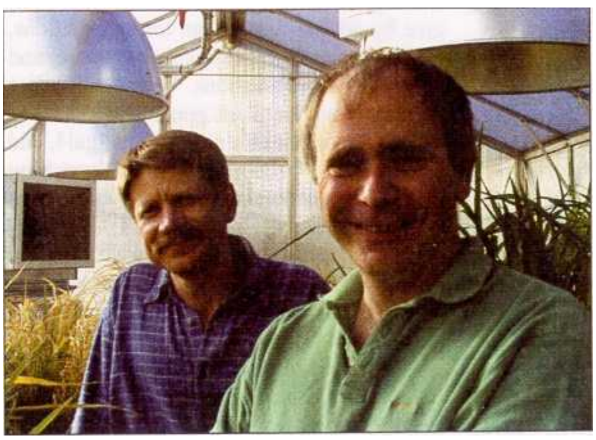
PLANT BIOTECHNOLOGY

Australian Center Develops Tools for Developing World

Richard Jefferson runs an institute in Canberra that helps plant scientists and farmers apply the latest technologies to overcome local problems

MELBOURNE-Richard Jefferson advocates grassroots genetic engineering for agriculture. He says that the approach taken by most universities and companies - producing single gene fixes tailored to model systems-is virtually irrelevant to the complex, diverse systems of the developing world. Instead, the 43-year-old molecular biologist argues passionately, what farmers need arc the knowledge and tools to develop and disseminate their own strains tailored to local conditions and practices. His Canberra-based institute, CAMBIA -the Spanish word for change and an acronym for the Center for the Application of Molecular Biology to International Agriculture-is dedicated to that goal. And a lot of people are rooting for him.

CAMBIA, founded in 1992 with rhizobial molecular geneticist Kate Wilson, is intended to be a genetic workshop for the developing world. It's also a clearinghouse for intellectual property issues. With support from the Rockefeller Foundation and smaller grants, Jefferson has already helped Chinese scientists develop a new strain of long-lived rice, and he and his colleagues are testing a technique for rapidly generating and screening genetic variants that will thrive in local conditions. Last month these efforts received a major boost when CAMBIA was chosen as the biotechnology arm of the Institute for International Tropical Agriculture OITA), the Nigeria-based research center that is part of the Consultative Group on International Agricultural Research (CGIAR).



A breed apart. Richard Jefferson, right, and Andrzej Kilian see CAMBIA as a way to improve agricultural technologies.

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Many plant scientists think this recognition is long overdue. "We all want to plow back our inventions to help developing countries, but ... CAMBIA's focus of developing new tools is unique, and I'm very pleased it's being recognized," says Roger Beachy, director of the Donald Danforth Plant Science Center in St. Louis, Missouri. "While we might train a student how to diagnose a specific disease in cassava, Richard is trying to develop brand-new technologies:" At the same time, they note that some of those technologies have yet to be tested. "They're either completely wrong or three jumps ahead," say Peter Raven, director of the Missouri Botanical Garden in St. Louis, about one of' CAMBIA's projects.

Born in the United States, Jefferson has an impressive record of crafting innovative tools for improving crops. In 1985, as a graduate student at the University of Colorado, Jefferson developed a technique that monitors the activity of transgenes by tagging them with the bacterial enzyme β–glucuronidase (GUS). Because GUS activity is easily detected by a color-producing enzyme assay, researchers use the assay to follow the activity of the transgene. The original paper is the most widely cited in the plant science literature. A few years later, at the Plant Breeding Institute in Cambridge U.K., he used GUS as a stethoscope to monitor transgenes in field trials of the world's first genetically engineered food crop, a potato. Jefferson quotes Henry Ford, another man who changed the face of an industry. I n describing the depth of his commitment to CAMBIA, which has relied heavily on self-funding from GUS royalties. "Obstacles are those things you see when you take your eyes off the goal," he quips.

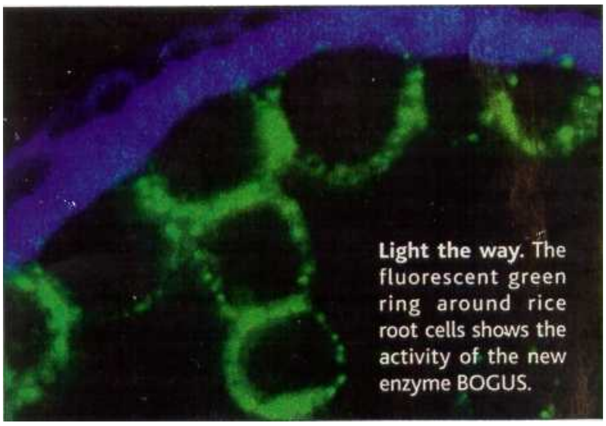
One of CAMBIA's current projects involves a new screening method for identifying transgenic plants through positive selection. The technique gives plants an exclusive energy source-in this case, cellobiuronic acid, a substrate that GUS breaks down to release glucose - and avoids the stress caused by the current approach of exposing plants to an antibiotic that onlv the transgenics are able to withstand. By using a novel secreted forth of GUS (Bacillus OZ GUS, or BOGUS) that can metabolize cellobiuronic acid outside the cell, the technique offers the prospect of producing healthier, more genetically stable plants and eliminates concern about producing plants with antibiotic resistance.

