Autosomal Dominant Polycystic Kidney Disease & PKD1

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Genetics 564

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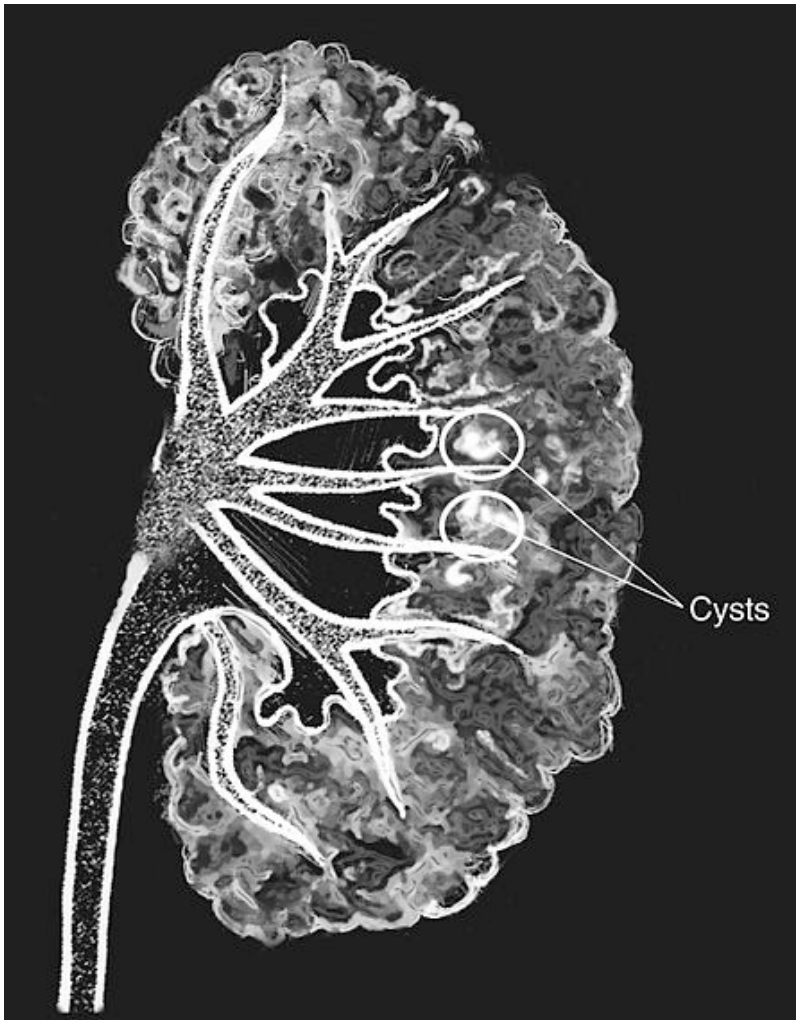
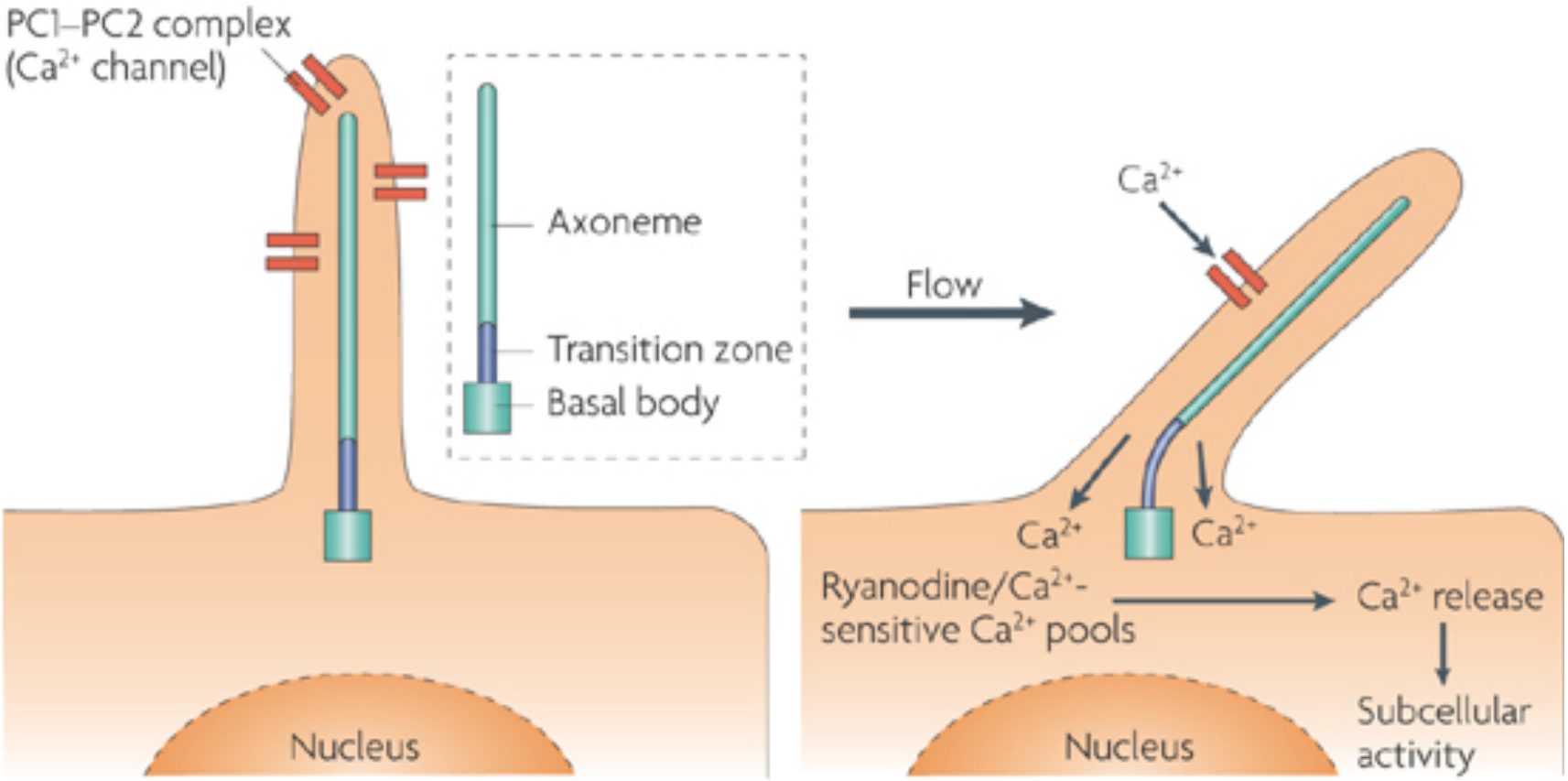
What is Polycystic Kidney Disease?



