Activity 3.2.2: The Genetic Code

Introduction
In the previous activity, you learned how DNA encodes the instructions for creating proteins. You also learned about the basics of the process of protein synthesis. In this activity you will apply your knowledge of transcription and translation to decode a secret message as well as investigate the effect that various mutations have on protein production. You will then look specifically at the genetic mutation that causes sickle cell disease.

Equipment
• Computer
• Laboratory journal
• DNA sequence
• Activity 3.2.2: mRNA
• Activity 3.2.2: tRNA
• Activity 3.2.2: Codon – Amino Acid Dictionary
• Scissors
• Tape

Procedure
Part I: Transcribing and Translating the Genetic Code
1. Work through the Transcribe and Translate a Gene animation from the Learn.Genetics: Genetic Learning Center’s website, available from http://learn.genetics.utah.edu/content/molecules/transcribe/.
2. Note that in this activity, you will simulate the protein synthesis process. In this simulation, you will translate the code and join letters to make sentences in the way amino acids join to form a completed protein.
3. Work in a group to obtain a pair of scissors, tape, a DNA sequence, an mRNA sheet, a tRNA sheet, and a Codon – Amino Acid Dictionary from your teacher.
4. Work as a group to cut out all of the mRNA molecules and place them in a pile.
5. Your teacher will assign your group one of the DNA sentence strips.
6. Use your knowledge of transcription to build an mRNA strand with your mRNA molecules that is complementary to your DNA sentence, base pair by base pair. Remember, in RNA, adenine pairs with uracil. Spread the base pairs on the floor or a long lab bench. Tape the mRNA molecules together.
7. Fill in the appropriate tRNA bases on the tRNA sheet.
8. Work as a group to cut out the tRNA molecules and assemble them complementary to the mRNA strand. Tape the tRNA molecules together.
9. Review the following key points about protein synthesis to use as your guide to help you translate your sentence in the next step.

   - The genetic code is a triplet code, with codons of three mRNA bases coding for specific amino acids. Each triplet codon specifies only one amino acid, but an individual amino acid may be specified by more than one codon. Remember that for this activity, amino acids are represented with letters and that you will be stringing these together to make sentences instead of proteins.

   - A start codon, AUG, sets the reading frame, and signals the start of translation of the genetic code. For this activity, when you see AUG at the beginning of the sequence, it signals the start of the translation and indicates that you should capitalize the next letter the codons indicate. Please note that AUG also codes for an amino acid. Therefore, whenever you see the AUG codon in the middle of the sequence, you should use it to code for the letter it indicates on the Codon – Amino Acid Dictionary.

10. Use the Codon – Amino Acid Dictionary to find the letter coded for by each codon. (Remember that codons are mRNA bases.)

11. Look at the resulting letters to determine the secret message.

12. Write the DNA, mRNA, and the resulting protein (sentence) in the space below.

   DNA Fragment #: ______

   DNA:

   mRNA (codons):

   Protein (sentence):

Part II: Mistakes Happen

The sequence of nucleotides in a DNA molecule determines the sequence of amino acids in a protein. If the nucleotide sequence is changed, then the amino acid sequence may also change. Any change in DNA is called a mutation. You will now investigate the effect of base pair mutations on your finished protein.

13. Make a mutation to your DNA code. Choose any base in your DNA sequence (with the exception of the first three bases, as these bases code for the start codon) and randomly change it to another base. For example, choose a C and make it a G.
14. Transcribe and translate the mutated DNA (as you did in Part I) below. NOTE: You will perform this part of the activity with pen and paper and do not need to cut out the associated pieces.

DNA:

mRNA (codons):

Protein (sentence):

15. Answer Conclusion question 1.

16. Make a different mutation to your DNA code. Randomly delete one of the bases in your original DNA strand. NOTE: Do not delete one of the first three bases. Remember that DNA will be read in groups of three. If a deletion occurs, all shifts over and the ribosome simply reads the next group of three in the chain.

17. Transcribe and translate the mutated DNA below.

DNA:

mRNA (codons):

Protein (sentence):

18. Answer Conclusion questions 2 - 5.

Part III: Sickle Cell Disease
Sickle cell anemia is an inherited blood disorder caused by a mutated gene. The gene affected in this disease codes for hemoglobin, a protein in red blood cells that carries oxygen throughout the body. A single genetic mutation in the hemoglobin gene can cause sickle cell anemia. You will analyze the first seven amino acids for normal versus sickle cell hemoglobin gene in order to determine what type of mutation is responsible for causing sickle cell disease. (Note that the gene coding for hemoglobin is 146 amino acids. In this activity you will only work with a small portion of this gene.) You will use a codon chart to determine the amino acids that correspond to the mRNA sequence.
Codon charts are often called the dictionary of the genetic code. Note that the codon chart, or genetic code, is listed by codons and not anti-codons. tRNA molecules are just the vehicle that shuttle in the amino acids. In order to use the codon chart, you start at the far left column entitled First Position. Find the first mRNA base of the codon you are trying to translate. Next, follow the row and find the appropriate Second Position column that corresponds with the second mRNA base of the codon you are trying to translate. Finally, find the appropriate Third Position row that corresponds with the third and final mRNA base of the codon that you wish to translate to determine the amino acid.

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<th>Third Position</th>
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19. Transcribe and translate the DNA sequence of bases for the first 7 amino acids in Normal hemoglobin below. Use the codon chart as your guide.

DNA: C A C G T G G A C T G A G G A C T C C T C

mRNA:

Amino Acids:

20. Transcribe and translate the DNA sequence of bases for the first 7 amino acids in Sickle hemoglobin below. Use the codon chart as your guide.

DNA: C A C G T G G A C T G A G G A C A C C T C

mRNA:
21. Answer the remaining Conclusion questions.

**Conclusion**

1. Describe (in words) the effect of the mutation.

2. Was the mutational effect greater in a substitution or a deletion? Explain your answer clearly.

3. Why do you think scientists call a substitution a “point mutation”? Why do you think scientists call a deletion (or an insertion) a “frameshift mutation”?

4. Note the two transcribed and translated DNA strips below. The two strips are identical except for a point mutation, where the 15th base was changed from a G to a T. Fill in the corresponding mRNA, tRNA, and letter in the blanks below for the mutated DNA strip. In the space below, explain how this point mutation changes the protein.

**Normal DNA:**

GTTGGCGAATGAACC\_GAGGCTGACGTCTAAGCCTAGAAAAATTGG

mRNA:

CAACCGCUUACUUG\_CUCCGACUGCAGAUCGGAUCUUU UUAACC

tRNA:

GUUGGC\_GAUGAACC\_GAGGCUUGACGUCUAAGCUCAGGAAUUUGG

Sentence:
5. What is the difference between normal and sickle hemoglobin at the DNA, RNA, and protein (amino acid) level?

6. What type of mutation is the sickle hemoglobin mutation? Explain.

7. Glutamic acid (Glu) and valine (Val) are two amino acids with different molecular structures. (Glutamic acid is a strongly hydrophilic molecule, and valine is a strongly hydrophobic molecule. This is something you will learn more about in the next activity). Why do you think switching the hemoglobin gene’s sixth amino acid from glutamic acid to valine would affect the hemoglobin protein?