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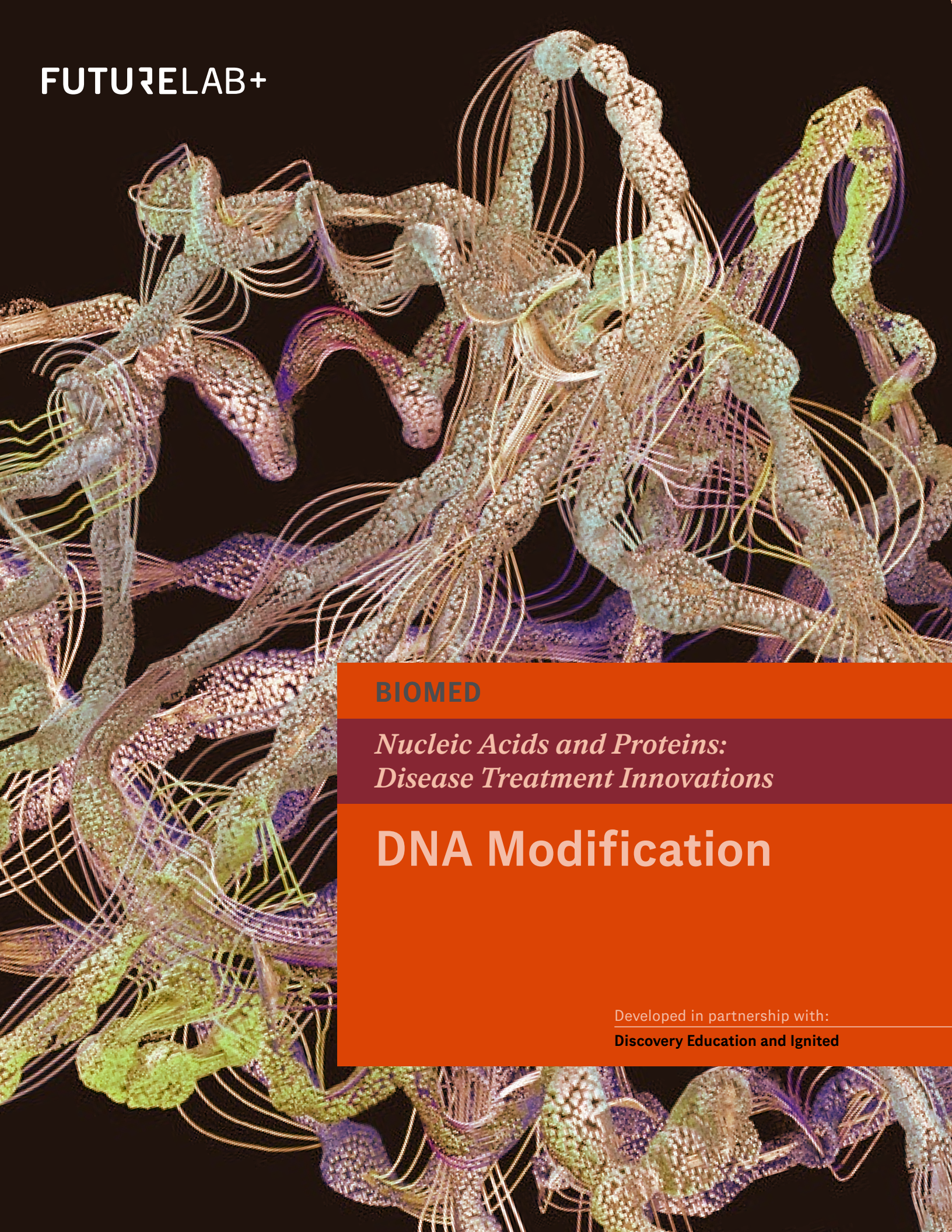

BIOMED

Nucleic Acids and Proteins: Disease Treatment Innovations

DNA Modification

Developed in partnership with:

Discovery Education and Ignited

In this Lesson Plan:

Print the **Teacher Section** →

Print the **Student Section** →

This document is separated into two sections, For Teachers [T] *and* Student Resources [S]*, which can be printed independently.*

Select the appropriate printer icon above to print either section in its entirety.

Follow the tips below in the Range field of your Print panel to print single pages or page ranges:

Single Pages (use a comma): T3, T6

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Cover Image
This is an illustration of a protein.

BIOMED / NUCLEIC ACIDS AND PROTEINS: DISEASE TREATMENT INNOVATIONS

DNA Modification

DRIVING QUESTION

How can DNA be intentionally modified to alter its sequence in organisms?

OVERVIEW

Genetic engineering has long been featured in science fiction, but it is now very real. While different techniques have been used over the years to achieve modification results, none have been as effective or as efficient as CRISPR technology. CRISPR is the short form for "clustered regularly interspaced short palindromic repeats."

In this lesson, students will learn how CRISPR technology works, its possible applications, and the ethical dilemmas that come from genomic manipulation. Students will explore how Cas9 (a bacterial RNA-guided endonuclease) works to edit DNA and apply it to the process of CRISPR, investigate the role of women in biotechnology, and explore a multitude of current and potential future applications of genetic manipulation.

ACTIVITY DURATION

Five class sessions
(45 minutes each)

ESSENTIAL QUESTIONS

How do scientists use Cas9 to modify DNA?

What are the controversies surrounding genetic modification?

How have women contributed to biotechnology?

How can genetic modification be applied to medical science?

OBJECTIVES

Students will be able to:

Articulate the structure of DNA used in modification.

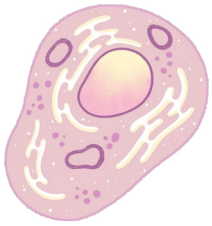
Explain the applications and controversy of CRISPR.

Model how Cas9 can be used in genetic modification.

Investigate the ethics of different biotech applications of CRISPR.

BACKGROUND INFORMATION

In 2012, Jennifer Doudna and her research partner Emmanuelle Charpentier made a discovery in a lab at UC Berkeley: they could use immune defenses of bacteria to "snip" DNA in a precise location. From there, they could effectively edit DNA at the point of the snip by adding in or removing genetic material. This technology became known as CRISPR, and its inventors were rewarded with the Nobel Prize in 2020. CRISPR has revolutionized biotechnology: it offers a way to make crops more nutritious, eradicate genetic diseases, and fight cancer. However, Jennifer Doudna herself now warns against using CRISPR to edit heritable genes until the scientific community knows how those edits will impact a person's offspring in perpetuity. As students learn more about the function of CRISPR in this lesson, they will be asked to wrestle with its ethical implications.



Materials

- **Computers with Internet Access**
- **Scissors**
- **Modeling Recombinant DNA Capture Sheet**
- **Bacterial Plasmid Nitrogen Base Sequences**
- **Human Nitrogen Base Sequences**
- **Restriction Enzymes**
- **Fix the Answer Capture Sheet**
- **CRISPR Paper Simulation Capture Sheet**
- **CRISPR Paper Simulation Student Materials**
- **Sequencing CRISPR-Cas9**
- **CRISPR Editing in the Body for Blindness**
- **What is CRISPR? Why are Doctors So Excited About It?**
- **Infographic Assignment—CRISPR Technology: Benefits and Concerns**
- **Design Journal**

Pedagogical Framing

Instructional materials are designed to meet national education and industry standards to focus on in-demand skills needed across the full product development life cycle—from molecule to medicine—which will also expose students and educators to the breadth of education and career pathways across biotechnology.

Through this collection, educators are equipped with strategies to engage students from diverse racial, ethnic, and cultural groups, providing them with quality, equitable, and liberating educational experiences that validate and affirm student identity.

Units are designed to be problem-based and focus on workforce skill development to empower students with the knowledge and tools to be the change in reducing health disparities in communities.

SOCIAL-EMOTIONAL LEARNING

Students will be given the opportunity to develop their own self-awareness as they explore the ethics concerning genetic modification—examining both sides of the discussion, and reacting to aspects of the conversation. As students work together in cooperative groups they will have opportunities to practice social management skills. Interacting with peers in a collaborative manner meets many social-emotional learning goals and builds a supportive classroom, all while teaching necessary soft skills like active listening, leadership skills, and compromise. Students will practice empathy through role playing.

CULTURALLY AND LINGUISTICALLY RESPONSIVE INSTRUCTION

Students will investigate a number of ways genetic modification is currently being used and how the modification of crops may impact those suffering from food scarcity. They will work with others of diverse cultures on activities with an emphasis being placed on inequalities in access. Culturally and linguistically responsive strategies are used throughout the lesson to address questions on the ethics of human genome manipulation.

ADVANCING INCLUSIVE RESEARCH

In this lesson, students examine why representation in science is important. They compare the experiences of two women in biotechnology and consider why the lack of representation had an impact on the number of women participating in science. They also explore whether current biotechnology companies would have a higher number of female employees if there had been more representation and other accountability measures in place.

COMPUTATIONAL THINKING PRACTICES

Genetic engineers and biotechnologists are heavily reliant on computational thinking in their day-to-day work. Logical problem-solving approaches such as building models to make predictions and abstracting key themes from data help these scientists make revolutionary advances like CRISPR a reality. In this lesson, students use the computational thinking strategies of building models, decomposition, developing algorithms, and abstraction to dig deeply into the processes behind and ethical concerns surrounding gene editing.

CONNECTIONS TO THE PRODUCT LIFE CYCLE

This lesson focuses on the **discovery** aspect of the product life cycle as students investigate different potential applications of gene editing and CRISPR technology. Only through understanding the essentials of gene manipulation can students hope to ultimately recommend delivery methods for two drug designs.

Have you ever wondered…

How are genetically engineered foods made?

Humans have been genetically altering food since they began domesticating animals. The difference between the genetic engineering done by the first farmers and the genetic engineering conducted by today's scientists has to do with how precisely an organism's genetic code can be manipulated. It used to take many generations of breeding before a desired trait would appear in an animal or plant, and even then there was a great deal of guesswork involved. Because of technological advances like CRISPR, scientists can make crops more resistant to drought, more abundant, and more resilient in the face of pests within just a generation or two.

