

Allele Profile

Marfan syndrome, Allele M1

Basic Information

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

Genetic Disorder – **Marfan syndrome**

Affected Gene – **FBN1**

Affected Protein – The affected gene codes for the protein **fibrillin-1**

Allele – **M1**

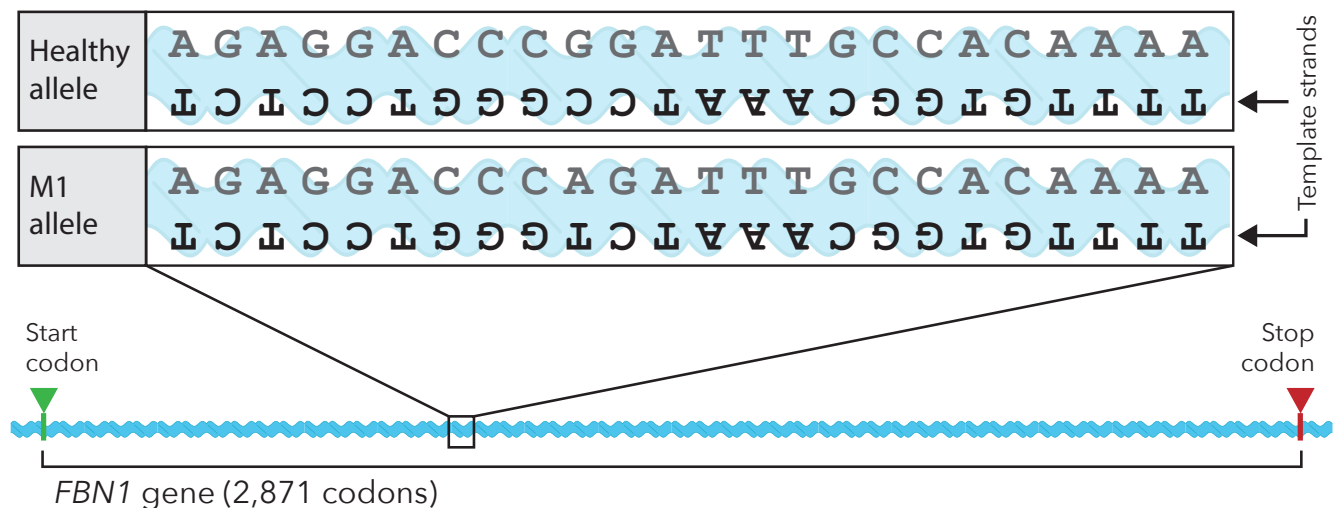
There are more than 2,000 versions, or alleles, of the *FBN1* gene. Some cause genetic disorders and some do not. Your assigned allele is one of over a thousand that can cause Marfan syndrome.

Mutations & Alleles

The protein-coding portion of the *FBN1* gene is 8,613 nucleotides long, and it has 2,871 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:

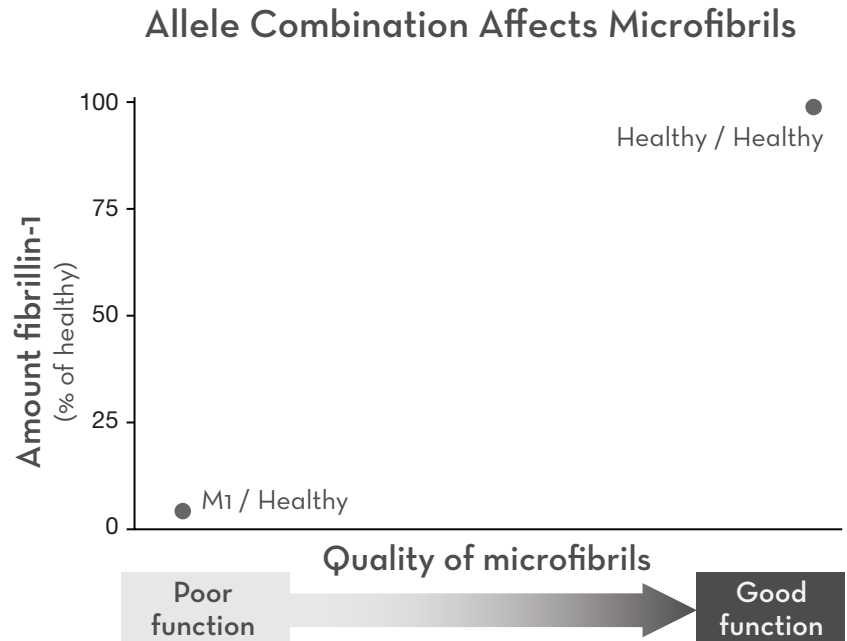
DNA sequences: codons 1,010–1,017



Inheritance

Everyone inherits two *FBN1* alleles, and fibrillin-1 protein is normally made (expressed) from both. Cells release fibrillin-1 protein into the space that surrounds them, where it is built into microfibrils. Each microfibril is made of many fibrillin-1 proteins, some from each allele.

