CHARACTERIZATION OF THE TUMOR MICROENVIRONMENT USING THE XENIUM IN SITU PLATFORM AND FFPE TISSUE ARRAY TECHNOLOGY

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Background Tissue array technology enables screening of multiple tissue samples on a single microscopic slide and is an assistive tool in the field of oncology, given its ability to investigate cancer markers in a high-throughput manner. Studying tumor tissues with high resolution in situ technologies further unlocks the potential to profile the tumor microenvironment and cancer cell heterogeneity at a subcellular resolution. Here, we used the Xenium Analyzer (10x Genomics) to characterize the gene expression profiles of formalin fixed & paraffin embedded (FFPE) cancer tissue sections with single cell and spatial resolution.

Methods We used Xenium Analyzer to profile 5 µm FFPE tumor sections from various tissue types in a tissue array format. Each tissue array was placed onto the 12 x 24 mm imageable area of each Xenium slide for deparaffinization and decrosslinking. The slides were incubated overnight with the Xenium Human Multi-Tissue and Cancer Gene Expression Panel and a custom panel of 100 additional genes, for a total of 477 genes which broadly targeted cell types across multiple human tissue types. Following ligation and amplification, the slides were then loaded onto the Xenium Analyzer instrument for automated in situ analysis. Transcript assignments, segmented cell boundaries, and clustering outputs were visualized using the Xenium Explorer software. H&E staining was performed after the instrument run to overlay histological imaging with in situ visualizations.

Results Cell type populations at subcellular resolution were identified and labeled in each FFPE tumor tissue section using unsupervised clustering. The 477-gene panel helped resolve biologically distinct subgroups of immune, cancer, and tissue-specific cells. H&E to Xenium DAPI image registration resulted in concordance between tumor regions identified in H&E images and clusters enriched for tumor-specific markers in Xenium Explorer.

Conclusions The Xenium Human Multi-Tissue and Cancer Gene Expression Panel and custom add-on genes allowed us to profile multiple human tissue types with subcellular resolution in a range of FFPE tumor tissues on a single slide. The Xenium platform is a powerful tool to study molecular targets pertaining to the tumor microenvironment in a spatial context.

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