

From Gene to Protein—Transcription and Translation

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This activity will help you to learn how a gene provides the instructions for making a protein.

What is a **gene**? Give a definition, and give some examples of genes.

What is a **protein**? Give a definition, and give some examples of proteins.

Proteins are very important in determining the characteristics of our bodies. For example, most of us have a protein enzyme that can synthesize melanin, the main pigment that gives color to our skin and hair. In contrast, albino people make a defective version of this protein enzyme, so they are unable to make melanin and they have very pale skin and hair.

The instructions for making a protein are provided by a **gene**, which is a specific segment of a DNA molecule. Each gene contains a specific sequence of nucleotides. This sequence of nucleotides specifies which sequence of amino acids should be joined together to form the protein. The sequence of amino acids in the protein determines the structure and function of the protein. For example, the defective enzyme that results in albinism has a different amino acid sequence than the normal enzyme for synthesizing melanin.

A gene directs the synthesis of a protein by a two-step process.

First, the instructions in the gene in the DNA are copied into a **messenger RNA (mRNA)** molecule. The sequence of nucleotides in the gene determines the sequence of nucleotides in the mRNA. This step is called **transcription**.

Second, the instructions in the messenger RNA are used by **ribosomes** to insert the correct amino acids in the correct sequence to form the protein coded for by that gene. The sequence of nucleotides in the mRNA determines the sequence of amino acids in the protein. This step is called **translation**.

Complete the following table to summarize the basic characteristics of transcription and translation.

	Original message or instructions in:	Molecule which is synthesized	Location where this takes place
Transcription	Nucleotide sequence in gene in DNA in chromosome		Nucleus
Translation			

¹Teachers are encouraged to copy this student handout for classroom use. A Word file (which can be used to prepare a modified version if desired), Teacher Preparation Notes, comments, and the complete list of our hands-on activities are available at http://serendip.brynmawr.edu/sci_edu/waldron/.

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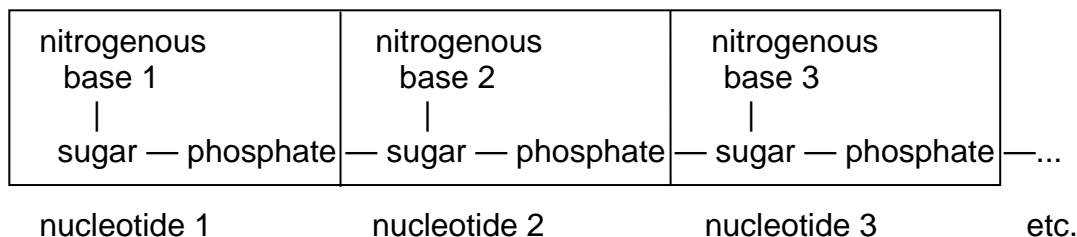
In this activity, you will use paper models to learn more about transcription and translation. Specifically, you will model how a cell carries out transcription and translation to make the beginning of the hemoglobin molecule.

What is hemoglobin?

Transcription

Since transcription is the process that makes messenger RNA (mRNA), we need to begin by understanding a little about the structure of mRNA. mRNA is a single-stranded polymer of **nucleotides**, each of which contains a nitrogenous base, a sugar and a phosphate group, similar to the nucleotides that make up DNA. mRNA is a ribonucleic acid because each nucleotide in RNA includes the sugar ribose, whereas DNA is a deoxyribonucleic acid because each nucleotide in DNA has a different sugar, deoxyribose.

