Team Lab Notebook (TLN)
Discovering the Genetics and Molecular Biology of Sickle Cell Anemia

Team Name:
By: (Enter the full names, and team roles of the team members who are present at today’s lab)

Date:

Part I. Meeting the Family Affected by Sickle Cell

Activity 1
1. Why do you think that Dr. Dufall wants a blood sample from Emily and Chaka, if neither of them has sickle cell anemia? What would looking at their hemoglobin tell us? (1 pt)

2. What’s wrong with Emily’s contention that they need not worry about sickle cell since he was not born in Africa, and there is no history of the disorder in his family? (1 pt)
Part II. Searching for Molecular Evidence of Sickle Cell Anemia

Activity 2.

1. As a team we discussed our answers to the homework and came to the following consensus on the predicted structural (size and shape) effects of each type of mutation on the resulting polypeptide. (An example is provided) (3 pts)

<table>
<thead>
<tr>
<th>Type of mutation</th>
<th>Predicted structural effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deletion, substitution or addition that results in a premature stop codon.</td>
<td>This would produce a smaller polypeptide. How small would depend on where the premature stop codon occurred in the gene ...near the end or at the beginning. This would likely change the shape of the protein substantially and therefore would probably alter its function.</td>
</tr>
<tr>
<td>Deletion, substitution or addition that alters the sequence of the stop codon.</td>
<td></td>
</tr>
<tr>
<td>Substitution of one nucleotide for another</td>
<td></td>
</tr>
<tr>
<td>Deletion of one nucleotide early in the gene.</td>
<td></td>
</tr>
<tr>
<td>Addition of three successive nucleotides early in the gene.</td>
<td></td>
</tr>
<tr>
<td>Deletion of an entire codon.</td>
<td></td>
</tr>
</tbody>
</table>

2. Our team thought that a mutation that changed a positively charged amino acid to a negatively charged amino acid would affect the rate of the polypeptide’s migration in a gel in the following way: (1 pts)
3. Our team generated the following hypotheses/predictions as to the effect of one of the possible mutations (from the table above) on the globin genes. *(Hint: A prediction can be a diagram of a completed gel!)* *(3 pts)*

Example: If a mutation resulted in a premature stop codon early in the beta globin gene, then we would predict the following gel results from our 5 tubes.

![Diagram of gel results](image)

- Normal beta globin polypeptide
- Normal alpha globin polypeptide
- Mutant beta globin polypeptide

If Emily is a carrier.

+ control  Chaka  Emily  Fatu  - control
4. Our team added the following solutions to the negative control tube (#5) for the following reasons (read the electrophoresis procedures in the lab manual before you make this decision): (1 pt)

Activity 3.

1. After watching the film, our team came up with the following explanation for the relationship between malaria and the frequency of the sickle cell allele in Africa and Southeast Asia. (2 pts)

2. Our team decided that the most likely survival probabilities for the populations living in West African countries would be: (2 pts)

   SS______; Ss (carriers)_______; ss________

   We chose these survival probabilities because
We observed the following general trend in the relative frequencies of the three genotypes in West Africa over time. *(Do not re-draw the graph from your computer, instead DESCRIBE how the genotypes change relative to one another!)* *(1 pt)*

Based on our knowledge of the relationship between sickle cell anemia and malaria in Africa, we developed the following explanation for the observed changes in the frequencies of each genotype: *(4 pts)*

1. Why does the frequency of each genotype change (increase or decrease) over time?

2. Why doesn’t the genotype with the lowest survival probability disappear from the population?

3. Explain why the frequency of the sickle cell genotype (ss) increases over time despite the fact that sickle cell anemia is such a debilitating disorder.
3. Our team decided that the most likely survival probabilities for people living in South Carolina would be: (2 pts)

SS______; Ss (carriers)_______; ss_________

We chose these survival probabilities because

We observed the following general trend in the relative frequencies of the three genotypes in South Carolina over time. (Again...don’t re-draw the graph from your computer, instead DESCRIBE how the genotypes change relative to one another!) (1 pt)

The most likely explanation for why the frequencies of each genotype changed as they did in South Carolina is... (In your explanation also comment on why the trends in the relative frequencies of genotypes are different from those in West Africa.) (3 pts)

Part III. A Best Guess.
Activity 4

1. Our team’s best guess at the probability of Emily and Chaka having a child with sickle cell is (please show and explain your calculations): (2 pts)
2. If Emily’s family were from Senegal our best guess at the probability of Emily and Chaka having a child with sickle cell is (please show and explain your calculations) (1 pt):

3. What do you think your (choose one member from your team) chances are of someday having a child with sickle cell anemia (please show and explain your work)? (1 pts)

Part IV. The Electrophoresis Results
Activity 5

1. The following is a picture of our gel with the various bands labeled: (1 pt)

   ![Gel Image]

Based on the above gel:

2. A mutation in which of the globin genes is responsible for the sickle cell anemia observed in this family? Who in the family inherited the mutation? (2 pts)

3. Use your results from your gel to determine which of the common mutations to the globin genes (shown in the table below) may have been inherited by members of this family. Justify your answer. (4 pts)
5. Our team wrote the following letter to Chaka and Emily explaining the results of the globin electrophoresis experiment. Make sure you read the guidelines for this letter in your lab manual. (4 pts)

<table>
<thead>
<tr>
<th>Name</th>
<th>Mutation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb Wayne</td>
<td>Single base deletion in alpha gene causes frameshift, changing amino acids 139–141 and adding amino acids</td>
</tr>
<tr>
<td>Hb Grady</td>
<td>Nine extra bases add three amino acids between amino acids 118 and 119 of alpha chain</td>
</tr>
<tr>
<td>Hb Chesapeake</td>
<td>Change from arginine to leucine at amino acid 92 of beta chain</td>
</tr>
<tr>
<td>Hb McKees Rock</td>
<td>Change from tyrosine to STOP codon at amino acid 145 in beta chain</td>
</tr>
<tr>
<td>Hb Constant Spring</td>
<td>Change from STOP codon to glutamine elongates alpha chain</td>
</tr>
<tr>
<td>Hb S</td>
<td>Change from glutamic acid to valine at amino acid 6 in beta chain</td>
</tr>
<tr>
<td>Hb Leiden</td>
<td>Amino acid 6 deleted from beta chain</td>
</tr>
</tbody>
</table>

Clean Up Checklist on the next page must be initialed by your lab instructor before you can leave the lab!
- Our work area is clean.
- Used buffer is poured down the sink.
- Our gel boxes are rinsed and dried and replaced neatly on our lab table. **DO NOT WRAP THE CORDS AROUND THE GEL BOX!**
- All microcentrifuge tubes have been rinsed clean with water, and placed in the plastic tub near the sink.
- Used micropipette tips have been rinsed clean with water, and placed in the plastic tub near the sink.
- Our lab table and stools are wiped down.
- Glassware is washed with soap and set in drying wracks above or next to the sinks.
- Class common work area is clean and materials/instruments are returned to their proper place.
- The computer desktop is clear of any files other than those that are supposed to be there for today’s lab.
- All applications (LoggerPro, Excel, Word etc…) on the computer are closed.
- The computer should remain on.

________ Your lab instructor must initial here, indicating that your work area is clean before you may leave the lab.

**Failure to clean up, or leave lab without your instructor’s initials, will result in 10 points deducted from this week’s TLN grade.**

*Please do not forget to complete the Peer Evaluation form, and turn it in to your lab instructor before you leave.*