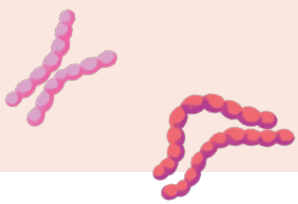
How might gene editing be used to cure disease?

Genomic therapies are already being used to treat patients with specific genetic ailments. One particular practice has shown promising results in curing genetic blindness. Another gene-editing practice may cure hemophilia. Scientists can use CRISPR to remove segments of problematic DNA or can even replace faulty genes with functioning ones. Through these modifications, we may be able to eradicate diseases with a straightforward genetic component. However, those with more complicated sources may not be readily remedied through this process.

MAKE CONNECTIONS!

How does this connect to the larger unit storyline?

As students learn more on the topic of drug delivery, eventually making their own recommendations on the topic, it is necessary they have a strong background in genetic modification. The delivery of drugs through modified biological organisms like proteins and nucleic acids may sound dangerous to some, but through understanding genetic modification, students will better grasp these techniques as being safe and essential to ensuring the health of many.



How does this connect to careers?

Molecular biologists work with DNA and RNA on projects such as cloning and DNA sequencing. They work for years conducting research that yields some of our greatest medical breakthroughs.

Biochemists use their knowledge of molecular processes to study the effects of drugs and other therapeutics on cells and cellular processes. These highly trained professionals utilize a variety of specialized equipment to study these effects and determine their safety and efficacy.

How does this connect to our world?

Genetic modification is complicated and controversial—not just the physical process but how we as consumers interact with and perceive these products. GMO foods are a big hot button issue for many, even those that normally trust scientific findings. The idea of altering the human genome raises large issues about scientists "playing God" while also potentially offering relief to innumerable sufferers of genetic ailments. Through study of the technical processes and discussion of the ethical dilemmas tied to genetic modification, students will be able to fully participate in these global conversations moving forward.

Day 1

Procedure

LEARNING OUTCOMES

Students will be able to:

Discuss how genetically modified organisms have agricultural, economic, and medical impacts on society.

Model the formation of recombinant DNA and its application in bacterial transformation.

Whole Group (10 minutes)

1 Have students pairs use the *Think-Pair-Share* strategy to answer the following questions:

- What would happen to a protein if the DNA sequence of a gene was modified?
- How would you determine if the change would be beneficial or harmful to the organism?

2 Then, project the following scenarios on the board from *Genetically Modified Foods*:

- You are a tomato farmer whose crops are threatened by a persistent species of beetle. Each year, you spend large sums of money on pesticides to protect your crops. A biotechnology company introduces a new strain of tomato plant that produces a natural pesticide, making it resistant to the beetle. By switching to this new strain, you could avoid both the beetle and the chemical pesticides traditionally needed to fight it.
- As a family physician, you often treat children who suffer from infectious diseases that could easily be prevented through vaccination. But the parents of many of your patients cannot afford the cost of vaccinations. You hear of a new approach that would reduce the cost to a fraction of its current price: genetically modified fruits and vegetables that contain various antigens. By simply eating a banana, a child could be protected against diseases without getting a shot!
- You are the leader of a developing nation. Hunger is a problem among your citizens: the salty coastal wetlands of your country can't support the growth of needed crops, and your slow economy can't support importing enough food for everyone. A biotechnology company has genetically modified a rice plant that can thrive in salt water, providing your nation with the opportunity to feed its citizens while bolstering its economy.

3 Show the class one scenario at a time. Read the scenario aloud and invite students to stand. Students will express their opinion using the *Vote with Your Feet* strategy. Explain where the imaginary continuum, or line, is in the room. Point out the ends of the continuum as "I would not accept the genetically modified organism." and "I would accept the genetically modified organism." Explain that participants can choose to stand anywhere on the line in between these two points. It is useful to read the prompt once so participants have time to consider their response, and then have them move once the response is read a second time. Participants will silently move in order to place themselves on the continuum in response to each prompt.

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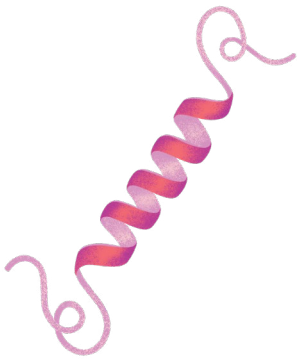
Day 1

Continued



COMPUTATIONAL THINKING IN ACTION

Computer scientists often use models based on data in order to make predictions and see how they play out as variables are changed. These tools allow for refinement and testing. In this activity, students use the computational thinking strategy of building models to examine recombinant DNA. This allows students to develop a deeper understanding of the gene editing process.

Procedure

4	Ask students to work with a partner from a different position on the continuum, in a quick *Turn and Talk,* to see why they would or would not accept the GMO and if they might be persuaded to change their opinion.
5	Repeat this process for the other two scenarios.

Small Group (10 minutes)

1	Place students in groups of four. Explain to students that humans have been doing various forms of genetic modification in agriculture since 8000 BC! Share the image or provide students with a copy of *What GMO CROPS are grown and sold in the United States?* Ask students to identify some foods that they eat regularly in their diet. Have them identify three different reasons for genetically modifying those foods and to discuss their answers within their group.
2	After a brief discussion within the groups, explain that there are many reasons why organisms are genetically modified. Agricultural benefits include growing more nutritious food and a reduction in the use of water and pesticides. Economic impacts include alleviating hunger and malnutrition around the world. Medical impacts include the production of pharmaceuticals, production of vaccines, and the research to prevent diseases.
3	Have students in the same groups read *How are GMOs made?* quietly to themselves and then describe the four step process of making a GMO plant using a *Tweet-Tweet* strategy to summarize each step in only 140 characters. Then, ask students to share at least one of their tweets with their group. Ask for volunteers to share a few tweets aloud with the whole class.
4	Explain to students that they are going to model step 3 from the GMO article by creating a model of recombinant DNA.

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Day 1

Continued

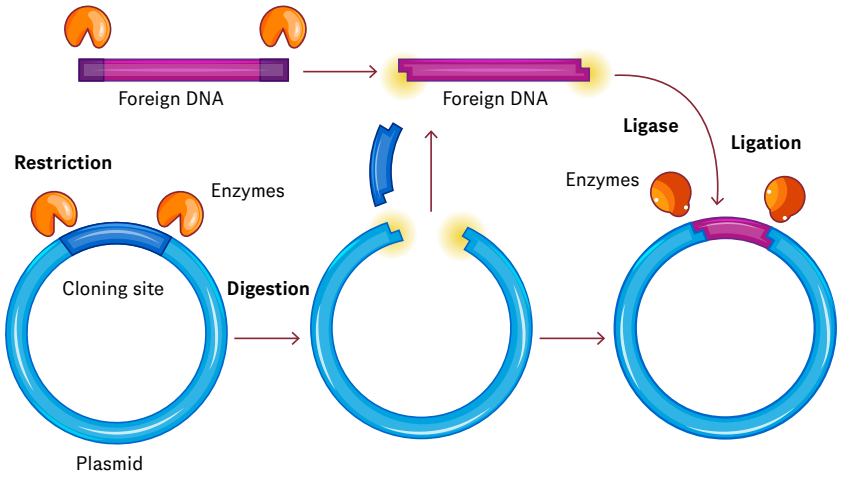
Procedure

Small Group (20 minutes)

1 Students will work in small groups of three to create a model of recombinant DNA that could be inserted into bacteria in the transformation process. Distribute the *Modeling Recombinant DNA Capture Sheet*, the *Bacterial Plasmid Nitrogen Base Sequences*, the *Human Nitrogen Base Sequences*, and the *Restriction Enzymes* capture sheets. Students will work together to model how restriction enzymes identify sequences of DNA to cut and how the structure of DNA allows it to be inserted into a foreign organism's genome. You may need to walk around the room and help students identify the restriction enzyme patterns in both the plasmid and human DNA.

2 When students have successfully created their recombinant DNA model, have them work together to answer the analysis questions.

Recombinant DNA



INDUSTRY AND CAREER CONNECTIONS

Students will need to be detail oriented in their research and summary with their group. They will focus on their openness to learning as they discover how GMOs are currently being used to aid the planet. Similarly, molecular biologists need to have these same skills when they conduct research and clone organisms.

Individual Work (5 minutes)

To review, ask students to create an illustrated flowchart of how they created the recombinant DNA and what criteria they would use to determine if the bacterial transformation was successful. This can be collected and evaluated as a formative assessment.

Day 2

Procedure

LEARNING OUTCOMES

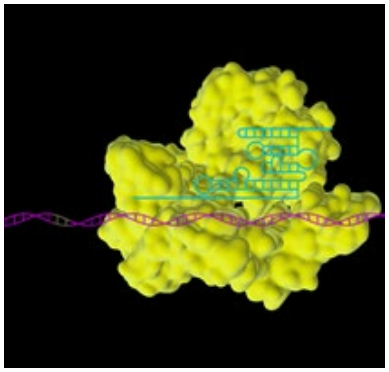
Students will be able to:

Apply knowledge of DNA structure, function, and base pairing to **describe** how CRISPR-Cas9 can be used to inactivate and edit genes.

Construct a paper model to explore how CRISPR-Cas9 is used to edit genes.

COMPUTATIONAL THINKING IN ACTION

As students use the computational thinking strategy of building models to examine how CRISPR-Cas9 edits genes, they are also using the computational thinking strategies of decomposition and developing algorithms to break the process of gene editing into steps and then arrange those steps in logical order.



Screenshot from the animation "Gene Editing Mechanism of CRISPR-Cas9."

Small Group (10 minutes)

Students will work in pairs to watch an animation, *Gene Editing Mechanism of CRISPR-Cas9*, that describes how CRISPR-Cas9 gene editing technology can be used to precisely disrupt and modify specific genes. While watching, students will complete the *Fix the Answer Capture Sheet*. When students are finished, use a non-volunteer strategy, like *Pick a Stick,* to call on some to share how they corrected each statement.

