NAME _____ DATE _____

Allele Profile

Hemophilia A, Allele H1

Basic Information

More information at Learn.Genetics.utah.edu/content/genetics/hemophilia/

Genetic Disorder – Hemophilia A

Affected Gene – ***F8***

Affected Protein – The affected gene codes for the protein **coagulation factor VIII**

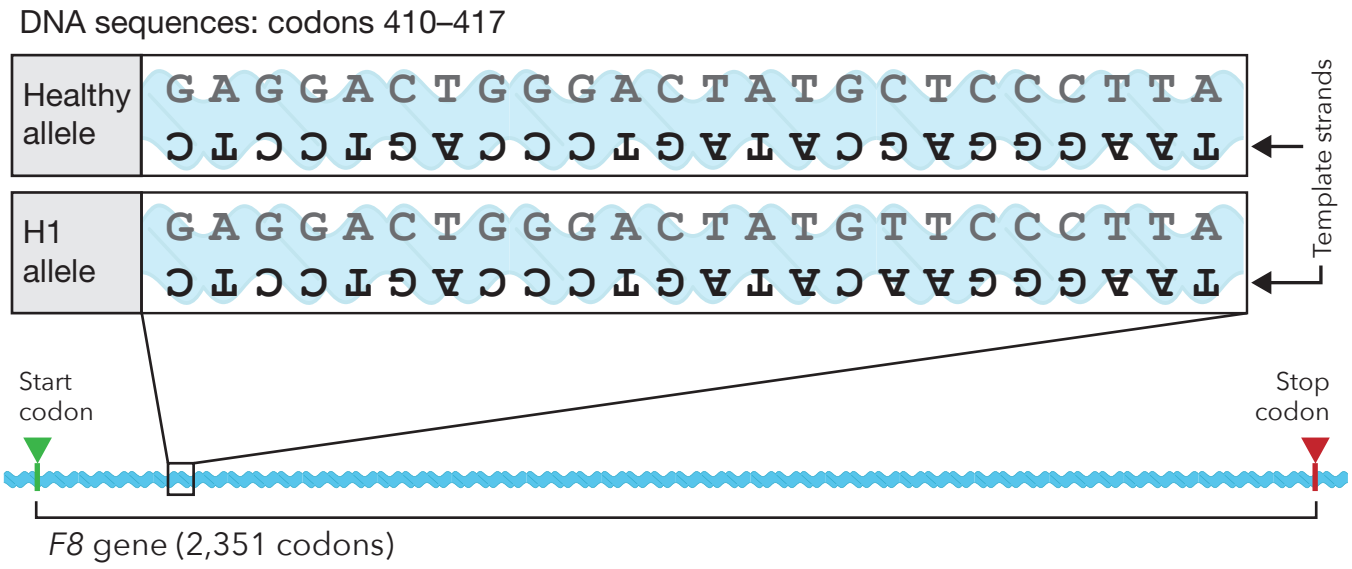
Allele – **H1**

There are more than 3,000 versions, or alleles, of the *F8* gene. Some cause genetic disorders and some do not. Your assigned allele is one that can cause hemophilia A.

Mutations & Alleles

The protein-coding portion of the *F8* gene is 7,053 nucleotides long, and it has 2,351 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:



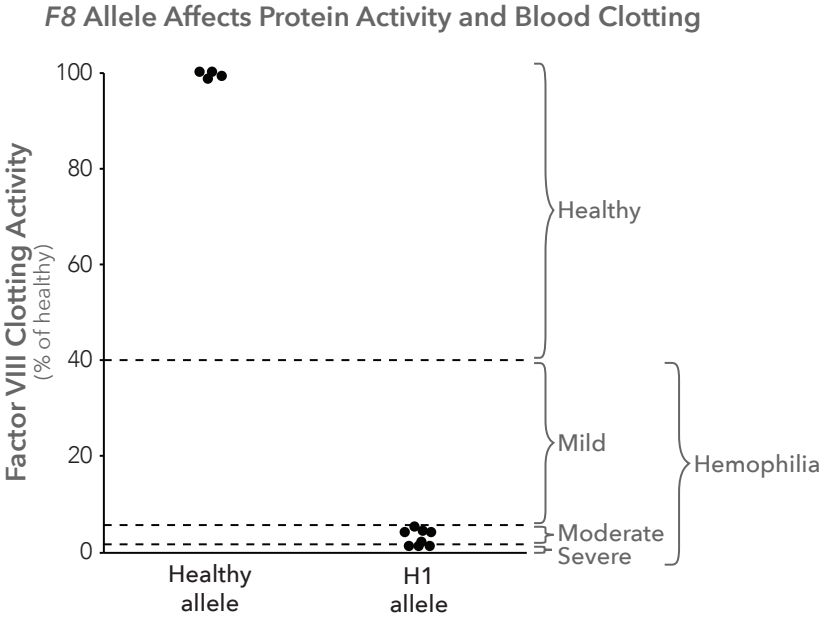
NAME _____ DATE _____

Inheritance

The *F8* gene is on the X-chromosome. XY males inherit one allele of *F8*, and XX females inherit two. Coagulation factor VIII protein is made from each allele a person has, then released into the blood stream.