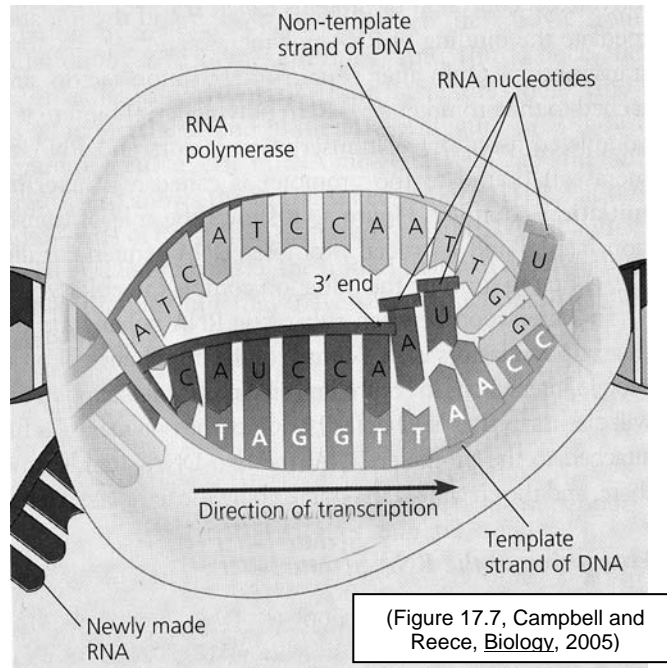
Simplified Diagram of Beginning of mRNA Molecule



How does the information in the DNA of the gene get copied into a message in the mRNA? When the mRNA is synthesized, RNA nucleotides are added one at a time, and each RNA nucleotide is matched to the corresponding DNA nucleotide in the gene. This nucleotide matching follows a **base-pairing rule** very similar to the base-pairing rule in the DNA double helix (see table).

Complementary nucleotides for base-pairing between two strands of DNA	Complementary nucleotides for base-pairing between DNA and RNA
G (guanine) pairs with C (cytosine).	G pairs with C .
A (adenine) pairs with T (thymine).	A in DNA pairs with U (uracil) in RNA. T in DNA pairs with A in RNA.

This base-pairing rule ensures that the message from the nucleotide sequence in the gene in the DNA is copied into a corresponding nucleotide sequence in the mRNA molecule. The diagram on the next page shows how the complementary RNA nucleotides are added one at a time to the growing mRNA molecule.



This figure shows that transcription requires an enzyme, **RNA polymerase**, which separates the two strands of DNA and adds RNA nucleotides, one at a time, to form the mRNA molecule. Why is RNA polymerase a good name for this enzyme?

Transcription Modeling Procedure

Note: You will work with a partner to model the actual sequence of steps used by the cell to carry out transcription. You probably will be able to think of a faster way to make the mRNA, but you should follow the sequence of steps described below in order to learn how the cell actually makes mRNA. Remember, enzymes like RNA polymerase do not have a brain, eyes or hands, so transcription must proceed in a step-by-step chemical process that adds one nucleotide at a time to the growing mRNA molecule.

1. To model the process of transcription, you and your partner will need:
 - a page showing an RNA polymerase molecule inside a nucleus,
 - a packet with a paper single strand of DNA labeled *Beginning of Normal Hemoglobin Gene* and RNA nucleotides
 - tape.

In addition, you should prepare by completing the following chart to summarize the base-pairing rule you will need to follow as you synthesize the mRNA molecule.

DNA nucleotide	Complementary nucleotide in RNA
G	
C	
T	
A	

2. One of you will act as the RNA polymerase, and the other one will be the cytoplasm which surrounds the nucleus and supplies the nucleotides which are used to make the RNA molecule.
RNA polymerase: Place the beginning of the DNA molecule on the dashed line in the RNA polymerase diagram.
Cytoplasm: Give the first RNA nucleotide (complementary to the first DNA nucleotide) to the RNA polymerase person.
RNA polymerase: Put the first RNA nucleotide in the box labeled RNA nucleotide.

With real DNA and RNA nucleotides, the shape and chemical makeup of the nucleotides ensure that only one type of RNA nucleotide can pair with each DNA nucleotide. In this paper model, all the nucleotides have the same shape, so you will have to use the nucleotide abbreviations and the base-pairing rule to match the appropriate RNA nucleotide with each DNA nucleotide.

3. Cytoplasm: Give the next RNA nucleotide (complementary to the next DNA nucleotide) to the RNA polymerase person.
RNA polymerase: Put this nucleotide in the box labeled "next RNA nucleotide" and join the two nucleotides together with transparent tape. The tape represents the covalent bond that forms between the adjacent RNA nucleotides as the mRNA molecule is synthesized. Then, move the DNA molecule and the growing mRNA molecule one space to the left.
4. Repeat step 3 as often as needed to complete the mRNA molecule, adding one nucleotide at a time. Be careful to follow the base-pairing rule accurately, so your mRNA will provide accurate information for synthesizing the beginning of the hemoglobin protein when you get to the translation step.

