CRISPR: The latest word in genetics

By MATEUSZ PERKOWSKI
Capital Press

When scientists in 1993 discovered the bacterial gene sequence now known as CRISPR, they didn't know what purpose it served.

It took about a decade to realize that the CRISPR sequence — an acronym for Clustered Regularly Interspaced Palindromic Repeats — acted as the bacteria's immune system.

The microbe had genes that normally belong to viruses in a specific location at regular intervals within its chromosomes.

"Scientists saw that and thought, What the hell is this?" said Steve Strauss, a forest biotechnology professor at Oregon State University. As it turned out, bacteria that survive a viral invasion use CRISPR to store the viral gene sequences within their own DNA to "remember" and destroy the virus if it returns.

"It's primed to recognize it and chop it up next time they meet," Strauss said.

The remarkable discovery proved to be more than a biological curiosity.

The basic mechanism of CRISPR — slicing DNA into pieces and inserting them into other genetic sequences — could also be used to edit the genes of plants and animals.

Instead of relying on entire bacteria to do the work, scientists isolated two genes to alter DNA: An enzyme known as a nuclease, which does the cutting, and some ribonucleic acids, or RNAs, to guide that tool to the right location.

"The CRISPR bacteria is gone, you're just using its technology," said Strauss.

Agricultural value

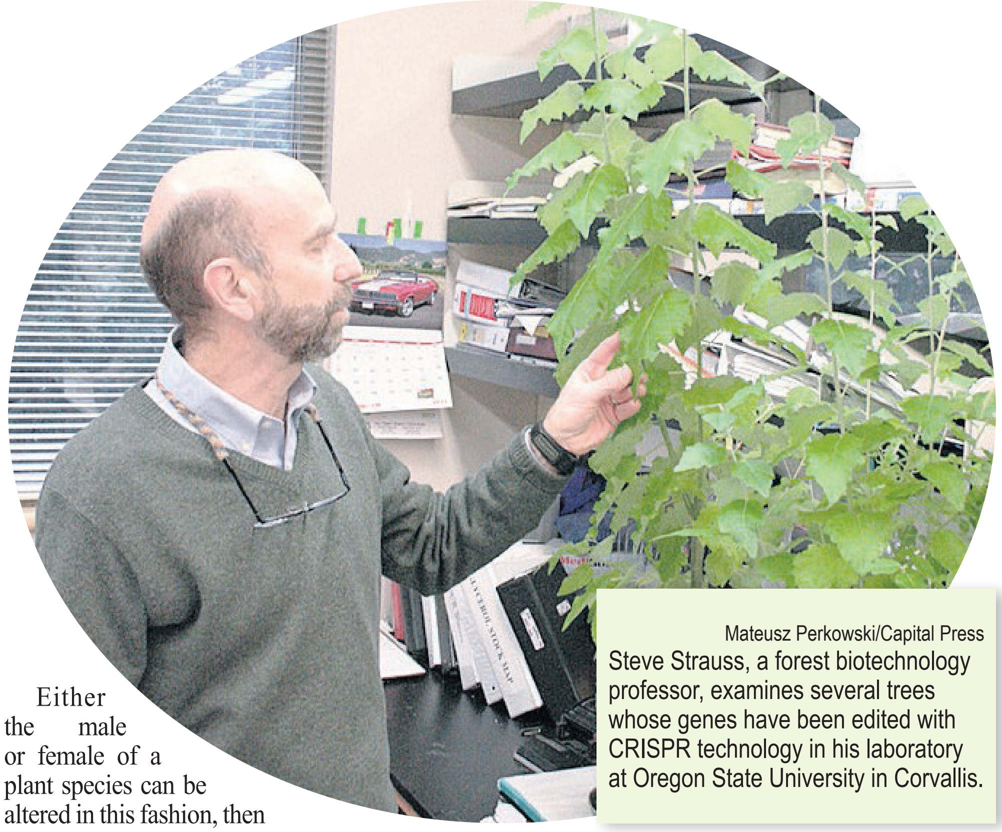
For agriculture, the technology is a new way to instill crops and livestock with desirable traits — or to remove unwanted ones — more quickly than traditional breeding, and without incorporating genes from foreign organisms. Whether the CRISPR method will encounter the same social opposition as genetic engineering is unclear, as is the global regulatory outlook for farm goods produced with the technique.

Before scientists can use CRISPR to genetically modify a plant, they must first identify the function and sequence of a gene. For example, one gene helps create gluten in wheat.

Once that's accomplished, they can use CRISPR to recognize that genetic sequence and then either mutate it, remove it or replace it with another sequence.