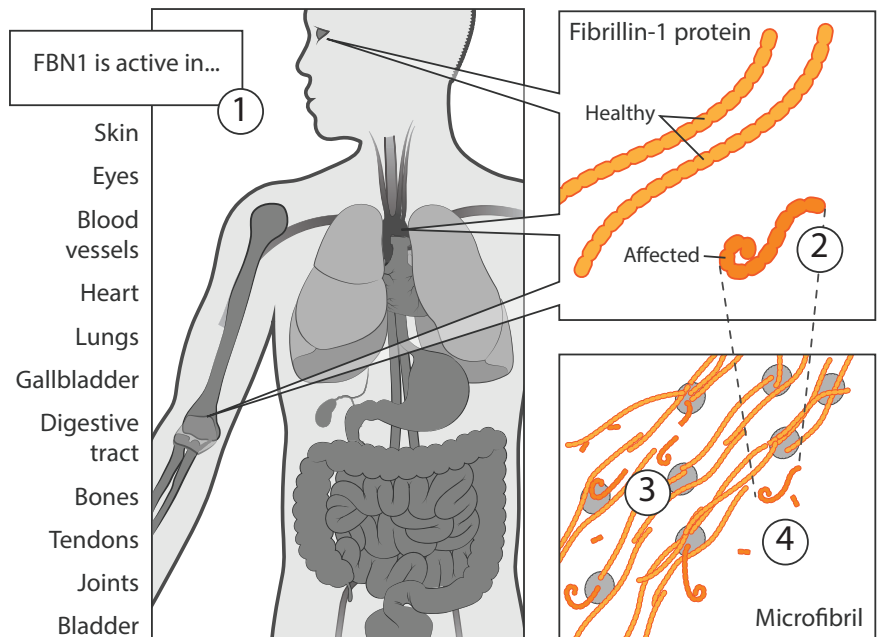
The combination of *FBN1* alleles a person has influences their microfibrils. People with Marfan syndrome either make too little fibrillin-1 protein, or their fibrillin-1 makes bad microfibrils, or both. The graph shows data about the microfibrils in people with a disease-causing *FBN1* allele compared to people with two healthy alleles.



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 M1 allele is switched on in cells that build connective tissue (same as healthy alleles). So cells do read the M1 allele and build proteins.
2. But the fibrillin-1 protein made from the M1 allele is altered.
3. The altered protein has two problems. First, it can't assemble into microfibrils very well, so it interferes with healthy fibrillin-1 protein.
4. Second, it breaks down too easily.



People with one M1 allele and one healthy allele make few microfibrils, and their quality is poor. They are at high risk for neonatal Marfan syndrome, a rare and very severe form that affects babies.

Allele Profile

Marfan syndrome, Allele M2

Basic Information

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

Genetic Disorder – **Marfan syndrome**

Affected Gene – **FBN1**

Affected Protein – The affected gene codes for the protein **fibrillin-1**

Allele – **M2**

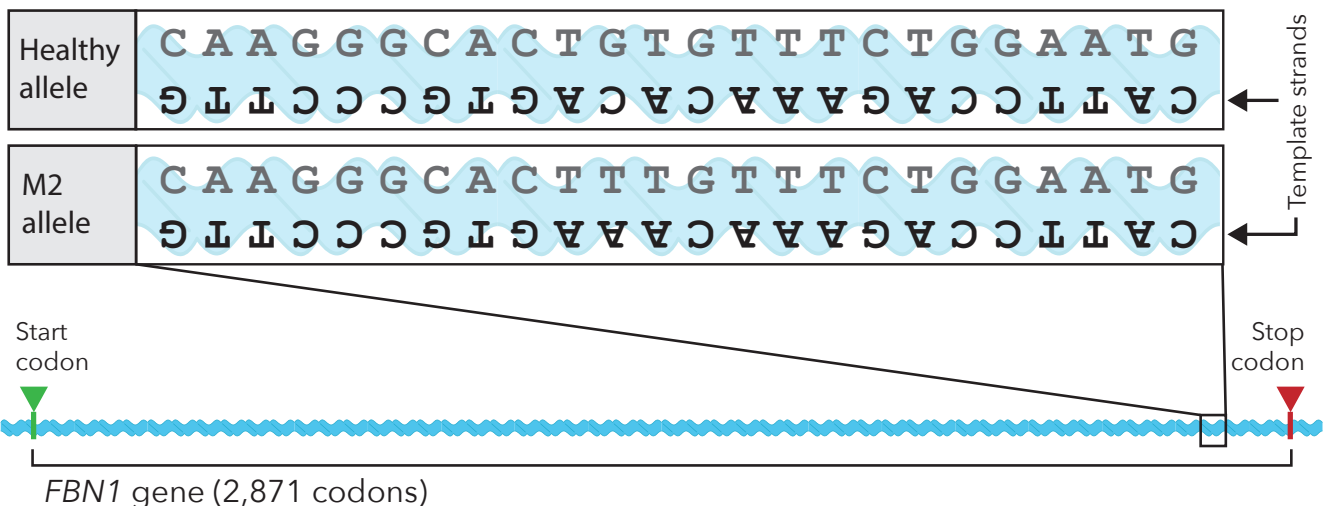
There are more than 2,000 versions, or alleles, of the *FBN1* gene. Some cause genetic disorders and some do not. Your assigned allele is one of over a thousand that can cause Marfan syndrome.

