

CHROMOSOMES TO GENES TO PROTEINS: The Story of Sickle Cell Anemia

Credits: Charlotte Mulvihill, DeAnn Campbell, and Megan Waugh, Oklahoma City Community College. Parts I & III reprinted with permission from *American Biology Teacher*. (To the teacher: Please note that a teacher answer sheet to the questions posed in this activity is available from Charlotte Mulvihill, via email request to cmulvihill@occc.edu)

Part I – Molecular Biology of Sickle Cell Anemia.

Recent research in biology has connected known “disease genes” first to specific sites on specific chromosomes, and then to the altered proteins these genes specify in the organism. Hemoglobin is a prime example; it is the well known protein that carries oxygen in the red blood cell. The hemoglobin protein is made of four polypeptide chains: 2 alpha chains (141 amino acids long) and 2 beta chains (146 amino acids long). Hence there is a gene for the alpha globin peptide chain and another gene for the beta globin peptide chain. There are many known mutations in the HBB gene (beta globin gene) leading to a variety of inherited diseases. The genetic disease sickle cell anemia is one example: the genetic code is altered such that the amino acid in position six is replaced by another amino acid.

Find out on which chromosome in the genome this gene is located: visit the NCBI (National Center for Biotechnology Information) home page at www.ncbi.nlm.nih.gov and on the right side of home page under “Hot Spots,” click on *Genes and Disease* part of the “Coffee Break, Genes and Disease, NCBI Handbook”, then click on Anemia, sickle cell to find out the chromosome number _____ and location/position _____ of this disease gene. From this page you can link to lots of other information about sickle cell anemia.

Making Normal beta-chain of Hemoglobin:

Here is the first part of the DNA sequence for the beta chain of **normal** hemoglobin; fill in the complementary DNA strand, using the base-pairing rules for making DNA:

Opposite adenine (A) put thymine (T) and vice versa
Opposite guanine (G) put cytosine (C) and vice versa

1
GTG CAC CTG ACT CCT GAG GAG

Now make the messenger RNA from this second strand of DNA, using the base-pairing rules for making RNA:

Opposite adenine (A) put uracil (U), opposite thymine (T) put adenine (A)
Opposite guanine (G) put cytosine (C) and vice versa

Now use the accompanying genetic code, and translate this messenger RNA into a sequence of amino acids.

This table shows the 64 mRNA codons and the amino acid each codon codes for.

		2nd base			
		U	C	A	G
1st base	U	UUU (Phe/F)	UCU (Ser/S)	UAU (Tyr/Y)	UGU (Cys/C)
		UUC (Phe/F)	UCC (Ser/S)	UAC (Tyr/Y)	UGC (Cys/C)
		UUA (Leu/L)	UCA (Ser/S)	UAA Ochre (<i>Stop</i>)	UGA Opal <i>Stop</i>
		UUG (Leu/L)	UCG (Ser/S)	UAG Amber (<i>Stop</i>)	UGG (Trp/W)
	C	CUU (Leu/L)	CCU (Pro/P)	CAU (His/H)	CGU (Arg/R)
		CUC (Leu/L)	CCC (Pro/P)	CAC (His/H)	CGC (Arg/R)
		CUA (Leu/L)	CCA (Pro/P)	CAA (Gln/Q)	CGA (Arg/R)
		CUG (Leu/L)	CCG (Pro/P)	CAG (Gln/Q)	CGG (Arg/R)
	A	AUU (Ile/I)	ACU (Thr/T)	AAU (Asn/N)	AGU (Ser/S)
		AUC (Ile/I)	ACC (Thr/T)	AAC (Asn/N)	AGC (Ser/S)
		AUA (Ile/I)	ACA (Thr/T)	AAA (Lys/K)	AGA (Arg/R)
		AUG (Met/M) <i>Start</i>	ACG (Thr/T)	AAG (Lys/K)	AGG (Arg/R)
	G	GUU (Val/V)	GCU (Ala/A)	GAU (Asp/D)	GGU (Gly/G)
		GUC (Val/V)	GCC (Ala/A)	GAC (Asp/D)	GGC (Gly/G)
		GUA (Val/V)	GCA (Ala/A)	GAA (Glu/E)	GGA (Gly/G)
		GUG (Val/V)	GCG (Ala/A)	GAG (Glu/E)	GGG (Gly/G)

