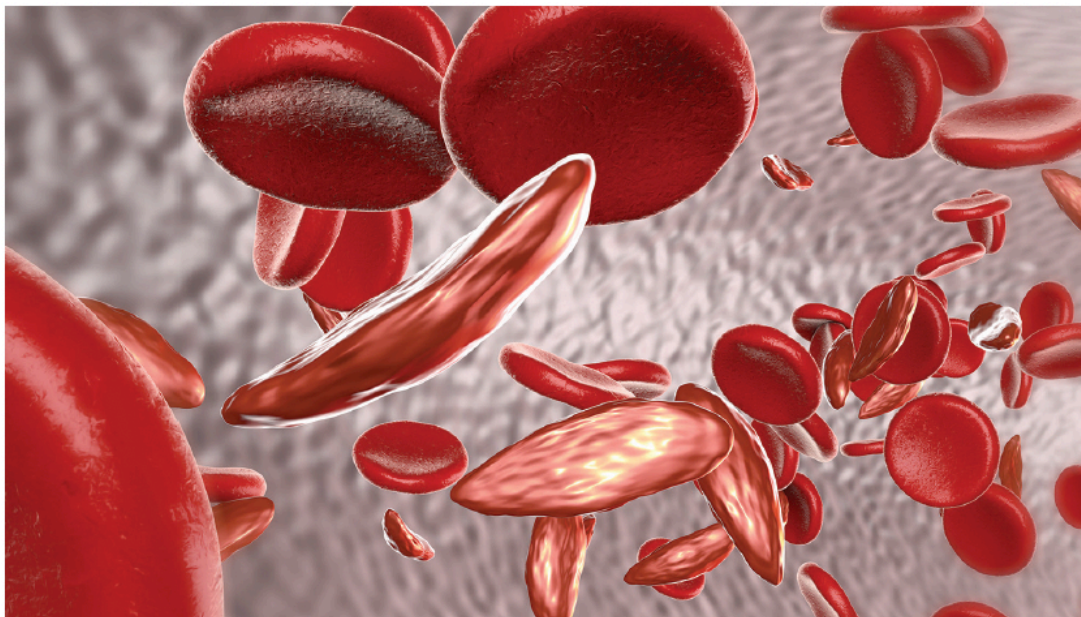




Sickle Cell Inheritance
MiniLab
Student's Guide

Cat# M3050
Version 010123



A special thank you to Crystal McDowell for her contribution that made this MiniLab possible.

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Laboratory Safety

1. Wear lab coats, gloves, and eye protection whenever possible.
2. Use caution with all electrical equipment such as electrophoresis units.
3. Heating and pouring molten agarose is a splash hazard. Use caution when handling hot liquids. Wear eye protection and gloves to prevent burns.
4. Wash your hands thoroughly after handling biological materials and chemicals.
5. Dispose of all materials in a biohazard bag or in a wash tub containing a 10% bleach solution.

Introduction

Monitoring and Surveillance Programs for Public Health

Crisis Episode - Year 2006

"You are late for rounds again, Ben," Sarah said as they rushed to catch up with the rest of the medical team.

"Right on time," Ben smiled as they both entered the room. Ben and Sarah were medical interns, first-year residents.

Dr. Grant, the attending physician, glared disapprovingly as Ben entered the room behind everyone else. "Dr. Thomas, why don't you present the first case today," Dr. Grant instructed as Ben entered the room.

"Yes, Dr. Grant. The patient is Jayden Smith. Good morning, Jayden," Ben said acknowledging the patient before proceeding.

"Good morning," Jayden replied, returning Ben's smile with her own. She was obviously very tired and weak from the crisis episode she had experienced.

"Jayden is a ten-year-old, African American girl who is presenting a number of clinical symptoms. Patient history reveals numerous episodes of unpredictable but excruciating pain. While Jayden feels well most of the time, these recurring events have been taking place throughout her childhood. Jayden was admitted last night. She was experiencing shortness of breath and fatigue. She complained of pain, particularly in her arms and legs at several joints and an intense soreness in her muscles. Short periods of exercise often leave her exhausted and very weak. When examined, it was also noted that the whites of her eyes were yellow in color and that her left abdominal area was tender to palpation. Her parents shared that she has a history of fevers and infections. Her parents and siblings do not exhibit these symptoms, but her maternal grandfather died at the age of 52 with similar symptoms throughout his life. The patient was dehydrated and her hematocrit levels are at 26% rather than the typical baseline of 36 to 48%. Leukocyte counts were higher than normal as well," Ben concluded his clinical presentation of the case.

