JAPAN

Consortia to Boost Efforts to Develop Genome Industry

TOKYO—Two years ago, venture capitalist Yoshihiro Ohtaki was becoming increasingly alarmed that Japanese pharmaceutical companies were all but ignoring the potential commercial value of work on the human genome. While European and U.S. drug giants were pouring hundreds of millions of dollars into start-up companies, databases, and academic labs, the only major Japanese company to show any real interest in turning genome findings into new drugs was Otsuka Pharmaceutical Co., which established a small genome research unit in 1993.

Ohtaki, fearing that these overseas commercial ventures were building up an insurmountable lead in genome work and putting a proprietary lock on genetic data, took his concerns to the government. He got a receptive hearing: The Ministry of International Trade and Industry (MITI) promptly set up a joint government-industry group, of which he was made a member, to study what should be done. The first fruits of its labor are expected to be announced within the next few months: a private company, backed by MITI and 20 large corporations, that will study gene function and develop automated technologies to advance genomic research. The company, tentatively called the Helix Institute, could be followed by a second venture, co-sponsored by the Ministry of Health and Welfare and industry, that would hunt for genes responsible for hereditary diseases, especially in children. Observers consider the MITI company a sure bet, while the Health and Welfare scheme is seen as a long shot.

"Two years ago, Japan's pharmaceutical companies did not realize the importance of genome research," says Ohtaki, president of Japan Associated Finance Corp. in Tokyo. "But now they finally understand the need to have their own base of intellectual property" to develop new drugs. Yasufumi Murakami, a genome researcher at the Institute for Physical and Chemical Research who has advised the MITI panel, says the rapid accumulation of genome sequence data and moves toward identifying gene function have forced the hand of Japanese industry.

Although some preliminary information about the prospective companies has appeared in the press, there has been no public announcement, and officials at both ministries will say only that the proposals are under study. News of the ventures has been percolating through the research community, however, and researchers have generally welcomed the plans. Kenichi Matsubara, a professor at Osaka University's Institute for Molecular and Cellular Biology, says, "I think it could be a very good thing—if properly operated."

The main objectives of the ventures are to develop technologies and generate basic knowledge that can support the new ventures and be shared among members of the consortia. The new companies are also expected to create a pool of talent, including scientists borrowed from participating companies. The first plan, presented by companies and under review by MITI, would have the trade ministry contribute as much as 70% of the $60 million to be put into the company over 6 years. The second proposal asks the health ministry to contribute 50% to 60% of a 6-year budget of $40 million.

Some genome researchers worry that these efforts will be too small to have a significant impact, and that the rules governing university-industry interactions and intellectual property rights may hinder collaboration with academic efforts. "With the stated goals, the [MITI] project should really be a bit bigger, maybe double," says Murakami.

Indeed, the annual budget of the MITI affiliate is only one-fourth that of Human Genome Sciences (HGS), a Rockville, Maryland, company formed to capitalize on the work of J. Craig Venter, formerly of the National Institutes of Health. Smith-Kline Beecham has provided $125 million to HGS. Even Otsuka Pharmaceutical will be outspending the MITI consortium: The company already provides its Otsuka Gen Research Institute with $15 million a year and projects rapid growth as it adds staff.

Otsuka will not be part of the MITI consortium, because it prefers to work on its own. The institute's deputy director, Hiroumi Maekawa, says 36 scientists have turned out some 30,000 partial sequences that serve to identify genes, and that the data on 12,000 partial sequences have already been deposited in an open, international database. The next step is to focus on gene function, he says, and Otsuka plans to hire 30 more researchers to tackle the job.

Ohtaki notes that the money the government and the private sector plan to put into the ventures is considered an investment, not a subsidy, and both companies are expected to show a return. The MITI affiliate expects to generate profits through a proprietary gene function database and by developing new automated methods to do such things as screen various proteins expressed by genes. That focus, he says, explains the presence of Hitachi Ltd. and Olympus Optical Co., which manufacture analysis equipment and precision instruments.

To be successful, the new ventures will have to overcome serious obstacles. To compensate for their small budgets, says Ohtaki, the companies need to form collaborations with research groups at Japanese universities and national research institutes. But unlike in the United States, professors at Japanese national universities cannot participate in start-up ventures or work directly for private companies.

Collaborations are a possibility, although these are complicated by questions about intellectual property rights. Universities typically do not have patent offices and are generally not set up to exploit the commercial potential of research discoveries. "There is

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	Helix Institute	Genome Pharmaceutical Science Research Center
Funding Agency	Key Technology Center, under International Trade and Industry and Posts and Telecommunications ministries	Ministry of Health and Welfare
Investment	$60 million over 6 years, 70% from government	$40 million over 6 years, 50%–60% from the government
Industrial Participants	20 companies, including Yamanouchi, Fujisawa, and Chugai Pharmaceutical Cos.; Hitachi; Mitsubishi Chemical; and Toray Industries	10 companies, including Eisai, Yamanouchi Pharmaceutical, Kirin Brewery, Olympus Optical, and Tanabe Seiyaku
Research Goals	Gene function and automated analysis and screening	Genes responsible for hereditary diseases, especially in children

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no mechanism to transfer intellectual property to the private sector," Ohtaki says.

