Science Societies

Genetic approaches to weed control

By Megan Sever

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Genetic Approaches to Weed Control, CSA News

- Weeds have evolved quicker than our ways to eradicate them with 264 species of weeds worldwide developing resistance to herbicides.
- Genetic weed control is one option being looked at by researchers with a particular focus on gene drive systems, which rely on using so-called selfish genes to bias Mendelian inheritance.
- There are a number of hurdles to overcome before this approach could be used, including ethical, regulatory, and ecological challenges, but it is an area of research that may be worth pursuing.

In May 2021, researchers unleashed a swarm of genetically modified mosquitoes in Florida. The mosquitoes' genes are designed so that half of the female offspring of the fathers don’t develop and grow into breeding adult females. Designed to halt the spread of disease-carrying mosquitoes, it’s a controversial population control mechanism.

Could a similar mechanism be unleashed to control weeds in agricultural systems? That’s what a small number of researchers worldwide are trying to figure out.

Problematic Weeds

Weeds have evolved quicker than our ways to eradicate them.

Weeds outcompete crops for nutrients, water, sunlight, and space, says ASA member **Vipan Kumar**, a weed scientist at Kansas State University. Some of the worst offenders can reduce yields by 95%—kochia (often called tumbleweed), for example, can reduce sugar beet yields by that amount, Kumar says. Horseweed can lower soybean yields by 83% and cotton yields by 46%. Palmer amaranth can reduce soybean yields by 80% and corn yields by 90%. Common waterhemp can reduce corn yields by 20% and soybeans by 44%. And the list goes on.

Biological characteristics of many problematic weeds make them really challenging to deal with, says **Pat Tranel**, a weed scientist at the University of Illinois who is working on genetic weed control options. Weeds are prolific seed producers. Common waterhemp, for example, produces up to a million seeds *per plant* while Palmer amaranth produces 500,000 seeds per plant. So imagine how many seeds can be released in a single field. Another problem, Tranel says, is that both species are dioecious, meaning plants are male or female. “That characteristic forces plants to outcross with the female plant receiving pollen from lots of males around it,” he says. “So the progeny produced by that one female have incredible genetic diversity.” That makes the weeds even harder to kill, and weeds create seedbanks—their seeds can lie dormant for years, sometimes even decades, in the soil.

Herbicide Resistance

Herbicides used to be extremely effective (and sometimes still are), but by the fall of 2021, 264 species of weeds worldwide had developed resistance to herbicides, according to the **International Herbicide-Resistant Weed Database**. Seventy-one countries have reported herbicide-resistant weeds in 95 different crops. In the U.S., all but two states have reported herbicide-resistant weeds (Alaska and Nevada just haven't reported).

Many weeds have developed resistance to multiple herbicides, and worse, multiple modes of action Photo courtesy of Adobe Stock/ivanvess.