Making Sickle Cell Hemoglobin:

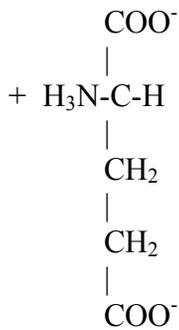
In sickle cell anemia, there is a mutation at the 17th nucleotide of DNA in this gene; the nucleotide (base) is changed from A to T; fill in the second strand:

1
GTG CAC CTG ACT CCT GTG GAG

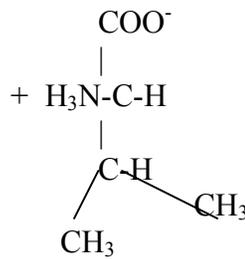
Now make the messenger RNA from this second mutated strand:

Now, using the genetic code, translate this new messenger RNA into a sequence of amino acids:

You can see that in normal hemoglobin, amino acid #6 is _____ and in sickle cell hemoglobin amino acid #6 is _____. Observe the structural formulae for these two amino acids:



Glutamic acid



Valine

Characterize the amino acid change in terms of polar versus nonpolar amino acids, or alternatively, which amino acid above carries an overall charge:

Although the altered hemoglobin has only one amino acid changed out of the total of 146, it's a crucial amino acid. When this new amino acid is at position #6 instead of the correct amino acid, the hemoglobin molecule is altered so that it becomes more hydrophobic. As a result, when the altered hemoglobin chains fold into their three-dimensional shape, they tend to stick to each other, forming long insoluble fibers of hemoglobin within the red blood cell. The red blood cell is deformed by this altered hemoglobin. It becomes more fragile, rupturing easily in tiny capillaries and clogging them up. Eventually, as the damaged red cells break down at an increased rate, the body experiences anemia along with other characteristic symptoms.

Check your understanding:

Tell how sickle cell hemoglobin differs from normal hemoglobin at the primary level of protein structure:

At the tertiary level of protein structure:

What is the effect on the red cell which contains this altered hemoglobin?

Part II. Genetics of Sickle Cell Anemia:

Sickle cell anemia is a classic Mendelian trait. That means that getting the disease is determined by the presence or absence of one particular gene, in this case, the gene for the beta chain of hemoglobin. So let's review basic genetics.

You can represent the single gene that codes for the beta chain of hemoglobin by using the letter **H** or **S** for the normal hemoglobin allele, **h** or **s** for sickle cell hemoglobin allele. This capital/small letter symbolism conveys that sickle cell anemia (h or s) is an autosomal dominant or recessive disease? _____

Allele is a genetic term that refers to different versions of the same gene, in this case the normal hemoglobin allele (H) or the sickle cell hemoglobin allele (h). Autosomal refers to a gene on any chromosome other than a sex-determining chromosome (X and Y).

Recall also that individuals have two copies of each gene, and if the individual is homozygous, the two gene copies are identical alleles, and if the individual is heterozygous, the two gene copies are different alleles.

Check your understanding:

An adult with homozygous normal hemoglobin would have the genotype:

_____ An adult with sickle cell hemoglobin would have the genotype: _____

An adult with normal hemoglobin, but heterozygous for the sickle cell trait, would have the genotype: _____. A heterozygote is sometimes referred to as a carrier because the person has no signs of the disease, he/she can pass on the disease gene to his/her offspring.

Gamete Formation:

Recall the process by which an adult forms reproductive cells called gametes that contain half the number of chromosomes; this process is called _____. Each gamete (egg or sperm in humans) will contain only one gene copy (one allele) for hemoglobin.

