Biotechnology
CRISPR
(Estimated running time: 05:15)

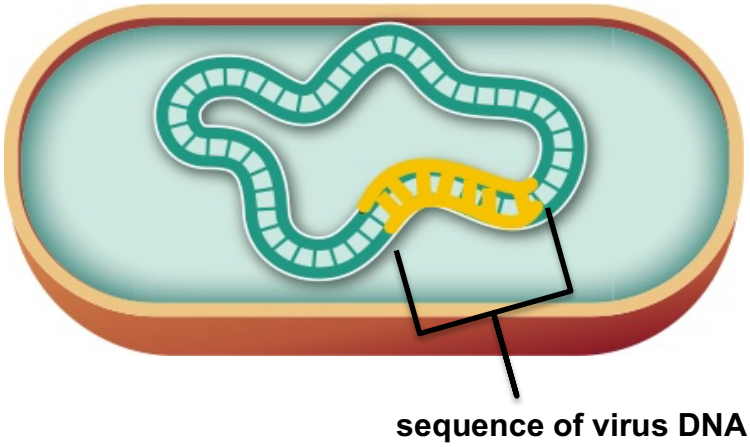
1.
A technology called CRISPR is proving to be a revolutionary gene-editing tool. CRISPR stands for "Clustered Regularly Interspaced Short Palindromic Repeats."

[Synced to narration:
Title graphic for **CRISPR** fades up. In time with narration, reveal definition of the acronym.]

CRISPR
"Clustered Regularly Interspaced Short Palindromic Repeats"

The name describes the addition of DNA that has originally come from viruses to produce a specific organization within the genomes of bacteria.

[Synced to narration:
Use bacterium from FIG 6-4 (3e). Zoom in on the bacterium, showing a **sequence of virus DNA** (labeled) incorporated into the loop of bacterial DNA.]



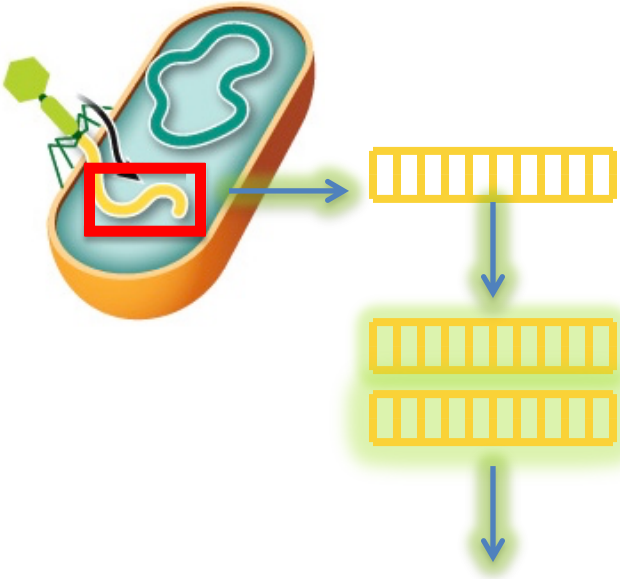
It turns out that bacteria commonly incorporate virus DNA into their own to serve as a sort of immune system that can help thwart infection by potentially lethal viruses.

[Sync to narration:
Cut to different view of bacterium containing the virus DNA, and animate a virus (from FIG 13-8 (3e)) attempting to infect the bacterial cell. Animators: maybe recolor this virus—dark red or black—so that it's a different color from the virus that attacks it in the next panel.]

2.

When a virus first infects a bacterium, the bacterium keeps a record of the encounter. It copies some of the virus' DNA and integrates it with its own.

[Synced to narration:
Use FIG 13-8 (3e) panel 2, animate virus attacking bacterium and inserting genetic material into the cell. Then zoom in on the virus DNA (use DNA from first panel from new FIG 7-7 (4e), recolor it yellow to match virus DNA from FIG 13-8). Show DNA being copied and then being integrated into the loop of its own DNA.]

