

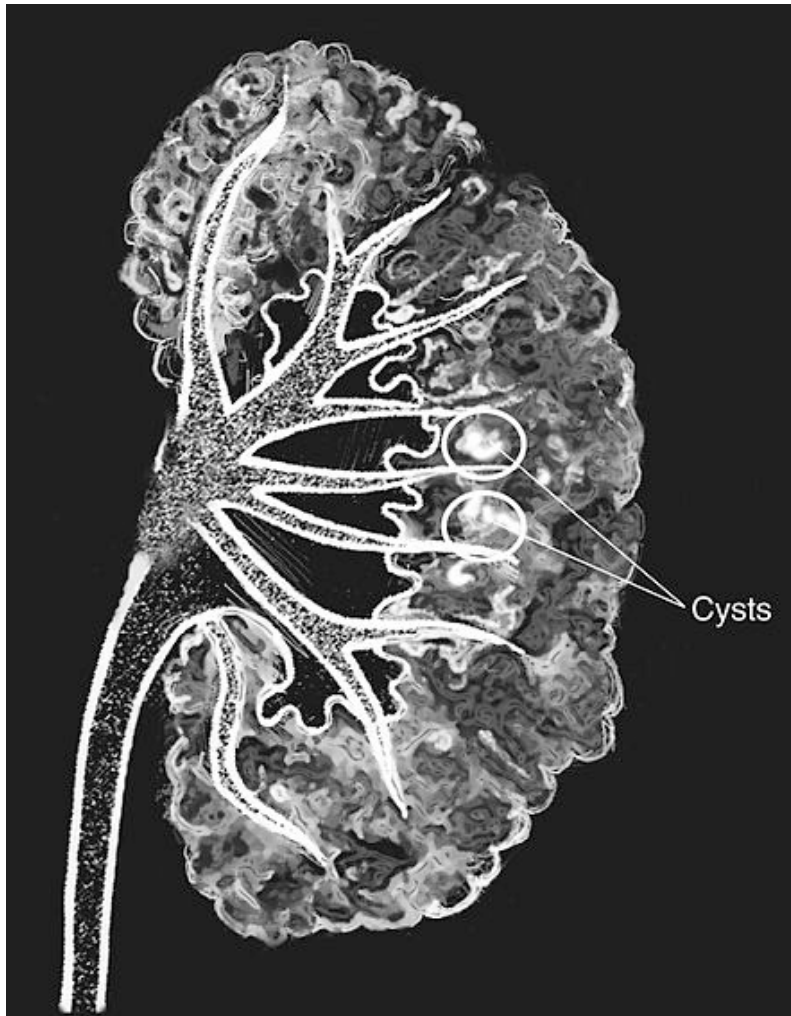
# Autosomal Dominant Polycystic Kidney Disease & PKD I

