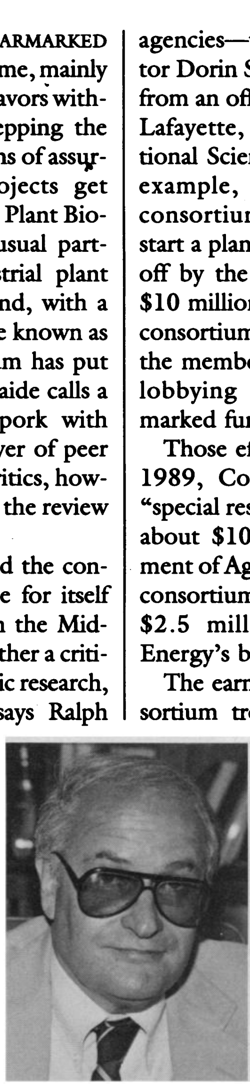
Can There Be a Better Grade of "Pork?"

The Midwest Plant Biotechnology Consortium says yes, but pork critics have not yet been convinced

IN THE ACADEMIC WORLD, THE EARMARKED research grant has earned a bad name, mainly because Congress bestows these favors without peer review, thereby sidestepping the scientific community's chief means of assuring that only meritorious projects get funded. Now comes the Midwest Plant Biotechnology Consortium, an unusual partnership of academic and industrial plant scientists in the nation's heartland, with a new twist on what has come to be known as "academic pork." The consortium has put in place what one congressional aide calls a "creative hybrid," combining pork with competitive peer review. The layer of peer review hasn't mollified all pork critics, however, and some observers say that the review isn't as rigorous as it should be.

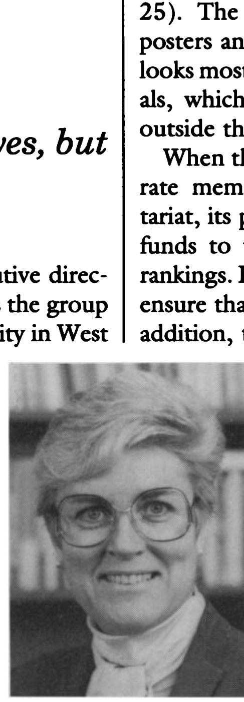
But such criticism is sparse, and the consortium has earned a good name for itself among many plant scientists. "In the Midwest, the consortium has put together a critical mass of good industry, academic research, and organizational structure," says Ralph Quatrano, a plant molecular biologist at the University of North Carolina who has served as a reviewer for the group.



Harvey Drucker

The consortium got its start in December 1985 at a meeting called by Harvey Drucker, associate director for energy, environmental, and biological research at Argonne National Laboratory outside of Chicago and Alan Schriesheim, the lab director. Their goal: to bring together researchers from federal, university, and industrial labs to spur the then nascent field of plant biotechnology. "If plant biotechnology was to be of any use," Drucker says, "we had to connect business with basic research." And at the meeting that began to happen. Barriers fell when industrial scientists defined their key problems—developing improved means for pest control and seed production, for example—and academic researchers realized that they had the skills to help solve them.

After the decision was made to put a consortium together, joining researchers from both camps, the organizers tried to get funding for it from the traditional granting agencies—to no avail, says executive director Dorin Schumacher, who runs the group from an office at Purdue University in West Lafayette, Indiana. The National Science Foundation, for example, turned down the consortium's application to start a plant science center, put off by the high cost—at least $10 million. At that point, the consortium organizers enlisted the member companies' aid in lobbying Congress for earmarked funds.


Dorin Schumacher

Those efforts paid off. Since 1989, Congress has written "special research grants" worth about $10 million into the U.S. Department of Agriculture (USDA) budget for the consortium and just this fall put another $2.5 million into the Department of Energy's budget.