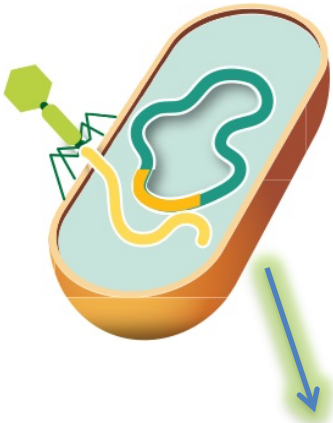


Note: zoom in on virus DNA that was introduced to the bacterium

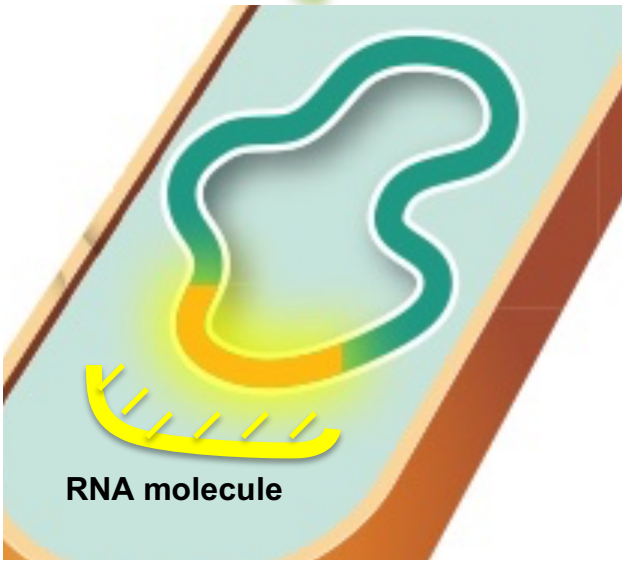
Note: bacterium makes a copy of the virus DNA

Note: bacterium integrates the copied virus DNA into its own loop of DNA

When the same type of virus invades again, the bacterium uses the stored virus DNA to quickly produce an RNA molecule.
[Synced to narration:
FIG 13-8 (3e) panel 2, a virus attacks the bacterium. We zoom in to see inside the bacterium. The stored virus DNA is used to generate the **RNA molecule** (label in figure).]

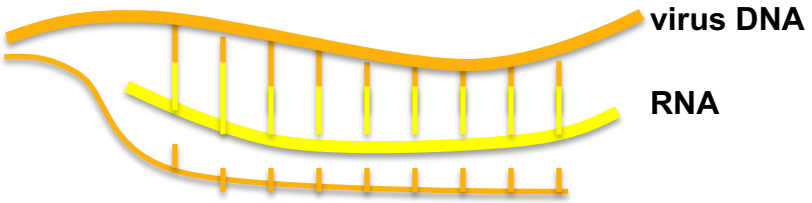


Note: virus attacks the bacterium and inserts virus DNA



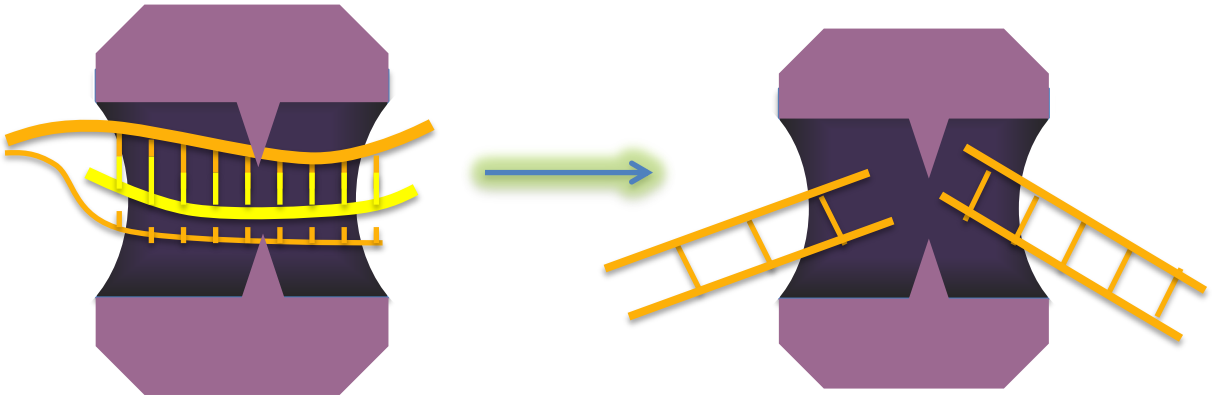
Note: zoom in to the interior of the bacterium. Highlight the yellow sequence of virus DNA in the loop of genetic material, and then have the RNA molecule fade in, indicating that it has been generated based on the virus DNA sequence.
Animators: can you make the RNA molecule look a little more like the one in the next frame?