A second project focuses on apomixis, the parthenogenetic reproduction of a plant from its seed. "Apomixis, if it's done right, could do more to revolutionize and democratize agriculture than any technology since the dawn of plant breeding;" says Jefferson. The technique would allow the small breeder to lock in the vigor of new genetic combinations, currently possible only by buying expensive hybrid seed or through labor intensive breeding protocols. It would also benefit crops like cassava or potato, by purging the pathogen load they aquirc during their vegetative propagation. CAMBIA is collaborating with its partner institute, IITA, and two other CGIAR centers to generate this trait using CAMBIA's new technologies.

Scientists in the developing world say that Jefferson's tools are just what they need. Qifa Zhang, a professor at Huazhong Agricultural University in Wuhan, China, has just developed a new transgenic rice strain carrying an antisenescence gene, which prolongs the grain-filling period of the plant. Results from the first test crop show it has increased productivity by 40%. "We and a lot of breeders have been helped by CAMBIA:" says Zhang, a member of Rockefeller's rice biotechnology network, whose student spent several months at CAMBIA constructing vectors and establishing the transformed rice lines.

Zhang is also excited about using the next generation of CAMBIA tools. One is TransGenomics, a strategy to reawaken what Jefferson and his colleague Andrzej Kilian believe is an untapped "Jurassic Park" of diversity lurking in the plant genome. TransGenomics is based on recent findings that suggest that new plant species evolve primarily by deploying relatively unchanged proteins in new functions rather than by making major changes to those proteins. Recent work by plant geneticist John Doebley and others at the University of Minnesota, St. Paul (*Nature*, 18 March, p. 236), for example, traces the difference between maize and teosinte, its wild grass ancestor with branches rather than a single spike, to changes in the regulation of the gene controlling this trait.

"TransGenomics takes a page out of evolution's own handbook in attempting to reorchestrate the activity of genes. Current techniques used in functional genomics programs disrupt gene function, affect all tissues, and fix the final mutations. Typically, these screens have not produced viable plants with useful new traits. TransGenomics is designed to kick-start the evolutionary engine by adding rather than losing functions, confining the changes to specific tissue, and permitting modifications. The screen relies on peppering the plant genorne with different combinations of a gene trigger. gal4 and its target, the UAS sequence, and watching as the combination of trigger and target fires up the activity of a new gene. Kilian hopes within 2 years that breeders around the world will be using CAMBIA's transgenomic rice seeds and creating their own crops with its tool kit.



Light the way. The fluorescent green ring around rice root cells shows the activity of the new enzyme BOGUS.

Many in the research community don't quite know what to make of the new technique. "I don't know if it will work or not," says Erie Kueneman special adviser for agriculture at the U.N. Food and Agriculture Organization. "But it takes the heat off using transgenic plants [because new traits are generated from the plant's own repertoire rather than from foreign genes]." IITA director Lukas Brader hopes the technique will aid African crops that have stubbornly resisted improvement. "Together we should be able to do something really good," he predicts.

However, future plant breeders and agroseientists will need more than science to succeed. They also must compete in a world where intellectual property (IP) issues can block the application of socially useful research. "Just about everybody in public institutes has been incredibly naive about IP rights;" says Gary Toenniessen director of Rockefeller's rice biotechnology program. "It's been a shock to us to realize that you cannot use the results of research you funded because almost everybody's product is tied up in IP [disagreements]."

That's why CAMBIA is developing a NVeb-based resource tool for IP issues, with support from Rockefeller. CGIAR, and the International Food Policy Research Institute, a CGIAR center based in Washington, D.C. "The resource should be of value to everyone from graduate students to agribusiness giants like DuPont, who can only gain from dealing with more sophisticated partners," explains Carol Nottenburg, an immunologist turned patent attorney who Jefferson recruited from from private practice in Seattle to Head the project.

Interactive software will allow users to address each step of the process, from ascertaining existing IP claims to formulating strategies to navigate (around them-with CAMBIA's own patented technologies as bargaining chips. Zhang welcomes this resource as he contemplates how to develop his new rice strains. "We have a lot of difficulty in dealing with documents, terms, rights. Basically we don't know how to negotiate," he confesses.

Although CAMBIA's freedom from institutional restrictions shortens its response tune, some wonder how the largely self-funded operation will muster the resources it needs to meet its ambitious goals. "It's somewhat distressing that, [despite Jefferson's] vision, it's been relatively difficult," says Beachy. "It's still a small operation."

But plenty of people hope CAMBIA beats the odds. "I told Richard years ago it was an absolutely brilliant idea that would never work," says Ed Rybicki, a professor of microbiology at the University of Cape Town in South Africa. "But I'm impressed [with how far he's come]" **-ELIZABETH FINKEL**

Elizabeth Finkel writes from Melbourne, Australia.