The inclusion of National Central University in Taipei indicates that the Chinese authorities are capable of putting science above politics. But some semantic maneuvering is required. Chen, who says that his peers are eager to strengthen their ties with Taiwan, stresses that BATC should be called an "interregional" collaboration. Asked why, he explains that the awkward word skirts the touchy issue of Taiwan's political status. U.S. participation also provides a buffer for Chinese authorities who might balk at a one-to-one link between Taiwan and the mainland.

J. D. MERVIS

Well-furnished. Han Jisheng's global ties support his research and books.

Moving mountains. Political realities are also impossible to ignore for geophysicists involved in the INDEPTH (International Deep Profiling of Tibet and the Himalayas) project. University of Syracuse geophysicist Doug Nelson helped to sell NSF on the $4 million project, which is probing the tectonic forces that have created the Himalaya uplift, after he visited Tibet in 1984. NSF geosciences program director Leonard Johnson now calls INDEPTH "the premier experiment in the world on continent collisions."

Nelson, who has spent two summers in Tibet setting off explosive charges along a 100-kilometer route and measuring the resulting seismic shocks, was the driving force on the U.S. side. But INDEPTH never would have gotten off the ground without Zhao Wenjin, senior scientist and former director of the Chinese Academy of Geological Sciences in Beijing. Zhao figures that he spent even more time—15 years—than Nelson did in trying to move the bureaucratic mountains that stood in the way of foreign researchers swarming over a politically sensitive region. "I remember how happy I was when the Army Chief of Staff signed off on permission to begin working in Tibet," recalls Zhao, who spends his full time coordinating the Chinese side of the collaboration. He's already been called on to soothe ruffled Chinese military feathers after a group of U.S. researchers accidentally wandered into a restricted zone.

The importance of Zhao's role is reflected in the order of authors on the first publication from the project, which began in 1991 (*Nature*, 9 December 1993, p. 557). Zhao is listed first, and Nelson is second. "The Chinese are good negotiators," explains Johnson, adding that authorship was just one of hundreds of items on their list.

While Johnson says that "good science is the sole reason" for NSF's support of the collaboration, Chinese officials have a host of potential benefits in mind from the deep profiling. These include getting a head start on oil and mineral exploration, gaining access to new technology, and winning international recognition for their scientists.

The lure of such mutual benefits seems to be drawing increasing numbers of Chinese and Western scientists into collaborations, although nobody is keeping any hard and fast numbers. The latest convert is NIDA's Leshner, who recently returned from a meeting in Beijing on drug abuse and HIV brimming with ideas for potential joint research. His reaction is typical of foreign scientists who have suddenly discovered the rich possibilities of working with China.

"Heroin addiction is increasing at an incredible rate in Yunnan Province [in southwest China]," says Leshner. "It's a tremendous opportunity to study the problem before it gets too big. And then there's acupuncture, both to treat the symptoms of withdrawal and for other purposes. It's not magic, but there are weird things going on that work for nonmagical reasons. There's just a lot of things that we can do together."

–Jeffrey Mervis

BIOTECHNOLOGY

Agriculture Finds a Niche; Drug Researchers Seek Help

GUANGZHOU—When Cornell University plant scientist Li Baojian accepted an invitation to set up a new molecular biology lab at his alma mater, Zhongshan University, he knew that his two children wouldn't be able to come with him. "It would have been very difficult for them to fit into the education system in China," Li explains with a wistful smile. "My son was weeping, 'Daddy loves China more than he loves me.' So I took out my checkbook and said: 'I am taking only a little for my expenses; the rest is for your education. I love China, but I love you, too.'"

Fortified by their parents' love and financial support, the children moved in with U.S. relatives while Li and his wife returned to their native China. Their arrival in 1986 coincided with the start of a major national program to boost biotechnology. "In the beginning, I had no people, no rooms, no equipment," says Li, recalling his situation at Zhongshan, south China's pre-eminent university. But thanks to a $150,000 grant from the education ministry and $25,000 from Guangdong province, he soon had a roomful of modern equipment. Within a few years, newly trained scientists were busy inserting genes into a cornucopia of crop plants at the university's Biotechnology Research Center.

