

Polycystic kidney disease (PKD), encompassing both autosomal dominant polycystic kidney disease (ADPKD) and autosomal recessive polycystic kidney disease (ARPKD), is characterized by the continuous formation of cysts in the kidneys and liver. ADPKD, prevalent in adults, results from mutations in PKD1 (polycystin1) and PKD2 (polycystin 2). On the other hand, ARPKD, affecting children, is primarily caused by mutations in the PKHD1 gene, encoding the Fibrocystin/Polyductin (FPC) protein, and a smaller subset by mutations in the DAZ interacting zinc finger protein 1 like (DZIP1L) gene. PC1/2 and FPC are transmembrane proteins located in the primary cilium, suggesting their role as signaling molecules. The precise mechanisms through which cilia regulate renal tubule morphology and prevent cyst formation remain unclear. Nevertheless, recent genetic and biochemical studies have provided insights into potential malfunctions and pathomechanisms underlying these diseases. This review summarizes genetic studies elucidating the functions of PC1/2 and cilia in cyst formation in ADPKD. It also discusses studies on the regulation of polycystin biogenesis and cilia trafficking. Additionally, it highlights synergistic genetic interactions between Pkd1 and Pkhd1, along with unique tissue patterning events controlled by FPC, not PC1. Notably, DZIP1L mutations compromise PC1/2 cilia expression, while FPC deficiency does not impact PC1/2 biogenesis and ciliary localization, indicating divergent mechanisms leading to cyst formation in ARPKD. The review concludes by outlining promising areas for future PKD research and suggesting potential therapeutic interventions for PKD treatment.