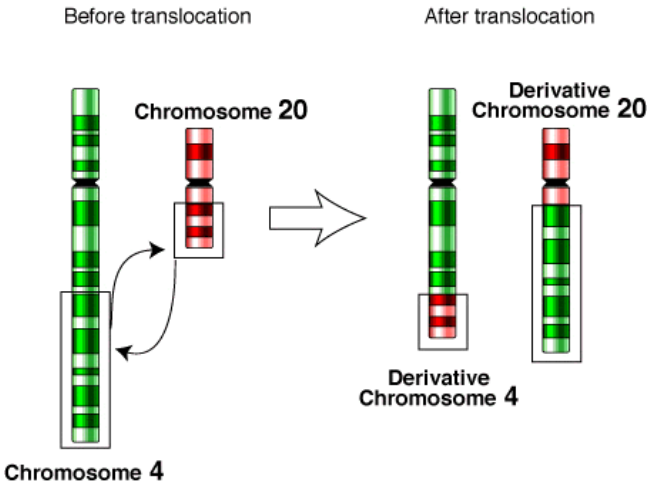
”What’s the Point?” --- Point, Frameshift, Inversion, & Deletion Mutations



http://members.cox.net/amgough/mutation_chromosome_translocation.gif

Introduction:

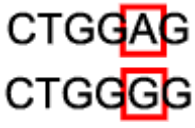
In biology, **mutations** are changes to the **base pair sequence** of the genetic material of an organism. Mutations can be caused by copying errors in the genetic material during cell division, by exposure to ultraviolet or ionizing radiation, chemical mutagens, or viruses. In multicellular organisms, mutations can be subdivided into **germ line mutations**, which can be passed on to descendants, and **somatic mutations**, which cannot be transmitted to descendants in animals.

Proteins are made of **amino acids** that are strung together in a chain. Each three-letter DNA sequence, or **codon**, encodes a **specific amino acid**. If a change in the DNA sequence occurs, the **instructions for making the proteins will be changed** producing a mutation.

Types of Mutations:

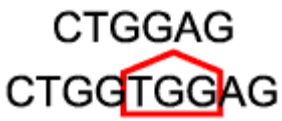
Substitution

A substitution is a mutation that **exchanges one base for another** (i.e., a change in a single “chemical letter” such as switching an A to a G).



Insertion

Insertions are mutations in which **extra base pairs are inserted** into a new place in the DNA.

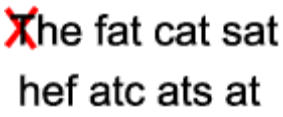


Deletion

Deletions are mutations in which a **section of DNA is lost**, or deleted.

Frameshift

Since protein-coding DNA is divided into codons three bases long, **insertions and deletions can alter** a gene so that its message is no longer correctly read and translated. These changes are called frameshifts.



Objective:

Students will use DNA sequences and corresponding paper templates of mRNA strands to show various mutations and the effect that changing these genes has on the construction of the amino acid sequence of proteins.

Materials:

- DNA strand template
- mRNA strand template
- Scissors
- Tape
- Crayons or colored pencils
- Small paper clips
- Computer with Internet Access

Procedure (Part A) – DNA Sequence & Proteins:

1. Color code the five genes on Template 1 as follows: Gene 1 – red, Gene 2 – blue, Gene 3 – green, Gene 4 – yellow, and Gene 5 – violet.

2. Cut out the 5 genes and tape them together in order, 1 – 5, to assemble a chromosome with its DNA base sequence. This is your **DNA template.**

3. Record the sequence of the DNA bases for each gene in Table 1.

4. Use the base-pairing rule to complete the mRNA nucleotide sequence that would read and copy the bases on each DNA gene in the DNA template you made. Write the correct letter for the base (a, T, C, or G) in each box of the mRNA gene. **REMEMBER: ADENINE (A) PAIRS WITH URACIL (U) AND CYTOSINE (C) WITH GUANINE (G) ON RNA.**

