The Phantom Forest: Research on Gene-Altered Trees Leaps Ahead, into a Regulatory Limbo

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At an industrial park in Walnut Creek, California, technicians and robots are sorting through the 550 million base pairs of genetic code in poplar DNA to sequence a tree genome for the first time. They are poised to unlock a fine, full toolbox for the work of genetic engineering in trees.

In Vermont, a group called Action for Social and Ecological Justice has just kicked off a national campaign to pressure companies to ban research on genetically engineered (GE) trees. The Sierra Club, the World Wildlife Fund, and the American Lands Alliance, among others, have called for a moratorium on commercialization of GE trees.

In Washington, a federal agency with key responsibility for judging the biological safety of GE trees is preparing its response for Congress to a report by the National Research Council (NRC), which cites a long list of misgivings about the agency's work.

Though results from most projects are either uncertain or years off, the research is well advanced on GE trees for industry and agriculture and on some that might be good for the environment. Engineered trees may grow faster or more compactly, or they may be more cheaply converted into pulp and paper. They may incorporate genes that confer insect resistance on an apple tree or drought resistance on a pine.

More than 200 notices of field trials have been filed with federal regulators for lab-engineered fruit, nut, and forest trees—also known as genetically modified, biotech, or transgenic trees. But aside from a virus-resistant, bushlike papaya tree grown in Hawaii, no one has yet sought regulatory approval for commercial use of a gene-altered tree.

"Maybe soon," says Vincent Chiang, codirector of the forest biotechnology group at North Carolina State University. Like others in this field of research, he feels little certainty about how the regulatory climate for GE trees will evolve. "But if we don't consider that factor, if we could grow transgenic trees just like we grow ordinary trees now, I would say in two years those trees could be put into the ground, so we could have wood available to a pulp mill in six years."

One of Chiang's projects has been to engineer trees to produce less lignin, which is expensive to remove during the process of turning pulp into wood. The process has been licensed to Arborgen, a $60-million joint research venture of the International Paper Company, the Mead Westvaco Corporation, and two New Zealand firms. Arborgen estimates that, if tests go very well, the product could be ready for the market in a decade.

Cloned cathedrals

Tinkering with tree DNA presents some issues for research and for public policy, however. Casting an uncertain light over all such projects is the fact that human society tends to revere trees and to embrace and mistrust new technologies.

"When you start doing genetic manipulation of what is widely considered to be a wild species, it raises a whole different set of issues than if you are doing it with agricultural plants," says molecular ecologist Stephen DiFazio of the Oak Ridge National Laboratory. "So even if there isn't a strong, credible scientific risk, there is a public perception issue that can be quite substantial."

"You hear people refer to forests as nature's cathedrals. Scientists I know who are working with trees have those feelings, too," says Gerald Tuskan, a senior scientist at Oak Ridge.

For some advocates of the technology, the fact that GE plants are regulated more closely than other plants is especially vexing. A tree that may or may not be good for the environment should be regulated accordingly, they argue, not on the basis of propaganda that stigmatizes its origins in a lab. They cite a scientific consensus: As the National Academy of Sciences has stated, introducing GE organisms "poses no risks different from the introduction of unmodified organisms and organisms modified by other mechanisms."

Some worry that an already onerous "regulatory load" that mixes politics with science has chilled investment interest and, under the guise of oversight, threatens to suffocate the infant industry along with the research it supports.

But opponents claim that the GE tree technology itself is unacceptable: It's too powerful to be relinquished to multinational corporation patent licensees whose environmental commitments are just lip service. Or it's too complex for our public science—haphazard, misdirected, and malnourished as it is—to predict the potential for catastrophic side effects. Or it's too much of a threat for cheerleading federal agencies to be allowed to regulate it.

Vincent Chiang, currently at North Carolina State, genetically altered the lignin content of aspen trees while director of the Plant Biotechnology Research Center at Michigan Tech. Here he examines the growth of genetically engineered aspen trees at different growing stages. Photograph: Michigan Technological University.

