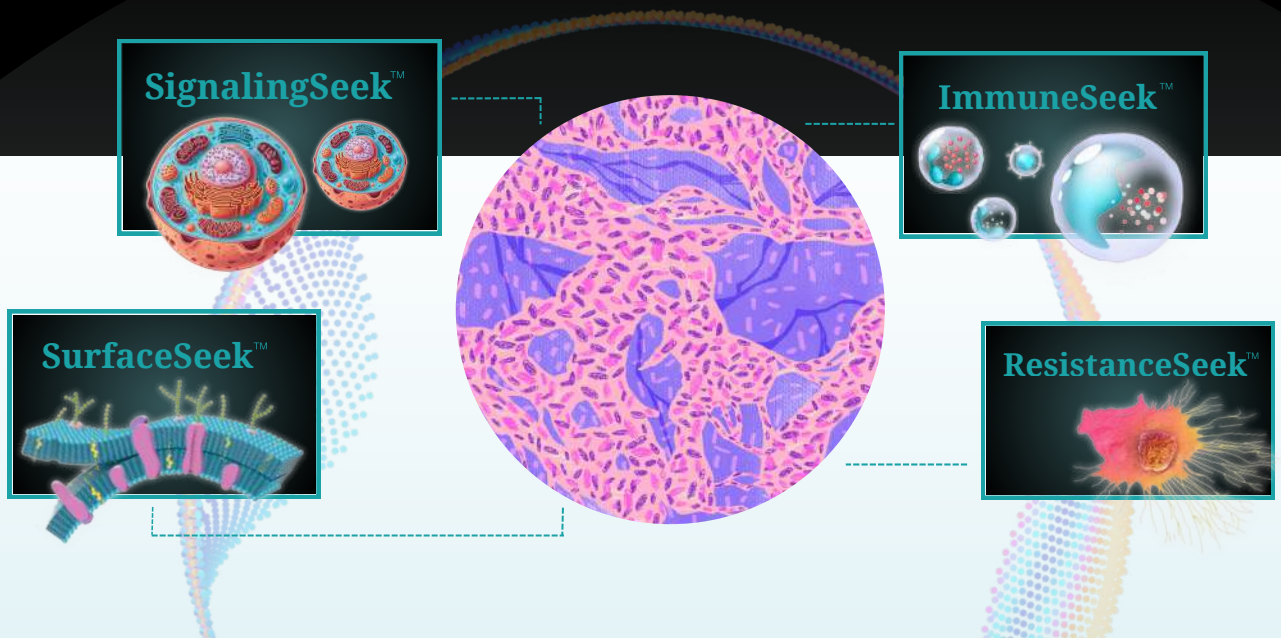
Reactive safety assessment → **Proactive,** data-driven target selection

Multi-Dimensional Proteomic Profiling

Each tissue in the DynamiQ Normal Human Tissue Proteomics Atlas has been profiled across multiple Sapient proteomics workflows. The atlas does not simply catalog which proteins are present – it **reveals how proteins are regulated, activated, and organized across normal human biology.**

Sapient Workflow	Biological Dimension	Depth and Insight
DiscoverySeek™	Global protein expression, including protein isoforms	Comprehensive measure of over 12,000 proteins across tissues
SurfaceSeek™	Cell surface protein expression	Surface protein density and accessibility in healthy biology
SignalingSeek™	Phosphorylation-driven pathway activity	Baseline pathway activation in non-tumor contexts
ImmuneSeek™	Immune cell composition and activation states	Resident immune biology and checkpoint expression by tissue
ResistanceSeek™	Baseline survival and stress response pathways	Tissues resilient or vulnerable to therapeutic pressure

By providing multi-dimensional proteomic context across normal tissues, the atlas enables **earlier, more informed safety and target selection decisions.**

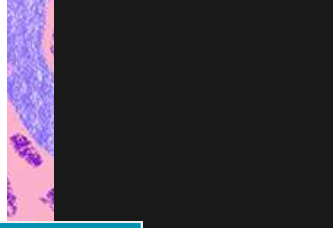


Key Questions Answered

On-Target, Off-Tissue Safety Assessment

The DynamiQ Normal Human Tissue Proteomics Atlas enables teams to evaluate whether a drug target is **expressed in normal tissues that could be affected by therapy:**

