

# Mapping the spatial whole transcriptome from normal to tumor tissue in renal clear cell carcinoma: Tumorigenesis and microenvironmental shifts at single-cell resolution



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## Introduction

Renal clear cell carcinoma (ccRCC) develops through significant molecular and spatial reprogramming, transforming normal kidney tissue into a malignant state and reshaping the tumor microenvironment. To investigate the transition from normal to cancerous tissue, we utilized the CosMx<sup>®</sup> Whole Transcriptome Atlas (WTX) assay to perform high-resolution spatial transcriptomic profiling of FFPE sections containing ccRCC and adjacent normal kidney. H&E staining on the same tissue sections enabled direct correlation of molecular profiles with histopathological features, uncovering novel insights into tumorigenesis and the potential for AI-driven diagnostic advancements.

## CosMx<sup>®</sup> WTX Assay + H&E Stain

CosMx WTX Assay: 19782 genes | 99.5% coverage of protein-coding genes



Fig. 1 The CosMx WTX assay has full coverage of human protein-coding genes.

## CosMx WTX Assay + Same-slide H&E Stain

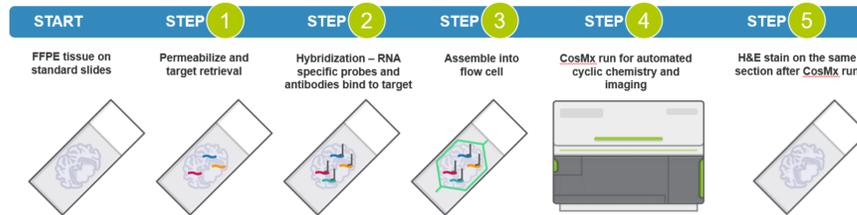


Fig. 2 CosMx assay workflow includes sample preparation, on-instrument readout run, and optional post-run H&E staining on the same section (imaged with Motic Slide Scanner).

## Co-detection of Whole Transcriptome and High-Plex Protein with Single-cell Subcellular Resolution

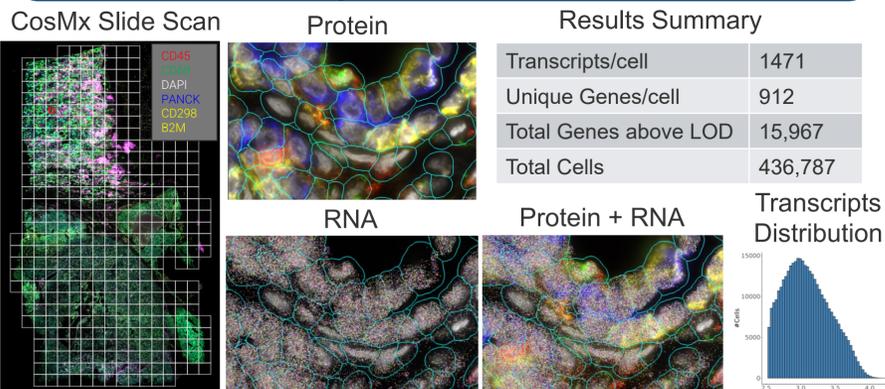


Fig. 3 CosMx WTX assay enables co-detection of 4 proteins and 19782 genes on the same slide. Results showed high throughput of hundreds of thousands of cells profiled per slide and high assay sensitivity with thousands of transcripts imaged in single cells.

## Integration of CosMx Results with H&E Post-Stain

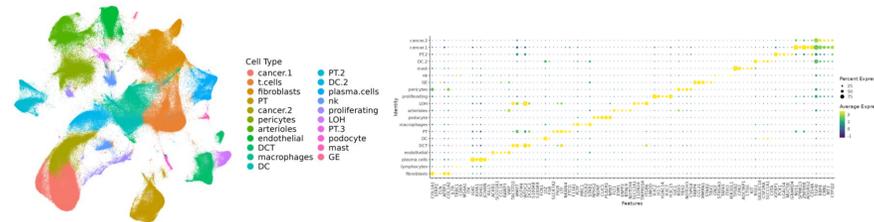


Fig. 4 UMAP and Marker gene heatmap from the CosMx WTX dataset on FFPE renal clear cell carcinoma.

