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Evolution of a Scientist-Vintner

Carole Meredith weighs in on genetic engineering of winegrapes

by Liza Gross

On a mild January day in 2003, Dr. Carole Meredith celebrated her 55th birthday as only she could. It's the rare scientist who walks away from a distinguished career at the top of her game, but the famed grape geneticist (Dr. DNA, as her fans call her) marked the day by giving herself an unusual gift. She quit the academic spotlight—and the grueling commute from her remote mountaintop winery home to her lab at the University of California, Davis—to concentrate on Lagier Meredith, the Napa winery she runs with her husband, winemaker Steve Lagier.

HIGHLIGHTS

- Dr. Carole Meredith, former University of California, Davis, professor and plant geneticist, now grows Syrah and runs a winery.
- The DNA sleuth who confirmed the parentage of Zinfandel and understands the benefits of genetic modification chose not to use transgenic vines in her vineyard.
- Meredith says she now understands the public's fears and discusses the dilemma facing researchers and grapegrowers.

For Meredith, who retains ties to UC Davis as professor emerita in the Department of Viticulture and Enology, choosing the road less traveled comes naturally. She earned a doctorate in plant genetics when few women studied botany, then briefly flirted with tomatoes, corn and other easy-to-manipulate subjects before tackling the notoriously intractable grapevine. (True to form, when Meredith and Lagier planted their first vines in 1994, they didn't choose Cabernet Sauvignon—the valley's undisputed king—but Syrah. "We really liked the flavor, and we thought we had a really good site for it," she explains. "Besides, who wants to be another Napa Cabernet winery?")

Meredith's gamble on a recalcitrant research subject proved prescient in the 1970s, when advances in molecular biology and DNA technology promised to revolutionize grapevine genetics. With potent new DNA analysis tools, researchers could capture a species' unique genetic fingerprint to trace its origins and evolutionary history. Once DNA markers for grapes became available, Meredith and her team at UC Davis quickly harnessed the power of DNA fingerprinting to identify classic vinifera varieties and resolve longstanding questions about their murky history. Meredith and grad student John Bowers even surprised themselves in

1996 by revealing a mixed heritage of white (Sauvignon Blanc) and red (Cabernet Franc) grapes for Cabernet Sauvignon. And in what many call her crowning achievement, Meredith—whose place in the wine pantheon was secured by a 2009 induction into the Vintners Hall of Fame—confirmed that Zinfandel, long claimed California's "historic" native, is the genetic twin of the nearly extinct Crljenak Kastelanski grape variety, once grown along Croatia's Dalmatian Coast.

But it was the ability to manipulate DNA, to "transform" grapevines with genes from distantly related species, that captured Meredith's scientific imagination. She heralded genetic engineering's dazzling potential to liberate grape breeders from the idiosyncratic constraints of their subject's biology.

"The most awesome aspect of this new technology is certainly the vastly extended range of genetic variability that will become available to the plant breeder," she wrote in a 1982 California Agriculture article. Genetic engineering, Meredith predicted, could give growers more flexibility by producing vines capable of tolerating inveterate vineyard pests or normally inhospitable conditions—all in a fraction of the time required by conventional breeding.

Although genetically engineered corn and tomatoes were commercially available by 1996, the disobliging woody perennial remained a challenge until the late 1990s, when a handful of groups had reported reliable transformation results. By 2000, Meredith's lab was routinely generating transgenic scion and rootstock cultivars to help growers ward off the dreaded Pierce's disease (PD)—a bacterial infection transmitted by sap-sucking insects like the glassy-winged sharpshooter, which can kill a grapevine in two years. Containing PD and GWSS has cost government and industry more than $300,000 million since 2000.

Conflicting values

As Meredith has settled into her new life, the grueling demands of high-profile research behind her, she has had second thoughts about promoting the technology responsible for her most celebrated discoveries. The turning point came after she first joined David Magnus, director of Stanford University's Center for Biomedical Ethics, on a 2005 panel discussing genetic engineering and the wine industry. Magnus argued that scientists must respect public concerns about genetic engineering and appreciate that there are other important values besides objective knowledge, Meredith recalls. "I took to heart a lot of what he had to say."

