Cystic fibrosis-related diabetes (CFRD) is the most significant comorbidity of CF, impacting >50% of adult patients. Studies in young children with CF indicate that perinatal defects in islet function is an early clinical feature of CF, but the cause of this dysfunction remains controversial. To begin to understand the potential origins of CFRD, it would be optimal to begin to study an animal model; however, CFRD is not well-modeled in mice and other animal models pose their own challenges. Alternatively, CFRD 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 patients with CF. Because the development of the fetal ferret pancreas has not yet been characterized, the purpose of this project is to characterize wild type ferret pancreas development as a baseline for future comparison with a CF ferret model. Immunofluorescent staining was employed to identify key markers of development and islet hormone expression patterns in fetal ferret tissues. In this study, we demonstrate that WT ferret and human islet development appear similar, and both species diverge from mouse pancreatic morphology. Future studies are underway to determine whether CF ferrets display altered pancreatic islet development and hormone expression.

**Abstract**

Cystic fibrosis-related diabetes (CFRD) is the most significant comorbidity of CF, impacting >50% of adult patients. Studies in young children with CF indicate that perinatal defects in islet function is an early clinical feature of CF, but the cause of this dysfunction remains controversial. To begin to understand the potential origins of CFRD, it would be optimal to begin to study an animal model; however, CFRD is not well-modeled in mice and other animal models pose their own challenges. Alternatively, CFRD 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 patients with CF. Because the development of the fetal ferret pancreas has not yet been characterized, the purpose of this project is to characterize wild type ferret pancreas development as a baseline for future comparison with a CF ferret model. Immunofluorescent staining was employed to identify key markers of development and islet hormone expression patterns in fetal ferret tissues. In this study, we demonstrate that WT ferret and human islet development appear similar, and both species diverge from mouse pancreatic morphology. Future studies are underway to determine whether CF ferrets display altered pancreatic islet development and hormone expression.

**Cystic Fibrosis-Related Diabetes (CFRD) is the Most Significant Comorbidity of CF**

**Methods**

We used n = 6 wild-type ferret embryos which were dissected for the pancreas, fixed, mounted, and sectioned. Immunofluorescence staining was performed as per a standard protocol. Image acquisition was performed using a Zeiss confocal microscope.

**Comparative Analysis of Ferret Pancreatic Development**

1. E15.5 / E34
2. E18.5 / E38
3. PO

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**Future Directions**

- Single cell RNA-sequencing using SPLiT-seqencing is underway to perform comprehensive comparative analyses between the ferret, human, and murine transcriptomes.
- Optimize protocol to improve primary antibody staining.
- Perform immunofluorescence staining at other time points in development and in CF ferrets

**Conclusions**

- Given the many similarities in islet morphology, pathology, and disease progression seen in CF ferrets and CF humans, ferrets appear to be a promising candidate as a model for the study of CF and CFRD.
- Our preliminary immunofluorescence data indicates differences in WT ferret development as compared to WT mouse development and appears to be more similar to published human data.