There is also a middle-ground discussion. Its boundaries are defined on one side by a call for an indefinite moratorium on commercial development of GE trees. This would last until important scientific issues are resolved and a credible and authoritative federal regulatory apparatus is in place. Faith Campbell, of the American Lands Alliance, says of the government's current role that "there's a lot of words there, but most of the time, it seems to boil down to next to nothing." Then there's the question of whether GE plants should be burdened more than conventionally bred crops by regulatory oversight. Campbell notes that the NRC justifies the scrutiny—and recommends far more—for GE and non-GE plants both, to ensure biological safety.

The other side of this range of thought favors commercial development of demonstrably benign GE tree innovations, as a public confidence builder. It also calls for extensive monitoring, under an improved regulatory system. DiFazio, for one, suggests controlled commercial releases with traits that carry negligible risk. Then long-term, large-scale studies can chart how far the genes disperse in the wild and provide answers about invasiveness.

One difference between GE trees and the many other transgenic plants that are already approved for commercial use is that, unlike corn and soybeans, trees endure. They exert a dominant influence in many ecosystems on the basis of size alone.

Just as important is their evolutionary history. Most crops have been domesticated for thousands of years and are now markedly different from their wild relatives. But the genetic makeup of forest trees, even those grown as row crops on industrial plantations, has been scarcely altered by humans.

"We're starting with organisms that are, today, exactly as they were 60,000 years ago, or millions of years ago in some cases," Tuskan says. Which means that genetically engineered pine or poplar trees, for example, may hybridize with wild relatives more easily. Clouds of wind-borne tree pollen can disperse over long distances and enormous areas.

Such concerns put a premium on finding a way to engineer sterility into trees, though few if any experts have concluded that this could be made 100 percent reliable. "The holy grail of a biotech improvement is a tree that is an elite producer, with a gene construct that prevents the tree from pollinating," says biotech industry consultant David Duncan. "First and foremost is the whole

An embryogenic American chestnut culture showing embryos in various stages of development. Unlike trees in the poplar family, chestnut has proven very difficult to clone, which slows progress on experiments to engineer a blight-resistant tree. *Photograph: Scott A. Merkle.*

issue of controlling the potential for outcrossing."

Single-gene theory

Duncan calls Oregon State geneticist Steve Strauss the world's foremost authority on modifying trees so they won't reproduce. Strauss says that at least some gene flow from biotech tree plantations to wild forests is likely to be inevitable but of little consequence: no deleterious effects and no accidental creation of a super-tree.

He rejects the possibility that engineered trees might behave like invasive exotics. They are "orders of magnitude more complex a unit to introduce into a new environment than a single gene." For example, the exotic melaleuca tree, a severely disrupting invasive in Florida, presents a whole suite of adaptations evolved over tens of millions of years. "Those are not single-gene traits," Strauss notes.

This view is shared by the Biotechnology Regulatory Service, the section of the federal Animal and Plant Health Inspection Service (APHIS) whose job is to judge the biological safety of GE plants, including trees.

"We don't necessarily believe that introduction of an alien species onto a new continent is a good or useful model from which to approach genetically engineered plants," says John Turner, acting supervisor for biotechnology risk assessment. "In that case, you have an entirely new organism being introduced. How it will behave is very unpredictable. In this case, we are dealing with plants that have been here for a long time, and it is usually changing a single trait. We think that's very different."

Perhaps not, however. The NRC panel that reviewed APHIS's work on regulating GE plants rejected the assumption that single-gene changes have small ecological effects. Its recent report also rejected any strict distinction between exotic invasives and transgenic plants on the basis of the environmental hazards they may present. "Introduction of biological novelty can have unintended and unpredicted effects" on ecosystems, the NRC report cautioned. In poplar, for example—the tree of choice for a wide range of GE projects—"the addition of a single transgene that improves some ecological characteristic could increase the weediness or invasiveness of the species, and these risks merit evaluation."

Other scientists echo the NRC's concerns about ecosystem effects. University of Wisconsin insect ecologist Kenneth Raffa, for example, has written, "The general lesson is that when you transfer a technology from closed, controlled conditions to open complex systems, there are almost always unforeseen parameters that affect system behavior." Raffa and colleagues have also written that unanticipated indirect effects are a "realistic" risk of introducing transgenic trees and could reduce populations of predators, parasites, scavengers, pollinators, and endangered or valued species.