The vast majority of scientists don't worry about theoretical risks of swapping genes among species, she explains, because they've studied the DNA sequence they're introducing, they understand how its gene product works, and they're convinced it doesn't present a risk. But consumers worry that genetic engineering might jeopardize things they value, like food safety, the environment and organic agriculture. They think scientists don't understand enough about genetic engineering to be "playing God."

"There's an element of truth in the concern expressed by skeptics that it's not fully understood, so you should be more careful," Meredith allows. "But I think critics tend to lump every single GE project into the same basket."

While it's true that some genes aren't well understood, others have been extensively characterized, giving scientists the ability to predict how they will function in a new genetic context. And some fears are simply unfounded. "I've seen surveys where people are very, very worried about eating DNA," Meredith says, clearly incredulous. "They don't realize that any time they eat an apple or a banana or fresh tomato they're eating DNA."

Still, she thinks that scientists should be “a little less arrogant” about the power of their technology, and recognize that they are part of a larger community that may hold different—but equally valid—values. “Magnus stressed how important it was to not try to say whether they were right or wrong, but to respect them,” Meredith explains. “And that’s a big part of the problem, the arrogance of trying to force something on the community.”

Allaying fears with facts

Indeed, Meredith points out, even “fairly knowledgeable” people have raised concerns about certain plant engineering techniques. One issue involves the way foreign genes are introduced. Most methods don’t direct the transgene to a specific site in the genome, so it’s not always clear where the gene will end up, and this could theoretically change how that gene functions. If the transgene has a counterpart in the grapevine, researchers could simply swap the transgene into the same place. But if there is no comparable gene in the plant, scientists can’t always predict where it will go, even though they can tell that it’s working as intended. “I think in the future that will be controllable, too,” Meredith says.

People also worry about the use of antibiotic resistance genes (taken from bacteria) as “selectable markers” during the transformation process. To engineer plants, researchers must deliver the desired gene into plant cells (typically using a soil bacterium as a gene-delivery system), isolate the transformed cells, and then add hormones and nutrients to trigger a regenerative process that yields (trans)genetically identical plants.

Since only a fraction of plant cells will incorporate the new gene, researchers use markers to distinguish the hits from the duds. One approach involves hitching the transgene to an antibiotic resistance gene, growing the cells in an antibiotic-soaked medium, and then separating the cells that survive on the (highly likely) assumption that the transgene and resistance gene were incorporated together. (Antibiotics kill plant cells, though not whole plants, by disrupting metabolic processes they share with bacteria.)

“People are concerned that the antibiotic-resistance sequences will recombine with microbes in nature and create pathogens that can’t be controlled,” Meredith says. Researchers think there’s little risk that these markers will aggravate this problem because they employ antibiotics with limited use in humans and animals. Still, scientists have started to take these concerns seriously, Meredith says. “There are other selectable markers being used and others in the pipeline, so the antibiotic resistance issue is going away.”

For Meredith, a bigger issue centers around the fact that two of the most widely used techniques—the bacteria gene-delivery system and the antibiotic resistance markers—are owned by Monsanto. “There’s a great deal of concern about intellectual property issues,” she says. Any U.S. researcher who wants to use these methods, which have become entrenched in transgenic plant research, must seek permission from Monsanto and, in some cases, pay royalties.

A question of sovereignty

Meredith is especially sensitive to worries about environmental contamination, that transgenes might “infect” wild relatives. “If a crop has wild relatives growing within a pollen grain’s jumping distance, like with oilseed rape or wild mustard, those will easily cross,” she explains. And Vitis vinifera does have a wild relative in California, V. californica. “Drive along Napa River, Dry Creek or into the Sierra Foothills during early fall,” Meredith suggests, “and you’ll see heart-shaped yellow leaves—that's all wild grape."

Unlike wild grapes, cultivated grapevines are largely self-pollinators, with pollination important for fruit set but not reproduction. Nonetheless, transgenic pollen carried by wind or insects could conceivably reach adjacent wild grapes.

A rogue pollen grain from a transgenic grapevine could also theoretically pollinate an organic grapevine in an adjacent vineyard. "Now it wouldn't turn that organic grapevine into a transgenic grapevine, but it might produce a single berry," Meredith says. "That one pollen grain would produce no more than one seed in one berry, and if you were to plant that seed out, then the little seedling would contain the transgene."

