Client: Example Client ABC123
123 Test Drive
Salt Lake City, UT 84108
UNITED STATES

Physician: Doctor, Example

[redacted]

Polycystic Kidney Disease, Autosomal Dominant (PKD1 and PKD2) Sequencing and Deletion/Duplication (Temporary Referral as of 06/09/20)

ARUP test code 2012250

ADPKD Seq and Del/Dup Specimen	Whole Blood
ADPKD Seq, Del/Dup Interp	Negative

TEST PERFORMED - 2012250
TEST DESCRIPTION - Polycystic Kidney Disease, Autosomal Dominant (PKD1 and PKD2) Sequencing and Deletion/Duplication
INDICATION FOR TEST - Predictive Testing

RESULT
No pathogenic variants were detected in the PKD1 or PKD2 genes.

INTERPRETATION
According to information provided to ARUP, this individual has a family history of polycystic kidney disease, but the familial variant is unknown. No pathogenic PKD1 or PKD2 gene variants were detected through bidirectional sequencing of the coding regions and intron-exon boundaries and deletion/duplication analysis. This result significantly reduces the possibility of, but does not exclude, a diagnosis of autosomal dominant polycystic kidney disease (ADPKD). Please refer to the background information included in this report for the clinical sensitivity and limitations of this test.

RECOMMENDATIONS
Medical screening and management should rely on clinical findings and family history. For optimal interpretation of this negative result, determination of the causative familial variant in an affected family member is necessary. Further testing may be warranted if there is a familial variant that is not detectable by this assay. Genetic consultation is recommended.

COMMENTS
Reference Sequences: GenBank # NM_001009944.2 (PKD1), NM_000297.3 (PKD2)
Nucleotide numbering begins at the "A" of the ATG initiation codon.
Likely benign and benign variants are not reported.

This result has been reviewed and approved by [redacted]

H=High, L=Low, *=Abnormal, C=Critical

BACKGROUND INFORMATION: Polycystic Kidney Disease, Autosomal Dominant (PKD1 and PKD2) Sequencing and Deletion/Duplication

CHARACTERISTICS: Autosomal Dominant Polycystic Kidney Disease (ADPKD) is typically an adult-onset, multisystem disorder. Renal findings include: bilateral renal cysts, renal insufficiency, renal pain, hypertension, dilated renal tubules, enlarged kidneys, and end-stage renal disease (ESRD). Extra-renal findings include cysts in other organs, including liver, pancreas, seminal vesicles, and arachnoid membrane. Connective tissue findings include intracranial aneurysms, dolichoectasia, dilation of the aortic root, aortic dissections, mitral valve prolapse, and abdominal wall hernias. Fifty percent of individuals with ADPKD will develop ESRD by age 60.

PREVALENCE: 1:500-1:1,000 in the U.S.

INHERITANCE: Autosomal dominant; 5-10 percent of cases are de novo.

PENETRANCE: Age-dependent; nearly all older adults develop multiple renal cysts. The average age of onset for ESRD in individuals with PKD1 and PKD2 mutations is 54 and 74 years, respectively.

CAUSE: Pathogenic PKD1 or PKD2 gene mutations. In cases with an identifiable molecular cause, 85 percent are attributed to PKD1 and 15 percent are attributed to PKD2.

CLINICAL SENSITIVITY: 90 percent for ADPKD. Approximately 87 percent of cases are due to sequence variants and up to 3 percent of cases result from large deletions/duplications in PKD1 or PKD2.

METHODOLOGY: Bidirectional sequencing of the entire coding region and intron/exon boundaries of the PKD1 and PKD2 genes. A large region of PKD1, including exons 1-33, is duplicated six times on the same chromosome; therefore, to distinguish the PKD1 gene from the PKD1-like pseudogenes, long range PCR followed by site-specific PCR is used to sequence PKD1 exons 1-33. Multiplex ligation-dependent probe amplification (MLPA) is used to detect large exonic deletions/duplications of PKD1 or PKD2.

ANALYTICAL SENSITIVITY AND SPECIFICITY: 99 percent.

LIMITATIONS: Diagnostic errors can occur due to rare sequence variations. Regulatory region mutations and deep intronic mutations in PKD1 or PKD2 will not be detected. Large deletions/duplications of PKD1 exons 1, 2, 4, 8, 17, 24, 28, 32, 34, and 45 will not be detected. Mosaic mutations in PKD1 or PKD2 may not be detected. Breakpoints for large deletions/duplications will not be determined. Mutations in genes other than PKD1 and PKD2 are not assessed by this assay.

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
ADPKD Seq and Del/Dup Specimen	20-092-124514	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
ADPKD Seq, Del/Dup Interp	20-092-124514	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

END OF CHART

H=High, L=Low, *=Abnormal, C=Critical