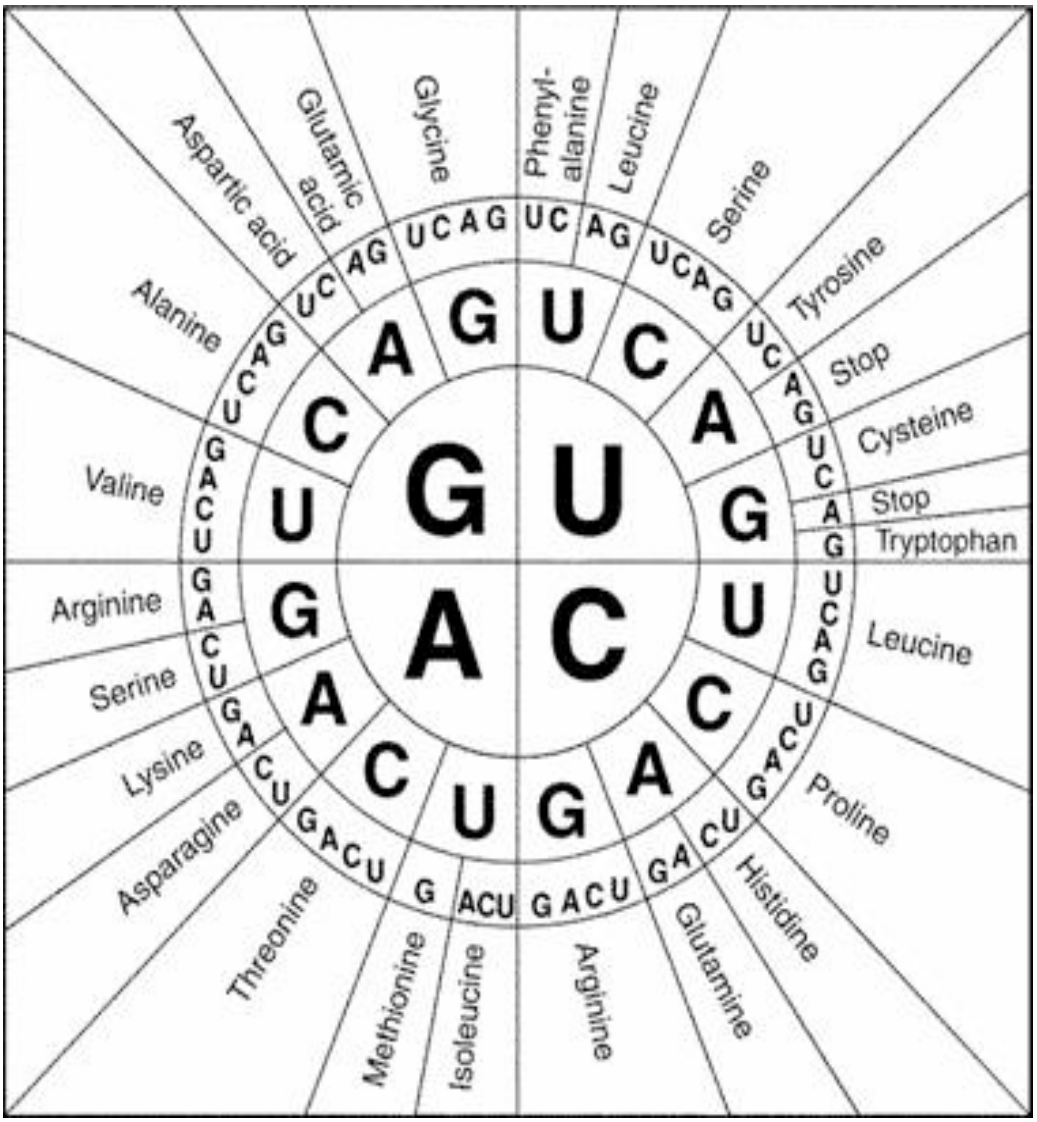
5. After each base is written on the mRNA genes, color code them as you did for the DNA genes; Gene 1 – red, Gene 2 – blue, Gene 3 – green, Gene 4 – yellow, and Gene 5 – violet.

6. Do **NOT** tape these 5 mRNA genes together. Instead, join them together in the correct order (1 – 5) with **small paper clips** so mutations can be made. This is your **mRNA template**.

