APPLICATION NOTE

SAPIENT

Cell Surface Proteomics for T Cell Engagers: Deep Profiling of Tumor-Associated Antigens

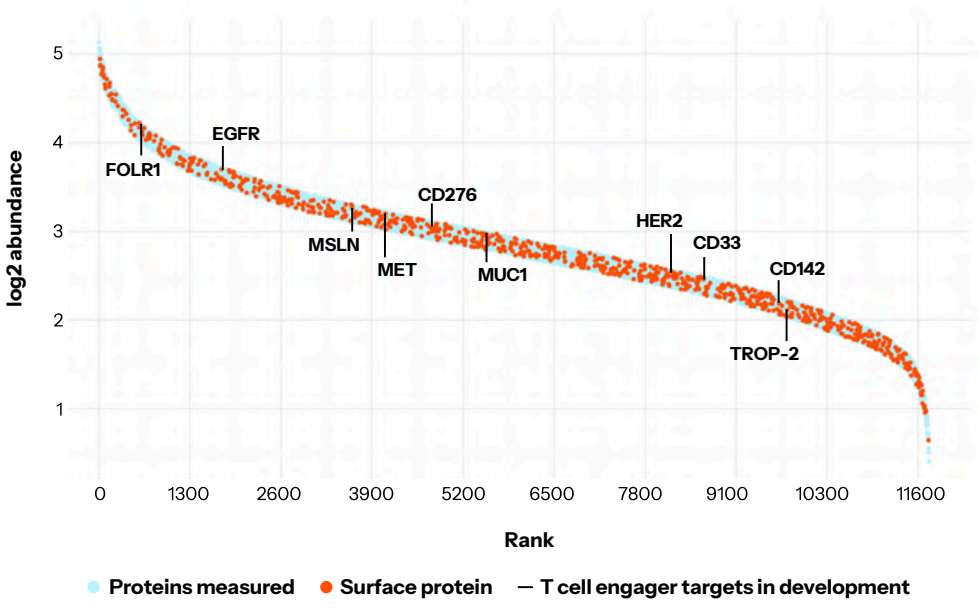
Introduction

T cell engagers are antibodies engineered to mobilize an immune response to cancer, directing T cell activity toward tumors that could otherwise evade the immune system. These innovative agents work by binding to both tumor-associated antigens (TAAs) expressed on the surface of a cancer cell and to a trigger protein on the T cell surface. Binding brings the T cell into close proximity so it can recognize and attack the cancer cell, stimulating it to release cytotoxic substances that penetrate the cancer cell membrane to cause cell death.

Comprehensive characterization of cell surface TAAs is among the most important criteria in developing T cell engagers, as efficacy and safety depends on the optimization of their binding 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.



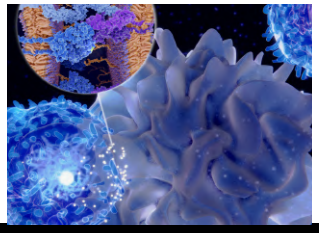
This /Deep/ **Cell Surface Proteomics** workflow is enabled by Evosep liquid chromatography coupled to state-of-the-art Bruker timsTOF HT mass spectrometers, which leverage label-free, data-independent acquisition (DIA) combined with Parallel Accumulation Serial Fragmentation (diaPASEF) to achieve deep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

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 T cell engager targeting.

Importantly, 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 key targets for T cell engagers.

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 T cell engagers.



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 T cell engager targeting

Conclusion

Sapient's /Deep/ **Cell Surface Proteomics** provides a robust solution for advancing the development of T cell engagers, enabling 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 T cell engagers for enhanced efficacy and safety as cancer therapy.

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