

# The Genetics of Sickle Cell Anemia

## I. What is Sickle Cell Anemia?

A **gene** is a segment of DNA that codes for a protein or a trait. Genes can be any length and sometimes involve multiple sections of DNA. The HBB gene provides instructions for making a protein called Beta-globin which is part of a large protein called **hemoglobin** that is found in red blood cells.

Each hemoglobin protein can carry four molecules of oxygen, which is delivered to the body's organs and tissues. If a person doesn't have enough red blood cells or the cells don't work properly, organs can become deprived of oxygen. This condition is called **anemia**. A person with anemia may feel tired all the time, experience difficulty with breathing, leg cramps, and dizziness.

There is one type of anemia that is related to the shape of the HBB protein. When a person has **sickle cell anemia**, the hemoglobin protein forms long chains that change the shape of the red blood cell. Instead of a disc shaped structure that moves easily through blood vessels, sickled blood cells are shaped like bananas. The reason they have a sickled shape is because the underlying gene has the wrong instructions. These misshapen blood cells get clogged in vessels and don't have the life expectancy of normal blood cells. A person with sickle cell disease will experience fatigue (feeling tired) and have episodes of extreme pain, called a **pain crisis**. Sickled blood cells that block vessels in the brain can even cause stroke.

Sickle cell anemia is a life threatening disease that affects about 100,000 Americans. It is an inherited disease that is passed from parents to their children, but parents can be **carriers** of the gene and not have any symptoms. If both parents are carriers, their children have a 25% chance of having sickle cell anemia.



*Normal Red Blood Cell*

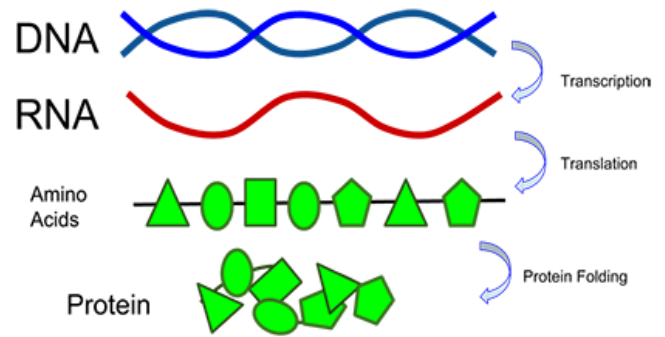


*Sickle Cell*

1. What is a gene? \_\_\_\_\_
2. What is hemoglobin? \_\_\_\_\_
3. How is a sickled blood cell different from a normal one? \_\_\_\_\_
4. Why are the blood cells the wrong shape? \_\_\_\_\_
5. What are the symptoms of sickle cell anemia? \_\_\_\_\_
6. What is a carrier? \_\_\_\_\_

## II. How DNA Makes Protein

Recall that DNA contains four bases: Adenine, Guanine, Cytosine, and Thymine. The sequence of A's, T's, G's, and C's are what determines the protein that is built. Each set of three bases will code for a single amino acid. **Proteins** are simply chains of amino acids. To make proteins, DNA must send its code sequence to the ribosomes in the cell, but it needs a messenger to do that. **Transcription** is the process where DNA is converted to a molecule of messenger RNA (mRNA). The mRNA is then used to build a protein like hemoglobin.



To determine the amino acid sequence of the gene, you must transcribe the DNA to RNA. The base pair rule is used to create RNA, but RNA does not contain thymine, it contains **URACIL** instead. This is why codon charts have U's in them and no T's.

A codon chart tells you what bases in RNA code for what amino acids. The ribosome combines all the amino acids to create a single protein, like hemoglobin. It takes three bases to determine one amino acid. Amino acids are usually abbreviated. GUC makes the amino acid valine, abbreviated as "Val" on the chart.

Here is how a codon chart could be used to determine the amino acid sequence:

		Second base in codon				
		U	C	A	G	
U	UUU	Phe	UCU } UCC } Ser	UAU } UAC } Tyr	UGU } UGC } Cys	U
	UUC					A
	UUA	Leu	UCA } UCG }	UAA Stop	UGA Stop	G
	UUG			UAG Stop	UGG Trp	C
C	CUU	Leu	CCU } CCC } Pro	CAU } CAC } His	CGU } CGC } Arg	U
	CUC					A
	CUA	Leu	CCA } CCG }	CAA } CAG } Gln	CGA } CGG }	G
	CUG					C
A	AUU	Ile	ACU } ACC } Thr	AAU } AAC } Asn	AGU } AGC } Ser	U
	AUA					A
	AUG	Met or start	ACA } ACG }	AAA } AAG } Lys	AGA } AGG } Arg	G
	AUA	Val	GCU } GCC } Ala	GAU } GAC } Asp	GGU } GGC } Gly	C
AUA	A					
G	GUU	Val	GCA } GCG }	GAA } GAG } Glu	GGA } GGG }	G
	GUC					C
	GUA	Val	GCU } GCC } Ala	GAU } GAC } Asp	GGU } GGC } Gly	U
	GUG					G