7. Record the sequence of the mRNA bases for each gene in Table 1.

8. **Ribosomes** read the bases on mRNA three at a time (called a **codon**) to assemble **amino acids**. Use the **codon table** to make a list of the correct sequence of amino acids that the ribosome would assemble when it reads the mRNA template strand. Record this amino acid sequence in Table 1.

mRNA Codon Table



Procedure (Part B) - Modeling Mutations:

Use the mRNA template strand that you assembled and paper clipped together to simulate each of these types of mutations:

Substitution

1. The last base triplet of DNA Gene#1 is **TTT** which is copied by mRNA as the codon **AAA**. **(Refer to your data for Gene #1 on your Sequence Table.)**

   What amino acid did this codon code for when it was read by the ribosome?

   _____

2. If the base **guanine (G)** is substituted for the **final base thymine (T)** on the DNA gene when **DNA is replicated**, write this new sequence for the DNA gene, mRNA gene, and amino acid sequence in Data Table 2.

   Did this base substitution change the sequence of amino acids --- **yes or no**?

3. If the base substitution for this same base had been cytosine, not guanine, would the amino acid sequence have been different --- yes or no? Explain why this did or did not produce a change in the amino acid sequence.

   _____

   _____

   _____

Deletion and Frameshift

1. The base sequence on DNA Gene #2 is --- **GGG CCC TAT TAA GCA**.

2. **Write** the mRNA sequence and amino acid sequence for Gene #2 in

   Data Table 3.

3. If the **last thymine (T)** in the DNA gene is **deleted**, the new base sequence will be --- **GGG CCC TAT AAG CA.** This will change the mRNA and amino acid sequence because it **changes the reading frame by shifting it**. **Write the NEW** sequences for mRNA and amino acids in **Data Table 3**.

Insertion & Inversion

1. In order for a ribosome to know when to **start and stop reading** an mRNA strand when assembling amino acids, specific **"start" and "stop" codons** appear at the beginning and end of the mRNA strand.

2. **AUG** on mRNA is the **start** codon called **methionine**, while **UAA, UAG, and UGA** do not code for an amino acid and signal the ribosome to **stop**.

3. Look at DNA Gene #5. What are the last 3 bases? _____

   What would be the mRNA codon for these 3 bases? _____

   What does the codon stand for? _____

4. The sequence of the bases on DNA Gene #5 is --- **CTG CAT CGG CGC ATT.**

5. Insert and **extra thymine** base (T) in the **7th position** (after the sixth T and the next letter C). Write the new base sequence (16 letters total).

   New DNA base sequence: _____

6. Determine the mRNA and amino acid sequence made from this changed DNA Gene #5. **REMEMBER, IF A STOP CODON APPEARS ON mRNA, NO MORE AMINO ACIDS WILL BE ASSEMBLED.**

   New mRNA Sequence: _____

   New Amino Acid Sequence: _____

   How did this gene mutation affect the building of the protein?

   _____

   _____

7. **Inversion** is a phenomenon in which a gene turns 180^{o} and attaches in reverse order.

   If Gene #5 inverts, what will be the first 3 bases on DNA? _____

   What is the mRNA codon for these 3 bases? _____

   What do these codon stand for? _____

   What happens to the protein? _____

Questions:

1. How many genes made up your DNA strand?_____

2. How many polypeptides would this DNA template code for?_____

Using the following four codons, answer these questions. **TAC GGT AAC CAT**

3. What is the mRNA transcript sequence?

   _____

4. What is the complementary DNA strand sequence?

   _____

5. If the 3rd DNA base is deleted, what is the new mRNA sequence?

   _____

6. If the base adenine is inserted in the 7th position on the DNA strand, what is the new mRNA sequence?

   _____

7. What is the amino acid sequence coded for by the original DNA strand?

   _____

8. What is the amino acid sequence after the deletion occurred?

   _____

9. What is the amino acid sequence after the insertion occurred?

   _____

The nucleotide sequence for the left template strand of human hemoglobin is ---

TAA TGT CGA CCG CTG GTC CAA GTC CTT TGA

10. Write the nucleotide sequence for the complementary DNA strand.

_____

11. What would be the mRNA transcript sequence? What is the amino acid sequence?

_____

_____

12. If the last two codons are inverted on DNA, what is the new mRNA sequence and amino acid sequence?

_____