Structure and Function of Molecular Genetics (Part 1 of 3) --Sickle Cell Disease

This 5E model for instruction can connect the concepts of mutations to gene therapy and is connected to bioethics in medicine.

Student Science Performance

Grade: 9-12 Biology	**Title:**
Topic: Sickle Cell Disease	The Way We Were

Performance Expectations for GSE:

SB2. Obtain, evaluate, and communicate information to analyze how genetic information is expressed in cells.

a. Construct an explanation of how the structures of DNA and RNA lead to the expression of information within the cell via the processes of replication, transcription, and translation.
b. Construct an argument based on evidence to support the claim that inheritable genetic variations may result from:
   - new genetic combinations through meiosis (crossing over, nondisjunction);
   - non-lethal errors occurring during replication (insertions, deletions, substitutions); and/or
   - heritable mutations caused by environmental factors (radiation, chemicals, and viruses).
c. Ask questions to gather and communicate information about the use and ethical considerations of biotechnology in forensics, medicine, and agriculture.
   (*Clarification statement:* The element is intended to include advancements in technology relating to economics and society such as advancements may include Genetically Modified Organisms.)

SB6. Obtain, evaluate, and communicate information related to the theory of evolution.

d. Develop and use mathematical models to support explanations of how undirected genetic changes in natural selection and genetic drift have led to changes in populations of organisms (microevolution). *(Clarification statement:* This element is intended to focus on basic statistical and graphic analysis. Hardy Weinberg would be an optional application to address this element.)

Performance Expectations for Instruction:

Group Performance:

1. Gather evidence to construct an explanation of the causes of mutations and effects in gene products.
2. Make a model of how mutation in DNA can lead to sickle cell disease and how gene editing can correct such gene defects.

Individual Performance:

1. Construct an argument for how gene editing can repair faulty genes.

Group Discussion:

1. Student groups ask questions regarding the ethical nature of gene therapy.
2. Student groups debate the ethical nature of gene editing and gene therapy to reverse disease.

Additional notes on student supports

Materials

Materials needed per group:	Materials needed for class size of 30:
Computer	gene editing role play manipulatives

Students will continuously be obtaining, evaluating, and communicating information. This is not a linear process. Students should be communicating through writing and discussions to allow for formative assessment. This benefits the teacher, student, and whole group to guide instruction to clarify misconceptions or extend content.

Engaging Learners	**Phenomenon** Sickle cell disease is a genetic disease caused by mutations that may be reversed with gene therapy.
	Obtaining Students obtain gene editing background information by watching short videos on gene editing with CRISPR Cas 9. Video from the Mayo Clinic: "CRISPR Explained" Video from UC Berkeley: "Gene editing with CRISPR Cas 9" Students will then obtain information on the possible cure of sickle cell disease by watching this video: Video from Stanford Children's Health: "Testing Gene Editing for Sickle Cell Disease"
	Evaluating Students, in groups, gather evidence to construct an explanation of the causes of mutations, and effects on gene/protein production. *Teacher Notes: Mutations that should be highlighted include insertions, deletions, and substitutions. Students will use resources found online, such as this article from Your Genome to construct their explanation.* Questions to initiate class discussion: Q: What types of environmental factors can cause a mutation? Q: Can mutations be inherited? Q: What would a mutation in a DNA sequence do to the resulting mRNA sequence? Q: If the original mRNA sequence is altered, what will happen to the resulting protein? Q: How does a change in a DNA sequence lead to a change in the traits of the organism? *Additional notes on topic, focus, and phenomena.*
	Communicating In groups, students make a model of how a mutation in DNA can lead to a change in a protein. Students should share their models with the class. This is a good opportunity for students to share the different types of mutations (insertion, deletion, substitution) and discuss what a frame shift means.

