NAME _____ DATE _____

Allele Profile

Alpha-1 Antitrypsin Deficiency, Allele D1

Basic Information

Genetic Disorder – **Alpha-1 Antitrypsin Deficiency**, also called Alpha-1 or AAT deficiency

Affected Gene – ***SERPINA1***

Affected Protein – The affected gene codes for the protein **alpha-1 antitrypsin** (AAT)

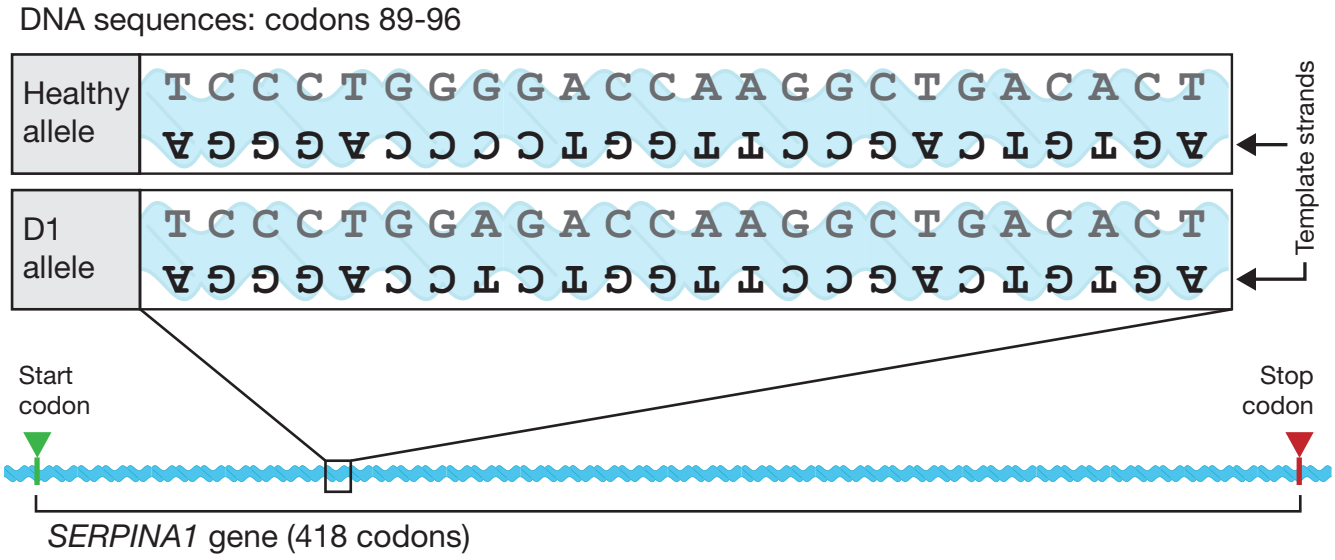
Allele – **D1**

There are more than 120 versions, or alleles, of the SERPINA1 gene. Some cause genetic disorders and some do not. Your assigned allele is one of several dozen that can cause alpha-1 antitrypsin deficiency.

Mutations & Alleles

The protein-coding portion of the *SERPINA1* gene is 1,254 nucleotides long, and it has 418 codons.

The DNA sequence of your allele is identical to a healthy allele for most of its length. The place where they differ is shown in detail:

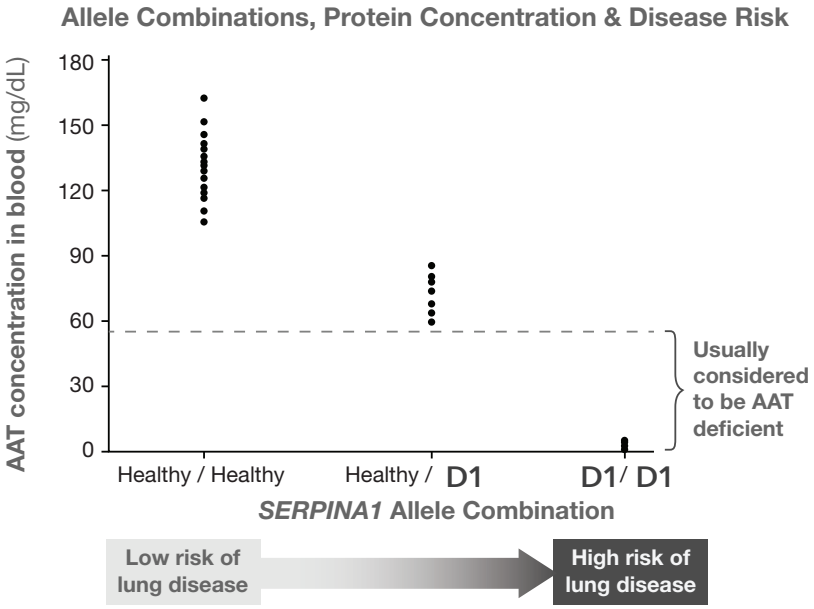


NAME _____ DATE _____

Inheritance

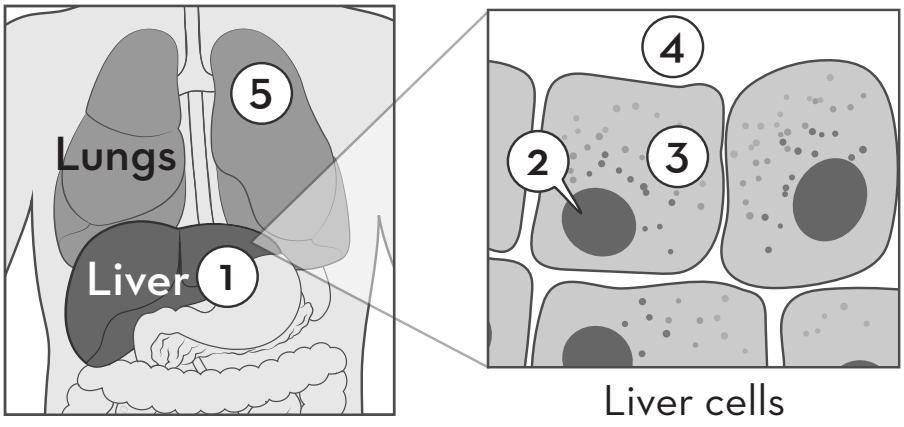
Everyone inherits two alleles of *SERPINA1*, and AAT protein is normally made (expressed) from both. AAT protein is normally released into the blood stream, where it can be measured by a blood test.

The *SERPINA1* alleles that a person has influences how much AAT protein they have in their blood. The graph shows how much AAT protein is in the blood of people with different allele combinations (each point represents one person). *[data based on Ferrarotti et al (2012) and Brode et al (2012)]*



Protein Function & Gene Expression

1. The D1 allele is switched on in liver cells (same as healthy alleles).
2. Liver cells do read the D1 allele and build proteins.
3. The AAT protein made from the D1 allele is altered. It isn't processed correctly, and it is broken down inside the cell soon after it's made.



4. The protein never gets out of the liver cells that make it, so it can't do its job.
5. People with two D1 alleles have a high risk for lung damage. Other organs usually are not affected.

NAME _____ DATE _____

Allele Profile

Alpha-1 Antitrypsin Deficiency, Allele D2

Basic Information

Genetic Disorder – **Alpha-1 Antitrypsin Deficiency**, also called Alpha-1 or AAT deficiency

Affected Gene – ***SERPINA1***

Affected Protein – The affected gene codes for the protein **alpha-1 antitrypsin** (AAT)

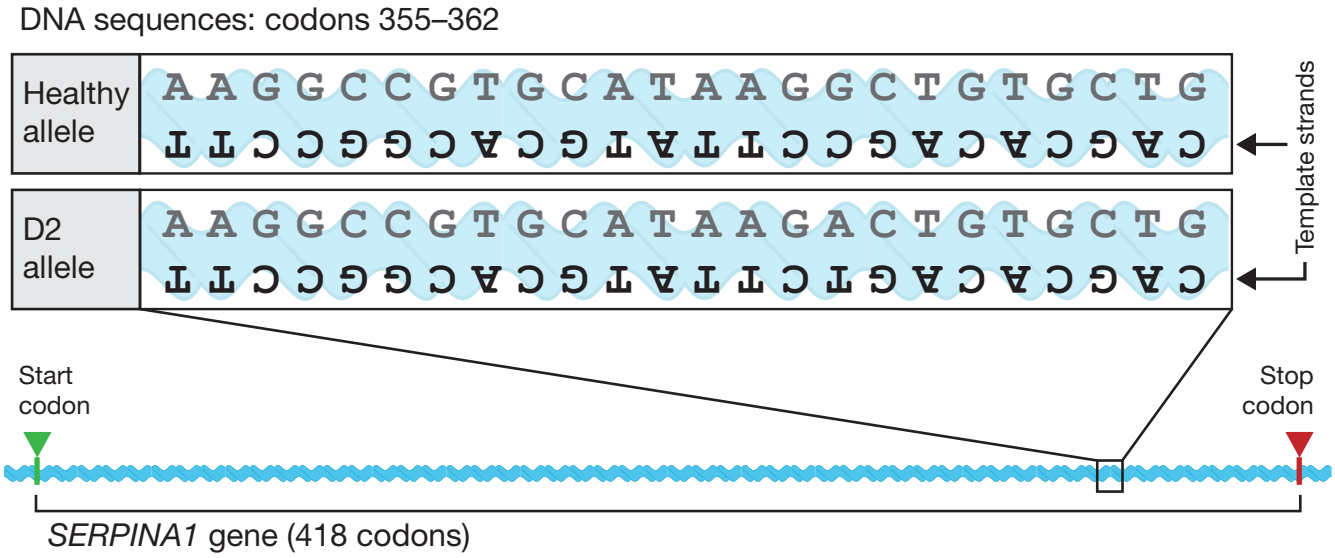
Allele – **D2**

There are more than 120 versions, or alleles, of the SERPINA1 gene. Some cause genetic disorders and some do not. Your assigned allele is one of several dozen that can cause alpha-1 antitrypsin deficiency.

Mutations & Alleles

The protein-coding portion of the *SERPINA1* gene is 1,254 nucleotides long, and it has 418 codons.