## Post-CosMx H&E CosMx Cell Typing Cell Type Composition

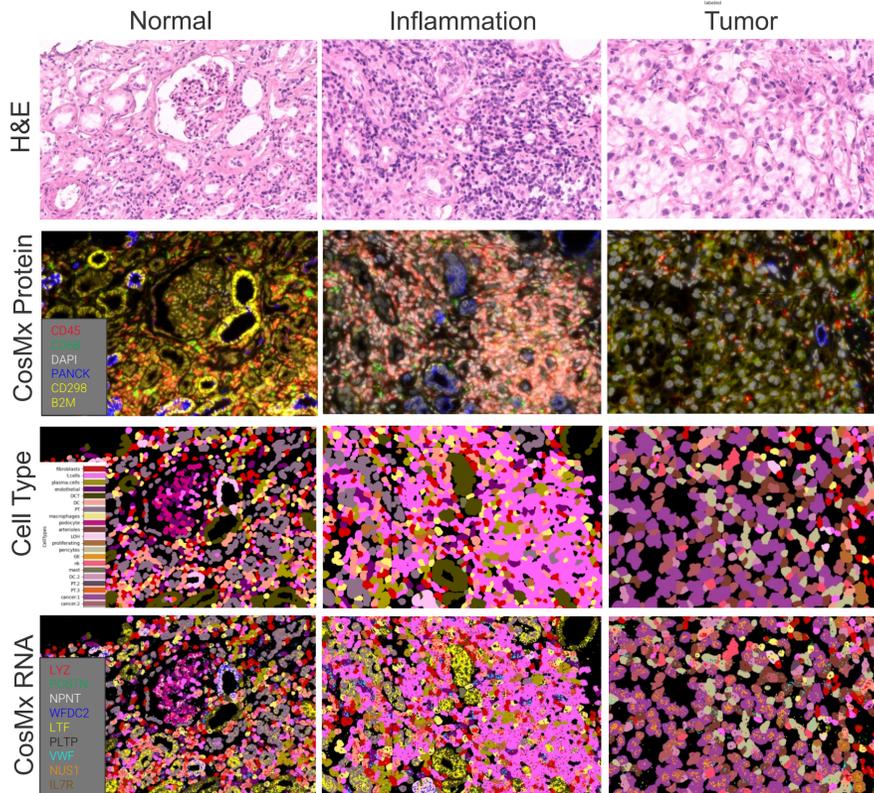
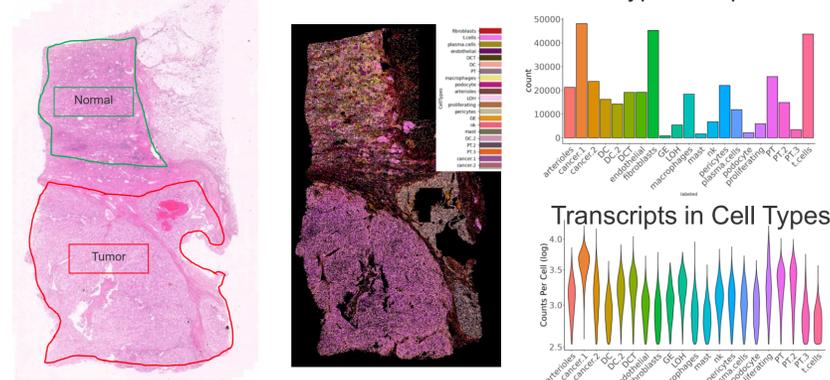


Fig. 5 Images from CosMx WTX assay were aligned with the post-run H&E image with high accuracy using custom software. Images from H&E, CosMx protein, Cell typing results using CosMx WTX data and a subset of CosMx RNA detected were shown in normal, inflammation, and tumor regions.

