CRISPR breathing new life into wheat and other crops—can it avoid GMO controversy?

One need not look far to find reasons for wheat growers to be clamoring for drastic improvements to the crop that represents their livelihood. The 2017 US wheat harvest was the lowest in 15 years, according to the USDA. The reasons ran from low prices and wet spring weather to pests and diseases. Meanwhile, bacterial blight in rice caused by *Xanthomonas oryzae* is decimating crops in Asia and Africa.

Farmers look upon the GMO technology that has improved corn, soybean and cotton crops and find themselves wishing for more. Some producers see hope for innovative gene-editing techniques to create hardier, more successful grains.

Ever since humans decided to settle down and raise their own food, they’ve been growing plants and selecting the ones that have the traits they want most. Plant breeding has since been accomplished through a range of techniques, including the basic plant-and-choose, directed mutagenesis, transferring germplasm from wild to domestic plants, and the transgenic combinations that have given us modern herbicide-resistant crops. But now, the new CRISPR gene editing offers the potential to radically change the way we breed crops.

Short for “clustered regularly interspaced short palindromic repeats,” these naturally occurring yet quirky sequences of DNA are used by bacteria to fight disease, and now are under scrutiny for their potential to create new traits in plants. But, like any new technology, there are a few shortcomings which may or may not block its way to commercial use—and not all of those are because of “anti” activism.

But the food industry would rather not take any chances with a technology that has yet to be part of any commercially available food. More specifically, they would like the benefits of CRISPR technology to avoid the public opinion and regulatory snags that have slowed down acceptance of transgenic and so-called “GMO” applications to plants, crops and food.

To that end, food industry members (like the US Pork Board, Monsanto, Syngenta and Bayer) have created the Coalition for Responsible Gene Editing in Agriculture. This organization hopes to spark more conversations with consumers to talk about food, CRISPR, and build trust between those consumers and food producers. “If people trust you, science doesn’t matter. If people don’t trust you, science does matter,” Charlie Arnot, CEO of the Center for Food Integrity and leader of the coalition, told Harvest Public Media recently.

On the regulatory side, so far the USDA is taking a hands-off approach to crops and other products that have been altered through CRISPR. Responding to a CRISPR-altered delayed browning mushroom, the agency said it would not regulate CRISPR-developed products because there is no foreign genetic material in the food. The FDA, meanwhile, has said it will continue to look at foods to determine if the final product is safe.

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Some groups that have opposed GMOs and transgenics have also issued cautions about CRISPR. Doug Gurian-Sherman, director of sustainable agriculture at the Center for Food Safety, warned that “we feel very strongly that this technology still needs to be regulated as we learn more about it. Maybe at some point it wouldn’t need to, but this is still a new technology.”

While no product has been introduced to the FDA for approval, several experiments are in the works:

- Francisco Barro, a plant biologist at the Institute for Sustainable Agriculture in Cordoba, Spain, and his team are using CRISPR to knock out genes in wheat that are responsible for gliadins, the part of gluten most responsible for causing celiac disease in susceptible people. The gliadin protein has 45 copies of the gene that produces problems; so far, Barro’s team has knocked out 35 of them.
- AddGene, a Cambridge, Massachusetts-based company that makes and stores plasmids for researchers, has recently started constructing CRISPR plasmids for a wide range of uses. The company claims it has handled more than 95,000 requests for CRISPR structures and assistance.
- Tomato breeders had long been frustrated by combining two (individually) beneficial traits, one that encouraged more fruit growth and another that eliminated a “joint” in tomato branches that made harvesting easier. Combining the traits by traditional means, however, produced tomatoes that branched out wildly, reducing their yields. Geneticist Zachary Lippman of Cold Spring Harbor Laboratory fond that CRISPR could shut down the specific genes behind the hyper-branching behavior.

The market for CRISPR research tools and products continues to increase, but scientists are still wary of off-target effects. The technique, while precise, can make precise cuts in the wrong parts of the genome sometimes, enough to (at least for now) thwart its ability to produce therapeutics.

In plant biology, however, these off-target effects could be less problematic. As the gliadin/gluten study above showed, plant genomes have many redundant genes, so many genes must be knocked out to shut down a particular trait-producing pathway. Aiming CRISPR at multiple families of genes may increase the risk of off-target effects, but researchers have found that very few or no off-target effects occur in plants. This could be because plants use nonhomologous recombination, which doesn’t require pairing up of structurally identical DNA ends, compared to animals that rejoin DNA breaks with homologous recombination, said Cara Soyars, a University of North Carolina graduate student working on CRISPR
breeding.

There’s also a long-standing issue with CRISPR-Cas9, comparing cutting a gene to edit it, and actually changing a base pair or adding DNA. It’s easier to cut, and adding base pairs is still much more challenging. Recently, researchers have introduced methods that do involve changing individual base pairs without cutting, so progress is continuing on expanding the effective applications of this new technique.

CRISPR took the research world by storm only within the past few years. Whether that storm will extend itself to crop breeding will depend on science, but also on public and regulatory acceptance.

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