Raffa believes that the technology holds promise for alleviating both commercial and environmental problems. But he finds the argument that genetically accelerated domestication of trees will make them feeble competitors in the wild unconvincing. "There are so many examples of organisms that are not competitive in one environment being extremely competitive in a different environment....We have to build attributes into the plants themselves, and into the growing systems, to provide safeguards."

Some scientists who are relatively untroubled by the possibility of gene flow into wild forests advocate long-term monitoring of GE trees and surrounding ecosystems just the same. "That's the way to do it, to tell you the truth," DiFazio says, "because these ecological questions are so complex. You can do preliminary small-scale tests of invasiveness, but the level of inference that you can have from those tests is extremely limited."

But discussions about long-term monitoring and other safety measures that depend on voluntary compliance have to take into account a record of breaches that have already occurred during the short history of transgenic plants. Along with the ill-famed StarLink episode (in which foods containing unapproved, genetically modified corn were sold commercially), some pharmaceutical-producing biotech corn was accidentally allowed to grow in Nebraskan soybean fields last year. The same company responsible for potentially contaminating the soybeans, Prodigene, was required to burn 155 acres of Iowa corn that might have cross-pollinated with a GE strain. Still other biotech firms were fined for violating Environmental Protection Agency regulations for field tests of insect-resistant GE corn in Hawaii last year.

Deserving of public trust

Other agencies share regulatory responsibility for some transgenes, but the focus of NRC's 2002 report is APHIS, which judges the safety of any genetically engineered plants—including trees—for agriculture and the environment. North Carolina State University entomologist Fred Gould, who chaired the NRC panel that produced the report, characterized its recommendations as "a means to help improve a functioning system." And the current regulatory process has its supporters, such as Arborgen, the private-enterprise GE tree research consortium.

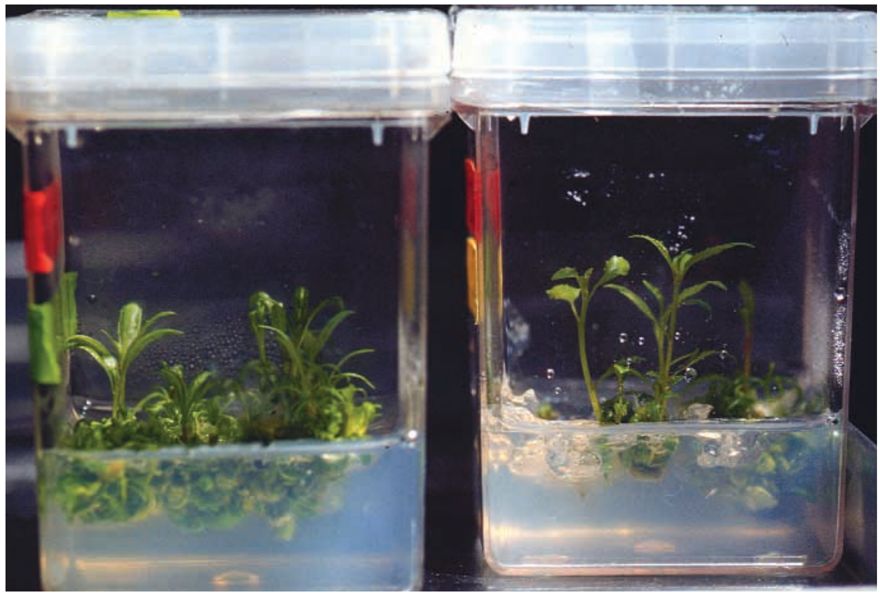
APHIS examines GE plants closely, says Les Pearson, Arborgen's director of regulatory affairs. "For us, that's just part of the landscape. There's a lot of learning for the public to do to understand about transgenic trees, and so that's perhaps appropriate." Adds Maud Hinchee, Arborgen's chief technical officer: "Private enterprise works with regulatory agencies, and we have a lot of faith in them. I think we have some of the best regulatory processes in the world, and other countries mimic the methods used in the US."

But the NRC report took sharp exception to much of the way APHIS evaluates the safety of transgenics, and it stressed that rigorous scientific risk analysis is not just the basis for good policy. It also "serves as evidence to the public that the decision making agencies are deserving of their trust," Gould wrote.

The NRC committee reached these conclusions:

- The APHIS section responsible for regulating transgenics is underfunded and understaffed, and its personnel are overworked. Their collective scientific training does not match their regulatory responsibilities.

