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ADPKD Genetics and Pathogenesis

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Autosomal Dominant Polycystic Kidney Disease (ADPKD) stands out as the predominant hereditary renal disorder affecting adults, with an estimated prevalence ranging from 1 in 400 to 1000 individuals. Beyond the well-known PKD1 and PKD2 genes, the genetic landscape of ADPKD exhibits notable heterogeneity. This exploration delves into the historical narrative of ADPKD genetics, elucidating the chronicles of its discovery, and presenting the current mutation panorama across various regions worldwide, with a specific focus on its prevalence and status in Taiwan.

The pathogenesis of ADPKD remains a complex puzzle, persisting unresolved despite more than four decades of intensive study. The mechanosensation of primary cilia, a cellular organelle implicated in the disease, remains a subject of debate. One prevailing hypothesis posits that the primary cilium functions as a unique mechano- and chemosensor, capable of detecting fluid flow and its composition, while also regulating calcium influx. Multiple pathways, including hormones and growth factors, the renin-angiotensin-aldosterone system, and mitochondria-related signaling pathways, are believed to play crucial roles in the intricate cascade leading to ADPKD.

Moreover, recent investigations have provided intriguing insights, suggesting that the progression of kidney cysts in ADPKD may be potentially reversible with the restoration of adequate dosage of the mutant genes' expression. This paradigm-shifting revelation opens new avenues for therapeutic approaches and underscores the dynamic nature of ADPKD research. As we navigate the intricacies of ADPKD genetics and its underlying mechanisms, a more comprehensive understanding emerges, offering hope for innovative treatments and potential reversibility in the progression of this challenging hereditary kidney disease.