From Gene to Protein – Transcription and Translation[1]

How do genes influence our characteristics?

A **gene is a segment of DNA** that gives the **instructions for making a protein**. Different versions of a gene result in different versions of a protein which can result in different characteristics. This chart shows an example.

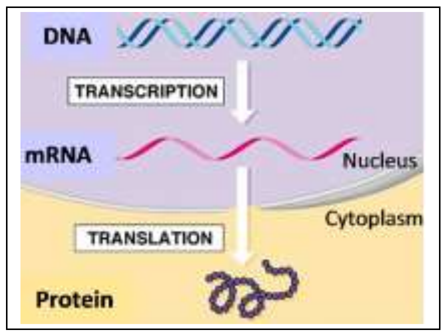
Gene in DNA	→	Protein	→	Characteristic
One version of a gene gives instructions for normal clotting protein.	→	When a blood vessel is injured, normal clotting protein results in prompt blood clot formation.	→	After an injury, a blood clot stops the bleeding.
Another version of the gene gives instructions for defective clotting protein.	→	Defective clotting protein results in slow blood clot formation.	→	Excessive bleeding = hemophilia

1. Explain how different versions of a gene determine whether or not a person has hemophilia.

How does a gene give the instructions for making a protein?

2a. The first step is **transcription** of the gene. During transcription, the instructions in the gene in the DNA are copied to **messenger RNA**, which is usually called _______________.
(DNA / mRNA / protein)

2b. The second step is **translation**. During translation, mRNA gives the instructions for making a _______________.
(DNA / mRNA / protein)

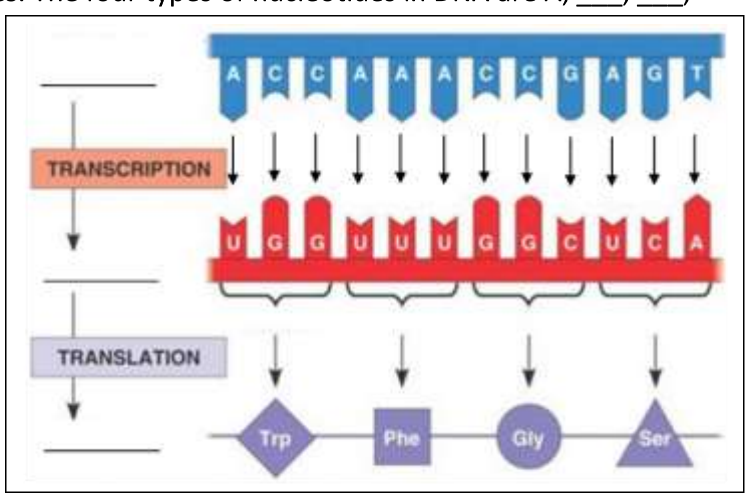


3a. The figure below shows more specifics. Fill in the blanks to label the DNA, mRNA and protein.

3b. DNA and RNA are polymers of **nucleotides**. The four types of nucleotides in DNA are A, ___, ___, and ___. The four types of nucleotides in RNA are ___, ___, ___, and ___.

3c. During transcription, the sequence of nucleotides in a gene in the DNA determines the sequence of ____________________ in mRNA.

3d. A protein is a polymer of **amino acids**. During translation, the sequence of nucleotides in mRNA determines the sequence of _____________________ in the protein.



[1] By Drs. Ingrid Waldron and Jennifer Doherty, Department of Biology, University of Pennsylvania, Copyright, 2019. Teachers are encouraged to copy this Student Handout for classroom use. A Word file (which can be used to prepare a modified version if desired) and Teacher Preparation Notes with instructional suggestions and background biology are available at http://serendipstudio.org/sci_edu/waldron/#trans .

You have seen that the sequence of nucleotides in a gene in the DNA determines the sequence of nucleotides in the mRNA which determines the sequence of amino acids in the protein.

The sequence of amino acids determines the structure and function of the protein. For example, the sequence of amino acids determines whether a clotting protein is normal or defective.