In the past decade, returnees like Li have helped implant biotech basics such as recombinant DNA and transgenic technology in Chinese soil. More than 120 companies, many of them joint ventures with foreign investors, have set up factories to produce biopharmaceuticals such as hepatitis B vaccine and recombinant insulin, interferons, and growth hormone. A team led by molecular geneticist Xue Jinglun of Fudan University in Shanghai has treated four patients for hemophilia B using the patients' skin cells engineered to express the gene for a blood-clotting factor. Trangenic fish are being raised in ponds, and transgenic tobacco now covers thousands of acres, boosting yields and profits for China's farmers.

Through such achievements, China has demonstrated that even a developing country with limited capabilities in basic research and product development can quickly master and apply the latest biotech tools. Indeed, although many Chinese labs still lag far behind the West and Japan scientifically, their willingness to move quickly into applied research has created pockets of strength that could well make China a significant player on the global stage in the next 20 years. To reach that goal, however, the country needs to strengthen both its research and its business skills, say experts both inside and outside China. Basic life sciences suffer from inadequate funding and poor infrastructure. Regulations are opaque and unenforced, resulting in low-quality drugs and concerns over field releases of bioengineered agricultural products (*Science*, 11 November 1994, p. 966). And too often, talented scientists work in isolation from one another and from the cutting edge.

Focus on agriculture. Despite such obstacles, China is already making its mark, especially in agricultural biotechnology. "China is clearly the most advanced country in the world in terms of using genetic markers and tools in rice breeding," says Gary Toenniessen, director of the rice biotechnology program at the Rockefeller Foundation. At the Huazhong Agricultural University in

Wuhan, Zhong Qifa, a plant geneticist trained at the University of California, Davis, and his co-workers are using genetic markers to select for rice strains that can be crossbred to enhance hybrid vigor. "His work is as advanced as any such work on any crop, anywhere," Toenniessen says.

Others are simply applying biotech tools developed overseas to Chinese crops. Researchers such as Li Lingcai at the Institute of Genetics have established reliable systems to introduce foreign genes into plants such as rice. And Li Baojian's lab reports it has inserted the genes for a viral protein into rice via an agrobacterium vector. "I've seen rice plants that I think have been genetically transformed," says one Western expert, adding that the lab has yet to document its claim rigorously. "The food crisis is very real to the Chinese," says Alvin Young, scientific director of the U.S. Department of Agriculture's (USDA's) office of agricultural biotechnology. "They're not going into novel work. They'll just use whatever technology the West and Japan develop."

War on hunger. Li Baojian's task is to fill his labs.

What sets Chinese efforts apart is the speed and scale with which transgenic plants are being introduced to fields and markets. Transgenic virus-resistant tobacco developed at Beijing University, for example, is grown on more than 50,000 hectares and used in cigarettes on sale. "The Chinese started with large plots, and they learned a lot about the overall environment in which they are grown," says Rudolph Kasper, former head of the Institute of Biochemistry and Plant Virology in Braunschweig, Germany, who last spring led an international inspection team that visited several sites in China. "The scientific progress I've seen since 1983 is fantastic. At the beginning the researchers were shy. Now they ask, 'How can we help you?' "

Trouble ahead. Mang Keqiang wants more research and clearer rules.

In biopharmaceuticals, by contrast, China is still a student rather than a teacher. While some biotech firms, such as Shanghai's Huaxin High Biotech Inc., are raking in millions of yuan manufacturing interferons and interleukins, "they are all making 'me-too' drugs," notes Mang Keqiang, vice director of the Chinese Academy of Science's Institute of Microbiology in Beijing and a member of the Ministry of Public Health's new drug evaluation committee. "And not one of them has been licensed from the company that holds the patents. We are headed for trouble here."

Mang is referring to China's ongoing bid to join the General Agreement on Tariffs and Trade and the World Trade Organization, which would require Chinese companies to honor international laws protecting intellectual property. "This is going to put pressure on Chinese scientists to do more original research," says Cornell plant scientist Raymond Wu, who advises the Chinese government on biotechnology.

Regulatory deficiencies. Developing a homegrown biotech industry won't be easy, however, say seasoned observers. One major liability is the lack of a strong regulatory infrastructure. "China is not so far behind in things like cloning," says Albert Chang, director of the Institute of Biotechnology in Hong Kong and a consultant to the Chinese government. "But they don't have a history of product development." Chang, who was previously director of strategic planning and international liaison at Upjohn Co., notes that "in the U.S., the Food and Drug Administration [FDA] laid the groundwork for streamlined development." But uniform guidelines for developing genetically engineered drugs and food crops are lacking in China, he says.

