Genetic Disorders of Kidney

Molecular Advances in ADPKD

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Autosomal dominant polycystic kidney disease (ADPKD) is the most common inherited kidney disease, and characterized by age-dependent occurrence of bilateral and multiple renal cysts as well as extrarenal manifestations. The discovery of the genes and their respective proteins that are associated with ADPKD has revolutionized the field of ADPKD biology. Dominantly inherited gene muations followed by somatic hit mutations result in renal tubular cyst formation and renal failure eventually. Mutations in two genes, PKD1 and PKD2, are responsible for ADPKD. The respective gene products, polycystin-1 and polycystin-2, have been localized to the primary cilium. Recent studies indicate that the pathogenesis of ADPKD is linked to abnormalities in the primary cilium in the kidney. Inactivation of ciliary proteins in the postnatal kidney has uncovered novel roles of primary cilia in regulating tubular growth and repair after injury. Furthermore, defective tubular repair after injury may contribute to the progression of ADPKD. Studies of signaling pathways that are perturbed in ADPKD have identified potential targets for pharmacological therapy. Better understanding of the downstream consequences of ADPKD mutations has identified a number of therapeutic targets that are now being tested in preclinical and clinical trials. The author summarized recent insights in the pathogenesis of ADPKD including the genetics of ADPKD, the properties of the respective polycystin proteins, the role of cilia, some cell signaling pathways and new therapeutic interventions.