NAME _____ DATE _____

Allele Profile

Hemoglobin Disorders, Allele HB1

Basic Information

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

Genetic Disorder – **Hemoglobin Disorder**: **Sickle Cell Disease**

Affected Gene – ***HBB***

Affected Protein – The affected gene codes for the protein **beta-globin**

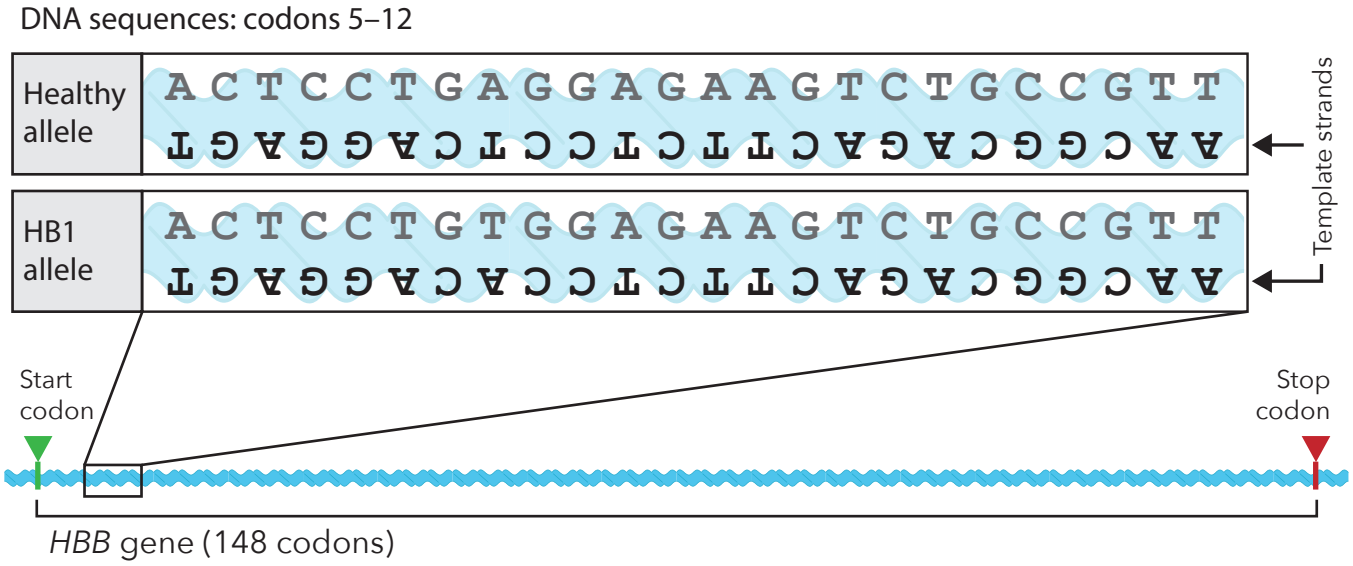
Allele – **HB1**

There are many versions, or alleles, of the *HBB* gene. Some cause inherited disorders and some do not. Your assigned allele is one of several hundred that can cause a hemoglobin disorder.

Mutations & Alleles

The protein-coding portion of HBB gene is 1,254 nucleotides long, and it has 148 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:

