Spatial whole transcriptomics uncovers unique functional insights into the histological structures of the human pancreas using Digital Spatial Profiling

#3844

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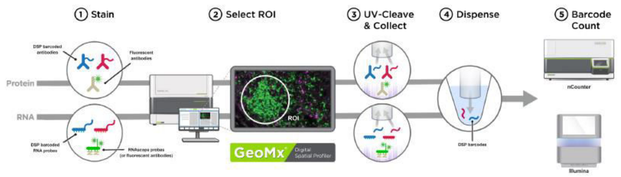
NanoString Technologies

Project Overview

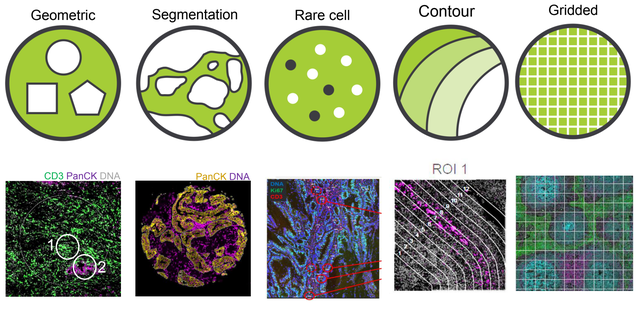
A thorough understanding of normal tissue biology is crucial to advances in disease treatment, but historically it has been challenging to spatially resolve gene expression profiles of the individual structures that comprise organ architecture and function. In this study, we report a deep characterization of pancreas function by analyzing whole transcriptomes of histological structures, encompassing both what decades of detailed molecular studies have unveiled along with novel insights into organ physiology.

Using the GeoMx® Digital Spatial Profiler (DSP) and accompanying Whole Transcriptome Atlas, we analyzed four non-diseased pancreas samples. We profiled functional structures including islets of Langerhans, acini, and ducts within the pancreas. We used a variety of profiling strategies the accurately and precisely optically segregate the functional regions and cells. These data can be used as standards to inform future profiling studies in normal and diseased tissue.

GeoMx Digital Spatial Profiler: Introduction & Workflow

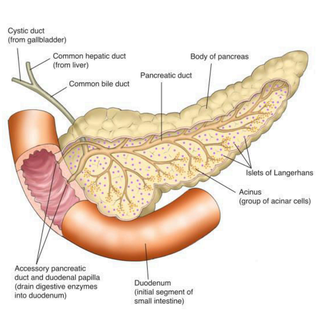


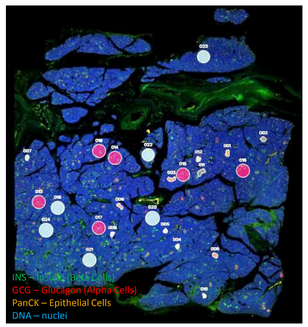
GeoMx DSP enables spatially resolved high plex profiling of either proteins or RNA transcripts from FFPE tissue sections. It uses target binding reagents (antibodies or ssDNA) labeled with photocleavable indexing oligos to bind targets of interest on a slide mounted tissue section, and in parallel tissue architecture is visualized with immunofluorescent imaging reagents. Regions of interest (ROI) are selected for molecular profiling, and those regions are sequentially exposed to UV light which cleaves the photocleavable linker and releases the indexing oligos, which are collected and stored off tissue. Indexing oligos are subsequently enumerated via nCounter® or next gen sequencing.

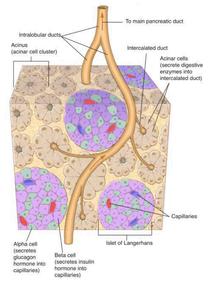


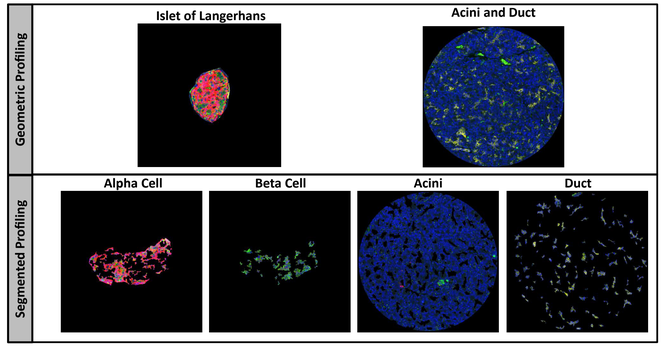
By using the visualization markers to mask specific areas within the ROI, the ROI can be further compartmentalized and molecular profiles of the different compartments profiled independently. This enables, for example, differential profiling of tumor vs stroma, or various immune cell types, within an ROI. NanoString® has developed panels of protein and RNA detection reagents for use with the GeoMx platform. Most recently, we have commercialized the Whole Transcriptome Atlas (WTA), an 18,000+ gene panel that enables characterizing the spatial biology of any human system.

