204 UNVEILING DIFFERENTIAL GENE EXPRESSION PROFILING AND POTENTIAL BIOMARKER IN BREAST CANCER WITH THE NANOSTRING GEOMX DIGITAL SPATIAL PROFILER

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Background The advancement of spatial biology technology, pioneered by Nanostring, has revolutionized genomic research by enabling the quantification of gene expression while preserving spatial and morphological information. This technology enriches the study of tumor microenvironment (TME) profiling especially benefits cancer research, it may provide a better understanding of cell population with functional segmentation. The aim of this study was to investigate the TME of breast cancer, and identify crucial biomarkers for discovery of potential drug targets.

Methods One formalin-fixed paraffin-embedded (FFPE) tissue microarray (TMA) was selected from BioChain's biorepository. It contains a total of 29 breast tissue samples, which consisted of 4 normal breast samples and 25 breast tumor samples (22 invasive ductal carcinoma samples and 3 invasive lobular carcinoma samples). After standard immunohistochemistry methodologies, tissue sections were performed in situ hybridization with probes conjugated to unique DNA indexing-oligonucleotides (DSP barcodes) via a UV photocleavable linker and stained with fluorescently labeled morphological markers PanCK and CD45. The biological compartments within a region of interest (ROI) were selected. The data from each ROI was stored in GeoMx DSP, integrated with imaging, and processed sequenced oligonucleotides information for analysis of spatially resolved whole transcriptomic expression.

Results Among more than 18,000 genes targeted across 88 ROIs, 12,893 genes were found to be expressed in 5% of the ROIs, with 919 genes expressed in 50% of the ROIs. This wide range of gene expression highlights the complexity and heterogeneity of breast cancer. Further analysis focused on the levels of gene expression, and the enrichment in either epithelial segments or immune segments. This result showed that gene expression levels and clustering of *ERBB2* were relative higher in epithelial segments than other segments, and the strong expression of *ERBB2* gene in tumor samples indicating its potential as a significant biomarker in breast cancer treatment.

Conclusions Our finding indicated that the relatively high expression levels of *ERBB2* in epithelial segments providing valuable insights into its potential as a biomarker in breast cancer treatment. The combination of BioChain's breast tumor TMA with Nanostring's GeoMx Human Whole Transcriptome Atlas provides the platform for mapping the architecture of TME and the groundbreaking capability in unraveling the complex dynamics of gene expression. This study paves the way for further exploration of spatial biology techniques for cancer pathogenesis and predict therapeutic response in the field of breast cancer research, with the approach to improve diagnostics and personalized treatment.

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