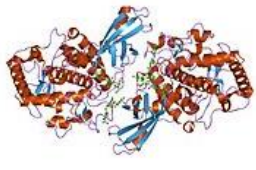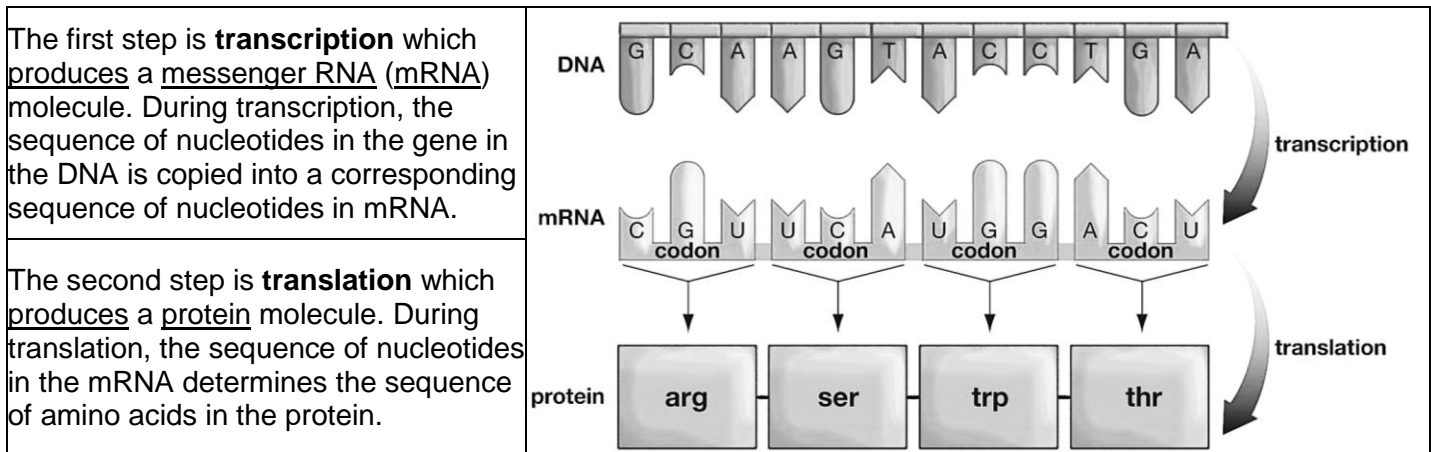# From Gene to Protein – Transcription and Translation[i]

In this activity you will learn how the genes in our DNA influence our characteristics. For example, how can a gene cause albinism (very pale skin and hair)?

Basically, **a gene is a segment of DNA that provides the instructions for making a protein** and **proteins influence our characteristics**. This chart describes how two different versions of a gene can result in either normal skin and hair color or albinism.

| DNA	→	Protein	→	Characteristic
	→		→	
Version of the <u>gene</u> that provides instructions to make normal protein enzyme	→	<u>Normal enzyme</u> that makes the pigment molecule in skin and hair	→	Normal skin and hair color
Version of the <u>gene</u> that provides instructions to make defective enzyme	→	<u>Defective enzyme</u> that does not make this pigment molecule	→	Albinism (very pale skin and hair)

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

The first step is **transcription** which <u>produces</u> a <u>messenger RNA</u> (<u>mRNA</u>) molecule. During transcription, the sequence of nucleotides in the gene in the DNA is copied into a corresponding sequence of nucleotides in mRNA.

The second step is **translation** which <u>produces</u> a <u>protein</u> molecule. During translation, the sequence of nucleotides in the mRNA determines the sequence of amino acids in the protein.

Thus, **each gene contains a specific sequence of nucleotides which gives the instructions for the specific sequence of amino acids that will be joined together to form a protein**. The sequence of amino acids in the protein **determines the structure and function of the protein**.

