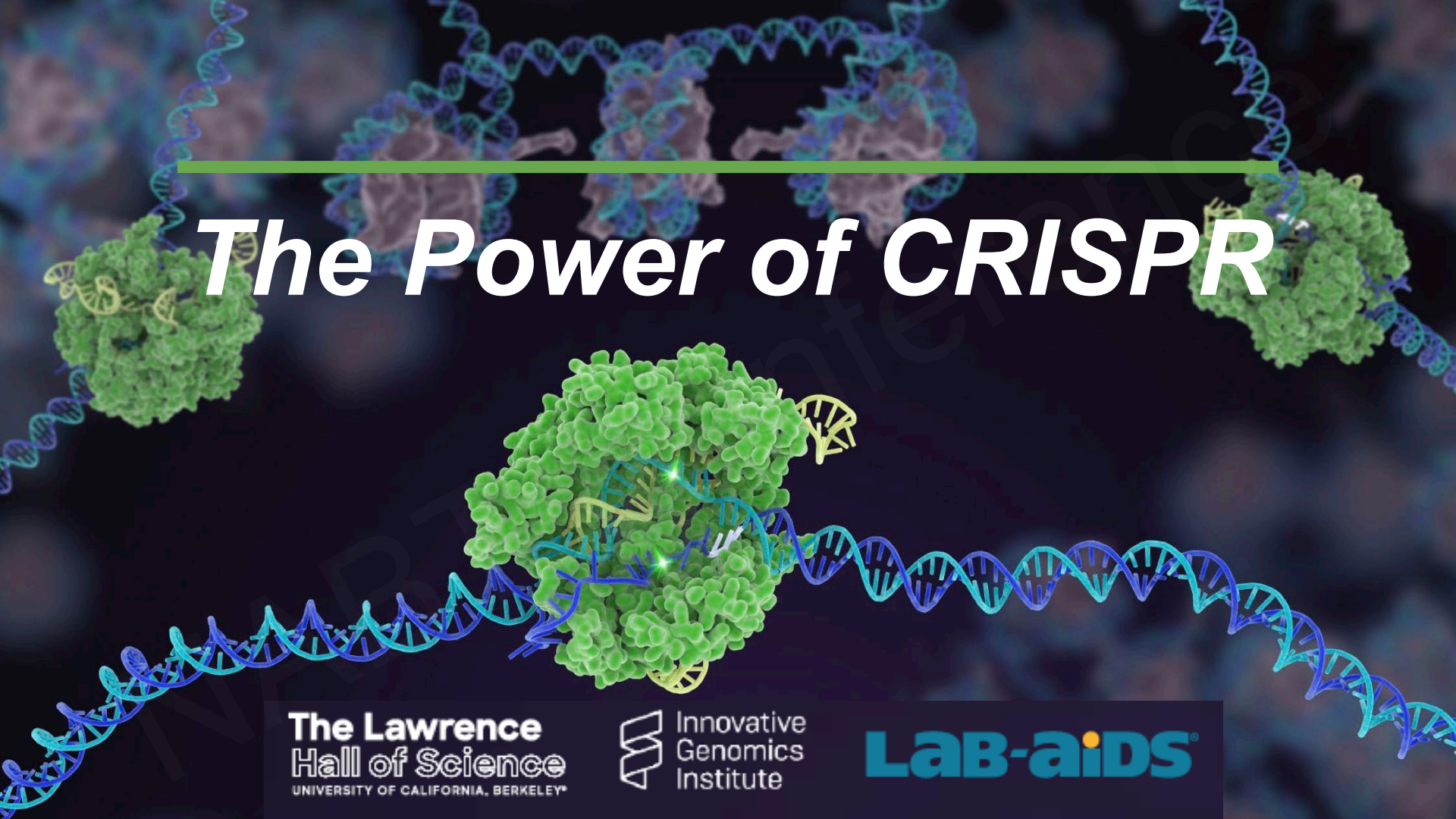
The Power of CRISPR

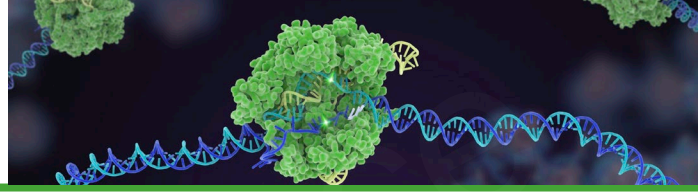


The Lawrence Hall of Science
UNIVERSITY OF CALIFORNIA, BERKELEY

Innovative Genomics Institute

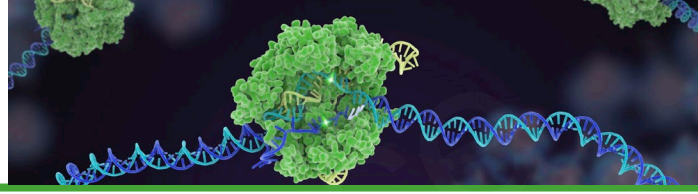
LaB-aiDS

Workshop Goals



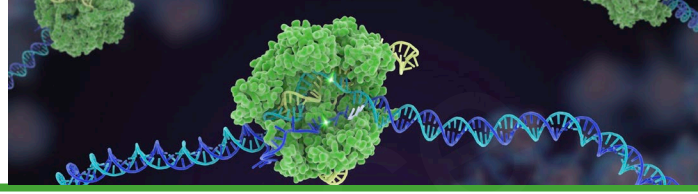
- Gain familiarity with the *Power of CRISPR* unit
- Understand how students construct their understanding of the mechanism of the CRISPR-Cas9 system and how it it can be incorporated into high school life science content.
- Gain interest and excitement in incorporating cutting edge research and current issues into your classrooms.