Teacher note > *There are several sites available, like Wheel of Names, that allow you to randomly choose students to share their ideas.*

Small Group (35 minutes)

1	Place students in small groups of two or three and explain that they will work cooperatively to build a two-dimensional paper model to explore how CRISPR-Cas9 is used to edit genes. They will apply their knowledge of complementary base pairing to model how CRISPR targets specific DNA sequences.
2	Distribute the *CRISPR Paper Simulation Capture Sheet*, *CRISPR Paper Simulation Student Materials*, scissors, and tape to each small group.
3	Small groups should follow the procedures to develop their two-dimensional model. Walk around the room to assist any groups that are having difficulty building their model by reviewing the procedures and diagrams with them.
4	To summarize, students should construct a flowchart that illustrates the steps of how CRISPR-Cas9 can be used to edit a gene. The flowchart must identify and briefly describe the four steps: targeting, binding, cleaving, and DNA repair. The flowchart can be hand-drawn or constructed digitally.

Day 3

LEARNING OUTCOMES

Students will be able to:

Explain the various ways CRISPR is being used in medicine.

Predict the impact of CRISPR on the future of medicine.

Procedure

Small Group (5 minutes)

Students will review the steps of using CRISPR-Cas9 to edit DNA. Invite students to use their flowchart from yesterday to complete this sequencing activity with their partner. Provide each pair with the *Sequencing CRISPR-Cas9 Capture Sheet* and have them work together to number each step in sequential order. When finished, invite students to share their results.

Whole Group (5 minutes)

Explain to students that they are going to identify how CRISPR is being used in the field of medicine by reading two articles.

CULTURALLY AND LINGUISTICALLY RESPONSIVE INSTRUCTION

The popular Think-Pair-Share model, and its variations, asks students to consider a question on their own, and then provides an opportunity for students to discuss it in pairs, and finally together with the whole class or another pair to form the square. This activity works ideally with questions that encourage deeper thinking, problem-solving, and critical analysis. It provides peer-to-peer scaffolding and support to learners who might have trouble with specialized vocabulary or general professional, scientific language structures.

Small Group (25 minutes)

1. Students will use a *Think-Pair-Share* to work first with one partner to read each article on the capture sheet and answer the questions to demonstrate their understanding. Distribute the *CRISPR Editing in the Body for Blindness* and *What is CRISPR? Why are Doctors So Excited About It?* capture sheets.

2. When student pairs finish answering the questions for each article, have them join with another pair of students to review their work and make any necessary corrections.

Teacher Note > *For struggling readers, you may want to make the article available at least the day before this lesson so that when the article is introduced, it is familiar.*

Individual Work (5 minutes)

As an exit ticket, have students select one of the writing prompts below to create a brief constructed response as a claim, with evidence and a reasoned argument. Have students record their responses in their design journal.

- What do you think the world of medicine will look like in 10 years with this new technology?
- What disease or disorder would you like scientists to focus on with CRISPR and why?
- Do you think there could be any dangers or ethical dilemmas that may come from the use of CRISPR in the future? Explain.

INDUSTRY AND CAREER CONNECTIONS

Students will need a strong attention span focusing on each article. They will need to have good time management skills to make sure they read and answer the questions for each article. Similarly, when biochemists plan complex research studies, they need to have a strong attention span to make sure they are not missing any details.

Day 4

LEARNING OUTCOMES

Students will be able to:

Explain important scientific contributions of women.

Develop an oral argument stating the importance of female representation in science.

Procedure

Whole Group (10 minutes)

1 Introduce students to Rosalind Franklin and her contributions to biotechnology through this video, *Rosalind Franklin and Her Contributions to Biotechnology* (watch up until 3:53 min).

2 Ask students, "Why is representation in science important and how might biotechnology be different if Rosalind Franklin had gained as much notoriety as Watson and Crick?" Students might respond that representation may have led to a larger number of women participating in science, more women publishing in science, and that current biotechnology companies may have a higher number of female employees if there had been more representation. Ask: How do we continue to change the culture of science-related fields? Ask students to specifically keep in mind the representation of women of color. Their stories are often "hidden" or untold. Allow students to investigate what structures are still in place that do not center around diversity. Representation is incredibly important but, it alone does not solve the problem. Instituting accountability measures for inclusive and non-discriminatory practices and policies along with employing women in decision-making roles and amplifying their work and voices may help dismantle structures or systems that are male-centered.

Teacher Note > *Current figures put female STEM employees at almost equal levels as men, but those numbers dramatically decrease when you look at leadership positions.[3] Advanced students may want to take this lesson further by conducting research and constructing a one-page report comparing the percentage and breakdown of males vs. females in the workforce in scientific fields in eight different countries around the world.*

Whole Group (15 minutes)

1 Show students the video of UC Berkeley biochemist Jennifer Doudna upon learning she had won the 2020 Nobel Prize in Chemistry. *Jennifer Doudna Wins 2020 Nobel Prize in Chemistry*

2 After discussing their thoughts of the video, have students read the article highlighting the two women who developed the CRISPR-Cas9 technique: *Genetic Scissors: a Tool for Rewriting the Code of Life.*

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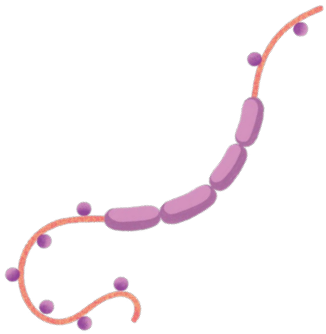
Day 4

Continued

Procedure



Individual Work (20 minutes)

Teacher Note > *A free account with Flipgrid will need to be created before students begin this assignment. However, a similar app or website may be used as a substitute.*

1. Explain to students that they will create a three-minute video discussing the important role of women in biotechnology. Say: Using what you've now learned about Rosalind Franklin and doctors Emmanuelle Charpentier and Jennifer Doudna, select and respond to one of the following prompts:

   a. If Rosalind Franklin had been given more recognition for her discovery, how might this have impacted young girls growing up at that time?

   b. Detail how Drs. Charpentier and Doudna's discovery culminated in their groundbreaking Nobel Prize in Chemistry.

   c. Compare and contrast the experiences of Rosalind Franklin and Drs. Charpentier and Doudna in the field of biotechnology.

2. The video can be made using any device and *Flipgrid* or similar free technology.

Day 5

Procedure

LEARNING OUTCOMES

Students will be able to:

Explain the controversies behind genome editing.

Construct an infographic that summarizes the benefits and concerns of using CRISPR technology.

COMPUTATIONAL THINKING IN ACTION

Infographics are useful tools that rely on the computational thinking strategy of abstraction. By identifying what should go into their infographic, students are refining their ability to identify central themes and communicate big-picture concepts.

INDUSTRY AND CAREER CONNECTIONS

Students will need to demonstrate professionalism in their writing and word choices. Writing in a business setting requires organization in order to articulate clear and concise information to a targeted individual. Similarly, biochemists need to be professional when writing out their designs for studies and experiments on the effects of certain drugs.

Whole Group (20 minutes)

Teacher Note > *Explain the thinking routine before you start the video; it is too long to watch twice.*

1. Explain to students that they are going to watch a TED Talk featuring a chemical biologist, David R. Liu, who shares a breakthrough: his lab's development of base editors that can rewrite DNA. This crucial step in genome editing takes the promise of CRISPR to the next level: if CRISPR proteins are molecular scissors, programmed to cut specific DNA sequences, then base editors are pencils, capable of directly rewriting one DNA letter into another.

2. As students watch the video *Can we cure genetic diseases by rewriting DNA?* (16 minutes), pause it occasionally and allow students time to reflect and complete a *3-2-1 Bridge* thinking routine.

   a. Students should write down three things that they learned, two questions, and one difference between base editing and CRISPR.

   b. Once complete, invite students to share their *3-2-1 Bridge* answers with two other students.

Whole Group (25 minutes)

1. Use *Stand and Share* to ask students what they think Liu meant at the end of the video when he said, "Engaging in other scientists, doctors, ethicists, and governments to maximize the likelihood that base editing is applied thoughtfully, safely, and ethically remains a critical obligation."

2. Explain to students that they are going to create an infographic summarizing what they have learned about CRISPR including benefits and concerns of its application. Students can use free websites like *Canva* or *Piktochart* to browse through infographic templates to get started.

3. Distribute and review the *Infographic Assignment—CRISPR Technology: Benefits and Concerns* criteria and rubric to answer any questions students may have.

4. As a wrap-up, ask students to complete the lesson questions in their **Design Journal**. The will summarize how scientists use Cas9 to modify DNA and the controversies surrounding genetic modification.

National Standards

Next Generation Science Standards

LS1.A: Structure and Function
Systems of specialized cells within organisms help them perform the essential functions of life. All cells contain genetic information in the form of DNA molecules. Genes are regions in the DNA that contain the instructions that code for the formation of proteins, which carry out most of the work of cells.

Science and Engineering Practices

Developing and using models
Develop, revise, and/or use a model based on evidence to illustrate and/or predict the relationships between systems or between components of a system.

Obtaining, evaluating, and communicating information
Communicate scientific and/or technical information or ideas (e.g. about phenomena and/or the process of development and the design and performance of a proposed process or system) in multiple formats (i.e., orally, graphically, textually, mathematically).

Crosscutting Concepts

Systems and System Models
Models (e.g., physical, mathematical, computer models) can be used to simulate systems and interactions—including energy, matter, and information flows—within and between systems at different scales.

Structure and Function
Investigating or designing new systems or structures requires a detailed examination of the properties of different materials, the structures of different components, and connections of components to reveal its function and/or solve a problem.

Career and Technical Education (CTE)

A3.1
Define and describe the structure and function of DNA, ribonucleic acid (RNA), and proteins, explain the consequences of DNA mutations on proteins.

