Test Definition: GSNZ

GSN Gene, Full Gene Analysis

Overview

Useful For

Diagnostic confirmation of amyloidosis V

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.

Reject Due To

No specimen should be rejected.

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, fibrinogen alpha chain, cystatin C, lysozyme, and gelsolin. Apolipoprotein AI, apolipoprotein AII, lysozyme, and fibrinogen amyloidosis present as non-neuropathic systemic

amyloidosis, with renal dysfunction being the most prevalent manifestation.

Gelsolin (*GSN*) amyloidosis (amyloidosis V) is characterized by corneal lattice dystrophy, cranial neuropathy, and skin changes. Peripheral neuropathy may be present but is typically mild. Like the other hereditary amyloidoses, it is an autosomal dominant disorder; however, homozygosity has been reported and is associated with accelerated renal disease.

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 have a diagnosis of amyloidosis V 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 amyloidosis V. For carrier testing, it is important to first document the presence of a gelsolin (*GSN*) gene mutation in an affected family member.

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, fibrinogen alpha chain, apolipoprotein AII, lysozyme 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

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. Kiuru S: Gelsolin-related familial amyloidosis, Finnish type (FAF), and its variants found worldwide. Amyloid 1998;5:55-66

4. 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 gelsolin (*GSN*) 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
GSNZ	GSN Gene, Full Gene Analysis	94203-7

Result ID	Reporting Name	LOINC®
53048	Result Summary	50397-9
53049	Result	82939-0
53050	Interpretation	69047-9
53051	Additional Information	48767-8
53052	Specimen	31208-2
53053	Source	31208-2

53054	Released By	18771-6