Alpha-1 Antitrypsin Deficiency

AAT deficiency is a genetic condition that can lead to lung and liver disease. It is caused by decreased levels of the alpha-1 antitrypsin (AAT) protein. This test includes the two most common variants linked to this deficiency.

Clark, while you have one of the two genetic variants we tested, you are **not likely at risk** for symptoms of AAT deficiency.

AAT deficiency is caused by certain combinations of genetic variants. However, people with only the variant detected are not likely at risk for developing lung or liver disease related to AAT deficiency.

1 variant detected
in the SERPINA1 gene

How To Use This Test

This test does not diagnose AAT deficiency or any other health conditions.

Please talk to a healthcare professional if this condition runs in your family, you think you might have this condition, or you have any concerns about your results.

Review the Genetic Health Risk tutorial
See Scientific Details
See Frequently Asked Questions

Intended Uses

- Tests for the PI*Z and PI*S variants in the SERPINA1 gene linked to AAT deficiency.

Limitations

- Does not test for all possible variants linked to AAT deficiency.

Important Ethnicities

- The variants included in this test are most common and best studied in people of **European** descent.

You are **not likely at risk** of developing lung or liver disease related to AAT deficiency based on your genetic result.

However, if you have a personal or family history of lung or liver disease, consider discussing this result with a healthcare professional.

We detected one variant called PI*S.
See Scientific Details

People who have only this variant are not likely at risk for lung or liver disease related to AAT deficiency.

Other combinations of variants can increase the risk for symptoms related to AAT deficiency.

You could pass this variant on to your children.

If your partner has a variant linked to AAT deficiency, your children could inherit a combination of variants that may put them at risk of developing lung or liver disease.

AAT deficiency is caused by certain combinations of genetic variants, and only some combinations increase risk for lung and liver disease.

People with your genetic result are not likely at risk for symptoms of AAT deficiency.

Smoking
Occupational and other exposures
Personal or family history of lung disease
Viral infections

Viral infections

Diseases like the flu can damage the lungs, and diseases like hepatitis A and B can damage the liver. It is important for people with AAT deficiency to stay up to date on their immunizations to prevent lung and liver disease from getting worse.

See Scientific Details for more information

About Alpha-1 Antitrypsin Deficiency

Also known as: Alpha-1 antitrypsin deficiency, AATD, A1AT deficiency, Alpha-1, A1AD, α1

When it develops

Because it is a genetic condition, AAT deficiency is present at birth. Symptoms of lung disease usually appear later in life, and age of onset is strongly affected by smoking. Some people may never have symptoms of lung disease, especially if they don't smoke. Liver problems may develop anytime from infancy to adulthood.

Potential signs and symptoms

- Shortness of breath and wheezing
- Chronic cough
- Recurrent lung infections
- Lung disease, including emphysema
- Liver disease, including cirrhosis

How common is the condition?

AAT deficiency is most common in people of Northern European descent. In the U.S., 1 in 3,000-5,000 people has this condition.

How it's treated

There is currently no known cure. People with AAT deficiency are encouraged to avoid smoking and consider getting certain vaccinations. For those with symptoms, treatment focuses on management of lung and liver problems. Direct replacement of the AAT protein into the blood may be used to slow the progression of lung disease. Lung and liver transplants may be beneficial in some cases.

Read more at: National Heart, Lung, and Blood Institute MedlinePlus GeneReviews Genetics Home Reference

Learn more about AAT deficiency.

See our Frequently Asked Questions for more information.
FAQs

If you have questions about your results or how they might affect you or your family, a genetic counselor may be able to help.
Learn more

If you have a personal or family history of lung or liver disease, consult with a healthcare professional.
Print report

Receive up to $20 when you refer family and friends to 23andMe. Get started today.

©2017 23andMe, Inc. All Rights Reserved.