The DNA sequence of your allele is identical to a healthy allele for most of its length. The place where they differ is shown in detail:

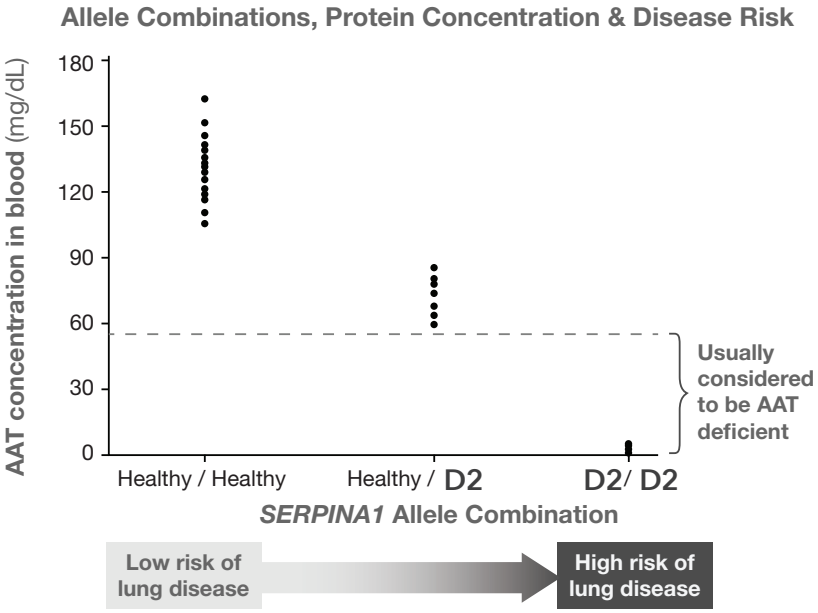


NAME _____ DATE _____

Inheritance

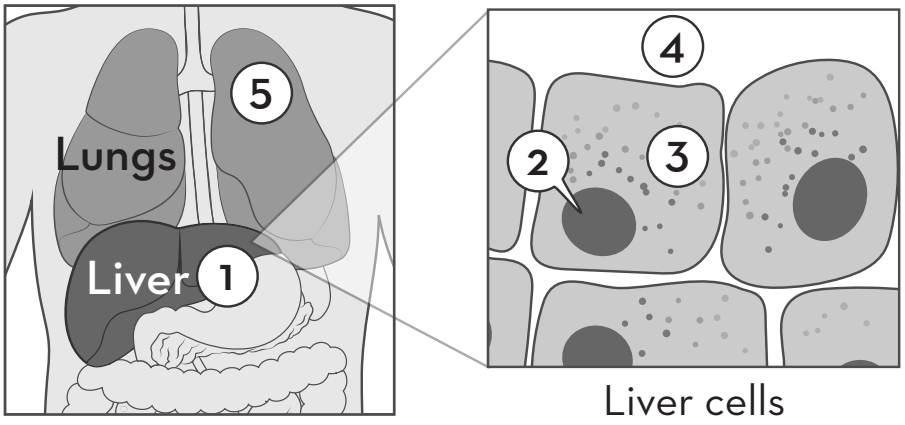
Everyone inherits two alleles of *SERPINA1*, and AAT protein is normally made (expressed) from both. AAT protein is normally released into the blood stream, where it can be measured by a blood test.

The *SERPINA1* alleles that a person has influences how much AAT protein they have in their blood. The graph shows how much AAT protein is in the blood of people with different allele combinations (each point represents one person). *[data based on Ferrarotti et al (2012) and Brode et al (2012)]*



Protein Function & Gene Expression

1. The D2 allele is switched on in liver cells (same as healthy alleles).
2. Liver cells do read the D2 allele and build proteins.
3. The AAT protein made from the D2 allele is altered. It isn't processed correctly, and it is broken down inside the cell soon after it's made.



4. The protein never gets out of the liver cells that make it, so it can't do its job.
5. People with two D2 alleles have a high risk for lung damage. Other organs usually are not affected.

NAME _____ DATE _____

Allele Profile

Alpha-1 Antitrypsin Deficiency, Allele D3

Basic Information

Genetic Disorder – **Alpha-1 Antitrypsin Deficiency**, also called Alpha-1 or AAT deficiency

Affected Gene – ***SERPINA1***

Affected Protein – The affected gene codes for the protein **alpha-1 antitrypsin** (AAT)

