MAYO CLINIC LABORATORIES

Test Definition: FGAZ

FGA Gene, Full Gene Analysis

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)

-Informed Consent for Genetic Testing-Spanish (T826)

2. Molecular Genetics: Congenital Inherited Diseases Patient Information (T521) in Special Instructions.

Reject Due To

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

Specimen Minimum Volume

0.5 mL

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Ambient (preferred)		
	Frozen		
	Refrigerated		

Clinical & 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

1. Richards S, Aziz N, Bale S, et al: Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med 2015 May;17(5):405-424

2. Benson MD: The hereditary amyloidoses. Best Pract Res Clin Rhematol 2003;17:909-927

3. Benson MD: Ostertag revisited: The inherited systemic amyloidoses without neuropathy. Amyloid 2005;12(2):75-87

4. Asselta R, Duga S, Tenchini ML: The molecular basis of quantitative fibrinogen disorders. Thromb Haemost 2006 Oct;4(10):2115-2129

5. Shiller SM, Dogan A, Highsmith WE: Laboratory methods for the diagnosis of hereditary amyloidoses. In Amyloidosis-Mechanisms and Prospects for Therapy. Edited by S Sarantseva. InTech 2011, pp 101-120

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 fibrinogen alpha chain (*FGA*) gene.(Unpublished Mayo method)

PDF Report

No

Specimen Retention Time

Whole Blood: 2 weeks (if available) Extracted DNA: 3 months

Performing Laboratory Location

Rochester

Fees & Codes

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-Unlisted molecular pathology procedure

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
FGAZ	FGA Gene, Full Gene Analysis	94199-7

Result ID	Reporting Name	LOINC®
53033	Result Summary	50397-9
53034	Result	82939-0
53035	Interpretation	69047-9
53036	Additional Information	48767-8
53037	Specimen	31208-2
53038	Source	31208-2
53039	Released By	18771-6