Questions

1. Notice that the process of transcription is similar to the process of DNA replication. What are some similarities between transcription and DNA replication?

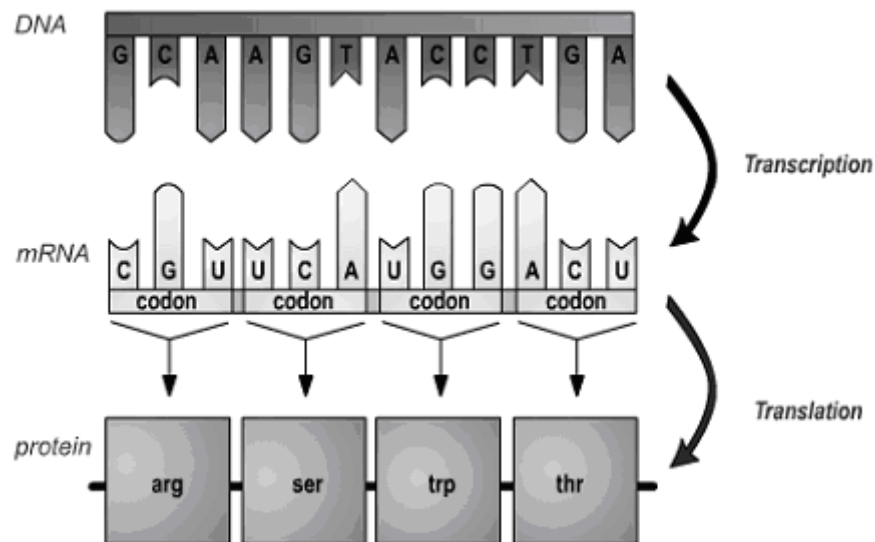
There are also a few important differences between DNA replication and transcription. Fill in the blanks in the following table to summarize these differences.

DNA replication	Transcription
The whole chromosome is replicated.	_____ is transcribed.
DNA is made. DNA is double-stranded.	mRNA is made. mRNA is _____-stranded.
DNA polymerase is the enzyme which carries out DNA replication.	_____ polymerase is the enzyme which carries out transcription.
T = thymine is used in DNA, so A pairs with T in DNA.	T = thymine is replaced by ___ = uracil in RNA, so A in DNA pairs with ___ in mRNA.

2. To summarize what you have learned, explain how a gene directs the synthesis of an mRNA molecule. Include in your explanation the words and phrases: base-pairing rule, complementary nucleotides, cytoplasm, DNA, gene, messenger RNA, nucleotide, nucleus, and RNA polymerase.

Translation

In the process of translation, the sequence of nucleotides in messenger RNA (mRNA) determines the sequence of amino acids in a protein. The figure below shows an example of how transcription is followed by translation.

