

## 4266/20: “Proteomics for Precision Oncology: Profiling the Proteome of Matching Tumor and Adjacent Normal Tissue Using Data-independent Acquisition”

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Precision oncology requires a deep understanding of the molecular mechanism in cancer biology. The predominant approach today focuses on genome structure and gene expression data, which have become available with the rise of next-gen sequencing technology. On a phenotypic level, however, protein expression and activation are arguably more directly related to cellular function. The availability of combined genome and proteome level data from the same tumor is therefore expected to provide a much more complete picture of a tumor in a particular state. Until recently, proteomics technology could not match the scale of next-gen sequencing and consequently, precision medicine research has almost exclusively been based on gene-level data. Here we show the first truly large-scale data set for protein expression and protein phosphorylation for a large collection of biospecimens derived from the IndivuType cohort of Indivumed, Germany. Matching fresh-frozen tumor and adjacent normal tissue samples from thousands of patients including various cancer entities were obtained from Indivumed’s network of partner hospitals Enabled by the novel data-independent acquisition (DIA) workflow, a mass spectrometric method that obtains peptide fragmentation data in a highly parallelized way with high reproducibility and sensitivity, more than 7,000 proteins in the whole proteome (WP) and 20,000 phospho-peptides in the phospho-proteome (PP) workflow were analyzed. Sample processing from 5 mg of tissue per sample was performed on 96-well plates with the help of a liquid handling robot. Phospho-peptide enrichment was carried out using a Kingfisher Flex device and MagReSyn Ti-IMAC magnetic beads (ReSyn Biosciences). Data-independent acquisition (DIA) LC-MS/MS was performed on multiple platforms consisting of a Thermo Scientific Q Exactive HF-X mass spectrometer coupled to a Waters M-Class LC. Chromatography was operating at 5  $\mu$ L/min, and separation was achieved using 45 min (WP) and 60 min (PP) gradients. With a throughput of 850 WP and 650 PP samples per month, thousands of samples were analyzed to date. The resulting proteome data is integrated into Indivumed’s IndivuType multi-omics database, supporting the identification and validation of new molecular cancer drug targets and biomarkers.

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