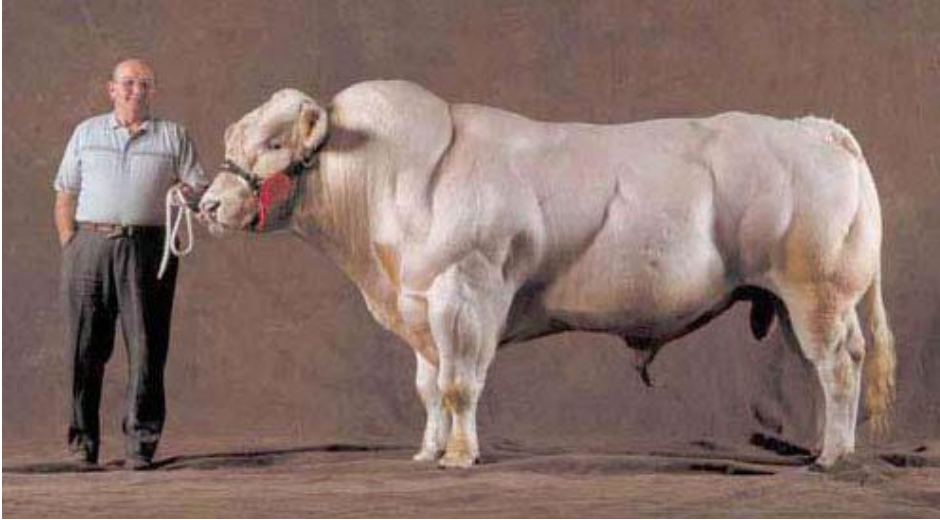


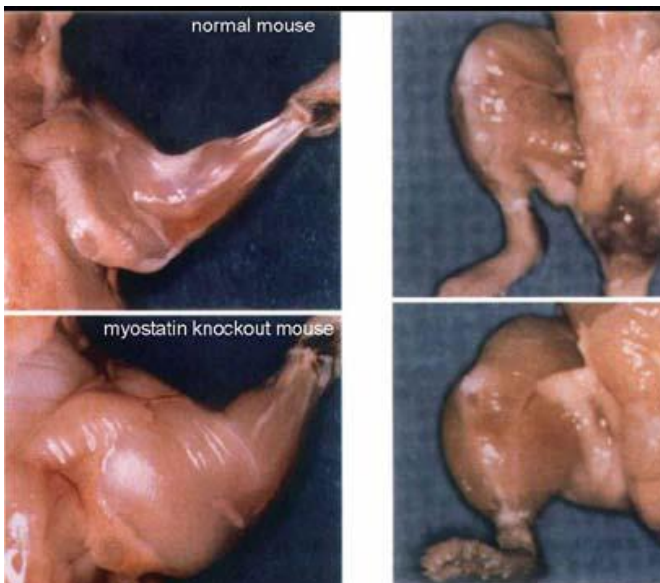
The Effects of Mutations

Part A: 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 1850s in Belgium as a result of breeding two different types of cattle. Biologists have discovered that the excessive muscle development is caused by a mutation.



Myostatin (also called growth differentiation factor-8) is a growth factor found in the skeletal muscle of mammals. Experimenters at Johns Hopkins University first discovered the role of the gene in mice. Myostatin knockout mice were engineered that developed two to three times more muscle than mice with 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.



iii) Nonsense mutation.

1. Define the terms growth factor and knockout mouse.

2. Provide a definition for each of the three general types of mutations that can occur:

- i) Point mutation.
- ii) Deletions.
- iii) Insertions.

3. Predict which type of mutation would have the most serious effect on an individual. Justify your answer.

4. Provide a definition for each of the three possible results of a point mutation:

- i) Silent mutation.
- ii) Missense mutation.

5. Tables 1 and 2 show the nucleotide sequence of a segment of the wild type and mutant myostatin genes. Complete the tables to identify amino acids 273-288 of the 375 amino acids in the protein.