The earmarking of the funds for the consortium troubles some observers, such as Paul Stumpf, former director of the USDA's competitive grants program, now called the National Research Initiative (NRI), and emeritus professor of plant physiology at the University of California, Davis. In a time of tight budgets, federal money that goes into this kind of work is money that can't be spent on competitive grants, he says, adding, "I think the money might be better spent if we transferred it to the NRI, where they already have in place a panel review system." Even Quatrano, although pleased with the work of the consortium, is unhappy that the group had to go the pork route. "I don't approve of the way funds are obtained," he says. "But the tragedy is that there is insufficient support for the kind of plant science research they do."

And consortium officials maintain that they are putting the money they get to good use, aided by a stringent peer-review system that has several components. After the consortium's corporate members establish a broad research agenda, academic researchers in the Midwest are invited to submit "preproposals" by presenting posters at the consortium's annual meeting (also see page 25). The industrial members screen the posters and invite researchers' whose work looks most promising to submit full proposals, which are sent to academic scientists outside the consortium for review.

When the reviews come back, the corporate members of the consortium's secretariat, its policy-making board, allocate the funds to those researchers who got high rankings. But passing this hurdle still doesn't ensure that a grant will be forthcoming. In addition, the successful applicant must get matching funds from nonfederal sources, such as foundations, universities, state or local governments, and companies, at least one of which must belong to the consortium. "They like that. It means that a company can see research carried out that it might not afford on its own," says Schumacher. And the academic researchers like the grants. With the matching funds, they range from $80,000 to $400,000 annually, a sizable sum in the plant sciences.

But not everyone agrees that the consortium's peer review is rigorous. One consulting scientist in the Midwest who asked to remain anonymous says that the money that goes into the consortium can be used only by members of this exclusive club, and no consideration is given to ideas from outside the Midwest. The result is that "you don't have real peer review," he asserts, but rather a system of "deals" in which awards are often preselected before review.

Schumacher bristles at suggestions that the peer review is anything but first class, however. "Our review procedures are just as rigorous as those of the National Science Foundation, the National Institutes of Health, and the USDA competitive grants. We have the same forms, reviewers, and procedures," she maintains, noting that last year the consortium didn't give out all the funds available because corporate members thought there weren't enough good proposals.

What's more, Drucker adds, the consortium is meeting its original objective of bringing together people in the applied and basic sciences. And the collaborations may soon pay off in more concrete results as consortium researchers have begun filing patent applications on the fruits of their work, such as new systems for getting novel genes into corn and for controlling gene expression, developments of value to both academe and industry. "There have not yet been any products," Drucker says. "But there will be." ■ ANNE SIMON MOFFAT

Plant Biotechnology Explored in Indianapolis

Every year the Midwest Plant Biotechnology Consortium has a meeting to showcase the progress its current grantees are making, as well as to provide an initial review of proposals from researchers who would like to be grantees (also see p. 24). Herewith follows a selection of the highlights from the 1991 meeting, which took place in Indianapolis on 12 to 14 November.

■ **Protecting plants against a fungal root disease.** When insects are used for pest control, there's usually little doubt about how they work. The beneficial insect eats its target, most often another insect. But the biocontrols used to combat disease-causing fungi and other microbes often work in ways that are not quite so easy to understand. Take the case of *Bacillus cereus UW 85*, a bacterium being tested as a possible means of controlling "damping-off disease" of roots, a fungal infection that destroys the roots of soybean and alfalfa seedlings and costs farmers tens of millions of dollars annually. *B. cereus* shows promise for controlling the disease, but researchers didn't know how it worked—until now. At the meeting, molecular biologist Jo Handelsman of the University of Wisconsin, Madison, reported that it produces an antibiotic that inhibits the disease-causing fungi.

Bad at the root. *One of the fungi that cause damping-off disease.*

F. SCHWENK, KANSAS STATE UNIVERSITY

But Handelsman's finding didn't come overnight. Back in 1985 she screened more than 100 species of soil bacteria, looking for any with antifungal properties. "We had faith in the variety of nature, that somewhere out there, there would be an organism that offers control," she says. *B. cereus* proved to be the only one that worked consistently. After that it took years of patient work to find out what the effective agent was. Now they've got that, but Handelsman and her colleagues still haven't solved all the mysteries about the antifungal action of *B. cereus*. Chemically, they have not yet fully characterized the antibiotic it produces. Nor do they understand why the bacterium provides significant protection against damping-off disease in field trials in the upper Midwest but is virtually useless in the South. They're working on that puzzle, they say, and on the genes the bug uses to make its antibiotic—all in hopes of creating a commercially useful biocontrol agent.

