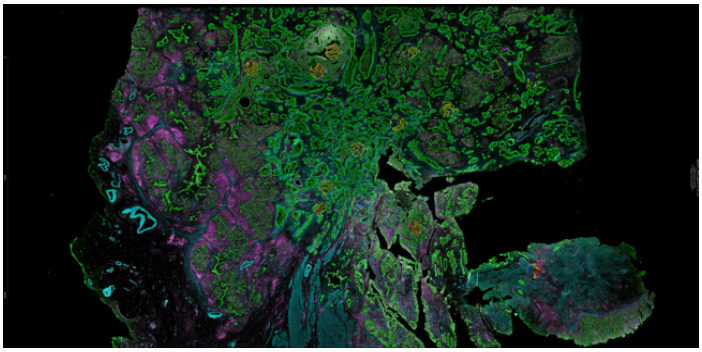
Spatial whole transcriptome profiling of pancreatic cancer redefines the molecular and cellular taxonomy associated with neoadjuvant therapy

Background

- Pancreatic Ductal Adenocarcinoma (PDAC) is highly lethal and challenging to treat
- Molecular subtyping remains to be resolved and does not inform therapeutic development
- Standard single cell methodologies have had limited success in this tumor setting

Research Question

1. What is the cellular composition of PDAC tumors?
2. What is the spatial localization of single cells and how are they interacting in space?
3. What is the mechanism of treatment resistance?



Experimental Setup

Instrument	GeoMx® DSP
Sample Type	FFPE
Tissue Type	Human Pancreas
Assay	Human Whole Transcriptome Atlas
Analyte	RNA
Readout	NGS

Why GeoMx?

"By integrating cell-type signatures and expression programs with whole-transcriptome digital spatial profiles, we identified distinct multicellular communities..."

"We discovered spatially defined intracellular receptor-ligand interactions … potential targets for improving therapy in pancreatic cancer."

Hwang WL et al.

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Results & Conclusions

Spatial whole transcriptome profiles of distinct molecular compartments withing regions of PDAC tumors enabled discovery of new molecular and cellular taxonomies that can be used for both patient stratification and therapeutic development in a disease considered to be difficult to treat.

- Spatial mapping of malignant and cancer associated fibroblasts (CAF) programs revealed program-specific inter- and intra-tumoral diversity of pancreatic cancer
- Enrichment of two malignant lineage programs, NRP and NEN, was revealed after neoadjuvant CRT, unraveling the treatment effect.
- Cell deconvolution analysis using WTA data and single nucleus RNA data revealed composition of ROIs profiled into malignant, CAF and immune cells. Correlation analysis across these tissue compartments revealed spatial organization into distinct cellular communities.
- Spatial receptor-ligand interactions reveal treatment-associated remodeling and potential targets for improving neoadjuvant and adjuvant therapy

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