Mutations & Alleles

The protein-coding portion of the *FBN1* gene is 8,613 nucleotides long, and it has 2,871 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 2,683–2,690

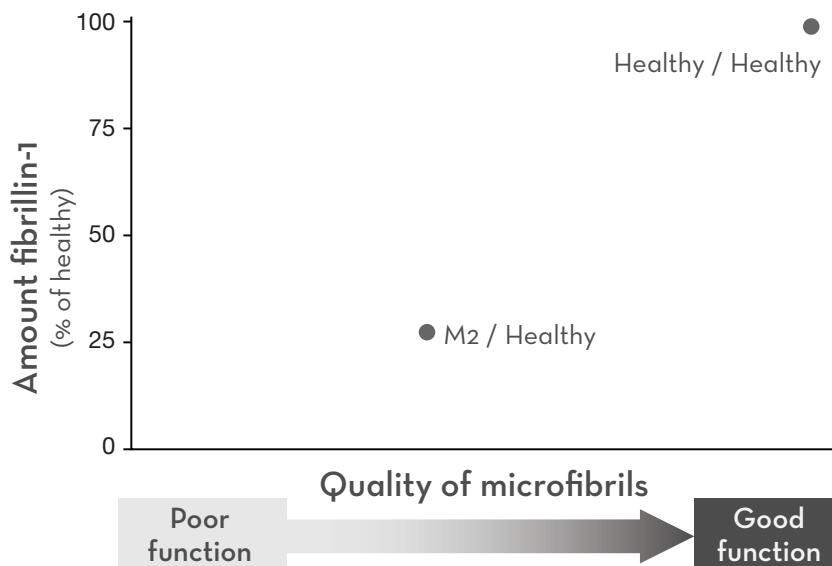


Inheritance

Everyone inherits two *FBN1* alleles, and fibrillin-1 protein is normally made (expressed) from both. Cells release fibrillin-1 protein into the space that surrounds them, where it is built into microfibrils. Each microfibril is made of many fibrillin-1 proteins, some from each allele.

The combination of *FBN1* alleles a person has influences their microfibrils. People with Marfan syndrome either make too little fibrillin-1 protein, or their fibrillin-1 makes bad microfibrils, or both. The graph shows data about the microfibrils in people with a disease-causing *FBN1* allele compared to people with two healthy alleles.