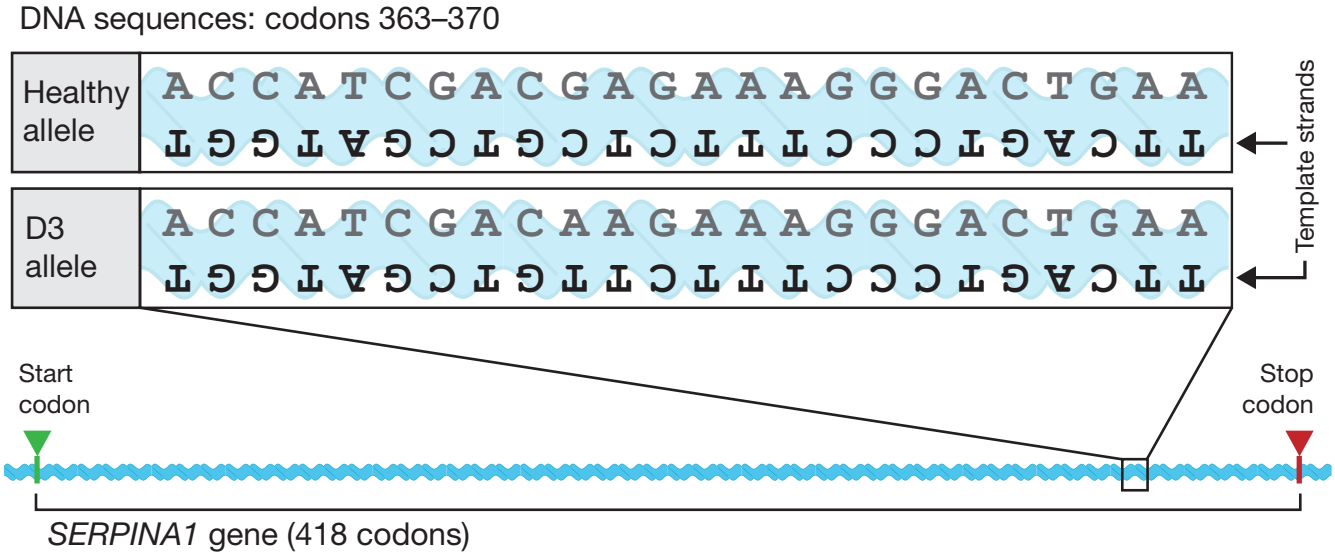
Allele – **D3**

There are more than 120 versions, or alleles, of the SERPINA1 gene. Some cause genetic disorders and some do not. Your assigned allele is one of several dozen that can cause alpha-1 antitrypsin deficiency.

Mutations & Alleles

The protein-coding portion of the *SERPINA1* gene is 1,254 nucleotides long, and it has 418 codons.

The DNA sequence of your allele is identical to a healthy allele for most of its length. The place where they differ is shown in detail:

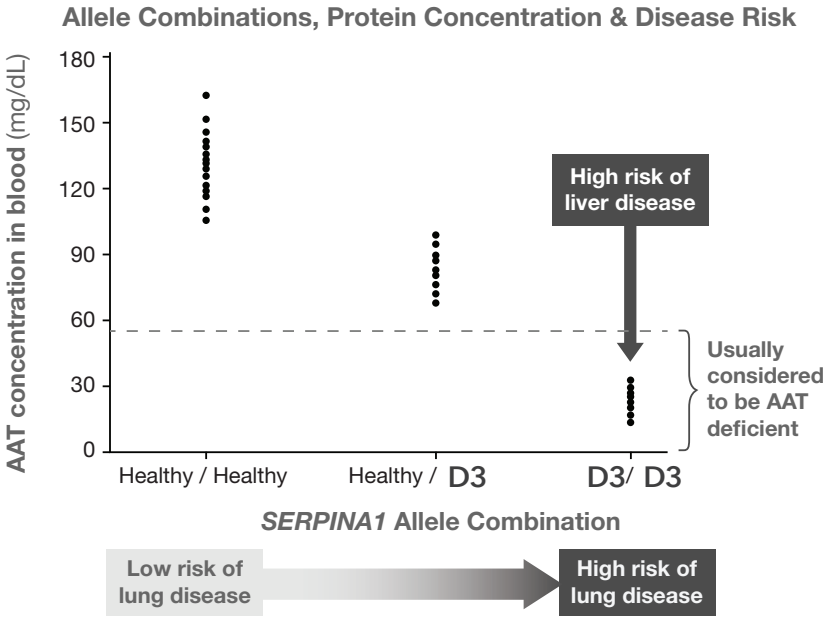


NAME _____ DATE _____

Inheritance

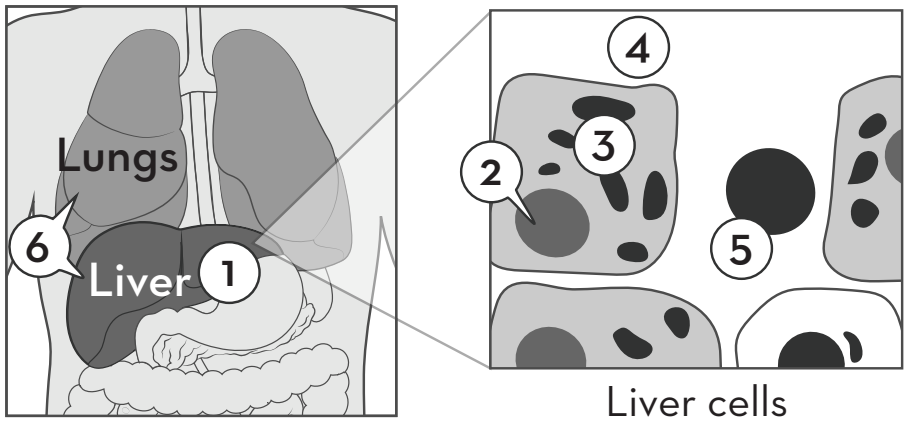
Everyone inherits two alleles of *SERPINA1*, and AAT protein is normally made (expressed) from both. AAT protein is normally released into the blood stream, where it can be measured by a blood test.