Exploring Revising Model	*Obtaining* Students gather evidence from their work with mutations and additional research (such as *this Berkeley Case Study and this National Library of Medicine article)* to make a model of how mutation in DNA can lead to sickle cell disease. This handout can be used to apply knowledge of protein synthesis to mutations. *Teacher Notes: Information on Sickle cell can be found at OpenStax: Sickle Cell. Students should be given 2 base sequences, 1 for the normal hemoglobin gene and a second mutated strand for sickle cell. Students should create a model that shows a single base substitution as the cause for the sickle cell mutation. In this part of the lesson, students should be able to use prior knowledge from the information they find on mutations to determine the type of mutation that causes sickle cell. Normal gene and sickle cell mutation can be found at the following link: Normal and Sickle Cell Gene Sequence* Students should be able to explain the phenomenon using the following concepts: ● Sickle cell disease is caused by a single point mutation in the DNA sequence. ● Because the mutated DNA sequence undergoes DNA replication, exact copies of the mutated sequence are in all somatic cells produces through mitosis. ● The mutated DNA is transcribed and translated into a misshapen protein that is not able to be used effectively.
	Evaluating Use A Model: Students use their model to explain how specific errors in the system of protein synthesis can lead to errors in protein structure causing sickle cell disease. *Teacher Notes: Models may be drawn on chart paper and hung around the room and presented to the group for discussion.* Questions to initiate class discussion: Q: What type of mutation causes sickle cell disease? Explain how the DNA has changed. Q: What is a frameshift? Did the mutation cause a frameshift? Q: How are the amino acid sequences different? Q: How might this mutation affect the function of the HBB protein?
Explaining Finalizing Model	*Obtaining* Students obtain information by role playing using manipulatives to make a model for how gene editing can affect the structure of genes to correct the protein product. *Teacher Notes: There are multiple sources online that include background information and possible gene editing activities. Gene editing manipulatives should include a portion of the normal hemoglobin gene sequence and a second sequence that codes for sickle cell. Students will form two lines; one line being the normal gene, and the second line the sickle cell gene. Each student in the line represents a nucleotide and is given the appropriate A, T, G, or C according to the sequence. Additional student roles needed include one student to play the role of CRISPR Cas 9 and the replacement sequence.*

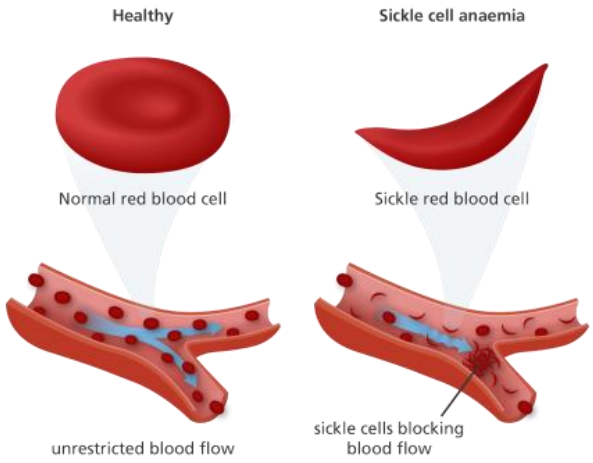
	Students role play CRISPR Cas 9 cutting out the defective gene in order to replace with the correct sequence.
	Evaluating Individually, students construct a written argument for how gene editing can repair the structure of faulty genes to restore proper function. *Teacher Notes: Students should be able to explain the phenomenon using the following concepts:* ● *Using biotechnology, scientists are attempting to reverse sickle cell disease with gene therapy.* ● *Gene therapy can replace a faulty gene with a good copy of the gene allowing for normal function to exist.*
	Communicating Students share their written arguments as a basis for class discussion. ***Formative Assessment of Student Learning*** Students may use a rubric to peer assess their arguments or teacher and students may assess the argumentation using a rubric. Feedback is an essential part of this stage of the process.
Elaborating Applying Model to Solve a Problems	**Phenomenon** Adenosine deaminase (ADA) deficiency is a disorder that has also been treated by gene therapy.
	Obtaining Students ask questions regarding the ethical nature of gene therapy *Teacher Notes: Additional background on gene therapy and the unintended side effects can be found at OpenStax: Gene Therapy and The American Society of Gene and Cell Therapy.* Questions: Just because we can, should we? What are the benefits and limitations of using this science?
	Evaluating Students engage in argumentation from evidence regarding the ethical nature of gene therapy
	Communicating Students carry out a debate on the ethical use of gene therapy.
Evaluation	***Assessment of Student Learning***
	Students carry out a debate on the ethical use of gene therapy which may be scored using a rubric.
SEP, CCC, DCI	**Science Essentials**
Science and Engineering Practices	● Developing and using models ● Engaging in argument from evidence ● Constructing explanations ● Asking questions and defining problems