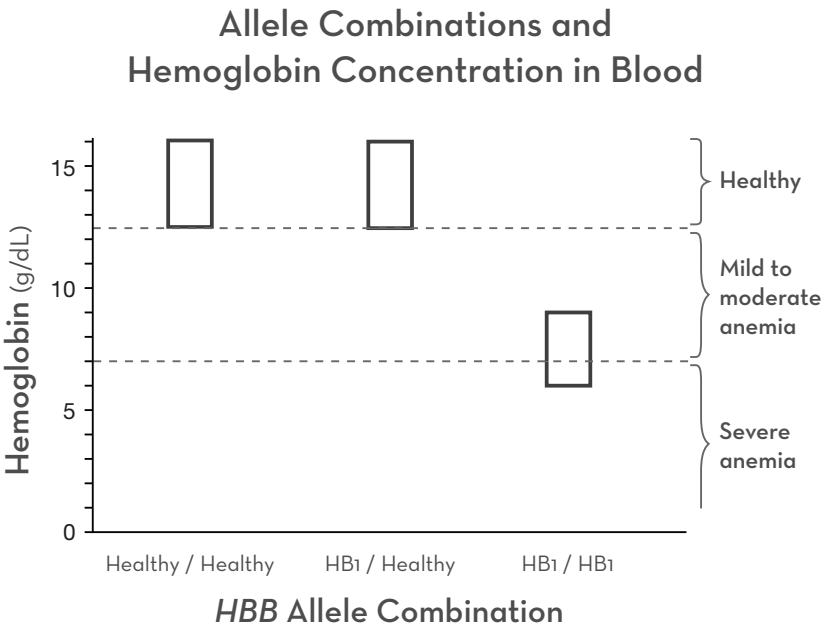


NAME _____ DATE _____

Inheritance

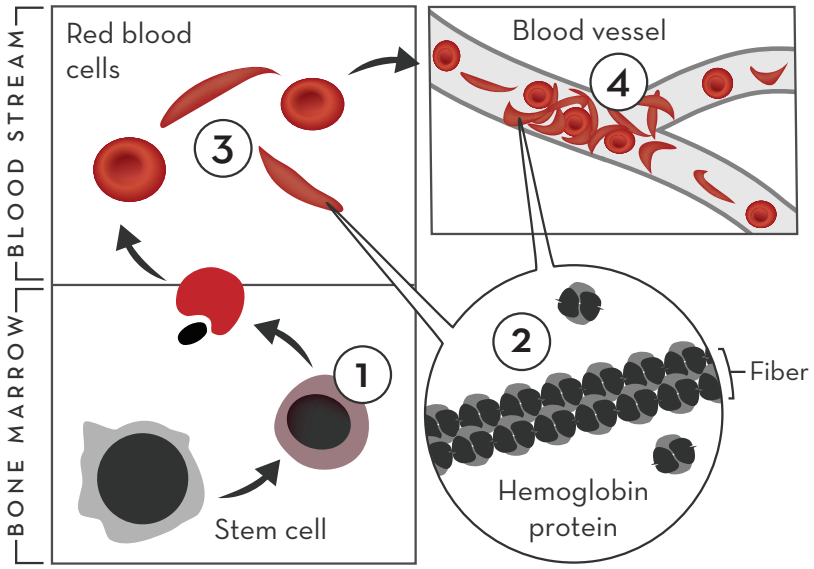
Everyone inherits two alleles of *HBB*, and beta-globin protein is normally made (expressed) from both. The *HBB* alleles that a person has influences how much and what type of beta-globin protein they make. This in turn affects the amount and type of hemoglobin in their red blood cells, and the number and type of red blood cells in their blood.

People who have hemoglobin disorders often have lower concentrations of hemoglobin in their blood, which leads to anemia. The graph shows how much hemoglobin protein is in the blood of people with different *HBB* allele combinations (and who are not receiving treatment). Data adaptedfrom Thein et al, 1990Kohne, 2011.



Protein Function & Gene Expression

1. The HB1 allele is switched on in maturing red blood cells (same as healthy alleles). The cells do read the HB1 allele and build beta-globin proteins.
2. The beta-protein made from the HB1 alleleis altered. It can do its job, but it sticks together, forming long, stiff fibers.
3. This causes red blood cells to easiliy become sickle-shaped.
4. Sickle-shaped cells are shorter-lived than usual, and they get caught in small blood vessels.



Most people with two HB1 alleles have a severe form of sickle cell disease. Often in children, the spleen stops working and must be removed. They are likely to have any of the symptoms of sickle cell disease, including pain episodes, organ damage, and anemia. But with good treatment, they typically live to middle age and beyond.

People with one HB1 allele and one healthy allele are generally healthy, though their red blood cells can sickle under some conditions. They are also resistant to infection by the malaria parasite.

NAME _____ DATE _____

Allele Profile

Hemoglobin Disorders, Allele HB2

Basic Information

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

Genetic Disorder – **Hemoglobin Disorder**: **Sickle Cell Disease**

Affected Gene – ***HBB***

Affected Protein – The affected gene codes for the protein **beta-globin**

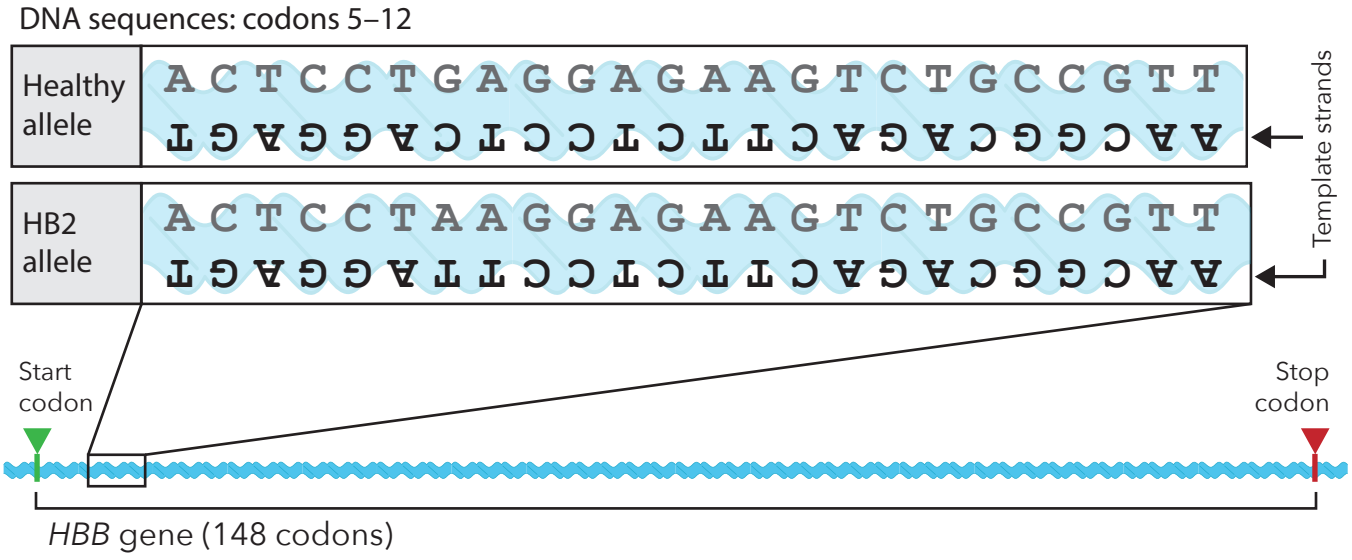
Allele – **HB2**

There are many versions, or alleles, of the *HBB* gene. Some cause inherited disorders and some do not. Your assigned allele is one of several hundred that can cause a hemoglobin disorder.

