CHARACTERIZATION OF HUMAN BREAST CANCER TISSUE WITH THE XENIUM IN SITU PLATFORM REVEALS A NOVEL MARKER FOR INVASIVENESS

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Background Breast cancer became the most diagnosed cancer globally for the first time in 2020. Of these breast cancers, approximately 20% are ductal carcinoma in situ (DCIS). Within the mammary gland ducts, myoepithelial cells and their surrounding basement membrane form a layer separating the breast epithelium from the surrounding stroma. Using Xenium, an in situ analysis platform capable of detecting gene expression patterns of hundreds of RNA targets with subcellular spatial resolution, we investigated the myoepithelial layer of human DCIS breast cancer tissue and observed gene expression alterations that may serve as markers of a transition to tumor invasiveness.

Methods Ten micron thick FFPE tissue sections were prepared from breast tissue blocks containing DCIS and invasive tumor areas. Tissue sections were screened using a Xenium In Situ gene panel of 205 markers and subsequently stained with H&E and imaged at 20X magnification using a light microscope. RNA expression was analyzed with Xenium Explorer software.

Results We analyzed FFPE sections of human DCIS tissues with invasive and non-invasive tumor regions with both H&E staining and with Xenium In Situ for spatial RNA expression profiles. Our data-driven and curated Xenium In Situ gene panel design allowed for the annotation of multiple cell types, including lymphocytes and macrophages, with specific immune subpopulations surrounding the cancerous lesions. In DCIS non-invasive tumor areas, we observed high KRT14 expression and intact myoepithelial tissue. Conversely, in invasive tumor areas, we observed low KRT14 expression and a disrupted myoepithelial layer. The same areas of low KRT14 expression were also positive for progesterone receptor (PGR).

Conclusions Progesterone receptor has previously been identified as playing a role in driving luminal B cell proliferation and invasion. In our study, Xenium In Situ analysis reveals that PGR is associated with regions where the myoepithelial layer appears to have broken down and may represent a novel marker for the transition between DCIS and invasive cancer in human breast tissue.

REFERENCES