**Supplementary Methods**

**Capture-based sequencing**

RNA probes were 120-bp long with a tilting density of 2× and 50-bp flanks into the intronic regions. Pooled, barcoded libraries for next-generation sequencing (NGS) were prepared using SureSelect® QXT kits (Agilent Technologies, Santa Clara, CA, USA) according to the manufacturer’s protocol. Genomic DNA samples were prepared using QIAamp® DNA Blood midi kit (Qiagen, KJ Venlo, Netherlands) following the man. The prepared libraries were sequenced via 150-bp single-end (SE) reads and an 8-bp barcode read using an Illumina MiSeq sequencer. Original files were aligned to the UCSC human reference sequence hg 19 using the Burrows-Wheeler Aligner v.0.7.12[1], and sequence alignment map (SAM) files were generated. These files were sorted and indexed using SAMtools (v.1.2)[2]. Then files obtained in BAM format were analyzed according to Genome Analysis Toolkit (GATK v.3.7) best-practice guidelines[3]. BAM files underwent further processing to remove duplicate reads (Picard MarkDuplicates v.1.119; http://broadinstitute.github.io/picard/) and for base quality recalibration (BaseRecalibrator v.0.1.19). Detection of single nucleotide variants (SNVs), indel detection, and genotyping were performed using GATK HaplotypeCaller (v.0.1.19). Variants were annotated with the GEMINI framework[4] and ANNOVAR[5]. Depth of coverage was calculated using GATK DepthOfCoverage (v.0.1.19). Copy number variations were analyzed with CONTRA software by calling copy number gains and losses for each target region through comparison with the normalized depth of sequencing in control samples.[6]

**Sanger sequencing**

Bidirectional Sanger sequencing was performed to confirm the presence of variants identified by NGS. For variants within the homologous region of *PKD1* (exons 1–33), the pertinent regions were first amplified by long-range (LR) -PCR using the primers reported previously. [7] Exon 1 of *PKD1* was also analyzed by Sanger sequencing in patients without pathogenic mutations according to NGS. [8]

**Variant filtering**

Filtering of candidate variants was done as described previously[9]. We first excluded SNVs with allele frequencies >0.01 in any population within the Exome Aggregation Consortium[10] (ExAC: http:// exac.broadinstitute.org), National Heart, Lung, and Blood Institute (NHLBI) Exome Sequencing Project exome variant server dataset ESP6500 (http://evs.gs.washington.edu/EVS/), 1000 Genomes catalog[11] (http://browser.1000 genomes.org/index.html), Human Genetic Variation Database[12] (HGVD: http://www. genome.med.kyoto-u.ac.jp/SnpDB/), or the genome cohort study of Tohoku Medical Megabank Organization[13] (ToMMo: https://ijgvd.megabank.tohoku.ac.jp). We also excluded SNVs with “LOW” impact severities based on the definition in the GEMINI software4, which includes the following functional predictions: “synonymous\_coding,” “intergenic,” “upstream,” “untranslated regions (UTR),” “intron,” etc. Missense variants of genes other than *PKD1* and *PKD2* were excluded if the depth of coverage was <20× and/or the alternative allele was found in <35% of reads. To interpret the significance of variants, we used the Polyphen2[14], SIFT[15], CADD[16], MCAP[17], and GERP conservation scores[18]. Interpretation of the significance of detected variants was based on American College of Medical Genetics and Genomics (ACMG) guidelines, Autosomal Dominant Polycystic Kidney Disease Mutation Database (PKDB, http://pkdb.mayo.edu), ClinVar (https://www.ncbi.nlm.nih.gov/clinvar/), and Human Gene Mutation Database Pro (HGMD Pro)[19].

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**Supplementary Figure legends**

**Figure S1: Mutations in *PKD1* truncating group patients.  
Figure S2: Mutations in *PKD1* non-truncating group patients.**

**Figure S3: Mutations in *PKD2* group patients.**

**Figure S4: Pathogenic mutations in Other group patients.**