

Decoding Mutations

Name: _____

Period: _____ Date: _____

Classify mutations by type and *draw conclusions* about the effect of each mutation.

Case Study: Regulation of the Lactase Gene

Howard Hughes Medical Institute

A gene is **expressed** when it is transcribed, translated, and processed to produce a protein. Lactase is an enzyme that helps infants break down lactose, a sugar in milk. A person can digest lactose when the lactase gene (LCT) is expressed in the cells of the small intestine. Most mammals (including early humans) do not drink milk after infancy, and the lactase gene is usually inactivated (i.e., shut off). If the gene is not expressed, or if expression is reduced, there may not be enough lactase enzyme to digest lactose. In most people with lactose intolerance, LCT gene transcription is drastically reduced, resulting in very low levels of lactase. Populations from northern Europe and regions in Africa have mutations near the LCT gene that cause lactase production to continue into adulthood. Lactose intolerance is very prevalent among non-European populations. Lactose tolerance is, historically speaking, the “mutant” form. Called **lactase persistence**, this is thought to be a human evolutionary adaptation to drinking milk from domesticated animals. Lactose tolerance is dominant over intolerance. In other words, lactose intolerance shows recessive inheritance. The mutation appeared at about the same time as the domestication of cattle, according to archaeological evidence.

It is important to note that genes themselves do not cause disease—genetic disorders are caused by mutations that make a gene function improperly. For example, when people say that someone has “the cystic fibrosis gene,” they are referring to a mutated version of the CFTR gene, which causes the disease. All people, including those without cystic fibrosis, have a version of the CFTR gene.

A gene mutation is a permanent, heritable change in the DNA sequence that makes up a gene. A **point mutation** is an insertion, deletion, or substitution of one or a few bases. A **frameshift mutation** is a deletion or insertion of a number of bases that is *not* a multiple of 3, so that the codon reading frame is shifted. Gene mutations can be classified by their effects on DNA structure and protein function.

Classification of mutations by effect on the **structure** of the gene:

- Insertion: one or more DNA bases are added
- Deletion: one or more DNA bases are lost
- Substitution: base is replaced by one of the other three bases
- Duplication: extra copy of all or part of a chromosome
- Inversion: 180° rotation of a DNA sequence
- Translocation: parts of non-homologous chromosomes change places

Classification of mutations by effect on the **function** of the gene (or protein):

- Missense mutation: changes the original amino acid to a different amino acid
- Nonsense mutation: a single nucleotide change that turns a sense codon (one coding for an amino acid) into one of the three stop codons, resulting in a premature end to the translation process
- Silent mutation: does not change the amino acid originally coded for

Below are descriptions of different mutations. Match each with the term that best describes this mutation. You may use the terms once, more than once, or not at all.

- A. Missense mutation
B. Nonsense mutation
C. Silent mutation
1. G is changed to C within an **intron** _____
2. TCA codon is changed to TCG _____
3. TCA codon is changed to CCA _____
4. TCA codon is changed to TAA _____

5. The RNA sequence below encodes a very short protein. Put a box around the codon where translation will STOP.

AUG-UCC-CAC-UAU-CCC-UAG-GCG-AUC

6. Decode the sequence of amino acids in the protein (remember that the protein only consists of the amino acids coded for up to the STOP codon).

7. If the underlined base changed from U to G, what would be the effect on the protein? How would you classify this mutation structurally and functionally?

8. If the underlined base changed from U to C, what would be the effect on the protein? How would you classify this mutation structurally and functionally?

9. Below is the DNA sequence for a short protein. Draw a box around the STOP codon.

ATG-GCC-ACT-GAA-TCC-TGA-ATG-GAC

10. How many amino acids will the protein translated from this mRNA have? _____

11. Give the amino acid sequence of the protein.

12. If a mutation occurs and the A nucleotide in the third codon is changed to a C, how will this affect the amino acids in the protein? How would you classify this mutation structurally and functionally?

13. Transcribe the following DNA sequence into RNA:

T T A C C C G A T G A A T C G G T G A T C

14. Translate the RNA sequence into amino acids:

On the next page, perform the following types of mutation on the **DNA sequence**. Show the **amino acid sequence** that would result from each mutation.

- Frameshift
- Base pair substitution
- Silent mutation
- Missense mutation
- Nonsense mutation

- 15. Frameshift: _____
- 16. Base pair substitution: _____
- 17. Silent mutation: _____
- 18. Missense mutation: _____
- 19. Nonsense mutation: _____

Sickle-cell Anemia

From Scitable: Genetic Mutation

Clancy, S. (2008) Genetic mutation. *Nature Education*1(1):187

Although the human genome consists of 3 billion nucleotides, changes in even a single base pair can result in dramatic physiological malfunctions. For example, sickle-cell anemia is a disease caused by the smallest of genetic changes. Here, the change of a single nucleotide in the gene for the hemoglobin protein (the oxygen-carrying protein that makes blood red) is all it takes to turn a normal hemoglobin gene into a sickle-cell hemoglobin gene. This single nucleotide change alters only one amino acid in the protein chain, but the results are devastating.

Molecules of sickle-cell hemoglobin stick to one another, forming rigid rods. These rods cause a person's red blood cells to take on a deformed, sickle-like shape, thus giving the disease its name. The rigid, misshapen blood cells do not carry oxygen well, and they also tend to clog capillaries, causing an affected person's blood supply to be cut off to various tissues, including the brain and the heart. Therefore, when an afflicted individual exerts himself or herself even slightly, he or she often experiences terrible pain, and he or she might even undergo heart attack or stroke—all because of a single nucleotide mutation

Transcribe and translate the following hemoglobin sequences.

DNA Sequence for Normal Hemoglobin:

ATGGTGCACCTGACTCCTGAGGAGAAGTCTGCCGTTACT

- 20. RNA: _____
- 21. Amino acids: _____

DNA Sequence for Sickle-Cell Hemoglobin:

ATGGTGCACCTGACTCCTGTGGAGAAGTCTGCCGTTACT

- 22. RNA: _____
- 23. Amino acids: _____

24. What is the specific nucleotide change between normal and sickle-cell hemoglobin?

25. How does this affect the amino acid sequence?

26. What type of structural mutation is this? _____

27. What type of functional mutation is this? _____