1. Draw a line to match each description below with the appropriate item in the diagram.

- the molecule that contains genes
- the molecule that could be the enzyme that makes the pigment in skin and hair
- a process that takes place in the nucleus
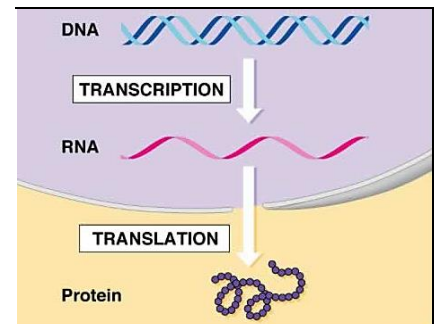
2. Complete the following sentence to describe how differences in a gene can result in normal skin and hair color *vs.* albinism.

Differences in the sequence of _____ in the gene

result in differences in the sequence of _____ in mRNA which

result in differences in the sequence of _____ in the protein which

result in normal *vs.* defective enzyme to make the pigment in skin and hair which

results in normal skin and hair color *vs.* albinism.

3. In this activity, you will learn more about transcription and translation by modeling how a cell carries out transcription and translation to make the beginning of the hemoglobin molecule. What is hemoglobin?

Transcription

Transcription uses the information in a gene in the DNA to make a messenger RNA (mRNA) molecule. **DNA** is a polymer of four types of nucleotides, **G**, **C**, **A** and **T**, and **RNA** is a polymer of four corresponding types of nucleotides, **G**, **C**, **A** and **U** (instead of **T**).

During transcription, the enzyme, **RNA polymerase,** separates the two strands of DNA and makes the mRNA molecule by adding RNA nucleotides, one at a time. Each RNA nucleotide is joined to the previous nucleotide by a covalent bond.

Each DNA nucleotide in the gene is matched by a **complementary** RNA **nucleotide** which has a matching shape and charge distribution. The **base-pairing rules** summarize which pairs of nucleotides are complementary. The base-pairing rules for transcription are very similar to the base-pairing rules in the DNA double helix.
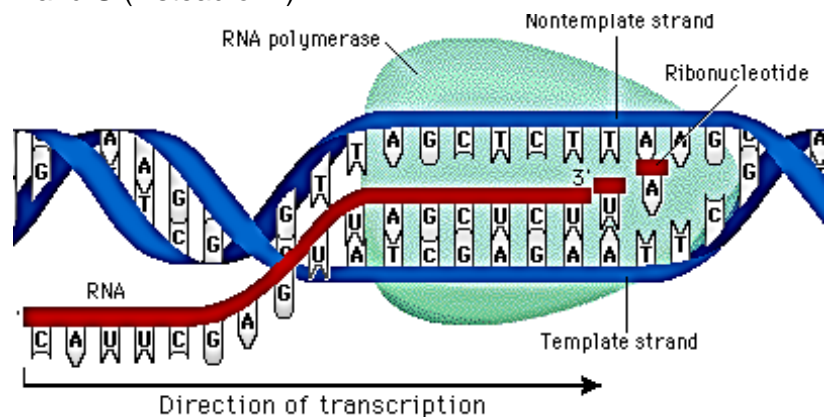
The template strand of the DNA contains the gene that is being transcribed.
A = adenine; **C** = cytosine; **G** = guanine; **T** (in DNA) = thymine; **U** (in RNA) = uracil
(http://www.phschool.com/science/biology_place/biocoach/images/transcription/startrans.gif)

4. Use the information in the figure to complete the following table.

Base-Pairing Rules for Complementary Nucleotides:	
between two strands of DNA	**between DNA and RNA (during transcription)**
G pairs with **C**.	**G** pairs with ____.
T pairs with **A**.	**T** in DNA pairs with ____ in RNA. **A** in DNA pairs with ____ in RNA.

The base-pairing rules ensure that the message from the nucleotide sequence in the gene in the DNA is copied into a corresponding nucleotide sequence in the mRNA molecule.

5. Why is RNA polymerase a good name for the enzyme that carries out transcription?

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, the goal is for you to simulate the actual molecular process of transcription in which the enzyme RNA polymerase carries out a step-by-step chemical process that adds one nucleotide at a time to the growing mRNA molecule.

➢ To model the process of transcription, you and your partner will need a page showing an RNA polymerase molecule inside a nucleus, a paper strip showing the single strand of DNA labeled "Beginning of Hemoglobin Gene", RNA nucleotides and tape.

