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MAYO CLINIC LABORATORIES

Test Definition: ADPKP

Focused Autosomal Dominant Polycystic Kidney Disease Gene Panel, Varies

Overview

Useful For

Providing a genetic evaluation for patients with a personal or family history suggestive of autosomal dominant polycystic kidney disease

Establishing a diagnosis of autosomal dominant polycystic kidney disease

Genetics Test Information

This test utilizes next-generation sequencing to detect single nucleotide, small deletion-insertion, and copy number variants in 8 genes associated with autosomal dominant polycystic kidney disease (ADPKD): *ALG8, ALG9, DNAJB11, GANAB, HNF1B, PKD1, PKD2, UMOD.* See Targeted Genes and Methodology Details for Focused Autosomal Dominant Polycystic Kidney Disease Panel in Method Description for additional details.

Identification of a pathogenic variant may assist with diagnosis, prognosis, clinical management, familial screening, and genetic counseling for ADPKD.

Special Instructions

- Informed Consent for Genetic Testing
- Informed Consent for Genetic Testing (Spanish)
- Hereditary Renal Genetic Testing Patient Information
- Targeted Genes and Methodology Details for Focused Autosomal Dominant Polycystic Kidney Disease Panel

Method Name

Sequence Capture and Amplicon-Based Next-Generation Sequencing (NGS)

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

Targeted testing for familial variants (also called site-specific or known mutation/variant testing) is available for the genes on this panel. See FMTT / Familial Variant, Targeted Testing, Varies. To obtain more information about this testing option, call 800-533-1710.

Customization of this panel and single gene analysis for any gene present on this panel are available. For more

information, see CGPH / Custom Gene Panel, Hereditary, Next-Generation Sequencing, Varies.

Shipping Instructions

Specimen preferred to arrive within 96 hours of collection.

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.

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 whole blood specimen in original tube. **Do not aliquot.**

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:

-Informed Consent for Genetic Testing (T576)

-Informed Consent for Genetic Testing-Spanish (T826)

2. Hereditary Renal Genetic Testing Patient Information (T918)
3. If not ordering electronically, complete, print, and send a Renal Diagnostics Test Request (T830) with the specimen.

Specimen Minimum Volume

1 mL

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 & Interpretive

Clinical Information

Autosomal dominant polycystic kidney disease (ADPKD) typically manifests in adulthood and is primarily characterized by bilateral kidney cysts, liver cysts, and an increased risk for intracranial aneurysm.(1) Less commonly, symptoms of ADPKD can manifest in childhood or adolescence.(2) Two genes, *PKD1* and *PKD2*, account for the majority of cases of ADPKD, with approximately 78% of cases being attributed to disease-causing variants in the *PKD1* gene and approximately 15% of cases being attributed to disease-causing variants in

2 other genes, *DNAJB11* and *GANAB*, are estimated to account for less than 1% of ADPKD cases. The lifetime penetrance of bilateral cysts is close to 100% in individuals with ADPKD, but disease manifestation is typically age-dependent and gene-dependent.(3)

ADPKD can have significant clinical overlap with other autosomal dominant conditions in which bilateral kidney cysts are a common feature, including autosomal dominant tubulointerstitial kidney diseases due to disease-causing variants in the *HNF1B* or *UMOD* genes.(1)

Rarer causes of autosomal dominant conditions with overlapping ADPKD features are emerging. The *ALG8* gene is most commonly associated with polycystic liver disease, however case reports have identified isolated, bilateral kidney cysts in a small number of individuals.(4) The *ALG9* gene is primarily associated with autosomal recessive congenital disorder of glycosylation, type I, but recent studies have identified isolated, bilateral kidney cysts in heterozygous carriers.(5)

Reference Values

An interpretive report will be provided.

Interpretation

All detected variants are evaluated according to American College of Medical Genetics and Genomics recommendations.(6) Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

Cautions

Clinical Correlations:
Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.

If testing was performed because of a clinically significant family history, it is often useful to first test an affected family member. Detection of a reportable variant in an affected family member would allow for more informative testing of at-risk individuals.

To discuss the availability of additional testing options or for assistance in the interpretation of these results, contact the Mayo Clinic Laboratories genetic counselors at 800-533-1710.

Technical Limitations:
Next-generation sequencing may not detect all types of genomic variants. In rare cases, false-negative or false-positive results may occur. The depth of coverage may be variable for some target regions; assay performance below the minimum acceptable criteria or for failed regions will be noted. Given these limitations, negative results do not rule out the diagnosis of a genetic disorder. If a specific clinical disorder is suspected, evaluation by alternative methods can be considered.

There may be regions of genes that cannot be effectively evaluated by sequencing or deletion and duplication analysis as a result of technical limitations of the assay, including regions of homology, high guanine-cytosine (GC) content, and repetitive sequences. Confirmation of select reportable variants will be performed by alternate methodologies based on internal laboratory criteria.

This test is validated to detect 95% of deletions up to 75 base pairs (bp) and insertions up to 47 bp. Deletions-insertions (delins) of 40 or more bp, including mobile element insertions, may be less reliably detected than smaller delins.

Deletion/Duplication Analysis:
This analysis targets single and multi-exon deletions/duplications; however, in some instances single exon resolution cannot be achieved due to isolated reduction in sequence coverage or inherent genomic complexity. Balanced structural rearrangements (such as translocations and inversions) may not be detected.