Mutations & Alleles

The protein-coding portion of HBB gene is 1,254 nucleotides long, and it has 148 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:

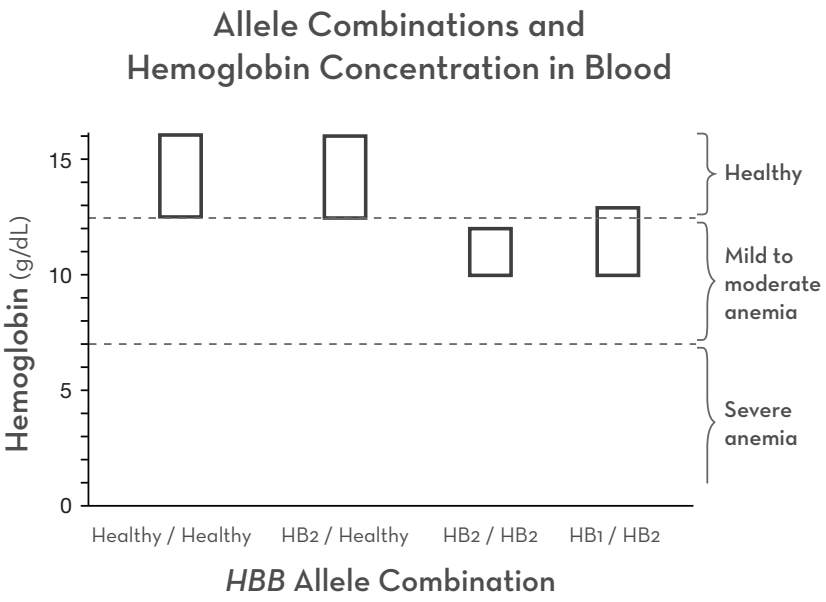


NAME _____ DATE _____

Inheritance

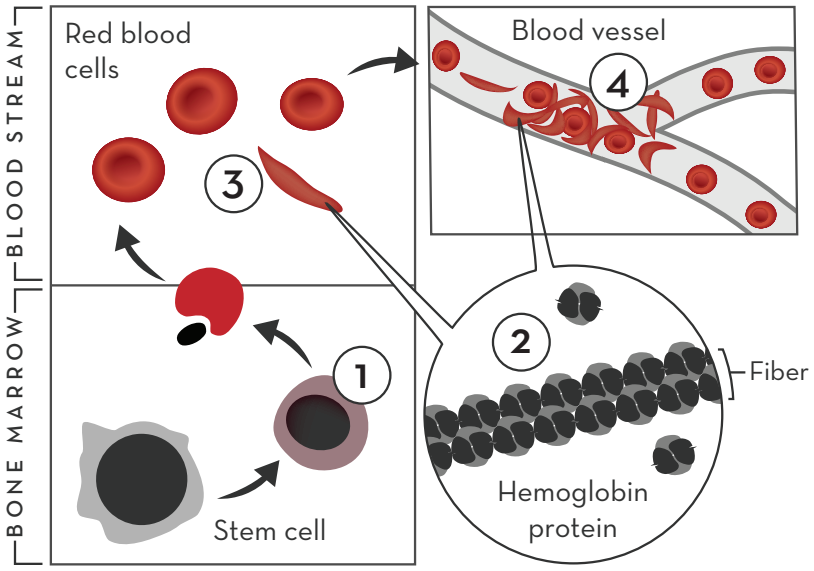
Everyone inherits two alleles of *HBB*, and beta-globin protein is normally made (expressed) from both. The *HBB* alleles that a person has influences how much and what type of beta-globin protein they make. This in turn affects the amount and type of hemoglobin in their red blood cells, and the number and type of red blood cells in their blood.

People who have hemoglobin disorders often have lower concentrations of hemoglobin in their blood, which leads to anemia. The graph shows how much hemoglobin protein is in the blood of people with different *HBB* allele combinations (and who are not receiving treatment). Data adaptedfrom Thein et al, 1990Kohne, 2011.



Protein Function & Gene Expression

1. The HB2 allele is switched on in maturing red blood cells (same as healthy alleles). The cells do read the HB2 allele and build beta-globin proteins.
2. The beta-protein made from the HB1 alleleis altered. It can do its job, but it sometimes sticks together, forming long, stiff fibers.
3. Red blood cells can sometimes become sickle-shaped.
4. Sickle-shaped cells can get caught in small blood vessels.



Some people with two HB2 alleles have no symptoms. Others have something like sickle cell disease but milder. Red blood cells are smaller, fewer in number, and shorter-lived than usual. This can cause mild anemia and an enlarged spleen, but not the more serious symptoms of sickle cell disease. People with two HB2 alleles and good medical care have a typical life expectancy. They are also significantly protected against severe malaria infection.

People with one HB2 allele and one healthy allele are healthy, and they have some protection against malaria. People with one HB2 and one HB1 allele have a mild form of sickle cell disease.