4a. Which process takes place in the nucleus? transcription ___ translation ___

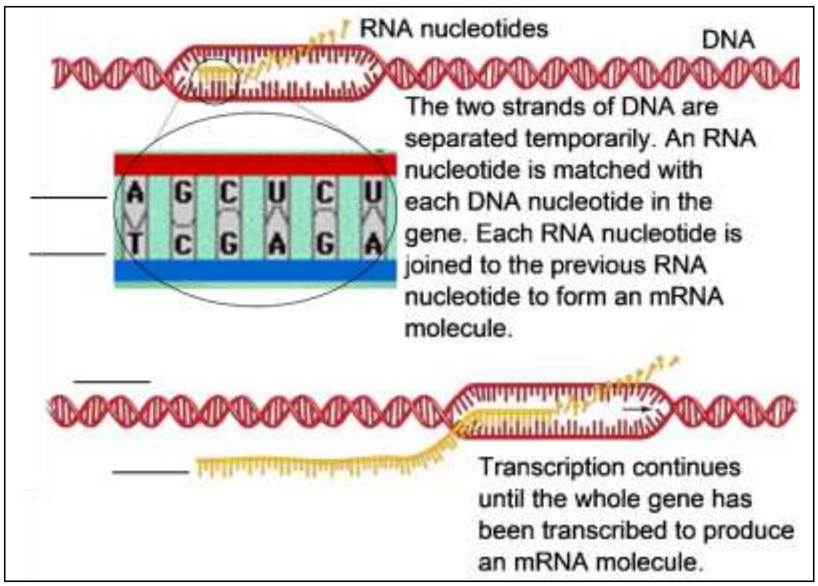
4b. Explain why this process must occur in the nucleus.

Transcription

This figure shows how a gene is transcribed to make an mRNA molecule.

5. Fill in each blank in the figure with DNA or mRNA.

During transcription, each DNA nucleotide in the gene is matched with a complementary RNA nucleotide which has a matching shape and charge distribution.



The base-pairing rules summarize which nucleotides are complementary. The base-pairing rules for transcription are similar to the base-pairing rules in the DNA double helix.

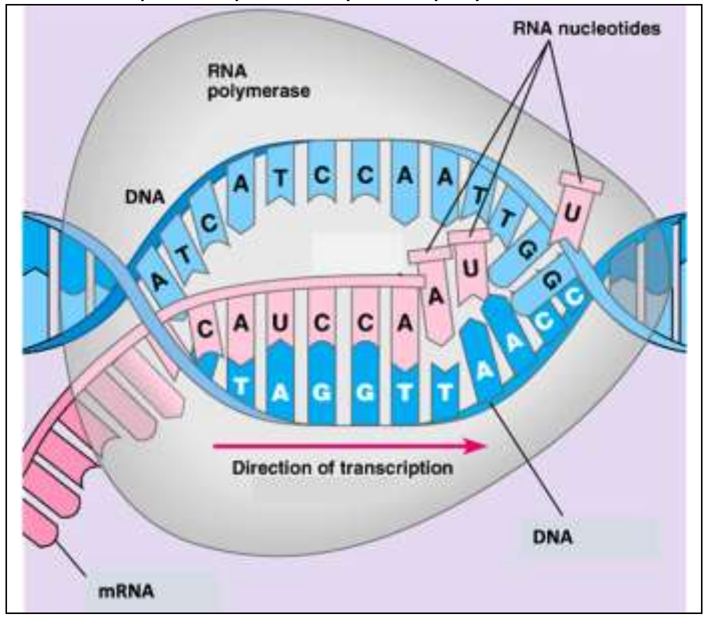
6. Use the information in the above figure to complete this table.

Base-Pairing Rules for Complementary Nucleotides:	
between the two strands of a DNA double helix	**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 nucleotide sequence in the gene in the DNA is copied into a corresponding nucleotide sequence in the mRNA molecule.

The enzyme **RNA polymerase** plays a crucial role in transcription. Specifically, RNA polymerase:

- separates the two strands of a DNA double helix
- synthesizes mRNA by adding RNA nucleotides one at a time
- uses the nucleotide sequence in a gene in the DNA to determine which RNA nucleotide to add next.



7. Why is RNA polymerase a good name for the enzyme that carries out transcription? Explain each part of the name: RNA, polymer and ase.

