**THE IMPACT OF MUTATIONS**

A mutation is any change to the normal DNA sequence of a gene for any protein. There are 3 basic types of mutations that can occur:

**Substitutions**: A change in any single nucleotide of a DNA sequence

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

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

There are 4 possible *results*:

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.

4) **Frameshift mutation**: A mutation of an insertion or deletion where the sequence is completely different from the where the change occurred.

**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 lbs., and females over 1100 pounds! This breed originated in the 1850’s in Belgium as a result of breeding two different types of cattle. Questions biologists have obviously asked are: What causes these cattle to develop such large muscles? Is it their diet, the exercise they get, or something in their DNA?

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.

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.***

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.

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

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**Analysis Questions:**

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

2) Which **type** of mutation occurred in the Belgian Blue myostatin?

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

4) What was the **result** of the mutation that occurred?

5) 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?

6) 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?

**PART 2:**  **Hemoglobin and Sickle Cell Anemia**

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 one another, but are called beta-globin subunits.

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 normalred blood cell lives for 120 days.

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.***

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 the sickle-cell beta-globin subunit as well, beginning with the triplet for amino acid number 1.

Either *circle* where the mutation for sickle-cell hemoglobin is located.



**Analysis Questions:**

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?

4. Only people who have inherited 2 bad genes (one bad gene from each parent) for hemoglobin actually have true 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 sickle 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. In the spaces provided below write a unique 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 \_\_\_\_\_\_\_\_\_\_**

6. What type of mutation did you just show and what is the result of the mutation?

PART 3: Complete the boxes below. Classify each as **Deletion**, **Insertion** or **Substitution** **AND** as either **frameshift**, **missense**, **silent** or **nonsense**

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| **Original DNA Sequence**: **T A C A C C T T G G C G A C G A C T** …  **mRNA Sequence:**  **Amino Acid Sequence:** |

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| Mutated DNA **Sequence #1** **T A C A T C T T G G C G A C G A C T** …  What’s the **mRNA** sequence? (*Circle the change*)  What will be the **amino acid** sequence?  What will be the results? What type of mutation is this? \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |

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| Mutated DNA **Sequence #2** **T A C G A C C T T G G C G A C G A C T** …  What’s the **mRNA** sequence? (*Circle the change*)  What will be the **amino acid** sequence?  What will be the results? What type of mutation is this? \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |

**Conclusions**:

Which type of mutation is responsible for **new variations** of a trait?

Which type of mutation does **not** result in an abnormal amino acid sequence?

Which type of mutation stops the **translation** of an mRNA molecule?

Which type of mutation probably has the most serious effect on an individual? Why?