

Overview

Useful For

Diagnosis of individuals suspected of having autosomal recessive polycystic kidney disease (ARPKD)

Prenatal diagnosis if there is a high suspicion of ARPKD based on ultrasound findings

Carrier testing of individuals with a family history of ARPKD but an affected individual is not available for testing or disease-causing mutations have not been identified

Genetics Test Information

This test includes next-generation sequencing to evaluate for mutations in the *PKHD1* gene. Sanger sequencing may be performed to confirm detected variants.

Reflex Tests

Test ID	Reporting Name	Available Separately	Always Performed
CULFB	Fibroblast Culture for Genetic Test	Yes	No
CULAF	Amniotic Fluid Culture/Genetic Test	Yes	No
MATCC	Maternal Cell Contamination, B	Yes	No

Testing Algorithm

For prenatal specimens only: If amniotic fluid (nonconfluent cultured cells) is received, amniotic fluid culture/genetic test will be added and charged separately. If chorionic villus specimen (nonconfluent cultured cells) is received, fibroblast culture for genetic test will be added and charged separately. For any prenatal specimen that is received, maternal cell contamination studies will be added.

Special Instructions

- [Molecular Genetics: Congenital Inherited Diseases Patient Information](#)
- [Informed Consent for Genetic Testing](#)
- [Informed Consent for Genetic Testing \(Spanish\)](#)

Method Name

Custom Sequence Capture and Targeted Next-Generation Sequencing (NGS) followed by Polymerase Chain Reaction (PCR) and Sanger Sequencing when appropriate

NY State Available

Yes

Specimen

Specimen Type

Varies

Additional Testing Requirements

All prenatal specimens must be accompanied by a maternal blood specimen; order MATCC / Maternal Cell Contamination, Molecular Analysis on the maternal specimen.

Shipping Instructions

Whole blood specimens preferred to arrive within 96 hours of collection.

Prenatal specimens can be sent Monday through Thursday and **must be received by 5 p.m. CST on Friday** in order to be processed appropriately.

Specimen Required

Patient Preparation: A previous bone marrow transplant from an allogenic donor will interfere with testing. Call 800-533-1710 for instructions for testing patients who have received a bone marrow transplant.

Additional Information: To ensure minimum volume and concentration of DNA is met, the preferred volume of specimen must be submitted. Testing may be canceled if DNA requirements are inadequate.

Submit only 1 of the following specimens:

Specimen Type: Whole blood

Container/Tube:

Preferred: Lavender top (EDTA) or yellow top (ACD)

Acceptable: Any anticoagulant

Specimen Volume: 3 mL

Collection Instructions:

1. Invert several times to mix blood.
2. Send specimen in original tube.

Specimen Stability Information: Ambient (preferred)/Refrigerated

Prenatal Specimens

Due to the complexity of prenatal testing, consultation with the laboratory is required for all prenatal testing.

Specimen Type: Amniotic fluid

Container/Tube: Amniotic fluid container

Specimen Volume: 20 mL

Specimen Stability Information: Refrigerated (preferred)/Ambient

Specimen Type: Chorionic villi

Container/Tube: 15-mL tube containing 15 mL of transport media

Specimen Volume: 20 mg

Specimen Stability Information: Refrigerated

Acceptable:

Specimen Type: Confluent cultured cells

Container/Tube: T-25 flask

Specimen Volume: 2 flasks

Collection Instructions: Submit confluent cultured cells from another laboratory.

Specimen Stability Information: Ambient (preferred)/Refrigerated

Forms

1. **New York Clients-Informed consent is required.** Document on the request form or electronic order that a copy is on file. The following documents are available in Special Instructions:

-[Informed Consent for Genetic Testing](#) (T576)

-[Informed Consent for Genetic Testing-Spanish](#) (T826)

2. [Molecular Genetics: Congenital Inherited Diseases Patient Information](#) (T521) in Special Instructions

3. If not ordering electronically, complete, print, and send a [Renal Diagnostics Test Request](#) (T830) with the specimen.

Specimen Minimum Volume

Blood: 1 mL

Amniotic Fluid: 10 mL

Chorionic Villi: 5 mg

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

Clinical and Interpretive

Clinical Information

Autosomal recessive polycystic kidney disease (ARPKD) is a disorder caused by mutations in the polycystic kidney and hepatic disease 1 (*PKHD1*) gene. The incidence of ARPKD is approximately 1:20,000 and the estimated carrier frequency in the general population is 1:70. ARPKD is characterized by enlarged echogenic kidneys, congenital hepatic fibrosis, and pulmonary hypoplasia (secondary to oligohydramnios [insufficient volume of amniotic fluid] in utero). Most individuals with ARPKD present during the neonatal period and, of those, nearly one-third die of respiratory insufficiency. Early diagnosis, in addition to initiation of renal replacement therapy (dialysis or transplantation) and respiratory support, increases the 10-year survival rate significantly. Presenting symptoms include bilateral palpable flank masses in infants and subsequent observation of typical findings on renal ultrasound, often within the clinical context of hypertension and prenatal oligohydramnios. In rarer cases, individuals may present during childhood or adulthood with hepatosplenomegaly. Of those who survive the neonatal period, one-third progress to end-stage renal disease and up to one-half develop chronic renal insufficiency.