Crosscutting Concepts	• Structure and Function • Systems and System Models • Cause and Effect
Disciplinary Core Ideas	From ***A Framework for K-12 Science Education:*** LS1.A: Structure and Function LS1.B: Growth and Development of Organisms LS3.A: Inheritance of Traits

Name: _____ Date: _____ Period: _____

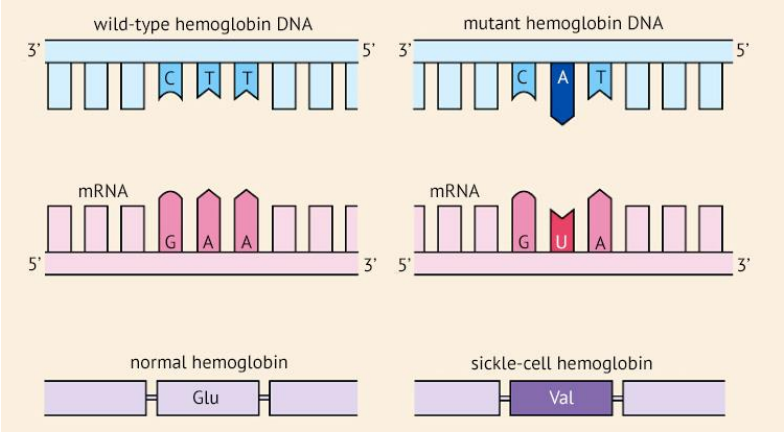
Sickle Cell Disease: Causes & Effects

Sickle Cell Disease is a group of heritable blood disorders that causes a problem with the hemoglobin inside red blood cells. Hemoglobin is the iron-containing protein in red blood cells that carries oxygen to cells throughout the body. In sickle cell, hemoglobin molecules clump together and can alter the shape of red blood cells. The altered shape of the cells makes it harder for them to easily roll through blood vessels and can cause blockages. If blood flow is reduced because of a blockage, red blood cells can deliver less oxygen to the body.



Affected individuals also have a shortage of red blood cells (anemia), which can cause pale skin, weakness, fatigue, infection, pain, and more serious complications. Sickle cell disease is a common blood disorder worldwide, with thousands of affected infants are born each year. Sickle cell occurs most frequently in people of African descent.

Sickle cell disease is caused by a mutation in the HBB gene, which is the gene that makes the hemoglobin inside red blood cells. In a normal (wild type) cell, the HBB gene has a DNA sequence that reads CTT. This leads to mRNA with the sequence GAA, and Glutamic Acid as the resulting amino acid. In people with sickle cell disease, a mutation substitutes the normal T (thymine) in DNA with an A (adenine). This mutated DNA sequences leads to mRNA with the sequence GUA, and Valine as the resulting amino acid.



The questions on the following page will ask you to apply your knowledge of the genetic code and protein synthesis to analyze some of the other mutations responsible for sickle cell and red blood cell disorders.

Apply What You Learned:

1. For the pair of normal and mutated DNA sequences given below, transcribe the corresponding mRNA sequence and translate the correct amino acid sequence.

Normal DNA Sequence 1: gga ctc ctc ttc aga

mRNA:

Amino Acids:

Mutated DNA Sequence 1: gga **a**tc ctc ttc aga

mRNA:

Amino Acids:

2. What type of mutation is this? Explain how the DNA has changed.

3. What is a frameshift? Did the mutation cause a frameshift?

4. How are the amino acid sequences different?

5. How might this mutation affect the function of protein coded by the original DNA (no change in the protein, reduced function, no protein formed, etc.)?

The Big Question: How does a change in a DNA sequence lead to a change in the traits of the organism? Answer this question in paragraph form.

Apply What You Learned:

1. For the pair of normal and mutated DNA sequences given below, transcribe the corresponding mRNA sequence and translate the correct amino acid sequence.

Normal DNA Sequence 2: cgg cgg acc cca ttc

mRNA:

Amino Acids:

Mutated DNA Sequence 2: cgg cgg **c**cc cca ttc

mRNA:

Amino Acids:

2. What type of mutation is this? Explain how the DNA has changed.

3. What is a frameshift? Did the mutation cause a frameshift?

4. How are the amino acid sequences different?

5. How might this mutation affect the function of protein coded by the original DNA (no change in the protein, reduced function, no protein formed, etc.)?