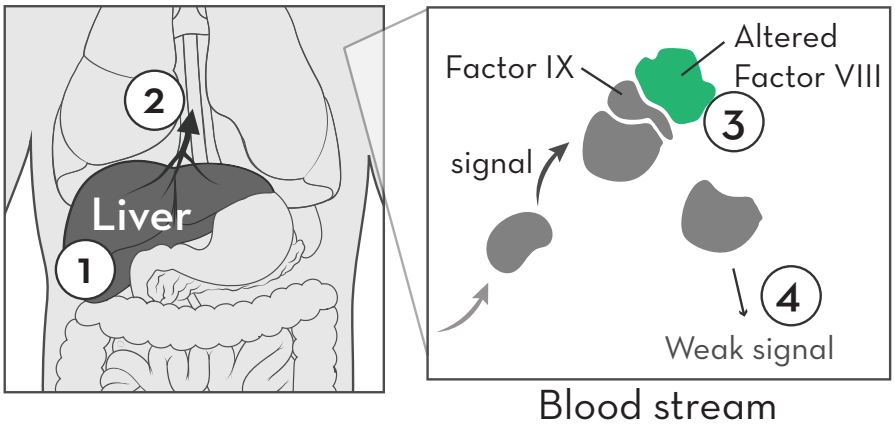
Depending on which *F8* allele/s a person has, blood can have higher or lower clotting activity. When activity is high, blood clots properly. In people with hemophilia A, activity is too low, and blood clots poorly.

The graph shows factor VIII clotting activity in XY males with different *F8* alleles. Each point represents one person.



In your Lab Notebook, page 4, the models in question 6 show the allele and protein combinations for females. For question 7, draw models to show the possible alleles and proteins for males.

Protein Function & Gene Expression



1. The H1 allele is switched on in liver cells (same as healthy alleles).
2. Liver cells read the H1 allele and build factor VIII proteins, and proteins are released into the blood stream.
3. But there is a small change to the protein's structure that makes it less able to do its job. It doesn't effectively carry the signal to tell blood to clot.
4. The signal is weak, and blood clots much more slowly than usual.

Men with the H1 allele have moderate to severe hemophilia. Without treatment, a cut or injury might cause dangerous blood loss. They are also at risk of joint damage from internal bleeding.

NAME _____ DATE _____

Allele Profile

Hemophilia B, Allele H2

Basic Information

Genetic Disorder – Hemophilia B

Affected Gene – ***F9***

Affected Protein – The affected gene codes for the protein **coagulation factor IX**

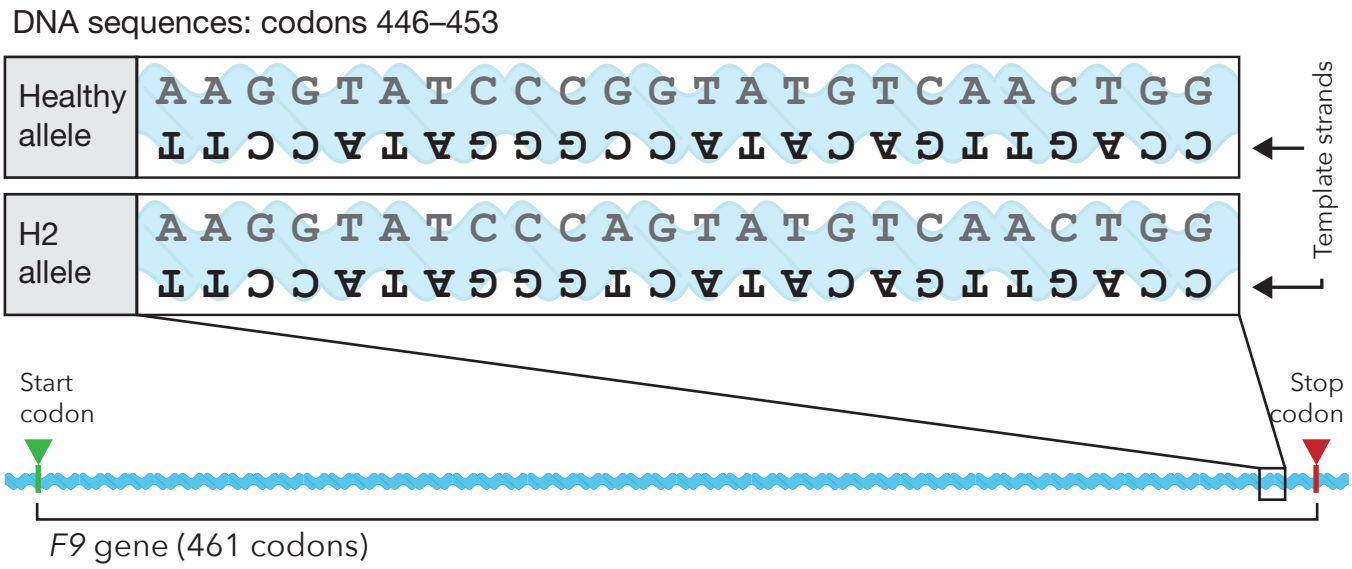
Allele – **H2**

There are more than 1,000 versions, or alleles, of the *F9* gene. Some cause genetic disorders and some do not. Your assigned allele is one that can cause hemophilia B.

Mutations & Alleles

The protein-coding portion of the *F9* gene is 1,383 nucleotides long, and it has 461 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:



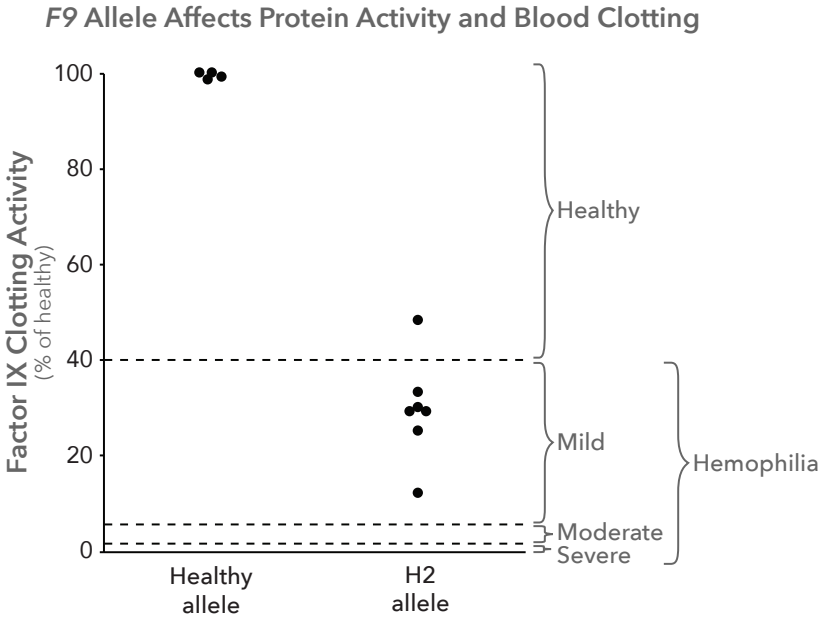
NAME _____ DATE _____

Inheritance

The *F9* gene is on the X-chromosome. XY males inherit one allele of *F9*, and XX females inherit two. Coagulation factor IX protein is made from each allele a person has, then released into the blood stream.

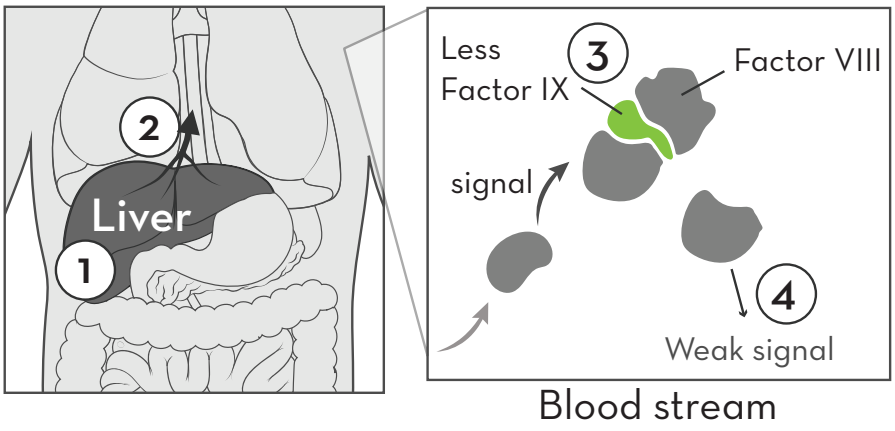
Depending on which *F9* allele/s a person has, blood can have higher or lower clotting activity. When activity is high, blood clots properly. In people with hemophilia B, activity is too low, and blood clots poorly.

The graph shows factor IX clotting activity in blood from XY males with different *F9* alleles. Each point represents one person.



In your Lab Notebook, page 4, the models in question 6 show the allele and protein combinations for females. For question 7, draw models to show the possible alleles and proteins for males.

Protein Function & Gene Expression



1. The H2 allele is switched on in liver cells (same as healthy alleles).

   Liver cells do read the H2 allele and build factor IX proteins—but the protein is altered.

2. Little factor IX protein makes it to the blood stream. Cells make less protein overall, and some of what they make is broken down before it can be released.

3. The clotting factor IX protein that does make it to the blood can do its job. But since there's less of it, it sends less signal than usual.

4. The signal telling the blood to clot is weak, so blood clots slowly.

Men with the H2 allele usually have mild hemophilia. Their cuts may heal slowly. They may bleed for a long time after a dentist visit or surgery.

NAME _____ DATE _____

Allele Profile

Hemophilia B, Allele H3

Basic Information

Genetic Disorder – Hemophilia B

Affected Gene – ***F9***

Affected Protein – The affected gene codes for the protein **coagulation factor IX**