Neither is it easy to hold joint patents on collaborative work. Although such arrangements are possible, says an official at the Ministry of Education, Science, Sports, and Culture, the procedures are cumbersome and not well known. The ministry is now studying ways to help universities benefit from intellectual property and work with the private sector. In the meantime, Murakami says he hopes academics will be willing to act as unpaid advisers to the new companies.

The biggest benefit of the new ventures for existing companies may be to stimulate their own human genome research efforts. A director of research planning at one of the participating drug firms, who requested anonymity, said his company sees participation as a step in developing "an infrastructure of genome research." The company plans to assign its own researchers to the consortia temporarily and then use them as the nucleus of the firm's own genome research team when they return. The consortia will focus on very basic work, he adds, leaving drug development in the hands of individual companies.

That arrangement is fine with Murakami, who sees such collaboration as the key to success. "If the tasks are separated in a well-organized manner, the new company could produce substantial [results] in conjunction with genome labs at each participating company," he says. The joint activity, he adds, could also contribute to global efforts.

–Dennis Normile

POLAR RESEARCH

Pressure on Budget Triggers Review of Antarctic Program

This month, under the brilliant 24-hour-a-day sunlight of high summer, a team of physicists at the U.S. South Pole station is drilling half a dozen holes deep into the ice as part of an experiment to flag down elusive cosmic neutrinos. Not far away, astronomers are peering into the cosmos with newly installed infrared and millimeter-wave telescopes that take advantage of the pole's high, dry, frigid environment. Other areas around the base are also a buzz of activity, as geophysicists, atmospheric scientists, and geologists probe the workings of Earth and its climate, both ancient and modern.

All this work is supported by the U.S. Antarctic program as part of a $195-million-a-year effort run by the National Science Foundation (NSF). It's by far the largest and most productive scientific presence on the continent, accounting for 40% of the roughly 3000 people working on the continent on any given austral summer day, by NSF estimates. But size is not always a virtue during times of fiscal austerity: The program has caught the attention of Congress, which has asked for a thorough review of U.S. policy in Antarctica.

At issue is whether the country still wants—and can afford—such a dominant effort. Last week more than a dozen federal officials gathered at the Old Executive Office Building to kick off the review, which could decide not only the future of these ongoing scientific activities but also the fate of NSF's plans for a $200 million replacement for its South Pole station. The review, requested by the Senate appropriations subcommittee that oversees NSF's budget and endorsed last month by the House, could also affect research by other countries that are partners in joint activities and whose own efforts are coming under closer scrutiny (see box).

The trouble is that Antarctic research doesn't come cheap. The current program—three year-round stations, two research vessels, and the world's only fleet of planes capable of landing on the ice—eats up 9% of NSF's overall research budget and requires $5.50 in logistical support for every dollar spent on research. Both figures will increase if the government replaces the 20-year-old Amundsen-Scott Station with a new structure that NSF officials say must be built in the next 5 to 7 years to meet the scientific, health, and environmental needs of those working at the South Pole (*Science*, 24 June 1994, p. 1836).

Hot spot. NSF hopes to avoid a meltdown of its plans to rebuild South Pole station.

Congress wants federal officials to think about ways to trim costs, including making the new station an international effort and operating it for only part of the year. And it's asking the Administration to look at these issues in a broad context: "It's not [just] how much money you can save," says a congressional aide who follows the issue closely, but "the rationale behind why you're there." The White House has assigned the job to a task force of the Committee on Fundamental Science, one of nine panels that make up the president's National Science and Technology Council, which includes 20 federal agencies with an interest in science. The Senate subcommittee wants a report by 31 March, in time to review NSF's 1997 budget request, which could include a downpayment on a new station.

Polar scientists seem confident that the research portfolio can withstand scrutiny by federal officials. "I've been going there since 1959, and the science is better now than it's ever been," says Robert Rutford, a geologist at the University of Texas, Dallas, and the U.S. representative to the international Scientific Committee on Antarctic Research, which coordinates the various national programs. "NSF rolled the dice when it decided to build a new station," he says, "and now it needs to be able to defend the value of the whole program."

But the debate is not just about science. Although the 1959 Antarctic Treaty binds the 26 signatory nations to peaceful scientific activity, the U.S. government long viewed Antarctica as an important outpost in its campaign to contain Soviet expansionism—a role underscored by the use of military personnel for logistical support. In addition, seven countries continue to hold territorial claims that the treaty puts in abeyance and that a U.S. station at the South Pole serves to blunt.

Those strategic concerns have helped NSF survive past reviews, and Cornelius Sullivan, head of NSF's Office of Polar Programs, says the fundamental issues haven't changed. "Is there something wrong with our policy over the past 40 years, or is it basically sound?" he wonders. In 1982, after soaring fuel prices threatened to curtail the program, the Reagan Administration endorsed "an active and influential presence" in Antarctica with the existing complement of facilities. A review early in the Clinton Administration, part of a 1994 directive that remains classified, cited along with science the importance of protecting the environment, cooperating with other countries, and preserving the region's living resources.

R. Tucker Scully, director of the department's office of ocean affairs and a veteran of Antarctic policy debates, is convinced that the current policy is correct. "I would be quite surprised if the task force concluded that our fundamental interests in Antarctica have changed, because I don't think that they have," he says.

However, NSF may have fewer allies at a time when budgets are shrinking, national