The Big Question: How does a change in a DNA sequence lead to a change in the traits of the organism? Answer this question in paragraph form.

Apply What You Learned:

1. For the pair of normal and mutated DNA sequences given below, transcribe the corresponding mRNA sequence and translate the correct amino acid sequence.

Normal DNA Sequence 3: cgg gac acc ccg ttc cac

mRNA:

Amino Acids:

Mutated DNA Sequence 3: cgg gca ccc cgt tcc ac

mRNA:

Amino Acids:

2. What type of mutation is this? Explain how the DNA has changed.

3. What is a frameshift? Did the mutation cause a frameshift?

4. How are the amino acid sequences different?

5. How might this mutation affect the function of protein coded by the original DNA (no change in the protein, reduced function, no protein formed, etc.)?

The Big Question: How does a change in a DNA sequence lead to a change in the traits of the organism? Answer this question in paragraph form.

Apply What You Learned:

1. For the pair of normal and mutated DNA sequences given below, transcribe the corresponding mRNA sequence and translate the correct amino acid sequence.

Normal DNA Sequence 4: cgg gac acc ccg ttc

mRNA:

Amino Acids:

Mutated DNA Sequence 4: cgg **c**ga cac ccc gtt c

mRNA:

Amino Acids:

2. What type of mutation is this? Explain how the DNA has changed.

3. What is a frameshift? Did the mutation cause a frameshift?

4. How are the amino acid sequences different?

5. How might this mutation affect the function of protein coded by the original DNA (no change in the protein, reduced function, no protein formed, etc.)?

The Big Question: How does a change in a DNA sequence lead to a change in the traits of the organism? Answer this question in paragraph form.

Apply What You Learned:

1. For the pair of normal and mutated DNA sequences given below, transcribe the corresponding mRNA sequence and translate the correct amino acid sequence.

Normal DNA Sequence 5: ctc cgg gac ctc tcc

mRNA:

Amino Acids:

Mutated DNA Sequence 5: ctc cgg gac c**t**t tcc

mRNA:

Amino Acids:

2. What type of mutation is this? Explain how the DNA has changed.

3. What is a frameshift? Did the mutation cause a frameshift?

4. How are the amino acid sequences different?

5. How might this mutation affect the function of protein coded by the original DNA (no change in the protein, reduced function, no protein formed, etc.)?

The Big Question: How does a change in a DNA sequence lead to a change in the traits of the organism? Answer this question in paragraph form.

Return to Instructional Segment

Structure & Function of Molecular Genetics GSE: **SB1a, SB1b, SB1c, SB2a, SB2b, SB2c, SB3c, SB4c, SB6a, SB6c**			
Anchoring Phenomenon: Sickle cell disease is a genetic mutation that may be reversed with gene therapy.			
Topic	**Focus**	**Lesson Phenomenon**	**GSE/Notes/Language**
Asexual Reproduction	Process of asexual reproduction seen in various organisms; include advantages and disadvantages that will be revisited in comparison with sexual reproduction.	**Biotechnology Link:** Bacteria are used in the production of insulin they can reproduce quickly through binary fission. Sea stars and salamanders can regrow lost limbs. Marine iguanas on the Galapagos Islands may be a result of parthenogenesis.	SB1b/SB2c/SB3c Reviewing the Cell Theory may be useful in connecting with instructional segments in **Patterns in Living Systems** units. Connect "All living organisms are composed of cells that are the basic unit of structure and function" with "All cells arise from preexisting cells". Marine iguanas are a great connection to revisit when discussing advantages and disadvantages of sexual reproduction (and connecting them back to asexual reproduction) in **Patterns of Heredity & Selection** instructional segment.
Mitosis & the Cell Cycle	Compare and contrast binary fission and mitosis; overview the phases of the cell cycle (G0, G1, S, G2); emphasize the phases of mitosis and chromosome movement; a parent diploid cell divides into two genetically identical diploid daughter cells.	Humans lose approximately one million skin cells daily. Brain MRIs show the loss of brain tissue in CTE and Alzheimer's patients.	SB1b Segue from asexual reproduction seen in other organisms to asexual reproduction seen in humans. Mental Image: Corded telephones are coiled to prevent tangles and allows for condensed storage. (DNA condenses into chromosomes.)
Cancer and DNA Mutations	Emphasize that cancer is a result of	The HPV vaccine is recommended for both	SB2b/SB1b/SB3c/SB4c Make connections between cancerous

