

3839 First Report of Spatial Whole Transcriptome Profiling of Histological Structures of Multiple Organs

Joseph M Beechem¹, Yan Liang¹, Alison Vanshojack¹, Wei Yang¹, Liang Zhang¹, Patrick Danaher¹, Jason Reeves¹, Erin Piazza¹, Megan Grout¹, Charlie Glaser¹, David Kroeppler¹, Emily Brown¹, Kathy Ton¹, Margaret Hoang¹, Gokhan Demirkan¹, Kit Fuhrman¹, Swati Ranade¹, Michael Rhodes¹, and Sarah Warren¹

¹NanoString® Technologies, Seattle, WA

Abstract

To realize the potential of spatial profiling to define normal organs at the cellular and molecular level, we have started an ambitious project to map the architecture of normal tissues using spatially resolved whole transcriptome profiling. In this pilot phase of the project, 5 organs (kidney, pancreas, brain, colon, and lymph node) were characterized with the GeoMx® Digital Spatial Profiler using region of interests (ROI) in the key multicellular structures that confer organ function (e.g. pancreatic islets). ROI consists of geometric areas centered on the functional unit or cell type-enriched ROIs to characterize particular cell populations within the functional units. Spatial transcriptomic data are then benchmarked to orthogonal platforms as independent validation of the results. Multiple ROI per tissue and multiple donors per organ have been profiled to permit evaluation of the diversity within and between individuals. All data will be made publicly available as a resource for the community. Future expansion of this program will encompass additional organs and larger cohorts for each organ to increase the utility of this resource.

Methodology

Non-diseased FFPE tissues were obtained from commercial vendors. Tissues were assessed by a pathologist before being used in the Spatial Organ Atlas project. For each organ, samples from 4 individuals were used. Five micron slices were taken and stained with morphology markers chosen to highlight the functional units of interest and probed with the GeoMx Whole Transcriptome Atlas Assay, a highly multiplexed set of probes designed to detect >99.5% of protein coding genes in humans. The GeoMx Digital Spatial Profiler uses the morphology markers to segment the selected Region of Interest (ROI) into individual Areas of Interest (AOI). This is shown in the central figure, demonstrating morphology marker-guided definition of cell populations or histological structures. The segmentation feature was used to collect whole transcriptome data from the individual AOIs. The resultant data allows analysis of spatially defined whole transcriptomes.

Samples

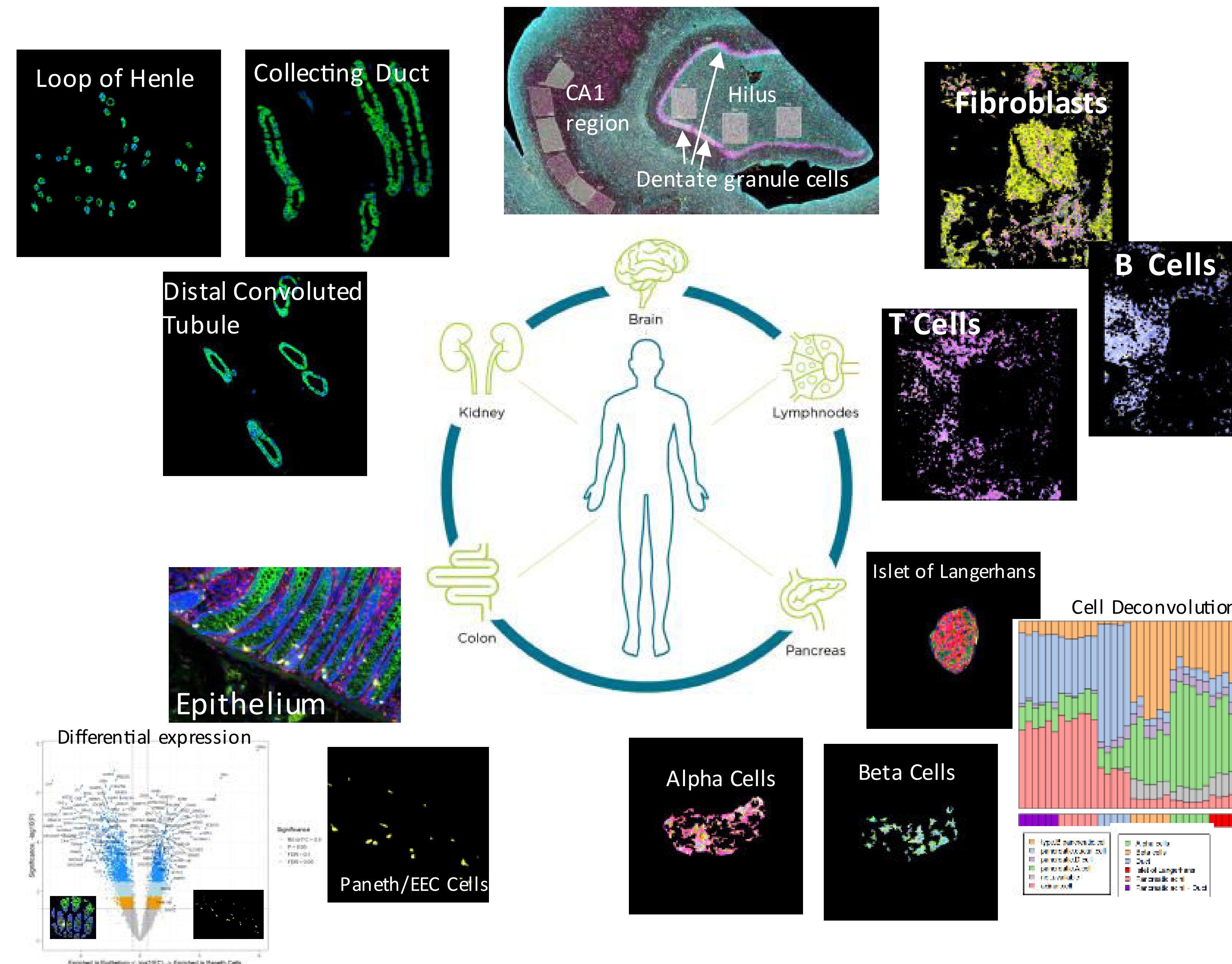
Organ	Segments Profiled	# AOIs Profiled
Pancreas	Islets (Alpha and Beta Cells), Acini, Ducts	142
Kidney	Glomeruli, Proximal & Distal Tubules, Collecting Ducts	203
Colon	Epithelium, Paneth Cells, Lamina Propria	172
Brain – Human + Mouse	Cortex and Hippocampus	190 (Human) + 361 (Mouse)
Lymph Node	B cells, T cells, Epithelial cells	188

