MAYO CLINIC LABORATORIES

Test Definition: APOL1

APOL1 Genotype, Varies

Overview

Useful For

Determining an individual's *APOL1* genotype

This test is **not useful for** clinical management of individuals with *APOL1* risk genotypes.

This test alone is **not useful for** determining eligibility for donation or receipt of kidney allografts.(12)

Special Instructions

- Informed Consent for Genetic Testing
- Pharmacogenomic Associations Tables
- Multiple Genotype Test List
- Informed Consent for Genetic Testing (Spanish)

Method Name

Real-Time Polymerase Chain Reaction (PCR) with Allelic Discrimination Analysis

NY State Available

Yes

Specimen

Specimen Type

Varies

Specimen Required

Multiple genotype tests can be performed on a single specimen after a single extraction. See Multiple Genotype Test List in Special Instructions for a list of tests that can be ordered together.

Submit only 1 of the following specimens:

Specimen Type: Whole blood
Container/Tube: Lavender top (EDTA)
Specimen Volume: 3 mL
Collection Instructions:
1. Invert several times to mix blood.
2. Send specimen in original tube.
Specimen Stability Information: Ambient (preferred) 9 days/Refrigerated 30 days

Specimen Type: Saliva

Patient Preparation: Patient should not eat, drink, smoke, or chew gum 30 minutes prior to collection.
Supplies: Saliva Swab Collection Kit (T786)
Specimen Volume: 1 swab
Collection Instructions: Collect and send specimen per kit instructions.
Specimen Stability Information: Ambient 30 days

Specimen Type: Extracted DNA
Container/Tube: 2 mL screw top tube
Specimen Volume: 100 mcL (microliters)
Collection Instructions:
1. The preferred volume is 100 mcL at a concentration of 50 ng/mcL.
2. Include concentration and volume on tube.
Specimen Stability Information: Frozen (preferred)/Ambient/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. If not ordering electronically, complete, print, and send a Renal Diagnostics Test Request (T830) with the specimen.

Specimen Minimum Volume

Blood: 0.4 mL
Saliva: 1 swab

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

The *APOL1* gene encodes apolipoprotein L-1, a serum apolipoprotein bound to high-density lipoprotein (HDL) particles. Two alleles, commonly called G1 and G2, have been associated with increased risk for development or progression of nondiabetic chronic kidney diseases, including HIV-associated nephropathy (HIVAN), primary focal segmental glomerulosclerosis (FSGS), and lupus-associated collapsing glomerulopathy.(1-4) The G1 allele is a haplotype consisting of 2 missense variants: c.1024A>G (p.Ser342Gly) and c.1152T>G (p.Ile384Met). The G2 allele is comprised of a 6 base pair deletion that results in the deletion of 2 amino acids: c.1164_1169delTTATAA (p.Asn388_Tyr389del). The G1 and G2 alleles are thought to be in complete linkage disequilibrium, meaning when both the G1 and G2 alleles are detected, they are on opposite chromosomes.(1) Risk for chronic kidney disease is only increased when 2 risk alleles are inherited

(ie, genotypes G1/G1, G2/G2, or G1/G2), following an autosomal recessive pattern of inheritance.(1) Individuals with one risk allele or no risk alleles do not appear to be at an increased risk.

The G1 and G2 risk alleles are enriched in individuals of African ancestry. Population studies show that in individuals of African descent, the G1 allele is found on 20% to 22.5% of chromosomes, and the G2 allele is found on 13% to 15% of chromosomes.(5-6) More importantly, it is estimated that 10% to15% of individuals of African descent carry 2 risk alleles.(5-6) The high frequency of the G1 and G2 alleles in this population is likely due to the protective effect these alleles confer against *Trypanosoma rhodesiense*, a parasite that causes trypanosomiasis, a disease endemic to Africa.(1) The G1 and G2 alleles are extremely rare or absent in individuals not of recent African descent (eg, European and Asian descent).(1,5) For this reason, increased risk associated with the G1 and G2 alleles has only been stratified in populations of recent African ancestry, and it remains unclear if similar risk effects associated with the *APOL1* risk genotypes are applicable to individuals without African ancestry. Currently, there are no guidelines for clinical management of individuals with *APOL1* risk genotypes.

