**Worms, genetics and healthy kidneys: the candidate PKD-2 localization factor, papl, may play a role in polycystic kidney disease.**

Madison Lucas, Molly Svoboda, and Anneka Johnson

Mentor: Dr. Jamie Lyman Gingerich

**BACKGROUND**

Polycystic Kidney Disease (PKD) causes cysts to form within the kidneys, leading ultimately to renal failure. Prior research in our lab demonstrated that expression of the papl gene is downregulated in a zebrafish model of cystic kidney disease. We asked whether the papl gene has a direct effect on proper localization of PKD2, one of the proteins known to be involved in cyst formation, and whether the papl gene influences cilia structure.

![Figure 1](image1.png)

**Figure 1.** The etiology of human polycystic kidney disease (a, left - normal kidney; right - diseased kidney) can be studied using zebrafish (b) and C. elegans (c), not to scale.

**papl-1**, not previously associated with PKD, belongs to a gene family associated with human disorders.

Neither the human ortholog (ACP7) nor the zebrafish ortholog (acp7/papl-1) has been associated with a specific function or organelle. *papl* encodes an acid phosphatase with putative hydrolase activity and a metal ion binding domain. Acid phosphatases have been associated with a number of human disorders, including prostate cancer (Araujo and Vihko 2013). Zebrafish *papl* ESTs have been identified in the kidney, olfactory rosettes and reproductive system.

**RNA INTERFERENCE REDUCES PAPL-1**

Reducing *papl-1* expression allows us to examine its effects on PKD-2 localization.

**Figure 2.** RNA interference (RNAi) downregulates *papl-1* transcript. When bacteria produce dsRNA, C. elegans ingest the bacteria and degradation of *C. elegans* papl-1 RNA is triggered.

**Assessment of neuron integrity by dye-filling demonstrates that downregulation of papl-1 does not affect cilia integrity.**

**Figure 3 (left).** Cilia Structure is unaffected by knockdown of *papl-1* expression. Wild type neurons exposed to DiI (a and c) appeared similar to neurons after *papl-1* RNAi treatment (b and d).

**papl-1 plays a role in PKD-2 localization in cilia.**

**Figure 4 (left).** The green shaded region shows the PKD-2 expression (*) in the cilia structure of the head of a wild-type *C. elegans* (Bae, 2006).

**Figure 5.** PKD-2::GFP localization (*), in male-specific cilia of the head, differs when *papl-1* gene expression is down-regulated. In wild-type *C. elegans*, localization is symmetric (a) while after RNAi treatment, localization is asymmetric (b). Anterior to left.

**papl-1** knockout leads to altered expression of PKD-2 in cilia.

**Figure 6.** *papl-1* knockdown resulted in abnormal PKD-2::GFP localization in cilia. Abnormal localization included asymmetric expression (left versus right) and increased localization compared to wild type. (Control n=29; Papl RNAi n=51)

**CONCLUSIONS**

- Downregulation of *papl* does not affect all cilia equally. *papl-1* knockout leads to overexpression of PKD-2::GFP in cilia in male specific neurons
- This suggests that *papl* is either specifically affecting PKD2::GFP localization in male specific neurons, structure of male specific, neurons or asymmetry of neurons.

**DISCUSSION AND FUTURE RESEARCH**

Our results suggest the *papl-1* gene may play a role in the proper localization of PKD-2 in cilia in *C. elegans*. Thus, *papl-1* may be involved in cyst formation and might play a role in PKD.

Future research includes confirming that *papl-1* expression is downregulated after RNAi using RT-PCR and examining whether zebrafish lacking *papl-1* develop cystic kidneys.

**Acknowledgements**

This research was supported by the Office of Research Sponsor Programs and the Department of Biology at UW-Eau Claire. We are grateful to our colleagues at the Mayo Clinic, Rochester, MN and our lab mates for sharing ideas, expertise, and reagents. We thank Blugold Commitment and ITS for printing this poster.

**References**