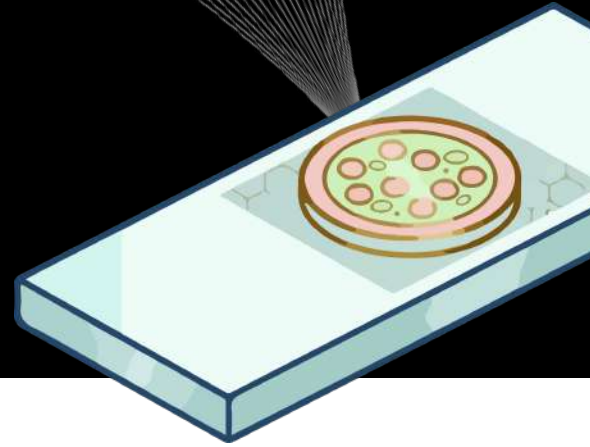




Next-Generation FFPE Proteomics

Revealing **functional tumor biology**
from FFPE tissue – **quantitatively,**
reproducibly, and at scale.



Unlocking Functional Biology from FFPE Tissue

While genomic profiling and RNA sequencing have transformed oncology, they reveal *potential*—not *function*. The proteome, which defines target expression, pathway activation, post-translational signaling, and drug response, has remained largely inaccessible in formalin-fixed, paraffin-embedded (FFPE) tissues, including by proteomics technologies that are optimized for plasma measures, such as Olink[®] Explore and SomaScan.

Sapient's next generation FFPE proteomics platform captures and quantifies proteins at scale in FFPE samples, transforming drug development by enabling:



Deep, direct measure of thousands of proteins in millions of existing tissue samples



Identification of responder subgroups or resistance mechanisms



Quantification of **drug tissue distribution, target engagement, and pathway modulation** in tumors

- ✓ **10,000+ protein groups measured** across tissue and tumor types
- ✓ **Phospho-, glyco-, and non-canonical** protein variant analysis
- ✓ Low sample requirement – **single 5 μ m FFPE slide**
- ✓ **Exceptional reproducibility** across **replicates, FFPE sections**, and in relation to **fresh-frozen samples**
- ✓ **Rapid turnaround** for thousands of samples

Turning archival tissue into discovery engines

FFPE tissue is one of the most accessible sample types available, but extracting protein insights from these biospecimens is challenging. The effects of fixation, such as formalin-induced cross-linking, can distort the structure of proteins and reduce the binding efficiency of antibody-based proteomic methods – which are also typically low-plex.

Sapient's next-generation **mass spectrometry-based FFPE workflows** overcome both fixation and coverage limitations via the **direct measure of proteins in FFPE tissue**.

From a 5 μm FFPE section, **Sapient quantifies >10,000 protein groups, including phospho- and glyco-proteins and isoforms** – revealing insights into tumor signaling, immune activation, and pharmacodynamic effects with single protein and pathway-level resolution.

Robust and Reproducible Methods

Sapient's FFPE proteomics method has been **applied across diverse tumor samples**, including lung, gynecologic, breast, colorectal, and pancreatic cancers, to show exceptional precision, robustness, and reproducibility.

- **Intra-section CV:** Technical variance of < 5% for repeat samples (Figure 1)
- **Inter-section CV:** Variance of < 8% with >97% overlap across serial FFPE sections (Figure 1)
- **Dynamic range:** Spans four orders of magnitude (Figure 2)
- **Protein-level concordance:** >90% protein matching with fresh-frozen tissues and correlation of > 0.8 (Figure 2)
- **False discovery rate (FDR):** < 1% at peptide level (Figure 3)
- **Key protein measures:** >200 oncogenes, >500 approved drug targets, and >100 pathways (Figure 3)

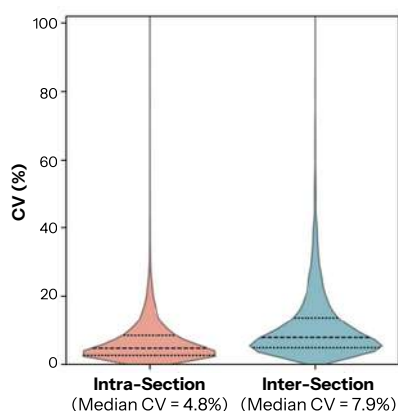


Figure 1: Technical intra- and inter-section variance.