Polycystin-1 is mutated in polycystic kidney disease



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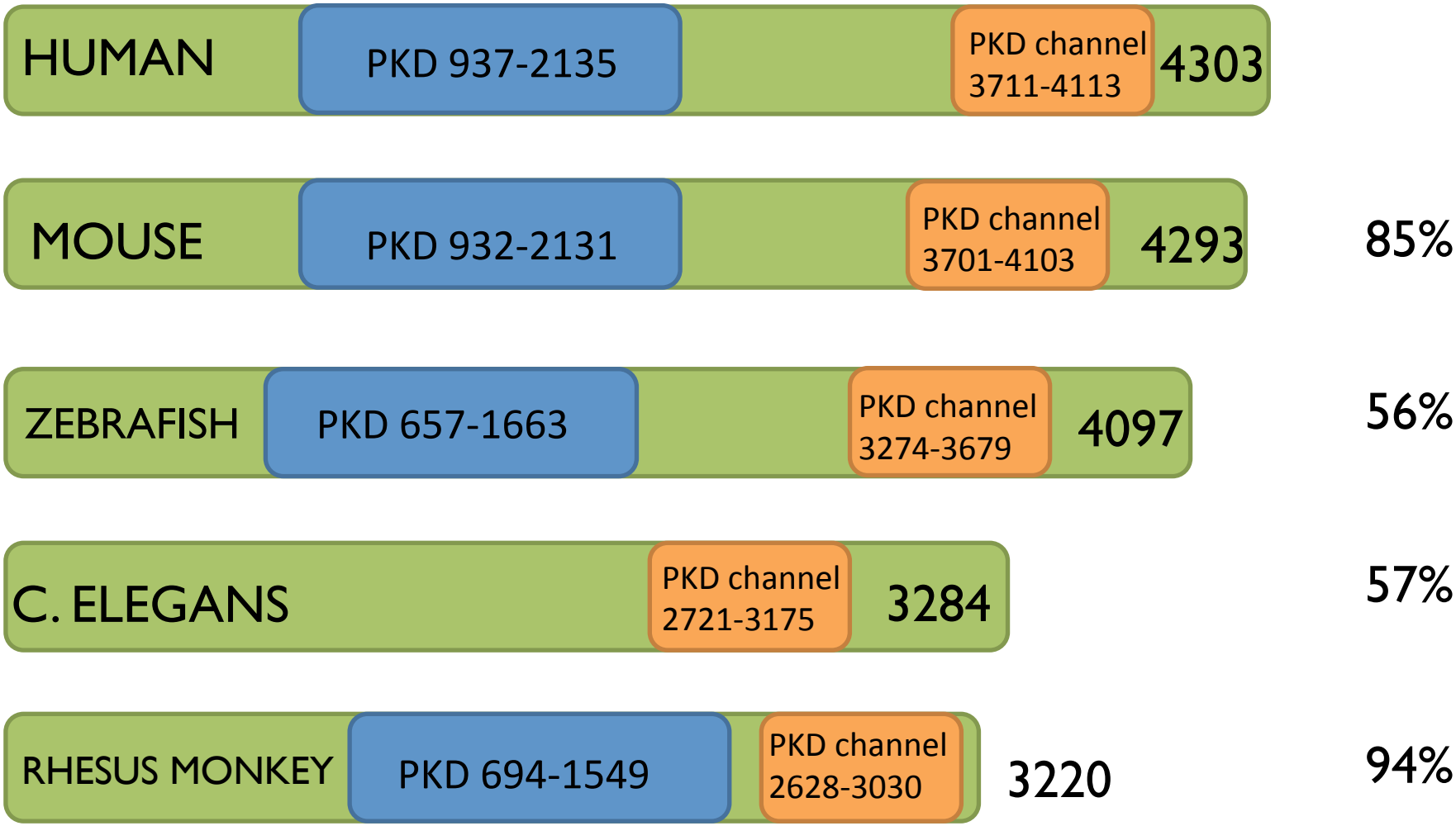
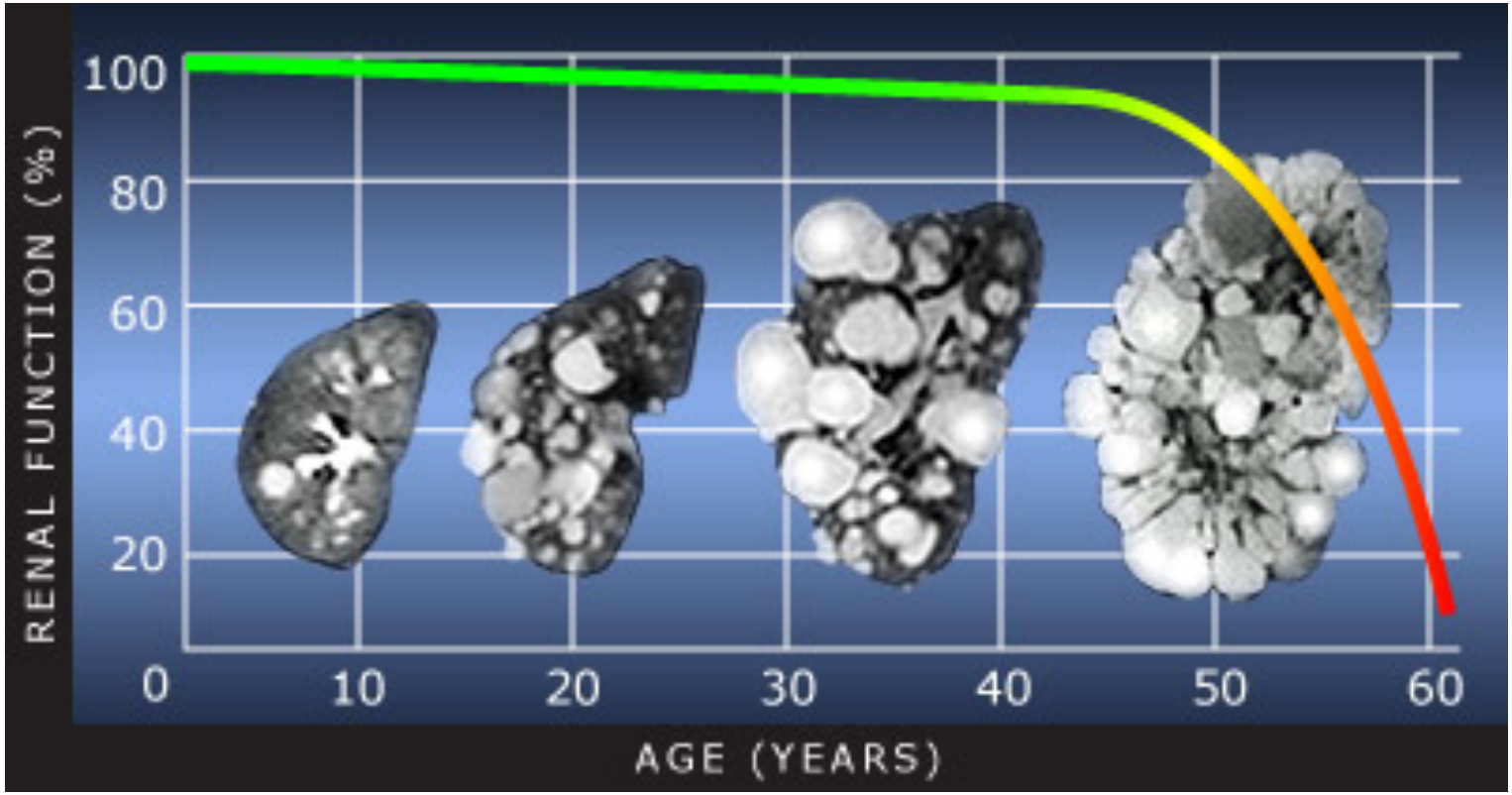
Polycystin-1 is well conserved

