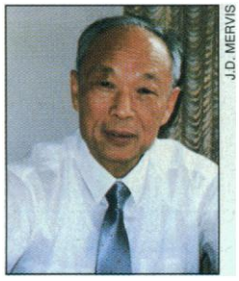
INTERNATIONAL COLLABORATION

The Right Ties Can Save Lives and Move Mountains

SHANGHAI—Wang Zhenyi says he'll never forget how ill the little boy looked when he was admitted to Rui-jin Hospital at Shanghai Second Medical University. Stricken with acute promyelocytic leukemia (APL), the 5-year-old child had not responded to standard chemotherapy. He was bleeding severely, running a high fever, and suffering many other symptoms. The only known treatment—a form of vitamin A called 13-*cis*-retinoic acid—had proved to be of limited success in treating patients in the West. And besides, the drug was too expensive for import into China. "It was a hopeless case," says Wang, director of the hospital's institute of hematology, thinking back to that day in 1986.



J.D. MERVIS

Clinical links. Wang Zhenyi's treatment for a rare form of leukemia won global acclaim.

But Wang didn't give up hope. Fortuitously, a variation of the drug, all-*trans*-retinoic acid, was already widely used in China to treat a skin disorder, and animal studies conducted in Wang's lab had found that it caused cancer cells to mature, differentiate, and die. So Wang decided to try the drug on his young patient. Four weeks after being treated with all-*trans*-retinoic acid, the child was well enough to walk into Wang's office for a checkup. Wang quickly followed up with 24 other patients, and 23 showed similar improvement.

"It was so incredible that at first it was widely disbelieved," says oncologist Raymond Warrell of the Memorial Sloan Kettering Cancer Center in New York, who was involved in later clinical trials of the drug. "But since then his work has been widely confirmed." Indeed, last year Wang shared a $100,000 prize from the General Motors Cancer Research Foundation for his efforts, and since then the drug has been approved to fight the roughly 2000 APL cases a year in the United States.

J. D. MERVIS

Rock solid. Geologist Zhao Wenjin helped clear way for worldwide seismic profiling project in Tibet.

Wang's story is a dramatic example of how a key insight in the laboratory can quickly translate into medical benefit. But it also illustrates the importance of a less obvious factor in the development of Chinese science: international collaboration. In Wang's case, links with Western scientists helped to legitimize his work and to extend it. "Trials in France and the United States proved that it worked," says Wang. "Now it has been used to treat more than 2000 cases of APL."

Wang's international connections run deep. They include Samuel Waxman, head of the cell differentiation lab at the Mount Sinai Medical Center in New York and medical director of an eponymous cancer foundation that provides $55,000 a year to support Wang's institute, as well as hematologist Laurent Degos at the Hôpital Saint Louis in Paris, with whom he shared the General Motors prize. It was Waxman who persuaded Wang to submit his results to *Blood*, where they received broad dissemination beyond the Chinese journal that had first carried the news. The ties to France begin with the hospital's founding in 1911 as a French medical university and run through one of Wang's students, Chen Zhu, who along with his wife Saijian were trained in Paris in the 1980s and who have since extended the research and linked it to the country's fledgling human genome project.

For many Chinese researchers, partnerships offer a chance to live and work in the United States or Europe, to get involved in projects their own government otherwise cannot afford, and to make contacts for future joint research. In addition, the presence of Western scientists and their governments can be an important factor when government officials decide who and what to fund.

It's not just Chinese scientists who benefit from collaborations. For many foreign scientists, collaborations with China represent an opportunity to lend a helping hand, to gain access to unique living or physical resources, and to do good science at bargain-basement prices.

DOUG NELSON

There's also the lure of cooperating with world-class scientists. For example, Western researchers speak favorably of work on high-temperature superconductivity at the Institute of Physics in Beijing, of both the scientific and technical skills of researchers at Nanjing University's state key lab of solid state microstructures, and of the innovative research going on at the Institute of Metal Science in Shenyang in northeastern China. And, on a commercial level, Western companies see an initial investment in research as a downpayment for access to a vast market, while the Chinese government sees Western funds as a way to boost economic development.

