The Relationship Between Genes in Maturity of Onset of Diabetes of the Young and Early Gastrulation

Kyle Ortiz[1], Lindsay Hayes[2], Matt McCoy[3]and Rosa Alcazar[4]

Clovis Community College, Stanford School of Medicine, Johns Hopkins School of Medicine,

Abstract

Foxa2, Foxa3, and HNF1B all have one thing in common: they are present in the maturity of onset diabetes of the young. This specific case of diabetes differs from Type 1 and Type 2 since it's caused by a genetic mutation. Since it results from a mutation that'd be from birth, I was curious to find out if these same genes that play into the pathway would also be present in early gastrulation. To test this, I used a single-cell RNA sequencing mouse gastrulation dataset that spanned from days 6.5-8.5. What I learned was that, sure enough, these same genes were relatively expressed in the early gastrulation dataset and didn't seem to disappear after day 8.5. So, the evidence supports my hypothesis that genes in MODY5 also appear in early gastrulation.

Introduction

I decided to research Foxa2 because I found it's in so many species from mice, to humans, and fruit flies. It's also apart of so many different important life processes like DNA-binding, transcription, regulation of fat metabolism, and much more. When I searched up Foxa2 on Kegg pathways and found the MODY pathway, I was intrigued since I had never heard of these unique diabetes. More specifically, this type of diabetes is in its own category because it runs strongly in families, causes primary insulin secretion defects, is typically diagnosed below the age of 25, and can be caused by 14 different genetic mutations. One of these 14 mutations so happens to be HNF1B, specifically MODY5, and this gene is also involved in type 2 diabetes and pancreatic cancer.When this gene mutates and causes diabetes, insufficient levels of insulin result from abnormal pancreatic beta cells. Meanwhile, Foxa2 (which appears in early embryonic development, type 2 diabetes, and the negative regulation of detection of glucose) and Foxa3 (which is involved in cellular glucose homeostasis) are both a part of the forkhead box protein family.

Methods

- Kegg Pathway:https://www.kegg.jp/pathway/map04950
  - I used this to find genes of interest in MODY to then research
- I used a single-cell RNA sequencing mouse gastrulation dataset in Rstudio to create the UMAPS, Violin Plots, and the graph of expression over stages.

Results

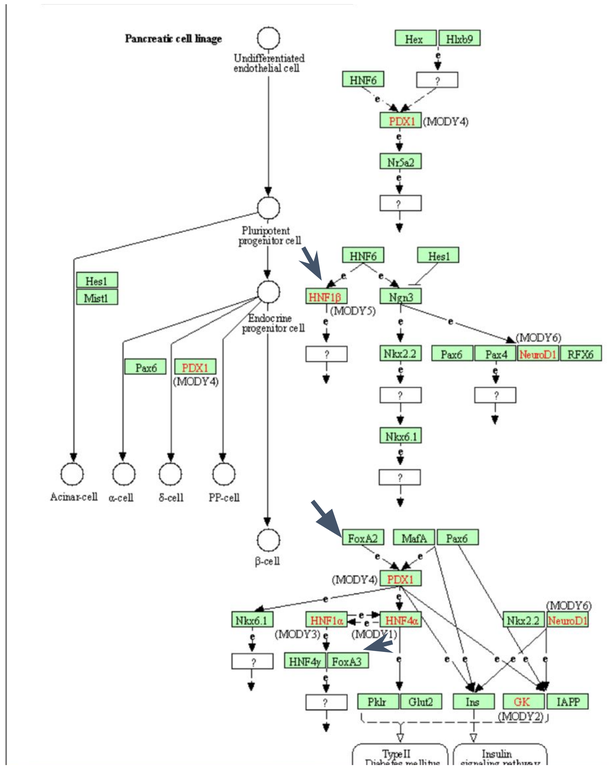

Figure 1: This is the human Kegg pathway for MODY which includes Foxa2, Foxa3, and HNF1B.

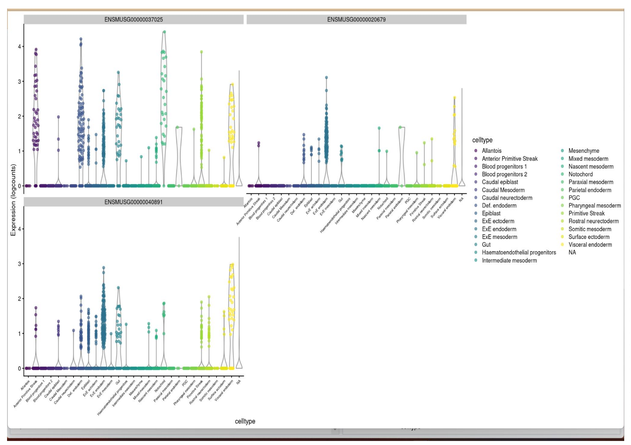

Figure 2: This is the expression of Foxa2 (top left), HNF1B (top right), and Foxa3 (bottom left) throughout all cell types in early gastrulation
***Major difference is Foxa2 has expression in APS while others don't and shared expression in ExE endoderm**