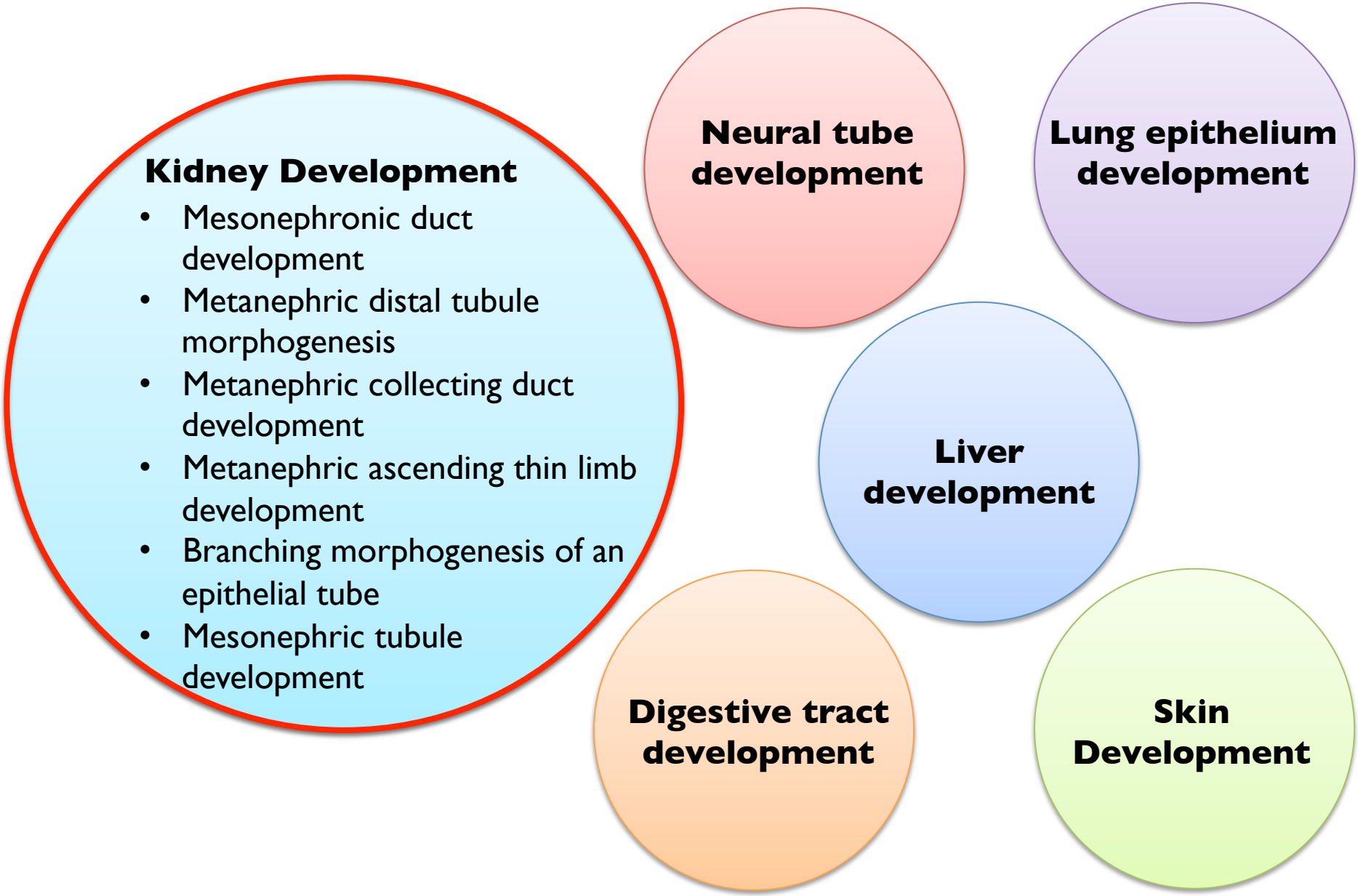


Cysts accumulate throughout lifetime



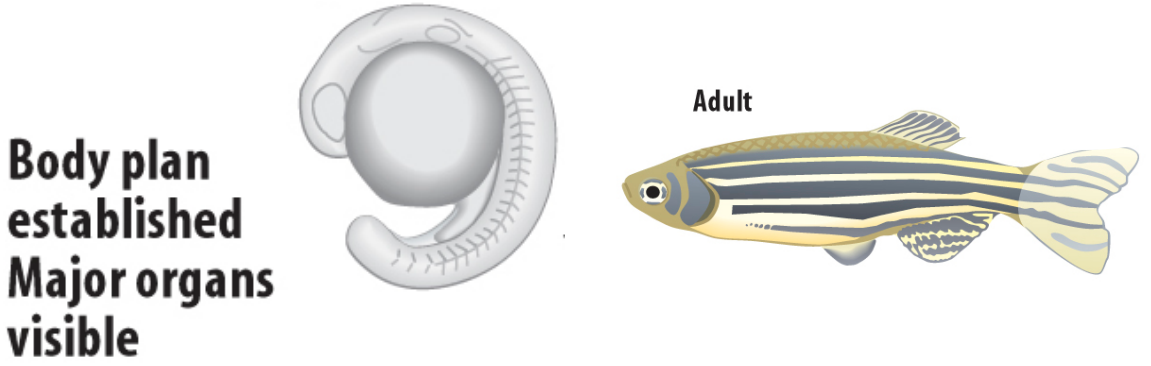
PRIMARY GOAL: to determine the role of PKD1 in development

