nPOD
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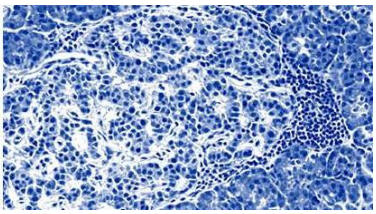

Temporal Analysis of Amylase Expression in Control, Autoantibody Positive, and Type 1 Diabetes Pancreatic Tissues

AUTHORS

Irina Kusmartseva[1], Maria Beery[1], Helmut Hiller[1], Myriam Padilla[1], Stephen Selman[1], Amanda Posgai[1], Harry S. Nick[2], Martha Campbell-Thompson[1], Desmond A. Schatz[3], Michael J. Haller[3], Clive H. Wasserfall[1], Mark A. Atkinson[1,3]

[1]Department of Pathology, Immunology and Laboratory Medicine, Diabetes Institute University of Florida, Gainesville, FL, USA

[2]Department of Neuroscience, College of Medicine, University of Florida, Gainesville, FL, USA

[3]Department of Pediatrics, College of Medicine, University of Florida, Gainesville, FL, USA

PURPOSE

Within the human pancreas, exocrine and endocrine cells control secretion of digestive enzymes and production of hormones to maintain metabolic homeostasis, respectively. While the vast majority of type 1 diabetes research efforts have focused on endocrine function and autoimmunity, recent studies identified a series of unique features (e.g., reduced weight and volume, increased density of leukocytes) within the exocrine pancreas in this disease. It remains unclear whether these alterations result from disrupted islet-acinar interactions secondary to the loss of functional β-cell mass, or contribute directly to type 1 diabetes development. In order to interrogate the potential relationship linking islet and acinar cell mass and function, a foundational understanding of cell phenotype and morphological organization within the exocrine pancreas is necessary.

METHODS

We histologically assessed pancreatic amylase expression patterns throughout the human lifespan from individuals with and without type 1 diabetes, representing what we believe to be the largest cohort and most extensive histological analysis of exocrine human pancreas reported to date.

SUMMARY OF RESULTS

Our analysis shows that amylase positive cells accumulate during early life development with the majority of acinar cells expressing amylase by age two, which is then maintained throughout the lifespan. Most significantly, pancreata from individuals over two years of age contained clusters of acinar cells devoid of amylase protein and mRNA expression. A majority of these amylase-negative cell clusters localized proximal to islets (i.e., peri-islet) and were positive for the exocrine enzymes lipase and trypsinogen. Type 1 diabetes pancreata displayed significant reductions in the frequency of these AMY^- cell clusters.

Interestingly, we observed an approximate 75% decrease in the number of peri-islet amylase negative cell clusters associated with insulin-negative versus AMY^- cell clusters associated with insulin positive islets.

CONCLUSIONS

These results support a contribution of the islet-acinar axis in pancreatic development and underscore a potential role for the exocrine pancreas in the pathogenesis of type 1 diabetes.