■ **Protein stability improved.** One of the major goals of the biotech industry is to use plants as "factories" for manufacturing useful proteins cheaply. Among the likely candidates for this approach are human proteins that can be used as drugs, and industrial enzymes such as subtilisin, a protein-splitting enzyme added to laundry detergents to improve their ability to dissolve tough stains. But before plant cells can be turned into little industrial plants, their production efficiency must be improved.

A common way of improving production of a particular protein is by tinkering with the regulatory region of the gene that encodes the protein—thereby boosting the gene's activity. But that strategy may not be enough by itself, because all cells contain protein-degrading enzymes called proteases that can reduce yields even when a protein is initially produced in ample amounts.

At the Indianapolis meeting, plant molecular biologist Richard Vierstra and his postdoc David Hondred of the University of Wisconsin, Madison, described a technique for improving the stability of novel proteins produced in plants. The key to the method is a protein called ubiquitin, shown by other researchers to enhance protein production in bacteria and yeast cells. To find out if the same is true of plant cells, the Wisconsin workers fused a ubiquitin gene to the gene for beta-glucoronidase (GUS), a marker protein commonly used in gene-transfer experiments because it turns cells that acquire it blue. When Vierstra and Hondred introduced their hybrid gene into tobacco plants, they found that GUS production was four times higher than in plants receiving a normal GUS gene.

While that's a promising finding, it does raise some questions that the Wisconsin group is now working on. One of them is why ubiquitin increased production of the hybrid protein in plants. In higher organisms, after all, ubiquitin attachment generally leads to protein degradation. But to get protein degradation, Vierstra says, several ubiquitins have to be attached to the protein—and they go on at an internal amino acid, not just on the end—as they do on the hybrid ubiquitin-GUS protein. In the hybrid, ubiquitin may physically shield the GUS portion from proteases, Vierstra suggests. Or, alternatively, it may facilitate the folding of GUS itself. Either way, the GUS portion would be protected. The next step, Vierstra says, is to see whether ubiquitin improves the stability of other, more economically useful proteins in plant cells.

■ **Plant regeneration genes located.** Given the right conditions, a single plant cell can regenerate into a whole plant. Indeed, this ability is a key element for the plant biotechnology industry. The reason: The industry generally creates novel plant strains by introducing foreign genes conferring desired traits into single cells, which are then induced to form whole plants. But finding the right conditions to induce such growth is now more art than science.

But help is at hand. Thomas Hodges of Purdue University in West Lafayette, Indiana, working with Charles Armstrong of Monsanto Corp. in St. Louis and Jeanne Romero-Severson of Agrigenetics Corp., has taken a giant step toward identifying the genes needed to trigger regeneration by mapping the chromosomal locations of at least three genes associated with corn plant regeneration. If the genes can be cloned, Hodges says, it may be possible to introduce them into plants whose cells regenerate poorly, thereby genetically engineering strains with improved regeneration capabilities. The problem so far has been that while some plant cells readily regenerate whole plants, many others don't, even after being doused with growth cereals.

To locate the critical regeneration genes, Hodges and his colleagues began with strains of corn that regenerate relatively well and crossed them with a poorly regenerating strain. The Hodges team then used gene markers known as RFLPs to identify the chromosomal locations that carry genes that facilitate regeneration. RFLPs that are consistently inherited with good regeneration ability should be very near the regeneration genes. Using this method, the joint academic-industry team identified regions on three separate chromosomes that appear to contain such genes. The next step is to try to pinpoint the genes so that they can be cloned—and then, perhaps, introduced into recalcitrant strains, coaxing them into regenerating. ■ **A.S.M**