5.4
Interpret information and draw conclusions, based on the best analysis, to make informed decisions.

CRISPR Editing in the Body for Blindness Questions

ANSWER KEY — **Do not share with students**

Directions
Read the article, CRISPR Editing in the Body for Blindness, and answer the questions.

1. Read the following paragraph from the section *New Era In Medicine*.

   Jason Comander, at Massachusetts Eye and Ear in Boston, a hospital that has plans to enroll patients in the study, has said that the surgery marks "a new era in medicine" using a technology that "makes editing DNA much easier and much more effective."

   Which idea is BEST supported by this paragraph?

   a. Treatments to edit DNA will be limited to diseases causing blindness.

   b. Doctors are encouraged by the possibilities of the CRISPR technology.

   c. Many patients are interested in participating in the gene editing study.

   d. Medical treatments will soon be dominated by technological treatments.

2. Why did the author conclude the article by explaining that the studies have government regulators' approval?

   a. to confirm that the studies are not taking unnecessary risks with patients

   b. to show that government approval is required to fund experimental treatments

   c. to explain the rigorous process of getting approval for experimental treatments

   d. to describe the unease that patients have with treatments that are not widely tested

3. Read the following statement.

   Scientists believe CRISPR technology can be more widely used.

   Which sentence from the article BEST supports the statement above?

   a. The companies have worked diligently to minimize that risk and to ensure that the treatment will cut only the intended area.

   b. Jean Bennett is a University of Pennsylvania researcher who helped test Luxturna at the Children's Hospital of Philadelphia, Pennsylvania. "The gene editing approach is really exciting. We need technology that will be able to deal with problems like these large genes," she said.

   c. Musunuru is a gene editing expert at the University of Pennsylvania. He noted that the treatment seems likely to work, based on tests in mice, monkeys, and human tissue.

   d. Other scientists are using CRISPR to edit cells outside the body to try to treat sickle cell disease, cancer, and other diseases.

4. How does the author analyze the claim that the CRISPR technology might be used to successfully treat diseases?

   a. by offering expert opinions, describing the treatment and addressing concerns about risks of the treatment

   b. by providing evidence of patients who have successfully received the treatment and the doctors who treated them

   c. by giving the details of government approval of the technology and describing successful outcomes in trial treatments

   d. by explaining the treatments that have been used in the past to correct DNA and showing that CRISPR technology is superior

5. Write a short paragraph that explains the central idea of the article. Use at least two details from the article to support your response.
   Answers will vary.

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What is CRISPR? Why are Doctors So Excited About It?

ANSWER KEY **Do not share with students**

Directions
Read the article, What is CRISPR? Why are Doctors So Excited About It?, and answer the questions.

1. According to the article, the study on gene editing to treat cancer has had mixed results up until this point.

   Which statement BEST supports the idea outlined above?

   a. The study showed varied results after two to three months. One patient was stable, and another's cancer has continued to worsen. The treatment was too recent in the third patient to know the response. Fifteen more patients are expected to be treated to assess the safety and efficacy of the trials.

   b. Dr. Aaron Gerds, an independent cancer treatment specialist at the Cleveland Clinic in Ohio says, "It's very early, but I'm incredibly encouraged by this.'

   c. Each had already failed multiple standard treatments. Two of the patients have a blood cancer called multiple myeloma. The third has a cancer known as sarcoma, which forms in the soft or connective tissue.

   d. "This is a brand new therapy," he said, "so it's not clear how soon any anti-cancer effects will be seen. Following these patients longer, and testing more of them, will tell."

2. Read the list of sentences from the article.

   The cells that are returned are now super-powered to fight their cancer — a form of immunotherapy that encourages a stronger immune system response in order to fight disease. (1)

   Chinese scientists have reportedly conducted the first studies of this type for cancer patients, but this is the first one outside of China. (2)

   It took over two years to get the United States government regulators to approve it as the treatment is so innovative. (3)

   The American Society of Hematology, which focuses on patients with blood disorders, released the early results and more details will be given at its annual conference. (4)

   Which two sentences taken together provide the BEST evidence to support the idea that gene editing as a form of cancer treatment is relatively new?

   a. (1) and (2)
   b. (1) and (4)
   c. (2) and (3)
   d. (3) and (4)

3. Which of the following details is MOST important to the development of the central ideas?

   a. It can be used to change DNA permanently and has been in use in labs for some time.

   b. Dr. Aaron Gerds, an independent cancer treatment specialist at the Cleveland Clinic in Ohio says, "It's very early, but I'm incredibly encouraged by this.'

   c. The American Society of Hematology, which focuses on patients with blood disorders, released the early results and more details will be given at its annual conference.

   d. The CRISPR tool allowed doctors to take immune cells from the patients' own blood and alter the genes in the cells so that they might help to recognize and fight the cancer.

4. The central idea of the article is developed by

   a. focusing on how cancer patients felt after they received the gene editing treatment

   b. describing some of the side effects patients experienced after gene editing

   c. comparing the specific results of gene editing in both China and the United States

   d. explaining how the gene editing treatment was conducted and what the results were

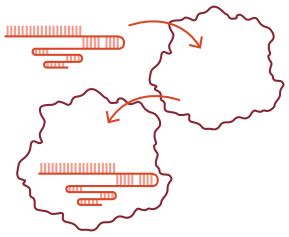
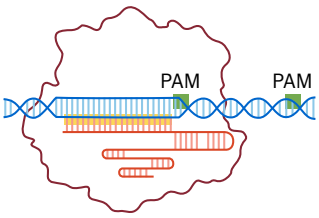
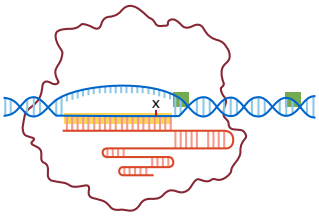
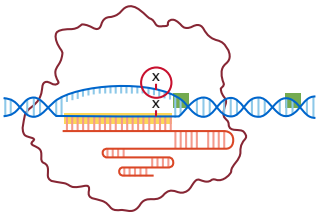
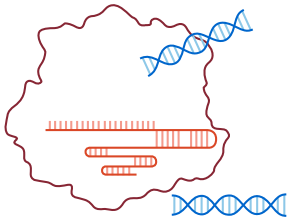
5. Make and support a claim about why someone should read this text. What makes this text worth reading? What will a reader gain or what might a reader do after reading this? Support your response with specific details from the text.

   Answers will vary.

Sequencing CRISPR-Cas9

ANSWER KEY **Do not share with students**

Directions
Read each step of Cas9 DNA cleavage and write the number of each step in sequential order.

Order	Description	Diagram
1	Cas9 binds an sgRNA. Cas9 recognizes and binds the scaffold (tracrRNA) region of a sgRNA. The nucleotide sequence of the scaffold region determines its structure, which is tailored to fit within the Cas9 protein as a key fits into a lock.	
2	The Cas9-sgRNA complex binds to a PAM site on the target DNA. Cas9 requires a particular PAM sequence (5'-NGG) to be present directly adjacent to the protospacer sequence. When the Cas9-sgRNA complex recognizes and binds a PAM, it separates the DNA strands of the adjacent sequence to allow binding of the sgRNA.	
3	The guiding region of the sgRNA binds to the target DNA sequence. The guiding region of the sgRNA attempts to base-pair with the DNA. If a match is found, the process continues. Otherwise, the complex releases and attempts to bind another PAM and target DNA sequence.	
4	Cas9 makes a double-stranded break in the DNA three base pairs upstream of the PAM.	
5	The complex releases from the DNA. The Cas9-sgRNA complex releases the cut DNA and is ready to repeat the process.	

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Modeling Recombinant DNA Capture Sheet

Objective

Students will model the formation of recombinant DNA using restriction enzymes to understand the process of bacterial transformation.

Background

Genetic engineering techniques are currently being used to study processes such as gene regulation, to develop products such as human hormones, to create disease-resistant plants, and to diagnose and treat genetic disorders. In this activity, you will model removing a functional human insulin gene and combining it with a bacterial plasmid to create recombinant DNA. This recombinant DNA would then be inserted into the bacteria where the gene for human insulin can be expressed.

Procedures

1. Use scissors to cut out the Plasmid Nitrogen Base Sequence strips and tape them together into one long strip. The letters should all be in the same direction. Tape the two ends of the long strip together to form a circle with the letters facing out. This is a model of your plasmid DNA.

2. Cut out the Human Nitrogen Base Sequence Strips and tape them together in numerical order. This is a model of your human DNA, which contains the gene for insulin production. The gene area is shaded.

3. Cut out the Restriction Enzyme Cards. Each card shows a sequence where a particular restriction enzyme cuts DNA.

4. Compare the sequence of base pairs on an enzyme card with the sequences of the plasmid base pairs. If you find the same sequence of pairs on both the enzyme card and the plasmid strip, mark the location on the plasmid with a pencil, and write the enzyme number in the marked area. Repeat this step for each enzyme card.

5. Some enzymes may not have a sequence on the plasmid DNA and will not cut it. Other enzymes may cut the plasmid DNA in several places. Choose the correct restriction to recombine your DNA. In doing so, you are modeling the process scientists follow. With hundreds of restriction enzymes available, scientists must determine which one will work for the DNA they want to recombine!

6. Once you have identified all enzyme sequences on the plasmid, identify those enzymes which cut the plasmid once and only once. Discard any enzymes that cut the plasmid in the shaded plasmid replication sequence. You don't want to cut out this particular gene, because it is necessary for the bacteria to replicate itself.

7. Which enzymes fit this criteria?

   _____

   _____

8. Next, compare the enzymes you chose in step 5 to the human DNA strip. Find any enzymes that will make two cuts in the DNA, one above the shaded insulin gene sequence and one below the shaded insulin gene sequence. Mark the areas on the DNA strip that each enzyme will cut and make a note of which enzyme cuts in that spot.