PKD1 is important for development



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

Approach: Microarray



	EARLY DEVELOPMENT	LATE DEVELOPMENT
KIDNEY		
LIVER		
SKIN		
LUNG		
DIGESTIVE TRACT		

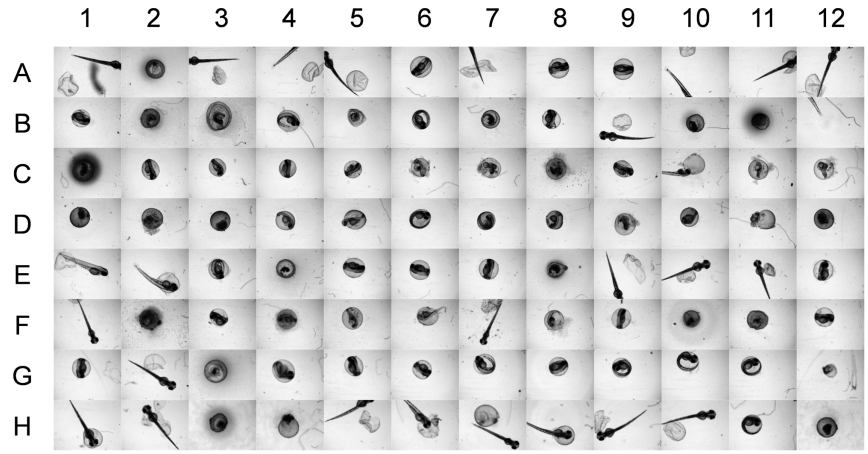
I expect that PKD1 will be expressed at high levels in the kidney and in low levels in other tissues during development

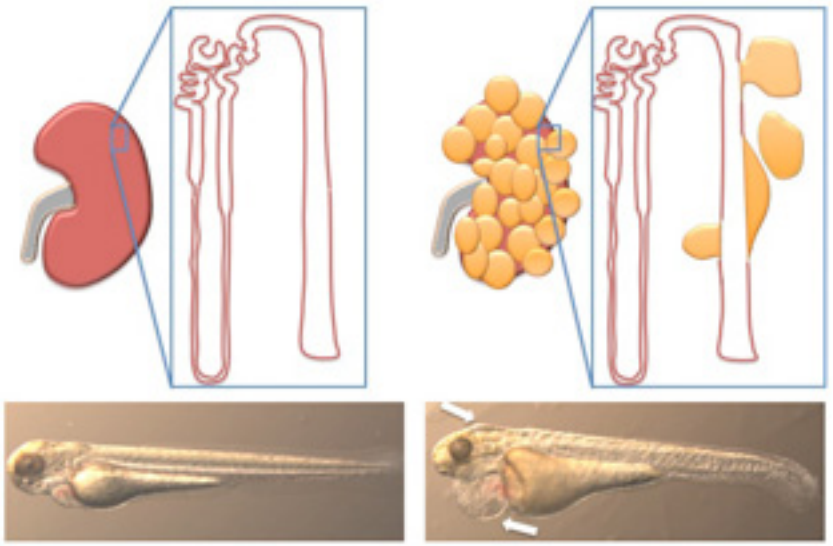
	EARLY DEVELOPMENT	LATE DEVELOPMENT
KIDNEY		
LIVER		
SKIN		
LUNG		
DIGESTIVE TRACT		