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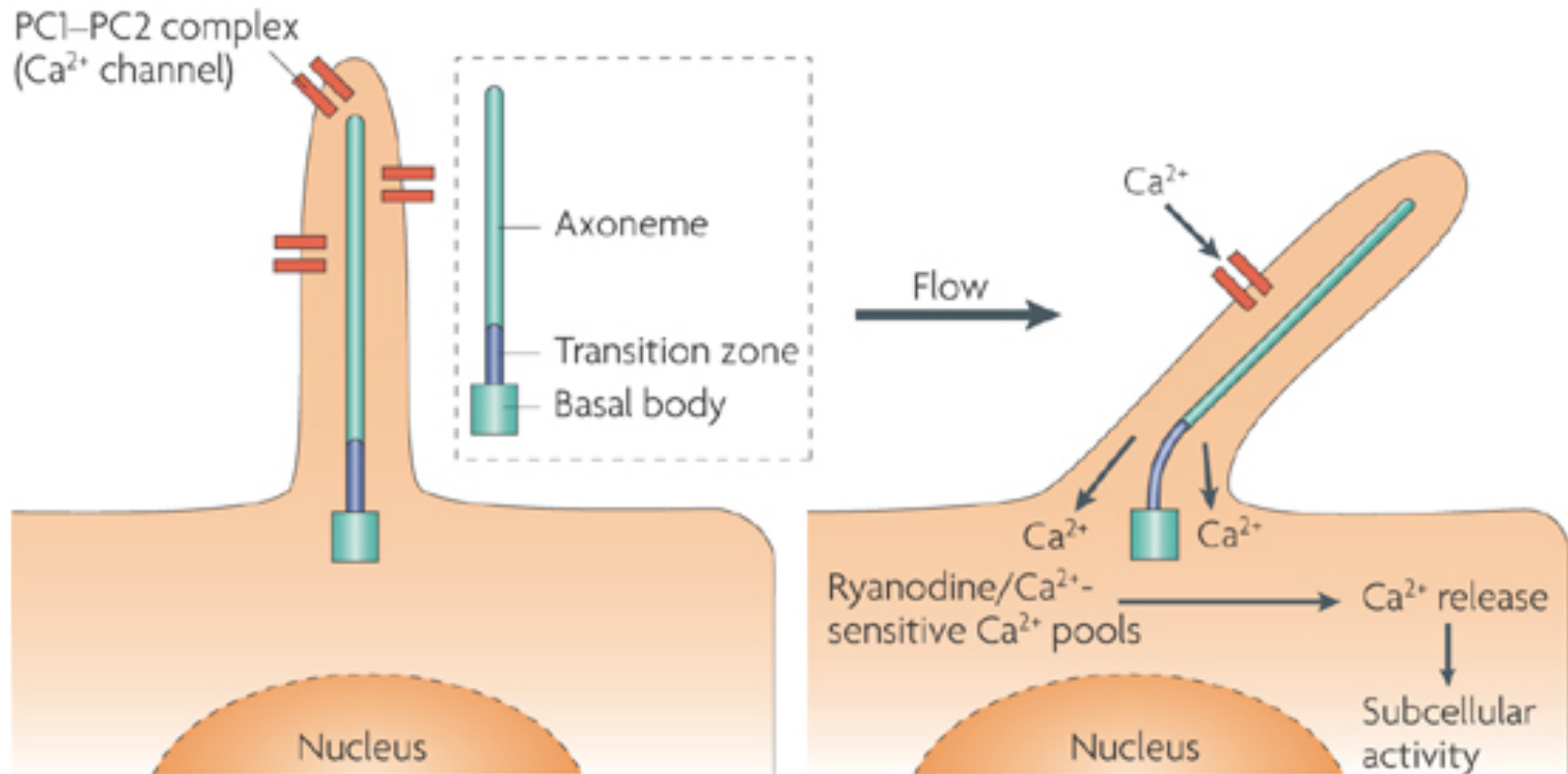
Genetics 564

