Overview

Useful For
Diagnosis of individuals suspected of having apolipoprotein A-I (APOA1) gene-associated familial amyloidosis

Special Instructions
- Molecular Genetics: Congenital Inherited Diseases Patient Information
- Informed Consent for Genetic Testing

Method Name
Polymerase Chain Reaction (PCR) Followed by DNA Sequence Analysis

NY State Available
Yes

Specimen

Specimen Type
Varies

Shipping Instructions
Specimen preferred to arrive within 96 hours of draw.

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.

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.

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

Forms
1. New York Clients-Informed consent is required. Please document on the request form or electronic order that a copy is on file. An Informed Consent for Genetic Testing (T576) is available in Special Instructions.
2. Molecular Genetics: Congenital Inherited Diseases Patient Information (T521) in Special Instructions

3. If not ordering electronically, complete, print, and send a [Neurology Specialty Testing Client Test Request](#) (T732) with the specimen.

**Specimen Minimum Volume**

0.5 mL

**Reject Due To**

No specimen should be rejected.

**Specimen Stability Information**

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<tr>
<th>Specimen Type</th>
<th>Temperature</th>
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<tbody>
<tr>
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**Clinical and Interpretive**

**Clinical Information**

The systemic amyloidoses are a number of disorders of varying etiology characterized by extracellular protein deposition. The most common form is an acquired amyloidosis secondary to multiple myeloma or monoclonal gammopathy of unknown significance (MGUS) in which the amyloid is composed of immunoglobulin light chains. In addition to light chain amyloidosis, there are a number of acquired amyloidoses caused by the misfolding and precipitation of a wide variety of proteins. There are also hereditary forms of amyloidosis.

The hereditary amyloidoses comprise a group of autosomal dominant, late-onset diseases that show variable penetrance. A number of genes have been associated with hereditary forms of amyloidosis including those that encode transthyretin, apolipoprotein A-I, apolipoprotein A-II, fibrinogen alpha chain, gelsolin, cystatin C, and lysozyme. Apolipoprotein A-I, apolipoprotein A-II, lysozyme, and fibrinogen alpha-chain amyloidosis present as non-neuropathic systemic amyloidosis, with renal dysfunction being the most prevalent manifestation. Apolipoprotein A-I amyloidosis is also associated with additional organ system involvement, including clinical manifestations in the liver, heart, skin, and larynx. In addition, the G26R APOA1 mutation has been associated with a neuropathic presentation.

To date, at least 16 amyloidogenic mutations have been identified within the APOA1 gene. The majority of these are missense mutations, although deletion/insertion mutations have also been described. There is some evidence of genotype-phenotype correlations. Mutations that occur near the amino terminal portion of the protein are more often associated with hepatic and renal amyloidosis, while mutations occurring near the carboxyl terminal portion of the gene are more often associated with cardiac, cutaneous, and laryngeal amyloidosis. The majority of mutations reported to date occur at 1 of 2 hot spots spanning amino acid residues 50 through 93 and 170 through 178.

Mutations in the APOA1 gene have also been linked to familial hypoalphalipoproteinemia. Patients carrying 1 APOA1 mutation typically demonstrate reduced levels of high-density lipoprotein (HDL) cholesterol, which is associated with increased risk for coronary artery disease. Comparatively, the presence of 2 APOA1 mutations generally results in complete absence of HDL cholesterol and may include additional clinical features such as xanthomas or corneal opacities.
Due to the clinical overlap between the acquired and hereditary forms, it is imperative to determine the specific type of amyloidosis in order to provide an accurate prognosis and consider appropriate therapeutic interventions. Tissue-based, laser capture tandem mass spectrometry might serve as a useful test preceding gene sequencing to better characterize the etiology of the amyloidosis, particularly in cases that are not clear clinically.

**Reference Values**

An interpretive report will be provided.

**Interpretation**

All detected alterations are evaluated according to American College of Medical Genetics recommendations. 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 apolipoprotein A-I (APOA1) gene-associated amyloidosis may have a mutation that is not identified by this method (eg, large genomic deletions, promoter mutations). The absence of a mutation(s), therefore, does not eliminate the possibility of positive carrier status or the diagnosis of APOA1-associated amyloidosis.

In some cases, DNA alterations 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.

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.

Mutations in other genes, such as those encoding transthyretin, lysozyme, fibrinogen alpha chain, apolipoprotein A-II, gelsolin, and others, have been shown to cause other forms of familial amyloidosis. Abnormalities in these genes are not detected by this assay.

**Clinical Reference**


**Performance**
Method Description
Bidirectional sequence analysis is performed to test for the presence of a mutation in all coding regions and intron/exon boundaries of the apolipoprotein A-I (APOA1) gene. (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
81479-Unlisted molecular pathology procedure

LOINC® Information

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### Test Definition: APO1Z
APOA1 Gene, Full Gene Analysis

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