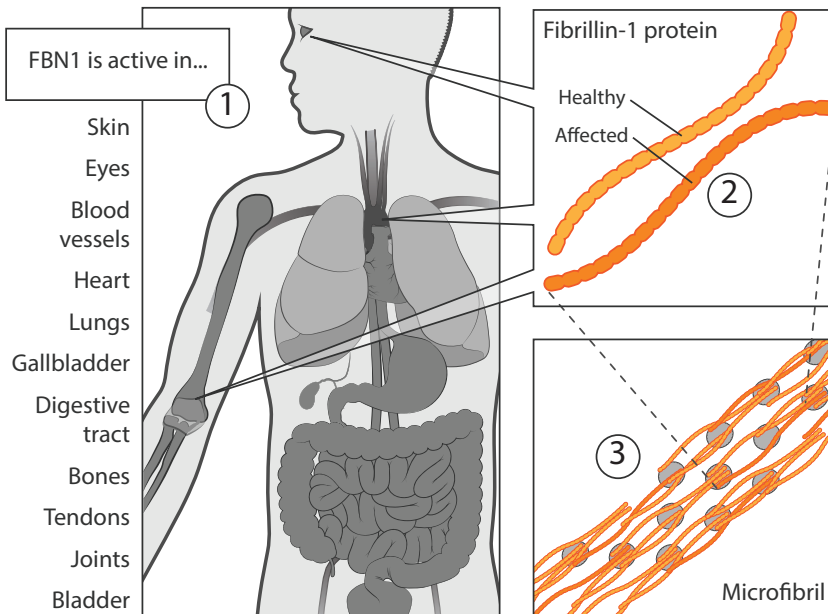
Allele Combination Affects Microfibrils



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 M2 allele is switched on in cells that build connective tissue (same as healthy alleles).
2. Cells do read the M2 allele and build fibrillin-1 proteins, but the proteins are altered. Cells have trouble processing it; they release it slowly and in smaller amounts than usual.
3. The altered protein also slows down the release of healthy fibrillin-1 protein. Microfibrils include less protein than expected, and they may not work properly.



People with one M2 allele and one healthy allele are at risk for any combination of the effects seen in Marfan syndrome. They may have a higher risk for dislocating the lens of their eye compared to people with other alleles.

Allele Profile

Marfan syndrome, Allele M3

Basic Information

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

Genetic Disorder – **Marfan syndrome**

Affected Gene – **FBN1**

Affected Protein – The affected gene codes for the protein **fibrillin-1**

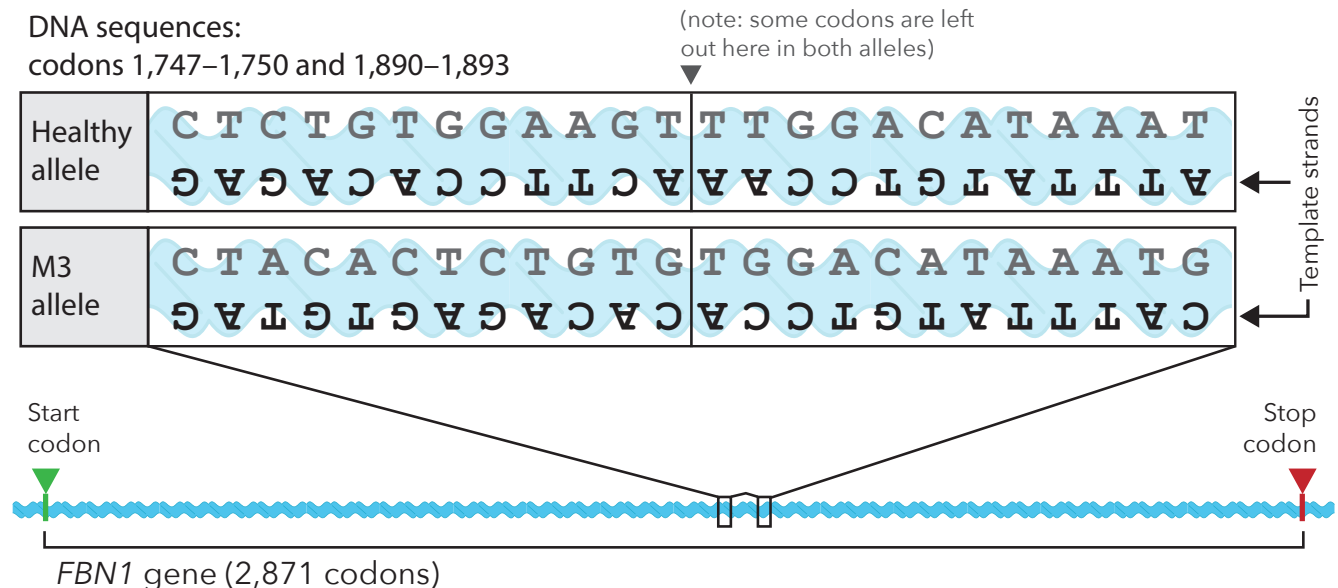
Allele – **M3**

There are more than 2,000 versions, or alleles, of the *FBN1* gene. Some cause genetic disorders and some do not. Your assigned allele is one of over a thousand that can cause Marfan syndrome.

Mutations & Alleles

The protein-coding portion of the *FBN1* gene is 8,613 nucleotides long, and it has 2,871 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:

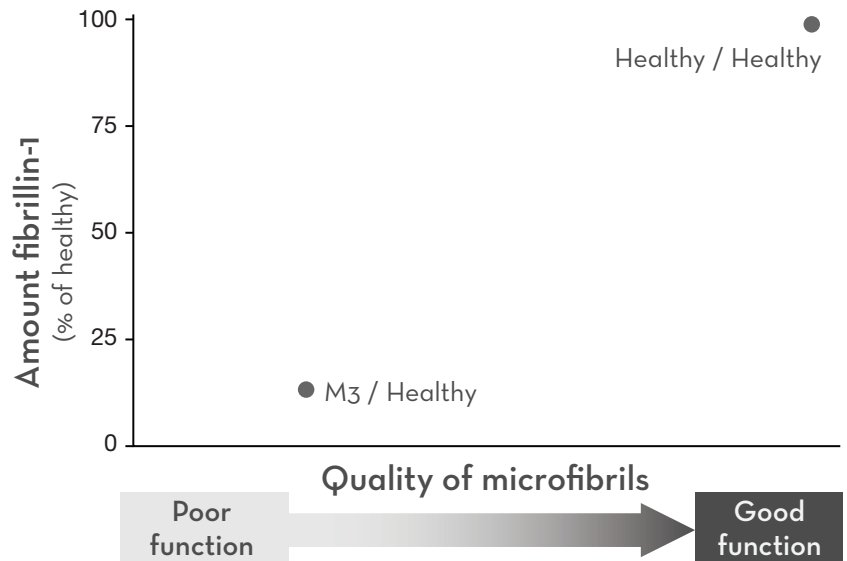


Inheritance

Everyone inherits two *FBN1* alleles, and fibrillin-1 protein is normally made (expressed) from both. Cells release fibrillin-1 protein into the space that surrounds them, where it is built into microfibrils. Each microfibril is made of many fibrillin-1 proteins, some from each allele.

The combination of *FBN1* alleles a person has influences their microfibrils. People with Marfan syndrome either make too little fibrillin-1 protein, or their fibrillin-1 makes bad microfibrils, or both. The graph shows data about the microfibrils in people with a disease-causing *FBN1* allele compared to people with two healthy alleles.

Allele Combination Affects Microfibrils

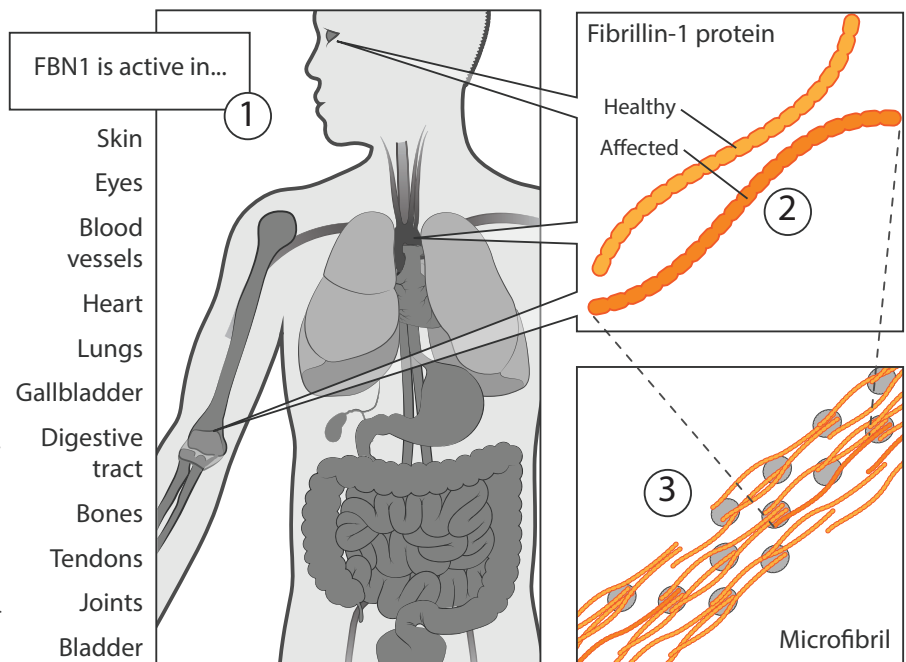


In your Lab Notebook, Page 4, Question 6: You do not have the information to answer the question about Person C – but what do you think might happen if someone had this allele combination?

Protein Function & Gene Expression

1. The M3 allele is switched on in cells that build connective tissue (same as healthy alleles).
2. Cells do read the M3 allele and build proteins, but the proteins are altered.
3. Very little of the altered protein can be built into microfibrils, and it interferes with healthy fibrillin-1 protein.

A person with one M3 allele and one healthy allele makes less than half the expected number of microfibrils. They are at risk for any combination of effects seen in Marfan syndrome.