Evidence exists that the donor *APOL1* genotype may impact both donor and recipient outcomes of kidney allografts. Results from 2 studies have shown that donor kidneys from individuals with 2 risk alleles were more likely to fail after transplantation when compared to donor kidneys from individuals with one or no risk alleles.(7-8) Another study suggests that living donors with two risk alleles may be at an increased risk for reduced kidney function following kidney donation.(9) At this time, there has been no association between the genotype of the allograft recipient and transplant outcomes, suggesting that allograft recipients with two risk alleles have similar outcomes to recipients with one or no risk alleles.(10) However, a prospective, large scale study to assess kidney allograft survival from donors with recent African ancestry based on donor and recipient *APOL1* genotypes is currently ongoing.(11) Based on presently available data, guidelines advise that an individual's *APOL1* genotype alone should not determine eligibility for donation or receipt of kidney allografts.(12)

Reference Values

An interpretive report will be provided.

Interpretation

An interpretive report will be provided.

Cautions

This assay will not detect all variants associated with an increased risk for development or progression of a chronic kidney disease. Therefore, the absence of an *APOL1* risk genotype does not rule out the possibility that an individual is at an increased risk for development or progression of a chronic kidney disease.

Specific *APOL1* genotypes are associated with an increased lifetime risk for chronic kidney diseases. Currently, there are no guidelines for clinical management of individuals with *APOL1* risk genotypes.

The *APOL1* genotype of a kidney donor may be associated with worsened outcomes in the allograft recipient. However. this assay cannot predict or rule out the development or progression of a chronic kidney disease in an individual. Current guidelines advise that an individual's *APOL1* genotype alone should not determine eligibility for donation or receipt of kidney allografts.(12)

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

Rare alterations may be present that could lead to false-negative or false-positive results. This assay does not identify less common apolipoprotein L1 alleles. Thus, an individual who appears to be homozygous for G1 or G2 may carry a rare allele that cannot be detected by this assay. If results obtained do not match the clinical findings, additional testing should be considered.

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

Samples may contain donor DNA if obtained from patients who received heterologous blood transfusions or allogeneic hematopoietic stem cell transplantation. Results from samples obtained under these circumstances may not accurately reflect the recipient's genotype. For individuals who have received blood transfusions, the genotype usually reverts to that of the recipient within 6 weeks. For individuals who have received allogeneic hematopoietic stem cell transplantation, a pretransplant DNA specimen is recommended for testing.

Clinical Reference

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2. Parsa A, Kao WH, Xie D, et al: APOL1 risk variants, race, and progression of chronic kidney disease. N Engl J Med. 2013;369(23):2183-2196. doi: 10.1056/NEJMoa1310345
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6. Duran CE, Ramírez A, Posada JG, et al: Prevalence of APOL1 risk variants in afro-descendant patients with chronic kidney disease in a Latin American Country. Int J Nephrol. 2019 Dec 18;2019:7076326 doi: 10.1155/2019/7076326
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11. Freedman BI, Moxey-Mims MM, Alexander AA, et al: APOL1 long-term kidney transplantation outcomes network (APOLLO): Design and rationale. Kidney Int Rep. 2019;5(3):278-288. doi: 10.1016/j.ekir.2019.11.022
12. Newell KA, Formica RN, Gill JS, et al: Integrating APOL1 gene variants into renal transplantation: Considerations arising from the American Society of Transplantation Expert Conference. Am J Transplant. 2017;17(4):901-911. doi: 10.1111/ajt.14173

Performance

Method Description
Genomic DNA is extracted from whole blood. Genotyping for each allele is performed using a polymerase chain reaction (PCR)-based 5'-nuclease assay. Fluorescently labeled detection probes anneal to the target DNA. PCR is used to amplify the section of DNA that contains the variant. If the detection probe is an exact match to the target DNA, the 5'-nuclease polymerase degrades the probe, the reporter dye is released from the effects of the quencher dye, and a fluorescent signal is detected.(Instruction manual: TaqMan SNP Genotyping Assay. Applied Biosystems Revision; A.0 January 2014)

PDF Report
No

Day(s) Performed
Monday through Friday

Report Available
3 to 8 days

Specimen Retention Time
Whole Blood/Saliva swab: 2 weeks; Extracted DNA: 2 months

Performing Laboratory Location
Rochester

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 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 US Food and Drug Administration.

CPT Code Information
81479

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
APOL1	APOL1 Genotype, V	In Process

Result ID	Test Result Name	Result LOINC® Value
610559	APOL1 Result	In Process
610561	Interpretation	69047-9
610562	Additional Information	48767-8

610563	Method	85069-3
610564	Disclaimer	62364-5
610565	Reviewed by	18771-6