



Division of Human Genetics

Alpha-1-antitrypsin (A1AT) deficiency secondary to *SERPINA1* mutations

Molecular Genetics Laboratory
CLIA#: 36D0965791
Phone: (513) 636-4474
Fax: (513) 636-4373
Email: moleculargenetics@cchmc.org

Additional information and test requisitions are
available at:
www.cincinnatichildrens.org/molecular-genetics



*Helping you fit the
pieces together*

Shipping Instructions

Please enclose test requisition with sample.
All information must be completed before
sample can be processed.

Place samples in Styrofoam mailer and ship
at room temperature by overnight Federal
Express to arrive Monday through Friday

Ship to:
Cytogenetics and Molecular Genetics
Laboratories
3333 Burnet Avenue NRB 1042
Cincinnati, OH 45229
513-636-4474

A1AT deficiency is one of the most common genetic disorders in Caucasian populations. In North America, approximately one individual in every 5,000-7,000 has A1AT deficiency. Clinically significant alpha-1-antitrypsin deficiency is typically the result of homozygosity for the PI*Z allele or compound heterozygosity for the PI*S*Z alleles, although other disease-causing alleles are identified in ~5% of affected individuals.

A1AT deficiency is characterized by liver disease from infancy and throughout adulthood and by lung disease in adults, particularly those who smoke cigarettes. A1AT is a serum protease inhibitor. In the adult liver, A1AT deficiency may lead to the accumulation of insoluble intracellular proteins in hepatocytes and bile ducts, leading to cirrhosis and fibrosis. However, the etiology of liver disease in children with A1AT deficiency is not well understood. In the lung, A1AT deficiency leads to a reduced inhibition of leukocyte elastase resulting in destruction of the elastin in the alveolae resulting in pulmonary disease. Hepatocellular carcinoma, panniculitis, and Wegener granulomatosis are rare complications of A1AT deficiency.

Approximately 2% of individuals with the PI*S*Z genotype develop severe liver disease in childhood while approximately 10% of adults over 50 years of age develop cirrhosis. In contrast, pulmonary disease is very rare in children with the PI*S*Z genotype, while adults with this genotype who smoke cigarettes have a significantly increased risk of developing chronic obstructive pulmonary disease (COPD). Heterozygotes for the Z allele are not at increased risk for liver disease, but may have a mildly increased risk of pulmonary dysfunction in adulthood, particularly among individuals who smoke. An individual's genotype and history of environmental exposures contribute to a highly variable phenotype, even among family members.

INDICATIONS:

- Obstructive jaundice in infancy or childhood
- Cirrhosis, fibrosis or hepatocellular carcinoma in adults
- Chronic obstructive pulmonary disease (COPD) in adults
- Presymptomatic testing of at-risk siblings
- Prenatal diagnosis of at-risk pregnancies
- Carrier testing in relative of a patient with A1AT deficiency

SPECIMEN:

At least 2 mls of whole blood in purple top (EDTA) tube. Label tube with patient's name, birth date, and date of collection. Phlebotomist must initial tube to verify patient's identity.

METHODOLOGY:

- TaqMan-based genotyping assay to detect Z and S alleles only
OR
- PCR-based sequencing of all five exons and exon/intron boundaries of the *SERPINA1* gene.

SENSITIVITY & SPECIFICITY:

- Genotyping Assay: This test detects only the Z and S alleles which account for 95% of disease causing mutations.
- DNA sequencing: The sensitivity of DNA sequencing is over 99% for the detection of nucleotide base changes, small deletions and insertions in the regions analyzed. Multiple exon deletions and insertions may not be identified by this methodology.
- *SERPINA1* is the only gene associated with A1AT deficiency. If the patient has received a liver transplant or recent blood transfusion, donor DNA may be present in the blood along with patient DNA (chimerism). In this case, additional testing may be required to rule out chimerism.

TURN-AROUND TIME:

- Genotyping Assay 2 business days
- *SERPINA1* full gene sequence analysis 3-4 weeks

COST:

Please call 1-866-450-4198 for current pricing or with any billing questions.

CPT CODES:

- Genotyping Assay: 83890, 83896(x2), 83900, 83909, 83912
- *SERPINA1* sequence analysis: 83890, 83898(x3), 83894(x3), 83891(x2), 83904(x7), 83909(x7), 83912
- Family specific analysis: 83890, 83898, 83894, 83891, 83904, 83912

Each test report includes a detailed interpretation of the genetic findings, the clinical significance of the result, and specific recommendations for clinical management and additional testing, if warranted. Results will be reported to the referring physician or health care provider as specified on the test requisition form.