Single Cell Atlases of the Pancreatic Islets of Langerhans Elucidate the Metabolic Dysfunction Associated with Type II Diabetes

CASE STUDY

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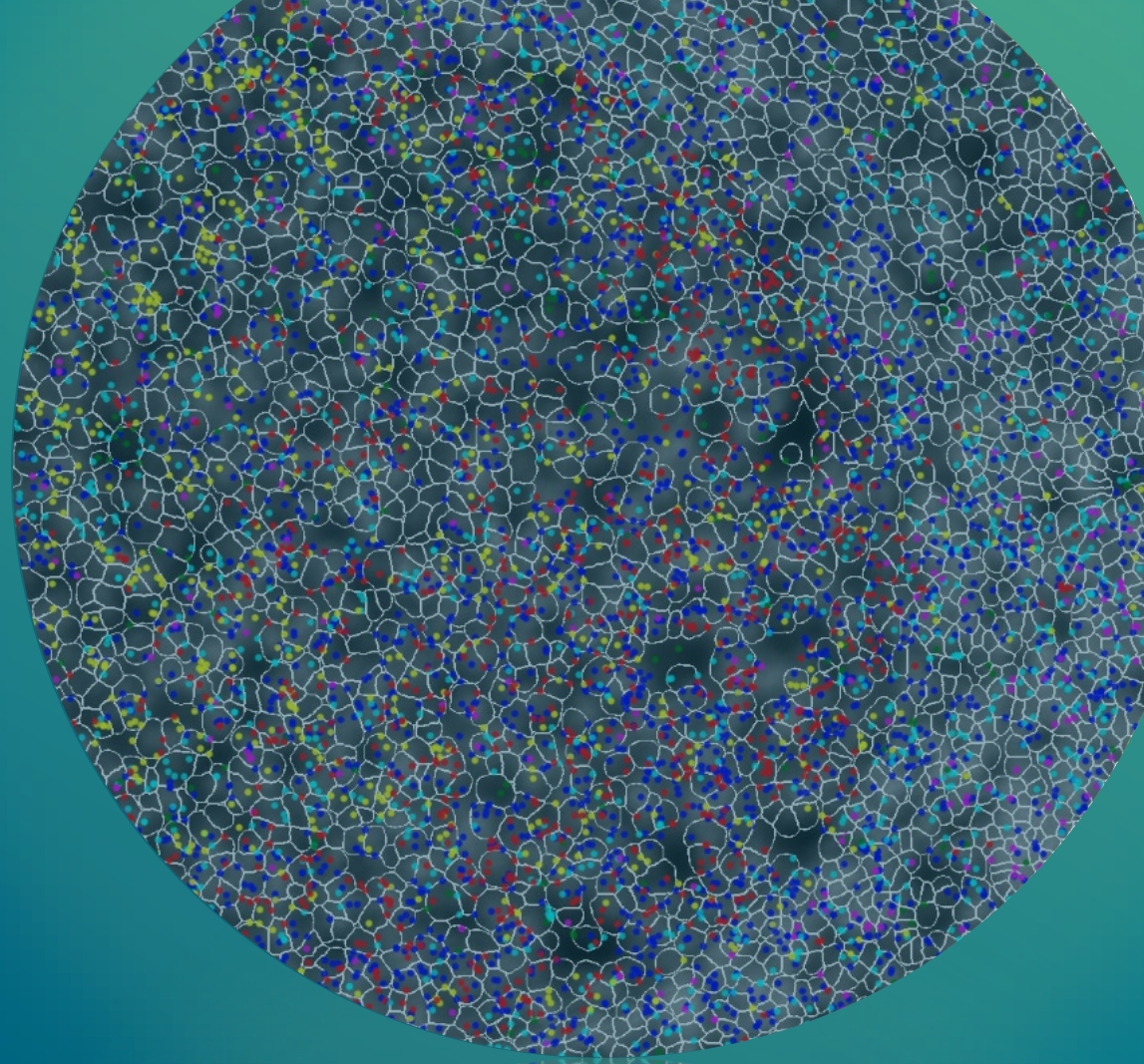