Fill in the following chart; use H= normal hemoglobin allele; h = sickle cell hemoglobin allele.

Adult phenotype	Adult genotype	Gametes Possible
Normal hemoglobin		
Sickle cell hemoglobin		
Normal hemoglobin, carrier for sickle cell hemoglobin		

Genetic Crosses:

Do a genetic cross, using the Punnett square, of a sickle cell individual with a person who is homozygous normal. List genotypes and phenotypes of offspring.

Do a genetic cross (Punnett square) of two normal heterozygotes (carriers) of the sickle cell trait; list genotypes and phenotypes of offspring.

One note on the subtlety of genetic disease: in parts of Africa where malaria is very common and claims many lives, 20% of the population may be carriers for the sickle cell gene. Although being homozygous for sickle cell anemia leads to early death and lowered likelihood to pass on the gene, the sickle cell heterozygotes (carriers) in high-malaria regions have improved survivability over the homozygous normal individuals. Why? It turns out that red blood cells of individuals who are heterozygous for sickle cell are less easily infected by the malaria parasite, thus improving the heterozygous individual's survival and ability to reproduce in that malaria-infested region. Hence the occurrence of the heterozygote is favored over the homozygous normal by selection pressures from the malaria parasite. What is the biologic lesson from this?

Genetic Testing and Counseling:

It is now possible to test people for the presence of the sickle cell hemoglobin. Testing can determine whether a person is homozygous normal or heterozygous normal (carrier) for sickle cell anemia. Sickle cell anemia is most frequent among African and Hispanic populations, and lower, but still present, among those of Italian, Greek, Arabian, Maltese, southern Asian, and Turkish ancestry.

Imagine that you are a genetic counselor and an African-American couple comes into the clinic and asks what is the likelihood that one of their children will have sickle cell anemia. They report no known family history of the disease; they both appear to have normal hemoglobin. No testing is done. You know that approximately one in ten African-Americans are carriers for the gene.

What are the possible genotypes for an individual who has the phenotype of normal hemoglobin: _____ and _____.

This couple, both of whom have normal hemoglobin phenotypes, could have sickle cell anemia offspring only if:

What is the overall risk for this couple, based on the incidence of the gene in the African-American population at large?

Do you think that people should be tested to see if they carry the gene? What are some pros and cons that you can think of for testing for the sickle cell gene? Make a chart:

PRO

CON

Oklahoma is one of the states that currently screens newborns for sickle cell trait or disease. Check out this link to find out what other diseases the Oklahoma newborn screening program looks for:

http://www.ok.gov/health/Child_and_Family_Health/Screening,_Special_Services_and_Sooner_Start/

Part III. Laboratory

To the teacher: Please visit

<http://www.occc.edu/mockbiotech/documents/Checklistsicklecell.html> for a list of equipment, materials and links to protocols for preparing this laboratory exercise.

You are a laboratory technician in the newborn screening section of the BBD Pathology Lab, a branch of the state health department. You and your coworkers are going to test today's samples of newborn blood to see if there are any cases of sickle cell anemia in the newborns.

You already know that individuals with sickle cell anemia have abnormal hemoglobin in their red blood cells. They make hemoglobin S instead of the normal hemoglobin A. Carriers of the disease make hemoglobin A and S. In the laboratory, you can use electrophoresis to detect abnormal hemoglobin protein because it is known that hemoglobin S moves slower than normal hemoglobin during electrophoresis.

Materials:

Agarose gel with special buffer for proteins

Electrophoresis chamber

Electrophoresis buffer

Power supply

Sample of blood containing normal hemoglobin A, labeled N for normal.

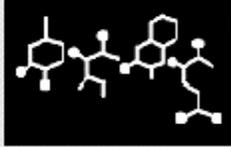
Newborn blood samples for screening, numbered P1, P2, etc. for Patient.

