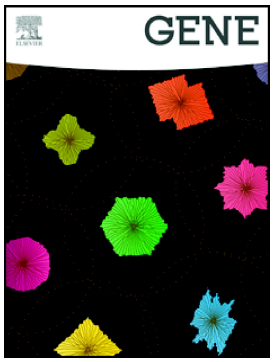

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Mutational analysis in patients with Autosomal Dominant Polycystic Kidney Disease (ADPKD): Identification of five mutations in the *PKD1* gene

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1. Introduction

Autosomal Dominant Polycystic Kidney Disease (ADPKD) is the most frequent genetic kidney disease, affecting approximately 1 in 400 to 1000 individuals (**Audrézet et al., 2012**). It belongs to the group of polycystic kidney diseases which are characterized by the presence of numerous cysts in nephron resulting in a decline of renal functions responsible for the end-stage renal disease (ESRD) (**Wu, Somlo, 2000**). ADPKD is characterized by the presence of non-cystic manifestations such as hypertension, hematuria, urinary infection, cardiovascular system abnormalities and the development of brain-aneurysms (**Gabow, 1993**). Furthermore, cystic manifestations can also be observed i.e. renal cysts in both kidneys, hepatic cysts, liver cysts, pancreatic cysts, splenic cysts, thyroid cysts, ovarian cysts**,** and seminal vesicle cysts (**Luciano, Dahl, 2014**). ADPKD is a heterogeneous disease with two principal causative genes: *PKD1* and *PKD2* genes. Approximately 85% of ADPKD cases are caused by *PKD1* gene mutations; whereas 15% are due to mutations in *PKD2* gene (**Harris, Torres, 2009**).

PKD1 gene (OMIM, 601313; NM_000296) is located on chromosome 16 (16p13.3) and contains 46 exons (**Hughes et al., 1995**). This gene is duplicated on six copies present as pseudogenes (PKD1P1–P6), which has made the analysis of the *PKD1* gene rather complex (**International Polycystic Kidney Disease Consortium Polycystic kidney disease, 1995**). It encodes a 4303 amino acid peptide called polycystin-1 (PC1) (**Hughes et al., 1995**). PC1 contains a large extracellular N-terminal region, 11 transmembrane domains (TRPP channel homology) and a short intracellular C-terminus (**Hughes et al., 1995**).

The N-terminal region consists of several protein motifs: two leucine-rich LRR domains (Leucine Rich Repeat), one WSC (cell wall integrity and stress response component) domain, one c-lectin domain, one LDL-A domain (Low Density Lipoprotein-A), 16 copies of PKD