Sarah and Ben had reviewed the cases the night before for the rounds. Sarah remembered this case well. She was determined to impress the attending physician so she examined each case carefully, noting the patient's symptoms and possible causes for each symptom.

Complete her analysis of Jayden's case below. The symptoms are **effects** of the underlying **cause(s)**. It is your job to figure out what the possible **causes** of the symptoms may be and to formulate a potential diagnosis for Jayden's crisis event.

Note the symptoms (**effects**) that Ben described in the clinical presentation from the patient chart and then brainstorm the possible causes, as well as organs or body systems affected.

Patient Analysis for Medical Rounds: Jayden Smith

Patient's Symptoms (Effect)	Thoughts about what could be causing this symptom. (Think about cells or parts of the body that could be causing this symptom.) Feel free to look up what could be causing the symptom. (Cause)
Preliminary Diagnosis	

Finding the Cause - Year 2006

Annotate: Underline Unusual Words, Circle Central Concepts

"Thank you, Dr. Thomas. Now, who can explain those symptoms?" Dr. Grant asked the room of first-year residents. "Yes, Sarah."

"The low hematocrit reading indicates a lack of red blood cells and thus anemia. Since red blood cells carry oxygen, the anemia would also explain a number of Jayden's symptoms. Her fatigue, muscle soreness, and weakness are likely due to the reduced number of RBCs carrying oxygen to her cells. The anemia is likely hemolytic rather than aplastic due to possible presentation of an enlarged spleen given the tenderness of the left abdominal region. The spleen's main function is to remove defective or older red blood cells. This suggests red blood cells are still being produced but that they are not lasting as long or they are abnormal in some way rather than the bone marrow not producing enough RBCs with aplastic anemia. The yellow tint in her eyes is likely due to jaundice and bilirubin building up from red blood cells that have lysed," Sarah finished.

"What about the excruciating pain, Dr. Thomas?" Dr. Grant asked Ben to explain.

"It is likely due to restricted blood flow, perhaps even with microcirculation of the capillaries. This may have also contributed to the enlarged spleen if occlusion is occurring in these small vessels that supply blood to the spleen. The organ is not getting enough oxygen, so hypoxia is another potential problem. This is known as a splenic sequestration crisis. It can result in death within 1-2 hours if left untreated, so it is good that Jayden came in when she did. Depending on the extent of the restricted blood flow, other organs could be affected as well. The reduced oxygen also explains the fatigue, weakness and shortness of breath," explained Ben.

"Yes, it is good that she came in. Now, what could explain the blockage in the capillaries and other small blood vessels? What is likely the ultimate cause here," asked Dr. Grant. "Yes, Sarah."

"It is likely a hemoglobinopathy disorder affecting red blood cells, most likely Sickle Cell Disease (SCD). Since there is possibly a family history of similar symptoms, that diagnosis would make sense. SCD most often results from the inheritance of two mutated alleles for a gene responsible for hemoglobin production. When a person is homozygous for HbS, the hemoglobin is abnormal and can cause the red blood cells to form a sickle shape. The sickled cells tend to adhere to each other and to capillary walls which would explain the occlusion and thus the pain. The joint pain could be explained by vascular necrosis in the head of the femur or the humerus. Sickle cells tend to only last about 10 to 20 days due to hemolysis versus the typical 120 days of a normal red blood cell. That would also explain the anemia other symptoms we have discussed. Sickle cell patients often experience a higher degree of infection which is likely why her white blood cells are higher than normal," Sarah affirmed.

"Nice analysis. Now, what should we do?"

"We should order a genetic screening test to confirm it is sickle cell anemia," said Ben.

Analysis: After reading and annotating this part of the case study, return to your table and use another colored pen or pencil to correct or add to the causes of the various symptoms. If there are reasons that Sarah and Ben did not address from class discussion, then note those as well.

Carrier Testing - Year 2006

Since Ben and Sarah led the discussion about Jayden's case during the morning medical rounds, they were chosen to speak to Jayden and her parents about the results of the genetic screening. The attending physician also suggested that Jayden's parents undergo carrier testing after learning they had not been screened when Mrs. Smith was pregnant with Jayden.