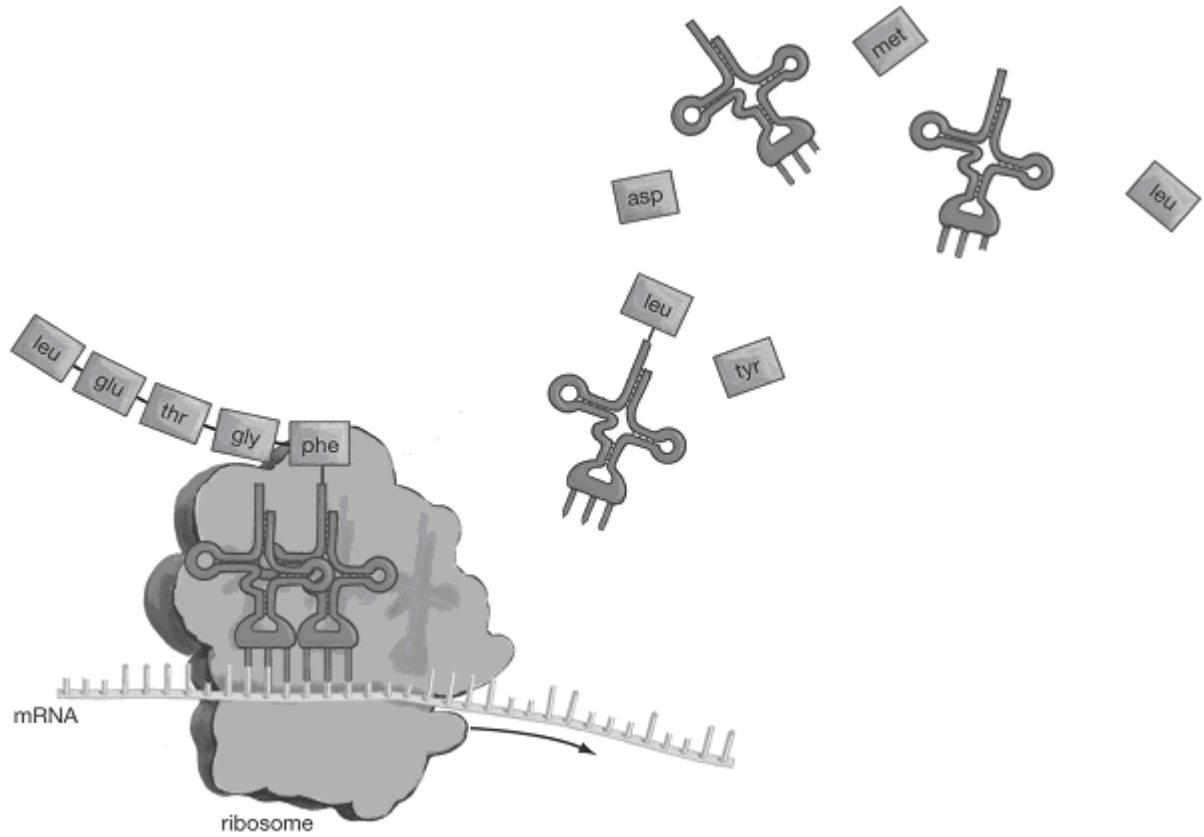


(Figure 14.6 from Krogh, *Biology, a Guide to the Natural World*, 2005)

In translation, each set of three nucleotides in an mRNA molecule codes for one amino acid in a protein. This explains why each set of three nucleotides in the mRNA is called a **codon**. Each codon specifies a particular amino acid. For example, the first codon shown above, CGU, instructs the ribosome to put the amino acid arg (arginine) as the first amino acid in this protein. The sequence of codons in the mRNA determines the sequence of amino acids in the protein. The table below shows the six codons that should be part of your mRNA molecule, together with the amino acid coded for by each of these codons.

mRNA codon	Amino acid
ACU	Threonine (Thr)
CAU	Histidine (His)
CCU	Proline (Pro)
CUG	Leucine (Leu)
GAG	Glutamic acid (Glu)
GUG	Valine (Val)

How does translation actually take place? Inside a cell, each tiny **ribosome** provides a workbench with the structure and enzyme needed for translation to take place. But how are the right amino acids added in the right sequence to match the sequence of codons in the mRNA? Translation is more complicated than transcription; the shape and chemical structure of each amino acid does *not* match the shape and chemical structure of the corresponding mRNA codon. Instead, a special type of RNA, **transfer RNA (tRNA)**, is required to ensure that the correct amino acid is brought in to match each codon in the mRNA.



(Figure 14.7 from Krogh, *Biology, a Guide to the Natural World*, 2005)

There are multiple different types of tRNA. Each type of tRNA molecule can bind to one specific type of amino acid on one end. On the other end, the tRNA molecule has three nucleotides that form an anti-codon. The three nucleotides in the tRNA **anti-codon** are complementary to the three nucleotides in the mRNA codon for that specific type of amino acid.

Circle the anti-codons in the tRNA molecules in the figure. Use *arrows* to indicate where anti-codons in tRNA are matched with complementary codons in mRNA.

In the cytoplasm there are enzymes that attach the correct amino acid to match the anti-codon of each tRNA. To show how the tRNA molecules would look after the correct amino acid has been attached, *draw* an asp amino acid attached to the top left tRNA and a tyr amino acid attached to the top right tRNA.