China has taken some steps toward that goal, creating a drug approval process and biosafety rules modeled on the FDA. But the trick is finding out what they are. "People applying to test the same product are told different things by different officials," says Mang. "We don't have uniform documents." In the case of food products, regulators can't keep pace with research. "We are doing field release of a transgenic tomato this year, but we don't have an office to which to apply for permission to put it on the market," says Chen Zhangliang, vice president of Beijing University and dean of the College of Life Sciences.

Even where regulations exist, they are not always enforced. Product quality, for example, is uneven. "The small drug samples that are sent to regulators are excellent, but large-scale production quality is not as good," complains Mang. Allan Hong, a Chinese-born chemical engineer and head of chemical portfolio management at Hoffmann-La Roche in Nutley, New Jersey, concurs. "The interferon made in China is not very good," he says. "I brought back samples to test in our labs. None of it could be sold here in the States."

Back to basics. Even if China does manage to improve the regulatory environment, it would still need to strengthen its foundation in basic life sciences. "Conditions even in the state key labs are not good," Mang says candidly. In many a life science institute in China, one finds room upon cavernous room with sparse equipment and dusty shelves supporting a few pieces of glassware capped with scraps of yellowing newspaper.

The government has been trying to improve working conditions by boosting funding for new equipment and projects, and the investments are beginning to make a difference, particularly at elite institutions. Beijing University's College of Life Sciences, for example, is one of the best equipped in China, with over $4 million in equipment purchased in part with World Bank loans. The university's prestige and improved conditions have helped the college to recruit two dozen scientists from labs abroad.

Even with such improvements, scientists still have to contend with the lack of supplies. "It used to take 6 months to get an enzyme," says Mang. "Now it takes 2 weeks. We can get animals and cell lines, but not the newest ones." Something as trivial as a burned-out microscope light bulb can halt work for weeks until a replacement arrives from the foreign maker. Tom Currier, a bacteriologist at Ciba-Geigy's agricultural biotech unit who has done joint research on insecticidal bacterial endotoxins at the Hubei Academy of Agricultural Sciences in Wuhan, recalls, "Things like a dissolved-oxygen probe can't be fixed over there. We have to hand-carry them back to the West. There's minimal infrastructure."

What frustrates many scientists is not just the poor infrastructure, but the inefficient use of what scarce resources exist. Scattered across China are 185 institutes and university labs with around 25,000 scientists and technicians doing biotech-related work, according to Mang's latest count. "Why so many?" he asks. "Each administrative center wants its own research centers. No one wants to give up control." Even within Mang's own institute, the custodians of the micro-organism library classify more than 10,000 specimens using traditional taxonomy and have no contact with the molecular biologists working literally next door.

Or take the case of germplasm collections. "China probably has the world's richest germplasm resources," says Cornell University rice researcher Susan McCouch. According to studies by Li Jiansheng at Huazhong Agricultural University, for example, maize diversity in southwest China is greater than in the United States. Unfortunately, says the USDA's Young, many of the germplasm libraries are maintained, with great effort, by provincial agricultural universities which scarcely communicate with one another. A national effort would be far more efficient, he says, allowing each collection to focus on germplasm resources

unique to its region.

Scientific isolation. Indeed, Chinese scientists feel their isolation within their own country keenly. When Young toured Chinese labs 2 years ago, he recalls, "the first thing people wanted us to tell them is not what's going on in the U.S., but what's going on elsewhere in China. Their ears were just burning." La Roche's Hong, who left China in 1980, says, "It's harder for Chinese to cooperate. We have less experience in dealing with win-win situations. It's our culture."

AL YOUNG

Open field. Nanjing trials with *Bt* toxin improve cotton yields.

Whether culture has anything to do with it or not, leaders in Shanghai, a stronghold of life sciences, have decided to try to break down the barriers that divide scientists. Last year, they set up the new Shanghai Research Center of Life Science to administer and fund research that promotes closer ties among two dozen life science labs scattered among the CAS institutes, universities, and medical colleges in Shanghai. "We want to organize research in frontier areas, provide good conditions for young researchers, promote interdisciplinary and international collaboration, and improve the research management system," says Xu Zhihong, one of the center's co-directors.