Allele Profile

Marfan syndrome, Allele M4

Basic Information

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

Genetic Disorder – **Marfan syndrome**

Affected Gene – **FBN1**

Affected Protein – The affected gene codes for the protein **fibrillin-1**

Allele – **M4**

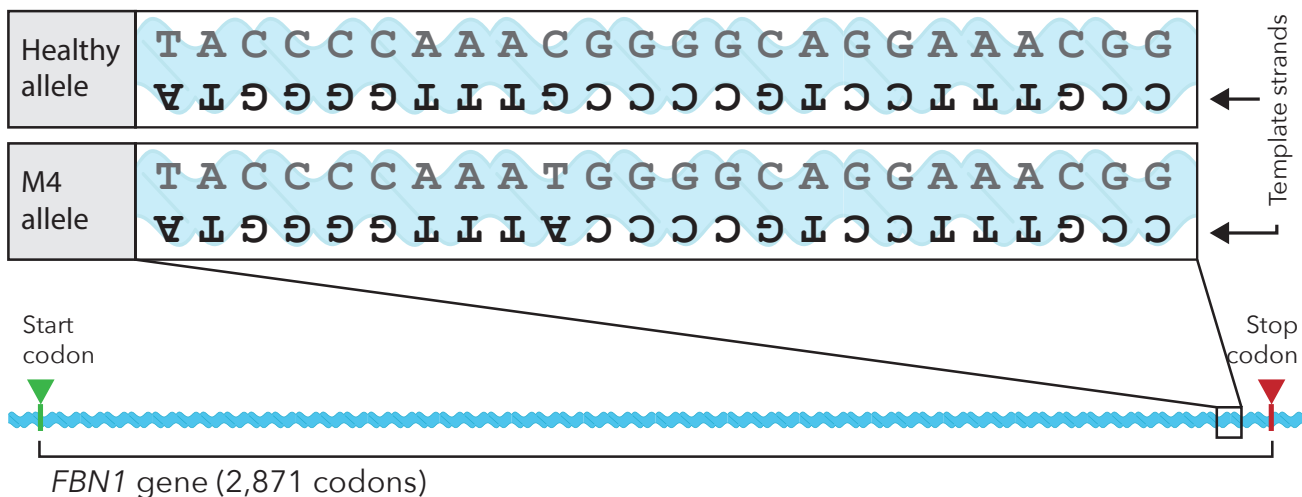
There are more than 2,000 versions, or alleles, of the *FBN1* gene. Some cause genetic disorders and some do not. Your assigned allele is one of over a thousand that can cause Marfan syndrome.

Mutations & Alleles

The protein-coding portion of the *FBN1* gene is 8,613 nucleotides long, and it has 2,871 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 2,723–2,730

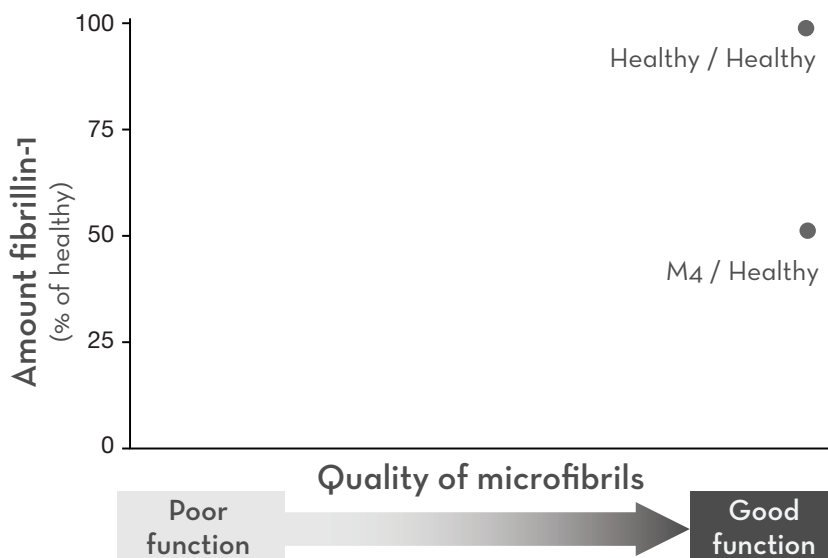


Inheritance

Everyone inherits two *FBN1* alleles, and fibrillin-1 protein is normally made (expressed) from both. Cells release fibrillin-1 protein into the space that surrounds them, where it is built into microfibrils. Each microfibril is made of many fibrillin-1 proteins, some from each allele.

The combination of *FBN1* alleles a person has influences their microfibrils. People with Marfan syndrome either make too little fibrillin-1 protein, or their fibrillin-1 makes bad microfibrils, or both. The graph shows data about the microfibrils in people with a disease-causing *FBN1* allele compared to people with two healthy alleles.