➢ 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: Insert the "Beginning of Hemoglobin Gene" DNA molecule through the slot in the RNA polymerase diagram so the first two nucleotides of the DNA are on the dashes labeled DNA.

➢ Cytoplasm: Use the base-pairing rules to choose an RNA nucleotide that is complementary to the first DNA nucleotide. Give this nucleotide to the RNA polymerase person.

➢ RNA polymerase: Put the first RNA nucleotide in the box labeled RNA nucleotide.

6. To show what your RNA polymerase looks like at this point, draw the first two nucleotides of the beginning of the hemoglobin gene and the first RNA nucleotide.
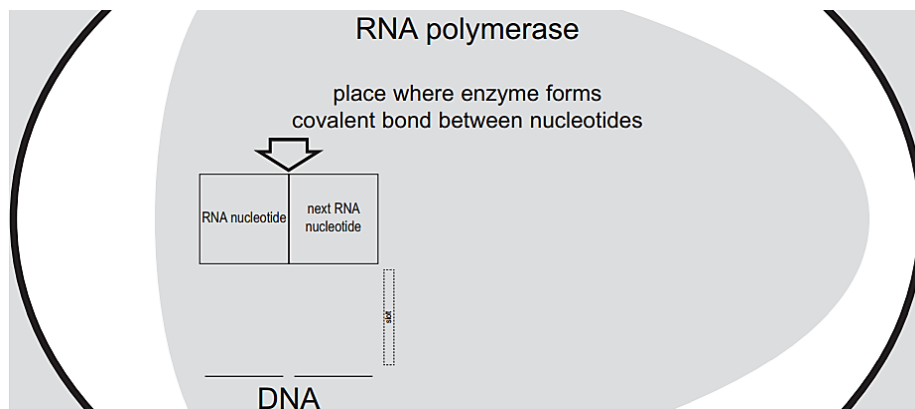
➢ Cytoplasm: Give the next RNA nucleotide (complementary to the next DNA nucleotide) to the RNA polymerase person.

➢ 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.

➢ Repeat this pair of steps as often as needed to complete transcription of the beginning of the hemoglobin gene, adding one nucleotide at a time to the mRNA molecule. 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 model translation.

7. What are some similarities between the process of transcription and the process of DNA replication?

8. Fill in the blanks in the following table to summarize the <u>differences</u> between DNA replication and transcription.

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.