As you saw on the previous page, the tRNA molecules translate between the codons in the mRNA and the sequence of amino acids in the new protein molecule. To ensure accurate translation, each type of tRNA must have the correct anti-codon to match the mRNA codon for the specific amino acid carried by that type of tRNA. For example, the mRNA codon for the amino acid threonine is ACU, so, using the base-pairing rule, you know that the anti-codon in the tRNA for threonine is UGA. Complete the following chart to indicate the appropriate anti-codons in the tRNA molecules for each of the other amino acids listed.

Amino acid	mRNA codon	Anti-codon in tRNA molecule that carries this amino acid
Threonine (Thr)	ACU	UGA
Histidine (His)	CAU	
Proline (Pro)	CCU	
Leucine (Leu)	CUG	
Glutamic acid (Glu)	GAG	
Valine (Val)	GUG	

Procedure:

1. To prepare for modeling translation, you will need to have a page showing a ribosome, the tRNA molecules and amino acids from your packet, and the mRNA you made during your simulation of transcription of the DNA labeled *Beginning of Normal Hemoglobin Gene*. One of you will play the role of the ribosome and the other one will act as the cytoplasm, which is the source of tRNA and amino acid molecules.

2. For tRNA molecules to function in translation, each tRNA must first pick up the appropriate amino acid that corresponds to the anti-codon in that particular tRNA.

Cytoplasm: Use the above table to match each model tRNA molecule with the correct amino acid for that particular type of tRNA. Tape the amino acid to the tRNA *very lightly*, because they will only be joined temporarily and will separate again soon, after the tRNA brings the amino acid into the ribosome.

Note: Each model tRNA molecule only shows the three nucleotides of the anti-codon and the binding site for the amino acid. A real tRNA molecule has many, many more nucleotides in an RNA polymer that is folded in roughly the shape shown in the figure on page 6.

Modeling Translation:

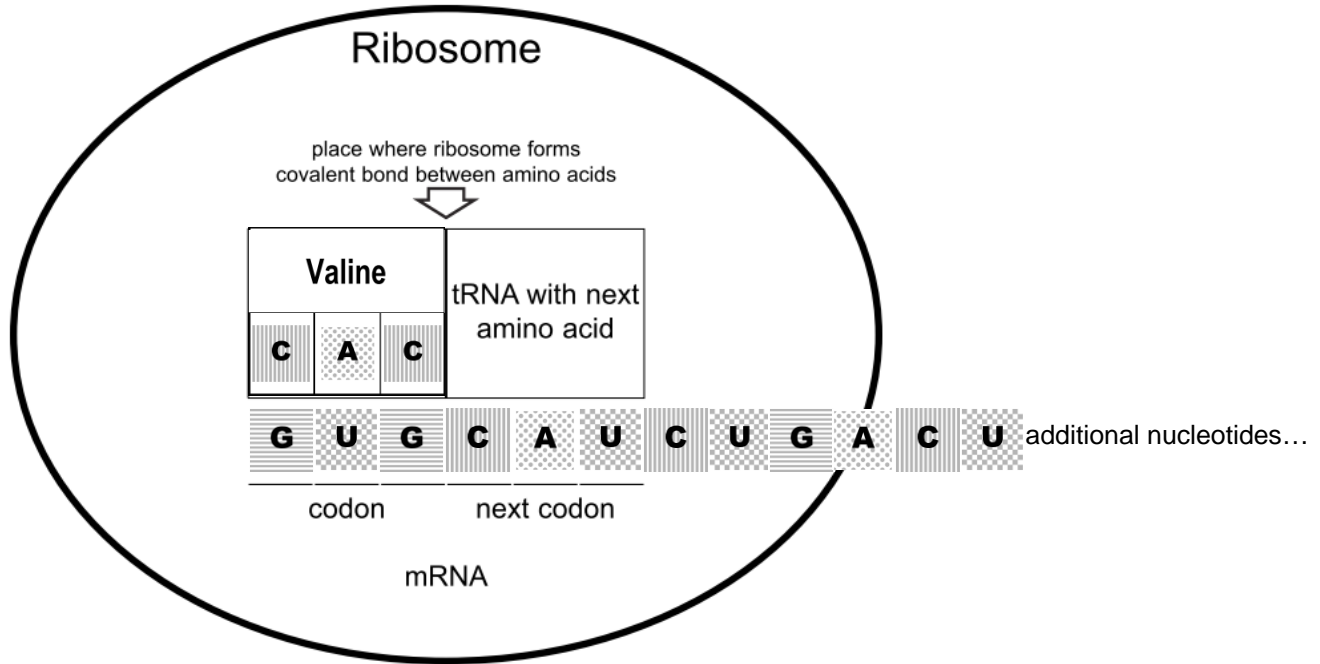
Note: You will be modeling the actual sequence of steps used by the cell to carry out translation. You probably will be able to think of a faster way to make the protein, but you should follow the sequence of steps described below in order to learn how the cell actually makes proteins.

