Your Alpha-1 Genotype: Why It's Important

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Genotype: What is it?

- ✓ Everyone inherits two gene alleles for alpha-1 antitrypsin (AAT): one from their mother and one from their father. The pair of gene alleles is called a genotype.
- ✓ The normal gene allele is called M. Individuals with two normal gene alleles have an MM genotype.
- ✓ Variants of each allele can have no health effects or can increase your risk for health problems.
- ✓ A variant that produces less AAT than a normal gene allele, produces AAT that is not functional, or produces AAT that gets trapped in the liver is referred to as a deficiency variant.
- ✓ There are many deficiency variants. The deficiency variants that are identified most often are Z and S.
  - ❑ You can have zero deficiency variants (example genotype: MM).
  - ❑ You can have only a single deficiency variant (example genotypes: MZ, MS).
  - ❑ You can have two deficiency variants (example genotypes: ZZ, SZ, SS).

Risk of Developing Disease

- ✓ The liver and lungs are the organs most at risk among individuals with at least one deficiency variant.
  - ❑ The risk of liver disease is due to abnormal AAT that gets trapped in the liver.
  - ❑ AAT protects the lungs. The risk of lung disease is due to a shortage of AAT in the lungs.
- ✓ In addition to alpha-1 genotype, the main risk factors for lung disease are smoking and environmental exposures. Additional risk factors for liver disease include obesity, smoking, diabetes, and alcohol use.
- ✓ If you have an increased risk of liver or lung disease due to your alpha-1 genotype, it is especially important to avoid or manage additional risk factors. In addition, you will need to work with your healthcare team to get appropriate medical tests to monitor your liver and lung health.

Treatment Options

- ✓ Currently, genotype does not influence treatment options for liver disease because there are no currently approved treatments specifically for liver disease due to AAT deficiency.
- ✓ Augmentation therapy is a treatment specifically for lung disease due to AAT deficiency. Genotype is one of the factors that influences whether augmentation therapy is a treatment option for you.

Clinical Trial Participation

- ✓ Several promising therapies for liver and lung disease due to AAT deficiency are being investigated in clinical trials. Genotype often is used to determine whether you can participate in these studies.
- ✓ Information on currently-enrolling alpha-1 clinical trials is available at clinicaltrials.gov.

Family Risk and Family Testing

- ✓ If you have at least one deficiency variant, your family members (especially parents, siblings, and children) should consider getting tested for AAT deficiency.
- ✓ Family members may have a higher risk of lung and liver disease than the general population. AAT test results may motivate them to lose weight, avoid smoking, or make other healthy changes.
- ✓ Genotype is one of the factors that will influence whether augmentation therapy is an available treatment option for family members with lung disease.
- ✓ Family members may want to learn about the risk of passing a deficiency variant to their children.
- ✓ Family members can talk with a genetic counselor before and/or after getting tested. The Alpha-1 Foundation provides free genetic counseling services, available at 1-855-476-1227.

Additional Information

- ✓ Information about lung and liver disease risk associated with various genotypes is available at the Alpha-1 Alleles website. You can enter your genotype in this interactive website, and learn the degree of risk for lung and liver disease associated with your genotype.
- ✓ AlphaNet's Big Fat Reference Guide (BFRG) has a section devoted to lung health and a section devoted to liver health. Anyone can access AlphaNet's BFRG. AlphaNet Subscribers can access the BFRG through their Subscriber Portal. The BFRG also provides information about additional health problems that occur less frequently due to AAT deficiency (panniculitis and vasculitis).
- ✓ AlphaNet has created a document about family testing and several 1-page documents that focus on lung and liver health. These documents are available here.