9. Select one enzyme to use to make the cuts. The goal is to cut the DNA strand as closely as possible to the insulin gene sequence without cutting into the gene sequence.

10. Make cuts on both the plasmid and the DNA strips. Make the cuts in the staggered fashion indicated by the black line on the enzyme card. It is important to leave unpaired nitrogen bases on the human insulin gene so that they can form hydrogen bonds with the nitrogen bases on the bacterial plasmid.

11. Tape the sticky ends (the staggered ends) of the plasmid to the sticky ends of the insulin gene to create their recombinant DNA. In the lab, DNA ligase is used to bind the strands together.

12. Congratulations! You have successfully created recombinant DNA with the human insulin gene that can be inserted into a bacterial cell. This bacteria will reproduce and create more bacteria with the gene. Bacteria grown in cultures can now mass produce insulin for diabetics.

Continues next page >

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Modeling Recombinant DNA Capture Sheet

Continued

Discussion Questions

1. Explain how the structure and function of DNA makes the creation of recombinant DNA possible.

2. Which restriction enzyme did you use? Why is it important to cut the plasmid and the human DNA with the same restriction enzyme?

3. Do restriction enzymes exist naturally in organisms? If so, what is their purpose?

4. Why would restriction enzymes that created "blunt" ends (ends that are not staggered) not be as useful in recombination as those that create sticky ends?

5. In this model, what did the scissors represent? What did the tape represent?

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Bacterial Plasmid Nitrogen Base Sequences

Directions
Cut strips along dotted lines. Tape the top of one strip to the bottom of another in any order.

G	C	C	G	T	A	T	A
C	G	G	C	G	C	A	T
C	G	A	T	G	C	A	T
C	G	G	C	T	A	G	C
A	T	T	A	G	C	C	G
G	C	T	A	G	C	C	G
A	T	A	T	G	C	G	C
G	G	A	T	G	C	T	A
T	A	C	G	G	C	A	T
T	A	G	G	C	G	G	C
T	A	T	A	A	T	G	C
C	G	A	T	A	T	T	A
T	A	G	C	G	C	T	A
T	A	G	C	G	C	C	G
A	T	A	T	T	A	G	C
A	T	G	C	T	A	A	T
G	C	G	C	A	T	A	T
G	C	G	C	T	A	C	G
T	A	C	G	A	T	G	C
C	G	C	G	C	G	C	G
T	A	C	G	T	A	C	G

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Human Nitrogen Base Sequences

Directions

Cut strips along dotted lines. Tape the bottom of Strip 1 to the top of Strip 2, the bottom of Strip 2 to the top of Strip 3, and continue until all are in one long strip in order (1-6). Shaded region = insulin gene

1	2	3	4	5	6
T A	G C	T A	T A	G C	T A
G C	A T	T A	T A	T A	T A
G C	G C	C G	C G	A T	C G
G C	A T	G C	G C	A T	G C
C C	T A	A T	T A	T A	A T
C G	T A	A T	C G	A T	A T
T G	C G	G C	A T	T A	C G
A A	T A	G C	T A	T A	G C
G T	T A	T A	G C	C G	G C
G C	A T	A T	T A	C G	G C
C C	A T	C G	G C	T A	G C
A G	G C	A T	C G	C G	C G
C T	T A	T A	C G	C G	C G
A G	C G	A T	T A	T A	C G
G T	A T	A T	T A	T A	T A
G C	A T	C G	T A	A T	A T
G C	G G	G C	T A	A T	G C
C C	C C	T A	A T	G C	G C
C G	A T	C G	A T	A T	A T
C G	G C	T A	A T	A T	C G
G C	G C	C G	T A	T A	C G
1	2	3	4	5	6

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Restriction Enzymes

Directions

Cut out each restriction enzyme along the dotted lines. There should be nine total cards. Compare each nitrogen base sequence to the sequences found on both the bacterial plasmid and human DNA. The solid lines that run between the base pairs represent where each restriction enzyme will "cut" the DNA.

Enzyme 1	Enzyme 2	Enzyme 3
C G C G T A G C G C	T A T A C G G C A T A T	C G C G T A A T G C G C
Enzyme 4	**Enzyme 5**	**Enzyme 6**
T A C G T A A T G C A T	G C G C C G C G	C G T A T A A T A T G C
Enzyme 7	**Enzyme 8**	**Enzyme 9**
C G T A C G G C A T G C	G C G C G C C G C G C G	A T A T C G G C

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Fix the Answer Capture Sheet

Directions
Work in pairs to watch an animation, Gene Editing Mechanism of CRISPR-Cas9, pausing as needed to complete the questions below.

Statement 1	CRISPR-Cas9 is a nucleic acid that naturally occurs in many viruses as an immunity mechanism.
Partner A: Fix the statement. Partner A is the student who has the most letters in their full name.	
Partner B Add on one extra detail to make the answer better.	

Statement 2	Cas9 acts like glue that can cut and paste almost any gene in any organism.
Partner A: Fix the statement. Partner A is the student who has the next birthday.	
Partner B: Add on one extra detail to make the answer better.	

Statement 3	When Cas9 finds a particular recognition sequence, it cuts the DNA.
Partner A: Fix the statement. Partner A is the student who has the most pets.	
Partner B Add on one extra detail to make the answer better.	

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Fix the Answer Capture Sheet

Continued

Statement 4	When DNA bases match the target sequence of the transfer RNA, Cas9 will cut one strand of DNA.
Partner A: Fix the statement. Partner A is the student who has the most items on their desk.	
Partner B Add on one extra detail to make the answer better.	

Statement 5	Cas9 causes a gene to be expressed in the cell.
Partner A: Fix the statement. Partner A is the student who has traveled the farthest outside the United States.	
Partner B: Add on one extra detail to make the answer better.	

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CRISPR Paper Simulation

Procedure

Objective

Apply *knowledge of DNA structure, function, and base pairing to* describe *how CRISPR-Cas9 can be used to inactivate and edit genes.*

Directions

1. Cut out the seven GFP gene sequence pieces on your capture sheet and tape the pieces together end to end in order to form the complete gene.

2. Your next step is to select a 20-nucleotide region somewhere within the GFP gene to serve as a target sequence. For the purposes of this activity, any stretch of 20 nucleotides within the gene will suffice, so long as it is not too close to either end of the gene. Write your chosen target sequence in double-stranded format in the space to the left.

   5′ example:

   CTCGTGACCACCCTGACCTA

   3′ example:

   GAGCACTGGTGGGACTGGAT

   Doudna and Charpentier modified the general structure of crisprRNA to make it easier to utilize under experimental conditions. Their modified crisprRNA is referred to as guideRNA.

3. Now it is time to design a crisprRNA capable of recognizing the GFP target sequence. Cut out the GFP guideRNA molecule and note the target region located at the 5′ (red) end. This is the region that will recognize the 3′ to 5′ GFP DNA target sequence that you wrote out. Write the required complementary guide RNA target sequence in 5′ to 3′ orientation in the space to the left. Remember, you are writing an RNA sequence, so be sure to use uracil in place of thymine.

   5′ example:

   CUCGUGACCACCCUGACCUA

4. Once you have double-checked the sequence, write the sequence on the paper guideRNA molecule. You are now ready to load the synthetic guideRNA into the Cas9 enzyme.

Continues next page >

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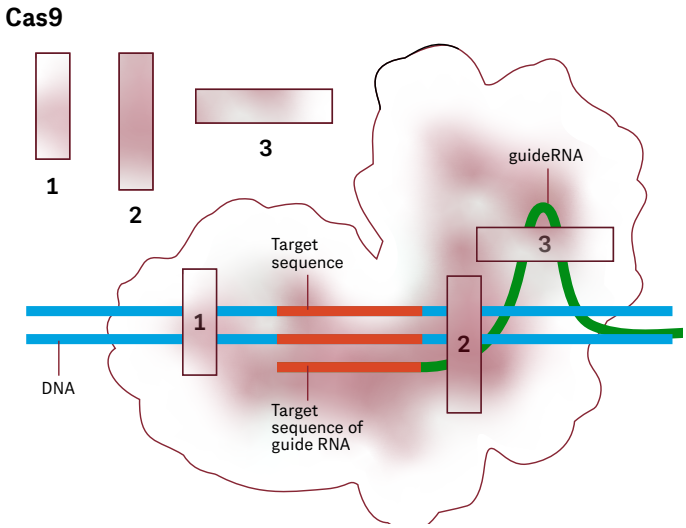
CRISPR Paper Simulation

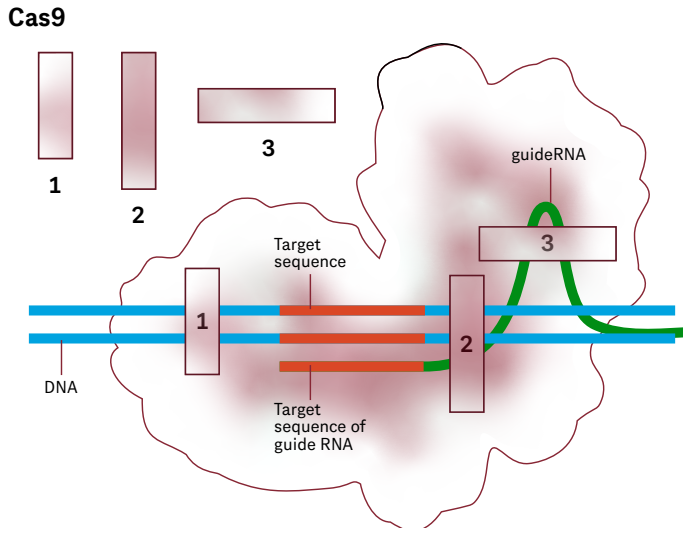
Procedure

Continued

5. Cut out the Cas9 enzyme and the three associated tabs. Staple or tape each tab onto the Cas9 enzyme at the appropriate location, so as to create three "belt loops".