The *SERPINA1* alleles that a person has influences how much AAT protein they have in their blood. The graph shows how much AAT protein is in the blood of people with different allele combinations (each point represents one person). *[data based on Ferrarotti et al (2012) and Brode et al (2012)]*



Protein Function & Gene Expression

1. The D3 allele is switched on in liver cells (same as healthy alleles).
2. Liver cells do read the D3 allele and build proteins.
3. The protein made from the D3 allele is altered: it's sticky. As the proteins are made, they form large clumps, which build up inside the liver cells.



4. The AAT protein doesn't get out of the cells that make it, so it can't do its job.
5. Liver cells can break down the clumps, but slowly. If there is too much sticky protein (like if someone has two D3 alleles), the clumps build up faster than the cells can break them down. Clumps can fill the cells, causing cell death, scarring, and other damage to liver tissue.
6. People with two D3 alleles have a high risk for damage to both the lungs and the liver. Liver problems can show up in babies, or they may appear later in childhood or adulthood. Even people with one D3 allele and one healthy allele can have liver damage.

NAME _____ DATE _____

Allele Profile

Alpha-1 Antitrypsin Deficiency, Allele D4

Basic Information

Genetic Disorder – **Alpha-1 Antitrypsin Deficiency**, also called Alpha-1 or AAT deficiency

Affected Gene – ***SERPINA1***

Affected Protein – The affected gene codes for the protein **alpha-1 antitrypsin** (AAT)

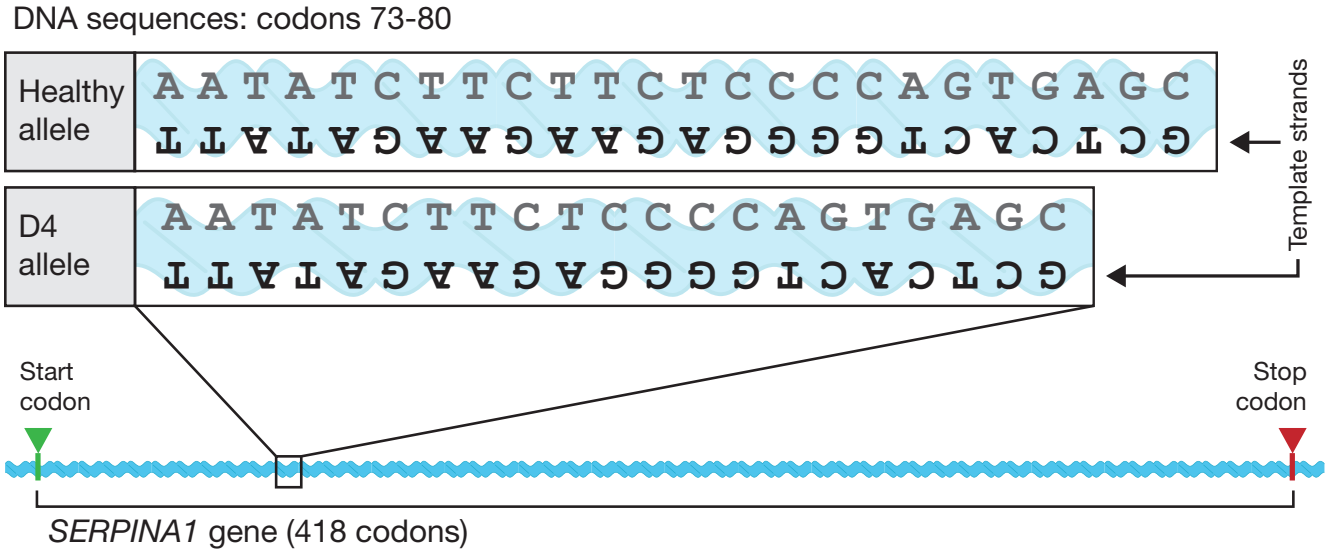
Allele – **D4**

There are more than 120 versions, or alleles, of the SERPINA1 gene. Some cause genetic disorders and some do not. Your assigned allele is one of several dozen that can cause alpha-1 antitrypsin deficiency.

Mutations & Alleles

The protein-coding portion of the *SERPINA1* gene is 1,254 nucleotides long, and it has 418 codons.

The DNA sequence of your allele is identical to a healthy allele for most of its length. The place where they differ is shown in detail:

