home. Although a few observers are grumbling privately that such largesse is a thinly veiled attempt by wealthy individuals to seize control of state assets, most view the charity drives as part of the long-awaited payback on India's massive brain drain of the last few decades. "We welcome the initiative," says Science and Education Minister Murli Manohar Josh, who says it recognizes the fact that India is fertile ground for growing future high-tech entrepreneurs. That receptivity is a change from the past, when rules prevented such individuals from making direct donations to universities and there was a feeling that it was not right for public institutions to accept private support.

The high-tech executives are already making an impact on their alma maters. In 1998 Rekhi gave $5 million to IIT-Mumbai to establish a school of information technology that has been named after him. Another successful computer scientist, Desh Deshpande, founder of Sycamore Networks of Chelmsford, Massachusetts, has pledged $100 million over the next 20 years to his alma mater, IIT-Madras.

All this philanthropy could not have come at a better time for the IITs. They were formed shortly after Indian independence as "institutions of national importance," but have struggled to keep up with the fast-changing and burgeoning fields for which they provide human capital. With enrollments up 35% to 40% in the past 4 years to an average of 2500, students endure packed lecture halls and overcrowded youth hostels. V. S. Raju, director of IIT-Delhi, estimates that the six IITs will need approximately $220 million in the next 3 to 4 years just to maintain existing facilities—an amount unlikely to come from the government, which provides roughly 80% of each institute's operational expenses.

What makes this new wave of private donations especially remarkable is that there is no history in India of academic philanthropy from expatriates. As recently as 1994–95, the total alumni contribution to all the IITs was less than $250,000. But that was before the New Economy began turning entrepreneurs into megamillionaires. Last August, N. R. Narayanamurthy, head of the fund-raising committee for IIT-Kanpur and chair of Infosys Technologies Limited of Bangalore, raised $1 million during a single lunch meeting in San Francisco. Narayanamurthy himself gave another $2 million to the school for a new computer lab. The $3 million represents roughly 30% of IIT-Kanpur's annual operating budget. Efforts to help IIT-Mumbai have been even more successful, with alumni in Chicago pledging $22 million in the span of a few days in December. That's more than the institute's annual operating budget of $20 million.

Many IIT alumni are content to give without asking anything in return, but others would like a bigger say in the way IITs are run. Although the prime minister's office had initially agreed with the idea of an independent board of trustees, Rekhi says, newspaper stories questioning whether the plan constituted a "takeover" that would threaten the institutes' independence have pushed the idea onto the back burner. The industry leaders say they never intended to seize control—"running the IITs is not such a good business," says Rekhi—but only wanted to ensure that the money was used for the desired ends. "I do not think it will make IITs beholden to anybody," says Nandan M. Nilekani, managing director of Infosys Technologies Limited in Bangalore, who so far has donated $1.4 million to IIT-Mumbai.

While some wealthy benefactors are trying to shore up their alma maters, others are trying to set up de novo private institutions. The Global Institute of Science and Technology (GIST) would consist of six research-centered institutes offering undergraduate, graduate, and postgraduate courses. Each institute would enroll up to 2000 students, with any surplus being plowed back into the facility. Some $300 million has already been pledged for the new institutes, which are currently before the influential Scientific Advisory Committee to the Indian Cabinet. Raghunath A. Mashelkar, director-general of the Council of Scientific and Industrial Research in New Delhi, says GIST addresses "a crying need" for another world-class research facility as well as additional training capacity.

Although the IITs and GIST are receiving most of the attention, other institutions are also getting into the act. K. B. Chandrashekar, co-founder and chair of Exodus Communications of Santa Clara, California, has funded a $600,000 center for excellence in Internet and telecommunications at his alma mater, Anna University in Chennai, as well as a remote learning center for students to take courses at any of the school's four campuses. "I got all my education in India, and the first 7 years of my work experience was in India," says Chandrashekar, who plans additional gifts.

Indian government officials see the new wave of philanthropy as the next step in boosting the nation's economy. Vajpayee has talked about creating "Silicon Valley–like conditions in India so that promising young Indians can create world-class ventures while living and working in India." Chandrashekar has an even more expansive vision: "By providing a better infrastructure and making it affordable for all people," he says, "we can make India a superpower through its intellectual capital and not through war."