Agenda

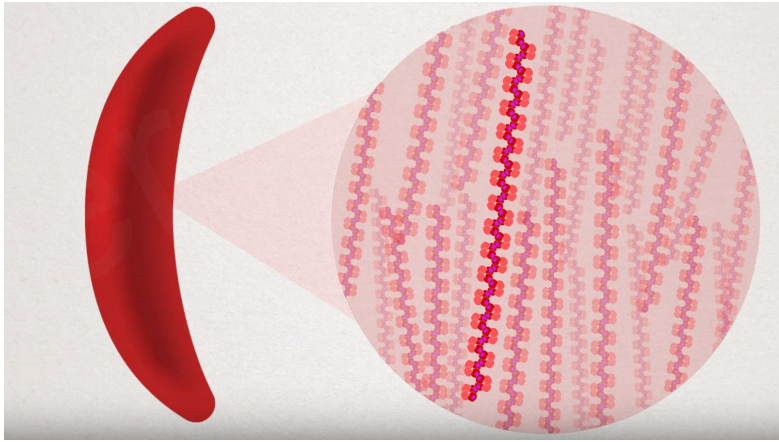


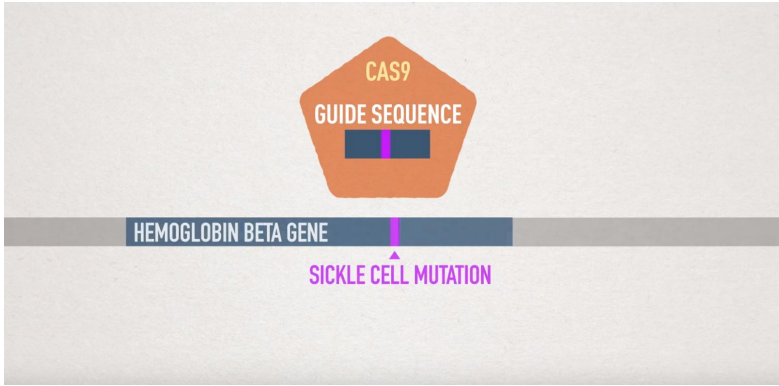
- Introduction
- Overview
- Activity Highlights
  - Hands-on model
  - Laboratory Experiment
  - Articles and Ethics
- Closing

Unit Overview

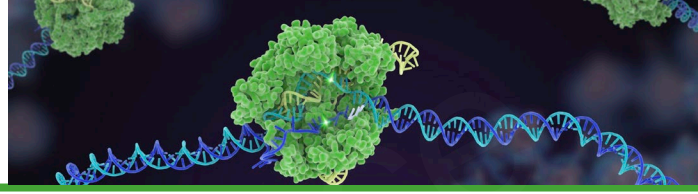


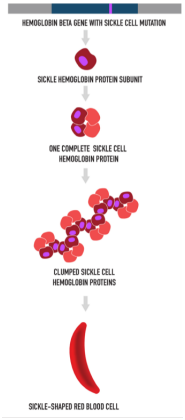
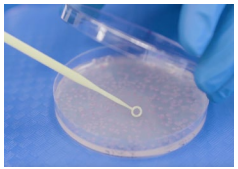
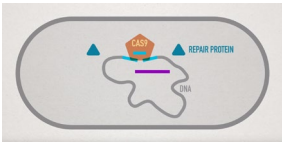
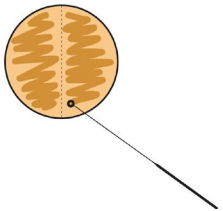
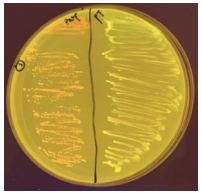
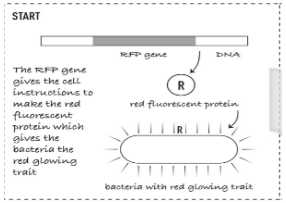
- Students learn about how CRISPR works in the context of using it to treat sickle cell disease, a genetic blood disorder.
- Main Learning Goals:
  - Genes → Proteins → Traits
  - CRISPR is a method of gene editing that allows scientists to insert, delete, or change sections of DNA in order to change an organism's traits.
- NGSS PEs HS-LS1-1 (DNA → Proteins) and HS-ETS1-1 (addressing challenges)



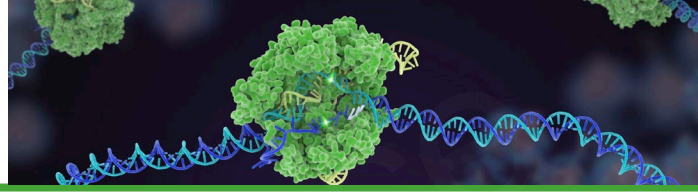


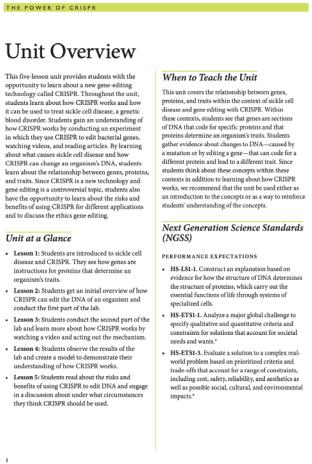
6 Lesson Unit



Lesson 1	Lesson 2	Lesson 3	Lesson 4	Lesson 5	Lesson 6
Intro to CRISPR and Sickle Cell	Lab Part 1 & CRISPR Overview	Lab Part 2 & CRISPR Details	Lab Part 3 & Acting Out CRISPR	Lab Results & Modeling Understanding	Ethics of CRISPR
		 		 	

What comes with the unit?





THE POWER OF CRISPR

Unit Overview

This five-lesson unit provides students with the opportunity to learn about a new gene-editing technology called CRISPR. Throughout the unit, students learn about how CRISPR works and how it can be used to treat sickle cell disease, a genetic blood disorder. Students gain an understanding of how CRISPR works by conducting an experiment in which they use CRISPR to edit bacterial genes, watching videos, and reading articles. By learning about what causes sickle cell disease and how CRISPR can change an organism's DNA, students learn about the relationship between genes, proteins, and traits. Since CRISPR is a new technology and gene-editing is a controversial topic, students also have the opportunity to learn about the risks and benefits of using CRISPR for different applications and to discuss the ethics gene editing.

Unit at a Glance

- **Lesson 1:** Students are introduced to sickle cell disease and CRISPR. They see how genes are instructions for proteins that determine an organism's traits.
- **Lesson 2:** Students get an initial overview of how CRISPR can edit the DNA of an organism and conduct the first part of the lab.
- **Lesson 3:** Students conduct the second part of the lab and learn more about how CRISPR works by watching a video and acting out the mechanism.
- **Lesson 4:** Students observe the results of the lab and create a model to demonstrate their understanding of how CRISPR works.
- **Lesson 5:** Students read about the risks and benefits of using CRISPR to edit DNA and engage in a discussion about under what circumstances they think CRISPR should be used.

When to Teach the Unit

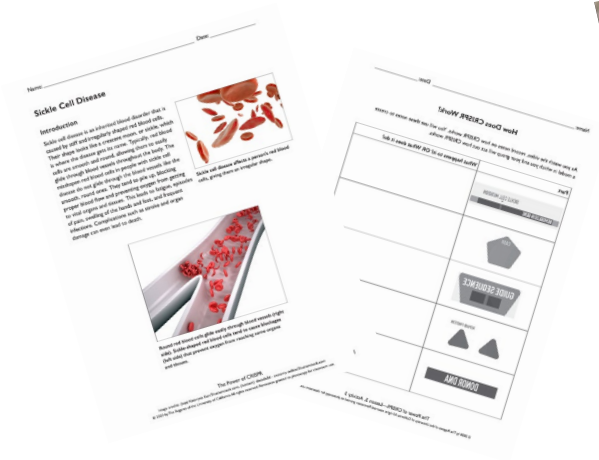
This unit covers the relationship between genes, proteins, and traits within the context of sickle cell disease and gene editing with CRISPR. Within these contents, students see that genes are sections of DNA that code for specific proteins and that proteins determine an organism's traits. Students gather evidence about changes to DNA—caused by a mutation or by editing a gene—that can code for a different protein and lead to a different trait. Since students think about these concepts within these contexts in addition to learning about how CRISPR works, we recommend that the unit be used either as an introduction to the concepts or as a way to reinforce students' understanding of the concepts.