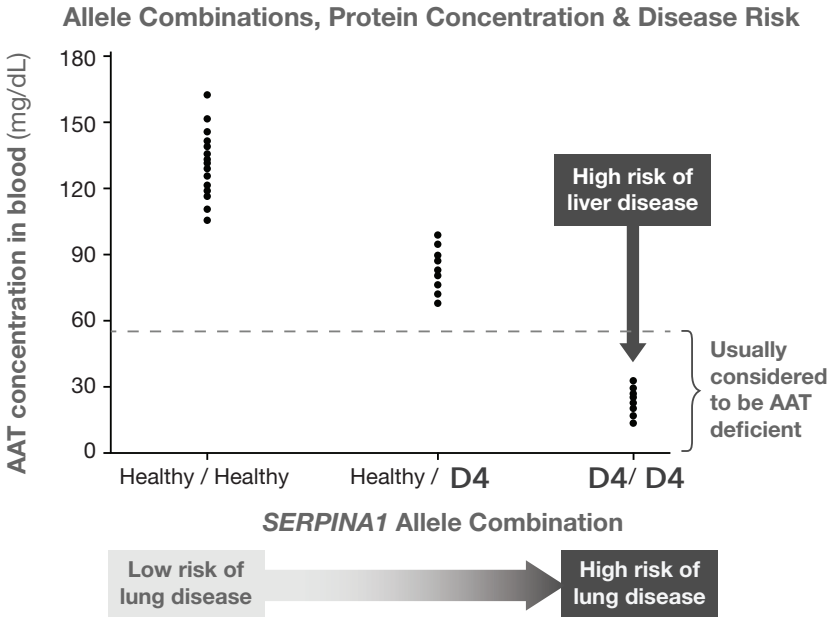


NAME _____ DATE _____

Inheritance

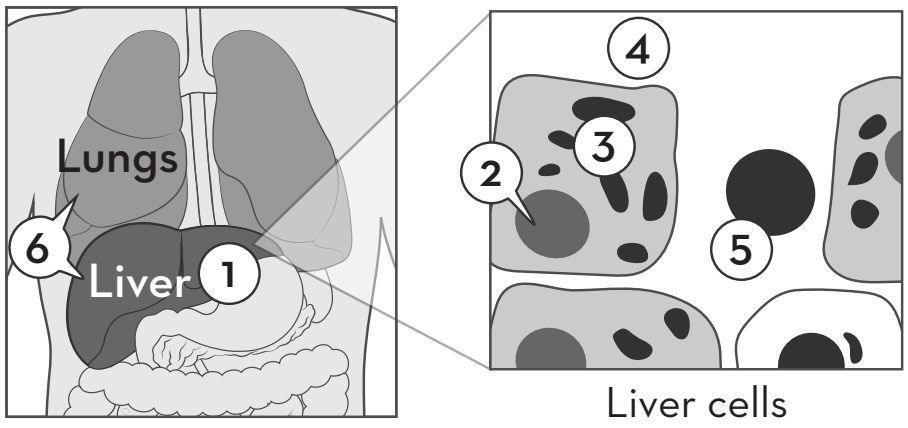
Everyone inherits two alleles of *SERPINA1*, and AAT protein is normally made (expressed) from both. AAT protein is normally released into the blood stream, where it can be measured by a blood test.

The *SERPINA1* alleles that a person has influences how much AAT protein they have in their blood. The graph shows how much AAT protein is in the blood of people with different allele combinations (each point represents one person). *[data based on Ferrarotti et al (2012) and Brode et al (2012)]*



Protein Function & Gene Expression

1. The D4 allele is switched on in liver cells (same as healthy alleles).
2. Liver cells do read the D4 allele and build proteins.
3. The protein made from the D4 allele is altered: it's sticky. As the proteins are made, they form large clumps, which build up inside the liver cells.



4. The AAT protein doesn't get out of the cells that make it, so it can't do its job.
5. Liver cells can break down the clumps, but slowly. If there is too much sticky protein (like if someone has two D4 alleles), the clumps build up faster than the cells can break them down. Clumps can fill the cells, causing cell death, scarring, and other damage to liver tissue.
6. People with two D4 alleles have a high risk for damage to both the lungs and the liver. Liver problems can show up in babies, or they may appear later in childhood or adulthood. Even people with one D4 allele and one healthy allele can have liver damage.

NAME _____ DATE _____

Allele Profile

Alpha-1 Antitrypsin Deficiency, Allele D5

Basic Information

Genetic Disorder – **Alpha-1 Antitrypsin Deficiency**, also called Alpha-1 or AAT deficiency

Affected Gene – ***SERPINA1***

Affected Protein – The affected gene codes for the protein **alpha-1 antitrypsin** (AAT)

