Case study

# Polycystic Kidney Disease

## Patient information

**A 32-year-old female was diagnosed with bilateral renal cysts at 16 years of age.** She has occasional hematuria likely due to ruptured cysts. Her glomerular filtration rate and creatine are normal. She has a strong family history of polycystic kidney disease.

## Previous genetic testing

**A next-generation sequencing (NGS) panel including *PKD1* and *PKD2* was negative.** However, *PKD1* has six pseudogenes affecting exons 1-33, making identification of variants in this gene challenging.

## How will genetic testing help?

Confirming a diagnosis is important for the management and surveillance of the patient and family members. In addition, genetic testing enables identification of potential related donors for kidney transplantation.

## Genetic testing

**A Blueprint Genetics Polycystic Kidney Disease Panel was requested which tests for 10 genes including CNV analysis as well clinically relevant non-coding variants.** This panel uses the IDT xGEN Exome Research Panel and the Illumina NovaSeq 6000 platform allowing for improved mapping quality and excellent coverage in difficult-to-sequence regions. It is ideal for patients suspected to have either autosomal dominant or autosomal recessive polycystic kidney disease.

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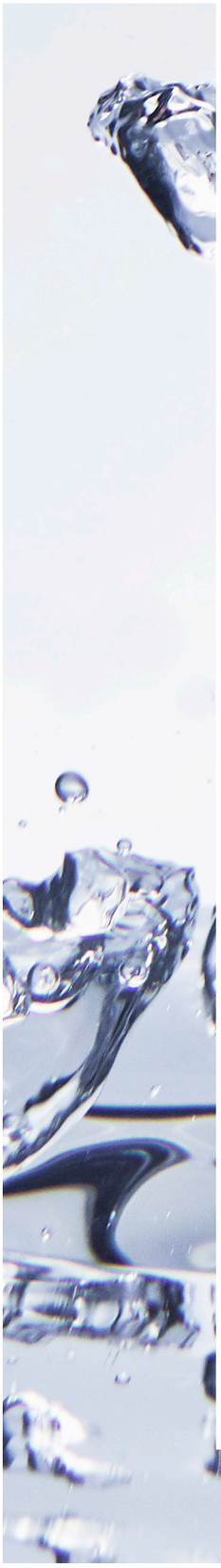

## Diagnostic summary

**Patient was heterozygous for *PKD1* c.2534T>C, p.(Leu845Ser), which was classified as pathogenic. The variant was confirmed with bi-directional Sanger sequencing.**

The *PKD1* c.2534T>C, p.(Leu845Ser) was first reported by Thomas et al. in a patient with autosomal dominant polycystic kidney disease (ADPKD) (PMID: 10364515). Since then it has been reported in several patients and families with ADPKD (http://pkdb.pkdcure.org).

Genome Aggregation Database (gnomAD) includes one individual previously identified with this variant. It is predicted to be damaging by SIFT, PolyPhen, and Mutation Taster *in silico* tools.

## Blueprint Genetics' nephrology test menu includes 24 panels

Our panels have been carefully curated to maximize the impact in clinical practice while minimizing the burden of variants of uncertain significance (VUS). Customization is available for all panels based on individual need.

## Diagnostic implications

**Due to pseudogene interference involving exons 1-33 of *PKD1*, detection of disease-causing variants in this gene is challenging.**

The clinical diagnosis in this patient is confirmed. The molecular diagnosis allows for asymptomatic family members to be tested and managed appropriately. In addition, identification of an unaffected related kidney donor is an option.

## Blueprint Genetics' Take Home

**We offer a customized NGS based solution that provides exceptional coverage for the *PKD1* and the ability to accurately map sequencing reads to the parent gene versus the pseudogenes.**

On our platform, *PKD1* has both high mean coverage (205x) and excellent mapping quality of MQ 20 with 99.96% of bp covered at least 20x, including the difficult-to-sequence GC-rich regions and exons affected by pseudogenes.

Read more about us, our services, and customer support at **blueprintgenetics.com**

Contact us with any questions, we're here to help!

*We are continuously developing our services and offering. We may amend service descriptions from time to time by posting new versions on our website. For up-to-date information, please visit blueprintgenetics.com.*

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