In spite of this diversity of interests and mutual benefits, all international collaborations with China are governed by one important fact: The government sets the rules. The latest reminder of that reality was the interruption or termination of several joint projects after the 1989 pro-democracy movement was crushed by tanks at Tiananmen Square. But scientific ties are resilient—this year, for example, Chinese and U.S. officials signed an agreement for a series of new joint projects to replace an earlier agreement that lapsed in 1989—and the Chinese government is often willing to stay in the background once a collaboration is under way.

Getting the point. One scientist who has benefited from both the close oversight of government authorities and from their free hand is Han Jisheng, director of the neuroscience research center at Beijing Medical University. Han has spent a quarter century studying the analgesic effects of acupuncture, exploring its biological and neurochemical mechanisms, and training generations of graduate students. "He runs a phenomenal operation," says Alan Leshner, head of the U.S. National Institute on Drug Abuse (NIDA), which funds part of Han's lab. "He's a good scientist, and he's worked with some of the best people."

At the top of Han's list is Stanford University neuroscientist Avram Goldstein, who discovered the brain chemical dynorphin, thought to be involved in the control of pain signals and possibly long-term potentiation. The two began collaborating in the 1970s as like-minded scientists pursuing a common line of research, and they became close friends. Sitting in his small office on a Sunday morning, Han confides proudly to a visitor that the tall wooden bookcase and couch in his office once belonged to his U.S. colleague and were given to him as a present when Goldstein retired.

But Han doesn't always have to settle for hand-me-downs. He is the head of a spanking new pain treatment center funded by the multibillion-dollar French pharmaceutical

Field Research Also Needs the Human Touch

MASHAN—Bicycling down a dusty road one sweltering Sunday morning last summer in rural southeastern China, U.S. agroecologist Erle Ellis was enjoying a rare break from his normal routine. The tall, sandy-haired postdoc had spent the past 2 years studying the nitrogen cycle of two villages in the Tai Lake region, south of the lower Yangtze River, which for centuries has been one of the country's most fertile areas. Now he was ready to return to Cornell University to pore over his data. But future publications were not the first thing on his mind as he traversed the flat expanse of rice fields and vegetable gardens. Instead, Ellis was reflecting on the trials and tribulations of planning and conducting field research in China, and the all-important human connections that can make or break a project like his.

Riding with him were two Chinese researchers who had been collaborating with him on his project, Yang Linzhang, director of the ecology department of the Nanjing Institute of Soil Sciences, and Li Ronggang of the office of environmental protection for the Jiangsu Department of Agriculture and Forestry. All were looking for the home of Xue Huailiang, village leader and agricultural expert. Ellis had set out with his companions to express his appreciation for the villagers' help in conducting his research, which attempts to measure all the nitrogen inputs to a traditional agricultural system, including human and other organic fertilizers, as well as to a modern system that relies on chemical fertilizers.

J. D. MERVIS

Hand-in-hand. Erle Ellis *(left)* and Li Ronggang check experimental rice patch.

Although his $70,000 grant from the U.S. National Science Foundation (NSF) has allowed Ellis to pay local officials and farmers for their work, as well as to provide his institutional collaborators with a monthly stipend, Ellis had a dozen watches in his backpack that meant more than money. They were a token of his gratitude at being welcomed into their homes and their lives. His first stop was to Xue, who not only provided a wealth of information about local practices but also made sure farmers kept daily journals of what fertilizers they used—when it was applied, and on what crops—and were available for lengthy interviews.

In addition to serving as thank-you gifts, the watches may also have been an unconscious reminder for Ellis of how much time had passed since he got the idea to study the country's tradition of sustainable organic agriculture. The idea grew out of a brief visit to China in 1990, with a group arranged by Robert Rodale, a pioneer in U.S. organic agriculture. A newly minted Ph.D. in plant physiology with no background in China, Ellis decided to spend a year teaching English at Nanjing Agricultural University. While there he became co-founder of the city's first pizza parlor, a job that gave him a chance to experience Chinese bureaucracy and culture first-hand. Those lessons, as well as a later stint with a Los Angeles company that arranged tours for visiting Chinese agricultural officials, paid off when he received an NSF environmental biology fellowship in 1993 and set about trying to find sponsors and sites for his work in China.

One contact, professor Cheng Xu of Beijing Agricultural University, helped him line up an affiliation with the school. Another, the minister of agriculture for Jiangsu Province, helped pave the way for a series of meetings that led to his eventual agreement with local officials. Finally, an old friendship between Cheng and the head of the district agriculture bureau assured him of access to the two villages. At each step, Ellis faced protracted negotiations with a host of scientific and governmental bodies, all wondering what value his work might have for their constituents and some looking for a reason to say no.