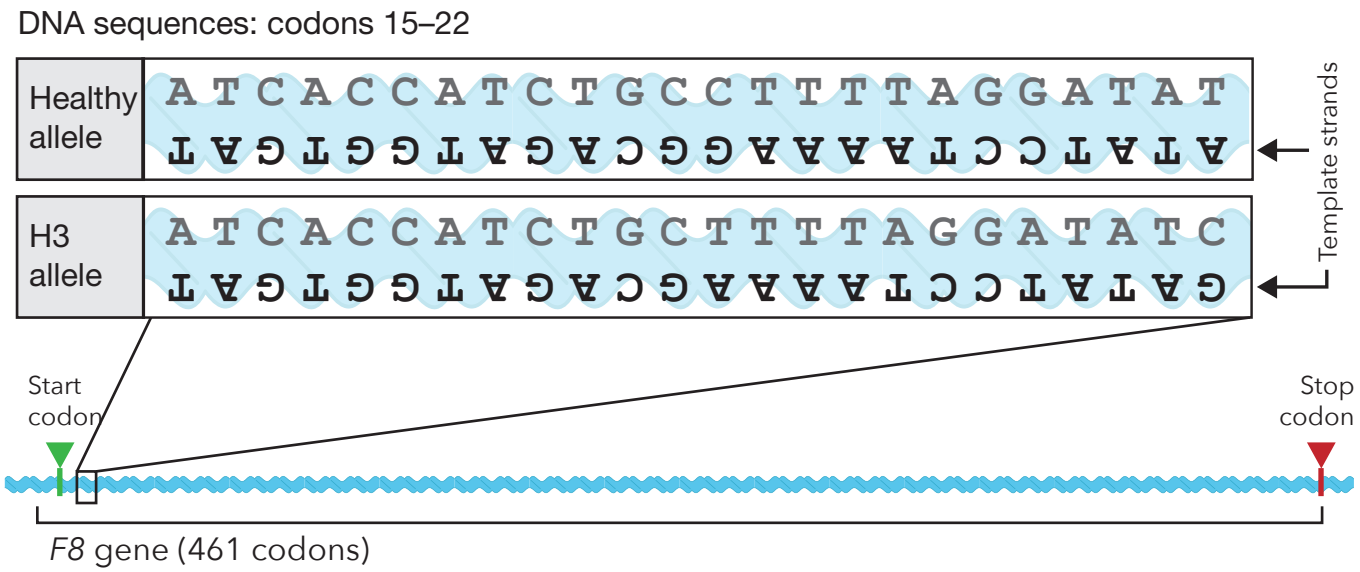
Allele – **H3**

There are more than 1,000 versions, or alleles, of the *F9* gene. Some cause genetic disorders and some do not. Your assigned allele is one that can cause hemophilia B.

Mutations & Alleles

The protein-coding portion of the *F9* gene is 1,383 nucleotides long, and it has 461 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:



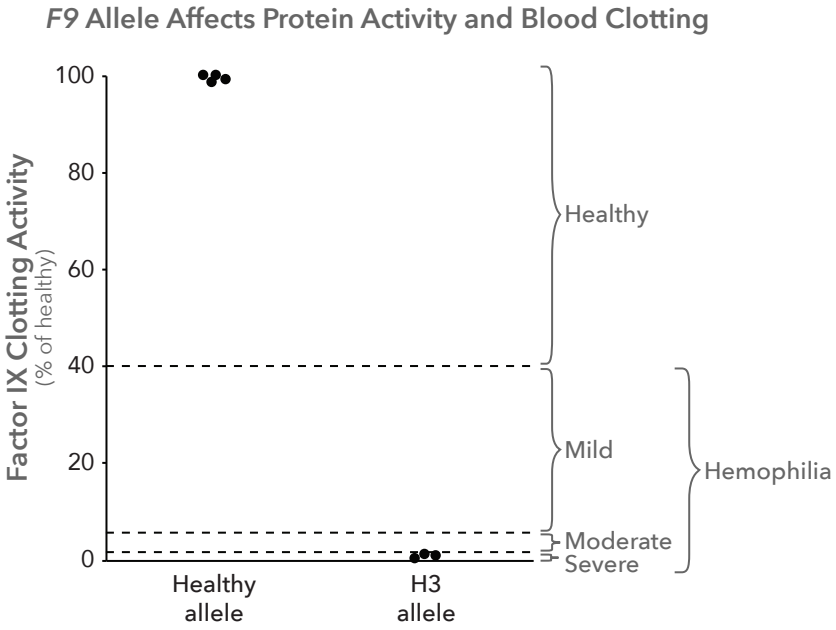
NAME _____ DATE _____

Inheritance

The *F9* gene is on the X-chromosome. XY males inherit one allele of *F9*, and XX females inherit two. Coagulation factor IX protein is made from each allele a person has, then released into the blood stream.

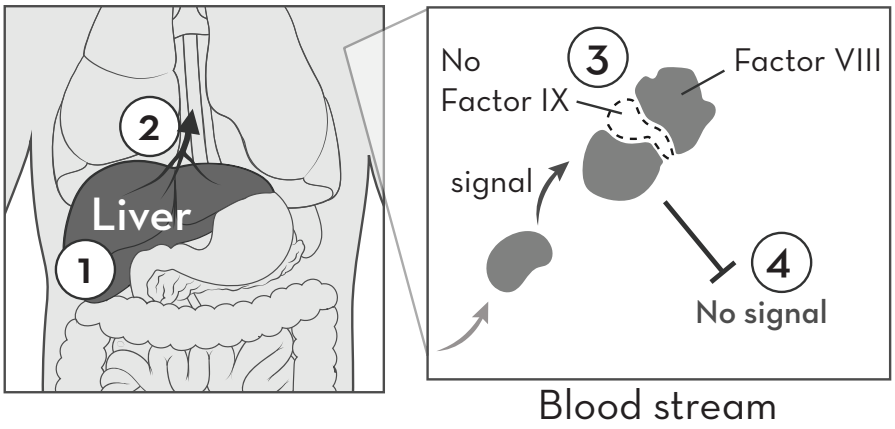
Depending on which *F9* allele/s a person has, blood can have higher or lower clotting activity. When activity is high, blood clots properly. In people with hemophilia B, activity is too low, and blood clots poorly.

The graph shows factor IX clotting activity in blood from XY males with different *F9* alleles. Each point represents one person.



In your Lab Notebook, page 4, the models in question 6 show the allele and protein combinations for females. For question 7, draw models to show the possible alleles and proteins for males.

Protein Function & Gene Expression



1. The H3 allele is switched on in liver cells (same as healthy alleles).

   Liver cells do read the H3 allele and build proteins– but the proteins are altered.

2. Only a tiny piece of factor IX protein is made. Little or no protein is released to the blood stream.

3. The blood is completely missing the function of Factor IX protein.

4. The signal telling blood to clot is not carried forward.

Men with the H3 allele have severe hemophilia. They have spontaneous bleeding that is hard to control. Without treatment, they're at risk for joint damage and seizures from internal bleeding.

