GENOME MAPPING

# Japan Picks a Winner in the Rice Genome Project

TSUKUBA—From outside, the five-story modern building that houses Japan's Rice Genome Research Program (RGP) is a cipher, its dark-tinted windows staring blankly out on rice paddies and vegetable fields that carpet the south rim of Japan's sprawling Tsukuba science city. But once past its nondescript exterior, a visitor is quickly swept up in a buzz of activity. Young men and women, some in spotless lab coats and others in plaid shirts and sweats, pad around laboratories glittering with the latest equipment or hunch over the glowing violet screens of their computer terminals. Their goal is to thoroughly understand the genetics of rice as part of a 7-year effort that will result, among other things, in a linkage map and ultimately the complete sequence of the rice genome. So far, they are right on schedule. "The genetic linkage map is almost complete," remarks project director Takuji Sasaki.

**Ripening harvest.** Rice serves as a model for cereal genomes.

In the 3 years since the project was launched, Japan has emerged as the world leader in rice genome research. "They are ahead of the United States in rice, which is a much more important crop for them," says molecular geneticist Saghai Maroof of the Virginia Polytechnic Institute and State University in Blacksburg, who has received genetic material from RGP scientists. The work of the program's 53 scientists, funded in part by the proceeds from racetrack betting, is also expected to provide insights into the genetics and evolutionary development of other cereal genomes, including wheat, maize, and barley. International interest in the RGP is also high: A majority of the 2200 subscribers to the RGP's newsletter, *Rice Genome*, work outside Japan. What's more, its single location has made it the envy of other, less centralized, genome projects elsewhere. "Our rice genome program, which supports several labs across the country, is attempting to do in the aggregate what RGP is doing with four units all in one location," says microbiologist Gary Toenniessen, deputy director for agricultural science at the Rockefeller Foundation in New York.

RGP germinated in the late 1980s as a joint government-industry effort to make Japan pre-eminent in the field of plant molecular biology. Discussions within the Ministry of Agriculture, Forestry, and Fisheries (MAFF) led to the creation of a rice genome project as a first step. The project really took off after MAFF found an unexpected source of funding—the Japanese Racing Association. The association is required to devote a portion of its take to activities that include scientific research, and in the late 1980s the sudden popularity of racetrack betting among Japan's women office workers sent its revenues soaring. As a result, the association agreed to spend $6 million on genome research and the construction of a new RGP building, which opened last November.

Today, the association provides more than half of the RGP's annual budget of $5.5 million. The project is run by the Society for Techno-Innovation for Agriculture, Forestry, and Fisheries (STAFF), a semigovernment organization that conducts research commissioned by MAFF. Its 160 industrial members include companies such as Japan Tobacco, Sanyo Electric Company, Hitachi Chemicals, and Kirin Beer, which occasionally participate in the rice genome–mapping effort.

Japan's staff of life might seem an obvious choice for a genome project, but Sasaki says "it wasn't a given. There were many candidates." Several factors tipped the scales towards rice. It has the smallest genome of the major cereal grasses, and its long breeding history has made its phenotype well known, with some 200 isolated traits such as growth cycle, disease resistance, and stalk height. In addition, rice is a staple food not only for Japan but for half the world's population, almost all of whom live in Asia and Africa. And traditional rice breeders in those regions are frantically seeking new strains that resist the growing menaces of fungal, bacterial, and viral diseases; insects; increased salinity; and drought.

**From maps to meals.** The ultimate goal of the rice genome project, says Sasaki, is to isolate and characterize agronomically important and scientifically interesting rice genes that could lead to more robust and productive strains. But the first priority is to construct a map of the 12 rice chromosomes and sequence its 450 million base pairs. As of this summer, the RGP had submitted 4342 nucleotide sequences of cDNA clones to the DNA Data Bank of Japan (DDBJ). The data bank is linked with two other international DNA sequence databases—GenBank in the United States and the data bank at the European Molecular Biology Lab in Heidelberg, Germany.

While the project is focused on genome mapping, says Sasaki, "we are also working on gene isolation—mostly to satisfy our funders." RGP researchers are on the verge of isolating several genes. They include *Se-1*, a gene that determines the flowering time of a plant, and a rice bacterial blight resistance gene, *Xa-1*. RGP is also hunting down genes that confer resistance to rice blast disease and is collaborating with a Japanese agricultural experimental station on a genetic linkage study involving several rice strains to segregate resistant and sensitive progenies. "After tagging these genes by DNA markers on our map," Sasaki predicts, "it will soon be possible to identify them."

Along the way, says Sasaki, RGP scientists expect to share with the world their growing store of knowledge and tools for identifying and cloning rice genes. Indeed, rice researchers from the United States, India, Thailand, Taiwan, the Philippines, South Korea, and China have visited Tsukuba to work elbow-to-elbow with RGP scientists. And RGP is exchanging DNA markers with the International Rice Research Institute (IRRI) in the Philippines as well as with rice genome mappers at Cornell University (see box on p. 1187).