Ellis hopes his efforts will shed light on the ecological basis for sustaining good yields in an agricultural system that has been productive for centuries but that is now under pressure from a growing population, rapid economic development, and changing food habits. Those changes have already affected his research: He discovered that the extensive use of commercial fertilizer for most crops made it hard to find a traditional system, and even harder to find one that is self-sustaining. He also learned that it's not easy to apply modern science to traditional agricultural methods. For example, after putting Xue in charge of replicating traditional levels of fertilizer on three experimental plots, Ellis found out to his chagrin that there was no such thing: The "traditional" method was to apply fertilizer as needed, depending on the leaf color of each plant.

But such analytical nightmares only reinforce the fact that data are only a small part of what he has learned from his work in China. Just as nitrogen is part of an elaborate cycle that leads to a productive harvest, so too a scientist hoping to do collaborative research in China must fit into an intricate and opaque network of human connections. As Ellis has discovered, the right blend of science and people skills is just as crucial to success as the right fertilizer.

–J.D.M.

company Upsa Laboratories. (Last year the company became a subsidiary of Bristol-Myers Squibb.) The 15-bed center is part of an international network that Upsa has created to foster research on pain, to increase scientific awareness of the condition, and to improve clinical care.

Jacques Wrobel, medical director of the Paris-based company, admits that he did not know Han or his work when Upsa decided to expand into China. But he did know how China works, and he followed the rules. "I approached the Ministry of Public Health and the Beijing municipal authorities," says Wrobel, "and they told me to go and see Han if I wanted a center in Beijing. They said he was the top man in the field and also president of the Chinese Association for the Study of Pain."

Wrobel accepted the official advice, and Upsa quickly decided to spend $100,000 to set up the center on campus. As a gesture of good will, it also agreed to finance a complete renovation of the three lower floors of a university-owned building that houses the center. Since May the center has been treating patients in a 15-bed unit and supporting pain research. Wrobel says there have been a few challenges in working with a different medical system: "Han is aware of pain, but he is not a [medical] doctor, so we needed to bring in someone to treat patients," says Wrobel. "And although we are interested in combining Western medicine with Eastern therapies, acupuncture is not something that most French doctors accept." Still, Wrobel considers Han to be "a good choice" for the project, and says his company hopes to begin training Chinese scientists in Paris "as soon as they learn some French."

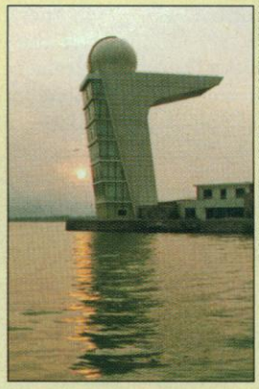
Universal links. Communication is no problem for the astronomers in the Beijing-Arizona-Taipei-Connecticut (BATC) col-

Astronomers Hang Out Help-Wanted Sign

Chinese astronomers are trying to drum up international support for two ambitious projects to be completed early in the next century—an orbiting, optical solar telescope and a radio telescope array with an unprecedented collecting area of 1 square kilometer. The Chinese government is offering to provide much of the infrastructure for the two projects as a lure to attract international funding and scientific expertise.

The Chinese want help in designing and building the space telescope, which would cost an estimated $45 million. They are prepared to provide the rocket and considerable technical support for the project, which would be China's first solar satellite. For the radio telescope, which could cost upwards of $200 million, China is prepared to provide a suitable ground site for an international team that would design, build, and operate the array.

These offers have already captured the attention of scientists from countries with strong programs in solar and radio astronomy. "We are very much interested in participating in the [solar space] program," says Reiner Schwinn, a solar physicist at the Max Planck Institute for Aeronomy in Lindau, Germany, which contributed several instruments to a joint European–U.S. mission that will be launched shortly from Cape Canaveral. This fall an international panel met in the sparsely populated Guizhou region of southwest China to discuss site characteristics and technical aspects of the proposed radio array.



BEIJING ASTRONOMICAL OBSERVATORY

Shining light. Solar astronomers are drawn to Huairou observatory.

