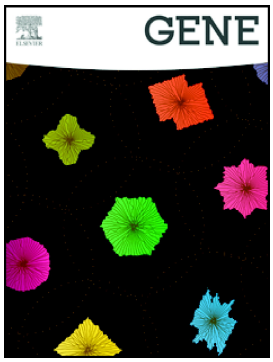

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Pathogenicity analysis of novel variations in Chinese Han patients with Polycystic Kidney Disease

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Abstract

Objective Locus and allellic heterogeneity in polycystic kidney disease (PKD) is a great challenge in precision diagnosis. We aim to establish comprehensive methods to distinguish the pathogenic mutations from the variations in *PKD1*, *PKD2* and *PKHD1* genes in a limited time and lay the foundation for precisely prenatal diagnosis, preimplantation genetic diagnosis and presymptom diagnosis of PKD. **Methods** Nested PCR combined with direct DNA sequencing were used to screen variations in *PKD1*, *PKD2* and *PKHD1* genes. The pathogenicity of de novel variations was assessed by the comprehensive methods including clinic data and literature review, databases query, analysis of co-segregation of the variants with the disease, variant frequency screening in the population, evolution conservation comparison, protein structure analysis and splice sites predictions. **Results** 17 novel mutations from 15 Chinese