Next Generation Science Standards (NGSS)

PERFORMANCE EXPECTATIONS

- **HS-LS1-1.** Construct an explanation based on evidence for how the structure of DNA determines the structure of proteins, which carry out the essential functions of life through systems of specialized cells.
- **HS-ETS1-1.** Analyze a major global challenge to specify qualitative and quantitative criteria and constraints for solutions that account for societal needs and wants.*
- **HS-ETS1-3.** Evaluate a solution to a complex real-world problem based on prioritized criteria and trade-offs that account for a range of constraints, including cost, safety, reliability, and aesthetics as well as possible social, cultural, and environmental impacts.*

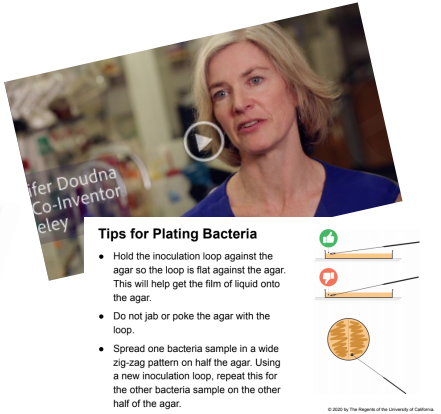
Teacher's Guide



Sickle Cell Disease

Introduction

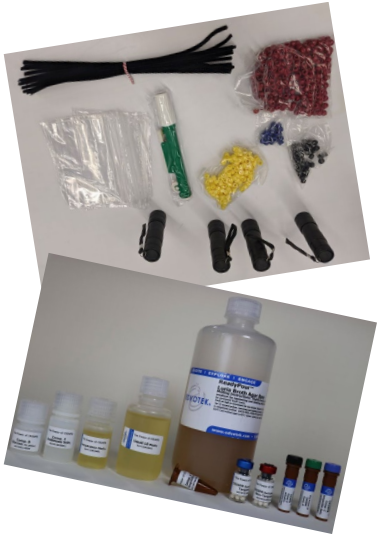
Student Facing Materials



Tips for Plating Bacteria

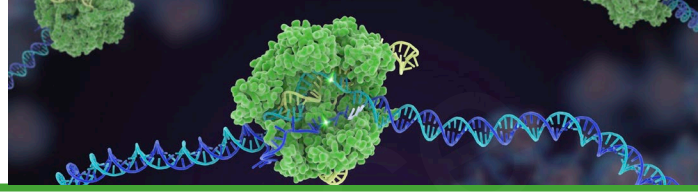
- Hold the inoculation loop against the agar so the loop is flat against the agar. This will help get the film of liquid onto the agar.
- Do not jab or poke the agar with the loop.
- Spread one bacteria sample in a wide zig-zag pattern on half the agar. Using a new inoculation loop, repeat this for the other bacteria sample on the other half of the agar.

Videos and Slides



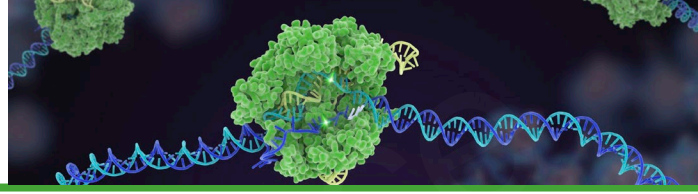
Hands-On and Lab Materials

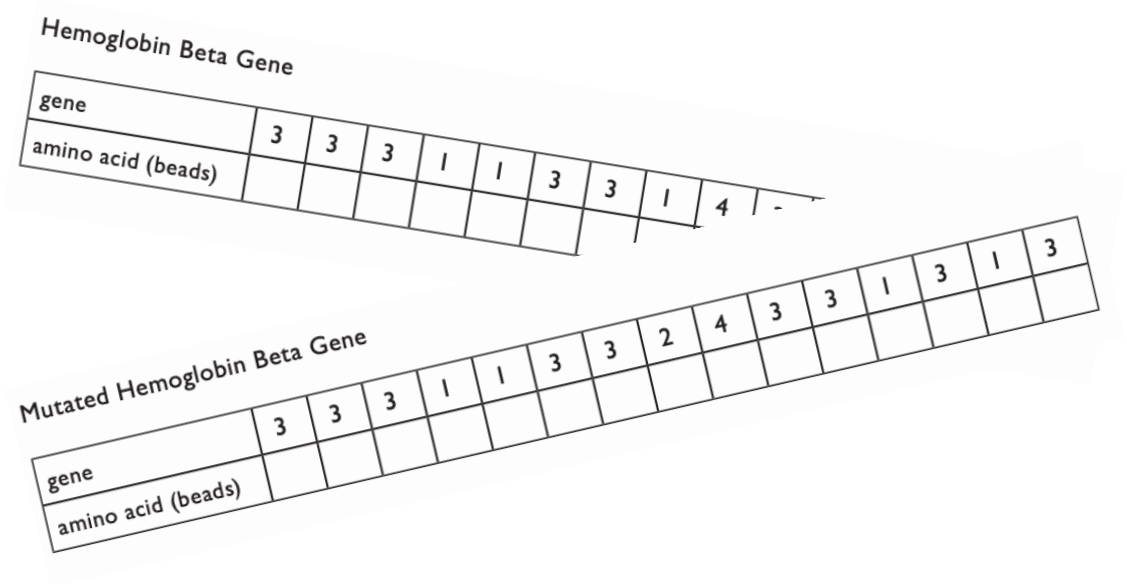
Intro to CRISPR Video



- Will be available soon at https://sepuplhs.org

Modeling Sickle Cell





Name: _____ Date: _____

Modeling Sickle Cell

Part 1

Sickle cell disease is caused by a mutation to a gene called the hemoglobin beta gene, one of the genes that codes for hemoglobin (a protein that carries oxygen in the blood).

Complete the following activity to better understand how the sickle cell mutation affects the hemoglobin protein. In this model, the different-colored beads represent different **amino acids**. A string of amino acids is a **protein**. The strips of paper with the code represent the **genes**.