NAME _____ DATE _____

Allele Profile

Hemoglobin Disorders, Allele HB3

Basic Information

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

Genetic Disorder – **Hemoglobin Disorder**: **Beta-Thalassemia**

Affected Gene – ***HBB***

Affected Protein – The affected gene codes for the protein **beta-globin**

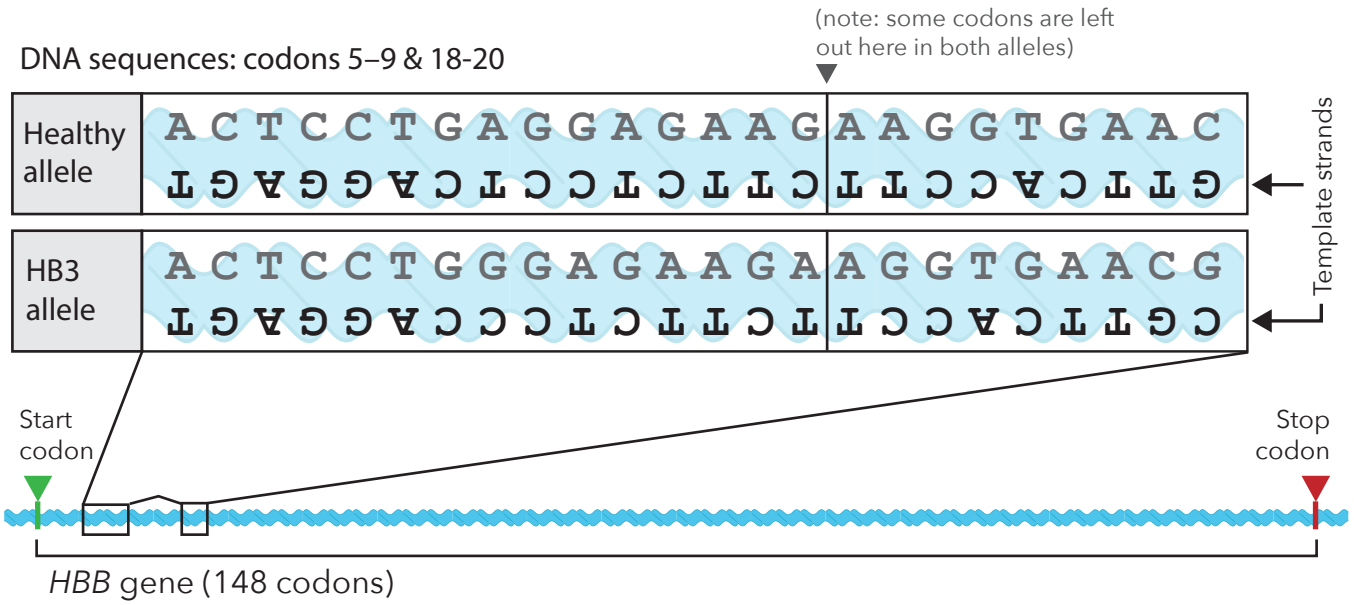
Allele – **HB3**

There are many versions, or alleles, of the *HBB* gene. Some cause inherited disorders and some do not. Your assigned allele is one of several hundred that can cause a hemoglobin disorder.

Mutations & Alleles

The protein-coding portion of HBB gene is 1,254 nucleotides long, and it has 148 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:

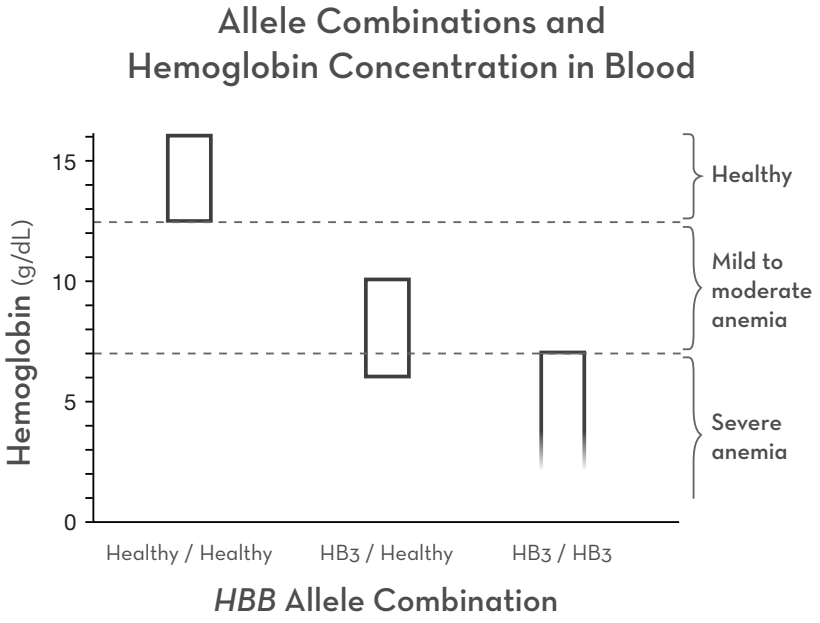


NAME _____ DATE _____

Inheritance

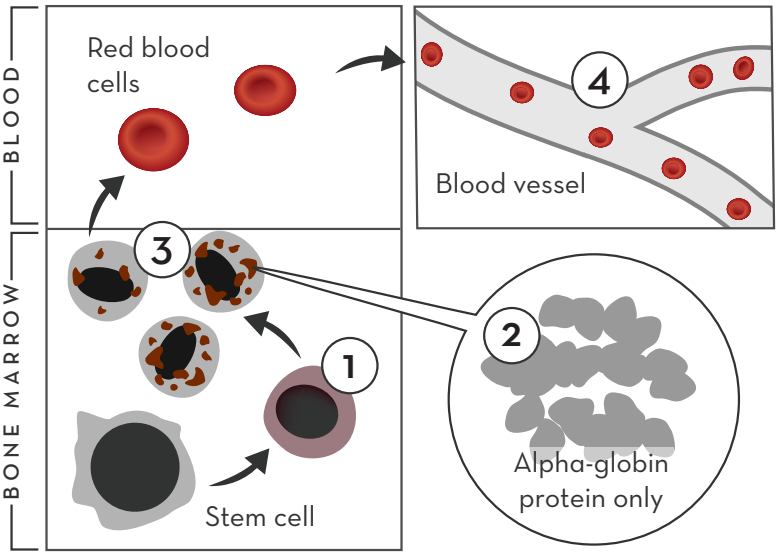
Everyone inherits two alleles of *HBB*, and beta-globin protein is normally made (expressed) from both. The *HBB* alleles that a person has influences how much and what type of beta-globin protein they make. This in turn affects the amount and type of hemoglobin in their red blood cells, and the number and type of red blood cells in their blood.

People who have hemoglobin disorders often have lower concentrations of hemoglobin in their blood, which leads to anemia. The graph shows how much hemoglobin protein is in the blood of people with different *HBB* allele combinations (and who are not receiving treatment). Data adaptedfrom Thein et al, 1990Kohne, 2011.



