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motoxylin/eosin and anti-insulin/glucagon/amyloid). Representative images of the stained sections and accompanying morphological evaluation will be uploaded on the IIDP website. Investigators may request histology sections for their research. Further, IIDP requires center reporting of Islet Index (reflects islet size distribution), purity (dithizone staining), viability (inclusion/exclusion dyes), sterility (aerobic, anaerobic, fungal and sentinel tests) and potency (Glucose Stimulated Insulin Secretion (GSIS) assay). Since January 2010, 112.3 million human islets have been distributed. The mean properties of pure and impure broadcasts respectively are as follows: Islet Index 1.2, 1.1; % Purity 85.3, 53.3; % Viability, 92.0, 89.5; Potency-Stimulation Index, 3.0, 2.7; Sterility, 99.1% of broadcasts were sterile. To further enhance the program, the IIDP is currently evaluating the isolation of islets from type 1 diabetic (T1D) donors. Offers for pancreata from T1D donors are rare and retrievable Islet Equivalents (IEQ), can be limited. However, the IIDP recently succeeded in distributing 60,000 IEQs from a T1D child isolated at University of Pennsylvania to 10 investigators for critical T1 research.

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2924-PO

Glutathione's Reduced Form Protects Beta Cells from Destruction Caused by Diabetogenic Ligands

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Glutathione Reduced form contain SH-group (GSH) possess ability to bind- ing with ligands.

Aim of work: To study effect of GSH on action of diabetoge-nic zincbinding ligands Diphenylthiocarbazone (DZ) and 8-para (toluenesul-phonylamino) quinoline (8PTSQ). Groups of rabbits: 1) injection of DZ 49,3-50,8 mg/kg 2) GSH 970-1020 mg/kg +DZ 48,9-51,6 mg/kg 10 min later; 3) GSH 985-1010 mg/kg+8PTSQ 47, 5-49, 7 mg/kg; 4) Glutathione Oxidized form (GOx) 980-1015 mg/kg+DZ 50, 9-51, 6 mg/kg. Blood Glucose level (BG)-3 times per 6 days. Other animals killed 10 min past 2nd injection.

Histology: aldehydefucshine method; insulin immunohistochemistry (IG); vital by DZ and 8PTSQ staining of Zn^{+2}-ions in B-cells with measuring of absorbance past injection of DZ (DZA) and 8PTSQ (IF).

Results: Group 1: BG: 5.4±0.7 mM before and 16.2±2.5 mM 6 days later; histology: necrosis and destruction of 85-90% B-cells; IG 1.07 ±0.03 (intacts-1.89±0.04); 2 animals early killed: binding of almost all amount of Zn^{+2}-ions in B-cells by DZ: DZA 1.95±0.04 (intacts-1.00±0.02). Group 2: BG: 5.2±0.5 mM before and 6.2±0.6 mM 6 days later; histology; islets without changes; 3 animals early killed: binding of 7-12% of Zn^{+2}-ions in B-cells: DZA 1.09±0.02 (intacts-1.00±0.03). Group 3: BG: 5.5 ±0.7 mM before and 6.8±0.9 mM 6 days later; histology: not marked necrobiosis in 5-10% of B-cells; 3 animals early killed: binding of 5-10% of Zn^{+2}-ions in B-cells by 8PTSQ: IF 1.12±0.03 (intacts-1.97±0.07). Group 4: BG: 4.8±0.5 mM before and 14.8±2.6 mM 6 days later; histology: necrosis and destruction of 80-85% B-cells; IG 1.09±0.02 (intacts-1.87±0.05); 2 animals early killed: binding of almost all amount of Zn^{+2}-ions in B-cells by DZ: DZA 1.92±0.05 (intacts-1.00±0.03).

Conclusions: 1) GSH protect B-cells of binding Zn^{+2}-ions by diabetogenic ligands, of destruction B-cells and of developing diabetes; 2) GOx not contain SH-group, not protect Zn^{+2}-ions in B-cells of binding by DZ that result destruction of cells and of developing of diabetes.

