

AGRICULTURAL RESEARCH

Crop Scientists Break Down Barriers at Ames Meeting

For years, crop science has been balkanized, with specialists in rice, corn, and soybeans, for example, working on their own commodities and attending their own meetings. But at the First International Crop Science Congress, held in July in Ames, Iowa—an 8-day event 3 years in the making—the discipline displayed a newfound hybrid vigor. More than 1000 researchers of various persuasions, including plant molecular biology, classical plant breeding, agronomy, and soil science, representing 85 countries, shared their expertise in basic and applied studies. Here are a couple of proposals for expanding world food production and another that shows the diverse roles crops can play.

Making Barren Areas Bloom

Many of the best farmlands have been in cultivation for decades, but their high yields are increasingly threatened by the collective impact of erosion, salinization, and nutrient and water loss. As a result, many crop scientists are turning their attention to lands that have been labeled marginal—areas abandoned as too cool, dry, or wet to support agriculture. The hope is that traditional plant breeding, coupled with a few new tricks offered by biotechnology and agronomic expertise, will produce crops tailor-made for these regions, allowing some desolate areas to become, if not a flourishing Eden, at least a bit more self-reliant when it comes to producing food.

Brian Fowler of the University of Saskatchewan, Saskatoon, Canada, for example, described efforts to move the cold hardiness genes of winter rye, a particularly tolerant crop, into wheat, a commercially more valuable one. Right now, wheat is grown in much of the United States but only on limited acreage in Canada. Fowler and his colleagues would like to engineer wheat so that it could prosper up to the 54th parallel, the latitude of the southernmost parts of Alaska and the northern Canadian prairies.

Fowler told the meeting that classical plant breeders have been able to incorporate the various rye genetic loci responsible for cold hardiness into wheat, but the snag is that they don't have a good handle on the genetic controls that could allow the expression of such genes in the new hosts. The recent successful genetic transformation of wheat by Indra Vasiland and colleagues at the University of Florida, Gainesville, and Monsanto (published in *Bio/Technology*, June 1992) has, however, raised hopes that new genetic engineering techniques can overcome the problems. The group used a "gene gun" and special cell culture techniques to insert a gene into wheat that conferred resistance to the herbicide Basta.™ These procedures, designed especially for wheat, should enable

plant breeders to introduce yet other genes, such as those that confer cold hardiness, with greater speed and precision than is possible with classical breeding techniques. "It is now just a matter of time to get improved cold hardiness," predicts Fowler. When that happens, the world's breadbasket could include the Canadian prairies and much of Siberia—an area Fowler describes as "the largest, harshest, agricultural region in the world."

Abraham Blum, an agronomist at the Volcani Center in Dagan, Israel, is aiming at the other end of the climate extreme, trying to develop wheat varieties that will prosper with only 8 inches of rain annually—less than one-half the normal requirement—and in temperatures approaching 100° Fahrenheit. But he's less sanguine than his cold-climate colleagues. Research over the past decade, he told the conference, has indicated that drought tolerance is a complex phenomenon that appears to depend on the interaction of several different genes.

Until 10 years ago, it was thought that drought-resistant varieties simply use less water to initiate growth. "That is wrong," says Blum. "They use water, but now we know that they use it more efficiently." Drought-resistant plants in fact use a variety of physiologic tricks to prosper in arid regions, including having tough, aggressive roots that seek out water; accumulating solutes so they retain water, which causes plant tissues to remain turgid even when it is very hot; and controlling the activity of leaf stomates, thus reducing water loss from inside the plant. Moreover, high-yielding, drought-tolerant species may be better able to mobilize their resources to the most important parts: the edible grains. Some drought-tolerant grains can produce plump kernels "even when the rest of the plant looks clinically dead, dried up with no chlorophyll," Blum says.