For more Detailed Analysis See:
Kidney - ASHG2021 Poster 3843
Pancreas - ASHG2021 Poster 3844

Selection of Available Organ Data

Digital Spatial Profiling allows the collection of spatial whole transcriptomes (over 18,500 gene targets) of tissue regions that exactly match the exact shape of tissue sub-structures.

The Spatial Organ Atlas will provide a reference database of healthy tissues for all the organs of human and mouse. For each of the Human tissues, an example is given of the ability to precisely measure whole transcriptomes on key histological substructures in Kidney, Colon, Brain, Pancreas and lymph nodes.



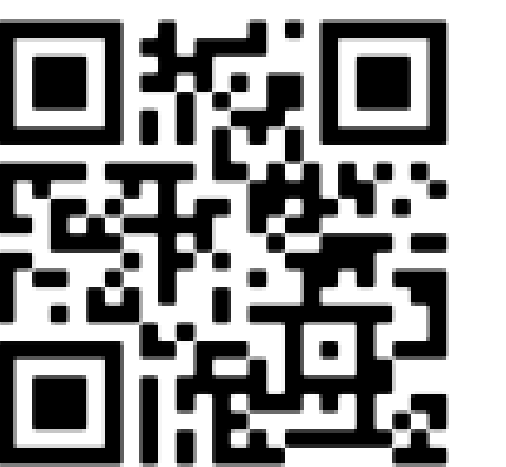
For the regions shown and many others, complete whole transcriptome data is available for download.

Data Availability

All data generated for these samples is available for download including

- Image files: OME-TIFF
- Sequencing data: FASTQ files
- All processed data files: Gene counts per AOI
- Vignette describing analysis process

Download data



Visualizing Analysis Results

Minerva stories enabling co-visualization of images and analysis results are available here: www.nanostring.com/spatial-organ-atlas/

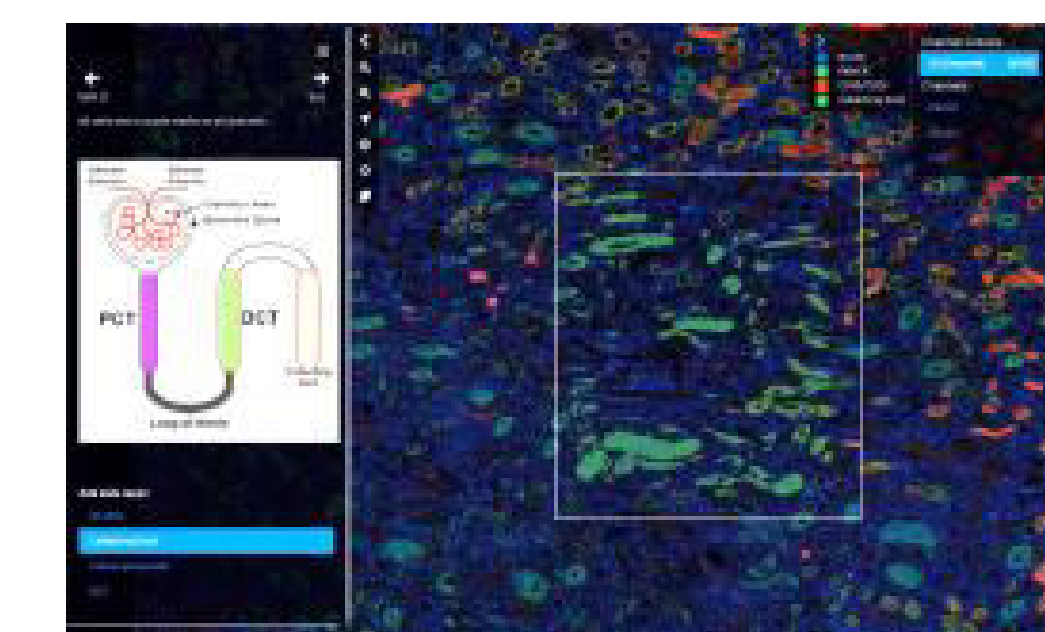


Fig 3: Minerva screenshot, showing ability to select a highlighted region on the diagram and highlight that feature on the actual sample

Hoffer et al., (2020). Minerva: a light-weight, narrative image browser for multiplexed tissue images. Journal of Open Source Software, 5(54), 1 2579

Conclusion

The Spatial Organ Atlas is the first community driven project to provide in-situ whole transcriptome data generated from FFPE, non-diseased organs. The 18,500+ gene targets map the exact shape of the molecular anatomy of functional histological features. This Atlas will serve as a reference for understanding of organs in health and disease.

