Overview

Useful For
Confirming a diagnosis of fibrinogen alpha-chain (FGA) gene-related familial visceral 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.

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)
Specimen Minimum Volume

0.5 mL

Reject Due To

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

Specimen Stability Information

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<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
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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 AI, apolipoprotein AII, gelsolin, cystatin C, lysozyme, and fibrinogen alpha chain (FGA). Apolipoprotein AI, apolipoprotein AII, lysozyme, and fibrinogen amyloidosis present as nonneuropathic systemic amyloidosis, with renal dysfunction being the most prevalent manifestation.

FGA-related familial visceral amyloidosis commonly presents with renal failure, which can often be fulminant, and is characterized by hypertension, proteinuria, and azotemia. Liver and spleen involvement may be seen in advanced cases. Neuropathy is not a feature of FGA-related familial visceral amyloidosis.

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 clinically clear.

It is important to note that there are rare disorders of hemostasis that are also associated with mutations in the FGA gene. Patients with afibrinogenemia, hypofibrinogenemia, and dysfibrinogenemia have all been reported to have mutations in FGA. Most dysfibrinogenemias are autosomal dominant disorders; afibrinogenemia and hypofibrinogenemia are more often autosomal recessive disorders. In general, truncating mutations in FGA result in afibrinogenemia and missense mutations are a common cause of dysfibrinogenemia.

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 have a diagnosis of fibrinogen alpha-chain (FGA)-related familial visceral amyloidosis may have a mutation that is not identified by this method (eg, large genomic deletions, promoter mutations). The absence of a mutation, therefore, does not eliminate the possibility of positive carrier status or the diagnosis of FGA-related familial visceral amyloidosis. For carrier testing, it is important to first document the presence of a FGA mutation in an affected family member.

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, apolipoprotein AII, 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**


**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 fibrinogen alpha chain (FGA) 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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