Biology-Driven Profiling of the Pancreas



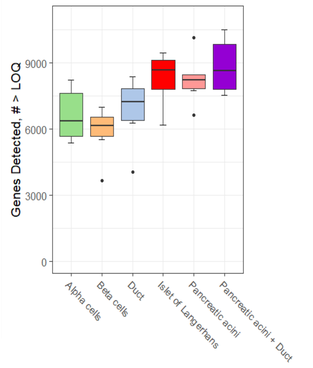




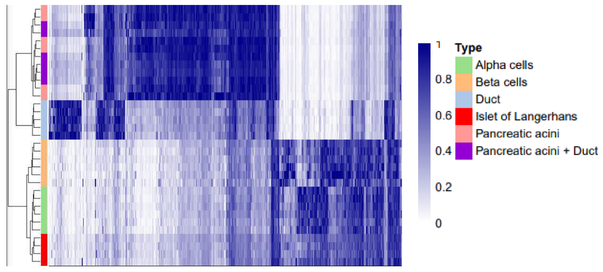


Sample Description and Profiling Strategy A non-diseased pancreas biopsy from a 68-year-old Caucasian woman was profiled via GeoMx DSP using the Whole Transcriptome Atlas (18,500+ genes). The tissue was stained with fluorescent antibodies to guide region of interest selection to functional units within the tissue. Regions of interest were placed on substructures within islets and acini, and geometric and segmentation AOIs were used to profile specific cell populations.

Robust Gene Detection from All AOIs

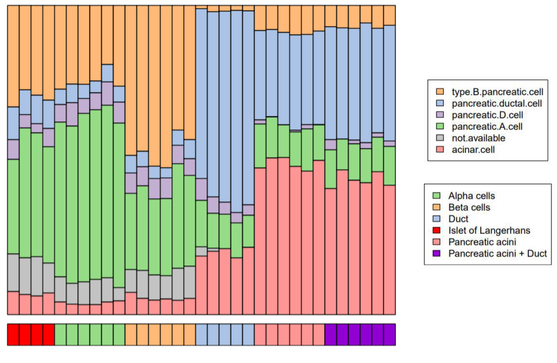


Histological Structures Accurately Identified by Unsupervised Clustering



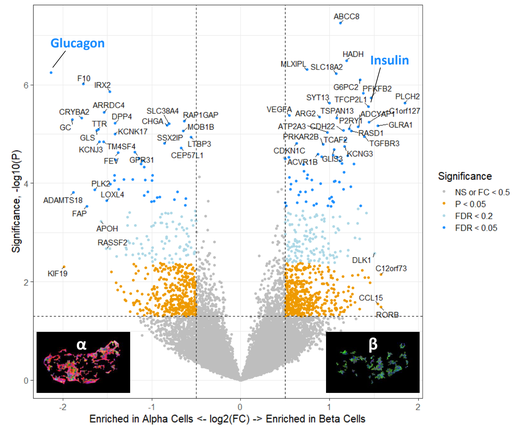
ROIs from the sample were analyzed via unsupervised hierarchical clustering and the molecular signatures of each ROI type was observed.

Cell Type Deconvolution of the Pancreas



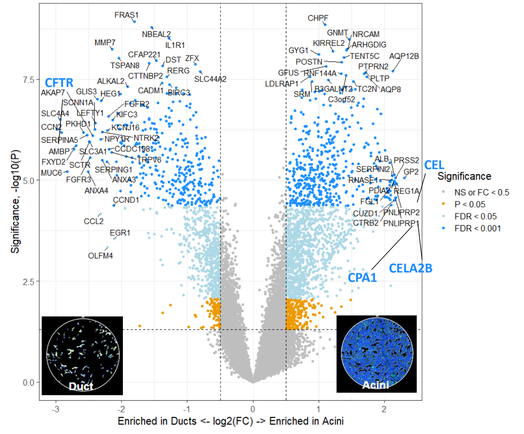
Cell type deconvolution was performed on each ROI/AOI to identify the specific population distribution of cells.

Transcriptional Profiling of Alpha and Beta Cells *In Situ*



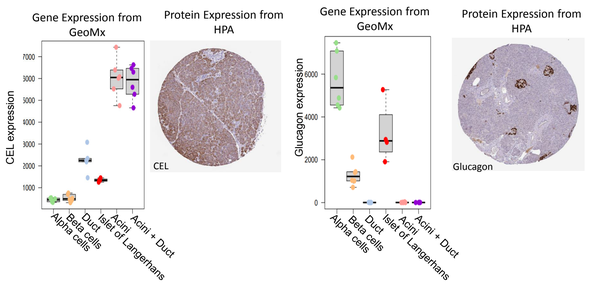
Differential expression was performed on AOIs from alpha and beta cells. Cell type marker genes (glucagon and insulin) were observed in their respective compartments, along with other cell type specific genes.

Transcriptional Profiling of Ducts and Acini *In Situ*

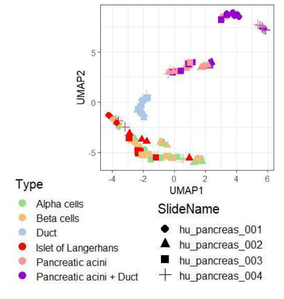


Differential expression was performed on AOIs from ducts and acinar cells. Cell type markers genes (CFTR and CEL) were observed in their respective compartments, along with other cell type specific genes.

Independent and Orthogonal Confirmation of Target Expression with the Human Protein Atlas



Cohort Analysis



Accessing the Data and Contributing to the Spatial Organ Atlas

These data can be accessed and freely downloaded at the Spatial Organ Atlas webpage:
www.nanostring.com/spatial-organ-atlas/

The Spatial Organ Atlas is growing! If you are interested in participating in the project, please contact geomx@nanostring.com

SPATIAL ORGAN ATLAS

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