3. Ribosome: Place the mRNA on the line in the model ribosome, with the first three nucleotides of the mRNA in the position for "codon" and the second mRNA codon in the "next codon" position.

Cytoplasm: Supply the tRNA that has the correct anti-codon to match the first codon in the mRNA.

Ribosome: Place this tRNA with amino acid in position.

Your model ribosome should look like:

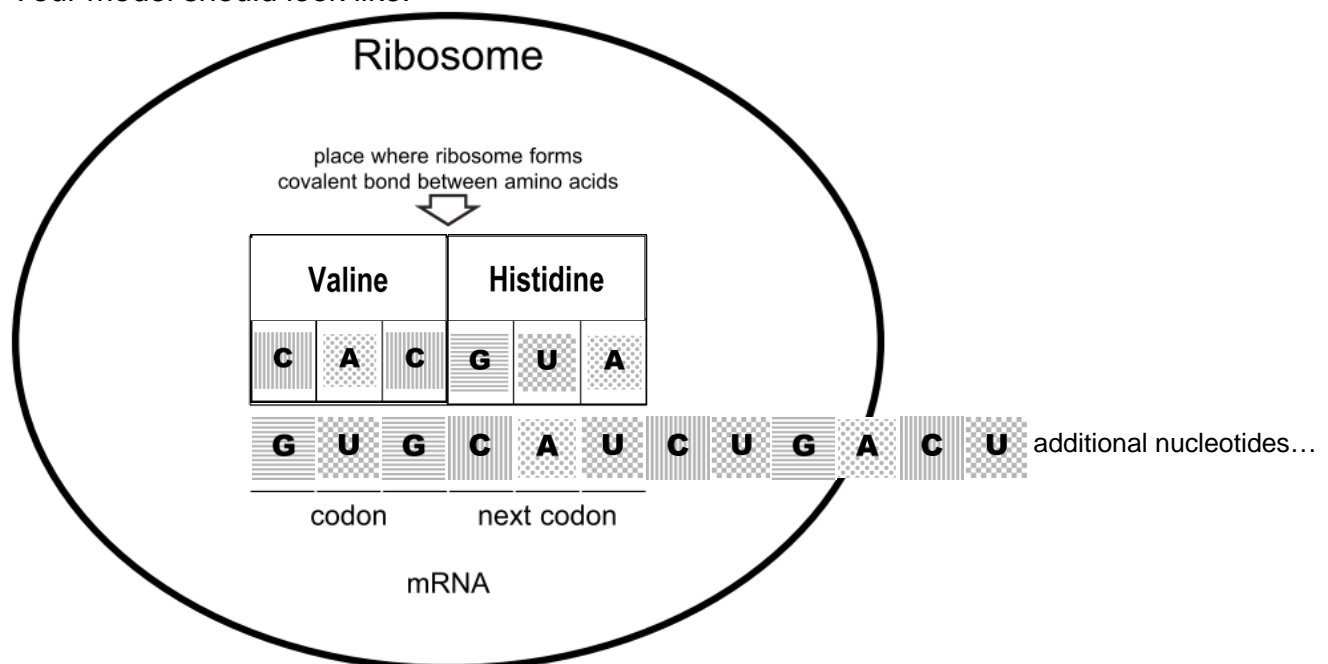


Use an *arrow* to indicate the anti-codon in the tRNA and use an * to indicate the amino acid. Put a *rectangle* around each codon in the mRNA.

4. Cytoplasm: Supply the tRNA that has the correct anti-codon to match the second codon in the mRNA and the ribosome person will place it in position. Now the ribosome is ready to link the first two amino acids in the hemoglobin protein.