Directions

1. **tRNA** and **ribosomes** are parts of the cell that help build proteins, using the DNA as a code. Decide which partner will be the tRNA and which partner will be the ribosome.
   - The tRNA will translate and read the code.
   - The ribosome will build the proteins.
2. **tRNA:** Translate the hemoglobin beta gene using the following code (1 = yellow, 2 = blue, 3 = red, 4 = black). Write the colors on the gene strip according to the code.
3. **tRNA:** Read the order of the amino acids and give the ribosome each amino acid in that order.
4. **Ribosome:** Create the hemoglobin beta protein by threading the amino acids (beads) onto the pipe cleaner in a straight chain as the tRNA hands them to you. Bend the ends of the pipe cleaner to keep the beads in place.
5. **tRNA** and **ribosome:** Repeat Steps 2–4 with the mutated hemoglobin beta gene to build the sickle hemoglobin beta protein.

Questions

What was the role of the gene in building the protein?

_____

_____

_____

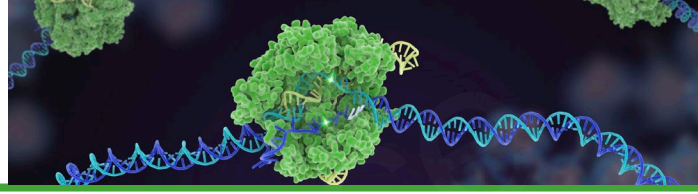
Compare the two proteins. How are they different? What led to the difference in the proteins?

_____

_____

_____

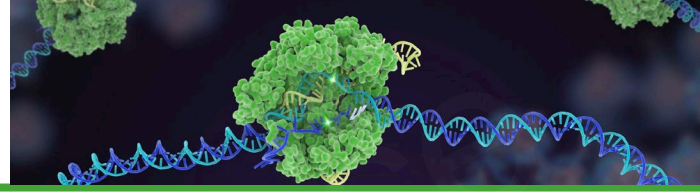
Modeling Sickle Cell

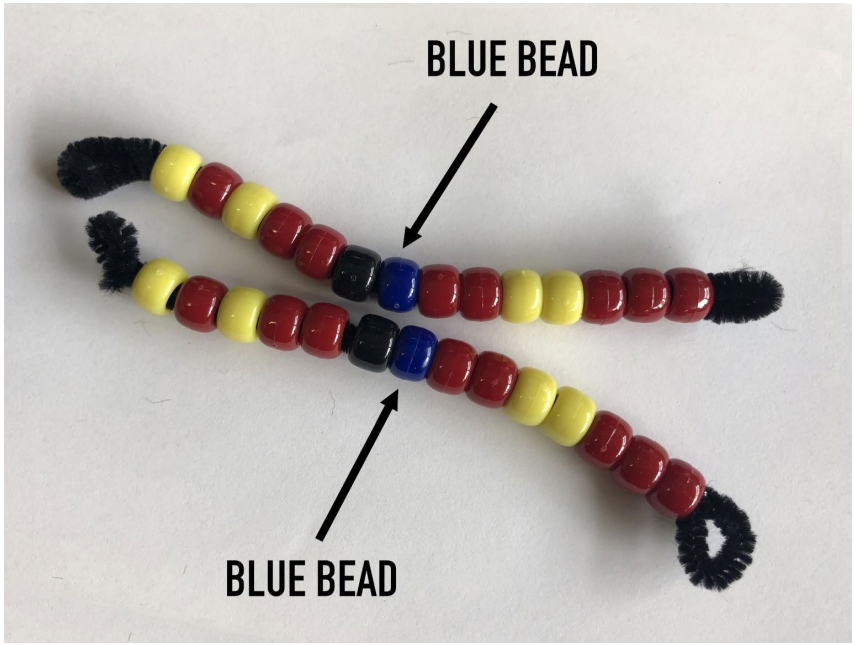


Use the code to read the DNA sequences:

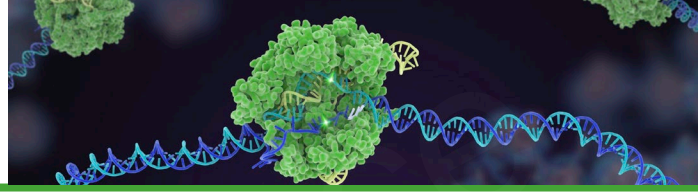
- GAG = yellow
- GTG = blue
- TCC = red
- GTA = black

Example completed models





Sickle Cell Disease Article



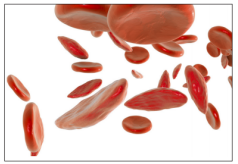
Students gather additional evidence about the causes of sickle cell disease by reading an article.

Name: _____ Date: _____

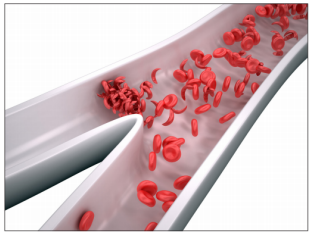
Sickle Cell Disease

Introduction

Sickle cell disease is an inherited blood disorder that is caused by stiff and irregularly shaped red blood cells. Their shape looks like a crescent moon, or sickle, which is where the disease gets its name. Typically, red blood cells are smooth and round, allowing them to easily glide through blood vessels throughout the body. The misshapen red blood cells in people with sickle cell disease do not glide through the blood vessels like the smooth, round ones. They tend to pile up, blocking proper blood flow and preventing oxygen from getting to vital organs and tissues. This leads to fatigue, episodes of pain, swelling of the hands and feet, and frequent infections. Complications such as stroke and organ damage can even lead to death.

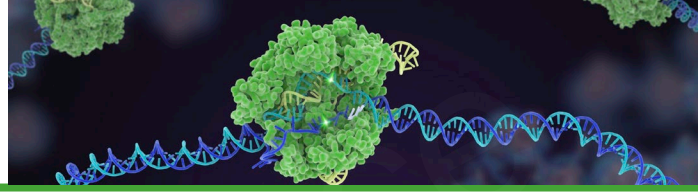


Sickle cell disease affects a person's red blood cells, giving them an irregular shape.



Round red blood cells glide easily through blood vessels (right side). Sickle-shaped red blood cells tend to cause blockages (left side) that prevent oxygen from reaching some organs and tissues.

Read, Think, and Take Note

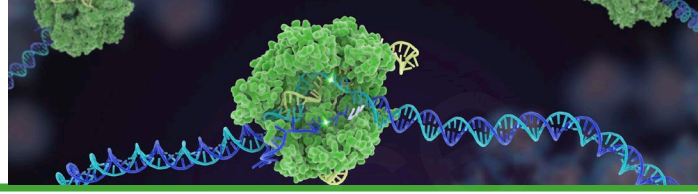


As you read, from time to time, use a sticky note to do one of the following:

- Explain a thought or reaction to something you read.
- Note something in the reading that is confusing or unfamiliar.
- List a word that you do not know.
- Describe a connection to something you learned or read previously.
- Make a statement about the reading.
- Pose a question about the reading.
- Draw a diagram or picture of an idea or connection.