Gurdeve S. Khush, head of plant breeding for IRRI's Genetics and Biochemistry Division, expects the project will increase the speed and efficiency of traditional methods of developing rice strains by its use of mark-

PHOTOS BY CAROLINE PARSONS/SYGMA

**Broad horizons.** Takuji Sasaki heads Japan's world-leading rice genome project.

ers to identify genes that determine important traits. However, he says it won't be long before rice genome research will lead to genetic manipulation of rice plants. Already, parallel research efforts in Japan, the United States, and Europe have used tissue culture to regenerate rice plants and produced fertile plants that contain and express foreign genes, says Toenniessen of the Rockefeller Foundation.

Manipulation of endogenous rice genes is also advancing rapidly. Hiroaki Shimada of Mitsui Toatsu Chemicals' Plant Biotechnology Lab expects the RGP's efforts to eventually boost the company's efforts to breed disease and stress-resistant strains. "Their molecular-based map and molecular markers that link with some important genes involved in rice quality will be very helpful for our rice-breeding process," he says.

Perhaps even more important are the expected benefits for the study of other crops, says Toenniessen. Because it is a small genome—one-sixth the size of wheat—rice is fast becoming the model cereal for studies in molecular biology and molecular breeding.

In a collaboration that began in 1991, Michael Gale, Graham Moore, and their colleagues at the John Innes Centre in Norwich, the largest plant molecular biology facility in Britain, worked with RGP scientists to identify markers that appear in the same relative positions on wheat and rice. Indeed, the correspondence between rice and wheat is so close that, in Gale's words, "wheat is rice." The colinearity observed among barley, wheat, and rye suggests there is colinearity "between markers on rice and all these species," says Moore. The ultimate goal, says Moore, is "a generalized map of the genome of the ancestral grass that gave rise to these cereals some 60 million years ago. Then all the information which has been generated by studying these cereals separately in the last 50 years could be combined."

Thanks to its well-funded and focused approach, Japan's RGP is ideally positioned to help lead this ambitious effort. And that's not all. Buoyed by the success of the project, the agriculture ministry is tapping its racetrack proceeds to start an animal genome project, using a pig model. Researchers hope it, too, will prove to be a winner.

–Jane E. Stevens

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## Send In the Clones

When Cornell University geneticists Susan McCouch and Steve Tanksley learned in the late 1980s about the Japanese rice genome–mapping project, they looked forward to a fruitful collaboration. The Cornell team was assembling its own rice genome map, so it proposed integrating the two efforts. Working with Akira Saitoh, then head of the Rice Genome Research Program (RGP) in Tsukuba, they exchanged 70 DNA markers.

But soon after the marker exchange, which occurred in 1990, the Japanese project was abruptly shut down and a new rice genome project was set up with an entirely new staff (see main text). Although a joint map was published in 1992, it took several years for outside groups like the Cornell team to regain access to material from the new project. "The project was absolutely closed, even to researchers in Japan," says McCouch.

Recently, however, McCouch and other researchers say the RGP has begun to open up once more. Last year, for example, 4342 sequences from the RGP's complementary DNA (cDNA) clones were deposited in public data banks, and another 1500 are to be added this fall. And RGP researchers have recently submitted a manuscript for publication that will give the locations of 1383 DNA markers, including 876 of the cDNA sequences already in the data banks. "After acceptance we will be able to release all mapped DNA clones, sequences, and additional information necessary for mapping work," says Takuji Sasaki, who became program director this past spring. And McCouch herself says that her group received a batch of cDNA clones from the RGP early in 1994.

According to Sasaki, there was never a policy against open collaboration. After the 1991 reorganization, the RGP's director, Yuzo Minobe, thought "clones should be widely distributed," says Sasaki, who succeeded Minobe in March of this year. The reason it took until this year to send out clones, he says, was that "we did not have so many clones to distribute" before then.

PETER MORENUS/CORNELL UNIVERSITY

**Taking root.** Cornell's Susan McCouch tends rice clones sent from Tsukuba.

Masahiro Nakagahra, who directed the initial RGP from 1988 to 1990 and presided over the 1991 reorganization, says the misunderstanding may have stemmed from his concern that an individual researcher might take DNA materials produced by the RGP team and "bring them into his small world," and that the project was reorganized and policies put in place "to avoid an accident." McCouch suggests, however, that RGP administrators feared that too-close collaboration might favor overseas teams.

Such an attitude would be understandable, because the RGP "was designed to make Japan pre-eminent in rice research," observes Gary Toenniessen, head of the agricultural science program at the Rockefeller Foundation in New York, which supports rice genome work at Cornell and a handful of other U.S. labs. Also, he notes, "The idea was to provide a place where corporate-sector scientists could work and then take materials back to their company and develop products. That never materialized," he says, and the project has since become more typical of an international scientific endeavor.

Molecular geneticist Saghai Maroof of the Virginia Polytechnic Institute and State University adds that there's nothing wrong with a research institute wanting to hold its cards close to the vest. "I don't think they are trying to hide [information]," he says, "but they want to make sure everything is right. Since they are calling the shots, it's up to them."

Whatever the reasons for the RGP's seesawing history, overseas researchers welcome the RGP's renewed openness. "We have found them very easy to work with," says British plant molecular biologist Michael Gale of the John Innes Center in Norwich, which has postdocs shuttling back and forth between Britain and Japan. "It's a very fruitful collaboration." Agrees McCouch: "This is a new era of collaboration. The RGP will be a major contribution to the international community."

–J.K. and Jeffrey Mervis