The bottom line, Blum said, is that "the various mechanisms that contribute to stable yield (in arid conditions) are not determined by a single or a few genetic entities but by a whole complex of factors at work." These recent findings mean that developing stress-resistant crops is a doable task, Blum said, but it is likely to be far more complex than engineering plants with herbicide resistance, which can result from tinkering with a single gene.

Novel Crops Gain Acreage

Of the 80,000 plant species that produce some part that is edible, just 50 are actively cultivated. Indeed, only seven crops—wheat, rice, corn, potatoes, barley, cassava, and sorghum—provide 75% of the world's food supply, and many of these, long the focus of plant breeders' attentions, are topping out in yields. Enter the so-called neglected crops: grains including quinoa, amaranth, and millet, and fruits and vegetables such as banana, sweet potato, and Andean tuber. For years, crop scientists have been arguing that such crops can be tapped for increased production; as R.S. Paroda of the Indian Council of Agriculture, New Delhi, explains, "Many of them are tolerant to adverse conditions and can grow on lands that are otherwise consid-



High and dry. Quinoa, a cereal plant, being cultivated at 10,000 feet in the arid Andean plateau.

ered marginal for agriculture." Now a few, scattered programs are putting that promise to the test.

Miguel Holle, of the Andean Agricultural Systems Project, Lake Titicaca bas, Peru, for example, told the Congress that quinoa (*Chenopodium quinoa*) is grown successfully in rotation with potato and barley in the 10,000-foot-high, dry, Andean plateau. This grain, a nutritious cereal, can be grown with few resources. Paroda adds that in India there has been a formal program since 1984 to give field trials to unexploited plants including amaranth, buckwheat, chenopods including quinoa, and the winged, rice, faba, and adzuki beans.

What is needed now, Paroda says, is a greater commitment from international agencies and the developing nations themselves to explore the potential of these crops. Experience in India and elsewhere has shown that most farmers are receptive to the idea of growing new plants if it can be shown that they will yield a profit, he says.

Plants as Cleanup Artists

In advanced nations, plants are valued largely as food, but in developing countries they serve more varied roles, often acting as the main source of food, fiber, fuel, and medicine. Now, several research groups have shown that plants can aid environmental cleanup, too—most recently by capturing heavy metals from groundwater and locking them in their tissues.

One hint of plants' cleanup abilities came a few years ago from Monash University in Victoria, Australia. Australian plant scientist Douglas R. Laing, who is in the process of moving from the International Center for Tropical Agriculture in Cali, Colombia, to become director of the Commonwealth Agricultural Bureau in Wallingford, England, reported that some colleagues at Monash conducted field experiments, using Australian swamp plants growing in a shallow, gravel-filled ditch, to filter suspended, finely divided organic matter from contaminated water supplies. "This is a fancy way of saying they used plants to take sewage out of the rural, local water supplies," he says. More recently, the Australians discovered that the plants were even more versatile as cleanup artists: They could also absorb a large proportion of the water's heavy metals.

Other researchers have tried to improve on this ability by genetic engineering. R. Keith Downey of the Agriculture Canada Research Station in Saskatoon, noted that a colleague at the University of Calgary, molecular biologist Lashitew Gedamu, has genetically engineered oilseed rape (*Brassica napus*), tobacco, and alfalfa, inserting a human gene for metallothionein, which chelates metals. He is now testing how various promoters may put this sequestering system into high gear to guide the metals into nonedible portions of plants. Gedamu's long-term goal is to use such transformed plants to trap metals and help clean the polluted areas around Canada's many mines.

But won't these metal-contaminated plants create a cleanup problem of their own? Laing suggests that if they are good enough at socking away precious metals along with the poisonous ones, they may be burned to reclaim, for example, gold and platinum. In any case, he says, it is far easier to dispose of heavy metals once they are trapped in plants rather than when they are floating free in the water system.