Of course, grapevines aren't grown from seed, but propagated by taking cuttings from the mother vine to retain that vine's unique characteristics. "The concern is that if one grape berry contains a seed with a transgene, does that jeopardize your standing as an organic grapegrower? I don't know."

For Meredith, this question goes to the heart of community values and whether people have the right to decide what types of agriculture should be allowed in their communities. "A concern that has been expressed by organic producers, particularly in Sonoma County," she says, "is that you, Mr. Big Corporate Grapegrower, who wants to plant a genetically modified grapevine that's resistant to something or that reduces your production costs—who gives you the power or the authority to jeopardize my economic viability?"

Finding common ground

If critics had "a little more knowledge," and scientists had "a little more humility," Meredith suggests, then maybe they could find common ground. Take the specter of promiscuous pollination. "If people were concerned not just about the presence of the transgene but about its effect," Meredith explains, "you could have that gene turned off in the pollen, turned off in the fruit. It could be a leaf-specific expression. But that would depend on what trait you want."

For example, you could introduce a PD-resistance gene that isn't expressed in the fruit, and the plant would still be protected because the disease attacks the leaves and stems. Or you could take advantage of the fact that PD spreads through the plant's vascular tissue, and engineer those microbes living in that tissue to thwart the disease's spread. "But that's just speculative at this po int," she cautions.

Given public resistance to genetic engineering, some researchers have stuck with conventional methods to achieve similar ends—albeit in a much longer time frame. Conventional breeding requires "a backcross program that takes about seven generations of breeding to end up with something that's 99.9% of your original type with just the introduction of the one trait you were trying to move over," Meredith explains. Each generation is five to seven years, minimum, "So you're talking 35-50 years."

Then add another seven to 10 years to evaluate your plant. "You still need to put it out in a vineyard in multiple locations for multiple years to evaluate the plant and fruit, make wine from it, and do sensory tests to make sure it's acceptable." With genetic engineering, it takes about two years to introduce a transgene, confirm it's there, and get ready for evaluation.

There is a middle ground. Andy Walker, a UC Davis professor of genetics and one of Meredith's first Ph.D. students, uses a DNA-based molecular marker linked to a gene associated with PD-resistance to rapidly identify seedlings—produced through conventional methods—that are more likely to contain the resistance gene. And by making educated guesses about which selections in the early generations are likely to make the best wines, he can save years of evaluation time by waiting until the end of the back-crossing program to evaluate the wines.

Any kind of breeding raises sticky issues for the tradition-bound wine industry. Some researchers have argued that since genetic engineering can introduce a single trait without changing the genetic underpinnings of a grape's flavor profile, it doesn't create a new variety. But Meredith isn't so sure. “In either case you're producing a new grape that's not a traditional grape, and there's a big question about what kind of name you can give that thing. With genetic engineering, even if you've only introduced one gene, it remains to be seen whether you could still call a Chardonnay that has a pear gene in it a Chardonnay.”

Traditionally, she explains, if it looks like Chard, tastes like Chard, makes wine that's like Chard, it would be a Chard. “But if you already know that you've changed it, that it's molecularly distinct, do those old rules apply anymore, and do new rules need to be written? That has not been tested.” Ironically, she adds, with conventional breeding, which involves moving whole chunks of DNA between plants, “it's even less likely that you could call it the same thing.”

These days, Meredith thinks more about what consumers will accept than about how to transform grapes. “My genetic knowledge is not that applicable to growing grapes,” she says, although she allows that a “pretty good grounding in how grapevines grow” helps when it comes to deciding when to spray for disease. Though most growers spray six to 10 times per year, “We spray just once,” she says, “and we've had no mildew.”

She has no interest in planting disease-resistant transgenic vines to eliminate spraying altogether. “If we had a huge disease problem where it was ‘replace the vines or go out of business,’ well sure, that would be different. But right now, we've got a place where the traditional grapes grow really well, and so we're not interested in changing everything.”

She pauses a minute, then adds: “I'm not interested in changing to another conventional variety, let alone a genetically engineered one.”

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