Procedure for Modeling Transcription

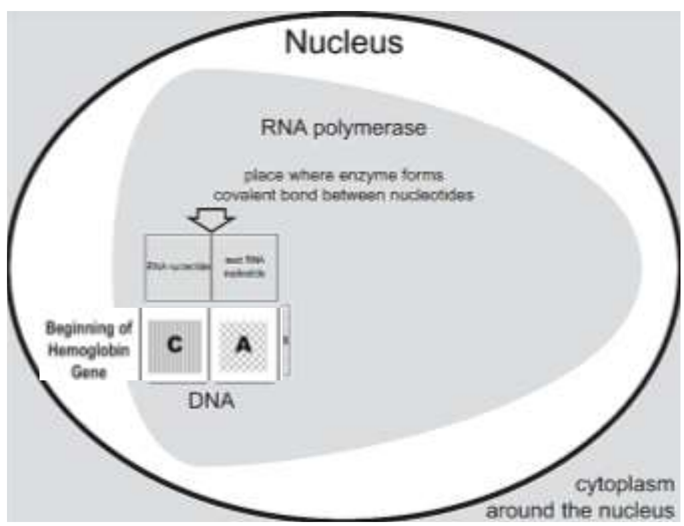
Note: In this modeling activity, your goal is to learn how RNA is made. During transcription RNA polymerase adds one nucleotide at a time to the growing mRNA molecule. To model transcription accurately, complete each step in the procedure and check the box before you begin the next step.

A. Your group should get a page showing an RNA polymerase molecule inside a nucleus,
a paper strip showing a single strand of DNA labeled "Beginning of Hemoglobin Gene",
RNA nucleotides and tape. ☐

One of you will be the RNA polymerase. Another group member will be the cytoplasm which surrounds the nucleus and supplies the nucleotides which are used to make the mRNA molecule.

B. 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 gene are on the dashes labeled DNA. ☐

Your RNA polymerase should look like this figure. (Note: A real RNA polymerase molecule and DNA and RNA nucleotides are much smaller than the nucleus.)



C. 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. ☐

D. RNA polymerase: Put this RNA nucleotide in the box labeled RNA nucleotide. ☐

E. Cytoplasm: Give the next RNA nucleotide (complementary to the next DNA nucleotide) to the RNA polymerase person. ☐

F. RNA polymerase: Put this nucleotide in the box labeled "next RNA nucleotide". Join the two RNA nucleotides together with transparent tape; the tape represents the covalent bond between these two nucleotides in the growing mRNA molecule. Then, move the DNA molecule and the mRNA molecule one space to the left. ☐

G. Repeat steps E and F as often as needed to complete transcription of the beginning of the hemoglobin gene by adding one nucleotide at a time to the mRNA molecule. ☐

8. Summarize how transcription makes mRNA. A complete answer will include:
DNA, gene, mRNA, nucleotides, RNA polymerase, one at a time, base-pairing rules.

9. The first column of this table describes DNA replication. Fill in the blanks in the second column to summarize the differences between DNA replication and transcription.

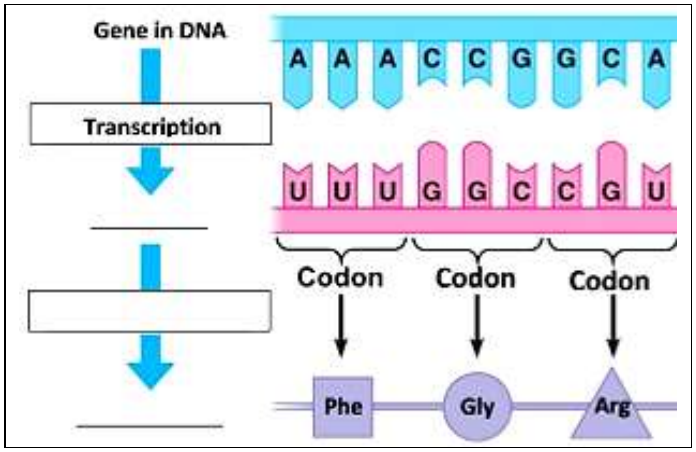
DNA replication	**Transcription**
The whole chromosome is replicated.	____________________is transcribed.
DNA is made. DNA is double-stranded.	mRNA is made. mRNA is ________________ -stranded.
DNA polymerase is the enzyme which carries out DNA replication.	_____ polymerase is the enzyme which carries out transcription.
T is used in DNA; **A** pairs with **T** in DNA.	In RNA, **T** is replaced by ___; **A** in DNA pairs with ___ in mRNA.

10. Fill in the blanks to describe the similarities between transcription and DNA replication.

Both transcription and DNA replication produce nucleic acids which are polymers of __________________ (C, G, A, and T or U). Both processes depend on a ____________________ enzyme which adds one _________________ at a time. To determine which nucleotide is added next, both transcription and DNA replication use the nucleotide sequence in a _______ strand and the ________________________________ rules.