- After transgenics are approved for commercial use, the agency's deregulation of them is absolute, with no further authority to monitor the GE plants. But detailed, long-term monitoring of ecosystem impacts, over a number of years and locations, is needed.



Richard Meagher of the University of Georgia's Genetics Department is working with eastern cottonwood trees genetically engineered for resistance to mercury compounds. The trees can clean up polluted soil by taking up mercury through their roots and converting it to a less toxic form—a process called phytoremediation. Shown are in vitro shoot cultures of two GE eastern cottonwood clones. The ability to clone GE trees for rapid propagation is essential. Photograph: D. Che.

- Individual GE traits that are approved for commercial use because they are presumed safe can be combined later in a single type of plant—this is called "gene stacking"—without further scrutiny by APHIS.

- There should be "substantial increases in public-sector investment" for research on the opportunities and risks associated with transgenics.

All of which would require a major surge of voltage for APHIS. It may not be at the scale envisioned by the NRC, but APHIS's budget for regulating transgenics and some related work has already increased from about $3 million in 1999 to $5.3 million in 2003.

Money and data

"Society so far—or maybe it's just the people who dole out the cash—have been unwilling to fund what is really necessary in terms of some of the long-term studies," says Bernd Blossey, a Cornell University invasive plant ecologist who served on the NRC committee. "One of the things we struggled with in the study is that we don't have good data on how organismal diversity in North America is being affected by anything: drought, herbicide or other pesticide use, or habitat loss.

"When we don't know that, it is very, very difficult to do something smart.... I don't think there is any data that would allow us to do a rigorous assessment of what transgenic tree plantations would actually do at the level required for commercial approval," he added.

For Raffa, one essential feature of a good regulatory system for GE trees would change how research money is allocated. As anyone who competes for grant money can testify, Raffa has written, the successful applicants propose tight, narrowly focused experiments that can be conducted under controlled conditions with quick results, using organisms that lend themselves to simple kinds of measurement. Unfortunately, the key questions about environmental safety are long-term and complex, and they operate across several species and multiple levels of the food web.

The NRC report also faulted APHIS's regulatory activity for its opacity. So much data is kept secret as "confidential business information" (CBI) that even the NRC committee itself was stymied at times in evaluating the agency's rulings. "Under this CBI stamp, all manner of data are hidden from public view and even from independent scientific scrutiny," the report said. APHIS's regulatory process for transgenics "should be made significantly more transparent and rigorous by enhanced scientific peer review, solicitation of public input, and...more explicit presentation of data, methods, analyses and interpretations."

Duncan says, "Private industry does not want an environmental catastrophe. They don't want a non-efficacious product in the marketplace, for obvious reasons. They have a huge liability. They have their very company at risk if something should go awry."

But Blossey contends that secrecy militates against credibility, and he doubts the claim that corporate liability can be relied on to guarantee the biosafety of GE trees. " I don't think the corporations have done a wonderful job in giving long-term stewardship. Particularly not the forest industry," he says.

Strauss directs the Tree Genetic Engineering Research Cooperative at Oregon State, some of whose work has been funded by the forest products industry. He says that corporate interest in keeping proprietary knowledge private will have to be reconciled with the intense level of public interest in GE trees, if progress toward commercialization is to be made. "Companies give lip service to doing things more openly and transparently," he said. "I don't see much of it happening yet. I don't know if it will happen. They have a whole different culture, a different mindset," especially in the wake of strident activist rhetoric and fire-bombing and vandalism incidents at GE tree research sites, including Strauss's own.

"What really bugs activists is, they don't trust corporations, and they're convinced that this technology wouldn't be done if it weren't for corporations seeking profits. They just ignore the fact that there's a lot of good uses for biotechnology, appropriately chosen and carefully developed. The activists like to beat themselves into a frenzy by thinking it's all multinational mind control, and it looks that way. There's grounds for those concerns. The companies don't share what they do very well, and that generates paranoia. But the next step the activists take is to demonize the whole technology."

Genomics research associate Lee Gunter and student intern Rebecca Tolbert shown here in the lab of Gerald Tuskan at Oak Ridge National Laboratory, examining the variability in DNA content among various poplar genotypes. This work was part of the development of the genetic map that will be used to help order and orient the data from the poplar genome sequencing project now under way. Photograph: Curtis Boles.

