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Class: _____

Explainer: How CRISPR Works

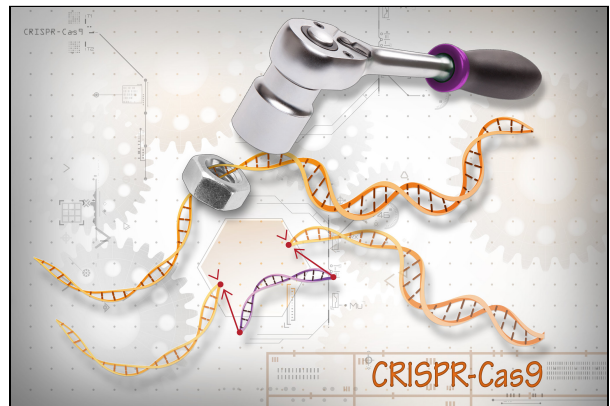
This technique lets scientists edit DNA in plants and animals

By Tina Hesman Saey
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In this informational text, Tina Hesman Saey discusses how scientists are able to edit organisms' genes. As you read, takes notes on how CRISPR changes DNA.

- [1] Scientists usually shy away from using the word miracle. Unless they're talking about the gene-editing tool called CRISPR, that is. "You can do anything with CRISPR," some say. Others just call it amazing.

CRISPR stands for "clustered regularly interspaced short palindromic repeats." Those repeats are found in bacteria's DNA.¹ They are actually copies of small pieces of viruses. Bacteria use them like collections of mug shots to identify bad viruses. Cas9 is an enzyme² that can cut apart DNA. Bacteria fight off viruses by sending the Cas9 enzyme to chop up viruses that have a mug shot in the collection. Scientists recently figured out how bacteria do this. Now, in the lab, researchers use a similar approach to turn the microbe's virus-fighting system into the hottest new lab tool.



"CRISPR-Cas9 Editing of the Genome" by
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This CRISPR/Cas9 tool was first described in 2012 and 2013. Science labs around the world soon started using it to alter an organism's genome — the entire set of its DNA instructions.

This tool can quickly and efficiently tweak almost any gene in any plant or animal. Researchers already have used it to fix genetic diseases in animals, to combat viruses and to sterilize³ mosquitoes. They have also used it to prepare pig organs for human transplants and to beef up the muscles in beagles.

1. the molecule that contains the genetic code of an organism
2. a protein molecule that causes chemical reactions
3. to make something free from bacteria

- [5] So far CRISPR's biggest impact has been felt in basic biology labs. This low-cost gene editor is easy to use. That has made it possible for researchers to delve into the basic mysteries of life. And they can do it in ways that used to be difficult if not impossible.

Robert Reed is a developmental biologist at Cornell University in Ithaca, N.Y. He likens CRISPR to a computer mouse. "You can just point it at a place in the genome and you can do anything you want at that spot."

At first, that meant anything that involved cutting DNA. CRISPR/Cas9 in its original form is a homing device⁴ (the CRISPR part) that guides molecular scissors (the Cas9 enzyme) to a target section of DNA. Together, they work as a genetic-engineering cruise missile that disables or repairs a gene, or inserts something new where the Cas9 scissors has made some cuts. Newer versions of CRISPR are called "base editors." These can edit genetic material one base⁵ at a time, without cutting. They're more like a pencil than like scissors.

Here's how it works

Scientists start with RNA. That's a molecule that can read the genetic information in DNA. The RNA finds the spot in the nucleus of a cell where some editing activity should take place. (The nucleus is a compartment in a cell where most of the genetic material is stored.) This guide RNA shepherds⁶ Cas9 to the precise spot on DNA where a cut is called for. Cas9 then locks onto the double-stranded DNA and unzips it.

This allows the guide RNA to pair up with some region of the DNA it has targeted. Cas9 snips the DNA at this spot. This creates a break in both strands of the DNA molecule. The cell, sensing a problem, repairs the break.

- [10] Fixing the break might disable a gene (the easiest thing to do). Alternatively, this repair might fix a mistake or even insert a new gene (a much more difficult process).

Cells usually repair a break in their DNA by gluing the loose ends back together. That's a sloppy process. It often results in a mistake that disables some gene. That may not sound useful — but sometimes it is.

