Evaluation of the timsTOF SCP for immunopeptidome applications

Susan Klaeger

Research Scientist, Proteomics Platform, The Broad Institute

Therapies that exploit the body's immune system to fight tumors have emerged as a promising therapeutic approach to cancer. The presentation of short peptide sequences from endogenous or foreign proteins to cytotoxic T-cells by human leukocyte antigen (HLA) molecules is at the center of these immune reactions. Mass spectrometry (MS) is the only technology to directly identify these peptides. However, HLA peptide analysis by MS is sensitivity limited, especially for deep profiling of HLA peptides using the small amounts of primary tumor samples obtained in a clinical setting. In low input tumor samples, increasing peptidome coverage is a crucial step in efforts aiming to detect neoantigens. Here, we evaluated the novel timsTOF SCP platform for analysis of HLA presented peptides in monoallelic and multiallelic cell lines. TimsTOF SCP files were searched with MSFragger against an Ensembl human proteome and compared to our standard workflow. The timsTOF SCP analysis provided deep immunopeptidome coverage and demonstrated increased sensitivity compared to current state-of-the-art approaches. In conclusion, we find that the timsTOF SCP provided comprehensive coverage of the peptidome and increased the ability to detect neoantigens in low input samples.