Congratulations to IMCB's latest PhD graduate - Stylianos Makrogkikas

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Thesis Title: Elucidation Of The Molecular And Cellular Mechanism Of Function Of The Pkhd111 Gene In Vertebrates

My thesis examined the molecular and cellular mechanism of function of the Pkhd1l1 gene in vertebrates – the zebrafish and the mouse. Foxj1, a master transcription factor of motile ciliogenesis, upregulates both pkhd1l1 zebrafish genes (pkhd1l1α and pkhd1l1β). Structurally, zebrafish Pkhd1l1 proteins resemble the human PKHD1 protein, which, when mutated, causes autosomal recessive polycystic kidney disease. We hypothesized that both pkhd1l1 zebrafish genes are involved in motile ciliogenesis. To examine our hypothesis, we generated double pkhd1l1 zebrafish knockouts using the CRISPR/Cas9 gene editing technique. We also examined Pkhd1l1 knockout mice for motile cilia defects. Double pkhd1l1 zebrafish knockouts show otolith defects with the ear 24, but they do not show any other motile cilia-specific defects. Pkhd1l1 knockout mice also do not show motile cilia defects. Double pkhd1l1 zebrafish knockouts show upregulation of the B-cell marker cd79a and the T-cell marker lck, suggesting that the pkhd11l1 genes may modulate inflammatory responses, and thus have immune functions.

Supervisor

Dr. Sudipto Roy

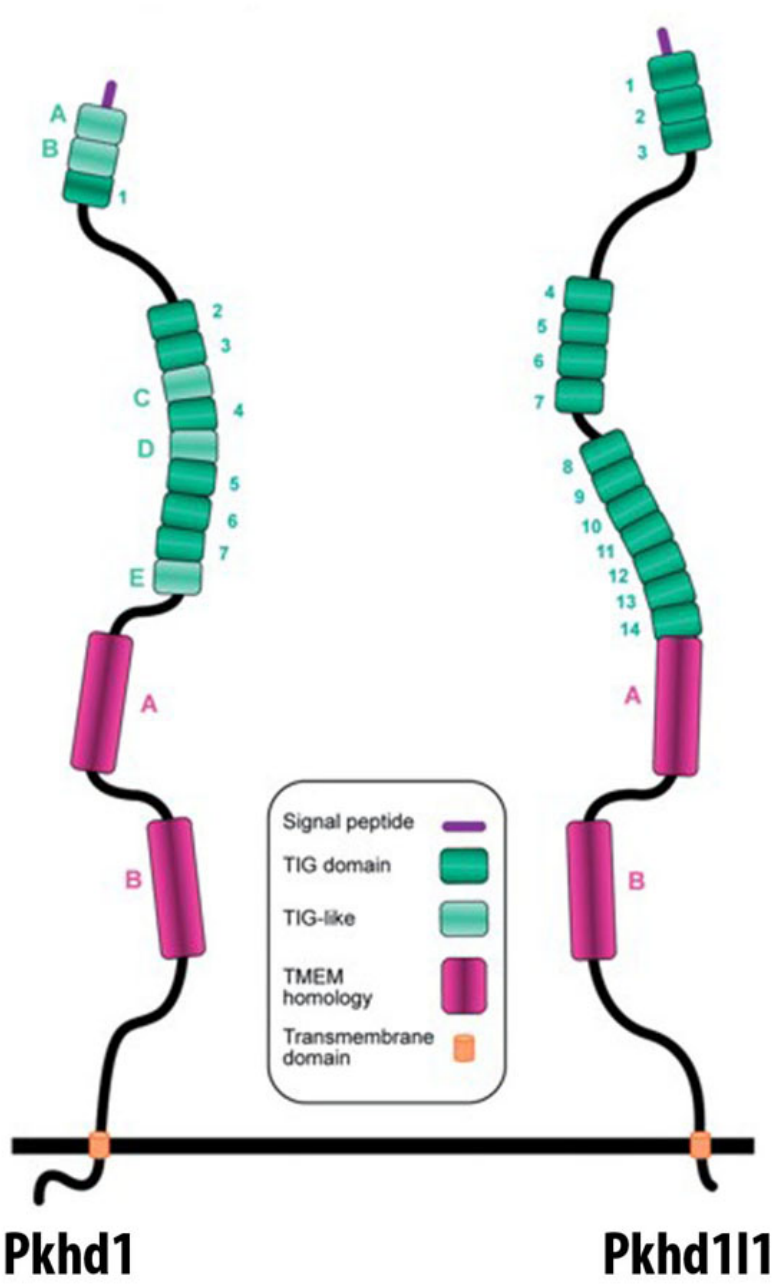

Fig.1 Pkhd111 is a paralog of Pkhd1 implicated in autosomal recessive polycystic kidney disease. Both proteins are very large (>4000 amino acids) membrane proteins, and their molecular functions are rather obscure.