6. Attach the guideRNA to Cas9 by sliding the hairpin end of the molecule under belt loop number 3 and the target sequence through belt loop number 2. The Cas9 has now been programmed to seek out DNA containing the specific target sequence of the guideRNA.



Before making the cut, predict the size of the fragments that will be generated if the cut occurs at the desired location. Specifically, Cas9 will cut the GFP gene at the 5′ end of the complementary DNA target sequence. This will generate two DNA fragments. What is the expected length of each fragment, as measured in the number of base pairs?

Fragment 1 = _____ base pairs

Fragment 2 = _____ base pairs

7. It is time to let the CRISPR-Cas9 complex do its job. Slide the GFP gene into the CRISPR-Cas9 complex through loop number 2 and then through loop number 1. Continue sliding the GFP gene through the CRISPR-Cas9 complex until the guideRNA recognizes its complementary 3′ to 5′ sequence in the GFP DNA.

8. Use a pair of scissors to cut the double-stranded DNA molecule at the 5′ end of the complementary DNA target sequence (near loop number 2).

   Are the fragments the sizes you expected? Explain.

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CRISPR Paper Simulation

Student Materials

Directions

Follow the procedures to develop a two-dimensional model.

1	5′ ATGGTGAGCAAGGGCGAGGAGCTGTTCACCGGGGTGGTGCCCATCCTGGTCGAGCTGGACGGCGACGTAAACGGCCACAAGTTCAGCGTGTCCGGCGAGGGCG	
	3′ TACCACTCGTTCCCGCTCCTCGACAAGTGGCCCCGCCGCGGGTAGGACCAGCTCGACCTGCCGCTGCATTTGCCGGTGTTCAAGTCGCACAGGCCGCTCCCGC	
2	AGGGCGATGCCACCTACGGCAAGCTGACCCTGAAGTTCATCTGCACCACCGGCAAGCTGCCCGTGCCCTGGCCCACCCTCGTGACCACCCTGACCTACGGCGT	
	TCCCGCTACGGTGGATGCCGTTCGACTGGGACTTCAAGTAGACGTGGTGGCCGTTCGACGGGCACGGGACCGGGTGGGAGCACTGGTGGGACTGGATGCCGCA	
3	GCAGTGCTTCAGCCGCTACCCCGACCACATGAAGCAGCACGACTTCTTCAAGTCCGCCATGCCCGAAGGCTACGTCCAGGAGCGCACCATCTTCTTCAAGGAC	
	CGTCACGAAGTCGGCGATGGGGCTGGTGTACTTCGTCGTGCTGAAGAAGTTCAGGCGGTACGGCGTTCCGATGCAGGTCCTCGCGTGGTAGAAGAAGTTCCTG	
4	GACGGCAACTACAAGACCCGCGCCGAGGTGAAGTTCGAGGGCGACACCCTGGTGAACCGCATCGAGCTGAAGGGCATCGACTTCAAGGAGGACGGCAACATCC	
	CTGCCGTTGATGTTCTGGGCGCGGCTCGACTTCAAGCTCCCGCTGTGGGACCACTTGGCGTAGCTCGACTTCCCGTAGCTGAAGTTCCTCCTGCCGTTGTAGG	
5	TGGGGCACAAGCTGGAGTACAACTACAACAGCCACAACGTCTATATCATGGCCGACAAGCAGAAGAACGGCATCAAGGTGAACTTCAAGATCCGCCACAACAT	
	ACCCCGTGTTCGACCTCATGTTGATGTTGTCGGTGTTGCAGATATAGTACCGGCTGTTCGTCTTCTTGCCGTAGTTCCACTTGAAGTTCTAGGCGGTGTTGTA	
6	CGAGGACGGCAGCGTGCAGCTCGCCGACCACTACCACGAGAACACCCCCATCGGCGACGGCCCCGTGCTGCTGCCCGACAACCACTACCTGAGCACCCAGTCC	
	GCTCCTGCCGTCGCACGTCGAGCGGCTGGTGATGGTCGTCTTGTGGGGGTAGCCGCTGCCGGGGCACGACGACGGGCTGTTGGTGATGGACTCGTGGGTCAGG	
7	GCCCTGAGCAAAGACCCCAACGAGAAGCGCGATCACATGGTCCTGCTGGAGTTCGTGACCGCCGCCGGGATCACTCTCGGCATGGACGAGCTGTACAAG	3′
	CGGGACTCGTTTCTGGGGTTGCTCTTCGCGCTAGTGTACCAGGACGACCTCAAGCACTGGCGGCGGCCCTAGTGAGAGCCGTACCTGCTCGACATGTTC	5′

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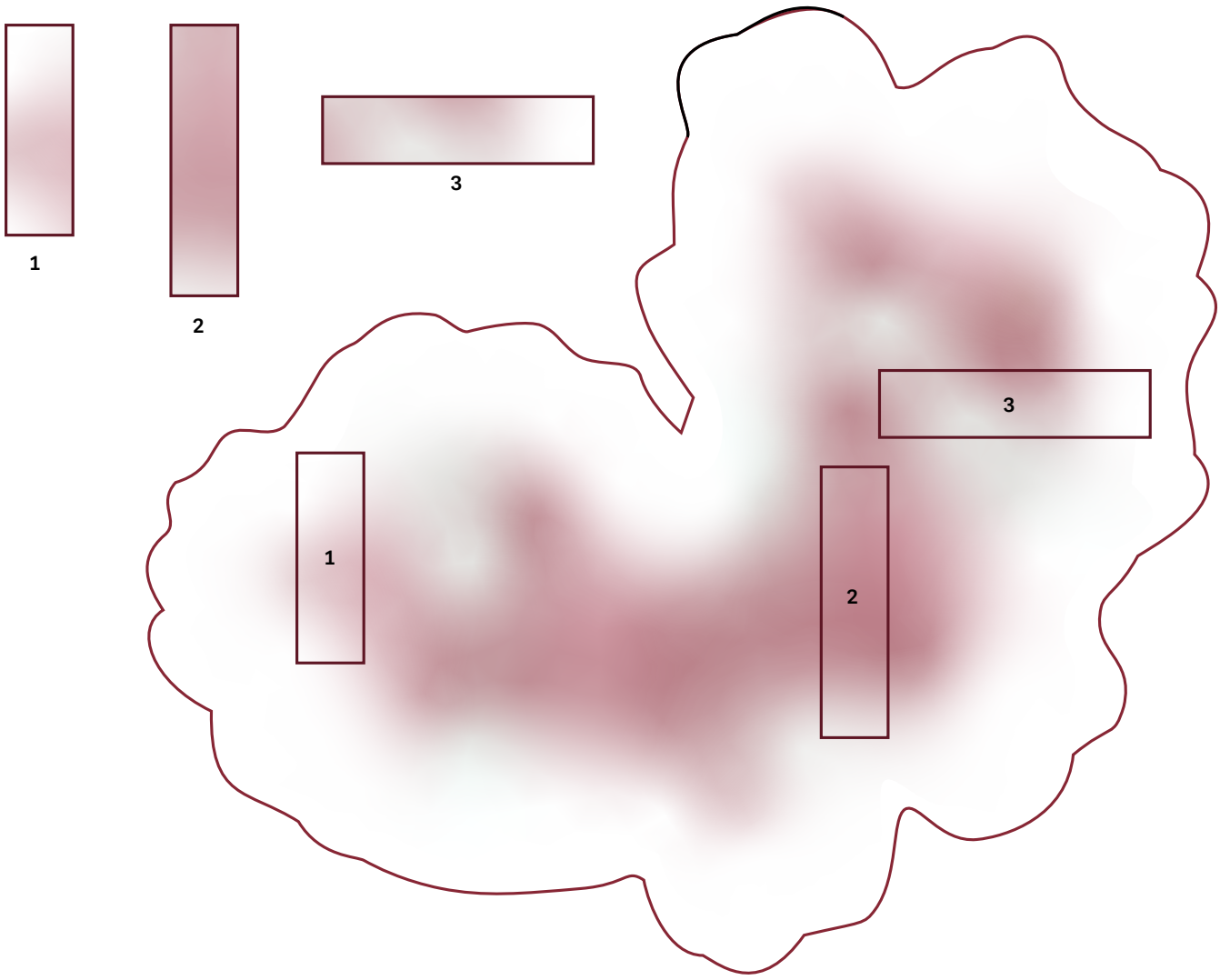
CRISPR Paper Simulation

Student Materials

Continued

Step 5

Cas9



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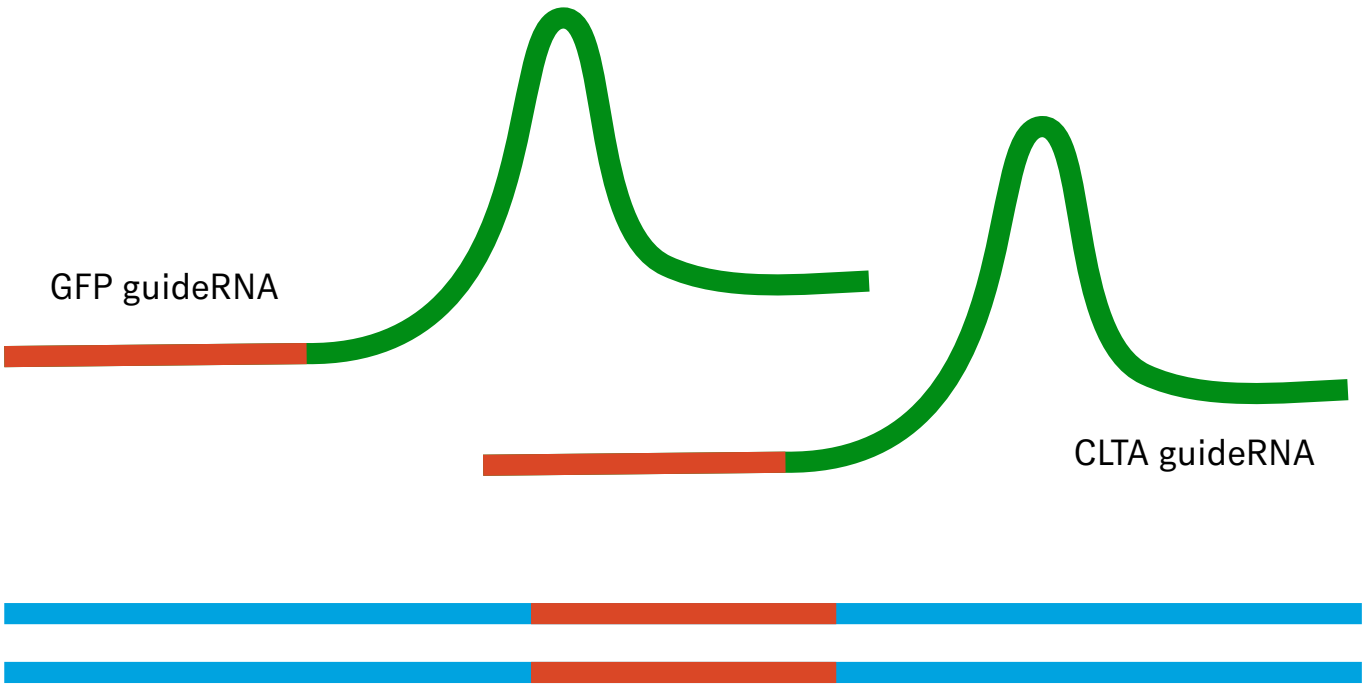
CRISPR Paper Simulation
Student Materials
Continued



