Name: Key Date: 2021 Honors Biology 2020

Mutations Review - An Application of Protein Synthesis

A **mutation** is any error or change in the DNA sequence.

Part I: Learning types of Point Mutations

Directions: For each DNA/mRNA strand provided break the mRNA strand into codons, then use the codon chart to translate the language from nitrogen bases to amino acids. Also, highlight the space in the DNA strand where the mutation has occurred.

1. Master: T A C C G T G G A T G G A A A C A T A C T
   mRNA: A U G | G C A | C C U | A C C | U U U | G U A | U G A
   Amino Acids: Meth, Ala, Pro, Thr, Phe, Val, STOP.

2. Master: T A C C G T G C A T G G A A A C A T A C T
   mRNA: A U G | G C A | C G U | A C C | U U U | G U A | U G A
   Amino Acids: Meth, Ala, Arg, Thr, Phe, Val, Stop.

   Compare this DNA/mRNA sequence to Question 1. Mark any difference you find.

   What kind of mutation is this? point mutation/substitution/missense

3. Master: T A C C G T G A T G G A A A C A T A C T
   mRNA: A U G | G C A | C U A | C C U | U U G | U A U | G A *missing C
   Amino Acids: Meth, Ala, leu, Pro, leu, Iso, _____.

   Compare this DNA/mRNA sequence to Question 1. Mark any difference you find.

   What kind of mutation is this? point mutation/deletion/frameshift/missense

4. Master: T A C C A G T G G A T G G A A A C A T A C T
   mRNA: A U G | G U C | A C C | U A C | C U U | U G U | A U G | A
   Amino Acids: Meth, Val, Thr, Tyr, leu, Cyt, Meth.

   Compare this DNA/mRNA sequence to Question 1. Mark any difference you find.

   What kind of mutation is this? point mutation/insertion/frameshift/missense

5. Master: T A C C G T G G A T G G A A G C A T A C T
   mRNA: A U G | G C A | C C U | A C C | U U C | G U A | U G A
   Amino Acids: Meth, Ala, Pro, Thr, Phe, Val, Stop.

   Compare this DNA/mRNA sequence to Question 1. Mark any difference you find.

   What kind of mutation is this? point mutation/substitution/silent mutation

6. Master: TAC CCT ACC TGC CA TAG TAT T
mRNA: AUG GGA UGG ACG GUA UCA UAA
Amino Acids: Meth, Gly, Try, Thr, Val, Thr, Stop.

7. Master: TACCC T ACT TGC CATAGT ATT
mRNA: AUG GGA UGA ACG GUA UCA UAA
Amino Acids: Meth, Gly, Stop, _____, _____, _____, _____.

Compare this DNA/mRNA sequence to Question 6. Mark any difference you find.

What kind of mutation is this? Point mutation/ Substitution/ nonsense

Identify the type of mutations in the examples above:
First decide whether the mutation is a **substitution**, **deletion** or **insertion** and then determine whether they are a **missense** mutation, a **nonsense** mutation or a **silent** mutation. Which mutation(s) result in a **frameshift** mutation?

Please note: The mutations shown above involving one nucleotide are called **point mutations**. There is another class of mutations called **chromosomal mutations**. Chromosomal mutations affect segments of chromosomes and involve multiple genes and long segments of nucleotides. A **Translocation** is an example of a chromosomal mutation (when a piece of one chromosome attaches to another, non-homologous chromosome). When entire segments of chromosomes are lost, that is referred to as a **deletion**. There could also be an **inversion** where a segment of a chromosome undergoes breakage and rearrangement within itself.

Part II: An Application of Mutations in Humans: Sickle Cell Anemia
How does a mutation in the gene for hemoglobin result in Sickle Cell Anemia?

Background: Different versions of the same gene are called **alleles**. These different alleles share the same general sequence of nucleotides, but they differ in at least one nucleotide in the sequence. Different alleles can result in different characteristics by the following sequence:

Differences in the nucleotide sequence in the gene

- ➔ *lead to differences in the nucleotide sequence in mRNA*
- ➔ *lead to differences in the amino acid sequence in the protein*
- ➔ *lead to differences in the structure & function of the protein*
- ➔ *lead to differences in a person's characteristics*

Hemoglobin is a protein inside red blood cells that binds to oxygen and allows for its transport throughout the body. If someone has an allele that codes for sickle cell hemoglobin, they will produce mis-shaped hemoglobin instead of typical-forming hemoglobin and their capacity for oxygen transport will be reduced. Additionally, the altered hemoglobin then can affect the overall shape of the red blood cell and the cells appear sickled in shape. The sickled red blood cells can then clump together and ultimately, the person with this condition suffers from anemia (the lack of enough red blood cells to adequately transport oxygen leading to fatigue, shortness of breath and other serious complications).