Ribosome: Tape these two amino acids together to begin the formation of the hemoglobin protein. The tape represents the covalent bond between the amino acids in the hemoglobin protein. At this time, the first amino acid detaches from the first tRNA, so remove that tape.

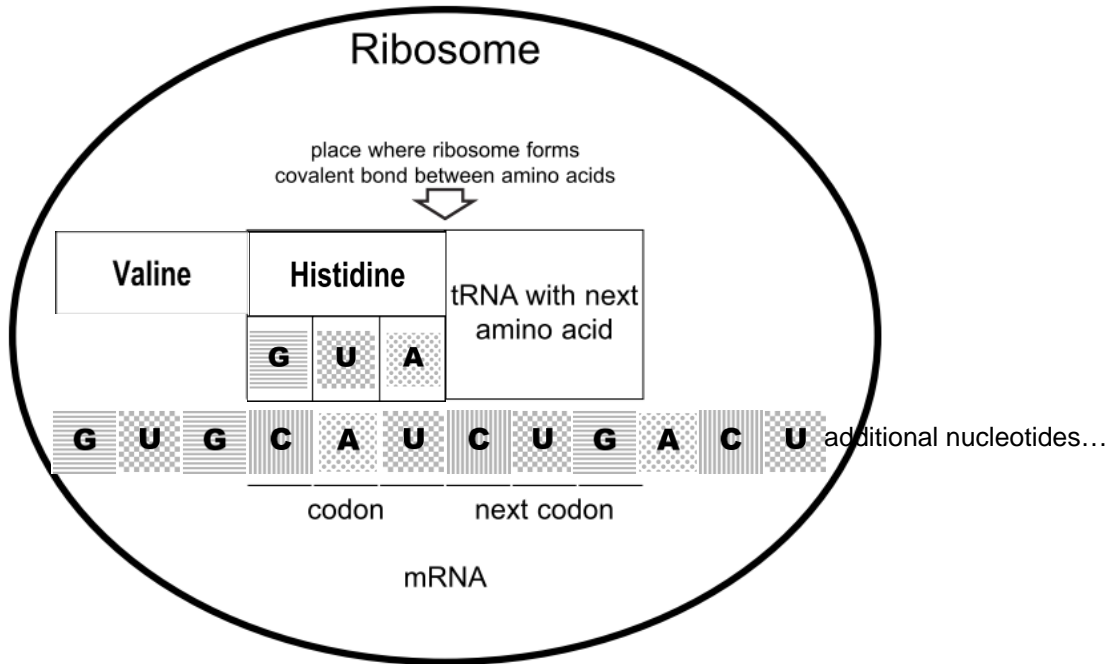
Your model should look like:



Draw a line to indicate the location where you put the piece of tape to represent the covalent bond between the first two amino acids in the new hemoglobin protein that the ribosome is making.

5. Ribosome: Move the mRNA to the left so the second codon is in the first position in the ribosome. The matching tRNA with amino acid also moves to the first position. Also, the first tRNA is released into the cytoplasm where it would be reused in a real cell.
Cytoplasm: Put the first tRNA in the packet.

Your model should look like:



Questions: What happened to the first tRNA? Why isn't it shown in this diagram?

Draw a *rectangle* around the third codon in the messenger RNA.

What is the anti-codon for that codon?

Which amino acid will be the third amino acid in the hemoglobin protein?

6. Cytoplasm: Supply the tRNA that has the correct anti-codon to match the codon in the "next codon" position.

Ribosome: Place the tRNA in position and tape the amino acid to the preceding amino acid.

Then, move the mRNA and matching tRNAs with amino acids one codon to the left. The first of these tRNAs will be released to the cytoplasm person who will put it in the packet.

7. Repeat step 6 until you have completed the beginning portion of the hemoglobin protein. Save your mRNA and protein, since you will need them for the next activity.

Questions

1. What is the function of mRNA?

2. What is the function of tRNA?

3. Describe one similarity in the structure of mRNA and tRNA.
4. Describe one difference between the structure of mRNA and tRNA.
5. The proteins in biological organisms include 20 different kinds of amino acids. What is the minimum number of different types of tRNA molecules that must exist in the cell?
6. Look at the figure on page 5 and explain why it makes sense to use the word translation to describe protein synthesis.