DNA: A A T C A G → (DNA sequence of gene)

RNA: U U A G U C → (transcribed from RNA; follow base pair rule, no T's)

Amino Acids: Leu Val → (find on codon chart)

7. In order to make a protein, the message on DNA must be converted to what? \_\_\_\_\_

8. How many bases in DNA are needed to code for a single amino acid? \_\_\_\_\_

9. What is a protein? \_\_\_\_\_

10. What base is found in RNA, but not DNA? \_\_\_\_\_

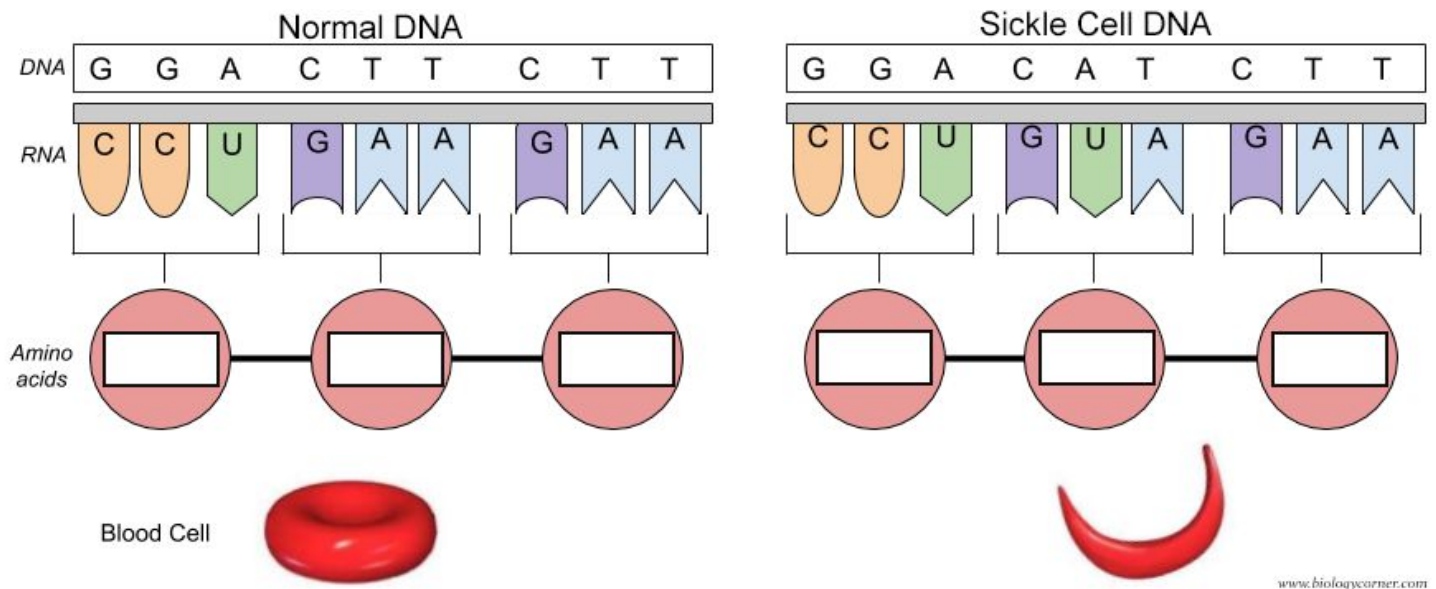
11. Consider the sequence shown, determine the complementary RNA and the amino acids

DNA	T A C	G T A	T T T	G C A	C A C
RNA					
Amino Acids					

### III. A Change in DNA Can Change the Protein

Sometimes, one of the letters in DNA gets switched with another letter, causing a mutation in the DNA. Many mutations don't have any effects, but some will change the amino acid made by the ribosomes. In the case of sickle cell anemia, just a single letter change alters the shape of the hemoglobin protein.

12. Use the codon chart to determine the amino acids created from each DNA.



13. Which codon in the sickle cell DNA is altered ? \_\_\_\_\_ (1st, 2nd, or 3rd)

14. What happens in people that have this difference in their DNA? \_\_\_\_\_

15. Explain how it would be possible to have a change in a single base of DNA, but have the protein NOT change and be functional. Hint: look at the codon chart.

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