APPLICATION NOTE

SAPIENT

Cell Surface Proteomics for ADC Development: Deep Profiling of Cell Surface Tumor-Associated Antigens

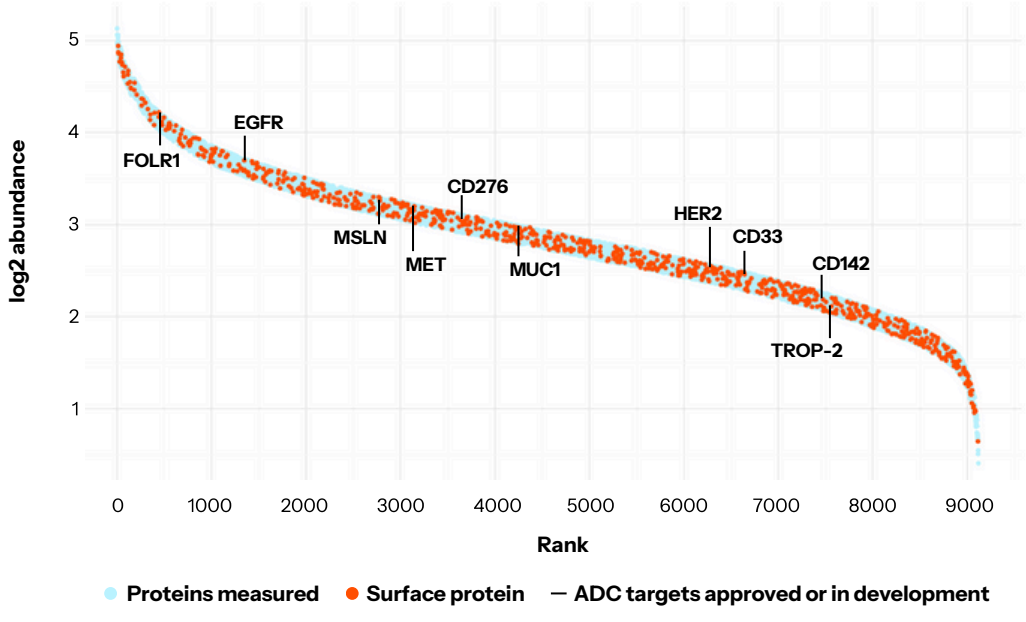
Introduction

Antibody-drug conjugates (ADCs) are a promising new class of cancer therapeutics, offering a powerful combination of specificity and potency via targeted delivery of cytotoxic agents to tumor cells. These drugs consist of an antibody linked to a cytotoxic drug, or payload, via a chemical linker. The antibody component of the ADC enables selective recognition of and binding to tumor-associated antigens (TAAs) on the tumor cell surface. The cytotoxic agent is then delivered directly into the cancer cell to destroy it while minimizing the impact on surrounding healthy tissue.

Comprehensive characterization of cell surface TAAs is among the most important criteria in developing complex ADC therapies, as efficacy and safety depends on the binding optimization of ADC to these targets. To limit toxic liability and enable a wider therapeutic window, it is imperative to identify and target TAAs that are differentially and abundantly expressed on tumors compared to healthy tissues.

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

Sapient provides a deep discovery proteomics method that is optimized to measure cell surface proteins at unprecedented depth and scale. This mass spectrometry approach captures and measures the abundances of **up to 1,000 well defined cell surface proteins** within tumor cells in as little as 20ug protein lysates.



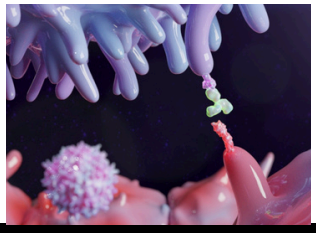
This /Deep/ **Cell Surface Proteomics** workflow is enabled by Evosep liquid chromatography coupled to state-of-the-art Bruker timsTOF HT mass spectrometers, which leverage label-free, data-independent acquisition (DIA) combined with Parallel Accumulation Serial Fragmentation (diaPASEF) to achieve deep 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 to drive timely decision-making in ADC development.

Applying cell surface proteomics for **comprehensive TAA profiling**

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 TAAs for ADC targeting.

In addition to providing information on the abundances of 1,000 surface proteins, our cell surface proteomics can provide an estimation of their copy numbers. Quantification of protein copy numbers within and across indications helps to prioritize TAAs as attractive targets for ADC development.

Using stable isotope labeling by amino acids (SILAC) approaches, Sapient can also provide estimation of protein half life for cell surface proteins, including turnover and resynthesis kinetics, which is central to the design and development of ADC therapies.



At a Glance

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

- Capture of **up to 1,000 cell surface tumor-associated antigens**
- **Quantification of TAA copy numbers** within and across cancer cell lines and tumor samples
- Evaluation of **differentially and abundantly expressed TAAs**
- Estimation of **protein turnover and resynthesis kinetics**
- Discovery of **novel TAAs** for ADC therapeutic targeting

Conclusion

Sapient's /Deep/ **Cell Surface Proteomics** provides a robust solution for advancing ADC development through comprehensive identification and characterization of TAAs.

By leveraging ultra-sensitive mass spectrometry and innovative workflows, we enable researchers to explore a broader landscape of protein expression across diverse cancer indications, facilitating high-specificity discovery of novel TAAs with differential abundance in tumor tissues. Through quantitative insights into protein copy numbers, our platform empowers informed decision-making in TAA selection, ultimately driving the optimization of ADCs for enhanced efficacy and safety as cancer therapy.

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