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

Translation

As discussed in the introduction, transcription is followed by translation. During translation, the sequence of nucleotides in mRNA determines the sequence of amino acids in a protein.
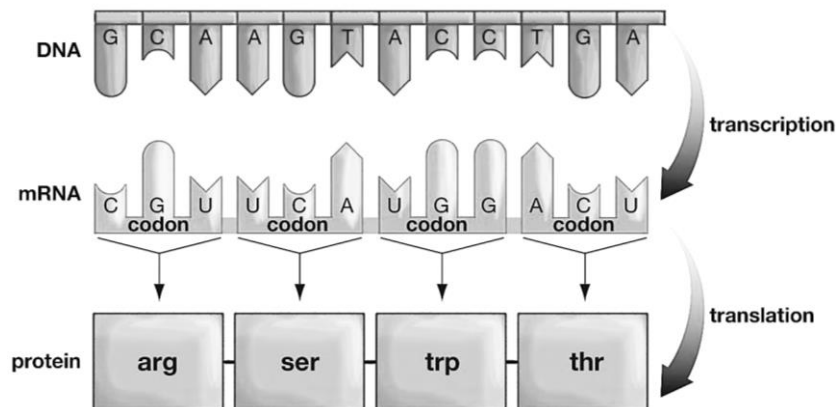
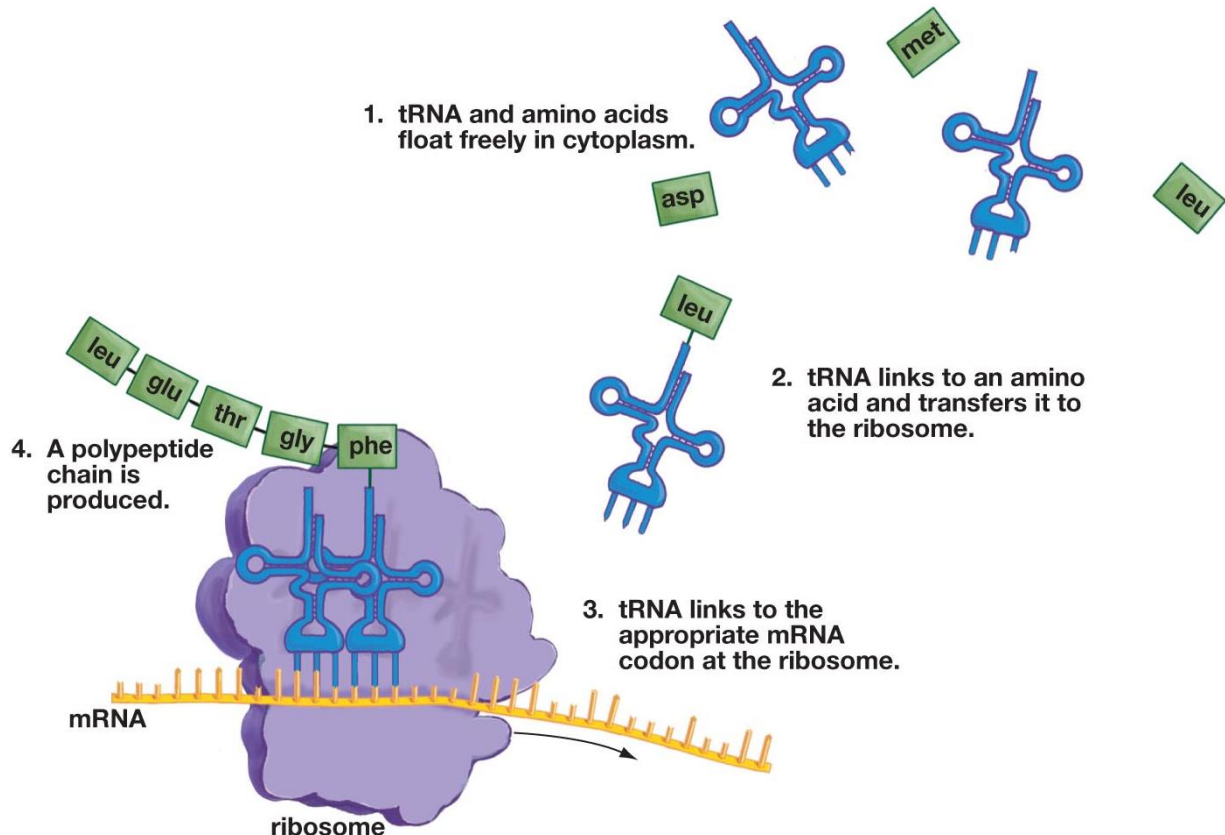(Figure 14.5 from Krogh, <u>Biology, a Guide to the Natural World</u>, 2005)

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) in the 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 will be part of your mRNA molecule, together with the amino acid coded for by each of these codons.

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

How does translation actually take place? Inside a cell, each tiny **ribosome** provides a workbench with the structures 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 do *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.

1. tRNA and amino acids float freely in cytoplasm.

2. tRNA links to an amino acid and transfers it to the ribosome.

3. tRNA links to the appropriate mRNA codon at the ribosome.

4. A polypeptide chain is produced.

mRNA

ribosome

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This figure uses the term polypeptide to refer to the amino acid chain before it folds into a protein.
(Figure 14.6 from Krogh, Biology, a Guide to the Natural World, 2011)

There are multiple different types of tRNA. Each type of 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 a specific amino acid. For each type of tRNA, there is a specific enzyme that recognizes the anti-codon and attaches the correct amino acid to the tRNA (step 2 in the figure).

Inside the ribosome, an mRNA codon is matched with the complementary anti-codon in a tRNA molecule. This tRNA brings the correct amino acid for that position in the growing protein molecule. Each amino acid is joined to the previous amino acid by a covalent bond (steps 3 and 4 in the figure). The ribosome moves along the mRNA, matching each codon with a complementary tRNA anticodon and adding the appropriate amino acid one at a time to produce the protein coded for by the mRNA.

