BILL #35

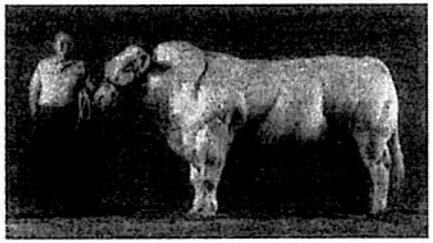
# THE IMPACT OF MUTATIONS

**BACKGROUND INFORMATION:**

**PART 1:**

**The Belgian Blue Mound of Beef**

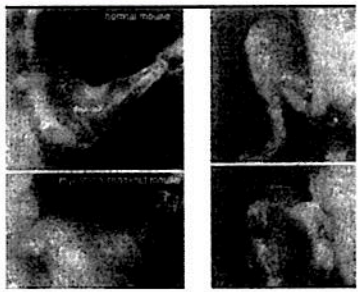
The Belgian Blue Mound of Beef is a breed of cattle that is extremely muscular. At two years of age, males can weigh over 1700 pounds, and females over 1100 pounds! This breed originated in the 1850's in Belgium as a result of breeding two different types of cattle. One question biologists have obviously asked is, what causes these cattle to develop such large muscles? Is it their diet, the exercise they get, or something in their DNA? We are going to look at some evidence today that suggests that the secret lies in their DNA.



**Myostatin:**

GDF-8

Myostatin (which is also called growth and differentiation factor-8) is a protein found in the skeletal muscle of mammals. It is a growth factor - a molecule that plays a part in controlling cell division, cell growth, and cell development. Experimenters at Johns Hopkins University discovered the role of the gene first in mice. Mice were engineered that had the myostatin gene "knocked out" (which means it didn't work). The resulting mice developed two to three times more muscle than mice with a normal version of the gene. The mice were described as looking "like Schwarzenegger mice" by the experimenters. Analysis of the muscle tissue of the mice showed that the number of muscle cells and size of muscle cells was two to three times greater in the muscle tissue of the knockout mice than in normal mice.



A mutation is any change to the normal DNA sequence of a gene for any protein. There are several different types of mutations that can occur.

1) Point mutation: A change in any single nucleotide of a DNA sequence

2) Deletions: The loss of one or more nucleotides in a DNA sequence

3) Insertions: The addition of one or more extra nucleotides in a DNA sequence

There are 3 possible results from a point mutation, deletion, or insertion occurring:

1) Silent mutation: The mutation does not result in a change the amino acid sequence.

2) Missense mutation: A mutation that causes one amino acid in the protein sequence to be changed to a different one.

3) Nonsense mutation: A mutation that results in a stop codon where there used to be a codon for an amino acid. This results in translation being stopped before the primary structure of the protein is complete.

**Pre-lab Questions:** Answer these using complete sentences. ~~Incomplete sentences will be marked wrong~~.

1. Where is myostatin found?

   _____

2. What is a growth factor?

   _____

3. What is meant by the term "knockout mice"?

   _____

4. Which type of mutation will have no effect on an individual?

   _____

5. Which type of mutation will probably have the most serious effect on an individual? Why?

   _____

1) Using the DNA sequence for normal myostatin below, determine the amino acid sequence for normal myostatin. ****NOTE** YOU ARE ONLY TRANSCRIBING AND TRANSLATING A SMALL PORTION OF THE DNA SEQUENCE FOR THIS PROTEIN. YOU HAVE THE DNA SEQUENCE FOR AMINO ACIDS 273 – 288 OUT OF A TOTAL OF 376 AMINO ACIDS IN THE PROTEIN.**

2) Using the DNA sequence for Belgian Blue myostatin below, determine the amino acid sequence for Belgian Blue myostatin. Again, you have only a small portion of the DNA sequence for the Belgian Blue myostatin as well, beginning with the triplet for amino acid number 273.

3) Using an arrow, point out where the mutation in the DNA sequence for Belgian Blue myostatin is located.

