



# 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](#)
- [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

**Patient Preparation:** A previous hematopoietic stem cell transplant from an allogenic donor will interfere with testing. For information about testing patients who have received a hematopoietic stem cell transplant, call 800-533-1710.

**Submit only 1 of the following specimens:**

**Specimen Type:** Whole blood

**Container/Tube:** Lavender top (EDTA) or yellow top (ACD)

**Specimen Volume:** 3 mL

#### Collection Instructions:

1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot.**
3. Whole blood collected postnatal from an umbilical cord is also acceptable. See Additional Information.

**Specimen Stability Information:** Ambient (preferred) 4 days/Refrigerated 4 days/Frozen 4 days

#### Additional Information:

1. Specimens are preferred to be received within 4 days of collection. Extraction will be attempted for specimens received after 4 days, and DNA yield will be evaluated to determine if testing may proceed.

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- To ensure minimum volume and concentration of DNA are met, the requested volume must be submitted. Testing may be canceled if DNA requirements are inadequate.
  - For postnatal umbilical cord whole blood specimens, maternal cell contamination studies are recommended to ensure test results reflect that of the patient tested. A maternal blood specimen is required to complete maternal cell contamination studies. Order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on both the cord blood and maternal blood specimens under separate order numbers.

**Specimen Type:** Saliva

**Patient Preparation:** Patient should not eat, drink, smoke, or chew gum 30 minutes prior to collection.

**Supplies:**

DNA Saliva Kit High Yield (T1007)

Saliva Swab Collection Kit (T786)

**Container/Tube:**

**Preferred:** High-yield DNA saliva kit

**Acceptable:** Saliva swab

**Specimen Volume:** 1 Tube if using T1007 or 2 swabs if using T786

**Collection Instructions:** Collect and send specimen per kit instructions.

**Specimen Stability Information:** Ambient (preferred) 30 days/Refrigerated 30 days

**Additional Information:** Saliva specimens are acceptable but not recommended. Due to lower quantity/quality of DNA yielded from saliva, some aspects of the test may not perform as well as DNA extracted from a whole blood sample. When applicable, specific gene regions that were unable to be interrogated will be noted in the report. Alternatively, additional specimen may be required to complete testing.

**Specimen Type:** Extracted DNA

**Container/Tube:**

**Preferred:** Screw Cap Micro Tube, 2 mL with skirted conical base

**Acceptable:** Matrix tube, 1 mL

**Collection Instructions:**

- The preferred volume is at least 100 µL at a concentration of 75 ng/µL.
- Include concentration and volume on tube.

**Specimen Stability Information:** Frozen (preferred) 1 year/Ambient/Refrigerated

**Additional Information:** DNA must be extracted in a CLIA-certified laboratory or equivalent and must be extracted from a specimen type listed as acceptable for this test (including applicable anticoagulants). Our laboratory has experience with Chemagic, Puregene, Autopure, MagnaPure, and EZ1 extraction platforms and cannot guarantee that all extraction methods are compatible with this test. If testing fails, one repeat will be attempted, and if unsuccessful, the test will be reported as failed and a charge will be applied. If applicable, specific gene regions that were unable to be interrogated due to DNA quality will be noted in the report.

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

**Specimen Minimum Volume**

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Blood: 0.4 mL

Saliva/DNA: See Specimen Required

**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 (CKD), including HIV-associated nephropathy (HIVAN) and focal segmental glomerulosclerosis (FSGS) with collapsing features.(1-4)

The *APOL1* (NM\_001136540.1) 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\_1169del (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) The risk for chronic kidney disease is only increased when 2 risk alleles are present (ie, genotypes G1/G1, G2/G2, or G1/G2), following an autosomal recessive pattern of inheritance.(1) Individuals with 2 risk alleles and nondiabetic CKD can be described as having *APOL1*-associated nephropathy. Individuals with one risk allele or no risk alleles do not appear to be at an increased risk for *APOL1*-associated nephropathy.

The G1 and G2 risk alleles are enriched in individuals of African ancestry. Population studies show that in individuals of African descent, the G1 and G2 alleles occur at a frequency of 20% to 22.5% and 13% to 15%, respectively.(5-6) Importantly, it is estimated that 10% to 15% of individuals of African descent have 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 brucei gambiense* and *Trypanosoma brucei rhodesiense*, which are parasites 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 these *APOL1* risk genotypes are applicable to individuals without African ancestry.

Currently, there are no guidelines for clinical management of individuals with *APOL1* risk genotypes and there are no specific treatments for *APOL1*-associated nephropathy.(7) However, several clinical trials are underway studying potential treatments.(8) Additionally, there currently is limited guidance on genetic testing strategies for *APOL1* risk genotypes.(9) One consensus statement suggests *APOL1* genotyping should be considered "in all patients of African ancestry with kidney disease and in any patient with kidney disease and a family member with a confirmed *APOL1* high-risk genotype."(7)

Evidence exists that the donor *APOL1* genotype may impact both donor and recipient outcomes of kidney allografts. Previous 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.(10-11) Another study suggests that living donors with two risk alleles may be at an increased risk for reduced kidney function following kidney donation.(12) Recent literature suggests that recipients with 2 *APOL1* high risk alleles may have lower graft survival one year after transplantation; however, additional research is required.(13-14) 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.(15) 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.(16)

**Reference Values**

An interpretive report will be provided.

**Interpretation**

The interpretive report includes an overview of the findings as well as the associated clinical significance.

**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.

Specimens may contain donor DNA if obtained from patients who received non-leukocyte reduced blood transfusions or allogeneic hematopoietic stem cell transplantation. Results from specimens obtained under these circumstances may not accurately reflect the recipient's genotype. For individuals who have received non-leukocyte reduced 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.

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**Clinical Reference**

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**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. (Unpublished Mayo method)

**PDF Report**

No

**Day(s) Performed**

Monday through Friday

**Report Available**

3 to 8 days

**Specimen Retention Time**

Whole blood: 28 days (if available); Saliva: 30 days (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**

81479

**LOINC® Information**

Test ID	Test Order Name	Order LOINC® Value
APOL1	APOL1 Genotype, V	104664-8

Result ID	Test Result Name	Result LOINC® Value
610559	APOL1 Result	104664-8
610561	Interpretation	69047-9
610562	Additional Information	48767-8
610563	Method	85069-3
610564	Disclaimer	62364-5
610565	Reviewed by	18771-6