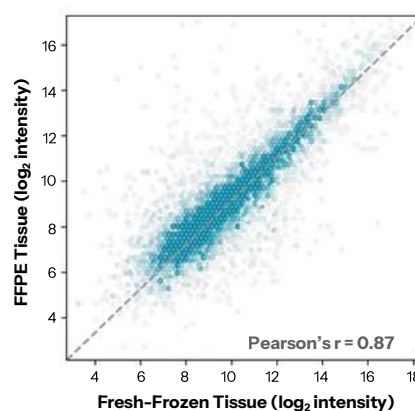


Figure 2: Protein group signal correlation between FFPE and matched fresh-frozen tissue.

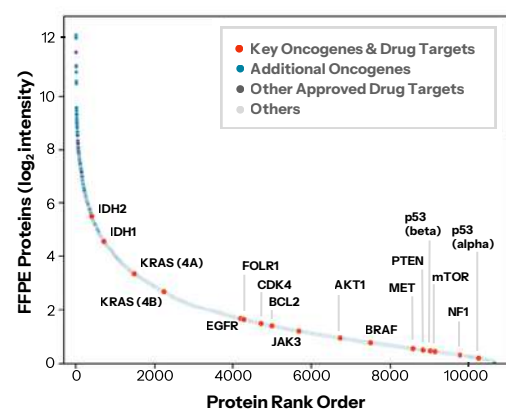


Figure 3: Proteins measured in FFPE tissue include key oncogenes and approved drug targets.

Multi-omic molecular mapping

Our FFPE proteomics **seamlessly integrates** with other omics offerings available through Sapient, including:



FFPE proteomics
for protein
expression and
pathway activity



**FFPE DNA
sequencing**
for mutation and
CNV mapping



**Single-cell
sequencing**
for cell-type
specific expression



**Spatial
profiling**
for tissue
contextualization

This multi-omic integration enables reconstruction of tumor biology from mutation to pathway activation, cell-type, and spatial localization, creating a **unified molecular map of each tumor**.

Category	Technical Specification
Protein Depth	>10,000 proteins in a single 5 μ m FFPE tumor section
Reproducibility	>97% overlap across sequential tissue sections, inter-section CV < 8%
PTM Coverage	Phospho-proteins and glyco-protein variants
Isoform Detection	Splice, truncation, indel, missense , and other non-canonical variants
Quantitation Range	Dynamic range spans four orders of magnitude
QC / FDR	< 1% peptide FDR ; isotopic spike-in controls
Turnaround Time	Optimized for discovery and clinical programs with hundreds to thousands of FFPE samples, with turnaround of < 6 weeks for up to 1,500 samples
Multi-Omic Integration	Integration with other omics offerings available through Sapient including FFPE DNA sequencing, single-cell sequencing, and spatial profiling workflows
Assay Quality	RUO assays to support clinical biomarker confirmation/verification
Data Output	Normalized matrices + pathway/PTM reports
Biorepository Access	Sapient's DynamIQ™ virtual biobank offers streamlined access to thousands of annotated FFPE tumors and tissues

Comprehensive biological insights

Through deep, quantitative profiling, Sapient's FFPE proteomics enables **comprehensive detection of hundreds of oncogenic and immune signaling pathways**, including PI3K/AKT/mTOR, MAPK/ERK, EGFR, KRAS, JAK/STAT, Wnt/ β -catenin, TGF- β , NF- κ B, p53, VEGF, and immune-checkpoint (PD-1, CTLA-4).

Applications across drug development

Stage	Use Case	Impact
Discovery	Identify functional targets and pathway dependencies in patient tumors	Higher-confidence, de-risked targets
Translational	Confirm target engagement and drug tissue distribution	Accelerated proof-of-mechanism
Clinical	Re-analyze archived trial biopsies for responders, biomarkers, and drug MOA	40–60% faster biomarker validation

Ready-to-access FFPE samples

Sapient's **DynamIQ™ virtual biobank** offers **streamlined access to thousands of annotated FFPE tumors and tissues**. We will help you tap into the diverse global inventory of existing archival tissue samples to support your specific study needs.

Data Delivery and Bioinformatics Output

Results are delivered as:

- **Normalized quantitative proteomic matrices**
- **Annotated pathway and PTM activity reports**
- **Drug–target engagement overlays**
- **Optional access via Sapient PrismatiQ™ data analytics package** for visualization of pathway activation and responder subgroup analysis

Faster validation, **deeper** biological insight, and **rapid access** to annotated tumor samples, without new trials or collections.

Sapient enables pharma teams to **extract quantitative pathway activation and target discovery and validation data** from FFPE tissues already used for genomics or IHC – turning decades of archived samples into functional translational data.

For prioritized access opportunities, contact discover@sapient.bio.