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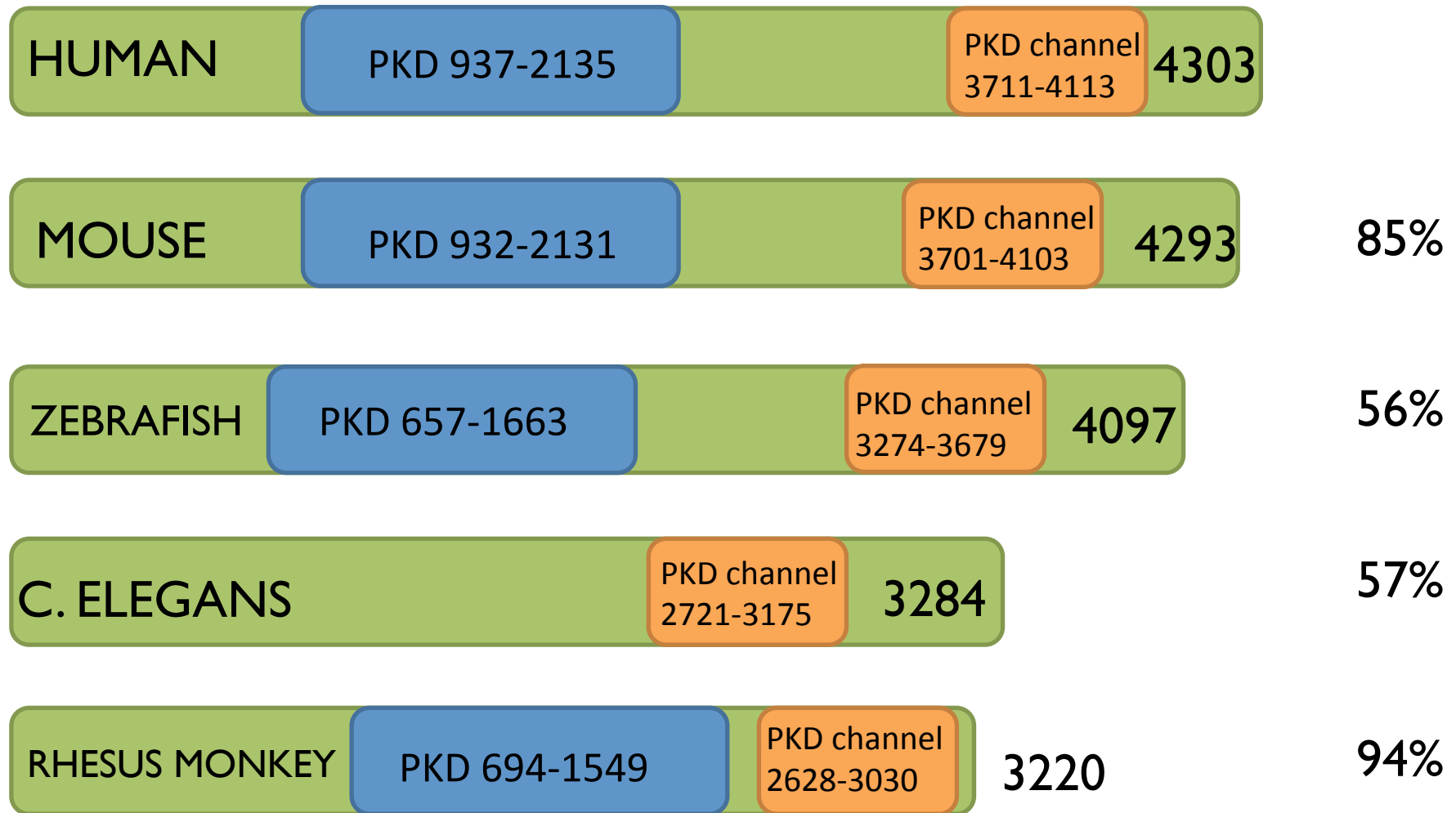
# What is Polycystic Kidney Disease?