The *PKHD1* gene maps to 6p12 and includes 67 exons. The *PKHD1* gene encodes a protein called fibrocystin, which is localized to the primary cilia and basal body of renal tubular and biliary epithelial cells. Because ARPKD is an autosomal recessive disease, affected individuals must carry 2 deleterious mutations within the *PKHD1* gene. Although disease penetrance is 100%, intrafamilial variation in disease severity has been observed. Mutation detection is often difficult due to the large gene size and the prevalence of private mutations that span the entire length of the gene.

Reference Values

An interpretive report will be provided.

Interpretation

All detected alterations are evaluated according to American College of Medical Genetics and Genomics (ACMG) recommendations.⁽¹⁾ Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

Cautions

A small percentage of individuals who are carriers or have a diagnosis of autosomal recessive polycystic kidney disease (ARPKD) may have a mutation that is not identified by this method (eg, large genomic deletions/duplications, promoter mutations, deep intronic mutations). The absence of a mutation, therefore, does not eliminate the possibility of positive carrier status or the diagnosis of ARPKD. For carrier testing, it is important to first document the presence of a polycystic kidney and hepatic disease 1 (*PKHD1*) gene mutation in an affected family member.

Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Errors in our interpretation of results may occur if information given is inaccurate or incomplete.

Technical limitations:

In some cases, DNA variants of undetermined significance may be identified.

Rare polymorphisms exist that could lead to false-negative or false-positive results. If results obtained do not match the clinical findings, additional testing should be considered.

Evaluation tools:

Multiple in-silico evaluation tools were used to assist in the interpretation of these results. These tools are updated regularly; therefore, changes to these algorithms may result in different predictions for a given alteration. Additionally, the predictability of these tools for the determination of pathogenicity is currently unvalidated.

Unless reported or predicted to cause disease, alterations in protein coding genes that do not result in an amino acid substitution are not reported. These and common polymorphisms identified for this patient are available upon request.

Reclassification of Variants-Policy:

All detected alterations are evaluated according to American College of Medical Genetics and Genomics recommendations. Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance. At this time, it is not standard practice for the laboratory to systematically review likely pathogenic alterations or variants of uncertain significance that have been previously detected and reported. The laboratory encourages health care providers to contact the laboratory at any time to learn how the status of a particular variant may have changed over time.

Clinical Reference

1. Richards S, Aziz N, Bale S, et al: Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. *Genet Med* 2015 May;17(5):405-424
2. Guay-Woodford LM, Desmond RA: Autosomal recessive polycystic kidney disease: the clinical experience in North America. *Pediatrics* 2003;111:1072-1080
3. Guay-Woodford LM, Bissler JJ, Braun MC, et al: Consensus Expert Recommendations for the Diagnosis and Management of Autosomal Recessive Polycystic Kidney Disease: Report of an International Conference. *J. Pediatr.* 2014 Sep;165(3):611-617
4. Gunay-Aygun M, Avner E, Bacallao RL, et al: Autosomal recessive polycystic kidney disease and congenital hepatic fibrosis: summary of a first National Institutes of Health/Office of Rare Diseases conference. *J Pediatr* 2006;149:159-164
5. Harris PC, Rossetti S: Molecular genetics of autosomal recessive polycystic kidney disease. *Mol Genet Metab* 2004;81:75-85

Performance**Method Description**

Next-generation sequencing is performed to test for the presence of mutations in 66 exons (exon 2-67) of the polycystic kidney and hepatic disease 1 (*PKHD1*) gene. Sanger sequencing is used to confirm alterations detected by next-generation sequencing when appropriate.(Unpublished Mayo method)

PDF Report

No

Day(s) and Time(s) Test Performed

Performed weekly; Varies

Analytic Time

14 days

Maximum Laboratory Time

20 days

Specimen Retention Time

Whole Blood: 2 weeks (if available); Extracted DNA: 3 months

Performing Laboratory Location

Rochester

Fees and Codes
Fees

- Authorized users can sign in to [Test Prices](#) for detailed fee information.
- Clients without access to Test Prices can contact [Customer Service](#) 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact [Customer Service](#).

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information

81408

Fibroblast Culture for Genetic Test

88233-(if appropriate)

88240-(if appropriate)

Amniotic Fluid Culture/Genetic Test

88235-(if appropriate)

88240-(if appropriate)

Maternal Cell Contamination, B

81265-(if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
ARPKZ	ARPKD Full Gene Analysis	94226-8

Result ID	Test Result Name	Result LOINC Value
53449	Result Summary	50397-9
53450	Result	82939-0
53451	Interpretation	69047-9
53452	Additional Information	48767-8

Result ID	Test Result Name	Result LOINC Value
53453	Specimen	31208-2
53454	Source	31208-2
53455	Released By	18771-6