Test Definition: SERPZ

SERPINA1 Gene, Full Gene Analysis, Varies

Overview

Useful For

Identification of causative mutations when a deficient serum level of alpha-1-antitrypsin is not explained by routine testing, such as proteotyping, genotyping, or isoelectric focusing phenotyping.

Determining the specific allelic variant (full gene analysis) for prognosis and genetic counseling

Testing Algorithm

See Alpha-1 Antitrypsin-A Comprehensive Testing Algorithm in Special Instructions.

Special Instructions

- Informed Consent for Genetic Testing
- Alpha 1 Antitrypsin-A Comprehensive Testing Algorithm
- Informed Consent for Genetic Testing (Spanish)
- Molecular Genetics: SERPINA1 Gene Patient Information

Method Name

Polymerase Chain Reaction (PCR) Amplification/DNA Sequencing

NY State Available

Yes

Specimen

Specimen Type

Varies

Shipping Instructions

Specimen preferred to arrive within 96 hours of collection.

Necessary Information

Molecular Genetics: SERPINA1 Gene Patient Information **is required.** Testing may proceed without the patient information; however, the information aids in providing a more thorough interpretation. Ordering healthcare professionals are strongly encouraged to fill out the form and send with the specimen.

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. Molecular Genetics: SERPINA1 Gene Patient Information (T521) **is required**
2. **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:
-Informed Consent for Genetic Testing (T576)
-Informed Consent for Genetic Testing-Spanish (T826)
3. If not ordering electronically, complete, print, and send a Gastroenterology and Hepatology Test Request (T728) with the specimen.

Specimen Minimum Volume

1 mL

Reject Due To

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

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

Alpha-1-antitrypsin (A1A) is a protein that inhibits the enzyme neutrophil elastase. It is predominantly synthesized in the liver and secreted into the bloodstream. The inhibition function is especially important in the lungs because it protects against excess tissue degradation. Tissue degradation due to A1A deficiency is associated with an increased risk for early onset panlobular emphysema, which initially affects the lung bases (as opposed to smoking-related emphysema, which presents with upper lung field emphysema). Patients may become symptomatic in their 30s and 40s. The most frequent symptoms reported in a National Institute of Health study of 1,129 patients with severe deficiency (mean age 46 years) included cough (42%), wheezing (65%), and dyspnea with exertion (84%). Many patients were misdiagnosed as having asthma. It is estimated that approximately one-sixth of all lung transplants are for A1A deficiency.

Liver disease can also occur, particularly in children; it occurs much less commonly than emphysema in adults.

A1A deficiency is a relatively common disorder in the Northern European White population. The diagnosis of A1A deficiency is initially made by quantitation of protein levels in serum followed by phenotyping-determination of specific allelic variants by isoelectric focusing (IEF), genotyping-DNA based detection of specific mutations, or proteotyping-using

liquid chromatography-tandem mass spectrometry (LC-MS/MS). While there are many different alleles in this gene, only 3 are common. The 3 major alleles include: M (full functioning, normal allele), S (associated with reduced levels of protein), and Z (disease-causing mutation associated with liver disease and premature emphysema). The S and Z alleles account for the majority of the abnormal alleles detected in affected patients. As a codominant disorder, both alleles are expressed. An individual of SZ or S- null genotype may have a small increased risk for emphysema (but not liver disease) due to slightly reduced protein levels. On the other hand, an individual with the ZZ genotype is at greater risk for early onset liver disease and premature emphysema.

Smoking appears to hasten development of emphysema by 10 to 15 years. These individuals should be monitored closely for lung and liver function.

Historically, IEF phenotyping has been the primary method for characterizing variants, though in some cases the interpretation is difficult and prone to error. Serum quantitation is helpful in establishing a diagnosis but can be influenced by other factors. IEF phenotyping, LC-MS/MS proteotyping, and DNA-based genotyping are routinely used to test for deficiency alleles but can miss disease alleles other than the S and Z alleles. In patients suspected to have alpha-1 antitrypsin deficiency based on clinical findings or serum alpha-1-antitrypsin (AAT) levels, who do not have evidence of the SZ or ZZ genotype by routine methods, this gene analysis assay may provide useful information. Full sequencing of the *SERPINA1* coding region is performed for the detection of rare non-S or non-Z disease mutations.

See Alpha-1-Antitrypsin-A Comprehensive Testing Algorithm in Special Instructions.

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 alpha-1 antitrypsin deficiency 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 alpha-1 antitrypsin deficiency. For testing of at risk family members, it is important to first document the presence of a *SERPINA1* gene mutation in an affected family member.

In some cases, DNA alterations of undetermined significance may be identified.

Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Errors in the interpretation of results may occur if information given is inaccurate or incomplete.

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.

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. Stoller JK, Aboussouan LS: Alpha-1-antitrypsin deficiency. Lancet 2005;365:2225-2236
3. McElvaney NG, Stoller JK, Buist AS, et al: Baseline characteristics of enrollees in the National Heart, Lung and Blood Institute Registry of alpha 1-antitrypsin deficiency. Alpha 1-Antitrypsin Deficiency Registry Study Group. Chest 1997;111:394-403
4. Snyder MR, Katzmann JA, Butz ML, et al: Diagnosis of alpha-1-antitrypsin deficiency: an algorithm of quantification, genotyping, and phenotyping. Clin Chem 2006;52:2236-2242
5. Graham RP, Dina MA, Howe SC, et al: SERPINA1 full-gene sequencing identifies rare mutations not detected in targeted mutation analysis. J Mol Diag 2015;17:689-694

Performance

Method Description
Bidirectional sequence analysis is performed to test for the presence of a mutation in all coding regions and intron and exon boundaries of the SERPINA1 gene.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Varies

Report Available
14 to 20 days

Specimen Retention Time
Whole Blood: 2 weeks (if available), Extracted DNA: 3 months

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

Fees & 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 account representative. 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. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

81479

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
SERPZ	SERPINA1 Gene, Full Gene Analysis	94222-7

Result ID	Test Result Name	Result LOINC® Value
113178	Result Summary	50397-9
113179	Result	82939-0
113180	Interpretation	69047-9
113181	Additional Information	48767-8
113182	Specimen	31208-2
113183	Source	31208-2
113184	Released By	18771-6