"Mr. and Mrs Smith, we have Jayden's results from the genetic screening and the test confirms that she has Sickle Cell Disease," Sarah explained. "You may recall some of the details about this inherited condition that we discussed previously. Basically, the results indicate that Jayden inherited a mutated allele, a version of the gene, for hemoglobin from each of you. That means you both are carriers. The genetic test we performed on your DNA confirmed that conclusion. You each have a normal copy of the hemoglobin gene which masks the mutated copy that you carry, so you do not exhibit any of Sarah's symptoms. But you each were able to pass the mutated allele on to Sarah. You have Sickle Cell Trait. One in ten African Americans have Sickle Cell Trait in the United States."

"Why was this test not performed when Jayden was a baby? Don't they perform blood tests on newborns? How did we miss this?" asked Mrs. Smith.

"That is an excellent question. Newborn screening for Sickle Cell Disease did not begin until this year (2006) in all 50 states, even though CA has been screening babies since 1990. Jayden was born in 1996, so she would not have been screened since you lived in another state when she was born. Unfortunately, even though sickle cell disease is a common genetic disorder, there has been limited funding and research in the past. Fortunately, that is starting to change," Ben explained.

"What can be done to help Jayden?" asked Mr. Smith.

"Unfortunately, the only drug that is approved for sickle cell disease is hydroxyurea and it is currently only approved for adults by the FDA. Jayden's best course of action right now is to avoid triggers. When she was admitted to the hospital, she was dehydrated which can be a trigger for a sickling or crisis event. Other triggers can be overexertion, exposure to cold weather, or even high altitudes. Antibiotics can be used to treat bacterial infections she may be more at risk of contracting, but otherwise she needs to avoid certain stressors to her body to minimize the crisis events. Because hemoglobin and red blood cells transport oxygen to body cells and organs, sickle cell affects multiple organs and systems. It is imperative that we monitor Jayden and limit exposure to triggers of these episodes. This is a lot of information to take in and there is much more that we could share. For now, we would like to set you up with an appointment with a genetic counselor to discuss the condition, treatment options, and the

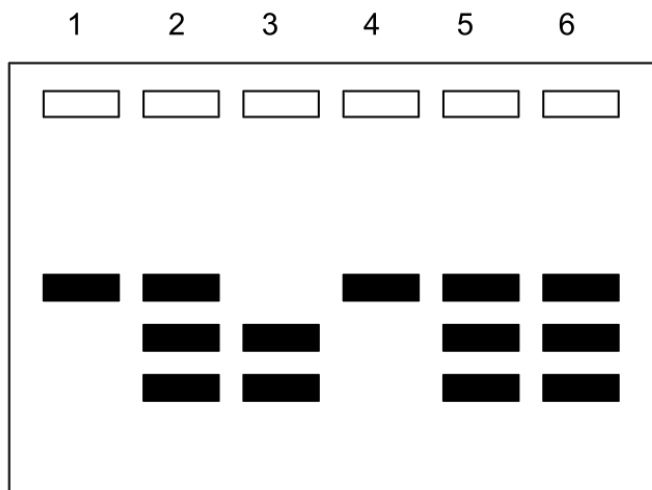
possibility you could have another child with Sickle Cell Disease," Sarah paused when she saw the look on Mrs. Smith's face. "Mrs. Smith, is something wrong?"

"I am pregnant," Mrs. Smith exclaimed. "What is the chance my next child could also have sickle cell disease?"

"Let's take this one step at a time, Mrs. Smith," Ben said. "The genetic counselor will go over the inheritance with you and let you know more information."

Pre-Lab Questions

1. Look at the genetic screening results from Jayden and her parents' DNA tests. Explain how this evidence supports the claims Ben and Sarah made about the test results?



- Lane 1: Positive Control for Sickle Cell Disease
- Lane 2: Positive Control for Sickle Cell Trait
- Lane 3: Positive Control for Normal Hemoglobin
- Lane 4: Jayden's Sample
- Lane 5: Mr. Smith's Sample
- Lane 6: Mrs. Smith's Sample

2. A person's genotype is a way of noting the two alleles or versions of a gene the individual has inherited. If the allele for the gene for normal hemoglobin is represented as Hemoglobin A (HbA) and the allele for the gene representing the mutated sickle cell hemoglobin is represented as Hemoglobin S (HbS), identify the genotype of Jayden, Mr. Smith and Mrs. Smith. Use the letters A and S. Also identify each person's phenotype, whether they will have Normal Hemoglobin, Sickle Cell Trait, or Sickle Cell Disease.