CLTA gene with target sequence

Random nucleotides

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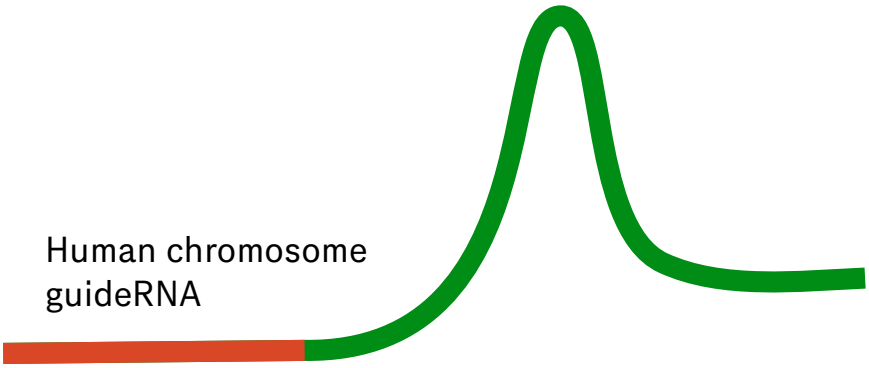
CRISPR Paper Simulation
Student Materials
Continued



Human chromosome with target sequence

Donor DNA with GFP gene

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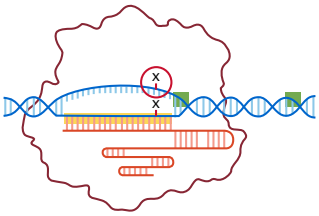
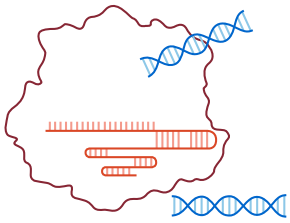
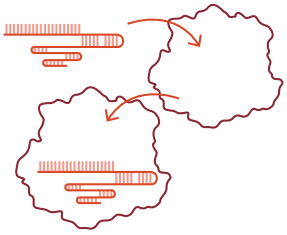
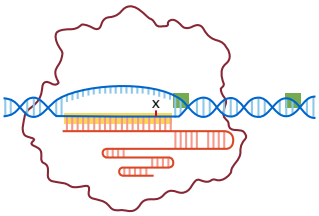
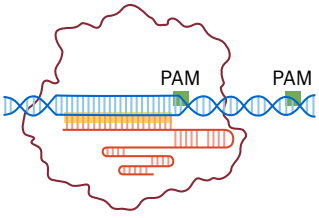
Sequencing CRISPR-Cas9

Directions
Read each step of Cas9 DNA cleavage and write the number of each step in sequential order.

Order	Description	Diagram
	Cas9 makes a double-stranded break in the DNA three base pairs upstream of the PAM.	
	The complex releases from the DNA. The Cas9-sgRNA complex releases the cut DNA and is ready to repeat the process.	
	Cas9 binds an sgRNA. Cas9 recognizes and binds the scaffold (tracrRNA) region of a sgRNA. The nucleotide sequence of the scaffold region determines its structure, which is tailored to fit within the Cas9 protein as a key fits into a lock.	
	The guiding region of the sgRNA binds to the target DNA sequence. The guiding region of the sgRNA attempts to base-pair with the DNA. If a match is found, the process continues. Otherwise, the complex releases and attempts to bind another PAM and target DNA sequence.	
	The Cas9-sgRNA complex binds to a PAM site on the target DNA. Cas9 requires a particular PAM sequence (5'-NGG) to be present directly adjacent to the protospacer sequence. When the Cas9-sgRNA complex recognizes and binds a PAM, it separates the DNA strands of the adjacent sequence to allow binding of the sgRNA.	

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CRISPR Editing in the Body for Blindness

First To Edit A Gene Inside The Body

The gene editing tool CRISPR (clusters of regularly interspaced short palindromic repeats) has been used successfully inside someone's body for the first time, according to scientists. This opens the way to treat diseases by operating directly with DNA, which is the chemical code of life.

CRISPR technology using the specialized area of DNA is a new and powerful tool for gene editing that allows scientists to alter the function of genes in the DNA itself.

In 2017, doctors used a tool called zinc fingers to first try an in-the-body gene editing. Because many scientists believe CRISPR is easier to use for locating and cutting DNA at a specific spot, there is a great deal of interest in the new research.

Treatment For Inherited Form Of Blindness

At the Casey Eye Institute at Oregon Health and Science University in Portland, Oregon, the new CRISPR treatment was used on a patient with an inherited form of blindness. However, no details were provided by the companies that make the treatment on the patient or when the surgery occurred.

Other companies, however, have offered insight into this treatment. Charles Albright is the chief scientific officer at Editas Medicine, a company in Cambridge, Massachusetts, that is developing the treatment with a company based in Dublin, Ireland, called Allergan. Albright said, "We literally have the potential to take people who are essentially blind and make them see. We think it could open up a whole new set of medicines to go in and change your DNA."

While it might take up to a month after treatment to know if the CRISPR treatment worked to restore vision, if the first series of attempts seem safe, there are plans to test it on 18 other children and adults.

New Era In Medicine

Jason Comander, at Massachusetts Eye and Ear in Boston, a hospital that has plans to enroll patients in the study, has said that the surgery marks "a new era in medicine" using a technology that "makes editing DNA much easier and much more effective."

The people taking part in the CRISPR gene editing study have a condition caused by a gene mutation which prevents the body from making a certain protein. The protein that is missing is needed to convert light entering the eyes into the signals to the brain to enable sight. People with this condition, called Leber congenital amaurosis, are often born with low vision and they frequently lose vision completely within a few years.

Editing Mutation

Standard gene therapy would simply supply a replacement gene. But, the replacement gene needed to treat this condition is too large to fit inside the disabled viruses that are used to carry it into the cells. Scientists are editing, or deleting, the mutation instead. By making two cuts on either side of the mutation to delete it, the hope is that the edges of the DNA will come together and allow the newly edited gene to work properly.

Doctors think they need to repair between one-tenth to one-third of the mutated cells to restore vision. The procedure is done in surgery under general anesthesia. Doctors drip three drops of fluid through a tube the size of a human hair. The fluid contains the gene editing mechanism and is placed just beneath the retina, which is the lining at the back of the eye. The retina contains light-sensing cells.

Eric Pierce is a scientist and study leader at Massachusetts Eye and Ear who was not involved in this first case. However, Pierce helped with the testing of a gene therapy called Luxturna for a different type of inherited blindness and who consulted for Editas. Because these cells do not divide, Pierce said, "Once the cell is edited, it's permanent and that cell will persist hopefully for the life of the patient."

In animal tests, according to Charles Albright, scientists were able to correct half of the cells with the treatment. Infections and bleeding are relatively rare complications. And doctors say that the eye surgery itself poses little risk.

Pierce, commented that one of the biggest risks from gene editing is that CRISPR could make unintended changes in other genes. The companies have worked diligently to minimize that risk and to ensure that the treatment will cut only the intended area.

Continues next page >

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CRISPR Editing in the Body for Blindness

Continued

Independent Experts Optimistic

Independent experts were optimistic about the new study with gene editing. Jean Bennett is a University of Pennsylvania researcher who helped test Luxturna at the Children's Hospital of Philadelphia, Pennsylvania. "The gene editing approach is really exciting. We need technology that will be able to deal with problems like these large genes," she said.

Three families looking for solutions to inherited blindness have called her about it. "It's a terrible disease," she said. "Right now they have nothing."

Kiran Musunuru is a gene editing expert at the University of Pennsylvania. He has observed that the gene editing tool stays in the eye and does not travel to other parts of the body, so "if something goes wrong, the chance of harm is very small," he said. "It makes for a good first step for doing gene editing in the body."

He noted that the treatment seems likely to work, based on tests in mice, monkeys, and human tissue.

Other Gene Editing

Gene editing has applications beyond the treatment of inherited blindness. Sangamo Therapeutics has been testing zinc finger gene editing to treat metabolic diseases. Other scientists are using CRISPR to edit cells outside the body to try to treat sickle cell disease, cancer, and other diseases.

All of the studies in the United States have been done openly with the government regulators' approval. However, some scientists do not work within the standard approvals and regulations. In 2018, a Chinese scientist named He Jiankui received international scorn for his work with CRISPR.

