Protein Profiling: Comparison of Modified DNA Aptamer Screening to Data Dependent Mass Spectrometry across Cancer Cell Lines

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Abstract

Proteomic profiling of biological fluids and cell lines by mass spectrometry has traditionally been limited by depth of coverage due to sample complexity. Techniques such as the use of antibody depletion columns or fractionation can improve proteome coverage by removing highly abundant species and reducing sample complexity, however this is at the expense of sample throughput. A modified DNA-aptamer technology (SOMAmer® assay and SOMAmer® reagents) developed for profiling thousands of proteins in a parallel and multiplexed high-throughput manner is being applied more commonly in the biomedical industry. We have screened eight cancer cell lines by the SOMAscan assay and compared the results to data dependent mass spectrometry profiling using TMT10 on the Q Exactive Plus. Although the total number of proteins measured by the SOMAscan assay is smaller than the number detected in the dependent discovery experiment, proteome coverage increases with use of the two complementary technologies. Twenty proteins were selected and analyzed in cell lysate by multiple reaction monitoring (MRM) after pull-down using the respective SOMAmer reagent. When compared to traditional fractionation approaches prior to MRM analysis, SOMAmer reagent pull-down increases sample throughput 10-fold. Incorporation of SOMAmer reagents into mass spectrometry workflows enables fast, multiplexed analysis of target proteins.

Large Scale Proteomic Profiling

Targeted SOMAmer Pulldown Mass Spectrometry (SP-MS)

Comparison of Quantitative Proteomic Technologies and RNA Seq

SOMAmers: Slow Off-Rate Modified Aptamers

SOMAmer Reagents

Protein profiling using the SOMAmer platform provides valuable complementary information to traditional data dependent profiling by mass spectrometry, as evidenced by the small overlap between the platforms. Targeted (MRM) proteomic results are more closely aligned with the SOMAscan results when compared to the discovery data, an expected result due to the established effect of TMT fold change compression. Incorporation of SOMAmer reagents into traditional targeted (MRM) mass spectrometry-based proteomics workflows greatly increases profiling throughput by reducing the need for offline fractionation. The complementarity of these approaches provides a means to profile hundreds of samples by SOMAmer in a high throughput manner then select the subsets of samples to follow-up with more depth-of-coverage profiling by discovery and targeted proteomics.

Advantages and Limitations of Each Platform

Conclusions