After writing each sticky note, place it next to the word, phrase, sentence, or paragraph in the reading that prompted your note.

CRISPR Lab Overview



Part 1
Add bacteria to liquid LB

Wait 24 hours

Part 2
Activate CRISPR genes

Wait 24 hours

Part 3
Move bacteria to agar dishes

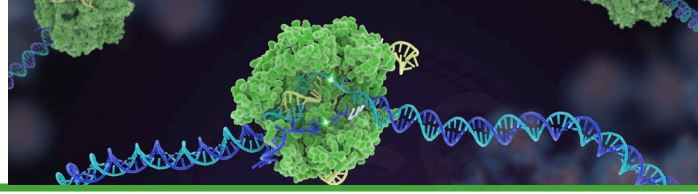
Wait 72 hours*

Observation
Observe bacteria

Everything at room temperature!
No special equipment? No problem!
PLAN AHEAD!
Follow the protocol!

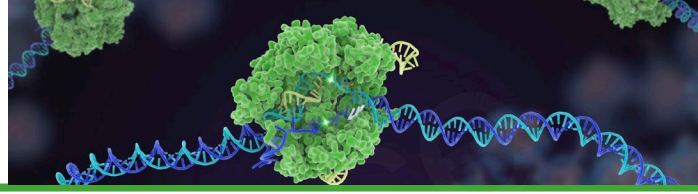
* Growth of bacterial cells on agar takes 72 hours at room temperature. This process can be sped up at higher temperatures.

Introduction to the CRISPR Lab



- Video available with purchase of the kit, at https://www.lab-aids.com

Conducting the CRISPR Lab



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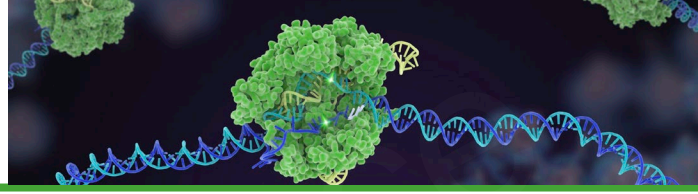
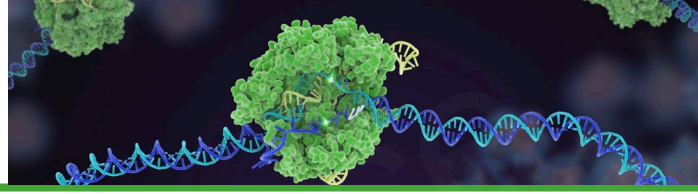
Curing Sickle Cell Using CRISPR



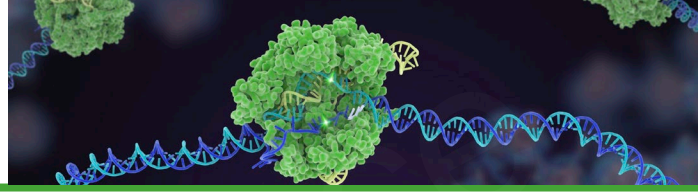
- Will be available soon at https://sepuplhs.org

How Does CRISPR Work?

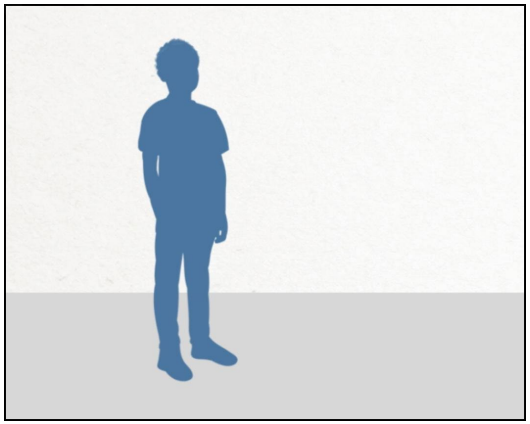


Component	What role does it play in the CRISPR system?	Is this component the same or different in the bacteria lab and in humans with sickle cell disease? Explain.
		
		
		
		
		

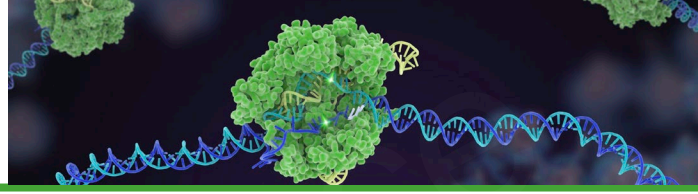
Gene Editing in Bacteria and Humans

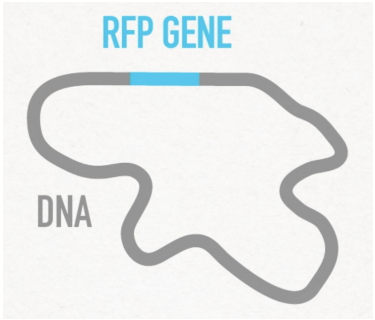


What is the target DNA sequence for CRISPR editing in your lab experiment? What is the target DNA sequence for CRISPR editing in sickle cell disease?

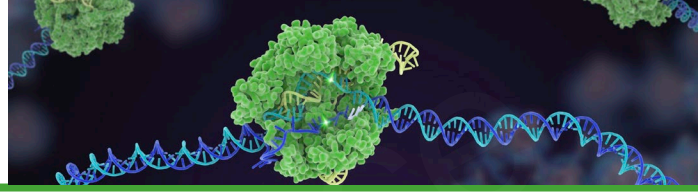


Comparing CRISPR Components

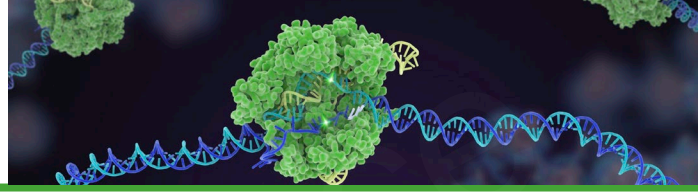


	Target Gene	Guide Sequence	Donor DNA
Our lab experiment			
Sickle cell disease			

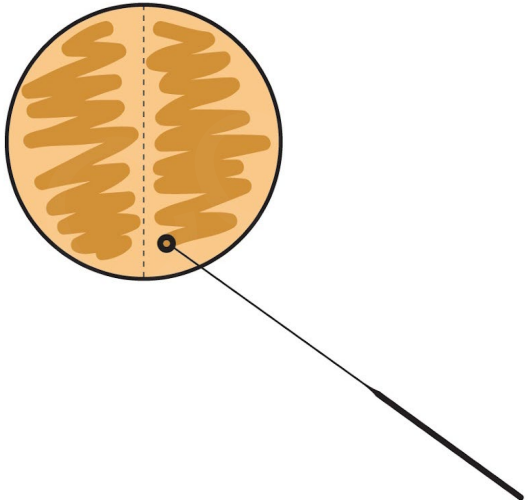
CRISPR Components



Lab Results

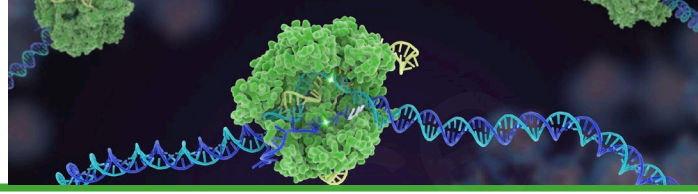


Non-targeting
(control)



