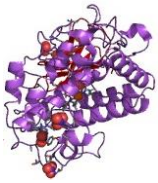
From Gene to Protein – Transcription and Translation[i]

How do the genes in our DNA influence our characteristics? For example, how can a gene determine whether a person is an albino with very pale skin and hair?

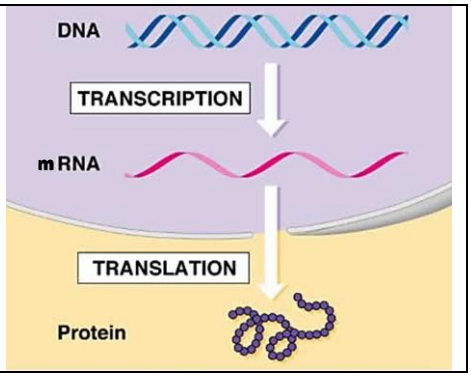
Basically, **a gene is a segment of DNA that provides the instructions for making a protein**, and **proteins influence our characteristics**. This chart describes how two different versions of a gene result in two different versions of a protein which in turn can result in either normal skin and hair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

DNA	→	Protein	→	Characteristic
	→		→	
Version of the gene that provides instructions to make normal protein enzyme	→	Normal enzyme that makes the pigment molecule in skin and hair	→	Normal skin and hair color
Version of the gene that provides instructions to make defective enzyme	→	Defective enzyme 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.

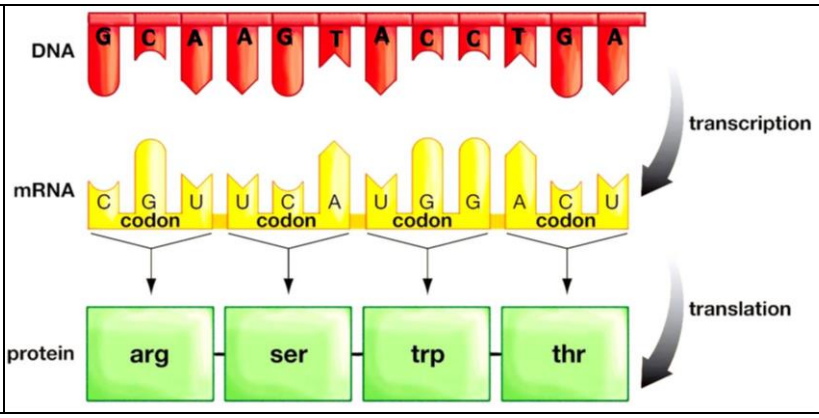
The first step is **transcription** of the gene in the DNA. Transcription produces a messenger RNA (mRNA) molecule.

The second step is **translation** of the mRNA molecule. Translation produces a protein molecule.



During **transcription**, the sequence of nucleotides in a gene in the DNA is copied to a corresponding sequence of nucleotides in mRNA.

During **translation**, the sequence of nucleotides in the mRNA determines the sequence of amino acids in the protein.



After translation, the sequence of amino acids in the protein determines the structure and function of the protein. Differences in protein function can influence characteristics such as normal skin and hair color vs. albinism.

1. Complete this flowchart to describe how a gene directs the synthesis of a protein. Label the process represented by each arrow and fill in the blank with the name of the appropriate molecule.

Gene in DNA ⟶ _____ ⟶ protein

2. Complete the following sentence to describe how different versions of 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

can result in normal skin and hair color *vs.* _____.

3. In this activity, you will model how a cell carries out transcription and translation to make the beginning of the hemoglobin molecule. What type of molecule is hemoglobin?

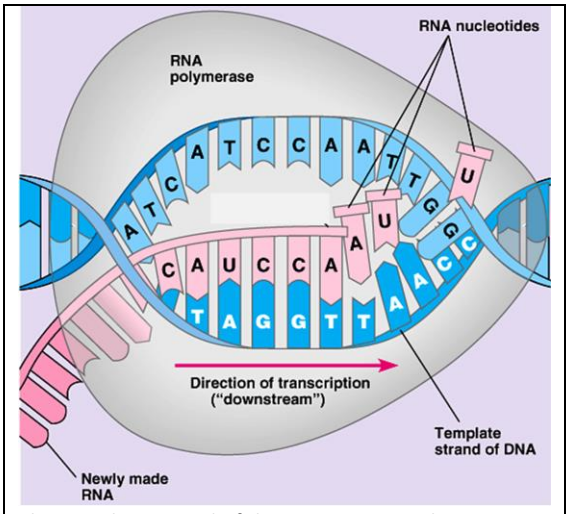
Transcription

During transcription, the enzyme, **RNA polymerase**:

- separates the two strands of a DNA double helix and
- makes an mRNA molecule by adding RNA nucleotides, one at a time.