Explain why it would not make sense to use the word translation to describe mRNA synthesis.

7. What part of translation depends on the same base-pairing rule that is used in transcription and DNA replication?
8. You have modeled how ribosomes carry out translation. Why is it appropriate to say that the function of ribosomes is protein synthesis?

How the Gene for Sickle Cell Hemoglobin Results in Sickle Cell Anemia

Different versions of the same gene are called different **alleles**. These different alleles share the same general sequence of nucleotides, but they differ in at least one nucleotide in the sequence. This difference in the nucleotide sequence results in differences in the amino acid sequence in the protein produced. Differences in the amino acid sequence can result in differences in the structure and function of the protein. Differences in the structure and function of proteins result in differences in a person's characteristics. For example, a defect in the enzyme that makes melanin results in albinism instead of normal pigmentation. In this section, you will learn about another example: normal vs. sickle cell hemoglobin.

You will work with your partner to understand how differences between the normal and sickle cell hemoglobin genes result in different hemoglobin proteins, and you will learn how the differences between the normal and sickle cell hemoglobin proteins can result in good health or sickle cell anemia. For this activity, you will need:

- the DNA for the *Beginning of the Sickle Cell Hemoglobin Gene*
- the DNA for the *Beginning of the Normal Hemoglobin Gene*
- the mRNA for the first part of hemoglobin which you made during the transcription activity
- the first part of the hemoglobin protein which you made during the translation activity.

Questions:

Compare the DNA for the *Beginning of the Normal Hemoglobin Gene* vs. the *Beginning of the Sickle Cell Hemoglobin Gene*.

What similarities do you observe?

What difference do you observe?

Think about the mRNA that would be produced by transcription from the *Beginning of the Sickle Cell Hemoglobin Gene*, and compare this to the mRNA produced by transcription from the *Beginning of the Normal Hemoglobin Gene*. How would these two mRNAs be similar?

What difference would there be?





Complete the following table.

<i>Beginning of Sickle Cell Hemoglobin Gene</i>	CACGTAGACTGAGGACAC					
Transcription produces:	codon 1	codon 2	codon 3	codon 4	codon 5	codon 6
<i>Beginning of Sickle Cell Hemoglobin mRNA</i>						
Translation produces:	amino acid 1	amino acid 2	amino acid 3	amino acid 4	amino acid 5	amino acid 6
<i>Beginning of Sickle Cell Hemoglobin protein</i>						
<i>vs. Beginning of Normal Hemoglobin protein</i>						

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

Each complete hemoglobin protein has more than 100 amino acids. Sickle cell hemoglobin and normal 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 normal 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 normal disk shape to a sickle shape. 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
<p align="center">SS (2 alleles for normal hemoglobin)</p>	→	<p align="center">Normal hemoglobin in red blood cells</p>  <p align="center">NORMAL HEMOGLOBIN</p>	→	<p align="center">Disk-shaped red blood cells → normal health</p> 
<p align="center">ss (2 alleles for sickle cell hemoglobin)</p>	→	<p align="center">Sickle cell hemoglobin in red blood cells</p>  <p align="center">CLUMPED HEMOGLOBIN</p>	→	<p align="center">Sickle-shaped red blood cells → pain, damage to body organs, anemia</p> 

Which arrows in this chart represent transcription + translation?

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 traits of an individual.

Questions

1. To summarize what you have learned, explain how a gene directs the synthesis of a protein. Include in your explanation the words amino acid, anti-codon, codon, cytoplasm, DNA, mRNA, nucleotide, nucleus, ribosome, RNA polymerase, tRNA, transcription, and translation. (Hint: You can use the answer to question 2 on page 5 for the beginning of the answer to this question.)

2. Why does the cell need both mRNA and tRNA in order to synthesize a protein like hemoglobin?

3. Why does the cell need to carry out transcription before it can begin translation?

4. How does your DNA determine whether you develop sickle cell anemia?

5. Considering that we are all made up of the same 4 nucleotides in our DNA, the same 4 nucleotides in our RNA, and the same 20 amino acids in our proteins, why are we so different from each other?

Bonus Question

In addition to the health disadvantages described above, sickle cell hemoglobin can result in an important health advantage. Describe this health advantage and the circumstances under which it arises.