Targeting
(experimental)

Lab Prediction Questions

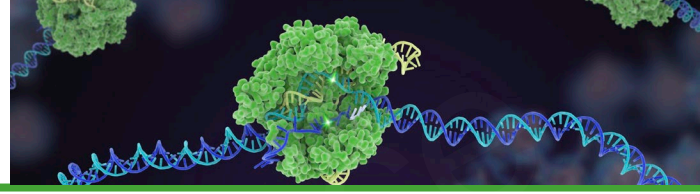


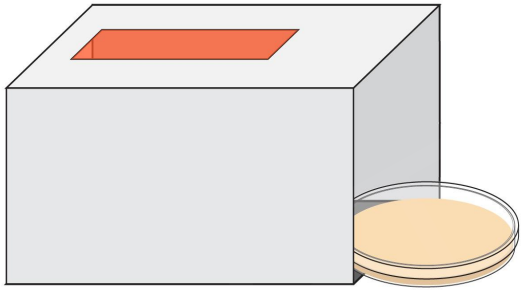
The bacteria need to multiply before you can see the trait for color. Answer the questions below to predict what the bacteria's traits will be.

What color will the bacteria from the "Control" tube be after they multiply on the agar petri dish? Explain your answer.

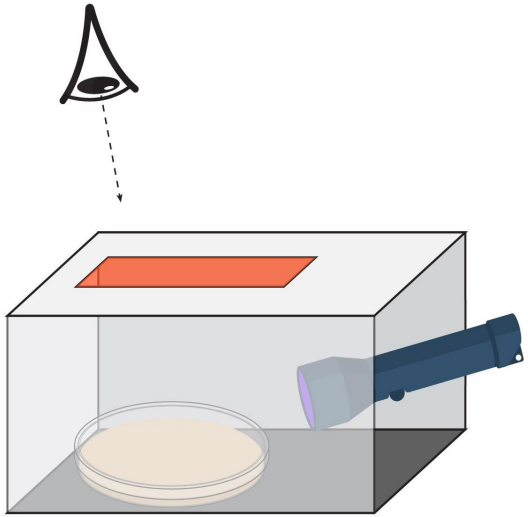
What color will the bacteria from the "Experimental" tube be after they multiply on the agar petri dish? Explain your answer.

UV Light-Viewing Boxes



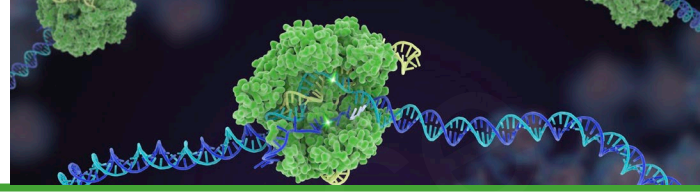


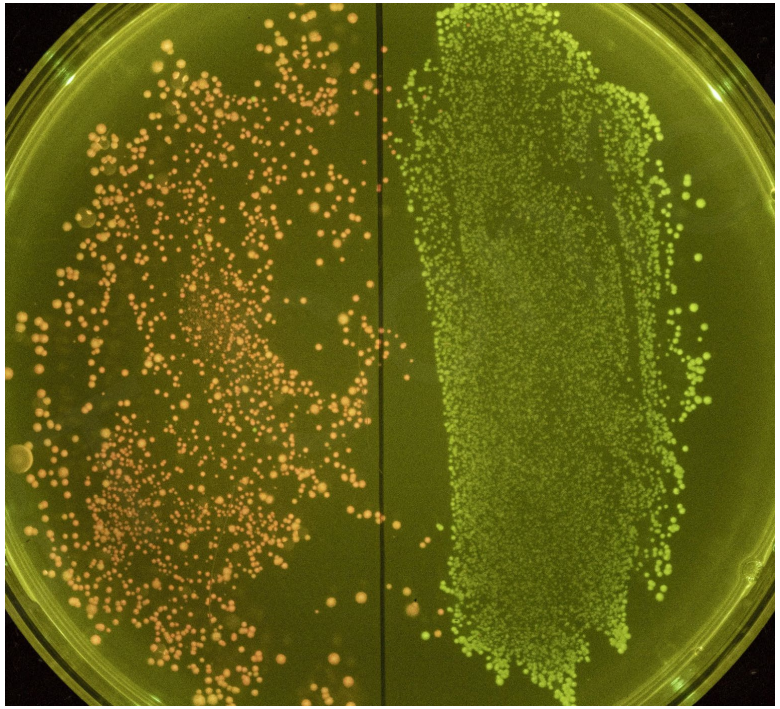
Insert the petri dish.



Shine the UV flashlight onto the dish and view the dish through the orange film.