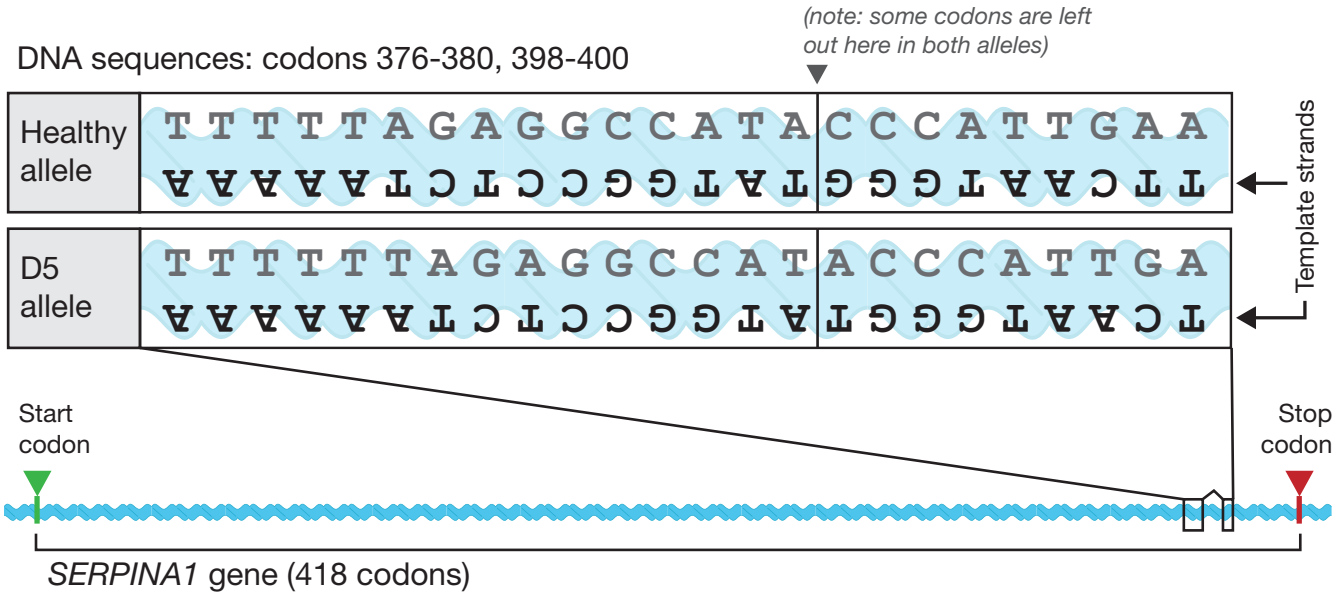
Allele – **D5**

There are more than 120 versions, or alleles, of the SERPINA1 gene. Some cause genetic disorders and some do not. Your assigned allele is one of several dozen that can cause alpha-1 antitrypsin deficiency.

Mutations & Alleles

The protein-coding portion of the *SERPINA1* gene is 1,254 nucleotides long, and it has 418 codons.

The DNA sequence of your allele is identical to a healthy allele for most of its length. The place where they differ is shown in detail:

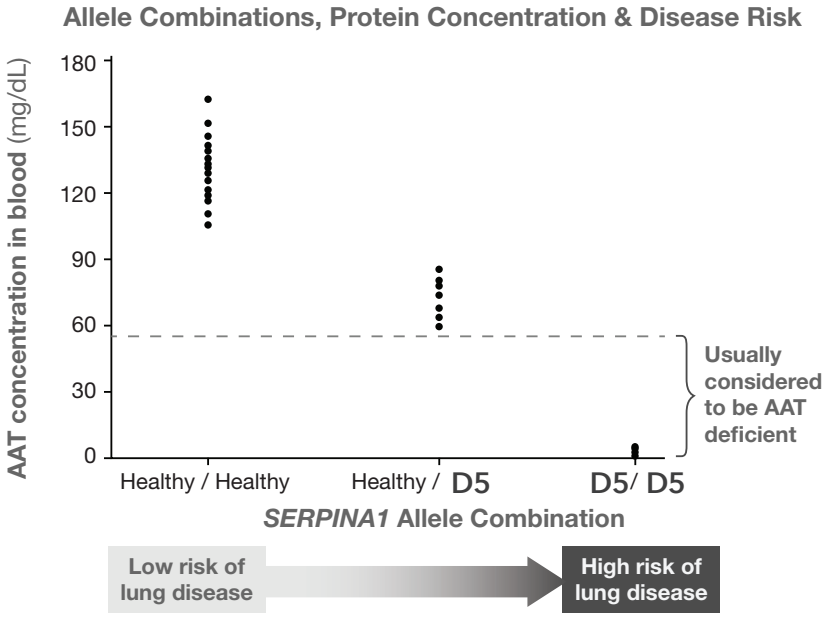


NAME _____ DATE _____

Inheritance

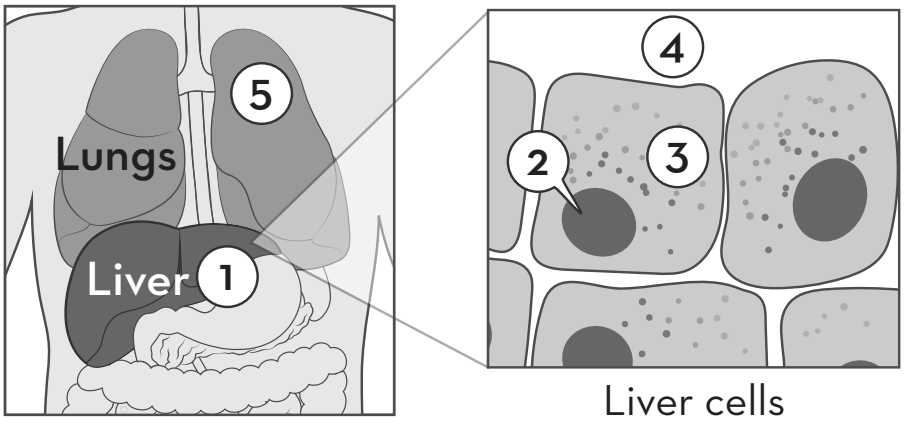
Everyone inherits two alleles of *SERPINA1*, and AAT protein is normally made (expressed) from both. AAT protein is normally released into the blood stream, where it can be measured by a blood test.

The *SERPINA1* alleles that a person has influences how much AAT protein they have in their blood. The graph shows how much AAT protein is in the blood of people with different allele combinations (each point represents one person). *[data based on Ferrarotti et al (2012) and Brode et al (2012)]*



Protein Function & Gene Expression

1. The D5 allele is switched on in liver cells (same as healthy alleles).
2. Liver cells do read the D5 allele and build proteins.
3. The AAT protein made from the D5 allele is altered. It isn't processed correctly, and it is broken down inside the cell soon after it's made.



