Overview

Useful For
Diagnosis of individuals suspected of having apolipoprotein A-II-associated familial amyloidosis

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

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.

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**

0.5 mL

**Reject Due To**

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

**Specimen Stability Information**

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<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
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<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-II amyloidosis typically presents as a very slowly progressive disease. Age of onset is highly variable, ranging from adolescence to the fifth decade. To date, all mutations that have been identified within the APOA2 gene occur within the stop codon and result in a 21-residue C-terminal extension of the apolipoprotein A-II protein.

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. (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 apolipoprotein A-II (APOA2) associated amyloidosis 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 apolipoprotein A-II associated amyloidosis.

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-I, gelsolin, and others, have been shown to cause other forms of familial amyloidosis. Abnormalities in these genes are not detected by this assay.

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.

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.

**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**


Performance

Method Description
Bidirectional sequence analysis is performed to test for the presence of a mutation in all 3 coding exons of the APOA2 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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