**NORMAL MYOSTATIN:**

| | 273 | | | | | | | | | | | | | | | 288 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **DNA** | TGT | GAT | GAA | CAC | TCC | ACA | GAA | TCT | CGA | TGC | TGT | CGC | TAC | CCC | CTC | ACG |
| **mRNA** | ACA | | | | | | | | | | | | | | | |
| **Amino Acid** | Thr | | | | | | | | | | | | | | | |

**BELGIAN BLUE MYOSTATIN:**

| | 273 | | | | | | | | | | | | | | | 288 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **DNA** | TGT | GAC | AGA | ATC | TCG | ATG | CTG | TCG | CTA | CCC | CCT | CAC | GGT | GGA | TTT | TGA |
| **mRNA** | | | | | | | | | | | | | | | | |
| **Amino Acid** | | | | | | | | | | | | | | | | |

**Analysis Questions:** Answer all sentences using complete sentences. Failure to follow these directions will result in the question being marked wrong.

1) Based on the appearance of the organisms that have a mutated version of the myostatin gene, what does the function of myostatin seem to be in mammals?

3) How many bases were changed, inserted, or deleted in the Belgian Blue myostatin?

4) What was the result of the mutation that occurred? i.e. Was this a silent mutation, missense mutation or nonsense mutation?

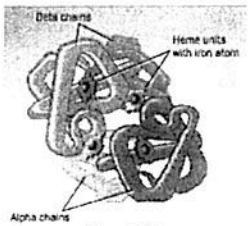
5) What level of structure of the Belgian Blue myostatin protein is the most directly affected by this mutation?

6) A breed of cattle called the Piedmontese cattle has the same type of extra muscle as the Belgian Blue cattle; however, the mutation to the myostatin gene is different. It is caused by a point mutation that changes a guanine to an adenine at DNA nucleotide number 941. This causes cysteine to be replaced with Tyrosine in the amino acid sequence. Is this a silent mutation, missense mutation, or nonsense mutation?

7) With both the Belgian Blue cattle and the Piedmontese cattle, which level of protein structure that is so important in determining how the protein will function is probably disrupted? Why is it disrupted?

**Hemoglobin:**

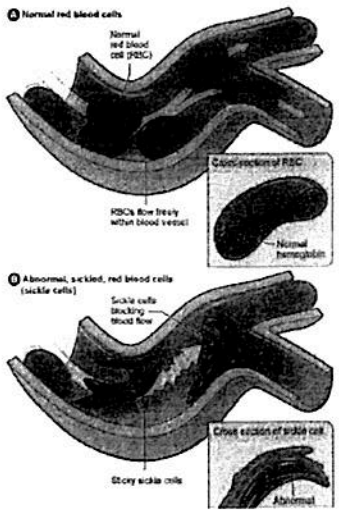
Hemoglobin is a protein found in the erythrocytes (red blood cells) of mammals. Its function is to carry oxygen from the lungs to all of the cells of the body, and carbon dioxide from all of the cells of the body to the lungs. The protein consists of 574 amino acids that are arranged into 4 subunits. 2 of the subunits are identical to each other and called alpha-globin subunits. The other 2 subunits are also identical to each other, but are called beta-globin subunits.




**Hemoglobin**

**Sickle Cell Anemia:**

In an individual with sickle cell anemia, the red blood cells, which are responsible for carrying oxygen and carbon dioxide throughout the body, are shaped like the letter "C". Normal red blood cells, on the other hand are shaped like a doughnut without a hole in the middle. The reason for the misshapen cell in individuals with sickle cell anemia is the hemoglobin protein in the red blood cells is abnormal. The sickle-shaped red blood cells don't pass through blood vessels easily, and tend to clump and stick together. This can lead to severe pain, serious infections, and organ damage.




Anemia is having less than the normal number of red blood cells. The red blood cells in individuals with sickle cell anemia only live 10-20 days, whereas a normal red blood cell lives for 120 days.

**Pre-lab Questions**: Answer these using complete sentences. Incomplete sentences will be marked wrong.

1. Where is hemoglobin found?

   _____

2. What is the role of hemoglobin in the body?

   _____

3. What is the name of the two different types of subunits that make up a hemoglobin molecule, and how many of each subunit are found in one hemoglobin molecule?

   _____

   _____

4. Compare the shape of a normal red blood cell to that of a red blood cell in someone with sickle cell anemia.

   _____

5. What is anemia, and why do people with sickle cell anemia have anemia?

   _____

1) Using the DNA sequence for normal hemoglobin on the below, determine the amino acid sequence for normal hemoglobin. ****NOTE** YOU ARE ONLY TRANSCRIBING AND TRANSLATING A SMALL PORTION OF THE DNA SEQUENCE FOR THE BETA-GLOBIN SUBUNIT OF THE PROTEIN. YOU HAVE THE DNA SEQUENCE FOR AMINO ACIDS 1-7 OUT OF A TOTAL OF 146 AMINO ACIDS IN THE BETA-GLOBIN SUBUNIT.**

2) Using the DNA sequence for sickle cell hemoglobin on the below, determine the amino acid sequence for sickle cell hemoglobin. Again, you have only a small portion of the DNA sequence for th sickle-cell beta-globin subunit as well, beginning with the triplet for amino acid number 1.