Table 1: Nucleotide sequence for wild-type myostatin gene

273

288

| | | | | | | | | | | | | | | | | |
|------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| DNA | TGT | GAT | GAA | CAC | TCC | ACA | GAA | TCT | CGA | TGC | TGT | CGC | TAC | CCC | CTC | ACG |
| mRNA | | | | | | | | | | | | | | | | |
| Amino acid | | | | | | | | | | | | | | | | |

Table 2: Nucleotide sequence for Belgian Blue myostatin gene

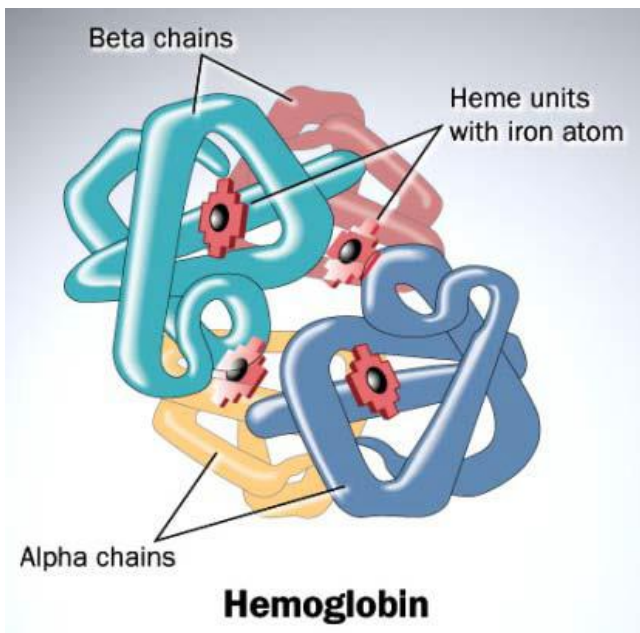
273

288

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

6. Indicate the location of the mutation in the DNA sequence for Belgian Blue myostatin.
7. a) Identify the type of mutation which resulted in the Belgian Blue myostatin. Justify your response.
b) Describe the result of the mutation.
8. Based on the appearance of the organisms that have a mutated version of the myostatin gene, suggest the function of myostatin in mammals.
9. 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. Identify the specific type of point mutation in the Piedmontese cattle.
10. In both the Belgian Blue cattle and the Piedmontese cattle, a change in the primary structure of a protein results in a physical change in the animals. Provide an explanation for how this is possible.

Part B: Hemoglobin is a protein found in the erythrocytes (red blood cells) of mammals. Its function is to carry oxygen in the blood to be delivered to all cells of the body. (It also carries some carbon dioxide from 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.



There is a particular mutation in the hemoglobin gene that results in red blood cells that have a sickle shape. Normal red blood cells are biconcave disks. The sickle-shaped red blood cells don't pass through blood vessels easily, and tend to clump and stick together. This can cause severe pain, bacterial infections, and stroke. Sickle cell hemoglobin carries less than the normal amount of oxygen. 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.

11. Repeat the steps you completed for the myostatin gene using the sequence for the normal and mutated hemoglobin gene below.

Table 3: Nucleotide sequence for wild-type hemoglobin

1

7

| | | | | | | | |
|------------|-----|-----|-----|-----|-----|-----|-----|
| DNA | CAC | GTG | GAC | TGA | GGA | CTC | CTC |
| mRNA | | | | | | | |
| Amino acid | | | | | | | |

Table 4: Nucleotide sequence for mutant hemoglobin

1

7

| | | | | | | | |
|------------|-----|-----|-----|-----|-----|-----|-----|
| DNA | CAC | GTG | GAC | TGA | GGA | CAC | CTC |
| mRNA | | | | | | | |
| Amino acid | | | | | | | |

12. Define anemia and state why people with sickle cell trait have anemia.

13. Identify the type of point mutation that causes sickle cell disease. Justify your response.

14. Only people who have inherited 2 copies of the mutated gene (one from each parent) for hemoglobin actually have sickle cell disease. About 90% of people with the disease survive to age 20, and close to 50% survive beyond age 50. 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. Suggest a reason why sickle cell trait and sickle-cell anemia are much more prevalent in the African-American population than in any other race of humans.

15. 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. Provide a reason for this observation.