Translation

11. To show how translation follows transcription, fill in the blanks and box in this figure.

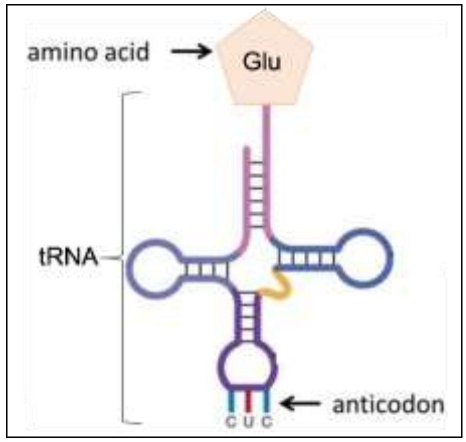


How do just 4 types of nucleotides in mRNA provide a unique code for each of the 20 types of amino acids in proteins?

The code for each type of amino acid is a sequence of three nucleotides, which is called a **codon**.

12. In the figure, circle the mRNA codon that codes for the amino acid Phe.

Special molecules called **transfer RNA** (**tRNA**) bring the right amino acid for each mRNA codon.



This figure shows one type of tRNA with the amino acid, Glu, attached. The other end of this tRNA has the anticodon for Glu. This anticodon has three nucleotides that are matched by the base-pairing rules to the three nucleotides in the mRNA codon for Glu.

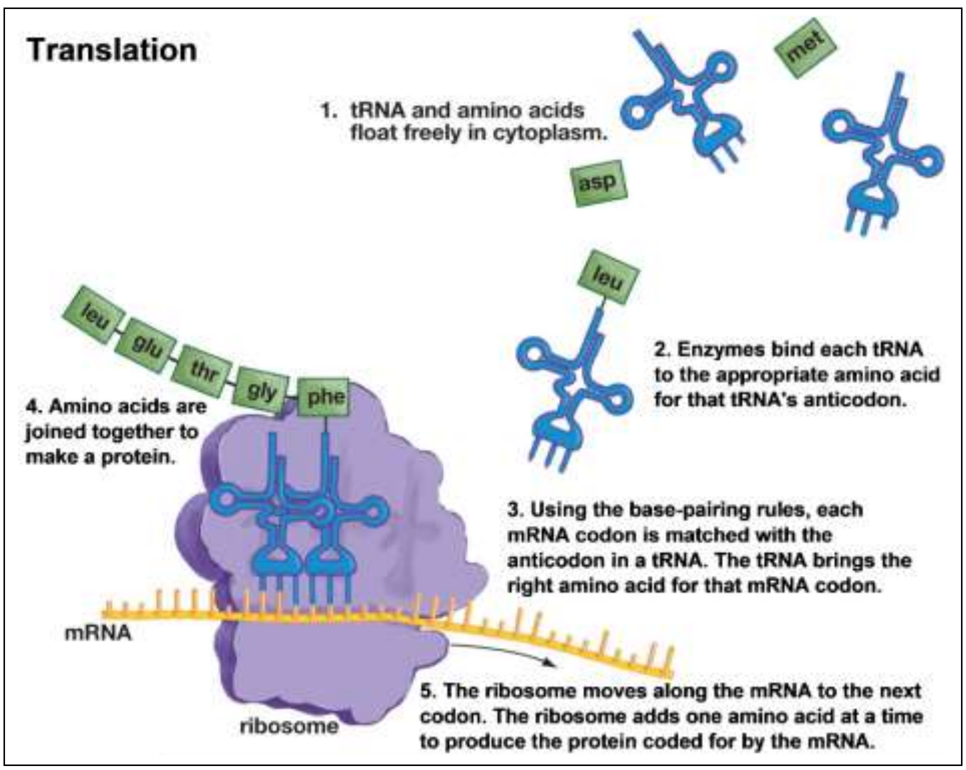
13. There are multiple types of tRNA. Each type of tRNA carries a specific amino acid and has an anticodon with three nucleotides that are complementary to the three nucleotides in the codon for that amino acid. What is the anticodon for the amino acid Phe?

14. For each type of tRNA, there is a specific enzyme that attaches the correct amino acid for the anticodon in that tRNA. These enzymes are needed for step ______ in the figure below.
(1/2/3/4)

Translation takes place in **ribosomes** (tiny structures in the cytoplasm).

Inside the ribosome, a codon in an mRNA molecule is matched by the base-pairing rules with an anticodon in a tRNA (step 3). This tRNA brings the next amino acid to be added to the growing protein molecule.