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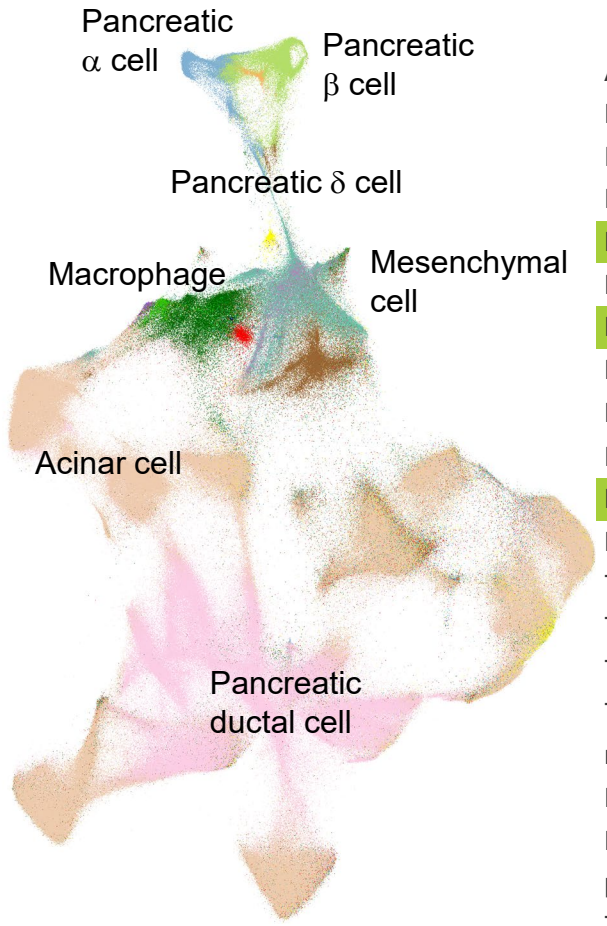
Single Cell Atlases of the Pancreatic Islets of Langerhans Elucidate the Metabolic Dysfunction Associated with Type II Diabetes

- "Spatially mapping the relative abundance and distribution of the cell subpopulations in endocrine micro-organs the islets of Langerhans using **CosMx™ SMI 1000 plex RNA Assay** provides invaluable views into the functioning of the pancreas."

- The **distribution and re-distribution of cellular sub-populations** within the islets of pancreatic tissue **in the context of MHO and T2D** is a unique application only possible with CosMx™ SMI. The percentage of endocrine cell types in the islet is higher for normal individuals than for type 2 diabetic (T2D) or metabolically healthy obese (MHO)

Abbreviations: ABV1, abbreviation 1; ABV2, abbreviation 2.