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 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

4. 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.

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

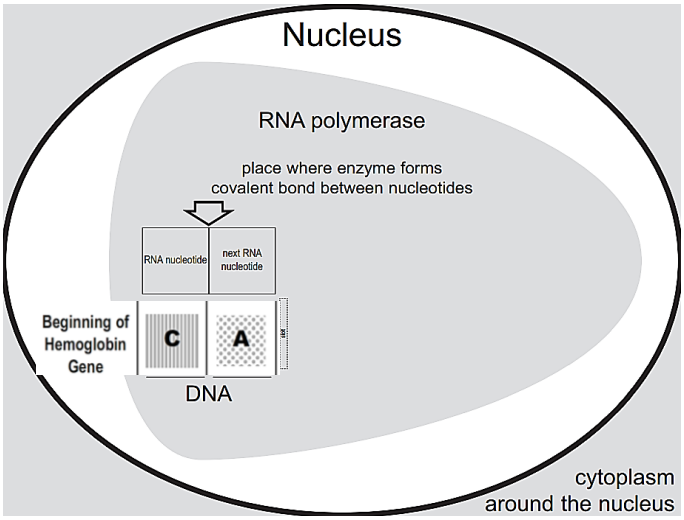
Transcription Modeling Procedure

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 process that adds one nucleotide at a time to the growing mRNA molecule.

- To model the process of transcription, your group will need 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 act as the RNA polymerase, and another will be the cytoplasm which surrounds the nucleus and supplies the nucleotides which are used to make the mRNA 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 gene are on the dashes labeled DNA.

  Your RNA polymerase should look like this figure.



- 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.

- 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". 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.

- Repeat the last two 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.

6. Fill in the blanks in this table 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 = 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.

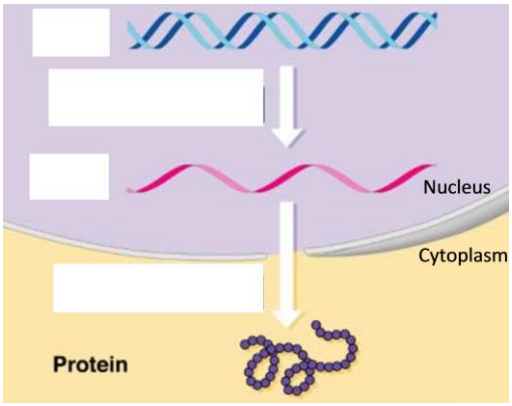
7. Fill in the blanks to describe the similarities between transcription and DNA replication.

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.

8. Summarize what you have learned about transcription in sentences or a labeled figure. Include these words and phrases:

transcription, gene, DNA, mRNA, nucleotides, sequence, base-pairing rules, one at a time, RNA polymerase.

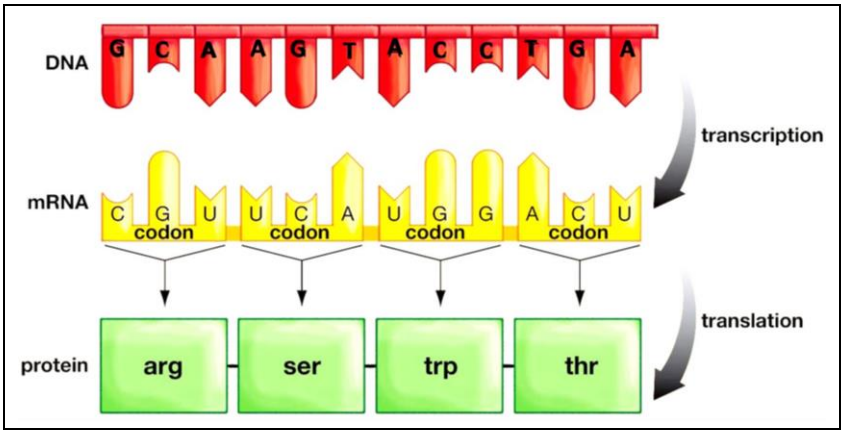
9. As you know, transcription is followed by translation. To give an overview of these processes, label the arrows and molecules in this figure.



Translation

During translation, the sequence of nucleotides in mRNA determines the sequence of amino acids in a protein.