This RNA molecule acts as a sort of homing device, finding and binding to the infecting virus' DNA.
[Synced to narration:
The RNA (labeled in animation) strand finds and binds to the virus DNA (labeled in animation).]



After latching onto the virus DNA, the bacterium employs a DNA-cutting enzyme, called Cas9, to cleave the virus DNA in two, rendering it harmless. An effective way for a bacterium to remember and resist virus infections, CRISPR turns out to be present in almost half of all bacteria.

[Synced to narration:
Cas9 enzyme from new FIG 7-7 (4e)—redrawn here (label in the animation)—fades up. As the enzyme moves along the strand, it cleaves the virus DNA in two.]



Cas9 enzyme

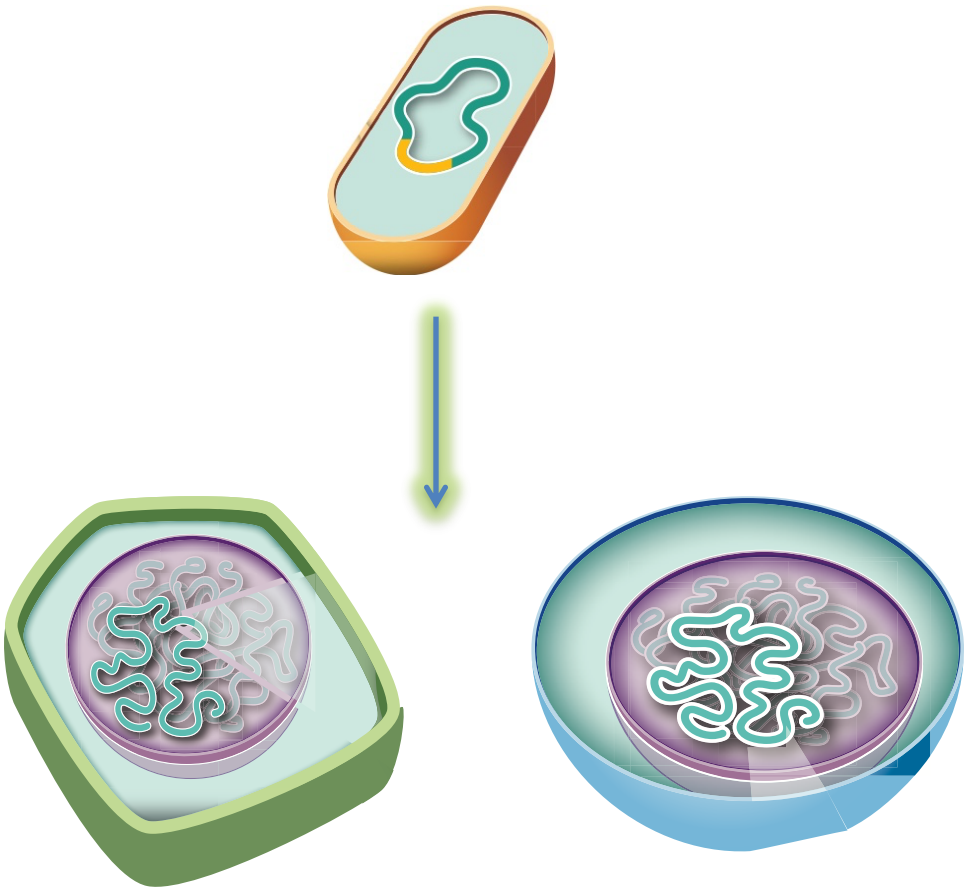
Note: Cas9 enzyme moves along strand of virus DNA with RNA bound to it.

Note: Cas9 enzyme cleaves the virus DNA into two harmless pieces.
Animators: main thing here is to show that the cut doesn't leave a "clean" edge on the virus DNA; there should be some overhanging "backbone".

3.