Micropipettors

Procedure:

- 1) Obtain two 0.5mL tubes, one containing the Normal (N), and one containing your Patient sample (P). Record the number of your particular patient sample_____.
- 2) Place a gel into the electrophoresis chamber. Fill the reservoirs with buffer, and then add just enough buffer to cover the gel.
- 3) Load 10-15 μ L of each sample into a separate well with a micropipette. Label the wells you used in the sketch below.
- 4) Note how your gel is oriented with respect to the positive and negative poles. (Remember- Run to red.)
- 5) Place the cover on the chamber and plug the electrodes into to the power supply, black to black, red to red.
- 6) Turn on power supply; look for bubbles rising from the wires at each end to ensure the electrophoresis box is working correctly.
- 7) Run your gel at 120-125 volts until the dye is about $\frac{3}{4}$ of the way down the gel. This should take about 10-15 minutes.
- 8) Turn off the power supply and disconnect the electrodes.
- 9) Draw your gel results below:

Discover INC



A Mock Biotechnology Company of OCCC

Technician _____

Date _____

Patient ID _____

Test ID Sickle Cell Anemia

Gene Testing Report

Test Results:

<input type="checkbox"/>							
--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------

Description of Results:

Analysis of Results:

Diagnosis: HbA HbA/S HbS

Signature: _____ Date: _____

Test Your Understanding:

1. If a person was carrier (heterozygous) for sickle cell hemoglobin, how many bands would you see? _____
2. If a person had sickle cell anemia, how many bands would you see? _____
3. If a person was normal for hemoglobin, how many bands would you see? _____
4. How does the gel distinguish normal from sickle cell hemoglobin?
5. Why do you need a Normal sample for each gel you run?
6. Would it be valid to use a known sickle cell sample instead of a known Normal sample for each gel you run?
Explain your answer:
7. When you report your class results for these newborns, which samples were positive for sickle cell anemia: _____
8. Did you detect any carriers and if so, list:

Part IV. Bioinformatics of Sickle Cell Anemia

Bioinformatics is the use of computers to make sense of biological data. In particular, the human genome project has generated lots and lots of sequences of DNA from many different organisms, not just humans. These sequences are stored in public databases, and there are so many sequences that it takes computer power to store, analyze and work with this data. One major gateway to the public databases is NCBI: the National Center for Biotechnology Information, maintained by the National Library of Medicine at the National Institutes of Health. These databases are not just for scientists; students can go to and learn from parts of these public databases. Let's mine these databases for some more information about sickle cell anemia.

Go to the NCBI sickle cell anemia "Genes and Disease" page, (<http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=gnd.section.98&ref=toc>) click on "Genome view" to visualize where on the chromosome this gene is located – would you describe its location as in the middle or near the end of the chromosome?

Back again to the sickle cell anemia "Genes and Disease" page. Let's look more closely at the HBB gene (symbol for the beta globin gene of hemoglobin). Click on "Entrez Gene" to get to the Entrez gene entry for HBB, and on that page, scroll down to "genomic regions, transcripts, products" – this item tells you a lot about this gene. For example, it reveals that the DNA for this gene is positioned on the chromosome between base # 5,203,272 and _____. How many nucleotides are in this sequence? _____ Within this stretch of DNA, how many coding regions are there: _____? The coding regions indicate what part of the DNA actually gets

translated from DNA into protein, and a coding region is termed an exon. The noncoding regions are called introns – how many are shown for this gene_____?

Click on black link NC_000011.8 (FASTA) to get entire nucleotide sequence of gene - this contains ALL the nucleotides of the gene, coding and non-coding. Next, go back one page and click on the blue link NM_000518 (FASTA) to get the mRNA sequence for this gene – what do you notice about this sequence – is it the same length? Longer? Shorter? What has happened to account for this difference?

Now go back one page and click on the red link CCDS7753.1 to get to the Consensus Coding Sequence page, scroll down to nucleotide sequence which is _____nts (nucleotides) long and see below the amino acid sequence which is _____amino acids long. Look at the seventh amino acid in the sequence – it is _____. (mouse over the symbol to get the amino acid name) You now know that in sickle cell anemia, this amino acid is replaced with _____ when the codon is changed from _____ to _____. Looking at the chromosomal locations chart above the CCDS sequence data, you can see the exact 3 locations on the DNA where the exons are located.