Protein Function & Gene Expression

1. The HB3 allele is switched on in maturing red blood cells (same as healthy alleles). But no working beta-globin protein can be made from this allele.
2. Alpha-globin proteins are still made—but with no beta-blogin to pair with, it clumps together.
3. Most red blood cells fail to mature. Instead, they are recycled.
4. The few cells that do mature have high levels of fetal hemoglobin, and they are smaller than usual.



People with two HB3 alleles usually develop severe beta-thalassemia by age 2. To survive, they need transfusions of healthy blood every 2–4 weeks. Though they are at risk for iron overload, most who receive proper care have a good quality of life and a near-normal lifespan.

People who have one HB3 allele and one healthy allele are usually healthy. But because they make less beta-globin, less hemoglobin, and fewer red blood cells than usual, they may have mild symptoms of beta-thalassemia, most commonly anemia.

NAME _____ DATE _____

Allele Profile

Hemoglobin Disorders, Allele HB4

Basic Information

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

Genetic Disorder – **Hemoglobin Disorder**: **Beta-Thalassemia**

Affected Gene – ***HBB***

Affected Protein – The affected gene codes for the protein **beta-globin**

Allele – **HB4**

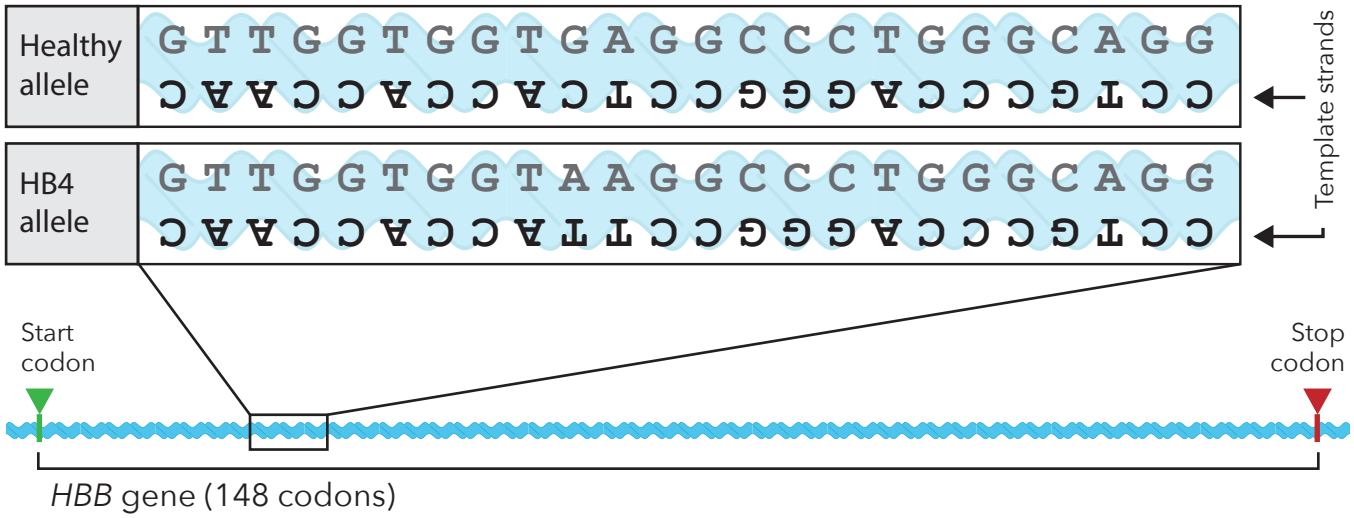
There are many versions, or alleles, of the *HBB* gene. Some cause inherited disorders and some do not. Your assigned allele is one of several hundred that can cause a hemoglobin disorder.

Mutations & Alleles

The protein-coding portion of HBB gene is 1,254 nucleotides long, and it has 148 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:

DNA sequences: codons 24–31

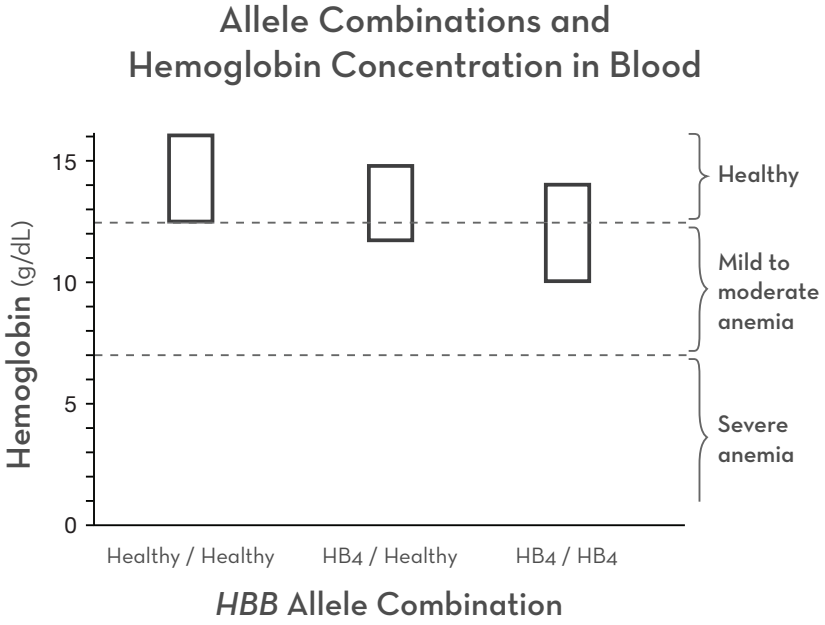


NAME _____ DATE _____

Inheritance

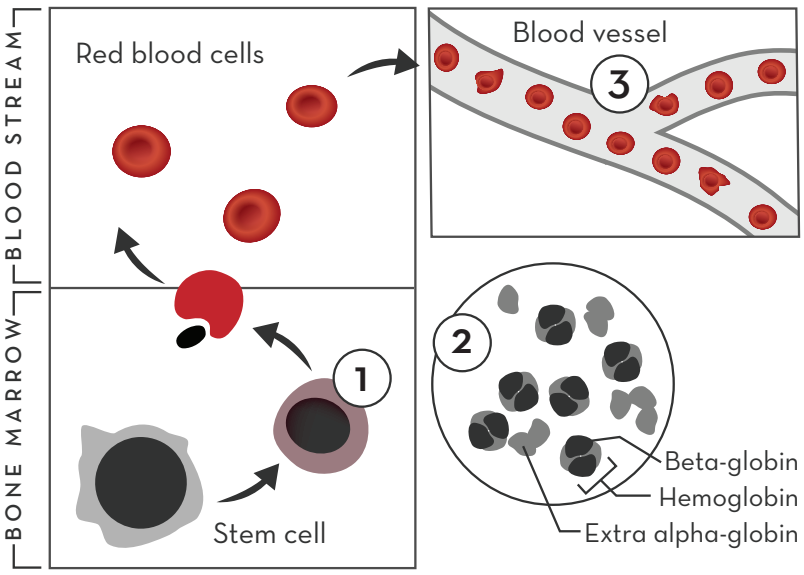
Everyone inherits two alleles of *HBB*, and beta-globin protein is normally made (expressed) from both. The *HBB* alleles that a person has influences how much and what type of beta-globin protein they make. This in turn affects the amount and type of hemoglobin in their red blood cells, and the number and type of red blood cells in their blood.

People who have hemoglobin disorders often have lower concentrations of hemoglobin in their blood, which leads to anemia. The graph shows how much hemoglobin protein is in the blood of people with different *HBB* allele combinations (and who are not receiving treatment). Data adaptedfrom Thein et al, 1990Kohne, 2011.



Protein Function & Gene Expression

1. The HB4 allele is switched on in maturing red blood cells (same as healthy alleles).
2. Cells do read the HB4 allele and build a version of beta-globin protein. But the protein is built slowly, and it is altered in a way that makes it less stable and shorter-lived than usual.
3. Red blood cells may be smaller, fewer in number, strangely shaped, and shorter-lived than usual.



Some people with two HB4 alleles never have symptoms. Others have mild symptoms of beta-thalassemia—mild anemia, jaundice, and/or an enlarged spleen. People with two HB4 alleles have a typical life expectancy, plus they are protected against severe malaria infection.

People with one HB4 allele and one healthy allele are healthy. They also have some protection against malaria. Those with one HB4 allele and one HB1 allele have a mild version of sickle cell disease.

NAME _____ DATE _____

Allele Profile

Hemoglobin Disorders, Allele HB5

Basic Information

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

Genetic Disorder – **Hemoglobin Disorder**: **Beta-Thalassemia**

Affected Gene – ***HBB***

Affected Protein – The affected gene codes for the protein **beta-globin**

Allele – **HB5**

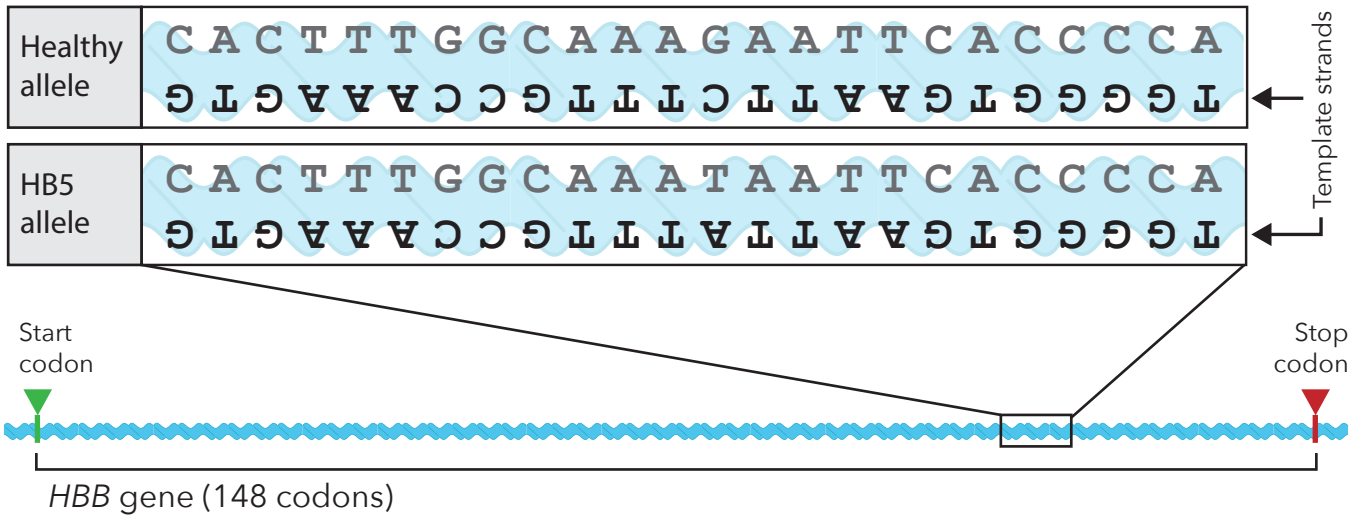
There are many versions, or alleles, of the *HBB* gene. Some cause inherited disorders and some do not. Your assigned allele is one of several hundred that can cause a hemoglobin disorder.