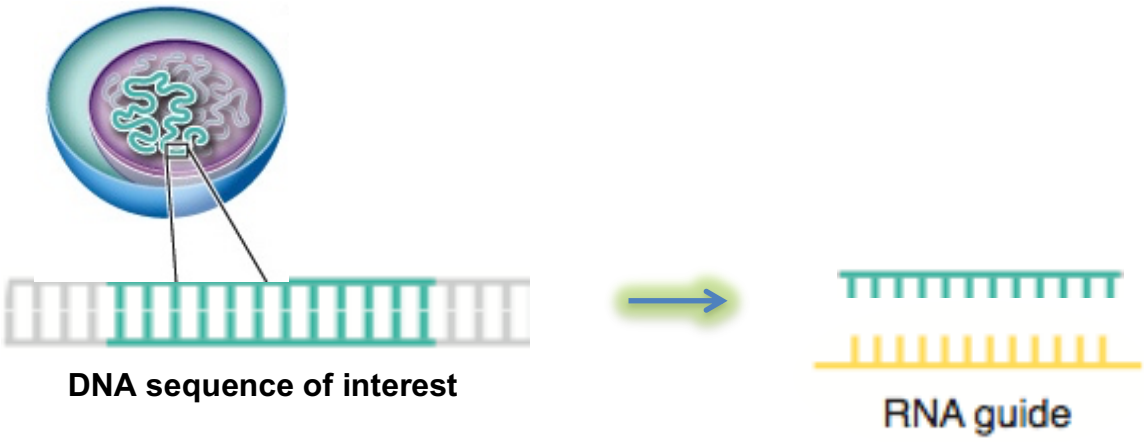
Although CRISPR is a tool initially discovered and isolated from bacteria, adapting the CRISPR system for biotechnology—including editing the genomes of eukaryotic organisms such as plants and animals—is straightforward.

[Synced to narration:
Bacterial cell fades up.
Bacterial cell fades out, and plant cell (from FIG 5-33) and animal cell (from FIG 5-27) fade up as narrator reads “adapting the CRISPR system for biotechnology—including editing the genomes…”.]



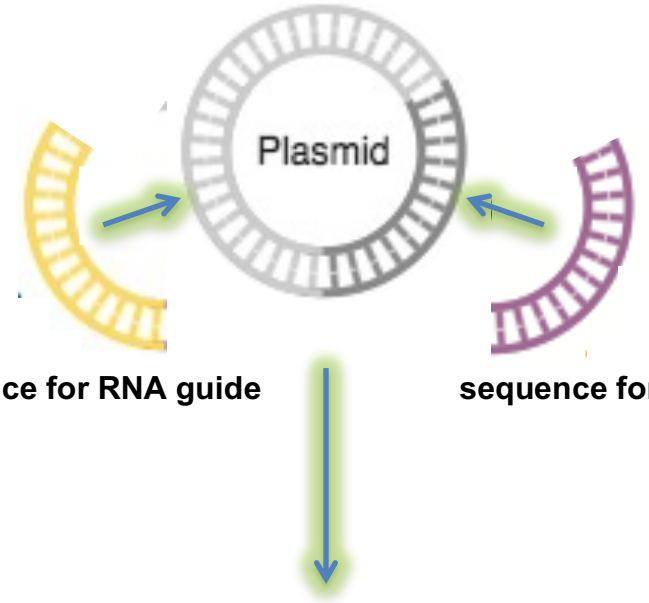
After identifying a particular DNA sequence of interest—maybe to fix or inactivate a defective gene, researchers isolate a DNA sequence that will be used to synthesize an RNA guide molecule with a sequence that matches the target gene to be sliced.

[Synced to narration:
Plant cell fades out; animal cell remains on the screen. We zoom in on the animal cell. Using the DNA sequence illustration from new FIG 7-7 (4e) have the **DNA sequence of interest** (label in the animation) pop out from the cell. Then show single strand of the DNA being used to generate the **RNA guide** (label in animation).]