The force behind the solar space telescope is Ai Guoxiang of the Beijing Astronomical Observatory, a major figure in Chinese solar astronomy. From its vantage point in earth orbit, the satellite would study the fine structure of solar flares and the photosphere. The 1-meter telescope would be larger than the 0.6-meter telescope planned for the Japanese Solar-B mission, currently on hold.

Ai has already received $1.5 million from the Chinese government to build a prototype and to test its tracking mechanism on a balloon flight. He says that government officials have told him a decision on the overall project hinges on a successful mission, now scheduled for next fall. "They've had a long interest in solar astronomy, and they have always wanted to do it on a rocket," says Hal Zirin, a California Institute of Technology professor and head of the Big Bear Solar Observatory, which served as the model for the Huairou observatory outside Beijing that Ai directs.

Zirin and others praise Ai's technical abilities, noting that he runs a successful factory that is the world's only source of a special filter for solar telescopes that sells for $100,000 or more. They say the balloon mission poses a major technical challenge for Ai because of the stability needed to observe the sun, but that China could become a major force in solar astronomy if Ai succeeds.

"China stands on the frontier of solar astronomy," says Wang Haimin, a former student of both Ai and Zirin who recently took a position at the New Jersey Institute of Technology. It's the first tenure-track opening in his field in the United States in a decade, Wang says, illustrating the dismal state of U.S. solar astronomy in contrast to the situation in his native China. "There are still many good opportunities for students in China," he says. "And if the space telescope succeeds, then China will be even stronger."

The proposed radio array would also propel China into the front ranks of radioastronomy—if it gets built. Its most alluring feature is the enormous collecting area of the telescope, the key to detecting faint radio emissions such as those from gases in evolving galaxies, explains Robert Brown of the U.S. National Radio Astronomy Observatory in Charlottesville, Virginia. The nearly completed Green Bank telescope will have a collecting area of 10,000 square meters, he notes; by contrast, the proposed array would cover 1 million square meters.

So far, foreign astronomers are intrigued by the idea, but there are many hurdles to clear. The Chinese site has certain features that are very attractive to radio astronomers, notes Richard Strom of the Dwingeloo Radio Observatory in the Netherlands, which has done pioneering work on the detection of neutral hydrogen in the early universe and is playing a leading role in the project. The site would offer minimal radio interference, and it contains hundreds of small valleys to house the reflecting dishes that would form the array. On the downside, he adds, the site's isolation would require a considerable investment in infrastructure. And there's the technological challenge. Because building 100 Green Bank telescopes would cost a few billion dollars, Strom notes, "the trick is to do it in a more clever manner" by linking up enough smaller, low-cost dishes.

–J.D.M.

laboration, many of whom have known one another for years. The 8-year project, begun in 1993, is an effort to obtain data on the full visible light spectra of about 1 million stars, galaxies, quasars, and nebulae in a 450-square-degree sector of the northern sky. Chinese astronomers are conducting the survey with a 0.6-meter Schmidt telescope located at Xinglong Station about 150 kilometers northeast of Beijing.

"This is the first international astronomical collaboration based on data collected by a Chinese telescope," says Chen Jiansheng, a professor at the Beijing Astronomical Observatory and coordinator for the three Chinese teams. China is not just supplying a telescope dedicated to the sky survey. The government has also provided astronomers with enough computing power to handle a nightly load of up to 1 gigabyte of data, and it has spent $100,000 on a pair of charge-coupled devices to capture the light collected by the telescope. "Ironically, our Chinese collaborators are far better equipped with [Western-made] computers than we are," notes Arizona State's David Burstein, who is leading the U.S. team.

For U.S. astronomers—who have received some support from the National Science Foundation's (NSF's) international program and are hoping for additional research funds—BATC offers a chance to participate in a major sky survey at a fraction of the cost of building a new telescope. Its data, including more detail on known objects as well as lots of information on new objects, will be fed to astrophysicists and cosmologists around the world. Among those participating in the data analysis will be Fang Lizhi, the University of Arizona theorist who became persona non grata in China in 1989 after his advocacy of political reforms.

The collaboration makes sense for Chinese astronomers, says Chen, because "the results will produce many good candidates that need detailed spatial observation beyond what we can do ourselves. We also need their connections to the rest of the U.S. astronomical community," he adds, to team up with the scientists best equipped to do the additional research suggested by the data from the BATC collaboration.

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