205 AI DRIVEN INTERROGATION OF SPATIAL PROTEOMIC AND TRANSCRIPTOMICS ATLASES IN THE TUMOR MICROENVIRONMENT OF TRIPLE NEGATIVE BREAST CANCER

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Background The limited efficacy of approved therapies for patients with triple negative breast cancer (TNBC) is driven by the highly heterogeneous tumor microenvironment (TME). In the context of response to immunotherapy, it is essential to spatially resolve the drivers of immune cell exclusion at both a transcriptomic and proteomic level to find better treatment combinations and biomarkers for response. Breast biopsies that contain malignant and benign tumor that while readily manually identifiable by pathologists using traditional histopathology methods, such as H&E or immunohistochemistry (IHC), can be challenging to identify without a pathologist's guidance on immunofluorescent (IF) images used in spatial-omics. Merging a traditional histopathology slide with the IF spatial-omics slide through digital image co-registration allows pathologist-derived annotations to inform spatial-omic region of interest (ROI) selection. However, this is a time-consuming, semi-manual aspect of the spatial-omics workflow. Here we use AI deep-learning-based algorithms to automatically distinguish tumor epithelium from benign regions. We then further profiled the selected tumor regions by spatial-omics to further characterize the TME.

Methods We characterized FFPE TNBC samples that had been previously assessed for bulk gene expression signatures using the nCounter® PanCancer IO 360™ assay. We utilize an integrated workflow of Visiopharm's Oncotopix® Discovery software and GeoMx® Digital Spatial Profiling (DSP). In this workflow, AI-driven ROI selection was performed to distinguish normal and malignant areas on a H&E sample, allowing the selection of diseased regions and exclusion of benign areas in an automated manner. We then interrogated tumor and stroma compartments within the AI identified tumor ROIs using the DSP with a novel human Immuno-oncology Proteome Atlas (IPA) containing 500 antibodies and the whole transcriptome atlas containing >18,000 genes.

Results We characterized transcriptomic and protein expression localized in the tumor and stromal compartments within TNBC tumors. Distinct niches of immune and tumor cells within the TME exhibited unique proteomic phenotypes and associated signaling pathways mapped to distinct ROIs of the tumor selected by AI.

Conclusions This integrated automated AI-driven high-throughput workflow for selection of ROIs to deeply characterize the whole transcriptome and 500 immuno-oncology-related proteins in tumor epithelium and stromal compartments of the TME. These findings provide an objective method to automatically select tissue regions for high-plex spatial-omic analysis, supporting discoveries that may improve the understanding of the underlying mechanism of TNBC tumor progression, potentially discover new combinations for drug targets and novel biomarkers that are easily translatable to large study cohorts.

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