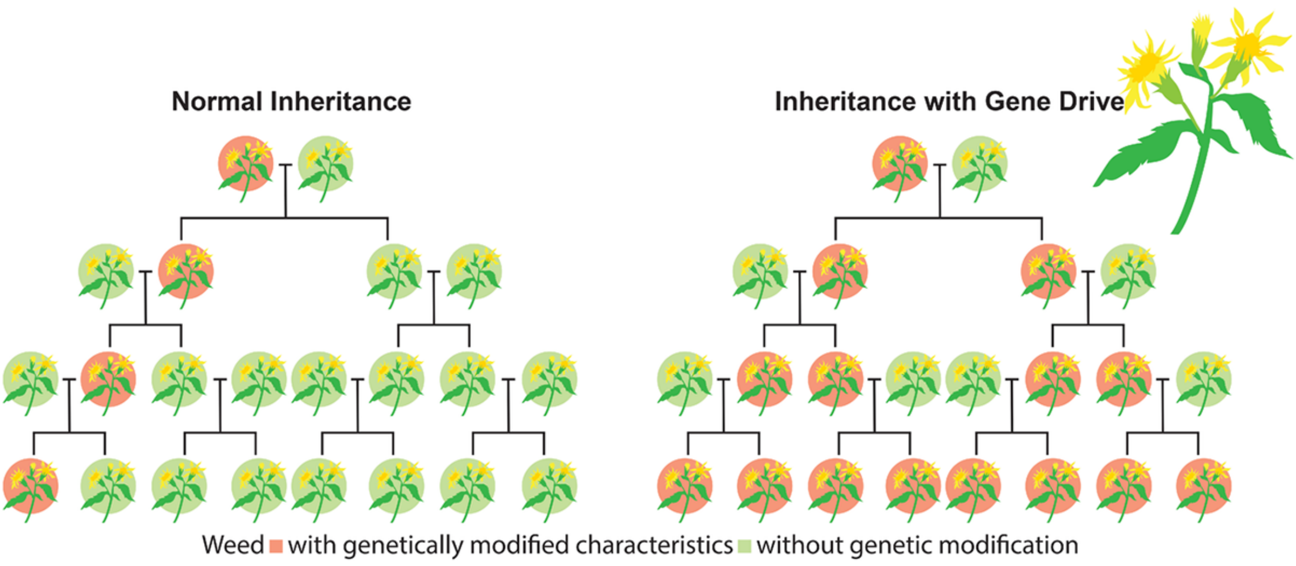
Herbicide resistance has been a problem for decades, but concerns were heightened during the last decade as glyphosate resistance became increasingly common. Now, many weeds have developed resistance to multiple herbicides, and worse, multiple modes of action (how the herbicide controls the plant) and sites of action (where the herbicide acts within the plant), Kumar says. Within those modes and sites of action, the weeds are developing resistance to different chemicals and chemical families, he says. Weeds have developed resistance to 23 of the 26 known modes of action, according to the weed database. In Kansas last year, Kumar says, one kochia population was found to survive four different herbicide modes of action, and one Palmer amaranth population had resistance to five different modes of action. Furthermore, Palmer amaranth has developed eight different resistance pathways. Waterhemp has evolved resistance to seven modes of action, Tranel says.

The genetic diversity of weeds like waterhemp and Palmer amaranth allows them to evolve resistance so quickly, Tranel says. They can "stack multiple resistances," he says. Say a farmer uses glyphosate in one field—the weeds develop resistance to that. An adjacent farmer uses dicamba in his field, and the weeds develop resistance to that. "Then pollen from one field goes to a female plant at the other field, and now you end up with a plant that has resistance to both of those herbicides," he says.

Growers and researchers are running out of options and starting to look for new ones, Tranel says. Enter genetics.

Genetic Weed Control

"In the broadest sense, genetic control strategies use genetically manipulated strains of a pest organism to achieve one of two main objectives: population suppression, aiming at lowering the densities of natural target populations or eliminating them entirely, or population replacement, aiming at replacing natural pests with less damaging individuals," wrote evolutionary biologists **Mathieu Legros** and **Luke Barrett** of CSIRO in Canberra, Australia, and colleagues in a **2021 paper** in *Evolutionary Applications*.



Gene drive systems rely on using so-called selfish genes to bias Mendelian inheritance, according to Luke Barrett of CSIRO in Canberra, Australia. Mendelian inheritance suggests that offspring inherit genes at a roughly 50–50 ratio. "A gene drive skews that ratio to give a higher than 50% chance of inheriting the genes—up to 100%," he says.

Although different types of genetic modification strategies exist, for the purposes of weed control, scientists are focusing on gene drives.

"At its core, the gene drive is some genetic element that is very good at being inherited to the next generation," Legros says. "We use that to introduce [traits] into a population, trying to transform populations," he says.

Engineering a Population Crash

Because the dioecy of waterhemp and Palmer amaranth is their strength, Tranel is trying to figure out a gene drive to use that strength against them. The idea is to use gene drive strategies to change the ratio of males to females in the weeds' populations.

He and his team have zeroed in on the regions of the Palmer amaranth and waterhemp genomes that make the weeds male and female. And they're close to finding the exact gene that controls maleness. Once they find that gene, the next step is determining how to manipulate it, Tranel says.

Say a waterhemp plant has a maleness gene in a gene drive: All of its progeny will be males, as will all of their progeny. The gene drive will carry the maleness gene through the generations. So over time, if all the offspring in a field were manipulated to be males, they couldn't produce seeds and the populations would crash.