- Query target protein expression across all 15+ normal tissues
- Quantify expression levels relative to tumor tissue to assess therapeutic index
- Identify specific organs at risk for on-target toxicity
- Assess surface protein accessibility via SurfaceSeek and pathway activation via SignalingSeek



USE CASE

Determine whether the tumor target for an ADC candidate is also expressed on the cell surface in heart, lung, and kidney tissue **prior to initiating IND-enabling studies.**

Novel Target Identification and Prioritization

By comparing tumor proteomics datasets against the atlas, teams can systematically identify proteins that are **highly expressed in tumors but absent or minimal in normal tissues:**

- Identify tumor-selective proteins with favorable normal tissue safety profiles
- Prioritize targets based on quantitative tumor-to-normal expression ratios
- Discover novel surface antigens for ADC, T-cell engager, and radioligand therapy development

USE CASE

Rank-order candidate protein targets by tumor-to-normal expression ratios, **highlighting those with maximal therapeutic index** for advancement.

Signaling, Surface, Immune, and Resistance Baselines

The atlas provides baseline biology across **multiple dimensions:**

- **Signaling:** Pathways that are functionally active in normal tissues, including those targeted by kinase inhibitors
- **Surface proteome:** Quantitative surface protein expression for ADC, T-cell engager, and radioligand therapy target assessment
- **Immune biology:** Resident immune cell populations, checkpoint expression, and tissues with high immune activation potential
- **Resistance pathways:** Baseline survival and anti-apoptotic programs that may affect therapeutic vulnerability

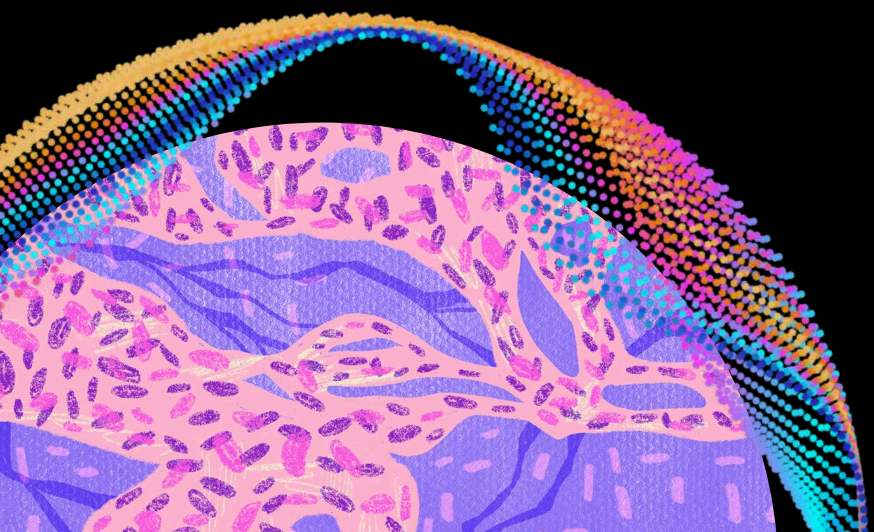
USE CASE

Evaluate baseline checkpoint and co-stimulatory protein expression across normal tissues, **identifying organs with pre-activated immune environments** susceptible to immune-related adverse events.

Your comprehensive reference map of normal human tissue biology

Unlike transcriptomic databases or single-marker IHC, the DynamiQ Normal Human Tissue Proteomics Atlas **delivers direct and diverse protein measurements,** including their abundance, surface accessibility, signaling states, and immune and resistance pathway context.

The atlas can be applied across early discovery, target selection, IND-enabling programs, and clinical development. It is **available through flexible data licensing and proteomics services models,** including data access for specific targets, integration with internal workflows, and custom proteomics studies using client-provided samples.



When the DynamiQ Atlas Is Most Valuable

This reference map is particularly valuable in programs where teams are asking:

- Where is my target expressed outside the tumor?
- Which organs should we monitor for on-target, off-tissue adverse events?
- Can we identify targets with better therapeutic index profiles?
- What does the surface proteome look like in normal tissues for our ADC, T-cell enager, or biologic target?
- What baseline signaling, immune, and resistance biology exists in normal tissues that may impact therapeutic response?

To access the DynamiQ Normal Human Tissue Atlas for your study, contact discover@sapient.bio.

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Discover more today.

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