SERPINA1 Gene

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serpin family A member 1

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1. Normal Function

The *SERPINA1* gene provides instructions for making a protein called alpha-1 antitrypsin, which is a type of serine protease inhibitor (serpin). Serpins help control several types of chemical reactions by blocking (inhibiting) the activity of certain enzymes. Alpha-1 antitrypsin prevents the digestive enzyme trypsin from breaking down proteins until trypsin reaches the intestines. Alpha-1 antitrypsin also inhibits other enzymes, including a powerful enzyme called neutrophil elastase that is released from white blood cells to fight infection.

Alpha-1 antitrypsin protects the lungs from neutrophil elastase, which can damage lung tissue if not properly controlled. Alpha-1 antitrypsin is produced in the liver and then transported to the lungs via the blood.

2. Health Conditions Related to Genetic Changes

2.1. Alpha-1 antitrypsin deficiency

More than 120 mutations in the *SERPINA1* gene have been identified. Some of these mutations do not affect the production of alpha-1 antitrypsin, while others cause a shortage (deficiency) of the protein. Without enough functional alpha-1 antitrypsin, neutrophil elastase destroys the small air sacs in the lungs (alveoli) and causes lung disease. Excessive damage to the alveoli leads to emphysema, an irreversible lung disease that causes extreme shortness of breath.

Many *SERPINA1* gene mutations change single protein building blocks (amino acids) in alpha-1 antitrypsin, which alters the protein's structure. The most common mutation that causes alpha-1 antitrypsin deficiency replaces the amino acid glutamic acid with the amino acid lysine at protein position 342 (written as Glu342Lys or E342K). This mutation results in a version of the *SERPINA1* gene called the Z allele that produces very little alpha-1 antitrypsin.

Abnormal alpha-1 antitrypsin proteins may bind together to form a large molecule, or polymer, that cannot leave the liver. The accumulation of these polymers results in liver damage. In addition, lung tissue is destroyed because not enough alpha-1 antitrypsin is available to protect against neutrophil elastase. Polymers of alpha-1 antitrypsin may also contribute to excessive inflammation, which may explain some of the other features of alpha-1 antitrypsin deficiency, such as a skin condition called panniculitis.

Other *SERPINA1* gene mutations lead to the production of an abnormally small form of alpha-1 antitrypsin that is quickly broken down in the liver. As a result, little or no alpha-1 antitrypsin is available in the lungs. While the liver remains healthy in individuals with these mutations, the lungs are left unprotected from neutrophil elastase.

3. Other Names for This Gene

- A1A
- A1AT
- A1AT_HUMAN
- AAT
- alpha-1 antiproteinase
- alpha-1 antitrypsin
- alpha-1 proteinase inhibitor

- alpha1AT
- PI
- PI1
- protease inhibitor 1 (anti-elastase)
- serine (or cysteine) proteinase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 1
- serpin peptidase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 1

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