—Anne Simon Moffat

MEETING BRIEFS

Chemistry Pitches Its Big Tent At Washington Gathering

When the American Chemical Society (ACS) held its 204th national meeting in Washington, D.C., last week, traditional, benchtop chemistry was all but eclipsed by the myriad of other disciplines—materials science, environmental research, and pharmacology, to name a few—that were gathered under the banner of chemistry. Several of the most intriguing sessions focused on a hot biomedical topic: cancer prevention and treatment.

Radioactive Antibodies Start Hitting Home

Since the early 1960s, doctors have routinely injected radioactive isotopes into patients in order to scan organs for disease. Some researchers also tried from time to time to develop isotopes for therapy, the idea being to destroy diseased tissue with the isotopes' radiation. But most such approaches have come up short, in part because of the difficulty of getting high doses of isotopes to home in specifically enough on diseased tissue. At a session of the ACS meeting last week, though, several researchers reported encouraging results in their effort to create the clinical equivalent of laser-guided missiles: isotopes attached to monoclonal antibodies that home in on aggressive cancers and deliver their cell-killing payloads.

The concept, known as radioimmunotherapy, isn't new—a team at Memorial-Sloan Kettering first attached iodine to rat antibodies in the 1950s. But for years radiopharmaceutical companies essentially ignored this work and concentrated on developing medical isotopes for diagnostic procedures. Attention began to shift toward therapy in the early 1980s, says Leonard Mausner, a nuclear chemist at Brookhaven National Laboratory. That was when new, nonradioactive techniques such as ultrasound began offering sharp competition in the diagnostic field, leaving isotope mavens to hunt for novel applications. And sure enough, new research showed how to attach isotopes to a variety of monoclonal antibodies.

That research is already paying off, National Institutes of Health (NIH) inorganic and nuclear chemist Otto A. Gansow told meeting attendees. Two years ago, Gansow and Thomas A. Waldmann, chief of the metabolism branch at NIH, began clinical tests of targeted isotopes in patients with adult T-cell leukemia, an aggressive cancer. The chemists attach yttrium-90, an isotope with a 64-hour half-life, to a monoclonal antibody designed by Waldmann that homes in on the interleukin-2 receptor of T cells. The yttrium-90 molecules shed beta particles that kill the T cells but spare other cells outside an 8

millimeter radius, reducing the damage to healthy tissue.

Gansow now reports that 10 of the 14 patients treated with the yttrium-antibody combination experienced at least a 95% reduction in tumor cells and eight went into partial or complete remission; five are still alive, and three appear to be completely free of cancer. "It's really lovely experimental work," says oncologist Steven Rosenberg of the National Cancer Institute. But Gansow warns that the technique needs refining; the isotopes sometimes detach from the antibodies before they reach their targets. "If your chemistry isn't perfect, the yttrium goes to the bone," he says. What's more, because the yttrium isn't as potent a weapon as some other isotopes, the NIH team, along with Johns Hopkins pharmacologist Mette Strand, envisions replacing it with bismuth-212, an isotope that emits both beta and alpha particles, which pack a greater therapeutic punch.

Besides tinkering with the weapon, researchers are toying with the antibody guidance system to get new anticancer weapons. Researchers at Newark-based Immunomedics Inc., in collaboration with the nuclear medicine group at Oak Ridge National Laboratory, are developing isotope-linked monoclonal antibodies targeted to a specific cancer antigen on colorectal cancers. The researchers recently began testing the efficacy of their system, based on rhenium-188, in monkeys. In addition, they've injected small doses of the antibody-rhenium conjugate into four patients with colorectal cancer. The doses weren't large enough to provide therapeutic benefit, but Gary L. Griffiths, director of chemistry at Immunomedics, points out that his team "hasn't seen any adverse effects yet."

Just how hopeful is this work? Robert E. Henkin, director of nuclear medicine at Loyola University of Chicago, warns that "therapeutic labeled antibodies are a few years away from becoming a common radiological tool." One potential stumbling block: Improving this sort of drug might prove to be a daunting task for the Food and Drug Administration (FDA), says Henkin, because "no one group at the FDA has experts on both antibodies and radioactivity." An FDA offi-