–PALLAVA BAGLA

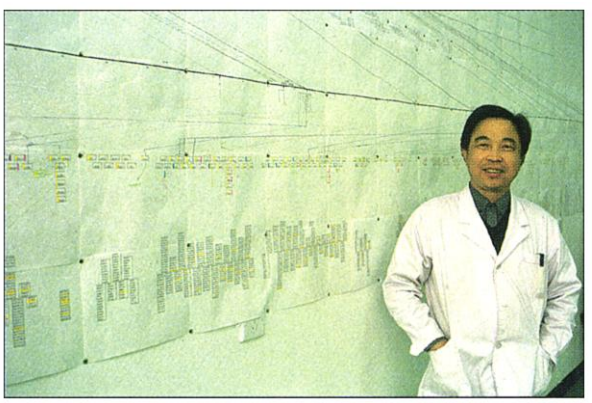
GENOMICS

Money and Machines Fuel China's Push in Sequencing

China hopes that a heavy investment in genomics will help it to fight disease, foster economic growth, and tap its vast biological diversity

BEIJING—Yang Huanming, who directs the human genome center at the Chinese Academy of Sciences' (CAS's) Institute of Genetics, is still unhappy with a deal that two Chinese laboratories struck last spring with a foreign-owned company based in China. The labs agreed to pay Shanghai GeneCore Biotechnologies $225,000 to sequence a prawn virus that threatens China's lucrative shrimp industry. They also ceded one-third of the intellectual property rights on the 300-kilobase sequence. The labs had to pay this steep price, Yang says, because they lacked the capacity to do the work in-house.

Negotiating from a position of weakness so rankled Yang that he and his colleagues lobbied the government for the capacity to do such sequencing jobs themselves. They prevailed: By the end of this month, Yang's center will have enough se-

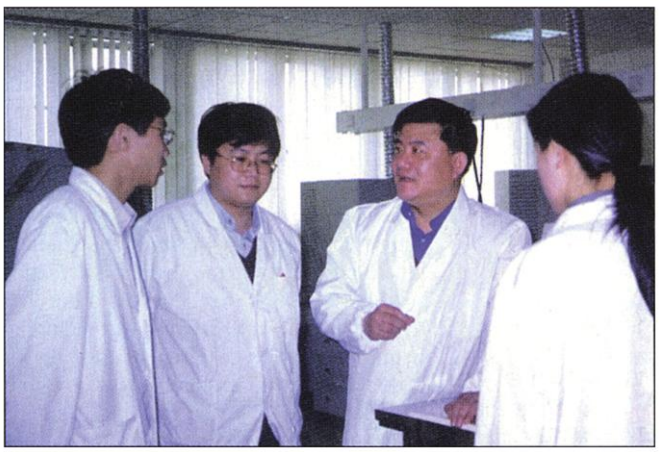


CREDIT: REN YUE

Small steps, big gains. CAS's Yang Huanming with a map showing the Beijing center's progress toward sequencing its allotted 1% slice of the human genome project.

quencing machines to process 15 million bases (Mb) of raw sequence a day. "That will give us the capability to do [such organisms] by ourselves," he says proudly.

A latecomer to the revolution in genomics, China is scrambling to catch up and become a major global player. Last year it joined the international consortium that is sequencing the human genome, agreeing to decipher 1% of the 3 billion base pairs. With all their machines, sequencing those 30 million bases 10 times over will be relatively easy, but the real work comes later, in piecing raw sequence into long stretches of DNA and filling in the gaps. In addition, it is stepping up investment in the scientific capacity to generate, analyze, and profit from genomic data.



Team effort. Shanghai's Chen Zhu, second from right, has forged ties between his center and various academic and corporate groups.

CREDIT: GANG FU CHINESE HUMAN GENOME CENTER

And to protect China's rights in any collaborative project with the public or private sector, the government is drafting new regulations on foreign access to the country's considerable genetic resources.

Chinese researchers welcome their country's entry into the field, but they are sharply divided over what path it should take. One group is pushing for the rapid sequencing of as many genomes—human, plant, and other animals—as possible, while another is hoping to concentrate on finding genes and sequencing only those species with the greatest impact on human health and the environment. "We caught the last bus, but everybody is pleased," says Yang, a prime mover in China's entry into the global human genome project, who is pushing an ambitious plan to sequence as much of China's vast biological diversity as possible. But others argue for a more targeted approach that uses sequencing selectively to explore specific disease genes, produce knockout animal modes, and spur development of related fields such as bioinformatics. "Sequencing is not everything," says Chen Zhu, an academician and hematology researcher at Rui Jin Hospital, Shanghai Second Medical University, who also heads the National South Genome Center in Shanghai.

China began its human genome sequencing project in 1994, with 20 research groups supported by the country's National Science Foundation (NSF). The initial emphasis was on genomic diversity and the identification of genes implicated in the country's major diseases, including hepatocellular carcinoma, nasopharyngeal cancer, essential hypertension, and neurological disorders. In early 1998 the Ministry of Science and Technology (MOST) set up two human genome centers, one in the north, in Beijing, and one in the south, in Shanghai. The country's work on the rice genome began even earlier, when the CAS National Center for Gene Research was created in 1992. Researchers there finished a physical map at the end of 1996. The sequencing was originally scheduled to be completed in 2002, but Hong Guofan, head of the center, said it may be done early.