More Bioinformatics Practice:

Open a second browser window or tab (while keeping the CCDS window open). Go to <http://www.ebi.ac.uk/> and pull down the “Tools” menu and select “sequence analysis – align” and the page EMBOSS Pairwise Alignment Algorithms pops up. You are now going to copy and paste DNA sequences to align into this tool.

Return to your first browser window or tab, showing the CCDS sequence data. Go back one page and click on NC_000011.8 (FASTA). Copy and paste this DNA sequence into sequence 1 of the EMBOSS window in your second browser.

Return to your first browser window, showing the Nucleotide page and go back one page. Click on NM_000518.4 (FASTA). Copy and paste this DNA sequence into sequence 2 of the EMBOSS window in your second browser.

Click on the RUN button. From the results, you'll notice that you get perfect alignment three times, with big gaps of no alignment. What does this illustrate?

Complete nucleotide sequence of HBB gene in FASTA format: DNA

```
>ref|NC_000011.8|NC_000011:c5204877-5203272 Homo sapiens chromosome 11,
reference assembly, complete sequence (1606 nt)
ACATTTGCTTCTGACACAACACTGTGTTCACTAGCAACCTCAAACAGACACCATGGTGCATCTGACTCCTGA
GGAGAAGTCTGCCGTTACTGCCCTGTGGGGCAAGGTGAACGTGGATGAAGTTGGTGGTGAGGCCCTGGGC
AGGTTGGTATCAAGGTTACAAGACAGGTTTAAGGAGACCAATAGAACTGGGCATGTGGAGACAGAGAAG
ACTCTTGGGTTTCTGATAGGCACTGACTCTCTCTGCCTATTGGTCTATTTTCCCACCCTTAGGCTGCTGG
TGGTCTACCCTTGGACCCAGAGGTTCTTTGAGTCCTTTGGGGATCTGTCCACTCCTGATGCTGTTATGGG
CAACCCTAAGGTGAAGGCTCATGGCAAGAAAGTGCTCGGTGCCTTTAGTGATGGCCTGGCTCACCTGGAC
AACCTCAAGGGCACCTTTGCCACACTGAGTGAGCTGCACTGTGACAAGCTGCACGTGGATCCTGAGAACT
TCAGGGTGAGTCTATGGGACGCTTGATGTTTTCTTTCCCCTTCTTTTCTATGGTTAAGTTCATGTCATAG
GAAGGGGATAAGTAACAGGGTACAGTTTAGAATGGGAAACAGACGAATGATTGCATCAGTGTGGAAGTCT
CAGGATCGTTTTAGTTTTCTTTTATTTGCTGTTTCATAACAATTGTTTTCTTTTGTTTAATTCTTGCTTTCT
TTTTTTTTCTTCTCCGCAATTTTTACTATTATACTTAATGCCTAACATTGTGTATAACAAAAGGAAATA
TCTCTGAGATACATTAAGTAACTTAAAAAAAACCTTACACAGTCTGCCTAGTACATTACTATTTGGAAT
ATATGTGTGCTTATTTGCATATTCATAATCTCCCTACTTTATTTTCTTTTATTTTTAATTGATACATAAT
CATTATACATATTTATGGGTTAAAGTGTAATGTTTTAATATGTGTACACATATTGACCAAATCAGGGTAA
TTTTGCATTTGTAAATTTAAAAAATGCTTTCTTTTAAATATACTTTTTTGTTTATCTTATTTCTAATA
TTTTCCCTAATCTTTTCTTTTTCAGGGCAATAATGATACAATGTATCATGCCTCTTTGCACCATTCTAAAG
AATAACAGTGATAATTTCTGGGTTAAGGCAATAGCAATATCTCTGCATATAAATATTTCTGCATATAAAT
TGTAAGTATGTAAGAGGTTTCATATTGCTAATAGCAGCTACAATCCAGCTACCATTCTGCTTTTTATTTT
ATGGTTGGGATAAGGCTGGATTATTCTGAGTCCAAGCTAGGCCCTTTTGCTAATCATGTTTCATACCTCTT
ATCTTCTCCCACAGCTCCTGGGCAACGTGCTGGTCTGTGTGCTGGCCCATCACTTTGGCAAAGAATTCA
CCCCACCAGTGCAGGCTGCCTATCAGAAAGTGGTGGCTGGTGTGGCTAATGCCCTGGCCCACAAGTATCA
CTAAGCTCGCTTTCTTGCTGTCCAATTTCTATTAAGGTTTCTTTGTTCCCTAAGTCCAACACTACTAACT
GGGGGATATTATGAAGGGCCTTGAGCATCTGGATTCTGCCTAATAAAAAACATTTATTTTTCATTGC
```