3) Either circle or highlight where the mutation for sickle-cell hemoglobin is located.

**NORMAL HEMOGLOBIN:**

| | 1 | | | | | | 7 |
|---|---|---|---|---|---|---|---|
| **DNA** | CAC | GTG | GAC | TGA | GGA | CTC | CTC |
| **mRNA** | | | | | | | |
| **ıino Acid** | | | | | | | |

**SICKLE CELL HEMOGLOBIN:**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **DNA** | CAC | GTG | GAC | TGA | GGA | CAC | CTC |
| **mRNA** | | | | | | | |
| **ino Acid** | | | | | | | |

**Analysis Questions:** Answer all questions using complete sentences. Failure to follow these directions will result in the question being marked wrong.

1. Which **type** of mutation occurred in the gene for sickle-cell hemoglobin?

_____

2. How many bases were changed, inserted, or deleted in the gene for sickle-cell hemoglobin?

_____

3. What was the **result** of the mutation that occurred? i.e. Was this a silent mutation, a missense mutatio or a nonsense mutation?

_____

have sickle cell anemia. The average life expectancy of someone with sickle cell anemia is around 45 years. If someone inherits one bad gene for hemoglobin and one good gene, they are said to have sickl cell trait. Individuals with sickle cell trait are less susceptible to malaria than individuals who inherit two normal versions of the hemoglobin gene. Given this information, why do you suppose that sickle cell trait and sickle-cell anemia are much more prevalent in the African-American population than in any other race of individuals in America?

_____

_____

_____

_____

5. Sickle cell anemia is more common in our modern population than in the past, and individuals with sickle cell anemia are living much longer lives than they used to. Why do you suppose this is the case?

_____

_____

6. In the spaces provided below write a 3 nucleotide DNA sequence, then transcribe and translate it. Then change one letter in the DNA sequence so that the amino acid does not change.

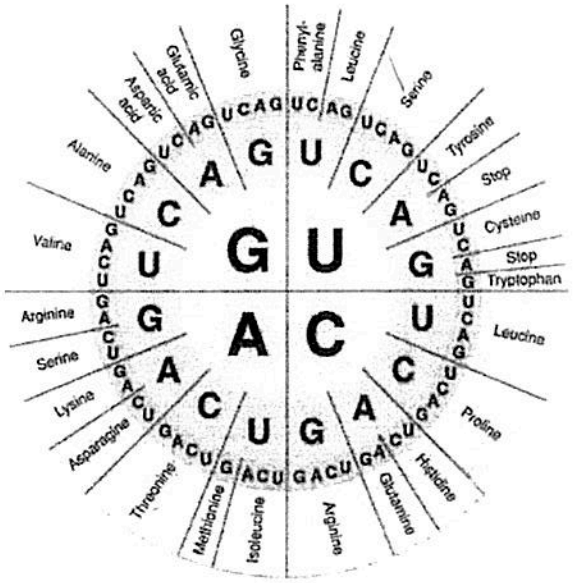
**DNA** _____ **New DNA** _____

**mRNA** _____ **mRNA** _____

**Amino Acid** _____ **Amino Acid** _____

What type of mutation is this? _____

_____




**3-LETTER AMINO ACID ABBREVIATIONS**

| AMINO ACID | ABBREVIATION |
|---|---|
| Alanine | Ala |
| Arginine | Arg |
| Asparagine | Asn |
| Aspartic Acid | Asp |
| Cysteine | Cys |
| Glutamine | Gln |
| Glutamic Acid | Glu |
| Glycine | Gly |
| Histidine | His |
| Isoleucine | Ile |
| Leucine | Leu |
| Lysine | Lys |
| Methionine | Met |
| Phenylalanine | Phe |
| Proline | Pro |
| Serine | Ser |
| Threonine | Thr |
| Tryptophan | Trp |
| Tyrosine | Tyr |
| Valine | Val |