4. The protein never gets out of the liver cells that make it, so it can't do its job.
5. People with two D5 alleles have a high risk for lung damage. Other organs usually are not affected.

NAME _____ DATE _____

Allele Profile

SERPINA1, Allele D6

Basic Information

Genetic Disorder – **Bleeding disorder**

Affected Gene – **SERPINA1**

Affected Protein – The affected gene codes for the protein **alpha-1 antitrypsin** (AAT)

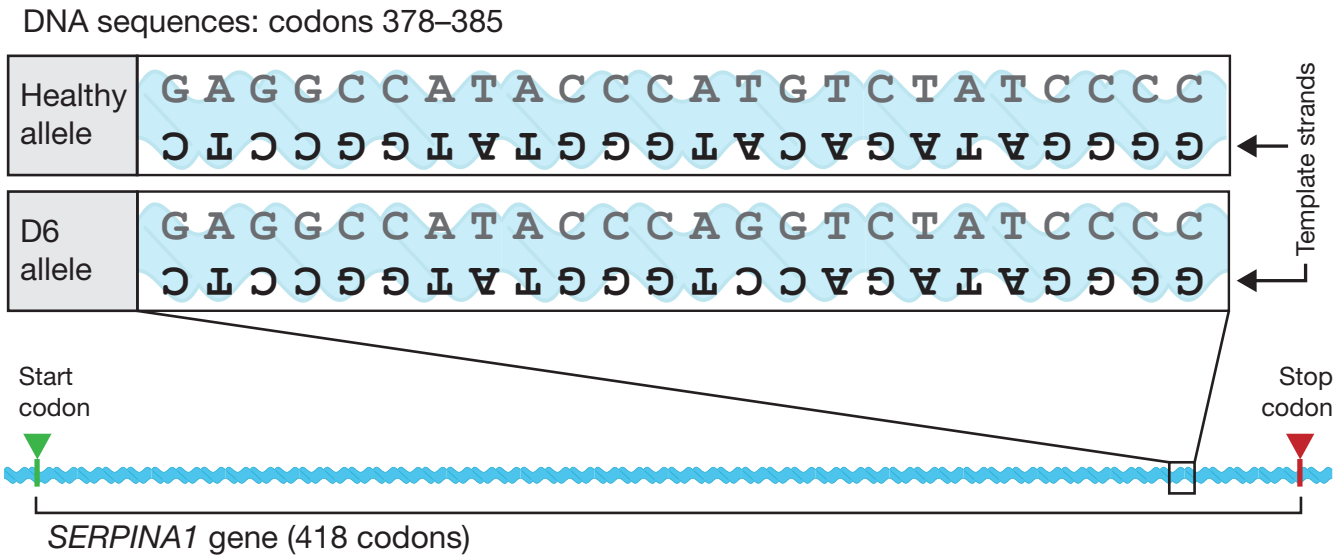
Allele – **D6**

There are more than 120 versions, or alleles, of the SERPINA1 gene. Some cause genetic disorders and some do not. Your assigned allele causes a severe bleeding disorder.

Mutations & Alleles

The protein-coding portion of SERPINA1 gene is 1,254 nucleotides long, and it has 418 codons.

The DNA sequence of your allele is identical to a healthy allele for most of its length. The place where they differ is shown in detail:



Inheritance

Everyone inherits two alleles of SERPINA1, and protein is normally made (expressed) from both. The SERPINA1 alleles that a person has influences both how much AAT protein they make, and how that protein functions.

Having just one D6 allele causes the blood to form clots very slowly. This can lead to severe bleeding from a bruise or a cut.

Everyone who has had a D6 allele has also had one healthy SERPINA1 allele. Thus, they still made enough working AAT to protect their lungs.

The D6 allele is incredibly rare. As of 2016, it has been found in only 5 individuals.

For the Inheritance section of your Lab Notebook, Pages 3–4:

- Question 4: Since there is no data table here, just interpret the information above.
- Question 5: Come up with a symbol to show a protein that has gained a new function.
- Question 6: You do not have the information to answer the question about Person C — but what do you think might happen if someone had this allele combination?
- Question 7: Draw a model for a person with a D6 allele in combination with an allele that can cause alpha-1 antitrypsin deficiency. What type of genetic disorder/s do you think they would have?

Protein Function & Gene Expression

Like with healthy alleles, the D6 allele is switched on in liver cells. So liver cells do read the D6 allele and build proteins. And, like with healthy AAT protein, the liver cells release these protein into the blood stream.

However, the D6 allele codes for an altered version of AAT protein. The change is small, but it completely changes the function of the protein. The protein no longer attaches to and deactivates elastase. Instead, it attaches to and deactivates a different protein: one that is necessary for forming blood clots. The effect is that the blood forms clots very slowly, leading to severe bleeding from a cut or bruise.

Other Factors

People with the D6 allele often have varied symptoms that first appear at different times. Clotting ability also tends to change over time. But since the D6 allele is so rare (it has been found in just a few people), it's unclear what causes these differences.

Bleeding episodes in people with a D6 allele usually happened after a severe injury, surgery, or another high-stress event. Usually, the bleeding stopped after patients were given blood, plasma transfusions, and/or medication to encourage clotting.