Background Despite years of studies and effort, the best strategies for treating prostate cancer and minimizing the complications of treatment remain unanswered questions. This gap in knowledge is partially due to the inability to dissect the complex heterogeneous tumor microenvironment (TME) and immune compartment. Spatially resolved molecular profiling of tumor sections will enhance our understanding of these complexities; However, it has been particularly challenging to do spatial molecular profiling in formalin-fixed paraffin-embedded (FFPE) tissues due to RNA degradation associated with this tissue-embedding method, which is routinely used in oncology workflows. The 10x Genomics Visium Spatial Gene Expression Solution for FFPE tissue overcomes these limitations, enabling spatial gene expression analysis of FFPE tissues combined with classical histology staining techniques such as Hematoxylin & Eosin (H&E) staining and immunofluorescence.

Methods We used the 10x Genomics Visium Spatial Gene Expression Solution for FFPE tissue to analyze and resolve tumorigenic profiles in sections of normal and adenocarcinoma prostate samples. This assay incorporates ~5,000 molecularly barcoded, spatially encoded capture probes in spots over which the tissue is placed, imaged, and permeabilized. Imaging and sequencing data are processed together, resulting in a spatially resolved transcriptional readout.

Results We profiled the whole transcriptome in normal, invasive adenocarcinoma, and acinar cell carcinoma FFPE human prostate tissues. Unsupervised clustering of the whole transcriptome data from normal, invasive adenocarcinoma, and acinar cell prostate carcinoma FFPE sections enabled the identification of 2 different regions, which had a well defined spatial distribution within the tissues. Well known prostate gland and prostate-cancer markers were over-expressed in the corresponding healthy and cancerous portions of the tissue, validating the performance of this method. We found that, while in healthy tissues basal cells and luminal cells are spatially organized, this pattern is lost in tumor samples, where luminal cells are greatly expanded in the invasive carcinoma region and do not colocalize with basal cells. Moreover, T lymphocytes are dispersed throughout the whole tissue section in the adenocarcinoma, while plasma B cells are located in the peritumoral region which could impact prognosis.

Conclusions Spatial whole transcriptome analysis opens new opportunities for better understanding the TME which can not only help discover novel predictive tumor biomarkers, but also enable identifying cell type and tumor region specific drug targets.