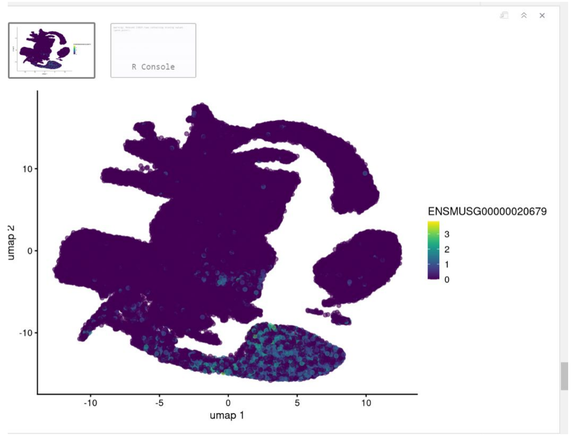

Figure 3A: HNF1B UMAP

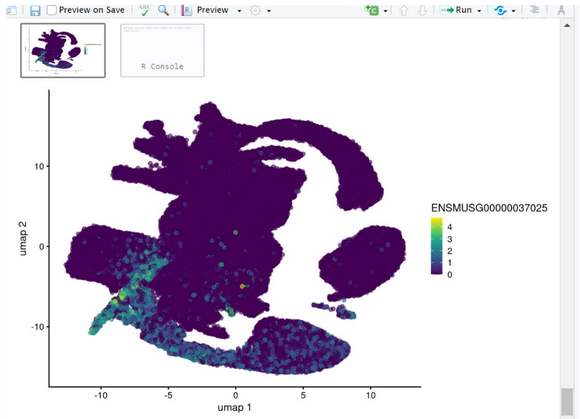

Figure 3B: Foxa2 UMAP

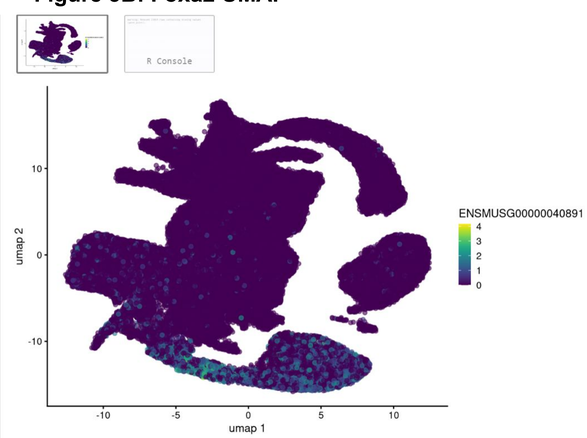

Figure 3C: Foxa3 UMAP

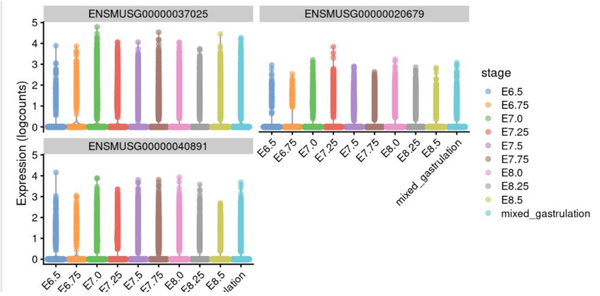

Figure 4: All 3 gene expression (Foxa2 top left, HNF1B top right, and Foxa3 bottom left) from day 6.5-8.5

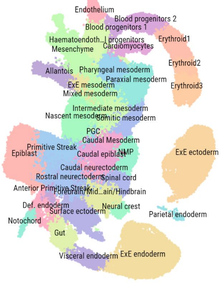

Figure 5: The cell type names in their respective regions.

Discussion

It can be seen that Foxa2, Foxa3, and HNF1B are prominent in gastrulation in both Figure 2, which shows the expression in different cell types, and then in Figure 4, which represents gene expression throughout the cell in a 2-day span. While the genes are similar in the abundant expression within the ExE endoderm, Foxa2 is more prominent all around with a lot of expression in the Anterior Primitive Streak. Then, Figure 3A-C just shows the respective gene expressions in their regions and how dense they are in that specific region. These findings support my research since it's clear that these genes that show up in Figure 1 (the pathway for MODY) are found way earlier in gastrulation. However, I expected this since MODY is a genetic mutation disease, and since genetic mutations happen at birth, the genes should also appear in early gastrulation. If I were to continue my research, I'd likely compare the HNF1B mutation variant to the other 13 mutations that also cause MODY.

Acknowledgements

PROVIDING OPPORTUNITIES DESIGNED TO EDUCATE AND RECOGNIZE
CLOVIS COMMUNITY COLLEGE

SciServer