Yang's center, affiliated with CAS, was created in August 1998, and he and his supporters immediately began lobbying to join the global consortium. Their success, however, meant that China needed to ramp up its sequencing operations, including the purchase of foreign-made sequencing machines.

That it has done. The CAS center, which is dedicated to China's 1% share of the human genome project, had been churning out 2 Mb daily by running its machines—three of the new, state-of-the-art MegaBACE1000 capillary machines made by Amersham-Pharmacia Biotech and 11 of the older ABI377 sequencers made by PE Biosystems—24 hours a day, 7 days a week. Last month, it installed another 30 MegaBACE1000 machines. Yang hopes to receive up to 100 more machines by the end of the year, raising his center's capacity for generating raw sequence to 50 Mb a day. The government's northern human genome center has five ABI377 sequencers and one of the latest ABI3700 machines from PE Biosystems, while the southern center has 10 ABI377s, two MegaBACEs, and one ABI3700. More sequencing machines will be added this year. While devoting a substantial portion of their capacity to the international sequencing project, the two centers are also sequencing other organisms, including the bacterium that causes the tropical disease leptospirosis.

Although China's capacity is impressive, it is not yet a match for the United States and Europe. For example, Celera Genomics Corp. of Rockville, Maryland, which has the highest concentration of sequencing firepower anywhere, has 300 of the new PE Biosystems 3700 machines, which make use of the new capillary technology for faster, more automated sequencing. But once the new machines arrive at CAS, China's overall capacity will be comparable to what's available at major Western centers like Washington University in St. Louis and the Sanger Centre in the U.K.

China's participation in the global human genome project has also forced it to grapple with the sensitive issue of access to data. Its human genome centers have followed the consortium's rules about depositing data immediately into a public database, but Chen's university lab also does proprietary work under contract with private companies. Chen also has a collaboration with the pharmaceutical giant SmithKline Beecham that will soon make public a large collection of expressed sequence tags, small pieces of expressed genes, from stem cells that give rise to blood cells and neuroendocrine tissue. "I think that the public sector and the private one can work together to accelerate the genome project as long as we strike a balance between protecting intellectual property and sharing data with the public," says Chen.

The sequencing work has been a boost to the entire field of biology, say officials. "The 1% project has stimulated the development of other disciplines and genome-related industries," says Gu Jun, CEO of the northern center. The project has given Chinese microbiology a big boost, Chen adds, noting that it greatly hastened work on the leptospira genome and force-fed the field of bioinformatics.

Yang wants the government to capitalize on that expertise by adopting an ambitious plan to generate working drafts of the genomes of most Chinese species—animals, plants, and microorganisms—that are economically or scientifically significant. He admits that the idea, temporarily called the National Bio-resource Genome Project, is an enormous undertaking that could take decades. But he estimates that an initial investment in equipment of roughly $20 million would be enough to get started. Yang has already received a $2.5 million down payment from CAS, and the science ministry and NSF are weighing their contributions. He estimates that, with those resources, his center could produce a working draft of one mammalian genome a year.

To clear the way for such bold projects, and make possible collaborations with for-

eign companies and organizations with sufficient sequencing power, Chinese authorities want to extend existing rules on foreign access to the country's human genetic materials to cover all organisms. Xu Xinlai, head of the MOST bioengineering center, which supervises the ministry's high-tech enterprises and drafts related regulations, says the new rules will uphold the idea that "resources have monetary values" and that China is entitled to its fair share. Under the draft, which has not been made public, Xu says that "if a foreign commercial company wants to make use of China's genetic resources, it has to do it through collaboration with a Chinese partner. The resources to be used should be considered as a kind of investment."

MOST began drafting the new regulations earlier this year in response to concerns raised by Chinese scientists when GeneCore was acquired by PE Corp., Celera's parent company. Yang says Chinese scientists were "alarmed" when Celera's president, J. Craig Venter, announced in January that the deal will "provide access to" many new sources of genetic information. "The intention expressed in Celera's wording is very obvious—to monopolize our country's genetic resources," says Yang. "We need foreign collaborations and even fair competition. But such collaboration and competition should abide by Chinese law."

Celera spokesperson Paul Gilman says Celera has no intention of monopolizing resources: "The only thing that we would negotiate is something that is satisfactory to all parties."