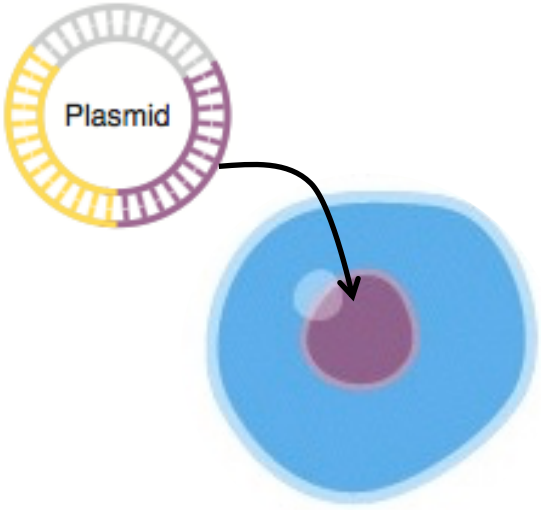


The sequences for the RNA guide and Cas9 enzyme are introduced to target cells, using a plasmid as a vector.

[Synced to narration:
The **sequence for RNA guide** and **sequence for Cas9 enzyme** (label in the animation) are inserted into the plasmid. Animate the plasmid (containing the RNA guide sequence and Cas9 sequence) being introduced to the **target cell** (this cell figure was pulled from FIG 6-20 (3e).]



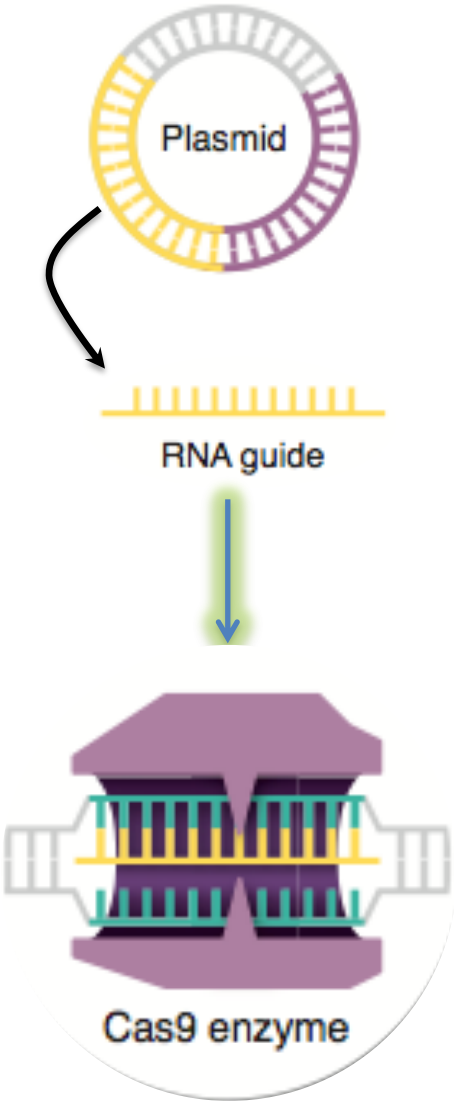
Note: RNA guide sequence + Cas9 sequence are inserted into the plasmid



Note: plasmid shrinks down as the target cell gets larger on the screen. The black line/arrow fades up, showing that the plasmid is being introduced into the cell. Then, the plasmid shrinks down and disappears into the target cell's nucleus.

Using the RNA sequence from the plasmid, the target cell produces the RNA guide. The RNA guide then leads the Cas9 enzyme to the desired location on the DNA, and the Cas9 enzyme cuts the DNA there.

[Sync to narration:
From the **plasmid** (labeled), the cell generates the **RNA guide** (labeled). The **RNA** guide then binds to the sequence of DNA from the target cell. Next, the **Cas9 enzyme** (labeled) from FIG 7-7 (4e) moves along the DNA strand. Animate the Cas9 enzyme cutting the DNA in two pieces.]

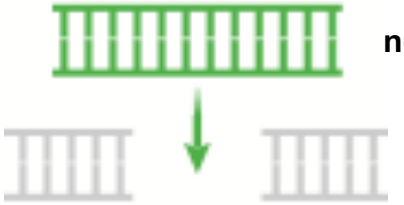


Note: show the plasmid containing the RNA sequence and Cas9 sequence. Arrow animates in from the RNA sequence on the plasmid, RNA guide molecule fades up on screen.

Note: The RNA guide binds to the target cell's DNA. Cas9 moves along the strand, and then cleaves the DNA into two pieces.

At the location where the DNA is cut, a sequence can then be inserted that repairs, or alters in some other way, the host cell's DNA.