NAME _____ DATE _____

Allele Profile

Hemophilia A, Allele H4

Basic Information

More information at Learn.Genetics.utah.edu/content/genetics/hemophilia/

Genetic Disorder – Hemophilia A

Affected Gene – ***F8***

Affected Protein – The affected gene codes for the protein **coagulation factor VIII**

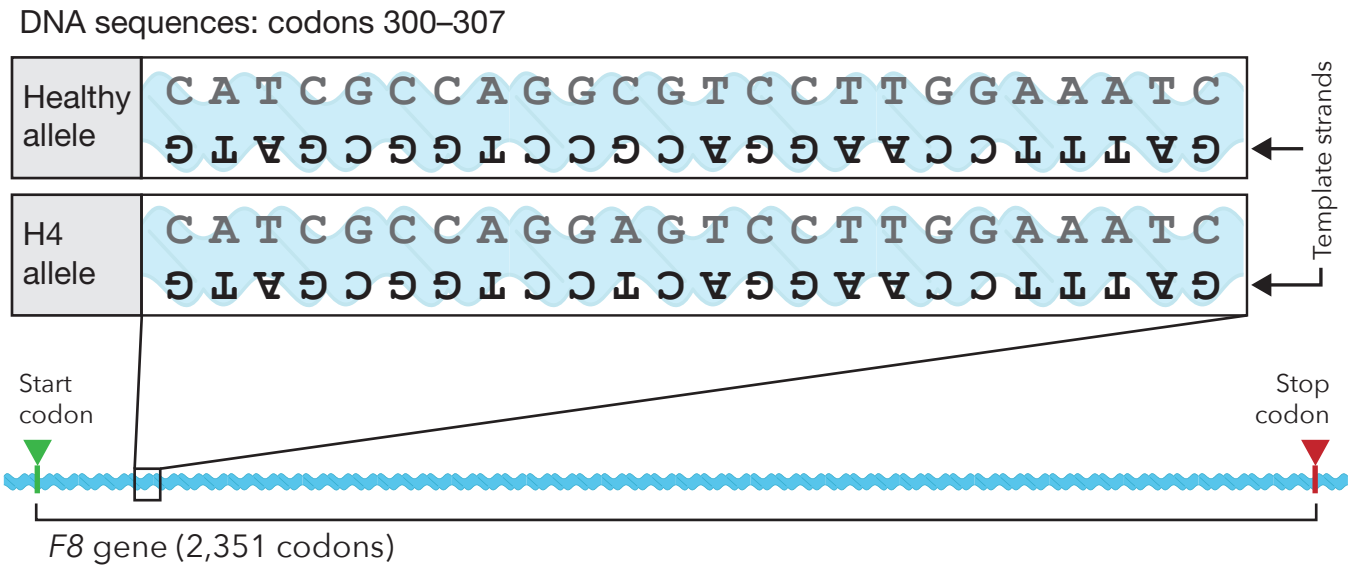
Allele – **H4**

There are more than 3,000 versions, or alleles, of the *F8* gene. Some cause genetic disorders and some do not. Your assigned allele is one that can cause hemophilia A.

Mutations & Alleles

The protein-coding portion of the *F8* gene is 7,053 nucleotides long, and it has 2,351 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:



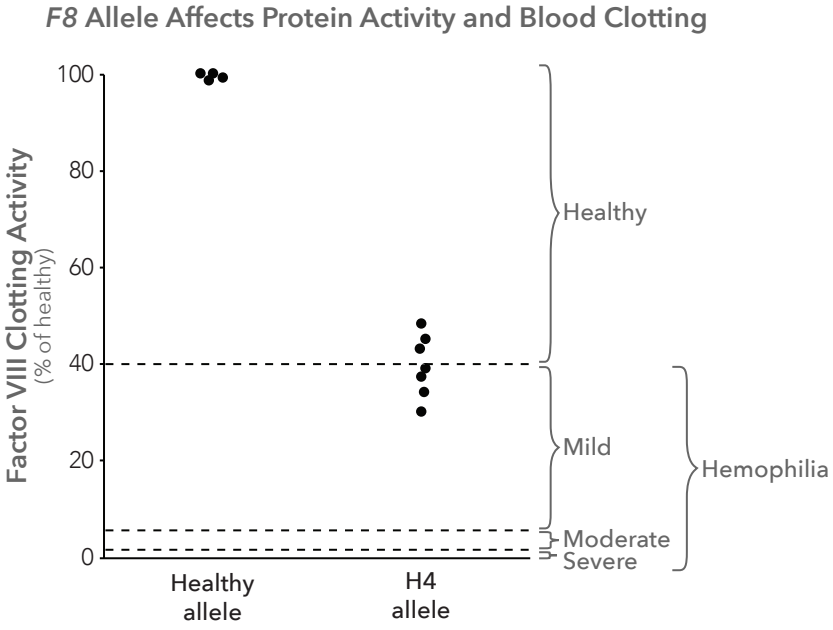
NAME _____ DATE _____

Inheritance

The *F8* gene is on the X-chromosome. XY males inherit one allele of *F8*, and XX females inherit two. Coagulation factor VIII protein is made from each allele a person has, then released into the blood stream.

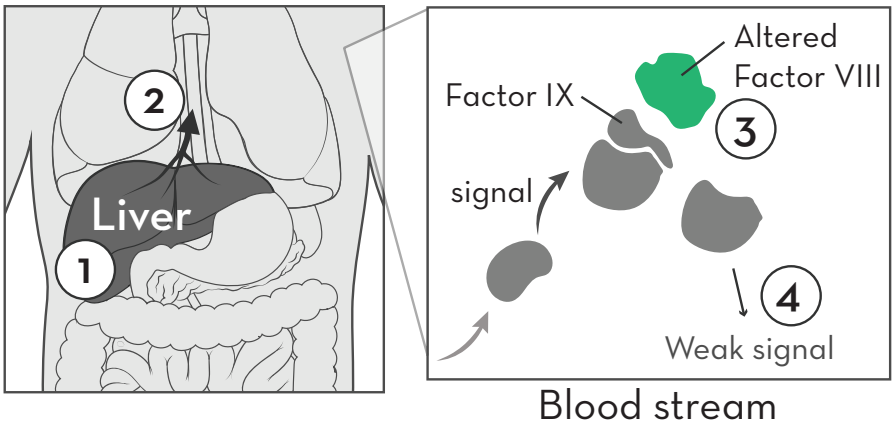
Depending on which *F8* allele/s a person has, blood can have higher or lower clotting activity. When activity is high, blood clots properly. In people with hemophilia A, activity is too low, and blood clots poorly.