mRNA of HBB in FASTA format: (444 nt)

```
>gi|28302128|ref|NM_000518.4| Homo sapiens hemoglobin, beta (HBB), mRNA
ACATTTGCTTCTGACACAACACTGTGTTCACTAGCAACCTCAAACAGACACCATGGTGCATCTGACTCCTGA
GGAGAAGTCTGCCGTTACTGCCCTGTGGGGCAAGGTGAACGTGGATGAAGTTGGTGGTGAGGCCCTGGGC
AGGCTGCTGGTGGTCTACCCTTGGACCCAGAGGTTCTTTGAGTCCTTTGGGGATCTGTCCACTCCTGATG
CTGTTATGGGCAACCCTAAGGTGAAGGCTCATGGCAAGAAAGTGCTCGGTGCCTTTAGTGATGGCCTGGC
TCACCTGGACAACCTCAAGGGCACCTTTGCCACACTGAGTGAGCTGCACTGTGACAAGCTGCACGTGGAT
CCTGAGAACTTCAGGCTCCTGGGCAACGTGCTGGTCTGTGTGCTGGCCCATCACTTTGGCAAAGAATTCA
CCCCACCAGTGCAGGCTGCCTATCAGAAAGTGGTGGCTGGTGTGGCTAATGCCCTGGCCCACAAGTATCA
CTAAGCTCGCTTTCTTGCTGTCCAATTTCTATTAAGGTTTCTTTGTTCCCTAAGTCCAACACTACTAACT
GGGGGATATTATGAAGGGCCTTGAGCATCTGGATTCTGCCTAATAAAAAACATTTATTTTTCATTGC
```

Protein sequence in FASTA format: (147 aa)

```
>gi|4504349|ref|NP_000509.1| beta globin [Homo sapiens]
MVHLTPEEKSAVTALWGKVNVDVGGGALGRLLVVPWTQRFESFGDLSTPDAVMGNPKVKAHGKKVLG
AFSDGLAHLNLRKGTFTLSELHCDKLHVDPENFRLLGNVLCVLAHFFGKEFTPPVQAAAYQKVVAGVAN
ALAHKY
```

Part V. Inquiry on Sickle Cell Anemia.

Students organize into groups, choose a scenario, and each group should discuss, investigate, and then present findings and generate further questions:

Scenario I. Imagine that you are a parent who has just been notified that your new baby has tested positive for sickle cell anemia.

1. Generate at least FIVE questions that a parent might have for the genetic counselor.
2. Then use some of the web resources below as a starting point to get some answers to those questions.
3. Groups share results with whole class.
4. List some *unanswered* questions that remain.