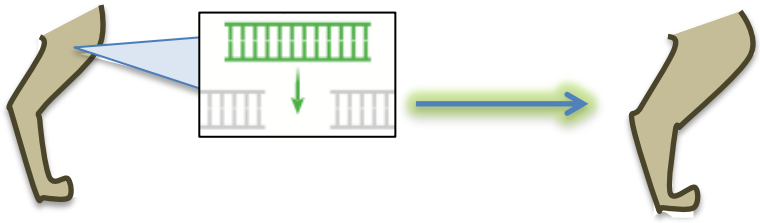
[Synced to narration:
Animate the **new DNA sequence** (label in the animation) from FIG 7-7 (4e) being inserted into location where section of DNA has been cut.]



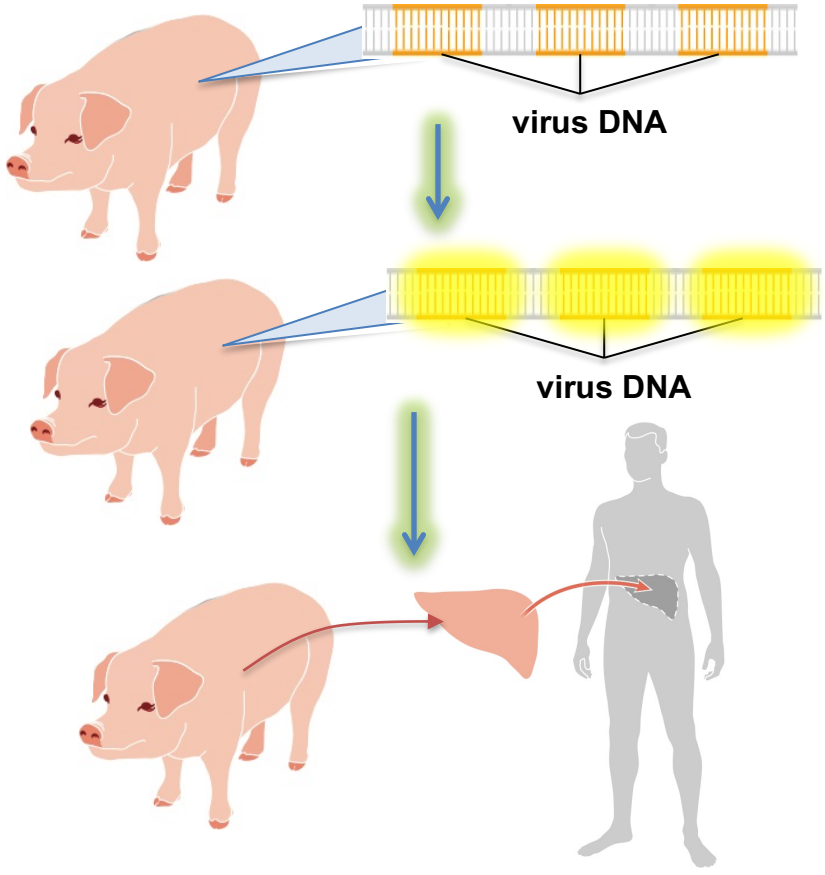
4.
CRISPR is considered a breakthrough in biotechnology because the ability to target and snip DNA precisely at a particular sequence opens the door to changing an organism's genes in almost any way imaginable. Just a few of the initial successful uses of CRISPR reveal the wide variety of potential applications.

[Synced to narration:
Reuse the same sequence from above, showing Cas9 cutting the DNA and then a new sequence of DNA being inserted into the resultant gap.]

Researchers have successfully increased muscle mass in the hind leg of a dog by inactivating a gene that inhibits muscle growth.
[Synced to narration:
Illustrate the hind leg of a dog that has very slender muscle mass, have a callout that pops up, showing gene being altered, and then have it cross dissolve to drawing of a hind leg with noticeably more muscle mass.]