Jayden's Genotype: _____

Jayden's Phenotype: _____

Mr. Smith's Genotype: _____

Mr. Smith's Phenotype: _____

Mrs. Smith's Genotype: _____

Mrs. Smith's Phenotype: _____

3. Mr. and Mrs. Smith visited the genetic counselor with Jayden to learn more about Sickle Cell Disease and the treatments. They also received information about Health Care Services available to help Jayden monitor her health and manage her condition. They were also concerned about their next child. If you were the genetic counselor, use the Punnett Square below and Mr. and Mrs. Smith's genotypes to predict the probability their next child will have sickle cell disease.

4. Describe what is meant by a newborn screening. Why do you think Sickle Cell Disease was added to the Newborn Screening for all states in 2006? Why was this an important public health decision? What benefits does the newborn screening program have on public health?

Registry and Surveillance System for Hemoglobinopathies (RuSH)

From 2010 to 2012, the National Heart, Lung, and Blood Institute, the National Institutes of Health and the Division of Blood Disorders at the Center for Disease Control developed an interagency state-based monitoring system for two hemoglobinopathies, Sickle Cell Anemia and Thalassemia. Thalassemia is another inherited disorder that affects red blood cells. The red blood cells do not make enough functional hemoglobin and red blood cells do not function properly or last as long. The goal of this collaborative effort was to identify and collect information about individuals with these two inherited conditions. Families like the Smiths participated in the program along with many other health organizations and institutions. The registry would serve as a means to develop an understanding of the patient population for each genetic disorder, the use of healthcare services and outcomes of those services. The data was from 2004 through 2008 and the sources of the data included: newborn screenings, birth and death records, hospital discharge, emergency room, clinical records, and state Medicaid claims. Seven states were involved in this effort. Let's imagine Mr. and Mrs. Smith agreed to participate in the registry in the state of California.

You are a medical geneticist in charge of evaluating the newborn screening (NBS) results at a hospital in California. You have several newborns that need to be tested for a variety of conditions but now Sickle Cell Disease is also routinely part of the NBS program. Alpha thalassemia has been part of the NBS for CA since 1999. You specialize in inherited hemoglobinopathy conditions and you have been assigned to these newborns because of the fact that they are at a higher risk for Sickle Cell Disease or another hemoglobinopathy based on family history.

Review the procedure with your Biotechnology Technicians so your lab can perform the genetic screening for Sickle Cell Disease on the blood samples from these newborns.

MiniOne Visual Instructions for Electrophoresis

Part I: Electrophoresis

Materials

- 1 Minione® Casting System
- 1 MiniOne® Electrophoresis System
- 1 agarose GreenGel™ cup (1.5 %)
- 9 DNA samples
- TBE running buffer (135 mL)
- 1 micropipette (2-20µL)
- 10 pipette tips