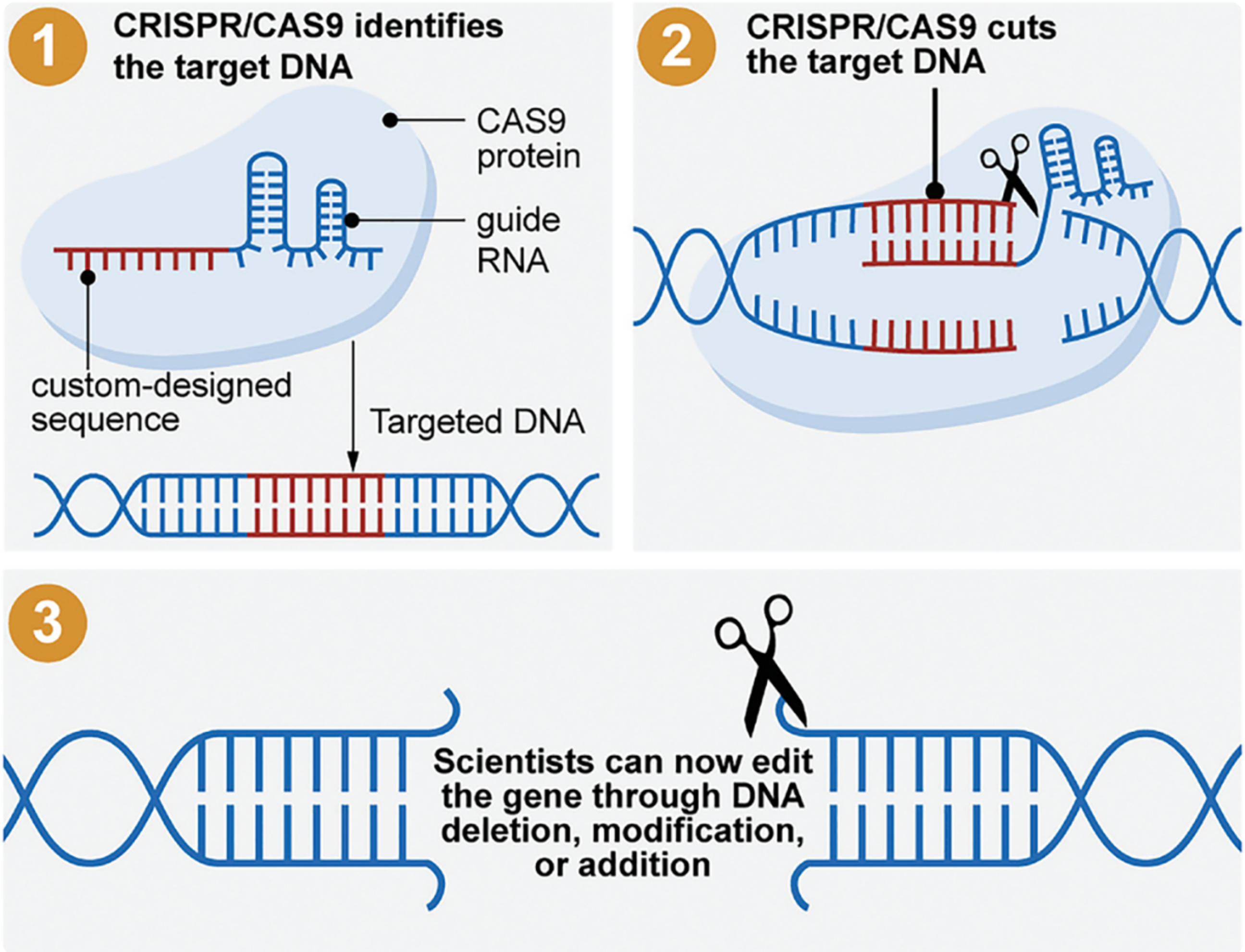
Researchers have been modeling how long such a population crash could take. With using a gene drive for maleness, Tranel says, "benefits—fewer females and therefore less total seed production—could potentially start occurring just a couple of years after introduction of the gene drive." That depends on introducing a high number of modified plants to start with—say 10%, he says. With a slower initial frequency, it might take 10 to 20 years to wipe out the local population, he notes. "And you could probably never completely wipe it out due to seed dormancy, but farmers could see benefits in just a few years."

