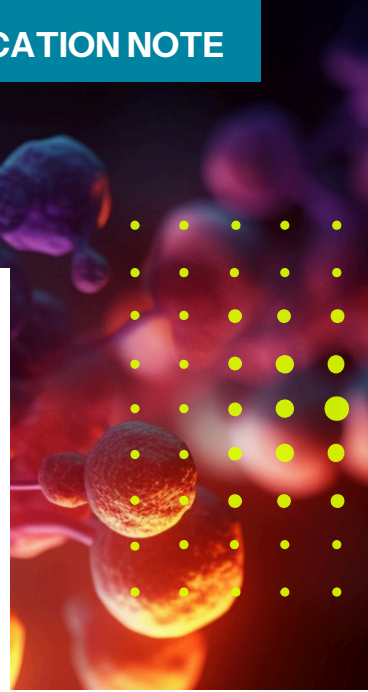# SAPIENT

# Cell Surface Proteomics for Radioligand Therapies: Deep Profiling of Cancer Cell Surface Receptors

Introduction

Radioligands are a powerful modality in cancer treatment, offering utility as both a diagnostic tool and as a precision therapy. Comprised of a radioactive isotope linked to a cell-targeting ligand, radioligands are designed to selectively bind to cell receptors that are overexpressed on tumor cells. The radioactive emissions from the bound radioligand can then be detected via imaging to assess tumor location, cancer cell concentration, and target activity. The radiation emitted by the radioligand can also be used to destroy or inhibit the target cancer cells while minimizing damage to surrounding healthy tissue.

The efficacy and safety of radioligand therapies depends on the binding optimization of radioligand to its cell receptor target. To limit toxic liability and enable a wider therapeutic window, it is imperative to comprehensively characterize cell surface receptors that are overexpressed, mutated, or uniquely expressed in cancer cells.

Sapient's mass spectrometry-based /Deep/ Cell Surface Proteomics

Sapient provides a deep discovery proteomics method that is optimized to measure cell surface receptors at unprecedented depth and scale. This mass spectrometry approach captures and measures the abundances of **up to 1,000 well defined cell surface proteins** in as little as 20ug protein lysates, to identify those receptors that are differentially expressed on cancer cells.
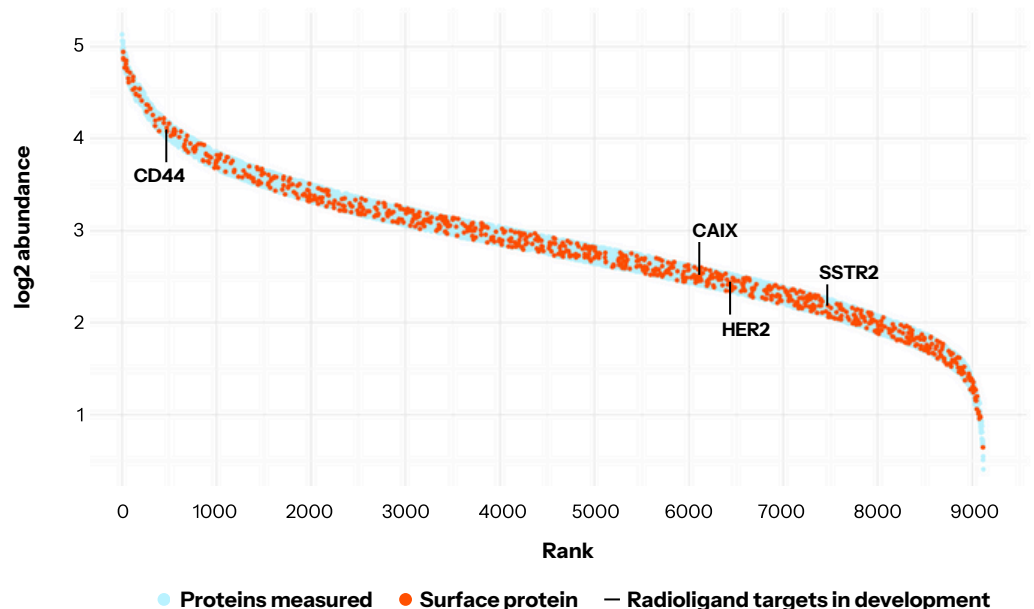
This /Deep/ Cell Surface Proteomics workflow is enabled by Evosep liquid chromatography coupled to state-of-the-art Bruker timsTOF HT mass spectrometers, which leverage label-free, data-independent acquisition (DIA) combined with Parallel Accumulation Serial Fragmentation (diaPASEF) to achieve deep proteome coverage and high confidence protein identification via direct peptide sequencing. Our method features fully automated end-to-end sample preparation for rapid turnaround and is readily scalable from tens to thousands of biosamples, delivering essential biological insights into radioligand binding selectivity to drive timely decision-making.

Applying cell surface proteomics for **comprehensive profiling of tumor cell receptors**

Using our /Deep/ **Cell Surface Proteomics** workflow, Sapient can rapidly perform global proteomic experiments or can selectively enrich cell surface proteins to screen different cell lines, tissues, and tumors. This can be performed within and across varied cell lines and tumor samples to discover novel cancer cell receptors for radioligand targeting.

Importantly, our workflow not only provides information on the abundances of tumor receptors but can also provide an estimation of their copy numbers. Quantification of protein copy numbers within and across indications helps to prioritize receptors as key targets for radioligand therapies.

In addition, using stable isotope labeling by amino acids (SILAC) approaches, Sapient can provide estimation of protein half life for cell surface receptors, including turnover and resynthesis kinetics, which is central to the design and development of radioligand agents.

At a Glance

Sapient's /Deep/ Cell Surface Proteomics method enables:

- Capture of **up to 1,000 cell surface proteins,** including cellular receptors

- **Quantification of cancer cell surface receptor copy numbers** within and across cancer cell lines and tumor samples

- Evaluation of **overexpressed** cancer cell surface receptors

- Estimation of **protein turnover and resynthesis kinetics**

- Discovery of **novel cellular receptors** for radioligand targeting

Conclusion

Sapient's /Deep/ **Cell Surface Proteomics** provides a robust solution for advancing the development of radioligand diagnostics and therapies, enabling comprehensive identification and characterization of cancer cell surface receptors.

By leveraging ultra-sensitive mass spectrometry and innovative workflows, we enable researchers to explore a broader landscape of protein expression across diverse cancer indications. Through quantitative insights into protein copy numbers, our platform empowers informed decision-making in cancer cell receptor selection, ultimately driving the optimization of radioligands for enhanced efficacy and safety as precision medicines for cancer.

Ready to discover more? Schedule a time to discuss your programs.

Visit: sapient.bio | **Email:** discover@sapient.bio | **Call:** 858.290.7010