The graph shows factor VIII clotting activity in XY males with different *F8* alleles. Each point represents one person.



In your Lab Notebook, page 4, the models in question 6 show the allele and protein combinations for females. For question 7, draw models to show the possible alleles and proteins for males.

Protein Function & Gene Expression



1. The H4 allele is switched on in liver cells (same as healthy alleles).
2. Liver cells read the H4 allele and build factor VIII proteins, and the proteins are released into the blood stream.
3. But there is a small change to the protein's structure that makes it less able to do its job. It doesn't attach to Factor IX very well, so it does its job slowly.
4. The signal for blood to clot is weakened, and blood clots more slowly than usual.

Men with the H4 allele usually have mild hemophilia. Blood takes longer to clot, but it eventually does. Some men with this allele may not notice symptoms. Others may heal slowly, or bleed for a long time after surgery or an injury.

NAME _____ DATE _____

Allele Profile

Hemophilia B, Allele H5

Basic Information

Genetic Disorder – Hemophilia B

Affected Gene – ***F9***

Affected Protein – The affected gene codes for the protein **coagulation factor IX**

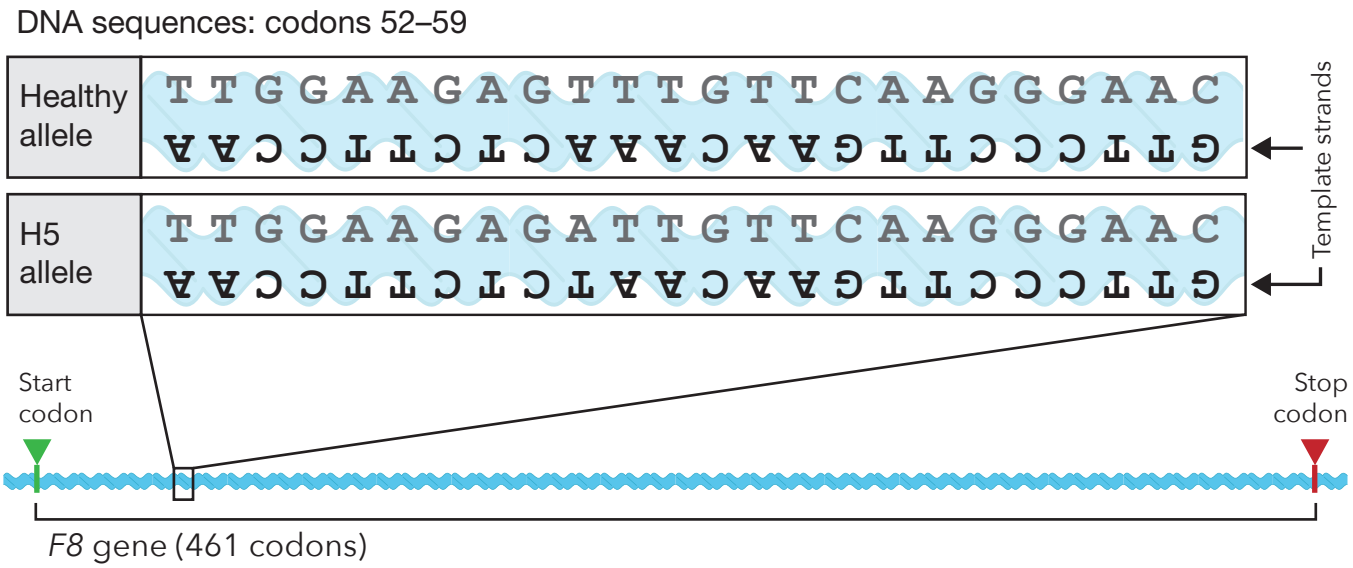
Allele – **H5**

There are more than 1,000 versions, or alleles, of the *F9* gene. Some cause genetic disorders and some do not. Your assigned allele is one that can cause hemophilia B.

Mutations & Alleles

The protein-coding portion of the *F9* gene is 1,383 nucleotides long, and it has 461 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:



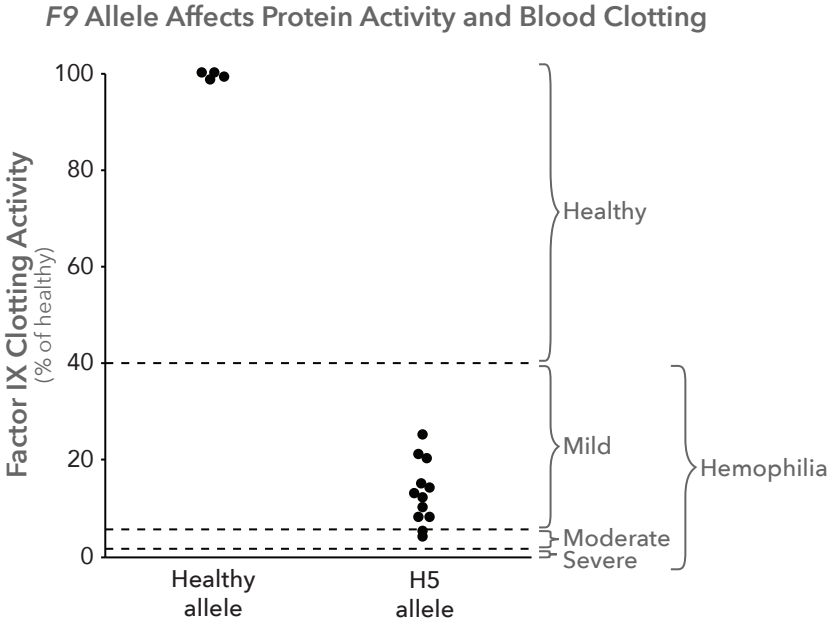
NAME _____ DATE _____

Inheritance

The *F9* gene is on the X-chromosome. XY males inherit one allele of *F9*, and XX females inherit two. Coagulation factor IX protein is made from each allele a person has, then released into the blood stream.