Alpha-1 Antitrypsin Deficiency

Scientific Details

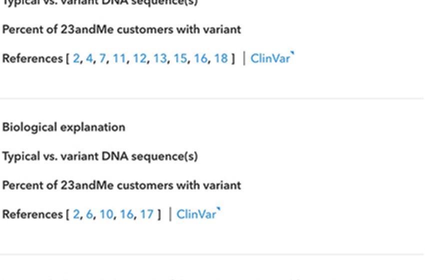
AAT deficiency is a genetic condition that can lead to lung and liver disease. It is caused by decreased levels of the alpha-1 antitrypsin (AAT) protein. This test includes the two most common variants linked to this deficiency.

AAT deficiency is caused by variants in the SERPINA1 gene.

SERPINA1

The SERPINA1 gene contains instructions for making a protein called alpha-1 antitrypsin (AAT). This protein is made in the liver, but is transported to the lungs where it has a protective function. Certain variants in SERPINA1 result in too little AAT protein getting transported to the lungs, and more AAT protein getting trapped in the liver. As a result, the lungs are less protected from damage, and the liver can become damaged as well.

Read more at Genetics Home Reference



You have one genetic variant detected by this test, called PI*S.

Variants Detected | View All Tested Markers

Marker Tested	Your Genotype*		Additional Information
PI*Z Gene: SERPINA1 Marker: rs28929474	**C** Typical copy from one of your parents	**C** Typical copy from your other parent	Biological explanation; Typical vs. variant DNA sequence(s); Percent of 23andMe customers with variant; References [2, 4, 7, 11, 12, 13, 15, 16, 18] | ClinVar
PI*S Gene: SERPINA1 Marker: rs17580	**A** Variant copy from one of your parents	**T** Typical copy from your other parent	Biological explanation; Typical vs. variant DNA sequence(s); Percent of 23andMe customers with variant; References [2, 6, 10, 16, 17] | ClinVar

*This test cannot distinguish which copy you received from which parent. This test also cannot determine whether multiple variants, if detected, were inherited from only one parent or from both parents. This may impact how these variants are passed down.

23andMe always reports genotypes based on the 'positive' strand of the human genome reference sequence (build 37). Other sources sometimes report genotypes using the opposite strand.

Test Interpretation

This report provides information about the risk of developing lung and liver disease in people of European descent who have the variants included in this test. Estimates for other ethnicities are not currently available.

Health Risk Estimates

Risk estimates are based on clinical studies that identify an association between a genotype and a health condition.

For certain genotypes, quantitative risk estimates may not be available.

Variants in the SERPINA1 gene can affect AAT protein levels differently. Severe AAT deficiency is defined by AAT levels below 11 µM/L. Lung diseases such as emphysema and COPD are most commonly associated with AAT levels below this protective threshold. This table provides AAT protein levels associated with each genotype for informational purposes only, and does not indicate a person's actual protein levels.

Consider talking to a healthcare professional if you have any concerns about your results.

References [1, 12, 16]

Risk estimates for developing lung and liver disease in people of European descent

Genotype	Average serum AAT levels, µM/L (5th to 95th %ile)	Lung Disease	Liver Disease
PI*MS	33 (18-52)	Not likely at increased risk of developing COPD, including emphysema.	Not likely at increased risk of cirrhosis.
PI*SS	28 (20-48)	Not likely at increased risk of developing COPD, including emphysema.	Not likely at increased risk of cirrhosis.
PI*MZ	25.4 (15-42)	People with this genotype who are non-smokers are not likely at increased risk of developing COPD, including emphysema. Smokers with this genotype have a slightly increased risk of developing COPD. More studies are needed to estimate risk in more detail.	Only a few studies have looked at risk for liver disease in people with this genotype, and findings have been inconclusive. More studies are needed to determine if there is any additional risk in these individuals.
PI*SZ	16.5 (10-23)	People with this genotype who are non-smokers are not likely at increased risk of developing COPD, including emphysema. However, scientists estimate that 20-50% of smokers with this genotype will develop signs of emphysema during their lifetime.	There are not enough studies of people with this genotype to determine whether they are at increased risk for cirrhosis.
PI*ZZ	5.3 (3.4-7.0)	Increased risk of developing COPD, including emphysema. Scientists estimate that greater than 80% of people with this genotype will develop signs of emphysema during their lifetime.	Increased risk of developing liver disease. Scientists estimate that people with this genotype have a 30-40% chance of developing cirrhosis after the age of 50.