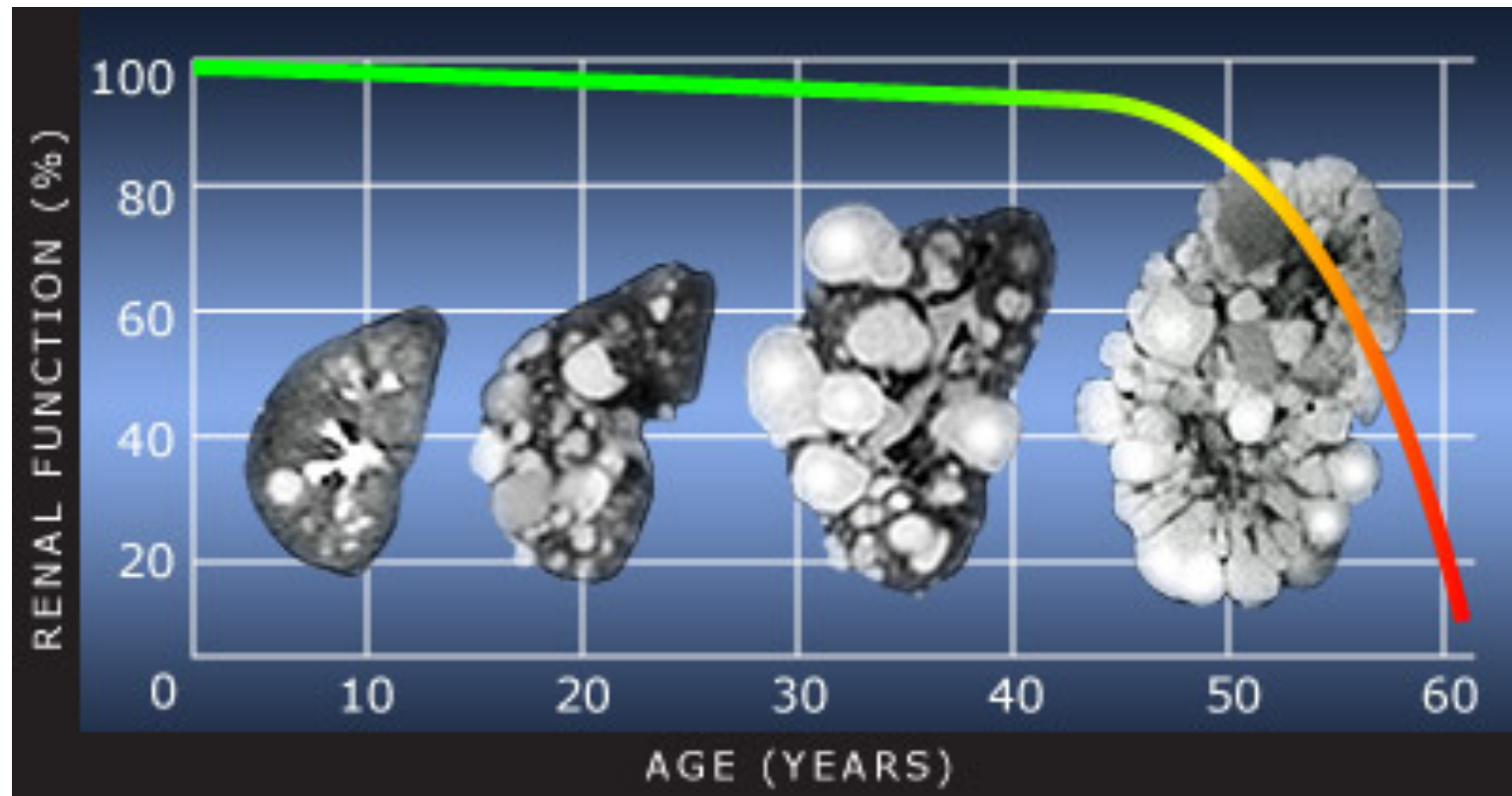
# Polycystin-1 is mutated in polycystic kidney disease



# Polycystin-1 is well conserved



# Cysts accumulate throughout lifetime



**PRIMARY GOAL: to determine the  
role of PKD I in development**

# PKD I is important for development

## **Kidney Development**

- Mesonephric duct development
- Metanephric distal tubule morphogenesis
- Metanephric collecting duct development
- Metanephric ascending thin limb development
- Branching morphogenesis of an epithelial tube
- Mesonephric tubule development

**Neural tube development**

**Lung epithelium development**

**Liver development**

**Digestive tract development**

**Skin Development**

**AIM 1: To determine the expression pattern of PKD1 in different developing tissues**



# Approach: Microarray

**Body plan  
established  
Major organs  
visible**



**Adult**



	EARLY DEVELOPMENT	LATE DEVELOPMENT
KIDNEY		
LIVER		
SKIN		
LUNG		
DIGESTIVE TRACT		

I expect that PKDI will be expressed at high levels in the kidney and in low levels in other tissues during development

	EARLY DEVELOPMENT	LATE DEVELOPMENT
KIDNEY	High	High
LIVER	Absent	Low
SKIN	Absent	Low
LUNG	Absent	Low
DIGESTIVE TRACT	Absent	Low

Expression level:



