212 INVESTIGATING CANCER AND IMMUNE CELL INTERACTIONS IN THE TUMOUR MICROENVIRONMENT WITH MERFISH

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Background Biological tissues are composed of heterogeneous cell populations intricately organized in 3D architectures. However, cell type composition and their spatial organization remain largely uncharacterized for most tissue types. Although single-cell sequencing analysis provides a systematic and quantitative approach to resolve cell type composition, the cell-cell interactions and cellular organization that define unique tissues are lost due to the requirement of cell dissociation for this approach. Spatial information is critical to better understand the spatiotemporal complexities of diseases such as cancer. Recently, spatially resolved, single-cell transcriptomic imaging platforms have provided a necessary solution to bridge this spatial information gap. The Vizgen® MERSCOPE® Platform, built on multiplexed error robust fluorescence *in situ* hybridization (MERFISH) technology, enables the direct profiling of the spatial distribution of hundreds of RNA species in intact tissue with subcellular resolution.

Methods Here, we demonstrate the power of MERSCOPE in combination with our Predesigned Immuno-Oncology Panel to characterize the immunological landscape of various human malignant tumor tissue samples. Using this 500-gene immune-oncology panel to characterize canonical signaling pathways of cancer and immune response within the tumor microenvironment, we spatially profiled gene expression across 16 human tumor samples, including breast, colon, prostate, liver, ovarian, lung, uterine, and skin cancer.

Results To demonstrate the capability of our immune-oncology panel to characterize many types of malignant tumor tissues, we clustered each MERFISH dataset. Then we annotated the combined clusters of all datasets to create a comprehensive cancer cell atlas. This unified characterization of the tested tumors revealed the presence of B and T cell populations in most of the malignancies tested. To further analyze the heterogeneity present within these critical immune cell populations, we combined spatial autocorrelation and gene expression clustering to subcluster the pan-sample populations of B and T cells. Using the spatial information embedded in our MERSCOPE data, we identified the tissue neighborhoods of these immune subtypes and further compared the neighborhoods between different B and T cell subtypes in the various cancer tumors tested.

Conclusions This analysis elucidated different patterns of immune cell localization related to immune hubs and the tumor-immune interface, as well as gene expression differences relating to inflammation and immune activation. These findings demonstrate the power of the MERSCOPE Platform and Vizgen Predesigned Panels for immune profiling in the tumor microenvironment.

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