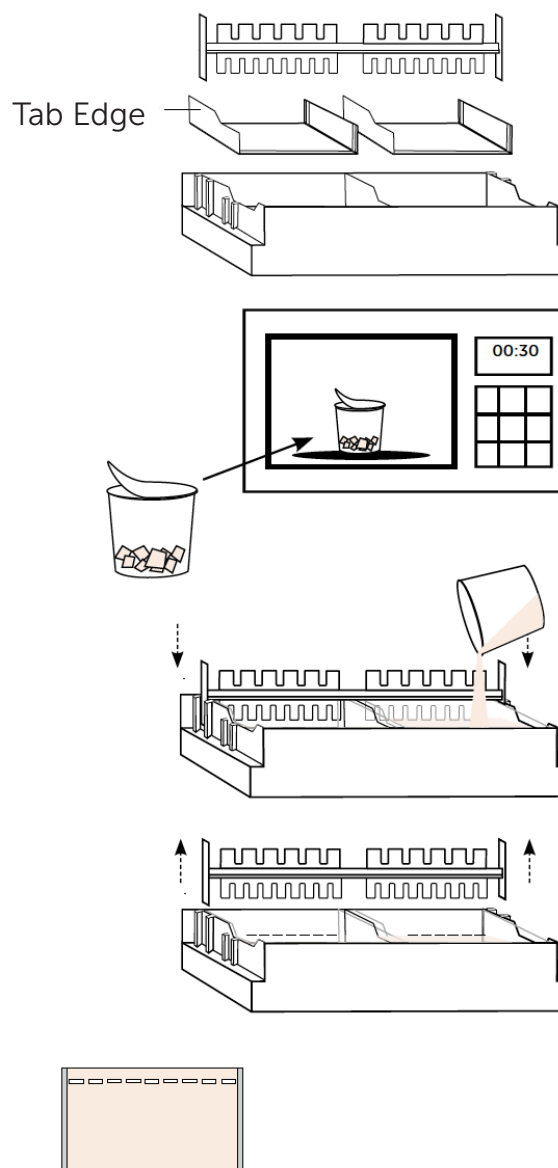
How to Cast a Gel

1. Place the MiniOne® Casting Stand on a level surface and place gel trays in the two cavities. For proper tray orientation place the tab edge of the tray on the left side. Insert the comb into the slots at the top of the casting stand with the 9-well side facing down.
2. **Partially** peel the film off a GreenGel™ cup and microwave for 25-30 seconds. Allow to cool for 15 seconds. DO NOT microwave more than 5 gel cups at a time.
3. One gel cup is for making one agarose gel! Slowly pour the hot agarose solution into a gel tray. Make sure there are no air bubbles in the agarose solution. Let the agarose gel solidify for 10 minutes or until opaque.


DO NOT disturb the gel until time is up.

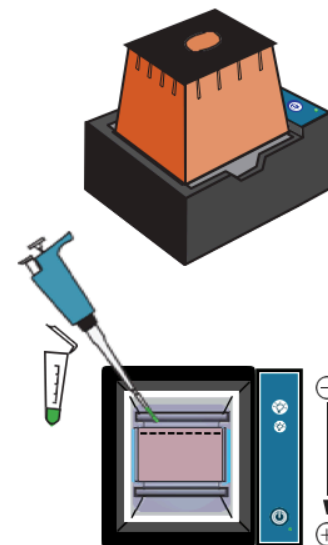
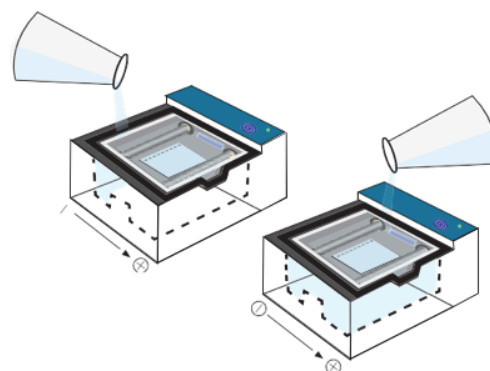
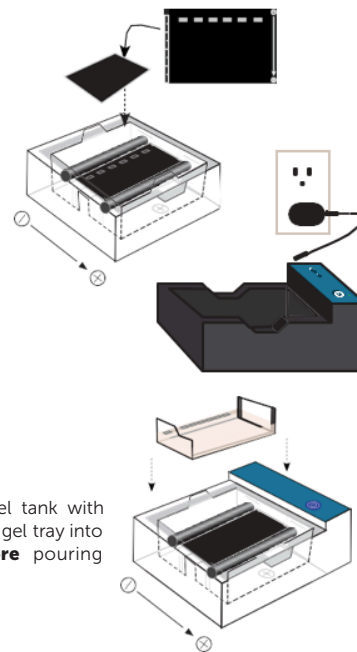
4. Carefully remove comb when gel is ready. Remove gel tray with solidified gel from Casting Stand and wipe off any excess agarose from the bottom of the tray.

Lane #	Sample Name	Volume
1	Positive Control, Sickle Cell Disease (SS)	10 µL
2	Positive Control, Sickle Cell Carrier (AS)	10 µL
3	Positive Control, Normal (AA)	10 µL
4	Camilia	10 µL
5	Eshin	10 µL
6	Juan	10 µL
7	Elaina	10 µL
8	Jamaal (Smith)	10 µL
9	MiniOne Marker	10 µL




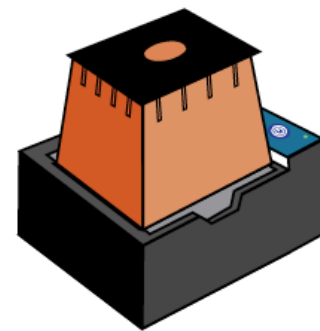
How to Load a Gel

1. Ensure the black viewing platform is in the gel tank. **Make sure the wells are aligned with the marks on the platform on the negative end.**
2. Plug the power supply into the wall and carefully insert the other end into the back of the MiniOne® Carriage.
3. Place the gel tank into the carriage so the carbon electrodes are touching the gold rivets and the tank sits level with the carriage.
4. Place the gel tray with the gel into the gel tank. The gel tank should not have any buffer in it when putting the gel tray with gel into it.
5. Turn the low intensity blue LED on by pressing the  button on the carriage.
6. Measure 135 mL of TBE running buffer and pour into **one side** of the gel tank. Watch the air push out between the gel tray and viewing platform. Once air has been removed from under the gel tray, pour remaining buffer into the **other side of the gel tank**.
7. Place photo hood on the carriage.
8. Press the power button which should now be a solid green light. If **green light is solid**, turn off the unit and proceed to loading gels.
9. Turn the low intensity blue light on by pressing the button on the carriage to help visualize the wells when loading.
10. Load 10 μL per well. Remember to change pipette tips for each sample. **Load your samples according to the order given in the sample chart.**