Biotech for the environment

"The naysayers want everybody to believe that there ought to be 30 years of testing before a product can go on the market," Duncan says. "Well, you've just killed the industry if you require that."

Some of the naysayers are demanding a good bit more. "The one way they could with certainty prove that this would be an innocuous technology if it were to contaminate native forests," says Brad Hash, of Action for Social and Ecological Justice (ASEJ), "is to grow genetically engineered trees that express every trait that's being researched. Continue that growth through the entire life of the tree, have it die and decompose into the soil, then conduct soil and water quality samples to determine whether this is truly benevolent." ASEJ is part of a campaign kicked off this spring to demand an indefinite moratorium on GE tree research at the International Paper Company. The hoped-for repercussions would halt such research at all US companies, Hash says.

Antibiotech activists face some paradoxes if they reject GE trees forever and all, though. Some of these innovations might prove to be good for the environment. Experiments are under way to engineer trees whose roots will take toxins up from polluted soil. Fast-growing populations of GE trees might ease the global pressure to log wild forests. Trees might be engineered so as to sequester more carbon and, when used as biofuel, could establish a closed-loop energy cycle that would mitigate global warming. Insect-resistant trees could reduce the need to spray pesticides or to use harsh chemicals during the wood-pulping process.

These possibilities are seen by critics as highly speculative or as introducing new, strong threats. One is the likelihood of a steady increase in insect resistance to the useful toxin generated by the soil microbe *Bacillus thuringiensis,* if trees are engineered to produce it, too. Other environmental claims for GE trees are dismissed as public relations maneuvers to justify a radical new technology. But the prospect of restoring chestnut, dogwood, hemlock, butternut, or elm trees to American forest ecosystems via genetic engineering seems less easy to shrug off.

One such project is making halting progress in labs at the State University of New York (SUNY) Environmental Science and Forestry School, in Syracuse, and at the University of Georgia. Work is under way there to create a transgenic chestnut resistant to the blight that erased the tree from the Appalachian ecoregion during the last century. SUNY molecular biologist William Powell and Charles Maynard of the forestry department have spent the last 12 years trying to incorporate two or three genes that would confer resistance into chestnut. One encodes a gene from wheat, used to detoxify a destructive acid that blight fungus produces. "We've done all the pieces but we haven't got everything together to get the gene in and regenerate the whole plant," Powell says. "I think within this decade, we will have a resistant tree."

The New York group is collaborating with Scott Merkle, a tree biotechnologist at the University of Georgia–Athens, whose specialties are propagating trees from cellular material and developing gene-transfer techniques—both very difficult with chestnuts. On both campuses, funding from government agencies has plummeted since September 11. Three-fourths of the annual budget that keeps Powell's work going now—about $75,000—has been donated by Arborgen as a public service project, along with a like amount for Merkle's research.

Ambitions

Biotech tree researchers are excited about the sequencing of the poplar genome, but the excitement is tempered by frustration: Will they be able to put these powerful new tools to use? The project, an international collaboration whose chief sponsor is the Department of Energy, is due for completion by the end of the year.

As the research clarifies, public and regulatory acceptance of its applications remains a foggy uncertainty. "I know that there are commercial crops—trees, economically viable right now—that have not been released because of those pressures," Tuskan, of Oak Ridge, says.

Strauss offers a backhanded salute to the success of activists who oppose GE trees. "In terms of round one of the war, they won and we lost.... I don't see how you can think of it any other way. There's much more and much better to come, but it's going to face more difficulty because of where we are."

University of Montana forestry professor Alan McQuillan shares the sense of resignation, but from the opposite perspective: The commercial development of GE trees, he says, is taken as assumed. "I think that society has made the decision that it's doing it," he says. "It's not just the United States, it's global."

Hash, on the eve of the new campaign to halt GE tree research, gives better odds for an extended debate. Bids for commercial development may be several years off, he noted. That offers time to mobilize public opinion, "so that we don't get into the situation that GE food is in. So that we don't have to stuff the genie back in the bottle. Once the organism has produced and spread the seed, you're not going to be able to recall it."

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