To insert the CRISPR into a plant, scientists rely on a method that's derived from conventional genetic engineering: agrobacterium, a microbe that infects plants and naturally changes their DNA.

"It has the machinery to put it into plant cells," Strauss said.



Mateusz Perkowski/Capital Press

Steve Strauss, a forest biotechnology professor, examines several trees whose genes have been edited with CRISPR technology in his laboratory at Oregon State University in Corvallis.

Either the male or female of a plant species can be altered in this fashion, then bred to each other. The progeny that don't inherit the CRISPR genes in their DNA aren't considered transgenic by some regulatory authorities.

For example, progeny that don't contain any genetic sequences from agrobacterium, a plant pest, aren't regulated as transgenic under the USDA's current biotechnology rules.

Relying on sexual reproduction to eliminate the CRISPR genes is fine for annual crops such as corn, but it's time-consuming in plants that take longer to reach sexual maturity, such as fruit trees or grape vines.

Scientists are also looking for ways to cleave the CRISPR from a plant without having it go to seed, said Strauss. In fruit trees, for example, selecting away the CRISPR in progeny is slow and difficult.

'Knocking out' genes

It's easier to "knock out" a gene with CRISPR than it is to replace one genetic sequence with another.

To replace genetic sequences, a scientist must first create a template from DNA that's synthesized in a laboratory.

When a plant is repairing its DNA that's been severed with CRISPR, sometimes it will use the synthesized DNA as a template, especially if the sequences are partly identical.

The likelihood of an organism using the template depends on the species. For example, it's more likely to occur in yeasts than plants.

Ensuring that plants use the template more often is another aspect of CRISPR that scientists are attempting to improve.

"There's a lot of innovation going on around the basic system," said Strauss.

Right now, CRISPR is often used to remove genes responsible for undesirable traits, but more ambitious uses will confer drought resistance, heat resistance and increased yields, he said.

Such goals will likely be accomplished as scientists develop a deeper understanding of CRISPR and plant genes, but there's another hurdle the technology faces — human acceptance of gene-editing, Strauss said.

Critics of traditional genetic engineering are also wary of CRISPR and other forms of gene editing, he said.

"The same political fights are going to happen," said Strauss. "In fact, they are already underway. It's always the people that are the mess. We can do the science and solve lots of problems if public fear and adverse regulations don't prevent it."

While the USDA doesn't consider gene editing to fall under biotech regulations today, other countries that trade with the U.S. will have their own definitions of genetic engineering.

The U.S. should work with trading partners to create workable systems that are hopefully less hostile than the ones that now exist for GMO crops in many countries, he said. "The way the rest of the world treats this matters."

Biotech critics argue that it makes sense for foreign countries to be cautious of the technology.

Biotech debate

It's likely the CRISPR mechanism serves another purpose than defending against viruses, as many bacteria don't have viral DNA in their genome even though they have CRISPR genes, said Bill Freese, science policy analyst at the Center for Food Safety, a nonprofit that's critical of USDA's biotech rules.

Given that scientists still don't know that much about what CRISPR does, the technology should be regulated, Freese said.

"We should have a thorough understanding before we rush to create new products," he said. "People are rushing to commercialize this prematurely."

The CRISPR mechanism can inadvertently remove or replace gene sequences that are similar but not identical to the DNA synthesized by scientists, he said.

For that reason, the technology can alter genes in ways that biotech developers weren't even expecting, Freese said.

"It turns out you don't have to have a perfect match for the CRISPR to target something," he said. "That gives rise to uncertainty."

It's possible that such unintended modifications could increase toxins within a plant or cause it to generate new toxins, he said.

"When you don't know what's going on, you could have changes that are harmful," Freese said.

The release of gene-edited crops into the environment could also cause trade disruptions, he said.

While the USDA doesn't regulate crops developed through CRISPR as genetically modified organisms, or GMOs, the technology does fall under the international definition of genetic engineering, he said.

"The U.S. is trying to bully its way to get its own definitions, and the world doesn't accept that," Freese said.

Trade partners could begin testing for gene-edited plants, potentially causing problems, as when Japan and South Korea suspended imports of U.S. wheat after a genetically engineered variety of the crop was discovered in Oregon in 2013, he said.

"Are you going to go through all this again with CRISPR products?" he said.

Yield10 Bioscience, a company developing crops with CRISPR, is optimistic that gene editing will be more socially accepted than transgenic GMOs, since there's no foreign DNA inserted into the plant.

"You're just using what's available in the crop," said Olly Peoples, the company's president and CEO.