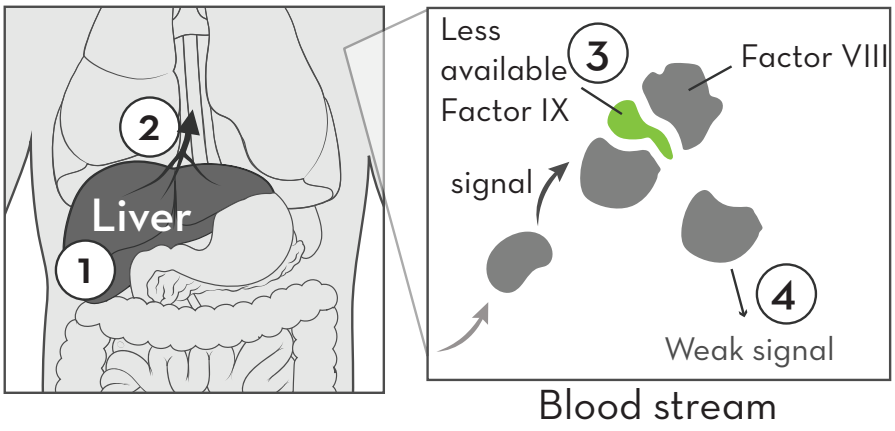
Depending on which *F9* allele/s a person has, blood can have higher or lower clotting activity. When activity is high, blood clots properly. In people with hemophilia B, activity is too low, and blood clots poorly.

The graph shows factor IX clotting activity in blood from XY males with different *F9* alleles. Each point represents one person.



In your Lab Notebook, page 4, the models in question 6 show the allele and protein combinations for females. For question 7, draw models to show the possible alleles and proteins for males.

Protein Function & Gene Expression



1. The H5 allele is switched on in liver cells (same as healthy alleles).
2. Liver cells read the H5 allele and build factor IX proteins, which are released to the blood stream.
3. But the factor IX protein is altered. It doesn't attach to platelets very well—which is where it needs to be to do its job. Less protein is available where it's needed.
4. With less factor IX protein doing its job, the signal is weak. Blood clots more slowly than usual.

Men with the H5 allele usually have mild hemophilia. Their cuts may heal slowly. They may bleed for a long time after a dentist visit or surgery.

NAME _____ DATE _____

Allele Profile

Hemophilia A, Allele H6 (Bonus Allele)

Basic Information

Genetic Disorder – Hemophilia A

Affected Gene – ***F8***

Affected Protein – The affected gene codes for the protein **coagulation factor VIII**

Allele – **H6**

There are more than 3,000 versions, or alleles, of the *F8* gene. Some cause genetic disorders and some do not. Your assigned allele is one that causes hemophilia A. In fact, almost half the people with a severe form of the disorder have this allele.

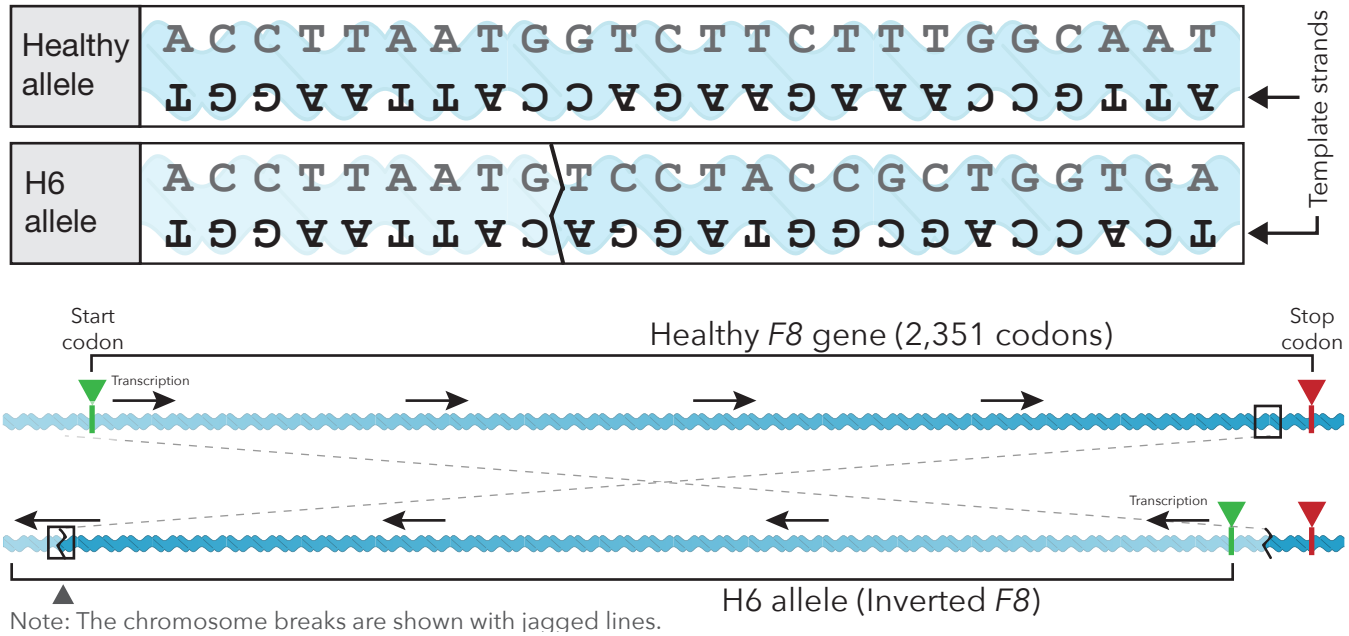
Mutations & Alleles

The protein-coding portion of the *F8* gene is 7,053 nucleotides long, and it has 2,351 codons.