10. *Circle* the anti-codon in one tRNA molecule in the figure. Use *arrows* to indicate where anti-codons in tRNA are matched with complementary codons in mRNA in the ribosome.

Translation Modeling Procedure:

Preparation:
In this section you will simulate the steps in translation to produce the beginning of a hemoglobin protein.

11. You will need to know which amino acid corresponds to each tRNA anti-codon. The table below shows the codons in your mRNA and the corresponding amino acids. Use the base-pairing rule to show the tRNA anti-codon for each mRNA codon.

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

➢ To prepare, you will <u>need</u> to have tRNA molecules, amino acids, the mRNA you made during your simulation of transcription, a strip labeled "Second Part of mRNA", and a page showing a ribosome.
➢ Tape the CUG end of the mRNA you made to the ACU end of the Second Part of mRNA strip.
➢ <u>One of you will play the role of the ribosome</u> and the <u>other one will act as the cytoplasm</u>, which is the source of tRNA and amino acid molecules.

➢ <u>Cytoplasm</u>: For tRNA molecules to function in translation, each tRNA must first be attached to the correct amino acid that corresponds to the anti-codon in that type of tRNA. Use the above table to match each model tRNA molecule with the correct amino acid for that type of tRNA. Tape the amino acid to the tRNA *very lightly*, because they will only be joined temporarily and will separate again soon.

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 5. Similarly, each mRNA molecule has many more nucleotides than shown in your strip.
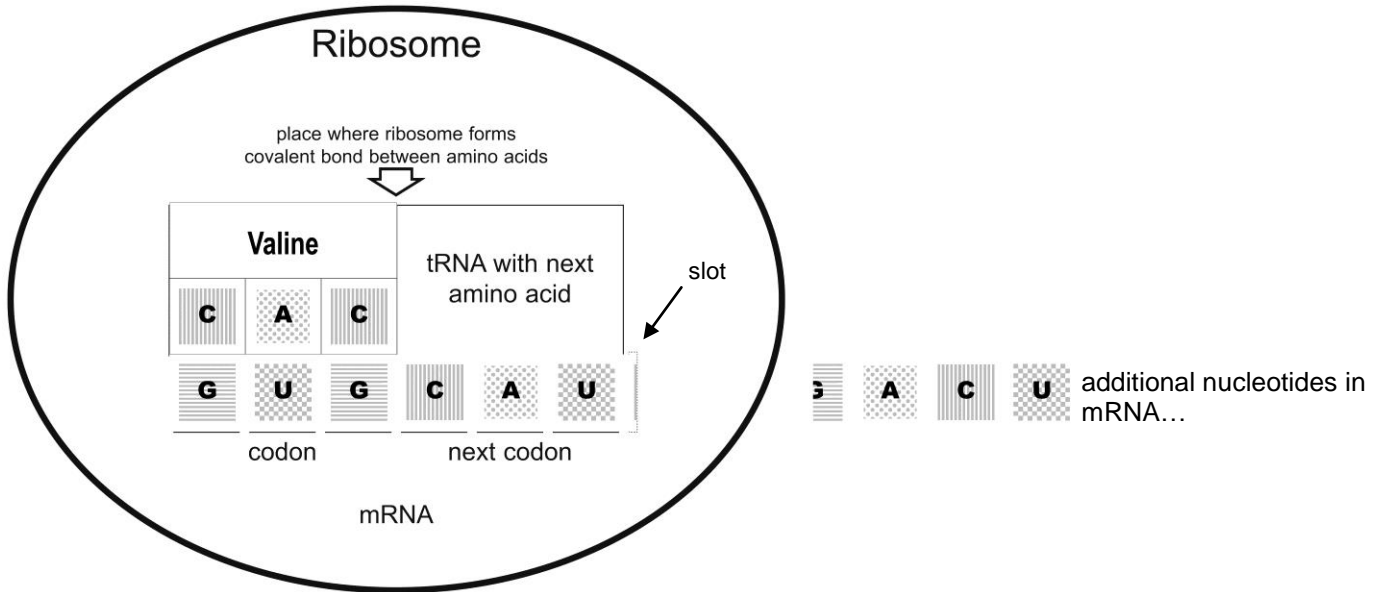
12. Your partner wants to move ahead quickly, so he lays out the mRNA strip with the appropriate tRNA molecules above each of the six mRNA codons and then tapes together all six amino acids. Explain why this would *not* be a good simulation of the actual sequence of steps used to carry out translation. (Hint: See page 5.)