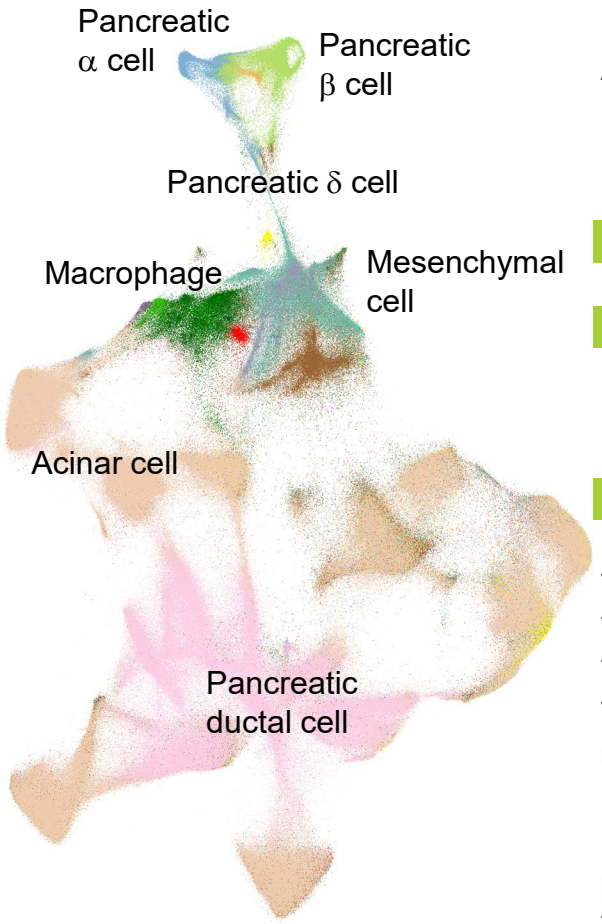


1,015,004 total cells

Cell types

	n	%
Acinar cells	469,428	46.25%
Pancreatic ductal cells	281,195	27.70%
Fibroblasts	58,023	5.72%
Endothelial cells	49,344	4.86%
Pancreatic β cells	**37,941**	**3.74%**
Macrophages	31,932	3.15%
Pancreatic α cells	**22,414**	**2.21%**
Mesenchymal cells	16,554	1.63%
Mast cells	15,089	1.49%
Plasmablasts	9,474	0.93%
Pancreatic δ cells	**4,547**	**0.45%**
Monocytes	3,505	0.35%
T CD4 memory cells	3,129	0.31%
T CD8 naïve cells	2,784	0.27%
T CD8 memory cells	2,299	0.23%
Tregs	2,090	0.21%
mDCs	1,386	0.14%
Neutrophils	1,335	0.13%
NK cells	1,094	0.11%
pDCs	904	0.09%
T CD4 naives	322	0.03%
B-cells	215	0.02%

Comprehensive Cell Atlas of 443 Human Islet of Langerhans



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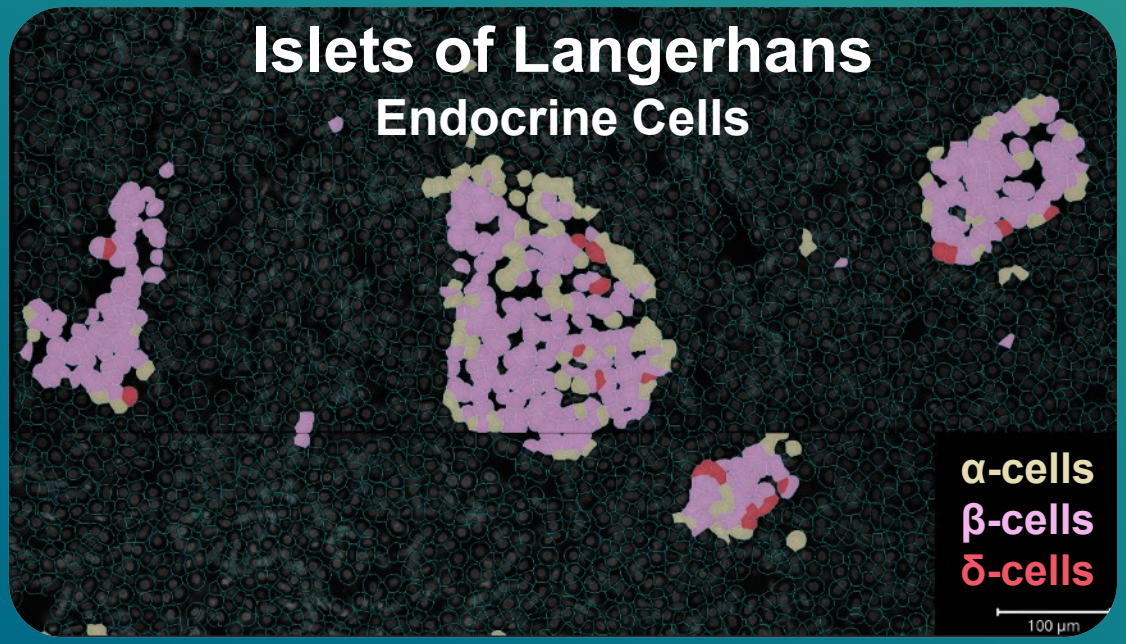