15. In the ribosome, circle a codon in the mRNA and the complementary anticodon in a tRNA molecule.



Each amino acid is joined to the previous amino acid in the growing protein molecule (step 4). Then, the ribosome moves along the mRNA to the next codon (step 5).

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

17. Why does a cell need tRNA to make a protein? Explain how tRNA works with mRNA to put the right amino acids in the right sequence as the protein is made.

Procedure for Modeling Translation

To simulate the steps in translation, one of you will be the ribosome, and another will be the cytoplasm. Complete each step in the procedure and check it off, before beginning the next step.

Preparation

A. Your group will need the mRNA you made during your simulation of transcription, a strip labeled "Second Part of mRNA", a page showing a ribosome, tRNA molecules, and amino acids. ☐

18. For tRNA to do its job, each tRNA molecule must be attached to the correct amino acid that corresponds to the anticodon in that type of tRNA. To know which amino acid should be attached to each tRNA molecule, use the base-pairing rules to complete this table.

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

19. Your partner wants to move ahead quickly, so he uses the mRNA strip and the table above to arrange the amino acids in the correct sequence; then he 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.

B. Cytoplasm: Use the above table to match each 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 soon separate. ☐

C. Cytoplasm: Tape the CUG end of the mRNA you made to the ACU end of the Second Part of mRNA strip. ☐

Note: A real mRNA molecule has many more nucleotides than your strip has. Also, a real tRNA molecule has many more nucleotides than the three nucleotides of the anticodon.

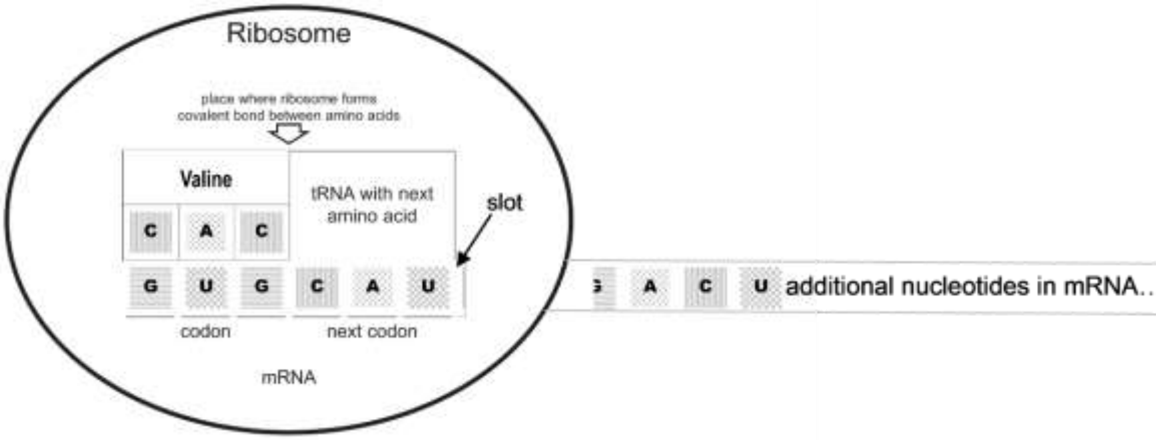
Modeling the Steps in Translation

D. Ribosome: 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. ☐

E. Cytoplasm: Use the base-pairing rules to supply the tRNA that has the correct anticodon to match the first codon in the mRNA. ☐

F. Ribosome: Place this tRNA with its amino acid in position. ☐

20. Your model ribosome should look like this figure. Circle the anti-codon of the tRNA.



G. Cytoplasm: Supply the tRNA that has the correct anticodon to match the codon in the "next codon" position. ☐

H. Ribosome: Place the tRNA in position. Tape the two amino acids together to represent the covalent bond between these two amino acids. Detach the amino acid on the left from its tRNA. ☐