Scenario II. Imagine that you are the genetic counselor for the parents in scenario I – how would you answer some of the following questions:

1. How would you describe the inheritance of sickle cell trait to the parents.
2. How would you give the family information about the risk of having another child with sickle cell disease if they have another baby.
3. What is the risk of being a carrier for the next baby?
4. Draw a pedigree (family tree) for this family indicating who might be carriers of sickle cell trait.
5. Develop some tools (diagrams, pictures, illustrations) to explain the inheritance of sickle cell trait to the family.
6. What are some of the signs and symptoms of sickle cell anemia?
7. What treatments are available for sickle cell anemia?

Groups share results with the whole class.

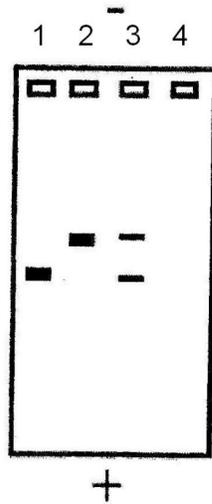
Web resources

- The Genetic Science Learning Center:
<http://learn.genetics.utah.edu/units/disorders/whataregd/sicklecell/>
- Genes and Disease from NCBI:
<http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=gnd.section.98&ref=toc>
- From the Science Education website, the Human Genetic Variation curriculum supplement, view the video about sickle cell anemia at
<http://science.education.nih.gov/supplements/nih1/Genetic/activities/activity2.htm>
- Fact Sheet from the National Heart, Lung and Blood Institute of NIH:
http://www.nhlbi.nih.gov/health/dci/Diseases/Sca/SCA_WhatIs.html?itool=books&referralid=gnd.section.98

- OMIM (Online Mendelian Inheritance in Man)
<http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=603903&itool=books&referralid=gnd.section.98>
- Sickle Cell Disease Association of America:
<http://www.sicklecelldisease.org/?itool=books&referralid=gnd.section.98>
- Oklahoma State Health Department:
http://www.ok.gov/health/Child_and_Family_Health/Screening_Special_Services_and_Sooner_Start/
- Check out the new law GINA: Genetic Information Non Discrimination Act at
<http://www.genome.gov/24519851>

Part VI. Assessment

1. People with Sickle Cell Anemia have distorted red blood cells. They make hemoglobin S instead of the normal hemoglobin A. Hemoglobin S moves slower during electrophoresis. Carriers of the disease make hemoglobin A and S. Look at the gel below and answer the next three questions.



Which lane was loaded with the sample from a person with sickle cell anemia?

- a. lane 1
- b. lane 2
- c. lane 3
- d. lane 4

Which lane was loaded with a sample from a normal person?

- a. lane 1
- b. lane 2
- c. lane 3
- d. lane 4

Which lane contains a sample from a carrier for sickle cell anemia?

- a. lane 1
- b. lane 2
- c. lane 3
- d. lane 4

2. Another Hemoglobin Genetic Variant: Hemoglobin Saverne:

The normal DNA for the end of the beta chain of hemoglobin reads:

143
CAC AAG TAT CAC TAA GCT CGC TTT CTT GCT GTC CAA TTT CTA TTA

Fill in the second strand of DNA on the line above.

Make a messenger RNA from this **second** DNA strand:

Translate the mRNA into a protein until you reach the STOP signal; do not translate further – why?

In the disease Hemoglobin Saverne, the A in triplet CAC #143 is deleted, causing a frameshift mutation. Delete that A in triplet #143, and reorder the remaining bases downstream as triplets, three at a time, without that A. The new DNA would then read:

143

Fill in the second strand of DNA above.

Now use the second strand of DNA to make the mRNA:

Translate the mRNA into protein; what is the result?

What effect do you think this would have on the functioning of the hemoglobin molecule? _____

3. If you look up the HBB gene on the OMIM database, # 141900, you will see that other kinds of mutations in this gene result in different kinds of beta-thalassemsias – what is the difference between sickle cell anemia and beta-thalassemsias?

4. Use the following terms to fill in the blanks below: chromosome, DNA, gene, genome, protein. The challenge is to use each term only once!

The _____ hemoglobin is coded by the _____ made of the molecule _____. The genes are organized in the nucleus within _____, and all together they make up the entire human _____.