Jiankui edited embryos at the time of conception with CRISPR to attempt to make them resistant to the AIDS virus. These types of changes to an embryos' DNA can pass to future generations. This is completely different from the work being done in adults, which does not pass forward, to treat certain diseases.

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CRISPR Editing in the Body for Blindness Questions

Directions
Read the article, CRISPR Editing in the Body for Blindness, and answer the questions.

1. Read the following paragraph from the section *New Era In Medicine*.

   Jason Comander, at Massachusetts Eye and Ear in Boston, a hospital that has plans to enroll patients in the study, has said that the surgery marks "a new era in medicine" using a technology that "makes editing DNA much easier and much more effective."

   Which idea is BEST supported by this paragraph?

   a. Treatments to edit DNA will be limited to diseases causing blindness.

   b. Doctors are encouraged by the possibilities of the CRISPR technology.

   c. Many patients are interested in participating in the gene editing study.

   d. Medical treatments will soon be dominated by technological treatments.

2. Why did the author conclude the article by explaining that the studies have government regulators' approval?

   a. to confirm that the studies are not taking unnecessary risks with patients

   b. to show that government approval is required to fund experimental treatments

   c. to explain the rigorous process of getting approval for experimental treatments

   d. to describe the unease that patients have with treatments that are not widely tested

3. Read the following statement.

   Scientists believe CRISPR technology can be more widely used.

   Which sentence from the article BEST supports the statement above?

   a. The companies have worked diligently to minimize that risk and to ensure that the treatment will cut only the intended area.

   b. Jean Bennett is a University of Pennsylvania researcher who helped test Luxturna at the Children's Hospital of Philadelphia, Pennsylvania. "The gene editing approach is really exciting. We need technology that will be able to deal with problems like these large genes," she said.

   c. Musunuru is a gene editing expert at the University of Pennsylvania. He noted that the treatment seems likely to work, based on tests in mice, monkeys, and human tissue.

   d. Other scientists are using CRISPR to edit cells outside the body to try to treat sickle cell disease, cancer, and other diseases.

4. How does the author analyze the claim that the CRISPR technology might be used to successfully treat diseases?

   a. by offering expert opinions, describing the treatment, and addressing concerns about risks of the treatment

   b. by providing evidence of patients who have successfully received the treatment and the doctors who treated them

   c. by giving the details of government approval of the technology and describing successful outcomes in trial treatments

   d. by explaining the treatments that have been used in the past to correct DNA and showing that CRISPR technology is superior

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CRISPR Editing in the Body for Blindness Questions

Continued

5. Write a short paragraph that explains the central idea of the article. Use at least two details from the article to support your response.

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What is CRISPR? Why are Doctors So Excited About It?

CRISPR stands for clusters of regularly interspaced short palindromic repeats and it is a gene-editing tool that can be used to edit a person's DNA at a particular point along the strand. It can change DNA permanently and has been in use in labs for some time. Now, however, it is being considered as a treatment tool for diseases such as cancer and other blood disorders.

Doctors are excited because the first attempt to use this tool in the United States has seen promising results. It was used to edit the genes of three cancer patients and, so far, seems to be safe for that use, with minimal side effects. The CRISPR tool allowed doctors to take immune cells from the patients' own blood and alter the genes in the cells so that they might help to recognize and fight the cancer.

The University of Pennsylvania's Dr. Edward Stadtmauer is the leader of the study of CRISPR's use with cancer patients. "It's the most complicated genetic, cellular engineering that's been attempted so far," he said. "This is proof that we can safely do gene editing of these cells."

The University of Pennsylvania, along with Tmunity Therapeutics, a biotech company, and the Parker Institute for Cancer Immunotherapy in San Francisco have invested money in the company. Some study leaders have invested as well, and may share in benefits from the study, like patents and licenses on the technology used.

Three patients were selected for the initial study. Each had already failed multiple standard treatments. Two of the patients have a blood cancer called multiple myeloma. The third has a cancer known as sarcoma, which forms in the soft or connective tissue.

T Cells Modified; Genes Deleted

T cells, the immune system's super soldiers, were removed from their blood by filtering them and modifying them in the lab. The T cells were then returned to the patients via an IV, as a one-time treatment. The desired outcome is that the modified cells would multiply and create the effect of a living drug within their bodies.

Stadtmauer said that the cells have survived and have been multiplying as was intended. "This is a brand new therapy," he said, "so it's not clear how soon any anti-cancer effects will be seen. Following these patients longer, and testing more of them, will tell."

The gene-editing adds a new feature to the cells to help them attack the disease, while it deletes three genes that might have been preventing their ability to attack it as needed.

The study showed varied results after two to three months. One patient was stable, and another's cancer has continued to worsen. The treatment was too recent in the third patient to know the response. Fifteen more patients are expected to be treated to assess the safety and efficacy of the trials. Dr. Aaron Gerds, an independent cancer treatment specialist at the Cleveland Clinic in Ohio says, "It's very early, but I'm incredibly encouraged by this." Other cell therapies for blood cancers "have been a huge hit, taking diseases that are uncurable and curing them," Gerds said, adding that gene editing may be a way to improve on those.

China Conducted First Studies

Chinese scientists have reportedly conducted the first studies of this type for cancer patients, but this is the first one outside of China. It took more than two years to get United States government approval, as the treatment is so innovative.

This study removes cells from the patient's body, modifies them, and gives them back to the patient. It does not attempt to change the DNA within a person's body. The cells that are returned are now super-powered to fight their cancer—a form of immunotherapy that encourages a stronger immune system response in order to fight disease.

The American Society of Hematology, which focuses on patients with blood disorders, released the early results and more details will be given at its annual conference.

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What is CRISPR? Why are Doctors So Excited About It? Questions

Directions
Read the article, What is CRISPR? Why are Doctors So Excited About It?, and answer the questions.

1. According to the article, the study on gene editing to treat cancer has had mixed results up until this point.

   Which statement BEST supports the idea outlined above?

   a. The study showed varied results after two to three months. One patient was stable, and another's cancer has continued to worsen. The treatment was too recent in the third patient to know the response. Fifteen more patients are expected to be treated to assess the safety and efficacy of the trials.

   b. Dr. Aaron Gerds, an independent cancer treatment specialist at the Cleveland Clinic in Ohio says, "It's very early, but I'm incredibly encouraged by this.'

   c. Each had already failed multiple standard treatments. Two of the patients have a blood cancer called multiple myeloma. The third has a cancer known as sarcoma, which forms in the soft or connective tissue.

   d. "This is a brand new therapy," he said, "so it's not clear how soon any anti-cancer effects will be seen. Following these patients longer, and testing more of them, will tell."

2. Read the list of sentences from the article.

   The cells that are returned are now super-powered to fight their cancer — a form of immunotherapy that encourages a stronger immune system response in order to fight disease. (1)

   Chinese scientists have reportedly conducted the first studies of this type for cancer patients, but this is the first one outside of China. (2)

   It took over two years to get the United States government regulators to approve it as the treatment is so innovative. (3)

   The American Society of Hematology, which focuses on patients with blood disorders, released the early results and more details will be given at its annual conference. (4)

   Which two sentences taken together provide the BEST evidence to support the idea that gene editing as a form of cancer treatment is relatively new?

   a. (1) and (2)
   b. (1) and (4)
   c. (2) and (3)
   d. (3) and (4)

3. Which of the following details is MOST important to the development of the central ideas?

   a. It can be used to change DNA permanently and has been in use in labs for some time.

   b. Dr. Aaron Gerds, an independent cancer treatment specialist at the Cleveland Clinic in Ohio says, "It's very early, but I'm incredibly encouraged by this.'

   c. The American Society of Hematology, which focuses on patients with blood disorders, released the early results and more details will be given at its annual conference.

   d. The CRISPR tool allowed doctors to take immune cells from the patients' own blood and alter the genes in the cells so that they might help to recognize and fight the cancer.

4. Which of the following details is MOST important to the development of the central ideas?

   a. focusing on how cancer patients felt after they received the gene editing treatment

   b. describing some of the side effects patients experienced after gene editing

   c. comparing the specific results of gene editing in both China and the United States

   d. explaining how the gene editing treatment was conducted and what the results were

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What is CRISPR? Why are Doctors So Excited About It? Questions

Continued

5. Make and support a claim about why someone should read this text. What makes this text worth reading? What will a reader gain or what might a reader do after reading this? Support your response with specific details from the text.

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Infographic Assignment
CRISPR Technology: Benefits and Concerns

Objective

Your job today is to summarize what you have learned about CRISPR technology and describe the benefits and concerns of its applications.

Assignment Criteria

1. *List* and *describe* the steps involved in using CRISPR-Cas9.

2. *Describe* the purpose of CRISPR.

3. *List* and *describe* three different benefits of this technology.

4. *List* and *describe* three different concerns of the use of this technology.

5. Provide pictures, diagrams, and relevant statistics that would visually *summarize* main ideas.

Assignment Criteria

Is CRISPR Worth the Risk? | Yale Insights

Policy Issues What are the Ethical Concerns of Genome Editing?

How CRISPR Tools are Unlocking New Ways to Fight Disease

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Infographic Rubric

Score	3	2	1
Procedure	All steps were properly identified and described.	All steps were identified but not properly described.	Many components were missing or not accurate.
Purpose	The description of the purpose of CRISPR is accurate and clear.	A description of the purpose was provided but was not accurate or clear.	A description of the purpose was not provided.
Benefits	Three different benefits were listed and described in enough detail for the reader to understand.	Two different benefits were listed and described in enough detail for the reader to understand.	Benefits were listed and described but were not accurate or not in enough detail for the reader to understand.
Concerns	Three different concerns were listed and described in enough detail for the reader to understand.	Two different concerns were listed and described in enough detail for the reader to understand.	Concerns were listed and described but were not accurate or not in enough detail for the reader to understand.
Visuals	Multiple use of pictures, models, or statistics to visually summarize important information.	Some use of pictures, models, or statistics to visually summarize important information.	Minimal use of pictures, models, or statistics to visually summarize important information.
Final Score			

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