Deletion/duplication events that extend past the genes included on the panel may occur. In these instances, genes included in the ordered test are provided on the report and interpreted, and genomic breakpoints are reported if they are confirmed. However, copy number variants for genes not listed in the Method Description are typically not reported or interpreted for haploinsufficiency/triplosensitivity. CMACB / Chromosomal Microarray, Congenital, Blood; WESPR / Panel to Whole Exome Sequencing Reflex Test, Varies; or WGSDX / Whole Genome Sequencing for Hereditary Disorders, Varies is recommended for a full interpretation of deletions/duplications predicted to extend past the genes included on the panel.

This test is not designed to detect low levels of mosaicism or to differentiate between somatic and germline variants. If there is a possibility that any detected variant is somatic, additional testing may be necessary to clarify the significance of results.

Genes may be added or removed based on updated clinical relevance. Refer to the Targeted Genes and Methodology Details for Focused Autosomal Dominant Polycystic Kidney Disease Panel for the most up to date list of genes included in this test. For detailed information regarding gene specific performance and technical limitations, see Method Description or contact a laboratory genetic counselor.

If the patient has had an allogeneic hematopoietic stem cell transplant or a recent blood transfusion, results may be inaccurate due to the presence of donor DNA. Call Mayo Clinic Laboratories for instructions for testing patients who have received a bone marrow transplant.

Reclassification of Variants:
At this time, it is not standard practice for the laboratory to systematically review previously classified variants on a regular basis. The laboratory encourages healthcare providers to contact the laboratory at any time to learn how the classification of a particular variant may have changed over time.

Variant Evaluation:
Evaluation and categorization of variants are performed using published American College of Medical Genetics and Genomics and the Association for Molecular Pathology recommendations as a guideline.(6) Other gene-specific guidelines may also be considered. Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance. Variants classified as benign or likely benign are not reported.

Multiple in silico evaluation tools may be used to assist in the interpretation of these results. The accuracy of predictions made by in silico evaluation tools is highly dependent upon the data available for a given gene, and periodic updates to these tools may cause predictions to change over time. Results from in silico evaluation tools are interpreted with

caution and professional clinical judgement.

Rarely, incidental findings or secondary findings may implicate another predisposition or presence of active disease. Incidental findings may include, but are not limited to, results related to the sex chromosomes. These findings will be carefully reviewed to determine whether they will be reported.

Clinical Reference

1. Harris PC, Torres VE: Polycystic kidney disease, autosomal dominant. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 2002. Updated July 19, 2018. Accessed June 7, 2022. Available at www.ncbi.nlm.nih.gov/books/NBK1246/
2. Gimpel C, Bergmann C, Bockenhauer D, et al: International consensus statement on the diagnosis and management of autosomal dominant polycystic kidney disease in children and young people. Nat Rev Nephrol. 2019 Nov;15(11):713-726
3. Lanktree MB, Haghighi A, Guiard E, et al. Prevalence estimates of polycystic kidney and liver disease by population sequencing. J Am Soc Nephrol. 2018;29(10):2593-2600
4. Besse W, Dong K, Choi J, et al: Isolated polycystic liver disease genes define effectors of polycystin-1 function. J Clin Invest. 2017 May 1;127(5):1772-1785. doi: 10.1172/JCI90129. Erratum in: J Clin Invest. 2017 Sep 1;127(9):3558
5. Besse W, Chang AR, Luo JZ, et al: ALG9 mutation carriers develop kidney and liver cysts. J Am Soc Nephrol. 2019 Nov;30(11):2091-2102. doi: 10.1681/ASN.2019030298
6. 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

Performance

Method Description

Capture-based and amplicon-based next-generation sequencing (NGS) are performed to test for the presence of variants in coding regions and intron/exon boundaries of the genes analyzed, as well as select other regions that have known disease-causing variants. The human genome reference GRCh37/hg19 build was used for sequence read alignment. At least 99% of the bases are covered at a read depth over 30X. Sensitivity is estimated at above 99% for single nucleotide variants, above 94% for deletions-insertions (delins) less than 40 base pairs (bp), above 95% for deletions up to 75 bp and insertions up to 47 bp. NGS based quantitative method is performed to test for the presence of deletions and duplications in the genes analyzed.

There may be regions of genes that cannot be effectively evaluated by sequencing or deletion and duplication analysis as a result of technical limitations of the assay, including regions of homology, high guanine-cytosine (GC) content, and repetitive sequences. See Targeted Genes and Methodology Details for Focused Autosomal Dominant Polycystic Kidney Disease Panel for details regarding the targeted genes analyzed for each test and specific gene regions not routinely covered.(Unpublished Mayo method)

Confirmation of select reportable variants may be performed by alternate methodologies based on internal laboratory criteria.

Genes analyzed: *ALG8, ALG9, DNAJB11, GANAB, HNF1B, PKD1, PKD2, UMOD*

PDF Report
No

Day(s) Performed
Varies

Report Available
28 to 42 days

Specimen Retention Time
Whole blood: 2 weeks (if available); Extracted DNA: 3 months

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

Fees & 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 account representative. 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. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information
81405
81406 x 2
81407
81479 (if appropriate for government payers)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
ADPKP	Focused ADPKD Gene Panel	51966-0

Result ID	Test Result Name	Result LOINC® Value
618003	Test Description	62364-5
618004	Specimen	31208-2
618005	Source	31208-2

618006	Result Summary	50397-9
618007	Result	82939-0
618008	Interpretation	69047-9
618009	Additional Results	82939-0
618010	Resources	99622-3
618011	Additional Information	48767-8
618012	Method	85069-3
618013	Genes Analyzed	48018-6
618014	Disclaimer	62364-5
618015	Released By	18771-6