Supported By: Family of Professor Gabit G. Meyramov

ISLET BIOLOGY—BETA CELL—DEVELOPMENT AND POSTNATAL GROWTH

2925-PO

Single-Cell RNA-Seq Reveals Alpha-Cell Maturation Stages in Pancreas Development

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The heterogeneous nature of the developing pancreatic epithelium and the low abundance of endocrine progenitors limits the information derived from traditional expression studies. The advent of single-cell transcriptomics allows the identification of important differences between cells otherwise sorted together using lineage markers. To characterize the transcriptomic landscape of pancreatic endocrine cells we performed single-cell RNA-seq of e13.5 mouse pancreata using Fluidigm C1. 76 individual libraries were generated. The data were analyzed by Monocle to sort cells in an order according to their progression through differentiation and to identify differentially expressed genes. Four cell states were identified: two appear to be early and terminal developmental stages, and two may represent intermediate stages. Glucagon (Gcg) was the major differentially expressed gene across the Monocle pseudo-differentiation stages, suggesting that Gcg+ cells at e13.5 are in different stages of maturation. A set of 152 genes had a similar expression profile to Gcg. Gene ontology (GO) analysis of this set showed enriched terms such as "cytoplasmic membrane-bounded vesicle" and "signaling and peptide hormone processing." Cells with very high Gcg transcript expressed other pancreatic hormones (insulin, ghrelin, peptide YY), albeit at lower levels, indicating that plurihormonal expression is a normal developmental stage in the maturation of α cells. Overall, Gcg+ cells expressed a variety of pro-endocrine factors (Sox9, MafB, Ngn3, Nkx2.2, FoxA2, Rfx6), and acinar lineage factors (Nr5a2, Rbpj, Cpa1, Gata4). At least at a transcriptional level, mouse pancreatic epithelial cells at e13.5 can concurrently express factors specific to different cell fates. Our study brings a new awareness of the maturational heterogeneity of mouse pancreatic endocrine cells at e13.5. It establishes the utility of single-cell RNA-Seq as an unbiased tool for analyzing pancreatic endocrine progenitors.

2926-PO

S 100-Positive Cells in the Human Islets of Langerhans

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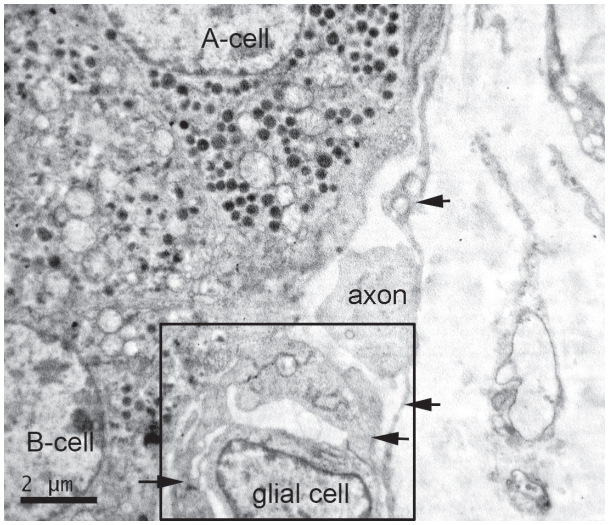
The current studies suggest that in the pancreas the structures of the nervous system are the primary target of the autoimmune attack in diabetes type one (DM1). Experiments on NOD (nonobese diabetic) mice have revealed an autoimmunization against neuronal and glial cell antigens (S-100, GFAP, GAD) at early stages of DM1. In order to characterize cells containing S 100-like immunoreactivity in the islets of Langerhans, we examined the autopsied pancreatic specimens from human fetuses, infants and adults using immunochemistry and electron microscopy. Two types of S 100-positive cells, which differ in shape and localization, were detected in the human islets of Langerhans.

Small oval, spindle or triangular cells with processes were revealed on the margin of the islets. The glial nature of these cells was confirmed by electron microscopy. In the fetal and children's pancreata, glial cells were often seen in the forming pancreatic islets. It has been suggested that these cells are a part of neuro-insular complexes and may be involved in the pancreatic islets morphogenesis.

S 100-positive cells, which were similar in shape and localisation with other endocrine cells, were found within the islets. We propose that these cells may play a role in synchronization of islets calcium-dependent hormone release. These findings suggest novel neural-islet regulatory mechanism and therefore advance basic knowledge of islet neurobiology.



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