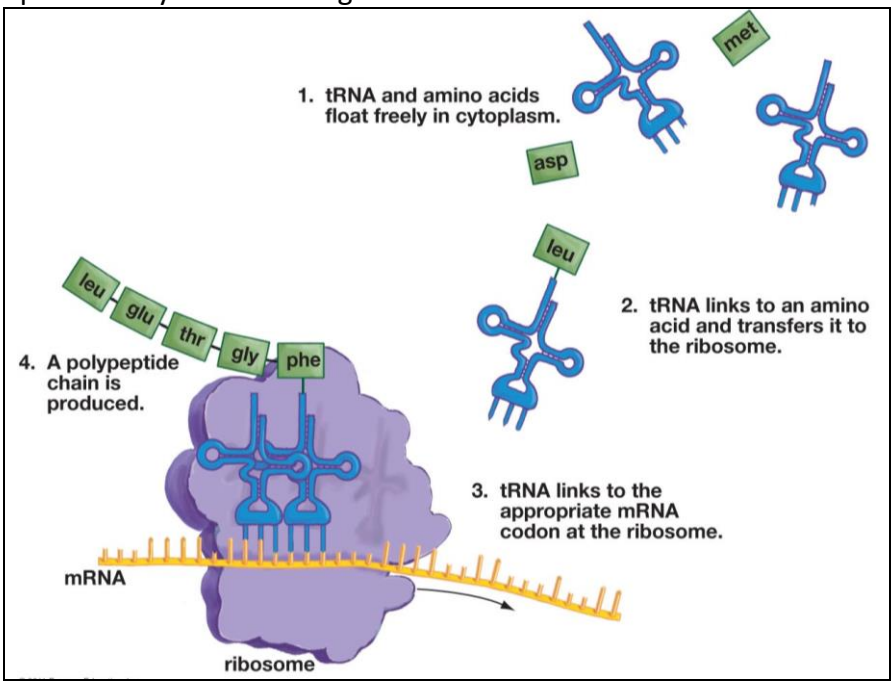
How can the four different types of nucleotide in mRNA provide a specific code for each of the twenty different types of amino acid in proteins? The code for each type of amino acid is a sequence of three nucleotides called a **codon**. (See figure.)



The cell uses **transfer RNA (tRNA)** to bring the correct amino acid for each codon in the mRNA. There are multiple different types of tRNA. Each type of tRNA molecule has three nucleotides that form an anti-codon. The three nucleotides in each **tRNA anti-codon** are complementary to the three nucleotides in the mRNA codon for a specific amino acid.

10. In the above figure, circle the mRNA codon that codes for the amino acid trp (tryptophan). What would be the anti-codon in the tRNA for trp (tryptophan)?

For each type of tRNA, there is a specific enzyme that recognizes the anti-codon in the tRNA and attaches the correct amino acid for that anti-codon (step 2 in this figure).



Translation takes place in **ribosomes**.

Inside the ribosome, a codon in an mRNA molecule is matched by the base-pairing rules with an anti-codon in a tRNA (step 3). The tRNA brings the correct amino acid for that position in the protein molecule.

Each amino acid is joined to the previous amino acid in the growing protein molecule (step 4). The ribosome moves along the mRNA, matching each codon with a complementary tRNA anti-codon and adding the appropriate amino acids one at a time to produce the protein coded for by the mRNA.

11. In the figure, *circle* the anti-codon in a tRNA molecule that is not in the ribosome.
- In the ribosome, put a *rectangle* around an anti-codon in a tRNA molecule and the complementary codon in the mRNA.

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

Translation Modeling Procedure

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

- One of you will play the role of the ribosome and another will be the cytoplasm.

Preparation:

- To model translation, you will need a page showing a ribosome, tRNA molecules, amino acids, the mRNA you made during your simulation of transcription, and a strip labeled "Second Part of mRNA". Tape the CUG end of the mRNA you made to the ACU end of the Second Part of mRNA strip.

13. For tRNA molecules to function in translation, each tRNA must be attached to the correct amino acid that corresponds to the anti-codon in that type of tRNA. To know which amino acid corresponds to each anti-codon in your tRNA molecules, use the base-pairing rules to complete this table.

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

- Cytoplasm: Use this 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 soon separate.