Run, Visualize and Capture Image

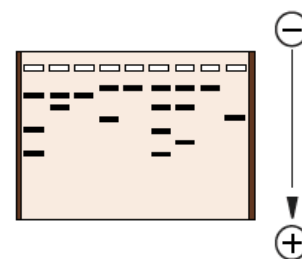
1. Once the gel is loaded, do not move it. Make sure the power supply is plugged in and place the photo hood on the carriage. Turn on the unit by pressing the  button. The green LED next to the button will turn on.



The green power LED will not turn on if:

- The tank is not properly placed inside the carriage. There is no buffer in the tank.
- The buffer is too diluted.
- The photo hood is not on the carriage. There is too little running buffer.
- The power supply is not plugged in. Check by turning on the blue LEDs.
- If the green power LED is blinking, please refer to the troubleshooting steps in the **MiniOne Electrophoresis Instruction Manual**

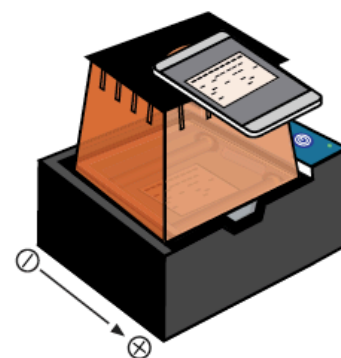
2. Have students periodically check the migration of the bands (~every five minutes).
3. Allow the gel to run **20 minutes** or until DNA separation is sufficient. Keep in mind small DNA samples run faster so it's important to periodically check where your bands are. After your run is complete, turn off the power by pressing the  button. Use the low intensity for viewing during the run. Light will weaken the fluorescent DNA signal.



4. Document your results.

Wipe off the condensation from the inside of the hood with a soft cloth if necessary, then place the hood back on the carriage. **Turn on** the high intensity light. Place your cell phone or camera directly on the photo hood to take a picture of the DNA. **DO NOT** zoom in as this will result in blurry pictures. (The photo hood is already at the optimal focal length for a smart device).

5. Clean up. Follow teacher's instructions on disposal and clean up.












Clean Up

Note: All reagents in this lab can be disposed of as non-hazardous waste.

1. After collecting data and documenting results, remove the photo hood and unplug the power supply from the wall and from the back of the MiniOne® Carriage. Remove the clear running tank from the carriage and remove the gel and tray from the running tank.
2. Pour the used running buffer down the drain or into a waste beaker. Throw the gel away AND SAVE THE GEL TRAYS. Rinse the clear plastic running tank, gel tray, comb, and casting system with DI or distilled water. Allow the tanks to fully air dry before storing.
3. Use a paper towel or Kimwipe™ to gently wipe the gold rivets in the carriage (where the electrodes connect) to ensure all moisture is removed. Wipe up any buffer that may have spilled into the black carriage. Follow any additional directions the instructor gives for clean up and storage.

Part II: Results

What does your gel look like? Record images of the gel in the gel below

1	2	3	4	5	6	7	8	9
								

Lane 1: _____
Lane 2: _____
Lane 3: _____
Lane 4: _____
Lane 5: _____
Lane 6: _____
Lane 7: _____
Lane 8: _____
Lane 9: _____

Post Lab Analysis Questions

1. Make a claim about which of the babies have Sickle Cell Disease.
2. Make a claim about which of the babies have Sickle Cell Trait.
3. If a baby does not have one of the sickle cell alleles, should that child be screened for thalassemia since these families had a history of symptoms related to hemoglobinopathies?
4. Examine the information about the newborns in Table 1 below. Fill in each patient's genotype from your gel electrophoresis genetic test for sickle cell anemia. Make any additional notes based on the data in the last column.