Other Factors

AAT deficiency is a genetic condition. People with this condition have a higher risk of developing lung and liver disease, but their risk is also influenced by other factors.

This is not a complete list of other factors.

The factors described to the right include the most common and well-established risk factors associated with lung or liver disease in people with AAT deficiency. Other factors not listed here may also influence risk for lung or liver disease in people with the condition.

Consult with a healthcare professional before making any major lifestyle changes.

Other Factors	References
Smoking People with AAT deficiency who smoke typically start to experience the symptoms of lung disease between 40 and 50 years of age. Smoking causes inflammation in the lungs. For people with AAT deficiency, AAT levels are not high enough to protect against the damage. There is also some evidence that the chemicals in cigarette smoke can further decrease AAT levels. In non-smokers, symptoms of AAT deficiency may be delayed until their 60s. Some non-smokers will never develop the symptoms of lung disease.	[1, 8, 16]
Occupational and other exposures A small number of research studies - mostly looking at men working in construction or farming - suggests that prolonged occupational exposure to industrial gases, metal fumes, and mineral dust may lead to a faster decline in lung function in people with AAT deficiency. Exposure to pollutants from kerosene heaters on a regular basis may also increase the chances of developing lung disease related to AAT deficiency. The effects of occupational and other exposures on symptoms of lung disease in people with AAT deficiency are still not fully understood.	[1, 14]
Personal or family history of lung disease People with AAT deficiency who have a personal history of lung problems such as asthma or wheezing are more likely to develop severe lung disease later in life. The risk of lung disease can also depend on family history. People with AAT deficiency whose siblings suffer from lung disease are more likely to develop lung disease themselves. This may be due to genetic and/or environmental factors.	[1]
Viral infections Diseases like the flu can damage the lungs. Diseases like hepatitis A and B can damage the liver. Yearly immunizations against influenza (a virus that causes the flu) and pneumococcus (a virus that causes respiratory infections) are generally recommended for people with AAT deficiency. This can prevent lung disease from getting worse. Immunizations against the viruses hepatitis A and B, which cause liver disease, may also be recommended by a healthcare professional.	[1, 5]

Test Details

Indications for Use

The 23andMe PGS Genetic Health Risk Report for Alpha-1 Antitrypsin Deficiency is indicated for reporting of the PI*Z and PI*S variants in the SERPINA1 gene. This report describes if a person has variants associated with AAT deficiency and a higher risk for lung or liver disease, but it does not describe a person's overall risk of developing lung or liver disease. This report is most relevant for people of European descent.

Special Considerations

- Testing for genetic variants associated with AAT deficiency is recommended under certain circumstances by several health professional organizations, including the American Thoracic Society.

Test Performance Summary

Clinical Performance [1]

More than 95% of all cases of AATD deficiency are caused by the PI*Z and PI*S variants in the SERPINA1 gene.

Analytical Performance

Accuracy was determined by comparing results from this test with results from sequencing for 409 samples. 409 out of 409 genotype results were correct. While unlikely, this test may provide false positive or false negative results.

Warnings and Limitations

- This test does not cover all variants that could cause this condition.*
- This test does not diagnose any health conditions.
- Share results with your healthcare professional for any medical purposes.
- If you are concerned about your results, consult with a healthcare professional.

See the Package Insert for more details on use and performance of this test.

* Variants not included in this test may be very rare, may not be available on our genotyping platform, or may not pass our testing standards.