Other modeling studies lean more toward the longer time frame. Introducing and spreading a gene drive in a wild weed population will be a significant challenge, says **Paul Neve**, a weed population biologist at Copenhagen University who wrote a **commentary** on gene drive systems for weed management in *Pest Management Science* in 2018. "If we extrapolate from modeling studies in other nonplant species, we can estimate that in a 10-ha field with a moderate weed population size, there would need to be release of 10,000 edited seeds in Year 1 to achieve a high frequency of the desired edited trait by year 10 (optimistically)," Neve says. "This assumes that there would be random mating in the population, that there would be little impact of the soil seedbank in slowing spread of the drive, that fitness costs of edited genes in wild populations were low, and that evolution of resistance to the drive could be prevented." Unfortunately, he adds, "there is some basis for questioning all of those assumptions." Putting all of that aside, he asks: "Will farmers wait for 10 years for a 'treatment' to become effective?"

Tranel counters, however, that generating 10,000 edited seeds for 10 ha is feasible, given that one waterhemp plant can produce a million seeds in a year.

But that brings up another important question: how would gene-drive-modified weeds be introduced to a field? Farmers couldn't just plant a few weed seeds in a field that's already chock full of waterhemp—it wouldn't make any difference, Tranel says.

Instead, Tranel says, theoretically, he would propose a situation like this: "Do your normal weed control. Spray a pre-emergence herbicide to give you some residual weed control, then maybe spray a post-emergence herbicide as your soybeans and the weeds start coming up. … After that, plant some seeds of your modified waterhemp." Those seeds would germinate and release their pollen to the native plants that survived the herbicide applications. Ideally, he says, maybe there would be 10 to 100 waterhemp plants left in an acre rather than the thousands that were there before herbicide application. So, if a farmer planted 10 to 100 gene-drive-modified seeds per acre after herbicide application, those males would effectively compete with the remaining natural males. As they pollinated the females to produce male-only offspring, eventually that population would collapse. It might be the kind of thing where you'd have to release more seeds every five years or so, he speculates.



The development of CRISPR technology has allowed genomic alteration to reach, almost, the masses. It's cheaper and easier than ever before, but it's still not cheap or easy, according to a review published by Sara Martin of Agriculture and Agri-Food Canada in Ottawa and her colleagues in Plants in 2019. Illustration courtesy of the U.S. GAO.

Engineering Weaknesses

Population collapse isn't the only potential use for gene drives. Another possibility is to weaken the weeds. For example, if researchers could determine which genes allowed the weeds to become resistant to herbicides, they could insert a gene drive that makes the plants sensitive again or even more sensitive than before, Legros says. Researchers could also insert a gene drive that changed seed dormancy, so seedbanks couldn't build up, or one that otherwise reduced the impact of weeds, he says. "The precise trait that you target might depend on the species," Barrett adds.

But to use gene drives for any type of weed control, researchers first need the complete genomes sequenced for weeds. And therein lies one of the big hurdles for this technology. Tranel and colleagues have assembled the most complete genomes yet for waterhemp, Palmer amaranth, and smooth pigweed, which they **released** in 2020 in *Genome Biology and Evolution*. For most other weeds, a genomic sequence is not yet available. Ultimately, scientists should have access to "assembled, annotated, and curated genomes" for about 30 weed species through the International Weed Genomics Consortium, Neve says. To get there will involve more people getting involved in the process, Tranel says, especially "people with the combination of skills and understanding of applied weed management and genomics."

Significant Hurdles

While Tranel and his team try to map weeds' genomes and find the maleness gene, population biologists and ecologists are trying to determine the feasibility of using gene-drive-modified weeds in wild populations. "Before we invest a whole lot of money in molecular biology [research], let's make sure that the species we're interested in is ecologically a good target for a gene drive," Barrett says. Indeed, Legros says, scientists first need to know how gene drive strategies would even work in various plant species. Outcrossing seems to be the most important factor determined so far. And for the maleness/population suppression technique, dioecy is necessary.

The population biology question is the biggest hurdle Neve sees. "I like the idea, but we need to address the challenges of spreading drives in a practical time frame up front," he says. "Biotechnological solutions that can be developed in the lab will fall at the first hurdle if ecological questions are not addressed at the same time." ("Ecology" in this case relates to the fitness and spread of gene drives in wild populations, rather than environmental impacts of gene drive, Neve notes.)