Dr. Grant Kohler, MD, Ph.D
Dr. Gina Yosten, Ph.D

St. Louis University

Single Cell Atlas of the Islets of Langerhans

Scan here to download or learn more

Background

- Islets of Langerhans are at the epicenter of the metabolic dysfunction associated with obesity and diabetes, but to date the abundance and spatial distribution of the beta, alpha, and delta cell subpopulations that comprise the islets are largely unknown

Research question

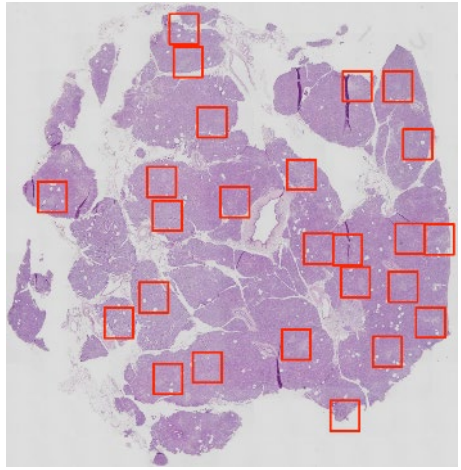
- How does the spatial distribution of cellular subpopulations within pancreatic islets affect the molecular and cellular changes associated with tissue dysfunction in diabetic patients?

Experimental design

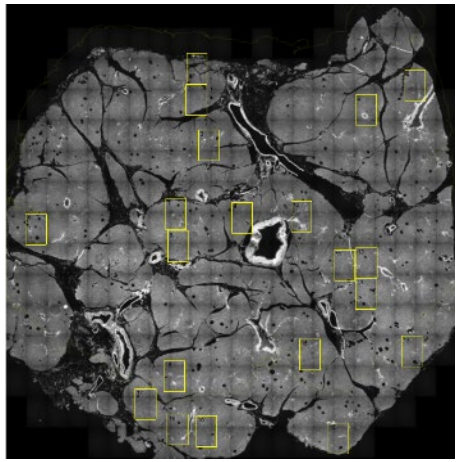
- Spatial atlasing of pancreatic islets in diabetic and non-diabetic patients by comparing differential gene expression in 3x normal, 3x Type II Diabetic, 3x Metabolically Healthy Obese tissues

Study Details	
Research area:	Type II Diabetes
Organism and tissue:	Human Pancreatic Tissue
Sample type:	FFPE
Instrument:	CosMx
Analyte:	• 1000 plex RNA • A custom panel of 30 genes
Readout:	CosMx
Publication Year:	AGBT 2022, poster 309