Table 1: Data from Carrier Testing of Parents and Newborn Screening Results

Patient	Ethnicity and Ancestry	Mom's Genotype	Dad's Genotype	Patient's Genotype	Notes (i.e., Claims, probabilities, etc)
Camilia	Hispanic America	AS	AS		
Eshin	Southeast Asian	AA	AA		
Juan	Hispanic America	AS	AS		
Elaina	Greek/ Mediterranean	AS	AS		
Jamaal	African American	AS	AS		

Sickle Cell Disease is more common in individuals of African descent but there are also high incidences in Hispanic populations originating from Central and South America. Other populations affected in higher frequencies include individuals of Middle Eastern, Asian, Indian and Mediterranean descent. Thalassemia occurs most often in individuals of African descent but also occurs with higher frequencies in populations of Mediterranean and Southeast Asian descent. Based on this information, explain why the data in the table makes sense?

- 1. Evolutionary Connection:** Research why the sickle cell mutation occurs more frequently in these populations. Identify any type of selective pressure in the environment that may have caused the mutated allele to persist in any of these populations.
2. How can a registry or a surveillance system help us to better understand these patterns in various populations? Why would that information be beneficial?

Enrichment Activity - Analyzing and Interpreting Data - Years 2010 through 2016

The CDC has published data from the Sickle Cell Data Collection Program from CA and GA. Use the following links to examine the data. Choose one of the states to explore.

- SCDC Program Data for CA:
<https://www.cdc.gov/ncbddd/hemoglobinopathies/scdc-state-data/california.html>
- SCDC Program Data for GA:
<https://www.cdc.gov/ncbddd/hemoglobinopathies/scdc-state-data/georgia.html>

First, try to simply identify and note trends and patterns in the data. Then try to interpret what those trends could indicate. Use what you learn to make two separate claims. Cite the evidence from the data you found and use scientific reasoning to connect the evidence to each claim. You may have to do some research to find the reasoning.

Claim 1:

Evidence 1:

Reasoning 1:

Claim 2:

Evidence 2:

Reasoning 2:

Interdisciplinary Enrichment Activity - Clinical Trials for New Treatments (2021) - Science and Society, Connecting Science to Social Studies through Public Health and Policy

Jayden's little brother, Jason, was also born with Sickle Cell Disease. In 2021, Jayden would be 25 years old and Jason would be 15. In 2021, "scientists at UC San Francisco, UC Berkeley and UCLA [announced they had] received U.S. Food and Drug Administration approval to jointly launch an early phase, first-in-human clinical trial of a CRISPR gene correction therapy in patients with sickle cell disease using the patient's own blood-forming stem cells" (Fernandes, L., 2021). Research CRISPR gene editing. Explain how it works and what it could mean for Jayden or Jason if they happened to be chosen as one of the six adults or three adolescents participating in the four-year study. What implications could this technology have on their health? Are there risks involved? Do the benefits outweigh the risks? How could this study impact public health and policies? How did programs like RuSH potentially influence these developments? How does monitoring and providing surveillance for genetic disorders impact future treatments and healthcare of individuals affected by the disease and society as a whole? What ethical considerations need to be evaluated. Hydroxyurea was approved in 2017 to treat children with SCD but what other treatments are in clinical trials.

Appendix A - What is Gel Electrophoresis?

Gel electrophoresis is a technique used in many areas of science to analyze the components of complex chemical mixtures. Mixtures of DNA, RNA, proteins, or dyes can be separated into their individual components based on molecular size and electrical charge using a separation matrix within an electric field.

The gel used in gel electrophoresis is a tangle of polymers forming a three-dimensional matrix with water-filled pores through which molecules migrate. A higher density of polymers creates smaller pores. Like the holes in a sieve or colander, the size of the pores has to be the appropriate size for the molecules being separated. Gels can be made from different substances depending on the application. One of the most commonly used and effective materials is agarose, a polymer extracted from seaweed. Agarose gels are formed (or cast) by pouring molten (melted) agarose into a tray where it solidifies into the desired shape as it cools. A comb is placed while the agarose is molten and then removed after it solidifies to create wells where the samples are loaded.

After the gel solidifies it is placed in an electrically conductive buffer between parallel positive ((+) anode) and negative ((-) cathode) electrodes.

A voltage is applied between the electrodes, creating a uniform electric field within the gel. Molecules in the wells begin to move under the influence of the electric field: positively charged molecules migrate toward the (-) cathode and negatively charged molecules migrate toward the (+) anode.