Modeling the Steps in Translation:

➢ <u>Ribosome</u>: Insert the mRNA through the slot in the model ribosome, with the first three nucleotides of the mRNA in the "codon" position and the next three nucleotides in the "next codon" position.
➢ <u>Cytoplasm</u>: Supply the tRNA that has the correct anti-codon to match the first codon in the mRNA.
➢ <u>Ribosome</u>: Place this tRNA with its amino acid in position.
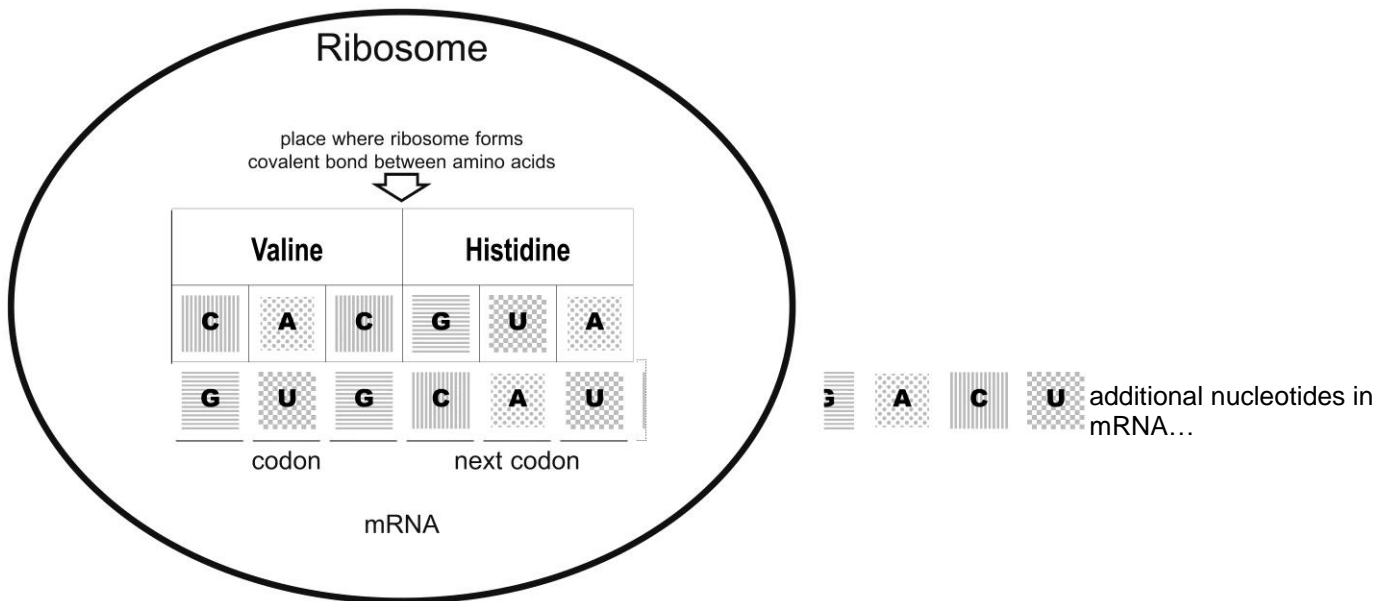
(See diagram on next page.)