## Pathway projection on tissue and InsituDiff reveals microenvironmental shift from normal to tumor region

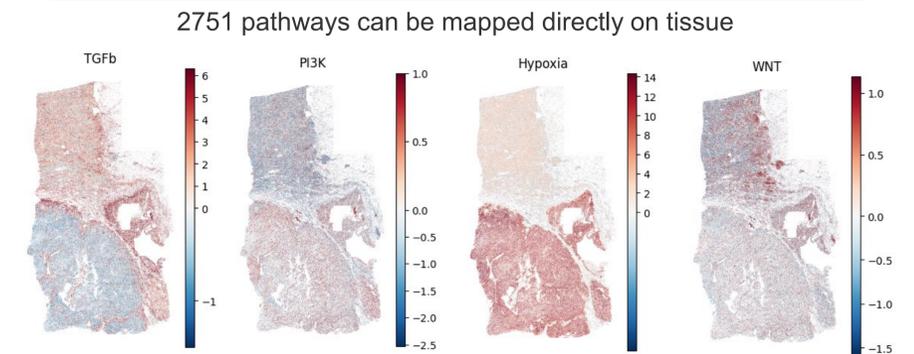


Fig. 6 CosMx WTX assay covers 2751 pathways, and the activity of each pathway can be mapped directly onto the tissue.

## InsituDiff is a CosMx data analysis tool to visualize perturbation in space

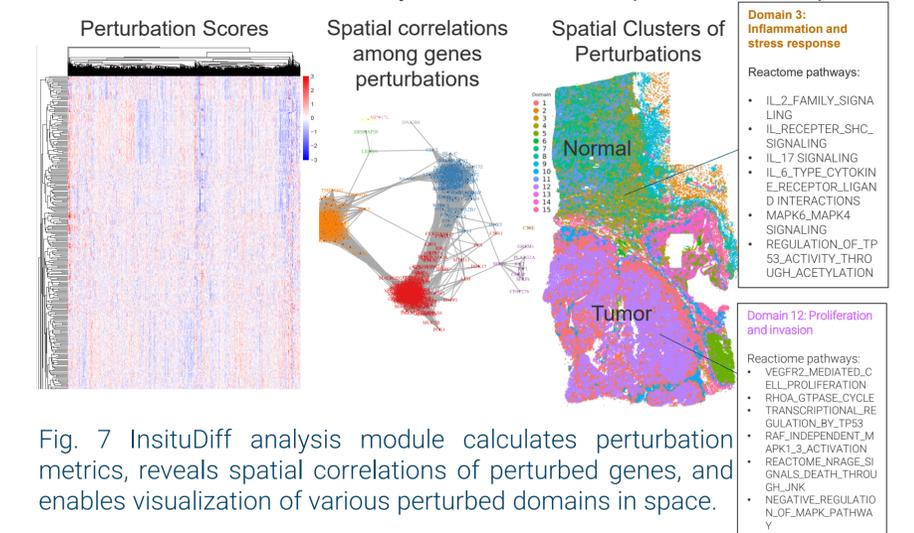


Fig. 7 InsituDiff analysis module calculates perturbation metrics, reveals spatial correlations of perturbed genes, and enables visualization of various perturbed domains in space.

## Conclusion

- This study presents a single-cell resolution spatial atlas of ccRCC using CosMx WTX assay, detailing molecular and cellular transitions from normal to tumor tissue.
- Integrating CosMx WTX with H&E-guided annotation highlights the potential for AI-powered diagnostic tools, setting the stage for future advancements in automated cell typing and transcriptome prediction, transforming research in clinical workflows and precision oncology.

CosMx Whole Transcriptome Assay

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