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

Approach: RNAi Screen

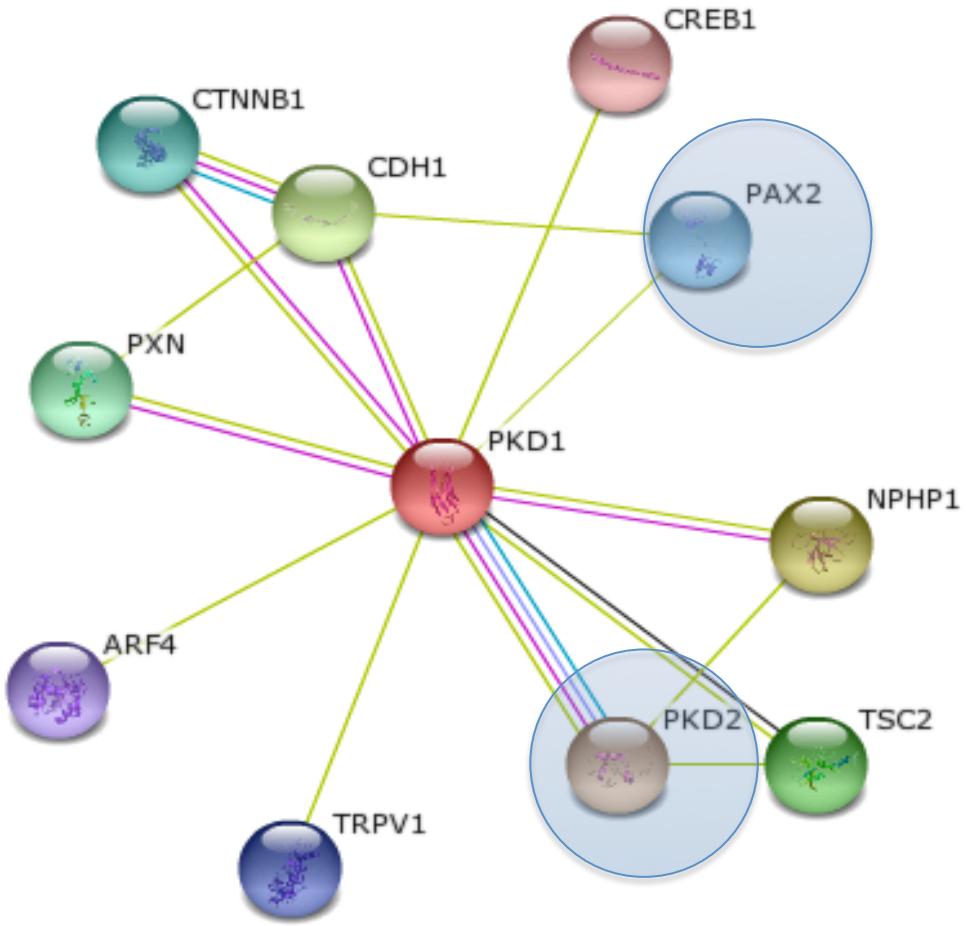
Add zebrafish embryos to 96-well plates with RNAi against genes associated with kidney function