Your model ribosome should look like:

Ribosome

place where ribosome forms
covalent bond between amino acids

Valine	tRNA with next amino acid
C A C	

slot

G	U	G	C	A	U
codon			next codon		

mRNA

G   A   C   U   additional nucleotides in mRNA…

13. In the above diagram, use an *arrow* to indicate the anti-codon in the tRNA and use an * to indicate the amino acid.
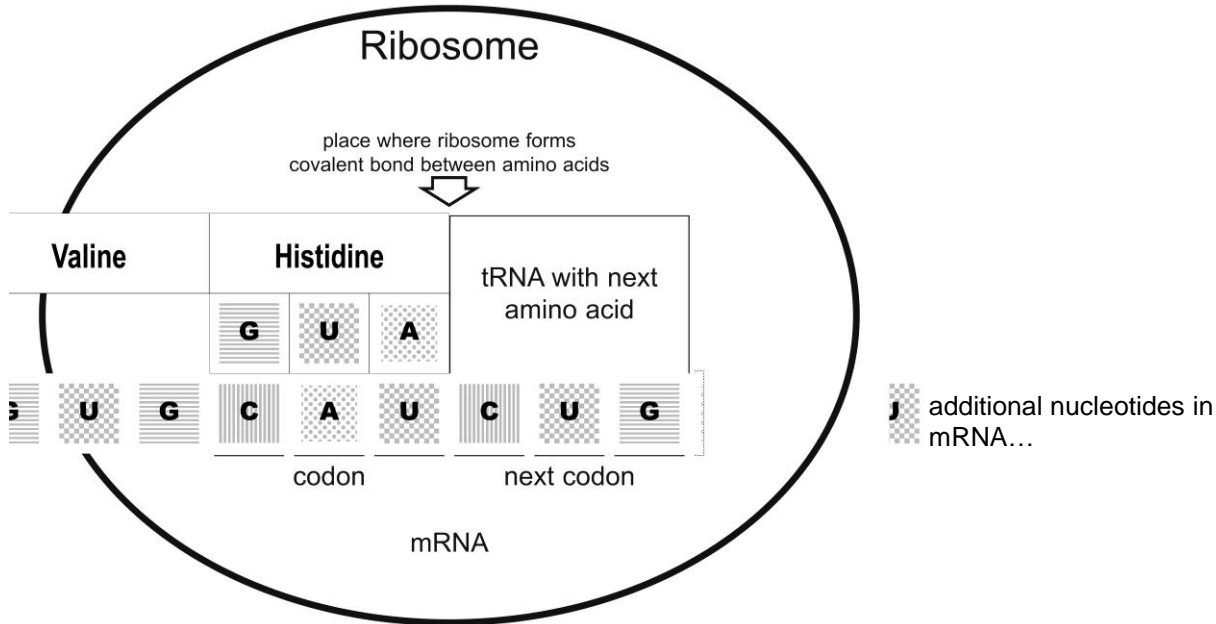Put a *rectangle* around each codon in the mRNA in the ribosome.

➢ Cytoplasm: Supply the tRNA that has the correct anti-codon to match the second codon in the mRNA.
➢ Ribosome: Place the tRNA in position. (Your model should look like the picture below.) Now the ribosome is ready to link the first two amino acids with a covalent bond to begin the formation of the hemoglobin protein. Tape these two amino acids together; the tape represents the covalent bond between the first two amino acids in the hemoglobin protein. At this time, the first amino acid detaches from the first tRNA, so remove that tape.

Ribosome

place where ribosome forms
covalent bond between amino acids

Valine			Histidine		
C	A	C	G	U	A

G	U	G	C	A	U
codon			next codon		

mRNA

G   A   C   U   additional nucleotides in mRNA…

14. *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.

- ➢ 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:

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

- ➢ 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, and release the tRNA on the left to the cytoplasm person who will put it in the packet.

- ➢ Repeat this pair of steps until you have attached all six amino acids to form the beginning portion of the hemoglobin protein.

16. Explain why a cell needs both mRNA and tRNA in order to synthesize a protein. Explain the function of mRNA, the function of tRNA, and how tRNA and mRNA work together to put the right amino acids in the right sequence as the protein is synthesized.

17. What part of translation depends on the base-pairing rules?

18. 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? Explain your reasoning.

19. Explain why it makes sense to use the word translation to describe protein synthesis and why it would *not* make sense to use the word translation to describe mRNA synthesis. (Hint: Look at the figure on the bottom of page 4.)