The speed of a molecule's movement in an electric field is determined by the strength of its electric charge relative to its molecular weight. This is quantified as the charge to mass ratio. Speed of movement within a gel is also influenced by the size of the molecule relative to the pores in the gel. The polymers in the gel are like an obstacle course: smaller molecules maneuver easily through the pores, traveling faster and farther than large, bulky molecules. However, a large molecule can move faster through a gel than a smaller molecule when the strength of its charge relative to its mass is significantly higher. Shape can also affect how a molecule moves through the gel. Long spaghetti-like molecules will move slower than compact molecules, which slip easily through the pores. Molecules of the same size, shape, and charge will move together and form a distinct band. If multiple types or sizes of molecules are present in the sample, they will separate from each other and each will form a distinct band.

Appendix B - Recommended Reading

https://www.sciencedaily.com/news/health_medicine/sickle_cell_anemia/ Sickle Cell Anemia News

<https://medlineplus.gov/genetics/condition/sickle-cell-disease/#frequency> Medline Plus

<https://www.cdc.gov/ncbddd/sicklecell/data.html#:~:text=SCD%20affects%20approximately%20100%2C000%20Americans,every%2016%2C300%20Hispanic%2DAmerican%20births.> CDC stats

<https://www.hematology.org/education/patients/anemia/sickle-cell-trait> American Society of Hematology

<https://www.acog.org/clinical/clinical-guidance/committee-opinion/articles/2017/03/carrier-screening-for-genetic-conditions> hemoglobinopathies

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4517422/> What is SCD?

<https://www.cdc.gov/ncbddd/hemoglobinopathies/features/keyfinding-state-based.html>

State-Based Monitoring for Selected Hemoglobinopathies

<https://www.cdc.gov/ncbddd/hemoglobinopathies/scdc.html> SCDC Sickle Cell Data Collection

<https://www.cdc.gov/ncbddd/hemoglobinopathies/scdc-factsheet.html> About SCD/SCDC

<https://www.cdc.gov/ncbddd/hemoglobinopathies/scdc-faq.html> CDC FAQs on SCDC

<https://www.cdc.gov/ncbddd/hemoglobinopathies/scdc-data.html> Data from CA and GA - Excellent for Extension Activity for students to go to this site and Identify and Interpret the data.

<https://www.cdc.gov/ncbddd/hemoglobinopathies/scdc-state-data/california.html>

<https://www.cdc.gov/ncbddd/hemoglobinopathies/scdc-state-data/georgia.html>

https://nap.nationalacademies.org/resource/25632/Sickle%20Cell%20Highlights_2020.pdf Social Studies Connection - Sept 2020 Consensus Study Report Highlights from national Academies - Addressing Sickle Cell Disease (Strategic Plan)

<https://www.nationalacademies.org/our-work/addressing-sickle-cell-disease-a-strategic-plan-and-blueprint-for-action>

<https://www.cdc.gov/ncbddd/hemoglobinopathies/data-reports/2018-summer/index.html> SCDC Report (Links to other information as well)

<https://www.cdc.gov/media/releases/2019/p0925-cdc-awards-funds-sickle-cell.html>

Press Release about Funding in 9 States

<https://www.cdc.gov/ncbddd/hemoglobinopathies/newborn-screening-genetics.html> NBS

<https://www.mdpi.com/2409-515X/5/2/20/htm> Sickle Cell Disease - Genetics, Pathophysiology, Clinical Presentation and Treatment

<https://www.cdc.gov/ncbddd/sicklecell/facts.html> CDC What is Sickle Cell Disease

<https://www.ucsf.edu/news/2021/03/420137/uc-consortium-launches-first-clinical-trial-using-crispr-correct-gene-defect> CRISPR Clinical Trial

<https://www.cdc.gov/ncbddd/hemoglobinopathies/surveillance-history.html> CDC Surveillance History

<https://www.acog.org/womens-health/faqs/carrier-screening-for-hemoglobinopathies> Carrier Screening

<https://www.medscape.com/answers/205926-15409/what-are-the-typical-baseline-blood-study-abnormalities-in-patients-with-sickle-cell-disease-scd> Hematocrit Levels for SCD

<https://www.redcrossblood.org/donate-blood/dlp/hematocrit.html#:~:text=Hematocrit%20is%20the%20percentage%20of,is%2036%25%20to%2048%25>. Normal Hematocrit Levels

<https://www.hematology.org/-/media/Hematology/Files/Education/Hydroxyurea-Booklet.pdf> Hydroxyurea and Sickle Cell

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4755934/> NBS for Hemoglobinopathies in CA

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