Scientists cut DNA with CRISPR/Cas9 to make gene changes, or mutations. By comparing cells with and without the mutation, scientists can sometimes figure out what a protein's normal role is. Or a new mutation may help them understand genetic diseases. CRISPR/Cas9 also can be useful in human cells by disabling certain genes — ones, for instance, that play a role in

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- 4. a device that provides direction to a location
 - 5. There are four main chemical bases for DNA.
 - 6. directs

inherited diseases.

“The original Cas9 is like a Swiss army knife with only one application: It’s a knife,” says Gene Yeo. He is an RNA biologist at the University of California, San Diego. But Yeo and others have bolted other proteins and chemicals to the dulled blades. That has transformed that knife into a multifunctional tool.

CRISPR/Cas9 and related tools can now be used in new ways, such as changing a single nucleotide base — a single letter in the genetic code — or adding a fluorescent protein to tag a spot in the DNA that scientists want to track. Scientists also can use this genetic cut-and-paste technology to turn genes on or off.

- [15] This explosion of new ways to use CRISPR hasn’t ended. Feng Zhang is a molecular biologist at the Massachusetts Institute of Technology in Cambridge. He was one of the first scientists to wield the Cas9 scissors. “The field is advancing so rapidly,” he says. “Just looking at how far we have come... I think what we’ll see coming in the next few years will just be amazing.”

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Text-Dependent Questions

Directions: For the following questions, choose the best answer or respond in complete sentences.

1. PART A: Which statement identifies the central idea of the text?
 - A. CRISPR can only be used on organisms with genetic diseases.
 - B. CRISPR has developed to alter DNA in impactful ways.
 - C. CRISPR is at risk of being used unethically.
 - D. CRISPR is dangerous to use on humans.

2. PART B: Which detail from the text best supports the answer to Part A?
 - A. "Bacteria fight off viruses by sending the Cas9 enzyme to chop up viruses that have a mug shot in the collection. Scientists recently figured out how bacteria do this." (Paragraph 2)
 - B. "CRISPR/Cas9 in its original form is a homing device (the CRISPR part) that guides molecular scissors" (Paragraph 7)
 - C. "Cells usually repair a break in their DNA by gluing the loose ends back together. That's a sloppy process." (Paragraph 11)
 - D. "CRISPR/Cas9 also can be useful in human cells by disabling certain genes — ones, for instance, that play a role in inherited diseases." (Paragraph 12)

3. Which statement describes how the author introduces CRISPR in the text?
 - A. She describes her own experiences using the tool.
 - B. She acknowledges the risks associated with the tool.
 - C. She emphasizes scientists' positive response to the tool.
 - D. She discusses the benefits and disadvantages of the tools.

4. How does paragraph 4 contribute to the development of ideas in the text?
 - A. It outlines some of the disadvantages of using CRISPR.
 - B. It shows how CRISPR is creating new species of animals.
 - C. It suggests that CRISPR is better used on animals than humans.
 - D. It provides examples of the effects of changing DNA using CRISPR.

5. What is the meaning of "delve" in paragraph 5?
 - A. to build
 - B. to predict
 - C. to examine
 - D. to improve

6. Which statement is the likely reason Robert Reed "likens CRISPR to a computer mouse" in paragraph 6?
- A. It is a small tool.
 - B. It is old technology.
 - C. It is easy to navigate.
 - D. It is shaped like a mouse.
7. How does the older version of CRISPR compare to the newer versions, "base editors"? (Paragraph 7)
- A. Base editors only erase DNA.
 - B. Base editors cannot cut DNA.
 - C. Base editors undo changes made to DNA.
 - D. Base editors can edit DNA without cutting it.
8. What is the author's purpose in paragraphs 13-14?

Discussion Questions

Directions: Brainstorm your answers to the following questions in the space provided. Be prepared to share your original ideas in a class discussion.

1. In the text, the author discusses the benefits of genetically editing animals' genes. How might gene editing improve food production and crop yields? Do you think there could be a downside to genetically editing plants or animals? Why or why not?
2. In the text, the author discusses editing human DNA to protect them from inherited genes. Do you think that humans' genes should be modified? Why or why not?