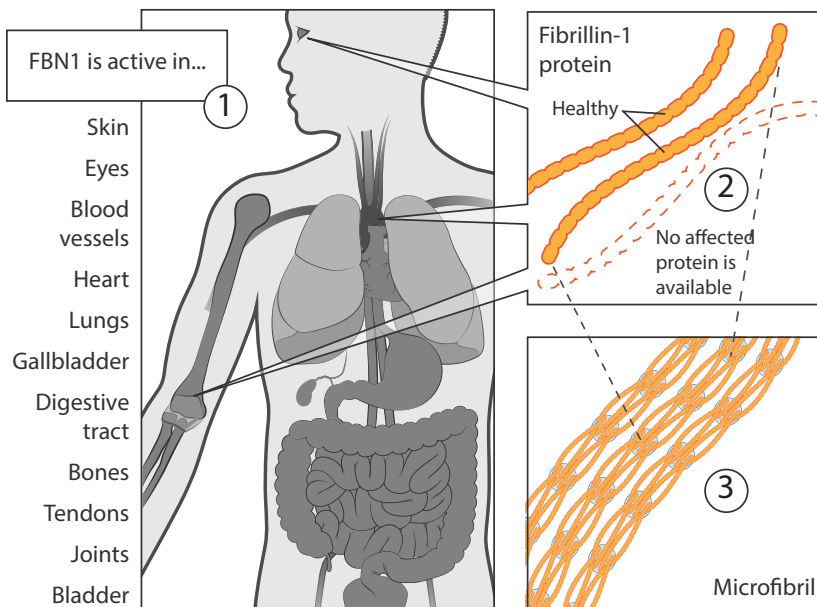
Allele Combination Affects Microfibrils



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 M4 allele is switched on in cells that build connective tissue (same as healthy alleles). Cells do read the M4 allele and build proteins.
2. Fibrillin-1 protein is normally cut by another protein before it can be used to build microfibrils. But the protein from the M4 allele can't be cut. The affected protein is released, but it can't be made into microfibrils.
3. The affected protein doesn't interfere with healthy protein. But overall there is less fibrillin-1 protein than usual.



People with one M4 allele and one healthy allele have a lower risk for many of the effects seen in Marfan syndrome. The allele was first discovered in a person with only skeletal features—long limbs, scoliosis (curved spine), and flat feet.

Allele Profile

Marfan syndrome, Allele M5

Basic Information

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

Genetic Disorder – **Marfan syndrome**

Affected Gene – **FBN1**

Affected Protein – The affected gene codes for the protein **fibrillin-1**

Allele – **M5**

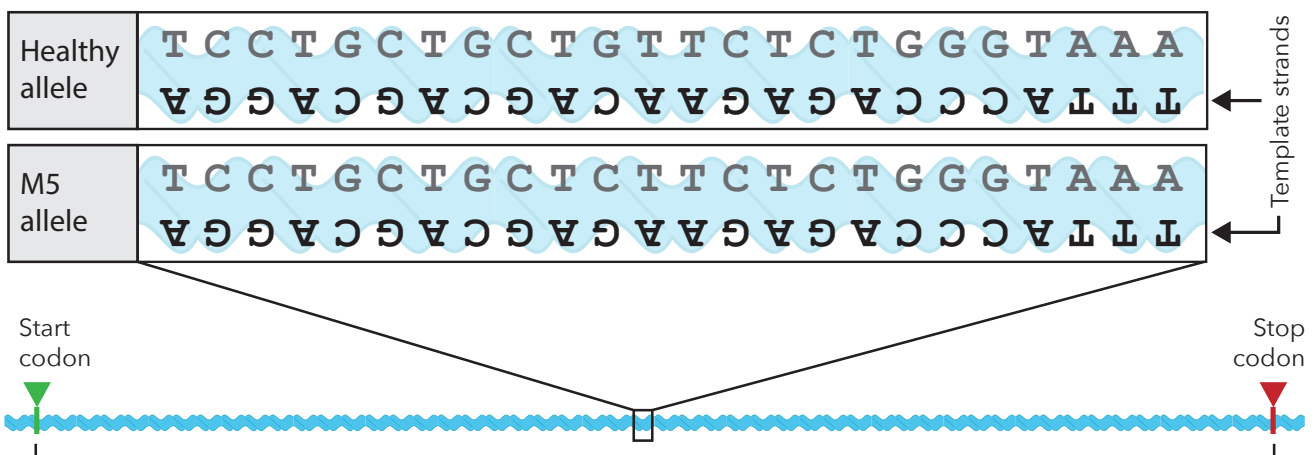
There are more than 2,000 versions, or alleles, of the *FBN1* gene. Some cause genetic disorders and some do not. Your assigned allele is one of over a thousand that can cause Marfan syndrome.