But a scientist familiar with the center's activities says that "right now it doesn't work well, because Chinese scientists traditionally do not have good experience collaborating on one project. It's basically an opportunity to ask for more funding from the local government." And even then, the funding has not had quite the impact the founders might have envisioned. The $350,000 spent by the center so far on genome mapping, gene diagnosis, and gene therapy has been carved up among several groups, which have ended up working independently.

An equally serious impediment to progress in biotechnology, says Hong, is Chinese scientists' isolation from the global cutting edge. "I'm surprised at the depth of biotech research the Chinese do," he says. "But the problem is they don't know the current state of research, or how to focus on promising areas. They're very active, but not well organized." What's more, he adds, Chinese scientists still have much to learn about conforming to international scientific standards.

But if Chinese biotech researchers can develop a more open, globally competitive outlook, their work could begin to pay off. Consider the possibilities of China's rice genome project. By the researchers' own admission, their mapping efforts fall far behind a much larger, well-funded Japanese effort (*Science*, 18 November 1994, p. 1186). But "the portions aimed at applications are moving well," says Rockefeller's Toenniessen. "Chinese scientists need to find an important niche that isn't duplicated elsewhere. I think that niche will be to link advanced tools to applications. There are all kinds of genes for disease resistance waiting to be discovered."

China still has a long way to go in biotechnology, but its biotech pioneers such as Mang Keqiang and Li Baojian have helped put the foundations in place. Li has lived apart from his children, now grown, for nearly a decade, but he has few regrets. "We are developing China's agriculture and helping farmers," he asserts. "At first, we didn't have many labs, and now we have many. My task now is to fill them with young scientists."

–June Kinoshita

EPIDEMIOLOGY

China's Unique Environment Favors Large Intervention Trials

BEIJING—The residents of Linqu, a poor county in Shandong Province in east-central China, have little formal education. But they know gastric cancer is killing them at a higher rate than anywhere else in the world. So when epidemiologist You Weicheng explained that they had a chance to participate in an experiment that could increase understanding of the disease and, maybe, save their lives, he had no shortage of volunteers.

J. D. MERVIS

Cancer killer. You Weicheng hopes that NIH trial will improve health of rural Chinese.

The experiment that began in September is the world's first randomized intervention aimed at inhibiting or preventing the development of gastric cancer. It extends earlier work by the 43-year-old You, who has spent almost 20 years exploring the origins and progression of the disease in China, at the Beijing Institute for Cancer Research, and the U.S. National Cancer Institute (NCI). The trial also builds on a large-scale nutritional intervention trial, which ended in 1991, in Linxian Province in north-central China, a region with one of the world's highest rates of esophageal cancer. The Linxian study, conducted by a team of U.S. and Chinese scientists, provided the first clear evidence that a nutritional supplement in pill form could arrest or prevent the development of a human cancer.

It's no accident that China is providing epidemiologists with some of the best data on ways to lower rates of diseases like gastric cancer. "China provides a tremendous opportunity for case-control and intervention studies," says Joseph Fraumeni, acting head of NCI's division of cancer epidemiology and genetics, which is funding the Linqu trial as well as projects in other parts of China. "There are striking variations in the incidence of various cancers and several extremely high-risk populations," he says. "For example, esophageal cancer just doesn't occur here often enough to get good results, but it's widespread in parts of China." Cultural and demographic factors also make it easier to conduct major epidemiological studies in China. "Its population is more compliant than in the West," notes Fraumeni, "which leads to very high participation rates. The studies are much cheaper to carry out—practically nothing compared to what a similar trial would cost in the U.S. And the population is more stable, so follow-up is much easier."

All these factors are evident in perhaps the largest intervention trial now under way anywhere in the world. It is aimed at reducing the high rate of neural tube defects in China, in particular spina bifida and anencephaly (SBA). Each year nearly 100,000 children in China are born with SBA, but small daily doses of folic acid, taken before and during the first weeks of pregnancy, are thought to be capable of lowering that number by at least half. So in 1993 the Chinese Ministry of Public Health, in conjunction with the U.S. Centers for Disease Control and Prevention, began signing up hundreds of thousands of women in three provinces