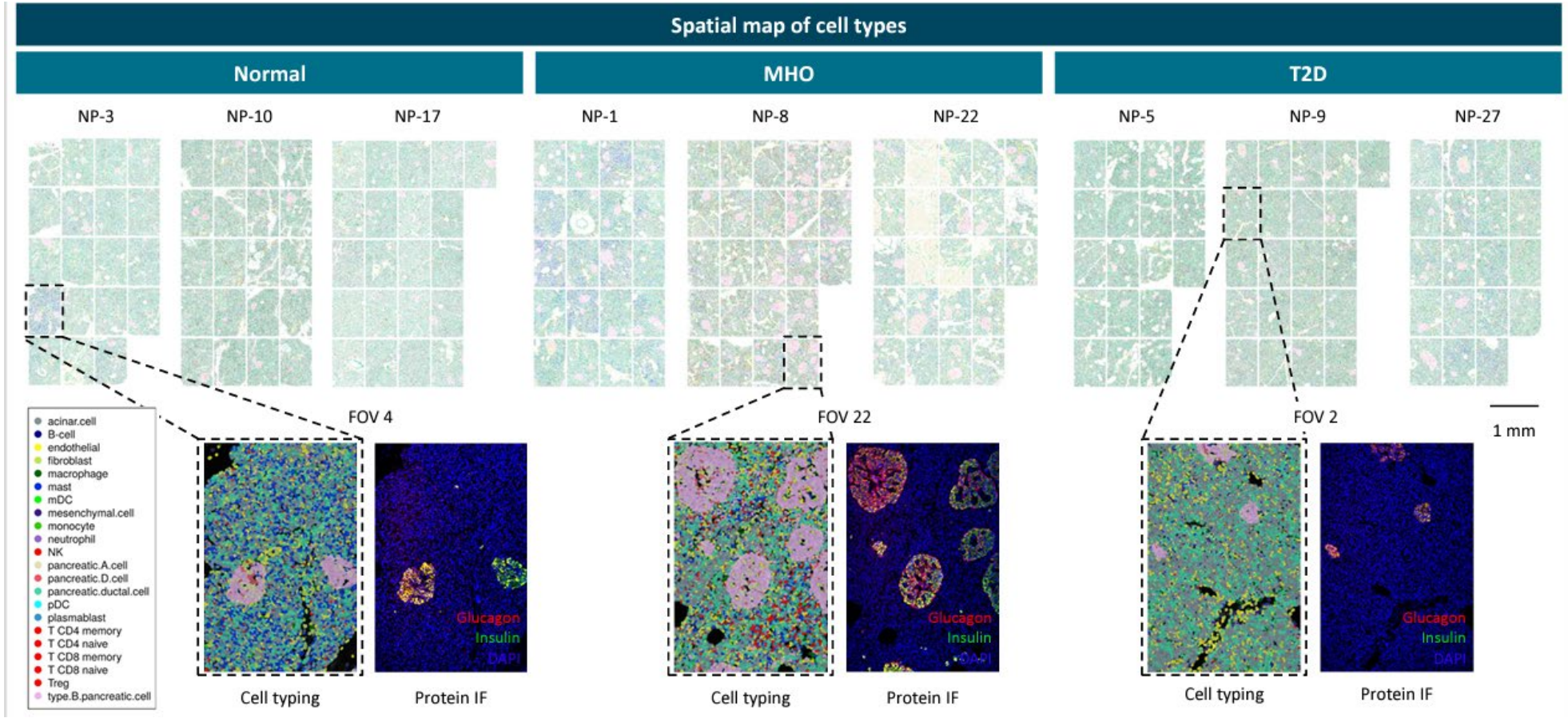
Profiling 1.2 million Single-Cells Across Nine FFPE Pancreatic Tissues



H&E to indicate FOV locations



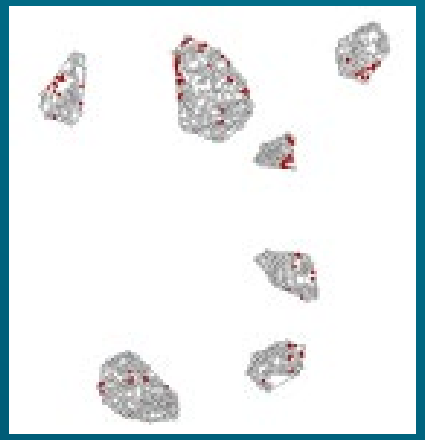
CosMx FOV selection on preview scan



CosMx Morphology Staining & FOV Selection Strategy

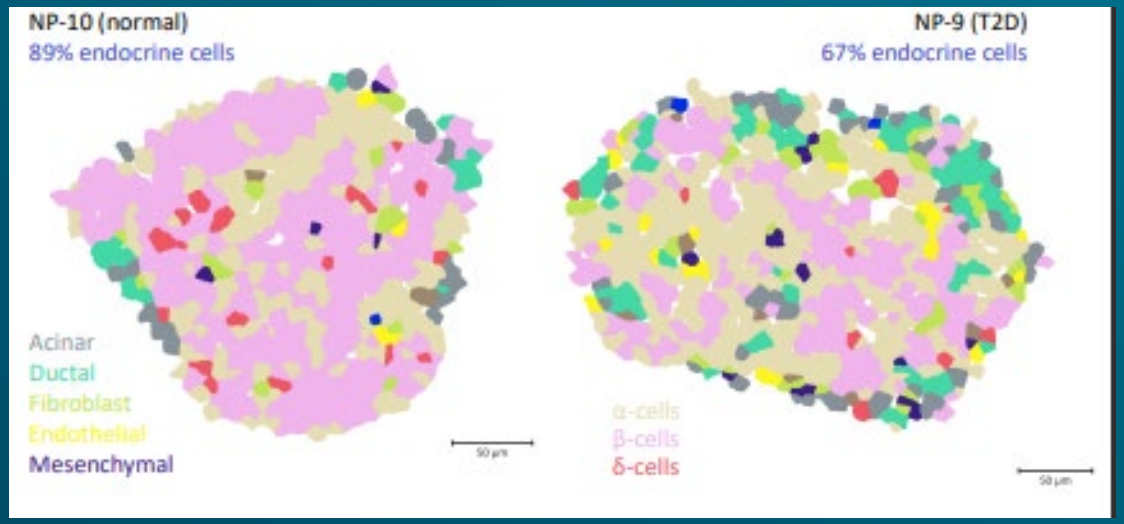
Glucagon (β-cells)
Insulin (α-cells)
DAPI (nuclei)

