1474 INVESTIGATING THE MOLECULAR ARCHITECTURE OF TRIPLE POSITIVE BREAST CANCER SAMPLES WITH SPATIAL OMICS TECHNOLOGIES

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Background Cancers are often heterogeneous in their presentation. These inherent differences affect the severity of the disease, choice of treatment, and treatment effectiveness. To profile these differences, subtyping categorizes cancers based on the expression of specific molecular, morphological, and clinical characteristics. For breast cancer, subtyping is commonly based on expression of ERBB2 (HER2), Estrogen Receptor (ER), and Progesterone Receptor (PR). In triple-positive breast cancer, all three markers are expressed, but the localization of these markers can vary between patients and within the same tumor. Spatial Biology technologies provide novel tools for deciphering the effects of this heterogeneity and allow for a more comprehensive approach to triple-positive breast cancer treatment. NanoString's® GeoMx® Digital Spatial Profiler and Canopy Biosciences® ChipCytometry® are two platforms that can answer questions about heterogeneity through spatial transcriptomic and proteomic analysis.

Methods To investigate triple-positive breast cancer (BRC), we developed custom morphology markers for use with the GeoMx DSP, including those for PR, ER, and HER2. These markers, in conjunction with a pathologists review of corresponding H&E sections, guided our selection of twelve total ductal carcinoma in situ (DCIS) and infiltrating ductal carcinoma (IDC) ROIs from each sample with variable PR expression. We transcriptionally profiled the tumor and tumor microenvironment (TME) from these ROIs with the Cancer (CTA), and Whole Transcriptome Atlas (WTA), which monitor expression of 1,800+ and 18,000+ targets, respectively. We use ChipCytometry® to help confirm that these transcriptional changes are correlated with changes in protein expression in individual cells.

Results Our results showed significant differences in gene expression between the DCIS and IDC regions in both tumor and TME, particularly in the expression of collagen and keratin transcripts. These differences reflect expected changes to tissue structure as tumor cells infiltrate surrounding tissue and are clear in both the CTA and WTA data. Additionally, we observe differences in fibroblast biomarkers and breast cancer regulators, like cyclin genes, when comparing tumor and TME segments.

Conclusions Taken together these spatial biology solutions will help increase our understanding of the molecular architecture of these tumor types by providing a glimpse into complex cell interactions that help shape tumor heterogeneity.

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