High

Low

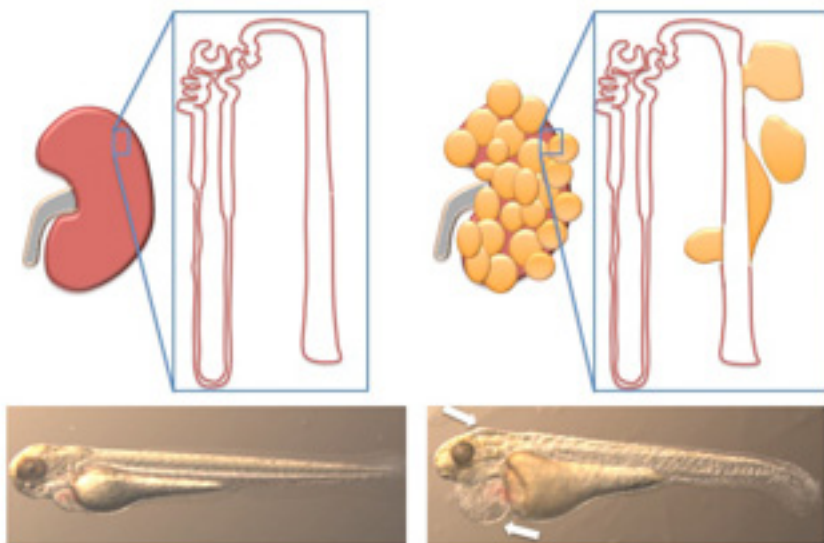
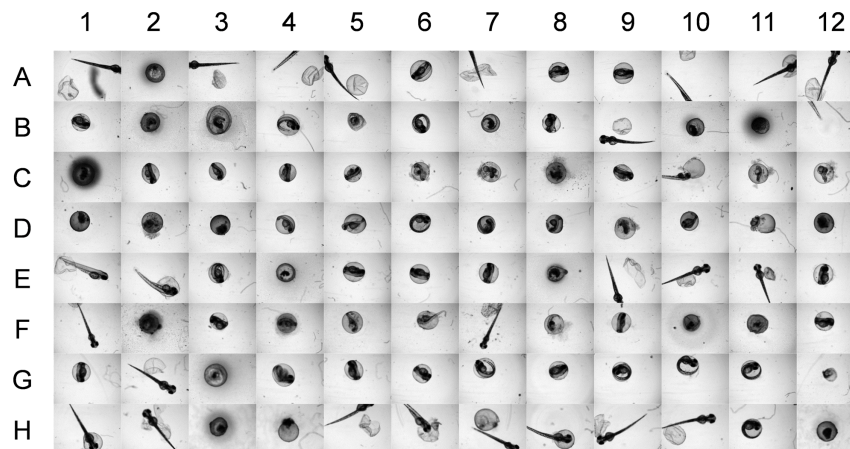


Absent

AIM 2: To determine whether  
knockdown of other kidney  
development genes can cause cystic  
kidneys