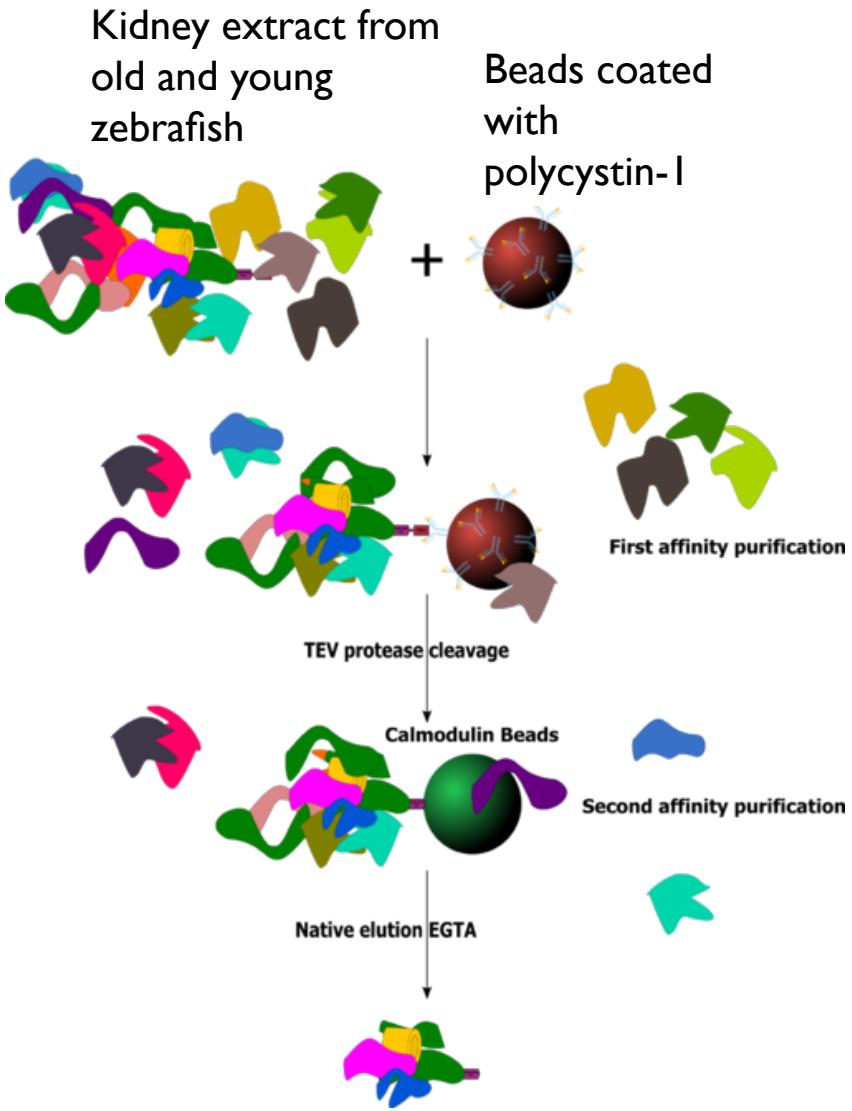
Screen for cystic kidneys

I expect that cysts will develop upon knock-down of development-related PKD1 interaction partners



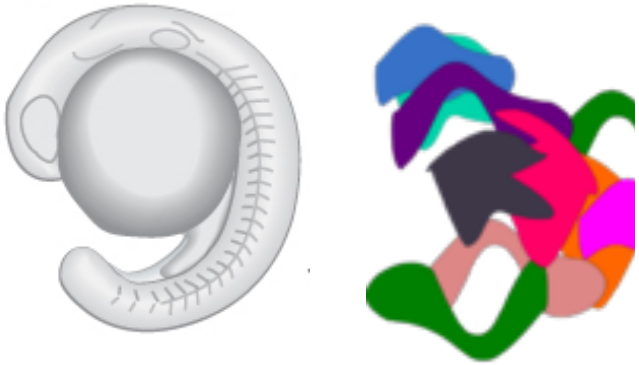
AIM 3: To determine if protein interactions with polycystin-1 are different in young and old zebrafish

Approach: TAP-Tag

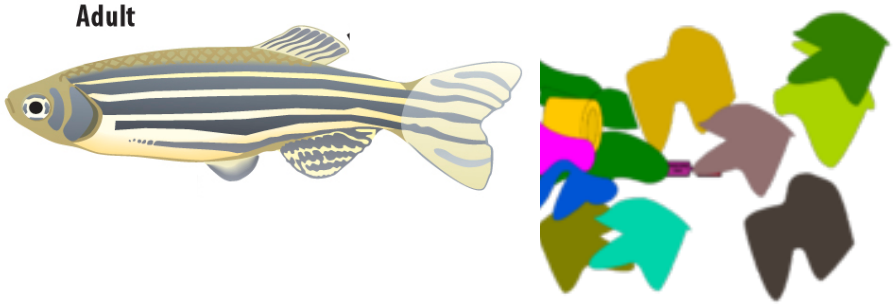


I expect that proteins that interact with polycystin-1 will be different in young and old embryos

Polycystin-1 interactors in young zebrafish



Polycystin-1 interactors in old zebrafish



Summary

PRIMARY GOAL: to determine the role of PKD1 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).