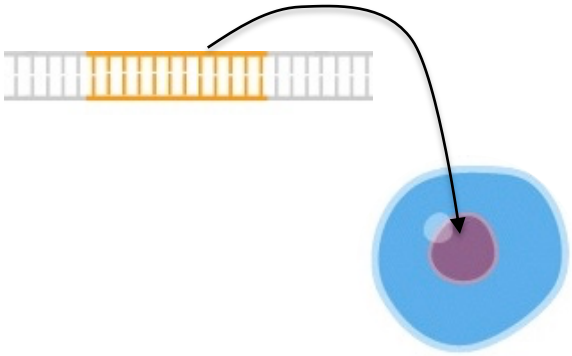


In pigs, researchers have found a way to simultaneously edit 62 sequences of virus DNA, which are encoded in pigs' genomes and are known to infect humans, in a way that could facilitate organ transplants into human recipients.
[Synced to narration:
Use pig figure from FIG 13-28 (3e). For the call-out, illustrate a chromosome that includes pieces of **virus DNA** (labeled). Use a highlight effect to indicate that the virus DNA sequences were altered. Have chromosome fade out, have arrow animate in, showing liver coming from the pig, and then arrow leading to the human figure (FIG 3-15, Phelan 3e).]

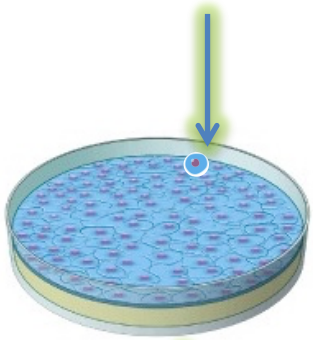


Researchers also have introduced mutations into human stem cells, producing tissue with disease properties that can serve as a model cellular system for studying common human diseases, such as cancer.

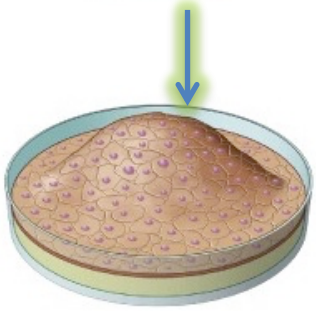
[Sync with narration:
Mutated gene sequence with arrow pointing to nucleus of stem cell. Then have that cell shrink down and blend into a few other cells in the Petri dish (FIG 6-16 (3e)). Next, have the cells change color and continue to divide and pile on top of each other, forming a tumor.]



Note: Show "mutated" sequence. The black arrow fades up, and the altered gene follows the path of the arrow and then disappears into the nucleus of the cell.



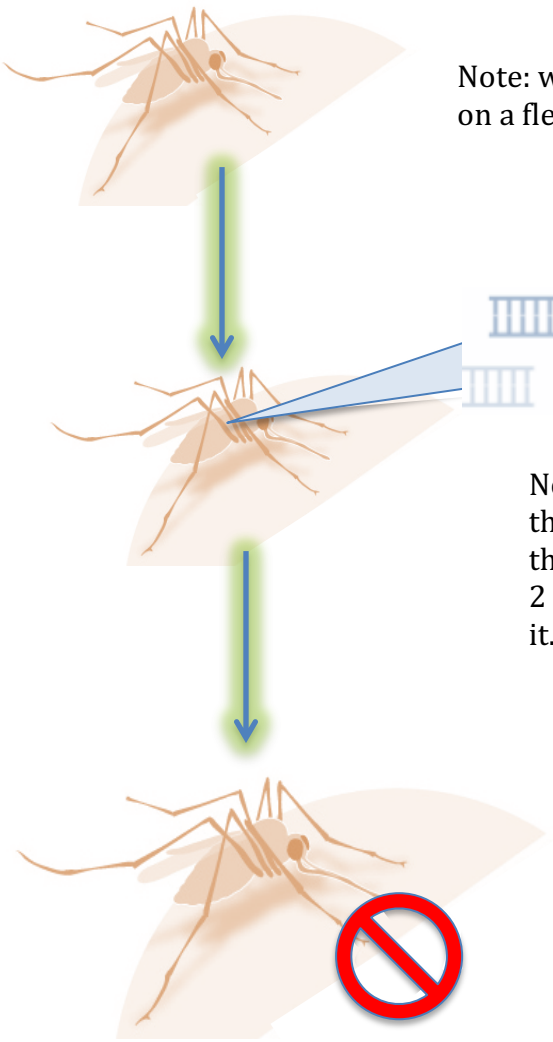
Note: Next, the cell shrinks down and "disappears" into other cells in the Petri dish.