Mutations & Alleles

The protein-coding portion of HBB gene is 1,254 nucleotides long, and it has 148 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:

DNA sequences: codons 112–119

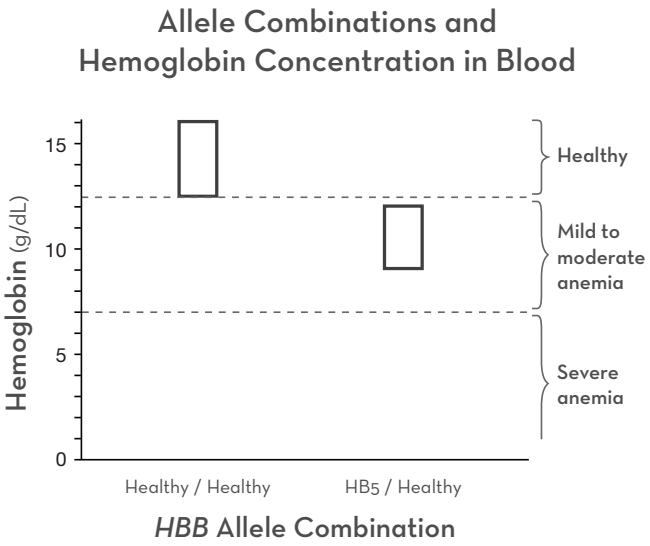


NAME _____ DATE _____

Inheritance

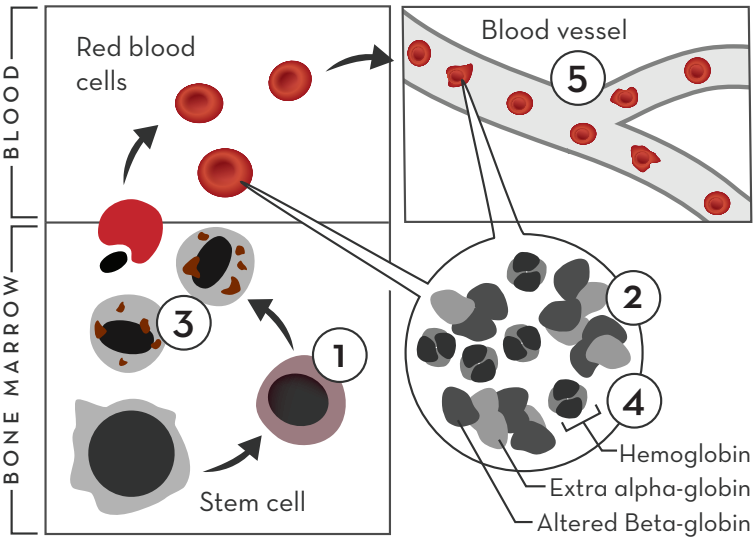
Everyone inherits two alleles of *HBB*, and beta-globin protein is normally made (expressed) from both. The *HBB* alleles that a person has influences how much and what type of beta-globin protein they make. This in turn affects the amount and type of hemoglobin in their red blood cells, and the number and type of red blood cells in their blood.

People who have hemoglobin disorders often have lower concentrations of hemoglobin in their blood, which leads to anemia. The graph shows how much hemoglobin protein is in the blood of people with different *HBB* allele combinations (and who are not receiving treatment). Data adapted from Thein et al, 1990Kohne, 2011.



In your Lab Notebook, Page 4, Question 6: You don't have the information to answer the question about Person C – but what do you think might happen if someone had this allele combination?

Protein Function & Gene Expression



1. The HB5 allele is switched on in maturing red blood cells (same as healthy alleles).
2. Cells do read the HB5 allele and build beta-globin protein—but it is missing the part that attaches to alpha-globin. These altered proteins are not incorporated into hemoglobin.
3. Inside maturing red blood cells, the unpaired beta-globin proteins and the extra, unpaired-alpha-globin proteins clump together.
4. People with one HB5 and one healthy allele make a combination of altered and healthy beta-globin. The beta-globin from the healthy allele does form proper hemoglobin.
5. Most red blood cells mature and function. But the protein clumps shorten the lifespan of the cells and can sometimes prevent them from maturing.

Most people with an HB5 allele develop beta-thalassemia, either in childhood or adulthood. Some have mild symptoms, such as anemia, jaundice, or an enlarged spleen. Others have more serious anemia, spleen damage, and iron overload. They may need transfusions of healthy blood. Yet with proper care, most people with an HB5 allele have a good quality of life and a typical lifespan.