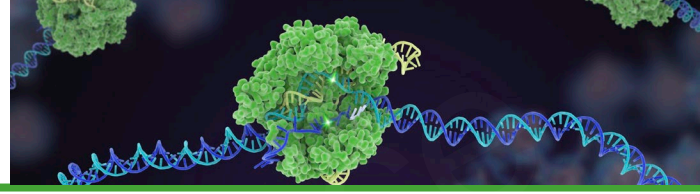
Ideal Lab Results

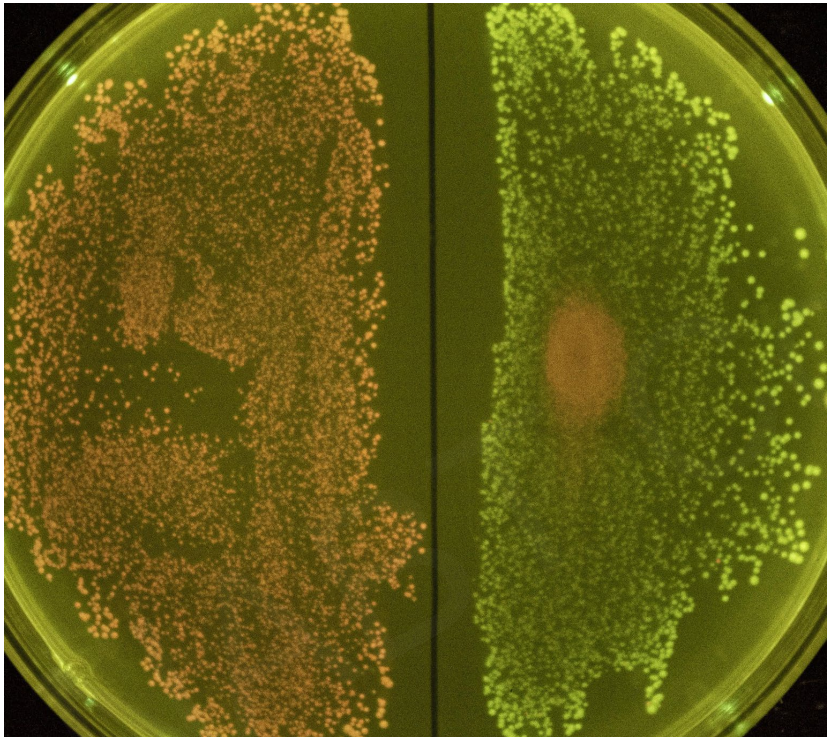




Control: Unedited cells *Experimental*: Edited cells

Other Lab Results



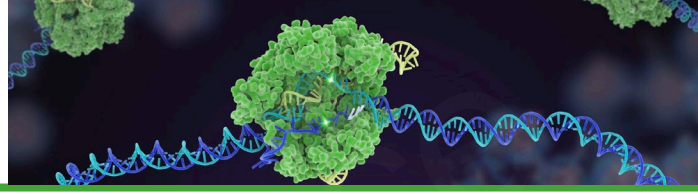


Control: Unedited cells *Experimental*: (Mostly) edited cells

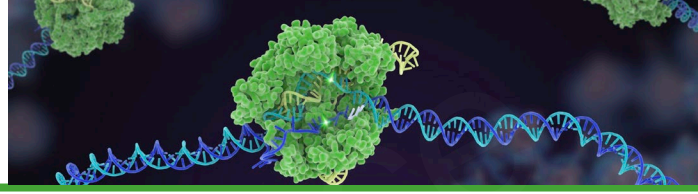
A pink color in the middle of a dense layer of green cells can be caused by transferring too much bacteria during the previous steps or by bacteria growing a little more than expected.

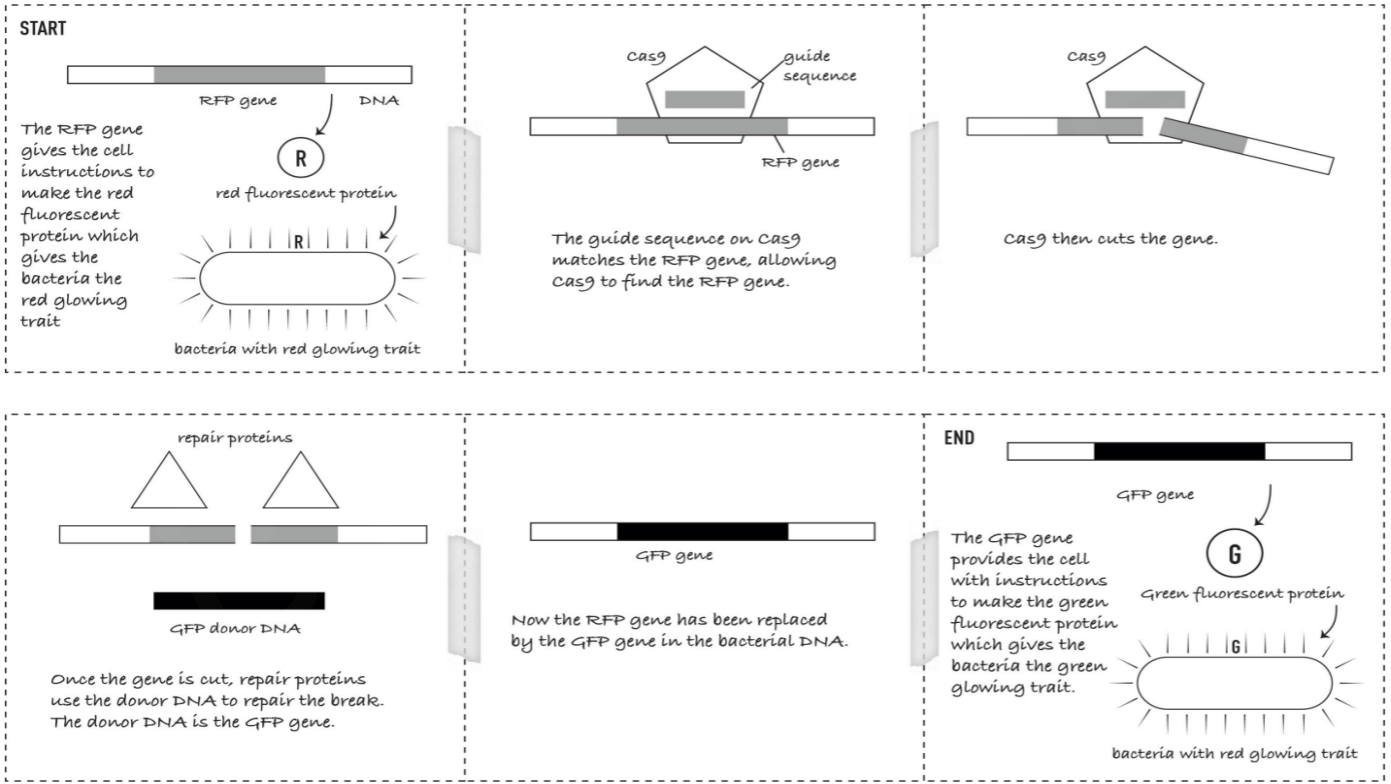
In areas of dense cell growth, the red fluorescence from a small number of unedited cells can overpower the comparatively weaker green fluorescence from the edited cells.