References

1. American Thoracic Society. et al. (2003). "American Thoracic Society/European Respiratory Society statement: standards for the diagnosis and management of individuals with alpha-1 antitrypsin deficiency." Am J Respir Crit Care Med. 168(7):818-900.
2. Dahl M et al. (2005). "The protease inhibitor PI*S allele and COPD: a meta-analysis." Eur Respir J. 26(1):67-76.
3. Fregonese L et al. (2008). "Hereditary alpha-1-antitrypsin deficiency and its clinical consequences." Orphanet J Rare Dis. 3:16.
4. Hersh CP et al. (2004). "Chronic obstructive pulmonary disease in alpha1-antitrypsin PI MZ heterozygotes: a meta-analysis." Thorax. 59(10):843-9.
5. Köhnlein T et al. (2010). "Diagnostic delay and clinical modifiers in alpha-1 antitrypsin deficiency." Ther Adv Respir Dis. 4(5):279-87.
6. Lieberman J et al. (1986). "Alpha 1-antitrypsin Pi-types in 965 COPD patients." Chest. 89(3):370-3.
7. Lomas DA et al. (1993). "Effect of the Z mutation on the physical and inhibitory properties of alpha 1-antitrypsin." Biochemistry. 32(2):500-8.
8. Lomas DA et al. (2004). "Alpha1-antitrypsin deficiency. 4: Molecular pathophysiology." Thorax. 59(6):529-35.
9. Marciniuk DD et al. (2012). "Alpha-1 antitrypsin deficiency targeted testing and augmentation therapy: a Canadian Thoracic Society clinical practice guideline." Can Respir J. 19(2):109-16.
10. McGee D et al. (2010). "Is PiSS Alpha-1 Antitrypsin Deficiency Associated with Disease?" Pulm Med. 2010:570679.
11. Miravitlles M et al. (1998). "Usefulness of a national registry of alpha-1-antitrypsin deficiency. The Spanish experience." Respir Med. 92(10):1181-7.
12. Molloy K et al. (2014). "Clarification of the risk of chronic obstructive pulmonary disease in α1-antitrypsin deficiency PiMZ heterozygotes." Am J Respir Crit Care Med. 189(4):419-27.
13. Seersholm N et al. (1998). "Intermediate alpha 1-antitrypsin deficiency PiSZ: a risk factor for pulmonary emphysema?" Respir Med. 92(2):241-5.
14. Senn O et al. (2005). "alpha1-Antitrypsin deficiency and lung disease: risk modification by occupational and environmental inhalants." Eur Respir J. 26(5):909-17.
15. Sidhar SK et al. (1995). "Mutations which impede loop/sheet polymerization enhance the secretion of human alpha 1-antitrypsin deficiency variants." J Biol Chem. 270(15):8393-6.
16. Stoller JK et al. (1993). "Alpha-1 Antitrypsin Deficiency".
17. Teckman JH et al. (1996). "The endoplasmic reticulum degradation pathway for mutant secretory proteins alpha1-antitrypsin Z and S is distinct from that for an unassembled membrane protein." J Biol Chem. 271(22):13215-20.
18. Turino GM et al. (1996). "Clinical features of individuals with PI*SZ phenotype of alpha 1-antitrypsin deficiency. alpha 1-Antitrypsin Deficiency Registry Study Group." Am J Respir Crit Care Med. 154(6 Pt 1):1718-25.

Change Log

Your report may occasionally be updated based on new information. This Change Log describes updates and revisions to this report.

Date	Change
April 17, 2017	Alpha-1 Antitrypsin Deficiency report created.

Receive up to $20 when you refer family and friends to 23andMe. Get started today.
©2017 23andMe, Inc. All Rights Reserved.

Alpha-1 Antitrypsin Deficiency

Frequently Asked Questions

AAT deficiency is a genetic condition that can lead to lung and liver disease. It is caused by decreased levels of the alpha-1 antitrypsin (AAT) protein. This test includes the two most common variants linked to this deficiency.