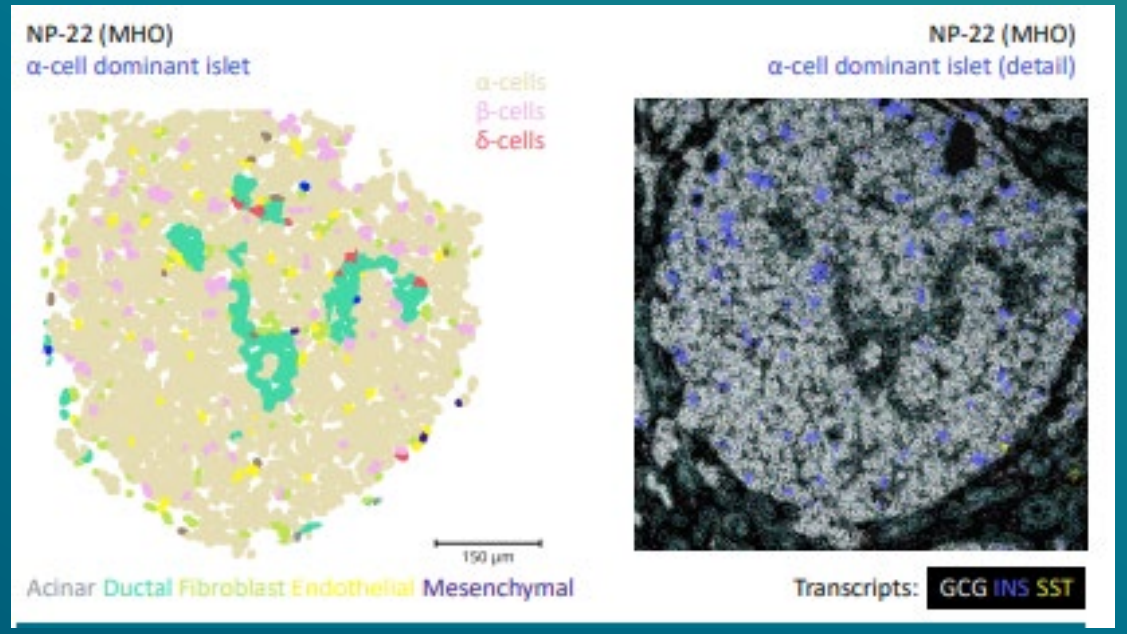
Single-Cell Atlases define Islets by endocrine cell cluster density



- Identify dense clusters of α, β, and δ cells
- Define the convex hull of these cells as islet region
- Assign any other cells in the enclosed space to the islet

463 individual islets were identified across nine samples





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Results

- **~1.2 million single-cells profiled** across nine FFPE pancreatic tissue
- Populations of **beta, alpha, and delta cells mapped** in the spatial context

Conclusions

- **Islet cell type composition varies** across disease and healthy tissue types
- Percentage of **endocrine cell types in the islet is higher for normal individuals than for type 2 diabetic (T2D) or metabolically healthy obese (MHO)**

Value of CosMx

- Spatially **mapping the relative abundance and distribution of the cell subpopulations** in endocrine micro-organs the islets of Langerhans only possible with the SMI capability of CosMx™ makes it a powerful tool to obtain **invaluable views into the functioning** of the pancreas