20. Why does a cell need to carry out transcription before translation?

21. To summarize what you have learned about translation, explain how an mRNA molecule directs the synthesis of a protein. Include in your answer the words amino acid, anti-codon, codon, mRNA, protein, ribosome, tRNA, and translation.

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.

Different alleles can result in different characteristics as follows:

Different nucleotide sequence in the different alleles of a gene

→ different nucleotide sequence in messenger RNA (mRNA)
transcription

→ different amino acid sequence in a protein
translation

→ different structure and function of the protein
(e.g. normal enzyme vs. defective enzyme)

→ different characteristics
(e.g. normal skin and hair color vs. albinism)

In this section, you will learn about another example of how different alleles produce different characteristics. To begin, you will work with your partner to understand how a difference between the alleles for normal and sickle cell hemoglobin results in two different types of hemoglobin protein.

22. In the table below, compare the nucleotide sequence in the DNA for the *Beginning of the Normal Hemoglobin Gene* vs. the *Beginning of the Sickle Cell Hemoglobin Gene.* What is the only difference?
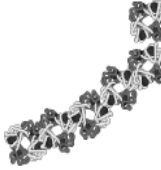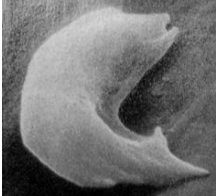

23. Complete this table. (Use the table on page 5 to help with translation.)

Beginning of **Normal** Hemoglobin **Gene**	CACGTAGACTGAGGACTC					
Transcription produces:	codon1	codon 2	codon 3	codon 4	codon 5	codon 6
Beginning of **Normal** Hemoglobin **mRNA**						
Translation produces:	amino acid 1	amino acid 2	amino acid 3	amino acid 4	amino acid 5	amino acid 6
Beginning of **Normal** Hemoglobin **Protein**						

Beginning of **Sickle Cell** Hemoglobin **Gene**	CACGTAGACTGAGGACAC					
Transcription produces:	codon 1	codon 2	codon 3	codon 4	codon 5	codon 6
Beginning of **Sickle Cell** Hemoglobin **mRNA**						
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**						

24. What is the difference in the amino acid sequence of the beginning 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 allele and produces only sickle cell hemoglobin, then the sickle cell hemoglobin molecules tend to clump together in long rods. These rods can change the shape of the red blood cells from their normal disk shape to a sickle shape. Sickle-shaped red blood cells can block blood flow in the small blood vessels. This causes pain and damage to body organs. In addition, sickle-shaped red blood cells do not last nearly as long as normal red blood cells, so the body cannot produce enough replacement red blood cells and the person develops anemia (not enough red blood cells).

Genotype (genes)	→	Protein	→	Phenotype (characteristics)
2 copies of the allele that codes for normal hemoglobin (**SS**)	→	Normal hemoglobin dissolves in the cytosol of red blood cells.	→	Disk-shaped red blood cells can squeeze through the small blood vessels → normal health
2 copies of the allele that codes for sickle cell hemoglobin (**ss**)	→	Sickle cell hemoglobin can clump in long rods in red blood cells.	→	When sickle cell hemoglobin clumps in long rods → sickle-shaped red blood cells → clogged small blood vessels + fragile red blood cells → pain, damage to body organs + anemia = sickle cell anemia

25. *Circle* the arrows in the chart that represent transcription + translation.

In <u>summary</u>, 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.

26. 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? For example, why do some people have sickle cell anemia and others don't?

A **model** is a simplified representation of a real world phenomenon such as transcription or translation. Models help us to understand complex phenomena by focusing on key features of a phenomenon and omitting less important features. Several different types of models have been included in this activity to help you understand:
- how genes influence a person's characteristics
- how genes determine the structure of proteins via transcription and translation
- the actual molecular processes that occur during transcription and translation.

27. Complete the following table to evaluate each type of model in this activity.

Type of model	What was an advantage of this type of model? What did these models contribute to your understanding?	What was a disadvantage or limitation of this type of model? Can you suggest how these models could be improved?
Flow charts (on pages 1 and 11)		
Diagrams (on pages 2 and 5)		
Modeling Procedures (on pages 3 and 6-8)		