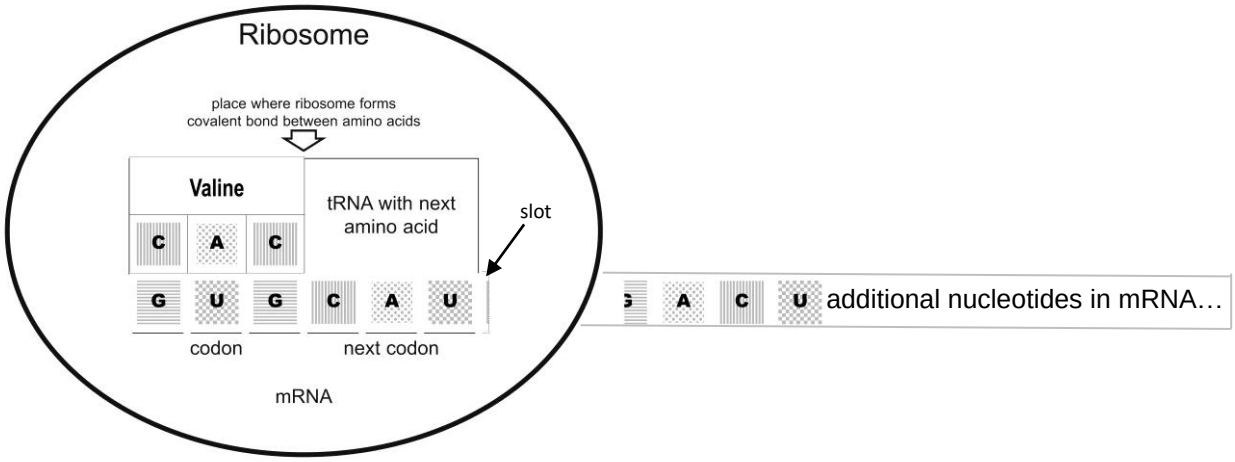
  Note: Each model tRNA molecule only shows the three nucleotides of the anti-codon and the binding site for the amino acid. A real tRNA molecule has many more nucleotides. Similarly, the mRNA molecule has many more nucleotides than shown in your strip.

14. Your partner wants to move ahead quickly, so he lays out the mRNA strip and puts the appropriate tRNA molecules above each of the six mRNA codons; 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. (Hint: See page 5.)

Modeling the Steps in Translation:

- 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.
- Cytoplasm: Use the base-pairing rules to supply the tRNA that has the correct anti-codon to match the first codon in the mRNA.
- Ribosome: Place this tRNA with its amino acid in position.

Your model ribosome should look like:



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

- 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. Tape the two amino acids together to represent the covalent bond between these two amino acids.
- Ribosome: Move the mRNA and matching tRNAs with amino acids one codon to the left. Release the tRNA on the left to the cytoplasm.
- Repeat these three 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. Why does a cell need to carry out transcription before translation?

18. 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 top of page 5.)

19. Summarize what you have learned about translation in sentences or a labeled figure. Include these words and phrases in your answer:

translation, ribosome, protein, sequence, amino acids, nucleotides, mRNA, codon, tRNA, anti-codon, base-pairing rules.

Understanding 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.

<u>Different alleles can result in different characteristics</u> as follows:

Different alleles of a gene have a different nucleotide sequence

→ 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)

Now you will analyze another example of how different alleles produce different characteristics. Specifically, you will analyze how a difference between the alleles for normal hemoglobin and sickle cell hemoglobin can result in normal health vs. sickle cell anemia.

20. 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?

21. Complete this table. (Use the table on page 6 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**						

22. Compare the beginning of the hemoglobin proteins synthesized by translating the beginning of the sickle cell vs. normal hemoglobin mRNA molecules. What difference in the amino acid sequence do you observe?

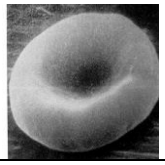
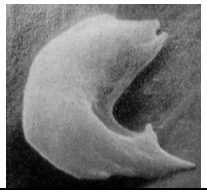
Sickle cell hemoglobin and normal hemoglobin differ in only a single amino acid out of more than 100 amino acids in the complete hemoglobin protein. This difference in a single amino acid results in the different properties of sickle cell hemoglobin compared to normal hemoglobin.

Specifically, normal hemoglobin is dissolved in the watery cytosol of red blood cells, but sickle cell hemoglobin is less soluble in the cytosol because:

- 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.

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 (see the protein column of the chart below). These rods can change the shape of the red blood cells from their normal disk shape to a sickle shape (see phenotype column of chart).

Sickle-shaped red blood cells can block blood flow in the smaller 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 can't produce enough replacement red blood cells and the person may develop anemia.

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 

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

In summary, sickle cell alleles result in production of the sickle cell hemoglobin protein, which results in the health problems observed in sickle cell anemia. This illustrates 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.

24. 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?