	uncontrolled mitosis that can arise from damaged DNA (inherited or from environmental factors).	sexes to help reduce the number of cancer cases. X-ray and UV radiation can cause cancer. Doctors use family medical histories of cancer when assessing patients.	cells with damaged DNA reproduce asexually via mitosis; these cancerous cells will produce genetically identical cancerous cells which can lead to the development of a tumor. Use the HPV phenomenon to review viral structure and brief overview of replication. Preview--Caused by a mutation in DNA that is copied during the S phase of Cell Cycle
Structure of DNA and Nucleotides	Nucleic acids are macromolecules formed from nucleotides; emphasize structure of nucleotide and connect to the structure of DNA.	The Human Genome Project mapped out the complete sequence for each chromosome.	SB1c/SB2a Practice complementary base pairing to prepare for protein synthesis. Emphasize hydrogen bonding to prepare for DNA replication. Connect nitrogenous bases to the nitrogen cycle with an emphasis on bacteria.
DNA Replication	Emphasize replication is a semi-conservative process needed to make an identical copy for asexual reproduction.	**Biotechnology Link:** The DNA segment that codes for Insulin are inserted into bacteria for mass production.	SB2a Preview the function of enzyme (speed up reaction) when discussing enzymes necessary for DNA replication: DNA helicase, DNA polymerase, and DNA ligase.
Protein Synthesis	Translation: DNA to RNA Emphasize RNA structure and the process of transcription; compare between DNA and RNA	The Human Genome Project mapped out the complete sequence for each chromosome. **Biotechnology Link:**	SB2a/SB2c Use the genetic code to analyze a DNA sequence. It may be beneficial to show students different examples of the code. (table/wheel)

	structure while noting both are nucleic acids composed of many nucleotides. Transcription: RNA to protein Emphasize that a codon codes for one amino acid; these amino acids are the monomers of proteins.	The DNA segment that codes for Insulin are inserted into bacteria for mass production. **Biotechnology Link:** Bt-corn is now able to ward off pests because of the insertion of a gene from *Bacillus thuringiensis.* Viruses cannot reproduce without infecting a host cell.	**Biotechnology Link:** Relate the medical and agricultural uses of DNA back to evolution with increasing fitness and/or combating resistance. Extend with macromolecule connection: Nucleic acids are composed of nucleotides that are genetic instructions, directing the production of an amino acid sequence that composes proteins. The connection between living organisms and viruses can be enhanced here. Viruses are composed of nucleic acid and a protein capsid. However, they lack ribosomes to produce the protein capsid. They are unable to produce the necessary proteins by themselves, so they must inject their nucleic acid into a host cell for protein synthesis to occur.
Effects of Gene Mutations	Effect of point and frameshift gene mutations (insertion, deletion, substitution) on the creation of proteins	Sickle cell disease is a point mutation that affects a red blood cell's shape and ability to carry oxygen. **Biotechnology Link:** Sickle cell disease may be reversed using gene therapy.	SB2a/SB2b/SB2c/SB6a/SB6c Make connections between these DNA mutations with natural selection arising from random genetic mutations.
Biotechnology	Enzymes are used to cut DNA at specific points into fragments that are used to create a DNA fingerprint	Investigators can use crime scene DNA evidence to determine suspects.	SB2c Compare DNA fingerprints from a variety of scenarios: crime scene, paternity, etc.