Note: We see the cells in the Petri dish starting to divide and pile up, forming a tumor, indicating that cells have become cancerous.

CRISPR also has the potential to fight some of the most harmful diseases to humans. Significant work has been aimed at altering mosquito biochemistry so they cannot host or transmit the parasite that causes malaria—a measure that could save half a million lives every year.

[Sync to narration:
Mosquito fades up (FIG 13-23 3e). The call-out shows an edited strand of DNA with two new sequences being added to it. The mosquito bites the individual but is incapable of infecting them with the malarial parasite.]



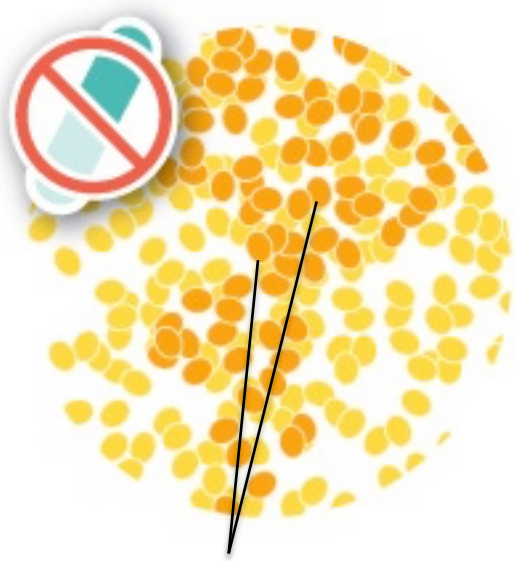
Note: we first see the mosquito, sitting on a fleshy-looking background.

Note: a call-out appears from the body of the mosquito. We see a strand of DNA that has had 2 sequences spliced out, and 2 alternate sequences are being added to it.

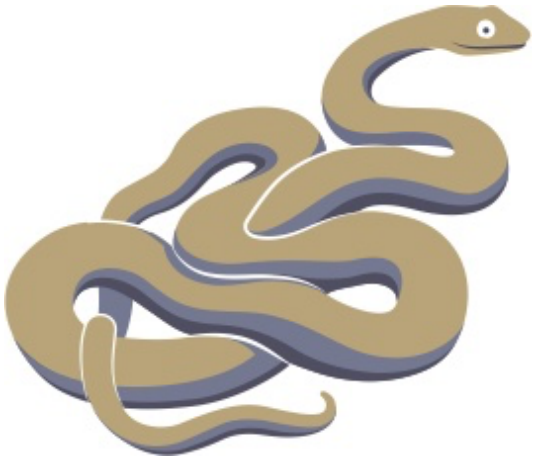
Note: the call-out fades, and we see the mosquito bite the person. The red strikethrough symbol fades up, indicating the mosquito is incapable of infecting the individual with the malarial parasite.

CRISPR might also make it possible to inactivate genes in disease-causing bacteria that confer antibiotic resistance, or target invasive species that damage environments and threaten native species.

[Synced to narration:
Left side of screen, resistant bacteria (from FIG 13-14, 3e) fades up. Right side of screen, brown tree snake (recolored from FIG 11-27, 3e) fades up.]



resistant bacteria



invasive species

5.
Although the potential of CRISPR is great, concerns and issues remain. For one, legal issues surround the technology, as several corporations and universities fight over who invented it and has the right to develop and profit from it.
Ethical issues also surround CRISPR, including concern about the potential for editing human embryos or germline cells—sperm or eggs, cases in which the gene changes could be passed down to subsequent generations.
What's more, the consequences of introducing new or altered genes into the genomes of natural populations are hard to predict. Even some desirable outcomes—such as eradicating mosquito populations that transmit malaria—might have secondary, harmful effects, such as harming bird or bat populations that rely on mosquitoes as a food source.

[Sync to narration:
Have title graphic **CRISPR** fade up. Then have **Concerns and Issues** title graphic fade up. Each bullet point fades up in time with narration.]

CRISPR
CONCERNS AND ISSUES

- Legal battle over ownership and rights to CRISPR technology
- Ethical concerns: editing embryos and germline cells
- Unpredictable or unintended consequences of gene manipulation