NAME _____ DATE _____

Allele Profile

Hemoglobin Disorders, Allele HB6

Basic Information

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

Genetic Disorder – **Hemoglobin Disorder**: **Oxygen transport disorder**

Affected Gene – ***HBB***

Affected Protein – The affected gene codes for the protein **beta-globin**

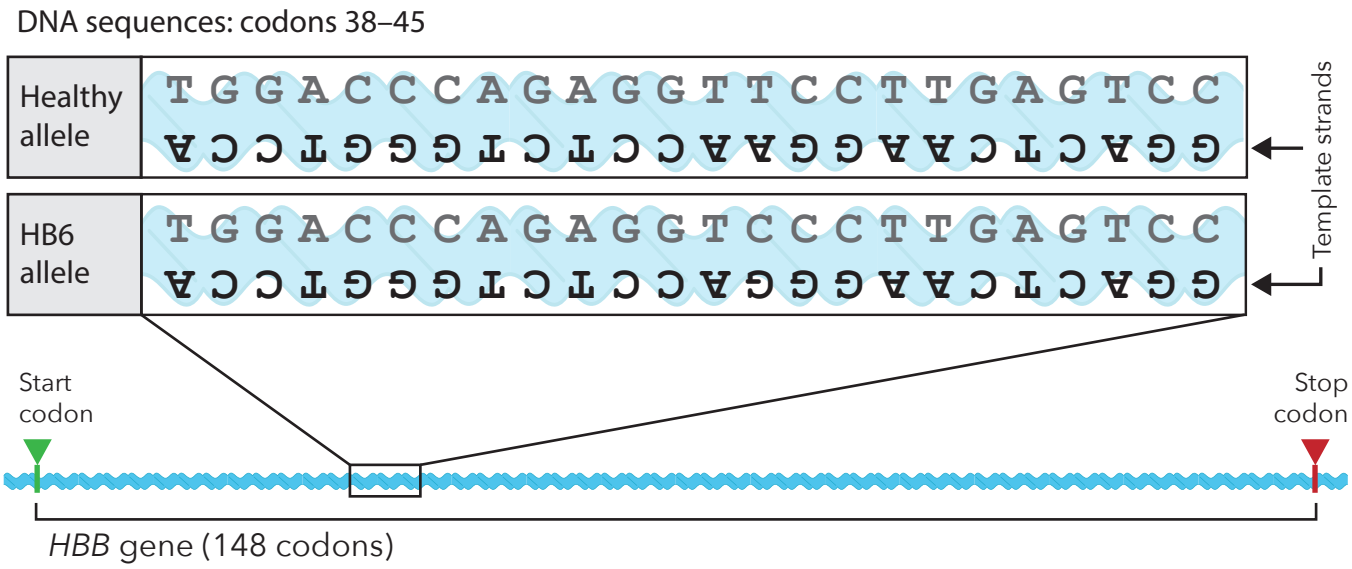
Allele – **HB6**

There are many versions, or alleles, of the *HBB* gene. Some cause inherited disorders and some do not. Your assigned allele is one of several hundred that can cause a hemoglobin disorder.

Mutations & Alleles

The protein-coding portion of HBB gene is 1,254 nucleotides long, and it has 148 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:

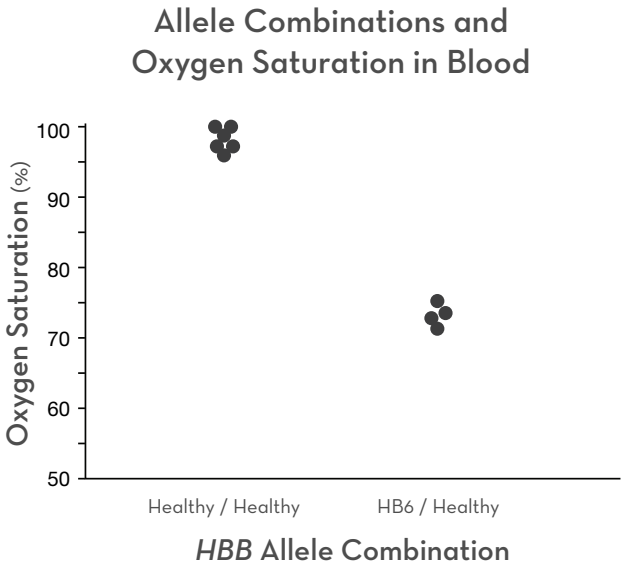


NAME _____ DATE _____

Inheritance

Everyone inherits two alleles of *HBB*, and beta-globin protein is normally made (expressed) from both. The *HBB* alleles that a person has influences how much and what type of beta-globin protein they make. This in turn affects the amount and type of hemoglobin in their red blood cells, and the number and type of red blood cells in their blood.

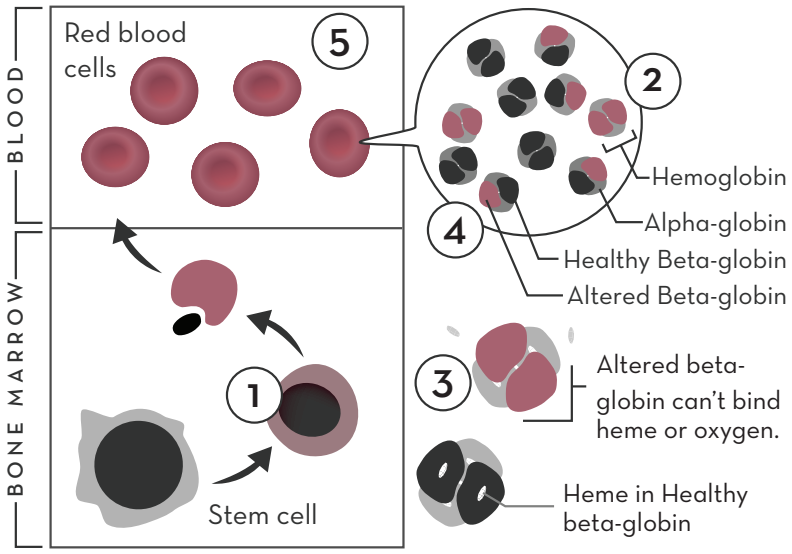
People who have oxygen transport disorders usually have healthy or near-healthy amounts of hemoglobin protein in their blood. But because their hemoglobin doesn't bind oxygen properly, it delivers less oxygen to the body's tissues. The graph shows the percent oxygen saturation in the blood of people with different *HBB* allele combinations. Each point represents one person (data adapted from Thein et al, 1990).



In your Lab Notebook, Page 4, 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?

Protein Function & Gene Expression

1. The HB6 allele is switched on in maturing red blood cells (same as the healthy allele).
2. Cells do read the HB6 allele and build beta-globin proteins.
3. But the HB6 allele codes for an altered version of beta-globin protein that binds weakly to oxygen. Hemoglobin made from it carries less oxygen than usual.
4. People with one HB6 and one healthy allele make both altered and healthy beta-globin proteins.



5. Their blood carries less oxygen, and it is more purple than red. The hemoglobin is also slightly unstable, making red blood cells shorter-lived. To compensate, they make more red blood cells than usual.

Some people with an HB6 allele are healthy, though low oxygen can cause a blue tint around the mouth, eyes, and fingernails. Others have added symptoms, including anemia or jaundice—especially during times of physical stress, such as illness, infection, or pregnancy.