Cellular Characterization of the Pancreas in Individuals with or at Increased-Risk for Type 1 Diabetes

**AUTHORS**

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**PURPOSE**

Once thought a disease primarily affecting β-cells, emerging evidence suggests that type 1 diabetes (T1D) also includes distinct alterations in both endocrine and exocrine pancreatic compartments. However, a quantitative histological description of pancreatic acinar, ductal, and other non-endocrine/non-exocrine tissues is lacking.

**METHODS**

We utilized HALO image analysis software to analyze scanned whole human pancreas cross-sections from nPOD donor cohort, stained for insulin and glucagon by IHC as well as H&E, from the PH, PB, and PT regions. We characterized pancreatic exocrine and endocrine tissue compositions by quantifying the proportion of endocrine, acinar, and ductal/other (non-endocrine, non-exocrine) areas as well as acinar and endocrine cell density, and size in subjects with or at-risk for type 1 diabetes as well as controls without diabetes.

**SUMMARY OF RESULTS**

The area of ductal/other tissues was greater in those with T1D lacking residual insulin containing islets (T1D ICI-) compared to non-diabetic autoantibody negative (ND AAb-) and non-diabetic autoantibody positive (ND AAb+) groups. Inversely, acinar area was lower in T1D ICI- donors vs. either ND group. However, despite having a similar proportion of acinar area to both ND groups, the cells were smaller and tissue denser in T1D individuals with residual insulin containing islets (T1D ICI+) compared to ND AAb- donors. Endocrine area was smaller, but density greater, in T1D donors compared to either ND group. Interestingly, endocrine cells were smaller in all T1D vs. ND AAb- donors, but also in T1D ICI+ vs. ND
AAb+ individuals. The main pancreatic duct was thicker and occupied area smaller in the tail vs. body region, regardless of disease status.

**CONCLUSIONS**

Further research is needed to address the role of whole-organ defects in T1D, but these data provide important insights into anatomical differences observed within the pancreas and highlights that alterations within the exocrine tissue may play a part in disease pathogenesis.