Whole transcriptome spatial profiling of fresh frozen tissue samples using two RNA-capture methods

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The Visium platform from 10x Genomics enables researchers to profile the whole transcriptome while retaining spatial context. The two approaches for this platform include reverse transcription (RT)-based, which captures mRNA directly, and probe-based that leverages RNA-templated ligation (RTL) to detect cellular transcripts by highly specific hybridization and ligation of probe pairs. Depending on the approach, either the mRNA or the successfully ligated probes are captured on a spatial barcoded oligo array and used to generate gene expression libraries. Visium CytAssist leverages RTL to produce high quality and sensitive mapping of the transcriptome while providing flexibility in sample preparation by decoupling the tissue preparation steps from probe capture. With Visium CytAssist, users select the tissue section and region to align to the Visium slide capture arrays based on the morphological or pathological landmarks of interest. The probe-based chemistry is advantageous for low quality samples with partially degraded RNA, as the probe-based chemistry does not require fully intact RNA. Here, we provide a detailed description and comparison of these distinct Visium workflows on human breast cancer and mouse brain, identifying use cases where a capture type is preferred. In particular, RT-based capture is leveraged for an unbiased view of the entire transcriptome while RTL-based capture is highly specific and sensitive, detecting low-expressing genes that could go unseen.