Mutations & Alleles

The protein-coding portion of the *FBN1* gene is 8,613 nucleotides long, and it has 2,871 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:

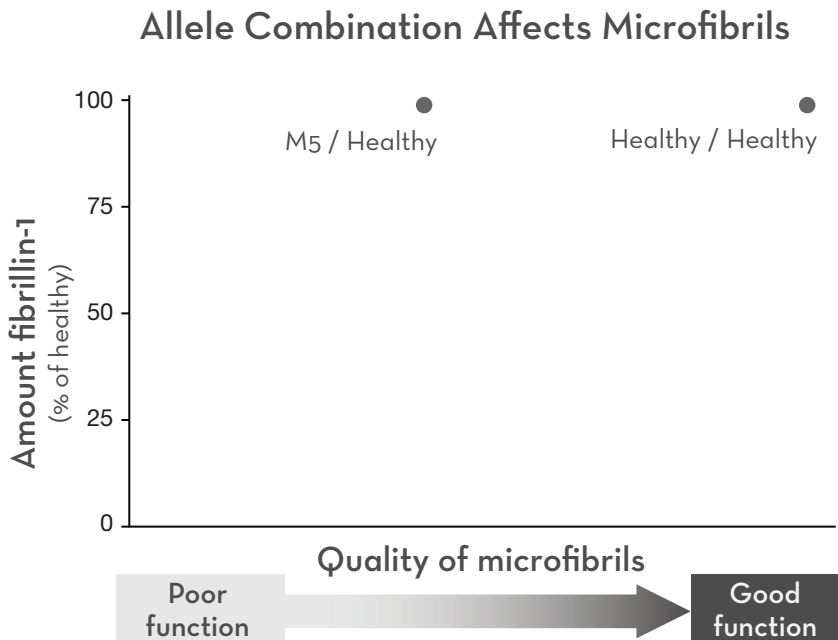
DNA sequences: codons 1,561–1,568



Inheritance

Everyone inherits two *FBN1* alleles, and fibrillin-1 protein is normally made (expressed) from both. Cells release fibrillin-1 protein into the space that surrounds them, where it is built into microfibrils. Each microfibril is made of many fibrillin-1 proteins, some from each allele.

The combination of *FBN1* alleles a person has influences their microfibrils. People with Marfan syndrome either make too little fibrillin-1 protein, or their fibrillin-1 makes bad microfibrils, or both. The graph shows data about the microfibrils in people with a disease-causing *FBN1* allele compared to people with two healthy alleles.

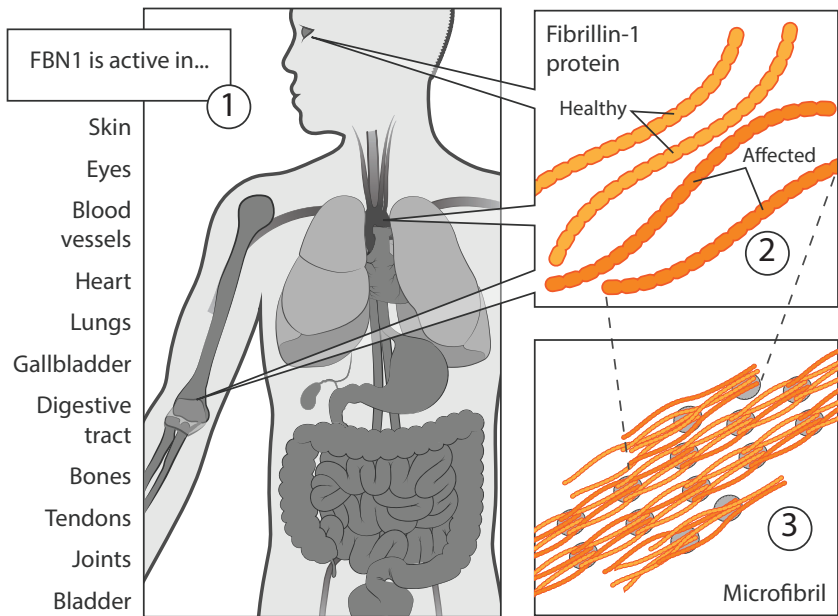


In your Lab Notebook, Page 4, Question 6: You do not have the information to answer the question about Person C – but what do you think might happen if someone had this allele combination?

Protein Function & Gene Expression

1. The M5 allele is switched on in cells that build connective tissue (same as healthy alleles).
2. Cells read the M5 allele and build proteins, but the proteins are altered.
3. The altered fibrillin-proteins are released from cells and built into microfibrils. But the microfibrils form clumps. They also don't wrap around elastin properly.

The altered protein interferes with the healthy fibrillin-1 protein. The microfibrils, especially ones that need to stretch, don't work very well.



People with one M5 allele and one healthy allele may be at lower risk for many effects of Marfan syndrome. In fact, the allele was discovered in someone with stiff skin syndrome. They had hard, thick skin, but none of the heart or skeletal effects of Marfan syndrome.