MAYO CLINIC LABORATORIES

Test Definition: SERPZ

SERPINA1 Gene, Full Gene Analysis, Varies

Overview

Useful For

Identification of causative variants 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

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
CULFB	Fibroblast Culture for Genetic Test	Yes	No
CULAF	Amniotic Fluid Culture/Genetic Test	Yes	No
_STR1	Comp Analysis using STR (Bill only)	No, (Bill only)	No
_STR2	Add'l comp analysis w/STR (Bill Only)	No, (Bill only)	No
MATCC	Maternal Cell Contamination, B	Yes	No

Testing Algorithm

For cord blood specimens that have an accompanying maternal blood specimen, maternal cell contamination studies will be performed at an additional charge.

For more information see Alpha-1 Antitrypsin-A Comprehensive Testing Algorithm.

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

Specimen Required

Patient Preparation: A previous hematopoietic stem cell transplant from an allogenic donor will interfere with testing. For information about testing patients who have received a hematopoietic stem cell transplant, call 800-533-1710.

Submit only 1 of the following specimens:

Specimen Type: Whole blood
Container/Tube: Lavender top (EDTA) or yellow top (ACD)
Specimen Volume: 3 mL
Collection Instructions:
1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot**.
3. Whole blood collected postnatal from an umbilical cord is also acceptable. See Additional Information
Specimen Stability Information: Ambient (preferred) 4 days /Refrigerated 4 days/Frozen 4 days
Additional Information:
1. Specimens are preferred to be received within 4 days of collection. Extraction will be attempted for specimens received after 4 days, and DNA yield will be evaluated to determine if testing may proceed.
2. To ensure minimum volume and concentration of DNA are met, the requested volume must be submitted. Testing may be canceled if DNA requirements are inadequate.
3. For postnatal umbilical cord whole blood specimens, maternal cell contamination studies are recommended to ensure test results reflect that of the patient tested. A maternal blood specimen is required to complete maternal cell contamination studies. Order MATCC / Maternal Cell Contamination, Molecular Analysis, Varies on both the cord blood and maternal blood specimens under separate order numbers.

Specimen Type: Extracted DNA
Container/Tube:
Preferred: Screw Cap Micro Tube, 2 mL with skirted conical base
Acceptable: Matrix tube, 1 mL
Collection Instructions:
1. The preferred volume is at least 100 mcL at a concentration of 75 ng/mcL.
2. Include concentration and volume on tube.
Specimen Stability Information: Frozen (preferred) 1 year/Ambient/Refrigerated
Additional Information: DNA must be extracted in a CLIA-certified laboratory or equivalent and must be extracted from a specimen type listed as acceptable for this test (including applicable anticoagulants). Our laboratory has experience with Chemagic, Puregene, Autopure, MagnaPure, and EZ1 extraction platforms and cannot guarantee that all extraction methods are compatible with this test. If testing fails, one repeat will be attempted, and if unsuccessful, the test will be reported as failed and a charge will be applied. If applicable, specific gene regions that were unable to be interrogated due to DNA quality will be noted in the report.

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:

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

Specimen Minimum Volume
See Specimen Required

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	Varies		

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 1129 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.

Alpha-1-antitrypsin 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 variants, 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 variant 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 variants.

For more information see Alpha-1-Antitrypsin-A Comprehensive Testing Algorithm.

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 variant that is not identified by this method (eg, large genomic deletions, promoter variantss). The absence of a variant, 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 variant in an affected family member.

In some cases, DNA variants of uncertain 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 genetic alterations (ie, 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;17(5):405-424
2. 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(2):394-403
3. 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(12):2236-2242
4. 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(6):689-694
5. Mornex JF, Traclet J, Guillaud O, et al. Alpha1-antitrypsin deficiency: An updated review. Presse Med.

2023;52(3):104170

Performance

Method Description
Bidirectional sequence analysis is performed to test for the presence of a variant 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: 28 days (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