In addition to the effort to sequence part of the human genome and the planned project to sequence China's key organisms, China has already begun deciphering the genome of its staple crop, rice. While an international consortium is working on the Japonica variety (*Science*, 1 October 1999, p. 24), China has pursued a different strain, Indica, grown throughout China and in most of the rest of rice-eating Asia. CAS's Hong says that parallel sequencing of the two rice varieties "provides a unique way to understand their functions." The decision to work on Indica was made early in 1992 at the beginning of the rice genome project. Since then the mapping and sequencing have been sticking with this strain.

With the government committed to raising its investment in genomics, the debate over how to distribute limited funds is likely to remain fierce. But China's research community appears increasingly confident that it will be able to keep up with the rest of the world. "Some scientists see Celera as a hungry wolf," says Chen. "But China is not as weak as it was 5 years ago. We should have confidence in our current capacity." **–LI HUI**

Li Hui writes for *China Features*. Additional reporting by Elizabeth Pennisi.

MEETING AMERICAN ASSOCIATION OF PHYSICAL ANTHROPOLOGISTS

From Field to Lab, New Insights on Being Human

SAN ANTONIO—More than 1100 researchers gathered for the 69th Annual Meeting of the American Association of Physical Anthropologists here, presenting a record 665 papers. Analyses ranged from field reports to lab experiments, including a genetic study of the evolution of a deadly gene, a description of a rare hominid fossil, and brain scans comparing humans and other apes.

Tracing the Genealogy of a Deadly Gene

If there were a Most Wanted list of common deadly genes, the apolipoprotein E (*APOE*) gene surely would be near the top. In its most dangerous form, this gene increases the risk of cardiovascular disease and Alzheimer's disease. Ever since geneticists discovered that there are three types of *APOE* proteins—the worst is known as *E4*—scientists have wondered where and when the killer variant arose. Now a powerful piece of evolutionary sleuthing presented at the meeting reveals the ancestry of the gene's three forms. An international team found that the dangerous *E4* type was inherited from our apelike ancestors and has given rise in the past 300,000 years to the two less harmful forms of the gene, *E3* and *E2*. *E3* is now moving through the world's populations and replacing the deadlier form. "We've actually caught a gene in the process of being changed to a favorable type," says S. Malia Fullerton, a population geneticist at Pennsylvania State University, University Park, and a member of the team headed by genetic epidemiologist Charles Sing at the University of Michigan Medical School in Ann Arbor.

The group also found that each of the three types of *APOE* has many variations, which may help explain why people who have inherited the *E4* type have different degrees of risk for developing heart disease or Alzheimer's. "This shows that it's important when we do these assessments of risk that we do not just use these simplistic three types," says pathologist George Martin of the University of Washington (UW), Seattle, who hopes that better diagnostic tests can now be developed.

The gene has been a target since 1985, when researchers found that people with the APOE4 protein have a higher risk of heart disease than those who inherit the other two types. In 1993, researchers linked *E4* to Alzheimer's (*Science*, 13 August 1993, p. 921), and soon after found that chimps only have *E4*. That sparked much debate about which type of *APOE* was ancestral, because *APOE3* is most common today.

To answer that question, the team sampled 96 people from four populations and began massive sequencing, done by UW geneticist Debbie Nickerson, of a 5491–base pair region of the gene on chromosome 19. When the team organized the sequences into a tree where the most similar sequences clustered together, they found 31 distinct subtypes of DNA that sorted into the three major types of *APOE*. Each of the variants within the three types preserves the genetic code necessary to produce one of the three *APOE* proteins, but the sequence varies in other regions. Those changes may subtly affect the way the *APOE* proteins are regulated and expressed, and may help explain why in some populations, such as African Americans, those with *E4* get Alzheimer's less than expected.

"It's ground-breaking that they did large-scale sequencing of a long stretch of DNA on so many people," says human population geneticist Jeffrey Long of the National Institutes of Health. Although geneticist Allen Roses's group at Glaxo Wellcome in Research Triangle Park, North Carolina, also has found variation at the DNA level within the three seemingly simple *APOE* types (*Science*, 15 May 1998, p. 1001), this new report also traces, step by step, the DNA changes that led from *E4* in the chimpanzee to *E3* and *E2*, and proves that *E4* was the ancestral form of the gene.

The limited variation within the *E3* and *E2* haplotypes shows that they emerged fairly recently, sometime in the past 300,000 years, according to a molecular clock based on the apparent rate of divergence between human and chimp. The good news, says Fullerton, is that the new and less dangerous *E3* type seems to be under selection pressure, as it is spreading most rapidly. Martin speculates that *E4* may have persisted for millions of years in human ancestors, offering some advantage, perhaps