Comparative Analysis of Fetal Ferret Pancreas Development

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Background

Cystic fibrosis-related diabetes (CFRD) is the most significant co-morbidity of cystic fibrosis (CF), impacting >50% of adult patients. Studies in young CF children indicate that defects in islet function is an early clinical feature of CF, but the cause of this dysfunction remains controversial.

Though CFRD is not well-modeled in mice, it occurs spontaneously in the ferret model of CF, suggesting this would be a useful model to characterize whether there is a developmental origin of pancreas dysfunction in CF patients.

Objectives

1. Characterize WT fetal ferret pancreas development as a baseline for comparison with a CF ferret model
2. Determine whether pancreatic developmental defects contribute to CFRD in adults

Methods

Formalin fixed, sucrose processed, and O.C.T embedded WT fetal ferret pancreatic tissues were selected at embryonic days 21, 22, 23, 33, and 38. The pancreas tissues were sectioned at 10µm, double immunofluorescence stained, and counterstained with DAPI.

Results

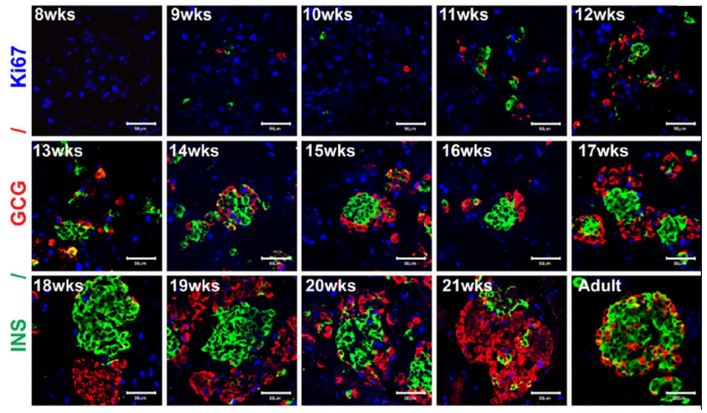

Image 2: INS/GCG expression in human pancreas development
Islet-like structures appear ~week 12 and are primarily formed by aggregation of insulin- and glucagon-producing cells.

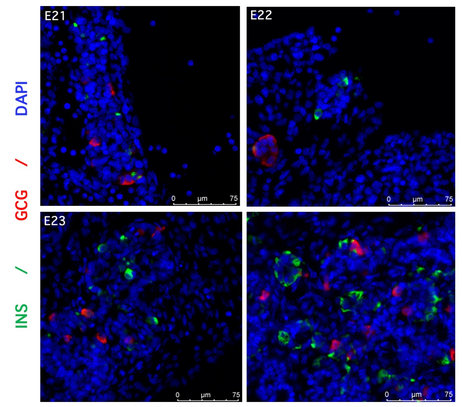

Image 3: INS/GCG expression in WT ferret pancreas development
Insulin- and glucagon-producing cells begin to aggregate ~E33, which approximately correlates with weeks 11-12 in human development.

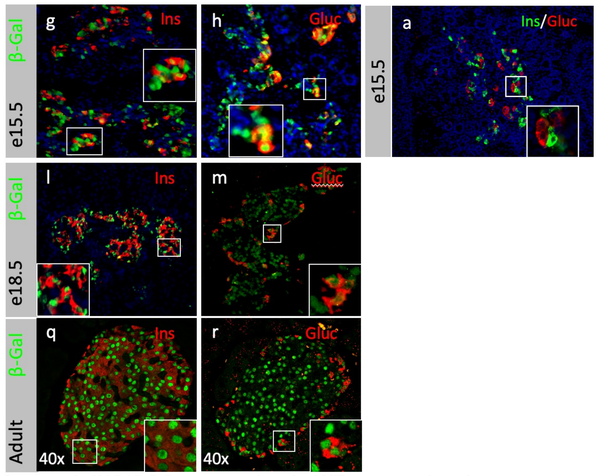

Image 4: INS/GCG expression in WT mouse development
Insulin- and glucagon-producing cells aggregate into a conformation where the glucagon surrounds the insulin.

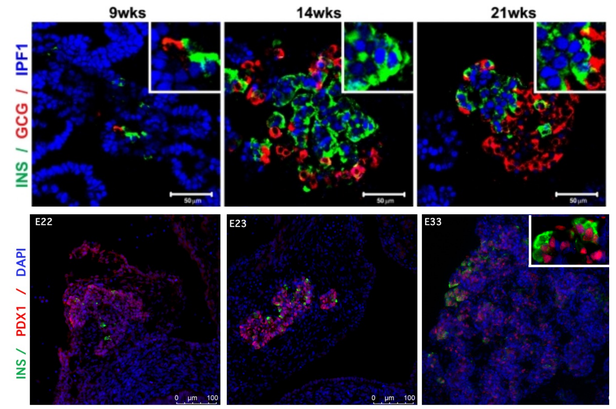

Image 5: INS/Pdx1(Ipf1) expression in human and ferret pancreas development
Human and ferret Pdx1/Ipf1 demonstrate similar morphologies on high magnification.

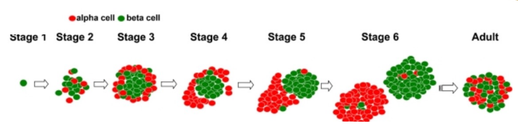

Image 1: Phases of islet-like cluster formation in human pancreas

Antibody	
Insulin	DAKO #IR002, monoclonal guinea pig IgG
Glucagon	CST #2760s, monoclonal rabbit
Glucagon	US Biologicals #G2040-01, monoclonal guinea pig IgG
Pdx1	BCBC #1858, monoclonal rabbit IgG
Somatostatin	Phoenix #H-060-03, monoclonal rabbit IgG
Nkx6.1	BCBC #AB1069, monoclonal rabbit IgG
Nkx2.2	DSHB #74.5a5-c, monoclonal mouse IgG
Nkx2.2	Sigma Aldrich #HPA003468, monoclonal rabbit IgG
Amylase	Sigma Aldrich, monoclonal rabbit IgG

Table 1: Antibodies used

Conclusions

- In early development, the ferret, mouse, and human pancreas appear similar.
- As development progresses, ferret pancreatic islet formation appears more similar to humans.
- Future studies will determine whether CF ferrets display altered pancreatic islet development.

Disclosures

No disclosures to report.

References

Jeon, J., Correa-Medina, M., Ricordi, C., Edlund, H., and Diez, J.A. 2009. Endocrine Cell Clustering During Human Pancreas Development. Journal of Histochemistry & Cytochemistry 57(9):811-824.