A field infested with Palmer amaranth. Photo courtesy of the United Soybean Board.

Environmental impacts are another potential issue, though. “We’re manipulating nature in ways that we may not understand all the consequences,” Tranel says. No one wants “to eradicate waterhemp or Palmer amaranth from the face of the earth, even though they’re really bad weeds,” he says. They may have value we don’t even know about yet. Maybe we find a drought tolerance gene in Palmer amaranth that we could use to make grain amaranth a better crop. Or maybe some important insect is dependent on these weeds, he adds. What are the possible unintended consequences? For stewardship reasons, “we want to make sure the gene drive is going to reduce the population but not spread uncontrollably throughout the world.” And once we release the gene-drive-modified weeds to nature, Tranel says, “they’re out there—and now you’ve lost control.” So we better hope we know what we released.

Then there are regulatory issues and public opinion issues. “This approach presents enormous ethical, regulatory, and ecological challenges,” wrote **Sara Martin** of Agriculture and Agri-Food Canada in Ottawa and her colleagues in a **review** of population genomic approaches for weed control in *Plants* in 2019. On the regulatory side, “I can’t just walk out of my lab here and plant some genetically modified waterhemp without getting into serious trouble,” Tranel says. And the public isn’t exactly keen on releasing genetically modified anything, much less weeds. One possible way to overcome that public reticence, Tranel mentions, might be to start with releasing a gene drive modification that people care about: their allergies. If we had the ragweed genome, for example, could we release a gene drive to get rid of that allergen? If so, he says, the general public might see the benefit of the technology and get more on board.

Yet another potential hurdle, Kumar notes, is that Mother Nature is really good at adapting to whatever we've thrown at her. So if we insert gene drives into these weeds, we need to think about how these plants will evolve around that. What then? he asks. Indeed, Tranel says, "we have to wonder about how long [a gene drive modification] would even work. We know that if you try to kill waterhemp with one tool, the waterhemp will evolve and come up with a way around it." That's hard to even think about right now, he adds, given that we don't even know yet what gene we'd be putting in a plant. Obviously there's a ton of research left to be done, the researchers agree.

The development of CRISPR technology has allowed genomic alteration to reach, almost, the masses. It's cheaper and easier than ever before, but it's still not cheap or easy, Martin and colleagues wrote. Genome assembly and sequencing is still "a significant investment of time and resources." It's going to take substantial time, funding, trial and error, and experiments before the idea of gene drive control of weeds goes anywhere, Tranel says.

Do We Even Want to Get There?

Despite all of the hurdles, gene drive control of weeds is still worth pursuing, according to the researchers. "This is a good strategy—a good, innovative way to look at the whole problem of weed control," Kumar says.

"The idea of gene drive is interesting, as for the first time, it offers the potential for direct genetic control of wild weedy plant populations," Neve says. "It is possible that the limitations [of gene drive] can be overcome by smart minds, but it is critical that these challenges are acknowledged and addressed up front."

"There's a lot of potential here for highly target-specific means of pest control," Barrett says. But we're so early in the research pipeline "that we don't know enough about it yet to be able to have a strong opinion either way"—whether it's good or bad, he says.

"There's a lot of research to be done and questions to be answered about where gene drives would be a valuable addition [to weed control strategies]," Legros says. "They're not going to be a silver bullet, but there's potential for them to be part of the arsenal of solutions for different kinds of pest control."

If gene drives are used in the future as a weed control strategy, they should still be used as part of an integrated weed management approach with other management strategies such as crop rotation, cover crops, strategic tillage, and mechanical methods like "harvest weed seed control" techniques (shown here). Photo courtesy of Michael Flessner.

Kumar and Tranel agree. "Diversity, integrated weed management should be the key," Kumar says. Tranel adds: "You'd use this in conjunction with other tools, including herbicides." Other tools also include crop rotation, cover crops, strategic tillage, and mechanical methods like "harvest weed seed control" techniques such as chaff lining and harvest weed seed destructors, Kumar says. Everything is on the table, he says. And in the future, that might include genetic modification.

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