	through gel electrophoresis.	DNA is used in determining paternity and maternity.	Discussions on why DNA fingerprints and physical appearance of offspring are different from parents and non-identical siblings may be beneficial in connecting the instructional segment, **Patterns in Heredity & Selection**. Emphasizing that sexual reproduction allowed the passage of mutated DNA for sickle cell and lactose tolerance to pass from parent to offspring may also be beneficial in the connection.
Biotechnology Connections	Several examples of genetic modification and genetic engineering may be addressed throughout this unit. Involve students in discussions on the scientific process and the advantages and disadvantages in each example. Discuss the logistics as well as impact on society, humans, ecosystems, and evolution/heredity. Preview for Patterns in Heredity & Selection by discussing how inserted genes pass from parent to offspring.		
Anchoring Phenomenon: Sickle cell disease is a genetic mutation that may be reversed with gene therapy. Students will explain the phenomenon using the following concepts: ● Sickle cell disease is caused by a single point mutation in the DNA sequence. ● Because the mutated DNA sequence undergoes DNA replication, exact copies of the mutated sequence are in all somatic cells produces through mitosis. ● The mutated DNA is transcribed and translated into a misshapen protein that is not able to be used effectively. ● Using biotechnology, scientists are attempting to reverse sickle cell disease with gene therapy.			

Return to Instructional Segment

Additional Supports for struggling learners:

The following supports are suggestions for this lesson and are not the only options to support students in the classroom. These supports target students that struggle with science material, this lesson or a previous lesson. These are generalized supports and do not take the place of IEP accommodations as required by each student's Individualized Education Program.

General supports for the following categories:

Reading:	Writing:	Math:
1. Provide reading support by reading aloud or doing partner reads 2. Have the teacher model what they are thinking when reading the text 3. Annotate the text with students so that they may refer to it as they work through the lab	1. The teacher can provide a sentence starter for the students. 2. The teacher can give students an audience to write to (i.e. Write a letter to your sibling explaining this topic). 3. The teacher can provide constructive feedback during the writing process to help students understand the expectations.	1. The students may need assistance from the teacher at identifying the initial patterns. The teacher can use guiding questions to get the students started down the path of identifying patters.

Supports for this specific lesson if needed:

Performance expectations for instruction:

Group performance*:*

1. Teachers should be intentional in grouping students to ensure that students get the most out of the lesson. Data driven grouping based on a prior assessment is best practice.
2. Students may require additional time to gather information and create models.
3. This lesson has groups of students explaining multiple topics that relate to sickle cell anemia. Explaining multiple topics may require additional processing time for students. The teacher should evaluate the lesson and deliver it in chunks that are understandable for the student population in the class.

Individual performance*:*

1. Provide choice for creating an argument such as in writing, verbally or drawing a picture.

Engaging Learners:

Obtaining

Evaluating and Communicating

1. The students may have questions after the video. The teacher should create a list of student questions and help the students determine which questions should be answered during this lesson. This will help students narrow their research topics and lessen time wasting.
2. The teacher should have some printed articles or websites that contain the information needed for the students that struggle to narrow the focus of their research.
3. The teacher should provide the questions that will be included in the class discussion to struggling learners in advance. Many struggling learners need additional processing time and giving questions in advance will increase the chances of struggling learners participating in the discussion.
4. Students may need additional time to construct their model.

Exploring:

1. During the research phase, the students may need some help focusing on what is important.
2. The student should have options to express their understanding of the phenomenon. These choices could include drawing a picture, creating a storyboard or cartoon, or verbally explaining their understanding.
3. The teacher should provide the questions that will be included in the class discussion to struggling learners in advance. Many struggling learners need additional processing time and giving questions in advance will increase the chances of struggling learners participating in the discussion.

Explaining:

1. The role playing may seem abstract to some students. The teacher should have a good formative assessment after this activity to support students that need additional help.
2. Students may struggle with writing a scientific argument. Some choice should be provided to students as to how they format their argument. Options could include writing the argument, creating a cartoon or story board, drawing a picture or verbally sharing their argument.
3. The teacher should provide a rubric for self-assessment of the student's scientific argument prior to asking to share with peers. This will cut down on the students feeling embarrassed to share because they have had the chance to evaluate their work.
4. The teacher can then provide a rubric for peer review as well.

Elaborating: 1. Some students may need to understand the definition of ethics. The teacher should share both the definition and some scenarios that give the students more understanding of what ethics are and how they might apply to gene therapy. 2. The students may need some assistance in determining what questions are important when evaluating the ethics behind a topic.
Evaluating: 1. The teacher should have a structured format for the debate and provide students with opportunities to express their knowledge in other ways if the students desire. Provide the students with an opportunity to support or refute an argument on paper or verbally, as needed, for students that are not ready to participate in a class debate.

Return to Instructional Segment