UAB MEDICAL GENOMICS LABORATORY

ARPKD Known *PKHD1* Mutation Linkage Analysis for Informativity (PKDL) and Prenatal Linkage (PKDPL)

Ordering Information

Acceptable specimen types:

- Please send samples from the parents and their children for informativity results
- Fresh blood sample (3-6 ml EDTA; no time limitations associated with receipt)
- Paraffin-embedded tissue blocks or whole tissue from affected individual
- For prenatal samples, 2 T25 flasks of cultured CVS (>70% confluent) or 2 T25 flasks of cultured amniocytes (>70% confluent)
- Please provide fresh blood sample (3-6 ml, EDTA) for maternal cell contamination studies with (or in advance) of submitted specimen. A delay in receipt may delay turnaround time

Turnaround time:

20 working days

6 working days for prenatal testing

Price, CPT codes, and Z code:

$400/individual tested, $500/individual for prenatal testing (USD – institutional/self-pay);

CPT: 81265

Z code: ZB67G

Candidates for this test:

ARPKD testing services are offered to established patients and families with previously identified *PKHD1* mutations who wish to know if they are carriers before initiating another pregnancy

720 Twentieth Street South, Suite 330 Phone: (205) 934-5562
Birmingham, Alabama 35294-0005 Fax: (205) 996-2929
www.uab.edu/medicine/genetics/medical-genomics-laboratory

Specimen shipping and handling:

- Please find acceptable specimen type above.
- All submitted specimens must be sent at room temperature. DO NOT ship on ice.
- Specimens must be packaged to prevent breakage and absorbent material must be included in the package to absorb liquids in the event that breakage occurs. Also, the package must be shipped in double watertight containers (e.g. a specimen pouch + the shipping company's diagnostic envelope).
- To request a sample collection kit, please visit the website or email medgenomics@uabmc.edu to complete the specimen request form.
- Please contact the MGL (via email at medgenomics@uabmc.edu, or via phone at 205-934-5562) prior to sample shipment and provide us with the date of shipment and tracking number of the package so that we can better ensure receipt of the samples.

Required forms:

- Test Requisition Form
- Form for Customs (for international shipments)

Note: Detailed and accurate completion of this document is necessary for reporting purposes. The Medical Genomics Laboratory issues its clinical reports based on the demographic data provided by the referring institution on the lab requisition form. It is the responsibility of the referring institution to provide accurate information. If an amended report is necessary due to inaccurate or illegible documentation, additional reports will be drafted with charge.

Requests for testing may not be accepted for the following reasons:

- No label (patients full name and date of collection) on the specimens
- No referring physician's or genetic counselor's names and addresses

- No billing information
- DNA samples must be extracted in a CLIA or equivalent certified lab

For more information, test requisition forms, or sample collection and mailing kits, please call: 205-934-5562.

Disorder Background

Autosomal Recessive Polycystic Kidney Disease (ARPKD) is characterized by enlarged cystic kidneys and hepatic fibrosis. The diagnosis is often made pre- or neonatally, but some patients are still diagnosed later in life. The severity varies widely, with a high mortality rate in the first months of life. ARPKD is one of the more common hereditary childhood nephropathies with an estimated incidence of 1:20,000-1:40,000. The carrier frequency in the general population is estimated to be 1 in 70 to 1 in 100. Mutations in *PKHD1* are scattered throughout the gene. Most families carry their own "private" mutations. For more information on the condition please refer to the review on the GeneTests website and Online Mendelian Inheritance in Man.

The gene for ARPKD, *PKHD1 (Polycystic Kidney and Hepatic Disease 1)*, resides on chromosome 6p21-p12, spans 470 kb of genomic DNA and is the only gene known to be associated with the wide clinical spectrum of autosomal recessive polycystic kidney disease. 86 exons have been identified and multiple alternative transcripts are known. Over 300 mutations have been reported. Missense, nonsense, frameshift, splicing and multi-exon deletions can occur and the mutations are located throughout the length of the gene, with no major mutational hotspots known, as shown in the *PKHD1* mutation database.

Test Description

We offer **targeted detection** of a previously characterized mutation within the family. From a fresh EDTA blood sample, DNA is extracted directly and the target region is amplified and directly sequenced. To offer this testing service, the proband's mutation must be identified by our laboratory before testing relatives.

Linkage studies are based upon the accurate clinical diagnosis of ARPKD in the affected family member and accurate delineation of the biological relationships in the family. Linkage studies also depend on the availability and/or willingness to be tested of at least the proband and both parents. Linkage analysis is performed by amplifying 6 highly informative microsatellite markers residing intragenically and closely flanking the *PKHD1* gene.

Paraffin-embedded tissue as well as a cell line, tissue biopsy or blood sample can be used as the starting material from the affected proband for testing. In cases where only 1 pathogenic mutation was identified by direct sequencing of the entire longest open reading frame, linkage studies can be applied for future prenatal diagnosis, if clinical diagnosis in the proband was accurate. Prenatal linkage based testing is available starting from direct or cultured CVS, fresh or cultured amniocytes.

REFERENCES available on website.

Other related testing options:

- ARPKD Known *PKHD1* Mutation Prenatal Testing (PT2)
- ARPKD Known *PKHD1* Mutation Linkage Analysis for Informativity (PKDL) & Prenatal Linkage (PKDPL)