

## Background

- Autosomal Dominant Polycystic Kidney Disease (PKD) is a genetic disorder that manifests as clusters of fluid filled cysts in the kidneys.
- Cysts can grow to various sizes, some eventually taking over the kidneys.
- Cysts cause the abdomen region to become stretched out (abdominal distension).

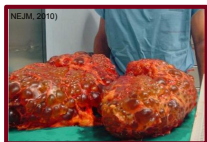


Figure 1: Phenotype PKD presentation. Left: cyst formation and kidney distension. Right: abdominal distension.

- PKD is a common genetic disorder and affects about 1 in 1000 people in the US. It is also the most common inherited cause of kidney failure in the US and the 4th most common cause of kidney failure worldwide.
- Zebrafish were used as the model since they are a conserved model of PKD and their genes behave similarly to human genes.
- Zebrafish with PKD have a higher collagen expression than wild type zebrafish (1,2)
- Overexpression of collagen causes notochord and dorsal axis curvature (tail curvature) (1,2).
- We studied the effect of iron on PKD since previous studies have provided evidence that iron altered another kidney disease, lupus nephritis (3).

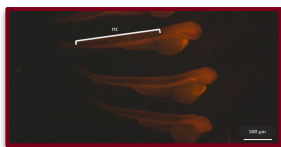


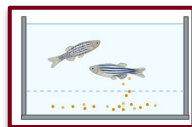
Figure 2: Antibody labeling showing collagen expression in the notochord of 2dpf zebrafish embryos

## Gap In Knowledge

- Not enough tools in clinics to diagnose PKD in the early stages.
- Extracellular matrix (ECM) plays big role in tissue architecture.
- Specifically, collagen in the ECM is the most abundant basement membrane protein in the kidneys.

Further studies are needed to elucidate the etiology of ECM in PKD progression. Also, we hope that observable changes to the ECM in kidneys will serve as a PKD early biomarker.

## Methods



Harvest embryos  
6 hours post  
fertilization

Control group  
n=½ total embryos

Test group  
n=½ total embryos  
Treatment: Ferric ammonium citrate  
added to the dish



Dechorionate 2  
days  
post fertilization

Tail curvature measured 2 & 3  
days post fertilization. Angle is  
determined via placing lines  
parallel to the body axis and tail  
tip and recorded.



Top image depicts "control" zebrafish. Bottom image depicts diseased zebrafish.

## Results

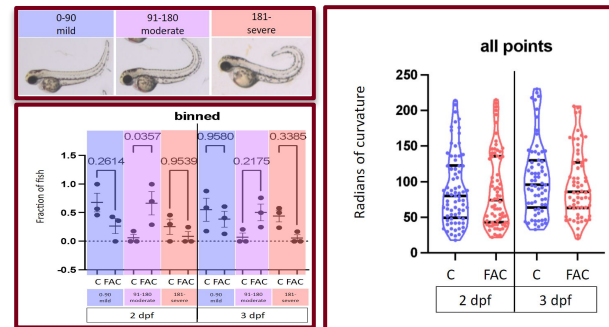


Figure 3: Left: fish were binned by radians of curvature into 3 bins, mild (0-90), moderate (91-180), severe (181-360). 2 dpf is shown on the left, 3 dpf on the right. Right: Violin plot depicting the degree of tail curvature in radians. Each dot represents one fish with a total of 3 batches of fish. Lines show median and quartiles. C is control. The median was around the same for the control and treatment groups.

## Conclusions & Future Directions

- FAC treatment did not significantly change tail curvature
- Previous findings indicate that iron decreases cyst size using mouse models
- Iron has been shown to modulate the immune response that contributes to PKD
- A caveat to the results is that iron precipitated out of solution which may have negatively impacted our results

We aim to expand the study to include adult zebrafish

## References

- Le Corre, S., Eyre, D., & Drummond, I. A. (2014). *Modulation of the secretory pathway rescues zebrafish polycystic kidney disease pathology*. Journal of the American Society of Nephrology : JASN, 25(8), 1749–1759.
- Zhang, Y. Reif, G. Wallace, D. (2020). *Extracellular matrix, integrins, and focal adhesion signaling in polycystic kidney disease*. Cellular Signaling, Volume 72.
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