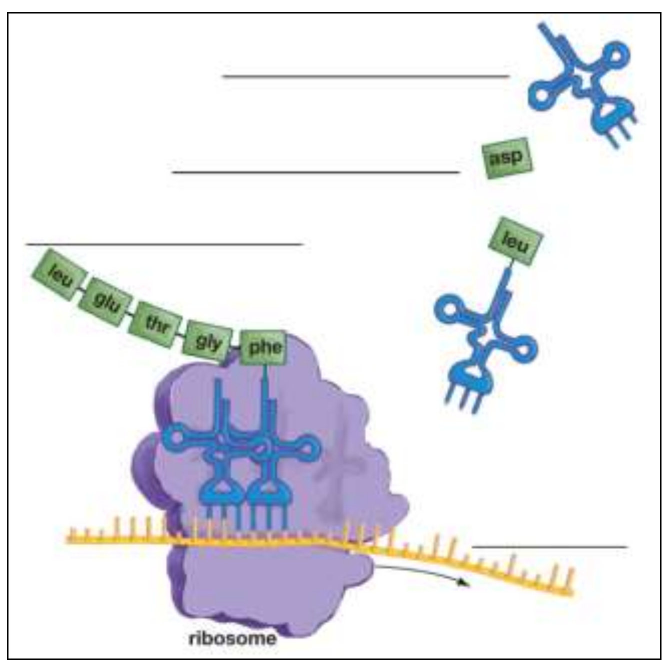
I. Ribosome: Move the mRNA and matching tRNAs with amino acids one codon to the left. Release the tRNA on the left to the cytoplasm. ☐

J. Repeat steps G-I as often as needed to attach all six amino acids to form the beginning portion of the hemoglobin protein. ☐

21a. Fill in the blanks to label each type of molecule in this figure.

21b. Name the process shown in the figure and explain each step in this process. A complete answer will include each of the molecules shown and these words:

anticodon, base-pairing rules, codon, nucleotides, ribosome, sequence.



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

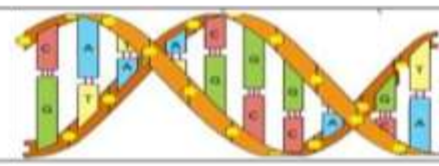
23. Explain why it makes sense to use the word translation to describe protein synthesis and why it would *not* make sense to use the word translation to describe mRNA synthesis.

The Hemoglobin Gene and 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.

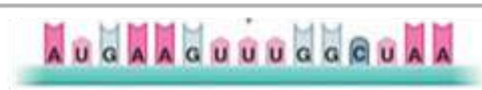
24a. Complete this flowchart to illustrate how different alleles can result in different characteristics.

In the DNA, different alleles of the hemoglobin gene have a different sequence of ____________________



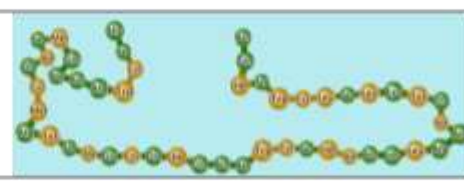
↓

different sequence of ____________________ in the mRNA



↓

different sequence of ____________________ in the hemoglobin protein



↓

different structure and function of the hemoglobin protein

↓

different characteristics (e.g. normal health vs. sickle cell anemia)

24b. Label the arrow that represents transcription.

24c. Label the arrow that represents translation.

25. Use this table to compare the nucleotide sequence in the "Beginning of Allele for Normal Hemoglobin" vs. the "Beginning of Allele for Sickle Cell Hemoglobin". What is the only difference?

Beginning of **Allele** for **Normal** Hemoglobin	**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 **Allele** for **Sickle Cell** Hemoglobin	**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**						

26. Complete the above table. Use the table below to help with translation.

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

27. Compare the amino acid sequence for the beginning of sickle cell hemoglobin vs. the beginning of normal hemoglobin. What difference do you observe?

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

Hemoglobin is carried inside red blood cells. Normal hemoglobin dissolves in the watery cytosol of red blood cells. Sickle cell hemoglobin tends to clump in long rods instead of dissolving in the cytosol. One reason why is:

- Valine (Val) is much less water-soluble than glutamic acid (Glu).
- Amino acid 6 is in a crucial location on the outer surface of the hemoglobin protein.

This chart shows how this difference between sickle cell hemoglobin and normal hemoglobin results in the symptoms of sickle cell anemia.

Genotype	→	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 inside red blood cells. 	→	When sickle cell hemoglobin clumps in long rods → sickle-shaped red blood cells → block small blood vessels → reduced oxygen supply → pain, damage to body organs. Also, these red blood cells die faster than they can be replaced → anemia (low red blood cells). Person has <u>sickle cell anemia</u>.

28. Circle the arrows in the chart that represent transcription + translation.

29. The alleles for normal hemoglobin and sickle cell hemoglobin differ in a single nucleotide. Explain how this small molecular difference can cause a person to experience pain and anemia. (Be specific.)

30. 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?