PKD1

The PKD1 gene provides instructions for making a protein called polycystin 1. This protein is most active in kidney cells before birth; much less of the protein is made in normal adult kidneys. Although its exact function is not well understood, polycystin-1 appears to interact with a smaller, somewhat similar protein called polycystin-2.

Polycystin-1 spans the cell membrane of kidney cells, so that one end of the protein remains inside the cell and the other end projects from the outer surface of the cell. This positioning of the protein allows it to interact with other proteins, carbohydrates, and fat molecules (lipids) outside the cell and to receive signals that help the cell respond to its environment. When a molecule binds to polycystin-1 on the surface of the cell, the protein interacts with polycystin-2 to trigger a cascade of chemical reactions inside the cell. These chemical reactions instruct the cell to undergo certain changes, such as maturing to take on specialized functions. Polycystin-1 and polycystin-2 likely work together to help regulate cell growth and division (proliferation), cell movement (migration), and interactions with other cells.

Polycystin-1 is also found in cell structures called primary cilia. Primary cilia are tiny, fingerlike projections that line the small tubes where urine is formed (renal tubules). Researchers believe that primary cilia sense the movement of fluid through these tubules, which appears to help maintain the tubules' size and structure. The interaction of polycystin-1 and polycystin-2 in renal tubules promotes the normal development and function of the kidneys.

Chauveau et al., from the Hôpital Necker, Paris, France, conducted a retrospective study on 77 ADPKD patients from 64 families presenting with ruptured (N = 71) or unruptured (N = 6) aneurysm. Information was collected on kidney disease, intracranial aneurysm and family history. Linkage to PKD1 locus was examined by five probes to obtain informative flanking markers. Within one year prior to rupture, blood pressure was normal in 29% of the patients. At the time of rupture, mean age was 39.5 years (range 15 to 69), renal function was normal in half of the patients and 11% were on renal replacement therapy. The ruptured aneurysm was usually located on the middle cerebral artery. Additional intact aneurysms (1 to 6) were detected in 31% of the patients. Surgical or endovascular treatment was performed in 54 (76%) patients whereas 17 (24%) had medical management only. Rupture of ICA was fatal in seven (10%) patients. On long-term follow-up 27 (38%) were left with severe disablement. Five patients bled from another aneurysm 2 days to 14 years after initial rupture. Only two of six patients with unruptured aneurysm alone were treated on a prophylactic basis. No clinical marker associated with aneurysm was found. A family history of aneurysm rupture was demonstrated in 10 (18%) kindreds. Linkage to the PKD1 locus was established in two of three tested families [1].

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Chauveau D, Pirson Y, Verellen-Dumoulin C, Macnicol A, Gonzalo A, Grünfeld JP. Intracranial aneurysms in autosomal dominant polycystic kidney disease. Kidney Int. 1994 Apr;45(4):1140-6. PubMed PMID: 8007584.