Alpha-1 Antitrypsin Deficiency

What does this test do?

This test looks for two specific genetic variants in the SERPINA1 gene called PI*Z and PI*S. These variants are linked to alpha-1 antitrypsin deficiency (also called AAT deficiency).

People with the genetic variants included in this test may be at risk for AAT deficiency. However, not everyone with these genetic variants has AAT deficiency or an increased risk of developing lung or liver disease.

This test does not include all possible genetic variants that may increase your risk for AAT deficiency.

Is this answer helpful? Yes No

What does this test not do?

This test does not diagnose alpha-1 antitrypsin (AAT) deficiency. Only a healthcare professional can do that.

This test does not tell you if you have lung or liver disease or if you will definitely develop these conditions in the future.

This test does not include all possible genetic variants linked to AAT deficiency.

This test does not provide a complete assessment of risk for lung or liver disease in people with variants linked to AAT deficiency.

Is this answer helpful? Yes No

The report says the variants included in this test are most common and best studied in people of European descent. What if I'm not of European descent?

The tested variants are expected to be less common in people who are only partly of European descent or not of European descent.

The effect of these variants on a person's risk of developing lung or liver disease related to alpha-1 antitrypsin deficiency is best understood in people of European descent. However, if a person who is not of European descent has one or more of these genetic variants, he/she is still expected to have a similar elevated risk of developing lung or liver disease. See Scientific Details for more information.

Is this answer helpful? Yes No

Where can I learn more about alpha-1 antitrypsin deficiency, support groups, and other resources?

You can learn more about alpha-1 antitrypsin deficiency from the following resources:

- Alpha-1 Foundation
- Alpha-1 Global
- AlphaNet

If you have questions about your results or how they might affect you or your family, a genetic counselor may be able to help. Learn more about genetic counseling.

Is this answer helpful? Yes No

My report says one variant called PI*S was detected. What does this mean?

This means you have one of the two genetic variants we tested. People with one copy of the PI*S genetic variant are not likely at risk of developing lung or liver disease related to alpha-1 antitrypsin deficiency.

Is this answer helpful? Yes No

What does not likely at risk of developing lung or liver disease related to AAT deficiency mean?

The alpha-1 antitrypsin (AAT) protein is important for protecting the lungs from inflammation. AAT deficiency is associated with decreased levels of the AAT protein in the lungs and a buildup of AAT in the liver. For people with certain combinations of genetic variants, these altered AAT levels can lead to lung and/or liver disease. However, research shows that people with one copy of the PI*S variant typically do not have significantly decreased AAT levels, so they are not considered to be at risk of developing lung or liver disease related to this condition. See the Health Risk Estimates table on the Scientific Details page for more information.

Is this answer helpful? Yes No

My report says one variant called PI*S was detected. What are some things I could do?

This result is not typically associated with an increased risk of developing lung or liver disease related to alpha-1 antitrypsin (AAT) deficiency.

Consider talking to a healthcare professional about additional testing if:

- You have a family history of lung or liver disease.
- You think you might have symptoms of AAT deficiency.
- You have concerns about your results.

Is this answer helpful? Yes No

How could my result affect my family?

Since you share DNA with your family members, they may also be interested in your result. If you are thinking about talking to family members about your results, see this article for a discussion of things to consider before having the conversation.

Because you have one variant, it is expected that:

- Each of your children has a 50% chance of inheriting this variant from you.
- At least one of your parents has this variant.
- Each of your siblings has a 50% chance of having this variant.

If your partner has a variant linked to alpha-1 antitrypsin deficiency, your children could inherit a combination of variants that may put them at risk of developing lung or liver disease.

Is this answer helpful? Yes No

Have more questions? Check out our Customer Care Help Center.

Receive up to $20 when you refer family and friends to 23andMe. Get started today.

©2017 23andMe, Inc. All Rights Reserved.