Your allele came about through a chromosomal rearrangement called an inversion. A piece of a chromosome broke away, rotated 180 degrees, then fused back in place. (See learn.genetics.utah.edu/content/disorders/rearrangements.)

Much but not all of the gene is included within the inverted sequence. At one end, the break was outside of the *F8* gene, before the start codon. At the other end, the break was within the gene, before the stop codon. Transcription machinery still begins reading the inverted gene correctly. So your allele has the same sequence as a healthy allele for most of its length. The boxed area near the end of the gene, where one end of the inversion happened , is shown in detail.

DNA sequences: codons 2,141–2,143 and 2,156–2,160



Note: The chromosome breaks are shown with jagged lines.

NAME _____ DATE _____

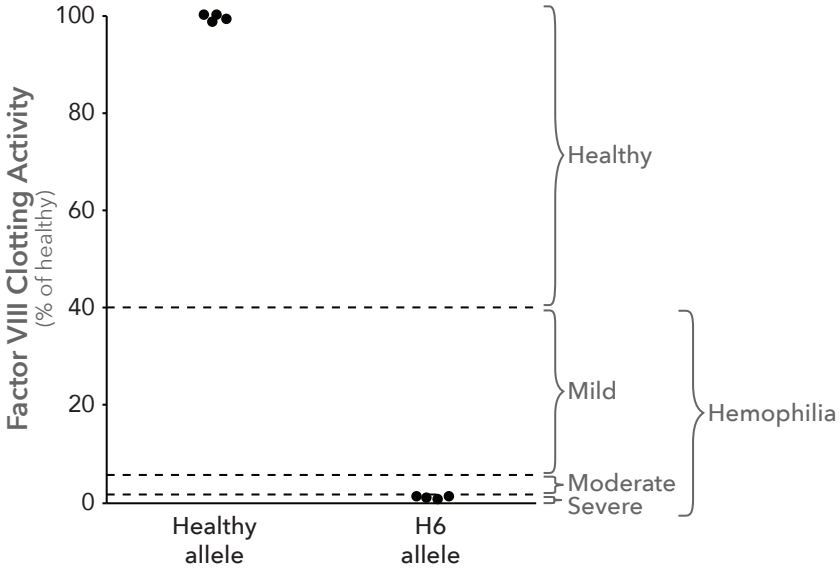
Inheritance

The *F8* gene is on the X-chromosome. XY males inherit one allele of *F8*, and XX females inherit two. Coagulation factor VIII protein is made from each allele a person has, then released into the blood stream.

Depending on which *F8* allele/s a person has, blood can have higher or lower clotting activity. When activity is high, blood clots properly. In people with hemophilia A, activity is too low, and blood clots poorly.

The graph shows factor VIII clotting activity in XY males with different *F8* alleles. Each point represents one person.

_F8_ Allele Affects Protein Activity and Blood Clotting



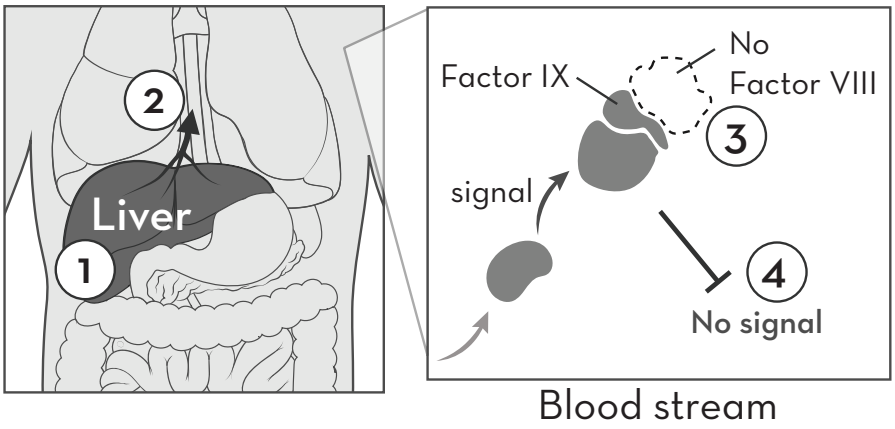
In your Lab Notebook, page 4, the models in question 6 show the allele and protein combinations for females. For question 7, draw models to show the possible alleles and proteins for males.

Protein Function & Gene Expression

1. The H6 allele is switched on in liver cells (same as healthy alleles).

Liver cells do read the H3 allele and build factor VIII proteins—but the proteins are altered.

2. The factor VIII protein is not processed correctly. It is trapped in liver cells, so it never reaches the blood stream to do its job.



3. The blood is completely missing the function of Factor VIII protein.

4. The signal telling blood to clot is not carried forward.

Men with the H6 allele have severe hemophilia with spontaneous, hard to control bleeding. Without treatment, they're at risk for joint damage or seizures from internal bleeding.