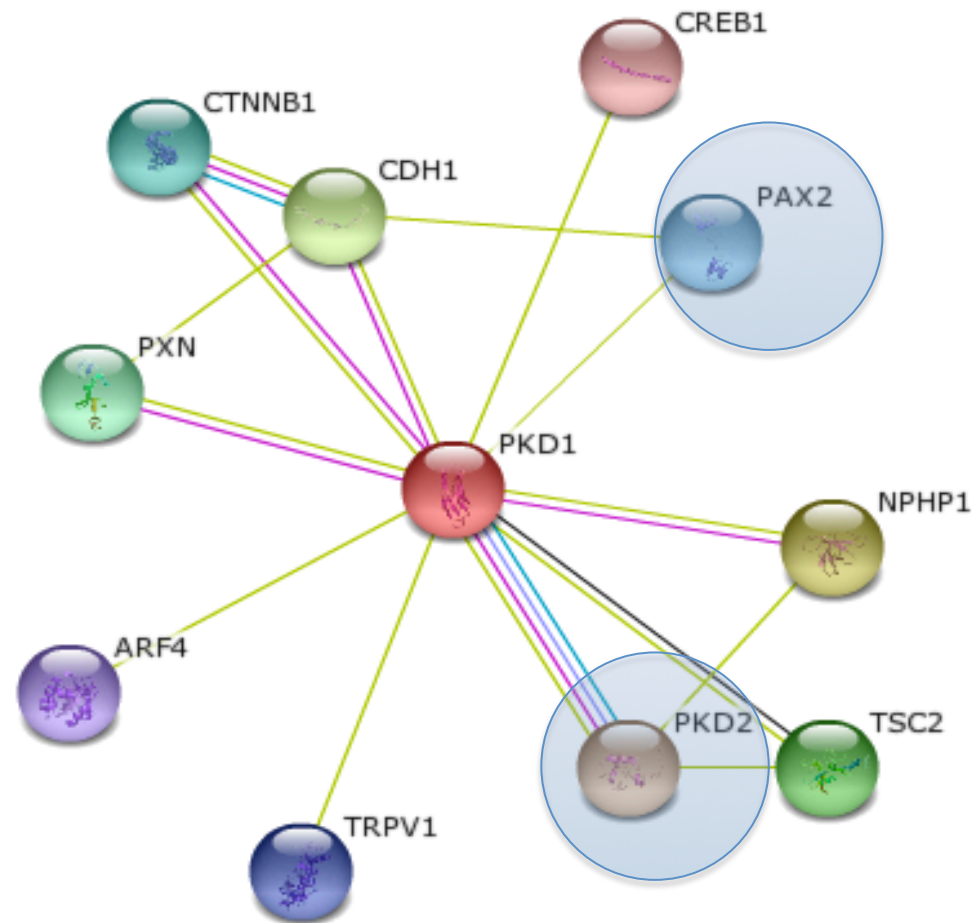
# Approach: RNAi Screen

Add zebrafish embryos to 96-well plates with RNAi against genes associated with kidney function