The following exercise will help you to understand how differences between the varieties of the hemoglobin gene can be expressed (either causing sickle cell or not). Then you will learn how the differences between the typical and sickle cell hemoglobin proteins can result in good health or sickle cell anemia.

1. In the table below, compare the DNA for the *Beginning of the **Typical** Hemoglobin Gene* to the *Beginning of the **Sickle Cell** Hemoglobin Gene*. Identify the difference.
2. Complete the table below. (Use the codon translator sheet)

Typical Hemoglobin Gene (more common in the population)

Beginning of a **typical** Hemoglobin ***Gene***	**CAC GTA GAC TGA GGA CTC**					
Transcription produces:	codon 1	codon 2	codon 3	codon 4	codon 5	codon 6
Beginning of a **typical** Hemoglobin ***mRNA***	GUG	CAU	CUG	ACU	CCU	GAG
Translation produces:	amino acid 1	amino acid 2	amino acid 3	amino acid 4	amino acid 5	amino acid 6
Beginning of a **typical** Hemoglobin ***Protein***	Val	His	Leu	Thr	Pro	Glu

Sickle Cell Hemoglobin Gene

Beginning of **Sickle Cell** Hemoglobin ***Gene***	**CAC GTA GAC TGA GGA CAC**					
Transcription produces:	codon 1	codon 2	codon 3	codon 4	codon 5	codon 6
Beginning of **Sickle Cell** Hemoglobin ***mRNA***	GUG	CAU	CUG	ACU	CCU	GUG
Translation produces:	amino acid 1	amino acid 2	amino acid 3	amino acid 4	amino acid 5	amino acid 6
Beginning of **Sickle Cell** Hemoglobin ***Protein***	Val	His	Leu	Thr	Pro	Val

3. What is the difference in the amino acid sequence of the hemoglobin molecules synthesized by translating the sickle cell vs. typical hemoglobin mRNA molecules?

Codon 6: Glutamic Acid is switched to Valine

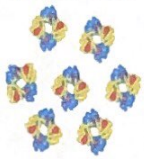
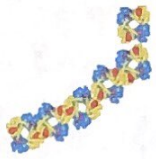
4. What kind of mutation is this?

Point mutation/substitution/missense

Part III (Extension): The effect of Sickle Cell Gene:

Each complete hemoglobin protein has more than 100 amino acids. Sickle cell hemoglobin and typical hemoglobin differ in only a single amino acid. This difference in a single amino acid results in the very different properties of sickle cell hemoglobin, compared to typical hemoglobin.

If a person inherits two copies of the sickle cell hemoglobin gene and produces only sickle cell hemoglobin, then the sickle cell hemoglobin will tend to clump together in long rods. These long rods of clumped-together sickle cell hemoglobin change the shape of the red blood cells from their typical disk shape to a sickle shape (see chart). The sickle-shaped red blood cells can block the blood flow in the tiny capillaries, causing pain and damage to body organs. In addition, the sickle-shaped red blood cells do not last nearly as long as normal red blood cells, so the person does not have enough red blood cells, resulting in anemia.

Genotype	→	Protein	→	Phenotype
HH (2 alleles for typical hemoglobin)	→	Typical hemoglobin in red blood cells  NORMAL HEMOGLOBIN	→	Disk-shaped red blood cells → healthy individual 
hh (2 alleles for sickle cell hemoglobin)	→	Sickle cell hemoglobin in red blood cells  CLUMPED HEMOGLOBIN	→	Sickle-shaped red blood cells → pain, damage to body organs, anemia 

In summary, the sickle cell allele results in production of the sickle cell hemoglobin protein, which results in the health problems observed in sickle cell anemia. This is a dramatic example of the importance of the nucleotide sequence in a gene, which determines the amino acid sequence in a protein, which in turn influences the characteristics of an individual.

In summary:

How does someone's DNA determine whether they develop sickle cell anemia?

People inherit their genes from their biological parents (sperm & egg). The genes are expressed in the form of proteins. Sometimes there are mutations which may cause a change in how the protein forms, which is the source of variation in populations. A mutation in the hemoglobin gene can cause Sickel cell.