Time Sequence Model: CRISPR Lab

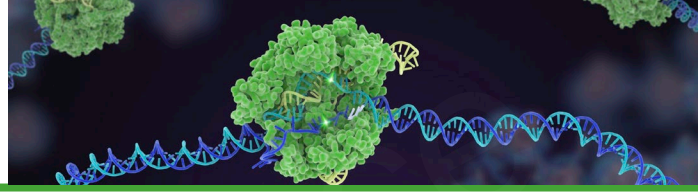


Completed Model



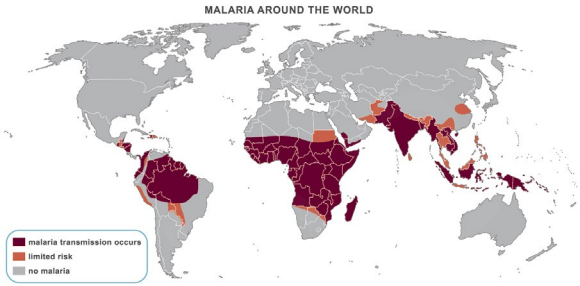


Articles: Ethics of CRISPR



Treating Sickle Cell Disease

Preventing Cystic Fibrosis

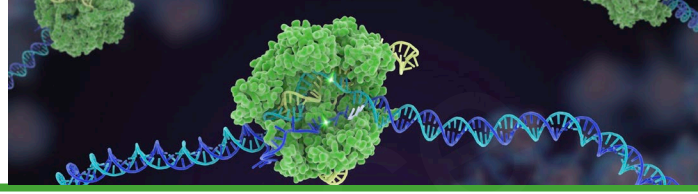


Fighting Malaria

Disease-Resistant Rice

Image credits: Patient: tiverylucky/Shutterstock.com; Rice field: Soichiro/Shutterstock.com

Read, Think, and Take Note

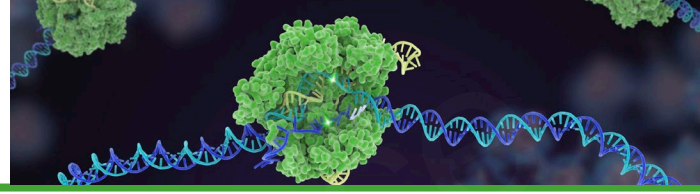


As you read, from time to time, use a sticky note to do one of the following:

- Explain a thought or reaction to something you read.
- Note something in the reading that is confusing or unfamiliar.
- List a word that you do not know.
- Describe a connection to something you learned or read previously.
- Make a statement about the reading.
- Pose a question about the reading.
- Draw a diagram or picture of an idea or connection.

After writing each sticky note, place it next to the word, phrase, sentence, or paragraph in the reading that prompted your note.

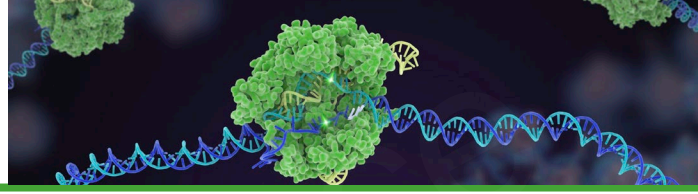
Ethics of CRISPR



Under What Circumstances Should CRISPR Be Used?

Image credits: Patient: tiverylucky/Shutterstock.com; Mosquito: nechaevkon/Shutterstock.com; Hand on grain: GrooveZ/Shutterstock.com; Babies: sirtravelalot/Shutterstock.com

Treating Sickle Cell Disease

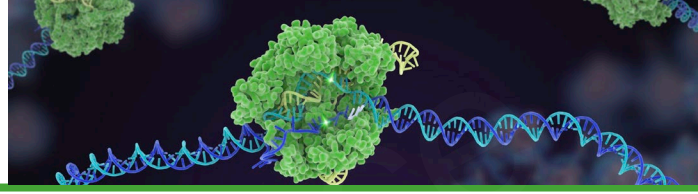


Should CRISPR be used to treat humans with diseases?

- What is the biggest risk?
- What is the biggest benefit?
- Do the risks outweigh the benefits, or do the benefits outweigh the risks?

Image credits: Patient with mask: tiverylucky/Shutterstock.com; Patient in bed: Thaiview/Shutterstock.com

Preventing Cystic Fibrosis



Should CRISPR be used to edit genes in embryos, sperm, or eggs?

- What is the biggest risk?
- What is the biggest benefit?
- Do the risks outweigh the benefits, or do the benefits outweigh the risks?

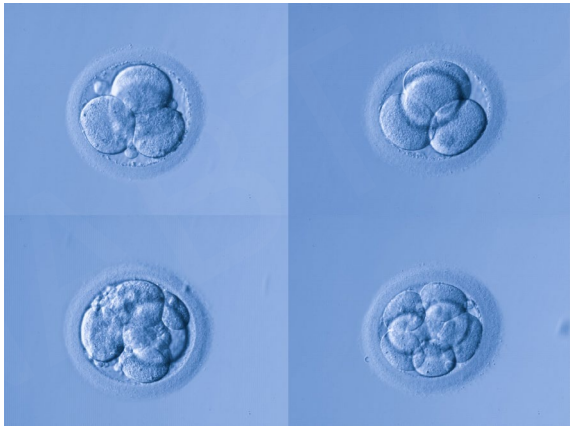
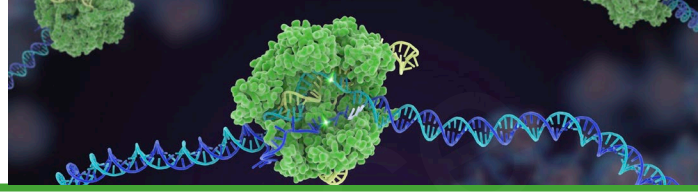


Image credits: Human egg cells: 895Studio/Shutterstock.com; Babies: sirtravelalot/Shutterstock.com

Fighting Malaria

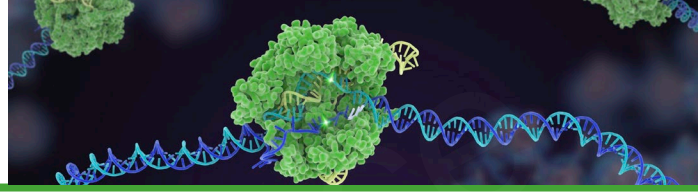


Should CRISPR be used to edit genes in insects to prevent the spread of disease?

- What is the biggest risk?
- What is the biggest benefit?
- Do the risks outweigh the benefits, or do the benefits outweigh the risks?

Image credits: Mosquito: nechaevkon/Shutterstock.com; Tse tse fly: Jaco Visser/Shutterstock.com

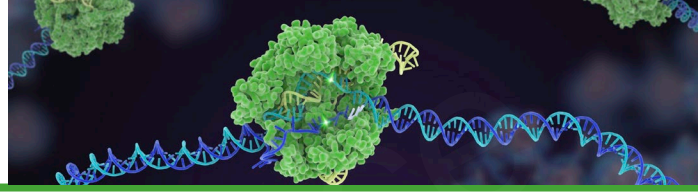
Disease-Resistant Rice



- What is the biggest risk?
- What is the biggest benefit?
- Do the risks outweigh the benefits, or do the benefits outweigh the risks?

Image credits: Hand on grain: GrooveZ/Shutterstock.com; Rice field: Soichiro/Shutterstock.com

Contact Information



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