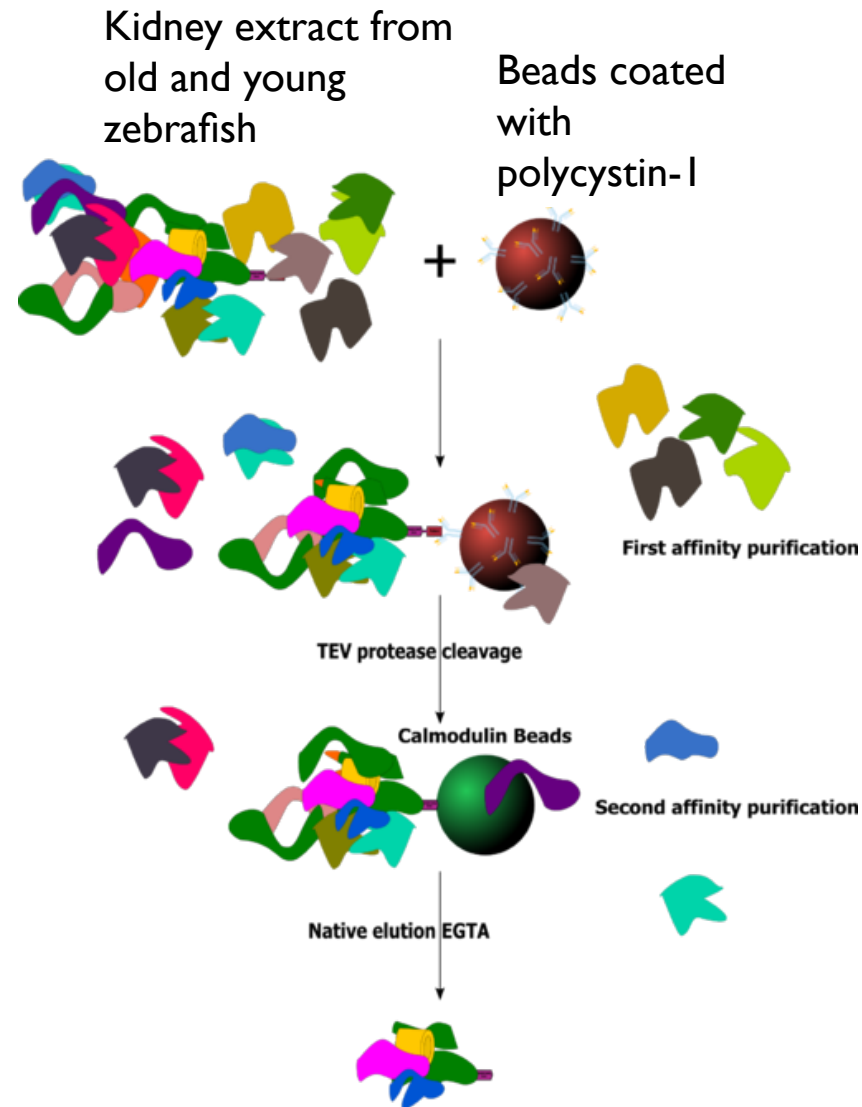
Screen for cystic kidneys

I expect that cysts will develop upon knock-down of development-related PKD I interaction partners



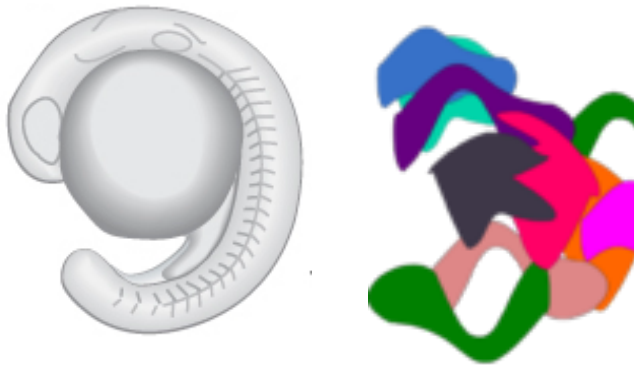
**AIM 3: To determine if protein interactions with polycystin-1 are different in young and old zebrafish**

# Approach: TAP-Tag

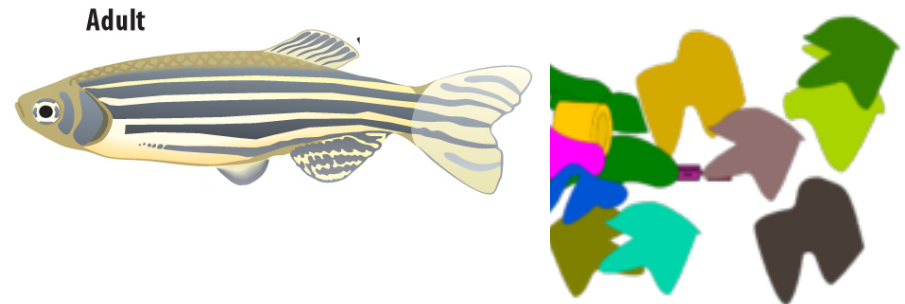


I expect that proteins that interact with polycystin-1 will be different in young and old embryos

Polycystin-1 interactors in young zebrafish



Polycystin-1 interactors in old zebrafish





# Summary

**PRIMARY GOAL:** to determine the role of PKD I in development

**Questions?**

# References

- [1] Gabow, P. (1993). Autosomal dominant polycystic kidney disease. *The New England Journal of Medicine*. 329(5) 332-342.
- [2] Fedeles, S.V., Gallagher, A-R., Stefan Somlo. (2014) Polycystin-1: A master regulator of intersecting cystic pathways. *Trends in Molecular Medicine*. E-pub ahead of print. Doi: 10.1016/j.molmed.2014.01.004
- [3] Reeders, S. T. et al. Prenatal diagnosis of autosomal dominant polycystic kidney disease with a DNA probe. *Lancet* 2, 6–8 (1986).