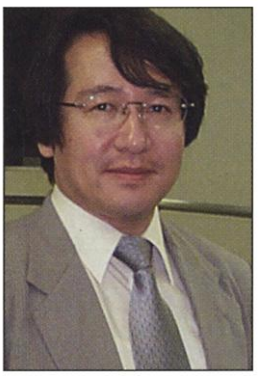
Japan and China Gear Up for 'Postgenome' Research

TOKYO AND BEIJING—When the human genome project was first conceived in the late 1980s, Japan hoped to play a major role. Funding, however, proved elusive. So although Japanese teams did decipher a good chunk of chromosomes 21 and 22, the country contributed just 6% to the draft sequence published last February. China managed even less. But now, as the focus moves beyond human sequencing, neither country will be content with a bit part.

"There is a feeling [among policymakers] that Japan was left behind in sequencing, and the country wants to be better prepared for the next stage of genomic research," says Akiyoshi Wada, director of the Genomic Sciences Center of the Institute of Physical and Chemical Research (RIKEN) in Yokohama. It will be, if Japan's Ministry of Education, Culture, Sports, Science, and Technology wins approval for an ambitious bundle of "postgenome" projects (see table). With a total proposed budget of $570 million for the fiscal year that begins next April, it would be considerably more than the U.S. National Human Genome Research Institute expects to spend.



Ambitious. Shigeyuki Yokoyama expects Japan to resolve 3000 protein structures within 5 years.

As elsewhere, debates have been intense over which aspects of genomic work should get priority (see main text). As a compromise, there is something in the proposal for just about everyone, although proteomics, with its expected payoffs in drug development, is getting the lion's share through the Protein 3000 Project. The goal of this project is to determine the structure and function of 3000 proteins over the next 5 years. That will be a challenge, acknowledges Kunio Miki, a protein crystallographer at Kyoto University—but he says it is probably doable "if anticipated advances in technology are actually realized, particularly in automating the time-consuming processes of sample preparation."

The work will be done at up to seven new protein structure centers to be created at universities and at RIKEN's new center for nuclear magnetic resonance (NMR) imaging, a key technique for determining protein structures. Japan also has the world's most powerful synchrotron radiation facility for x-ray crystallography: SPring-8, located near Kobe. This facility will be used to handle the larger, more complex proteins that can't be resolved with NMR.

Shigeyuki Yokoyama, who heads RIKEN's protein research group, says that the 3000 proteins will be Japan's share of an emerging international effort, involving at least 11 countries, that aims to determine 10,000 protein structures over the next 5 to 10 years. Yokoyama, who is on the organizing committee, explains that the 10,000 proteins are a first step toward resolving the structure of at least one representative protein from the estimated 15,000 to 20,000 protein structure families. "We believe that once you have the structure of one protein in a family, you will be able to model the others," he says.

The International Structural Genome Organization, as it will probably be called, will likely be officially launched late this year or early next. The group's first scientific meeting is scheduled for October 2002 in Berlin. Yokoyama says the group hesitates to put a price tag on the project because current costs—about $80,000 per structure—make it unreasonably expensive. "We need to improve the success rate and make the whole process more efficient," he says.

Japan's new centers should have plenty of proteins to analyze, thanks to several Japanese efforts to accumulate libraries of complementary DNAs (cDNAs). These are synthesized strands of DNA containing only the transcript sequence that codes for proteins. Next spring, when a RIKEN group led by Yoshihide Hayashizaki finishes a 3-year, $45 million project, data and clones of more than 80,000 mouse cDNAs will be available, one of the largest such collections for any organism. Other groups are working on human cDNA libraries and the plant model organism *Arabidopsis thaliana*. The cDNAs themselves will also be used in microarrays for profiling gene expression patterns.

After a late start on genomics, China rallied and recently announced its 1% contribution to human sequencing and is forging collaborations to sequence the genomes of the pig and chicken. China is also contributing to an international rice sequencing effort while tackling two other rice varieties on its own.

Although work is currently focused on mapping and sequencing, Chinese scientists anticipate moving beyond, perhaps "to focus on identifying genes, compare the pig genome with the human genome, and find pig models for human diseases," says Merete Fredholm of the Royal Veterinary and Agricultural University in Copenhagen, Denmark, which is collaborating with the Beijing Genomics Institute (BGI) in the Sino-Danish Pig Genome Sequencing Project.

In addition to the purely scientific benefits, the collaborations are strengthening ties among research institutes in China, the United States, and Europe. The latest tie is a new sister center relationship between BGI of the Chinese Academy of Sciences and the Whitehead Institute Center for Genome Research at the Massachusetts Institute of Technology. The two institutes expect to exchange researchers and collaborate on developing technologies. Eight BGI computer specialists were to have traveled to Whitehead in September to explore joint software development; the trip was postponed when flights were halted because of the recent terrorist attacks in the United States.

—DENNIS NORMILE AND YANG JIANXIANG

Yang Jianxiang writes for *China Features*.

SELECTED POSTGENOME RESEARCH PROJECTS IN JAPAN

Protein 3000 Project, $160 million (¥19.1 billion)*
Determine the structure and function of 3000 proteins within 5 years

National Bioresources Project, $86 million (¥10.3 billion)
Sequence model organisms, develop embryonic stem cell lines, assemble collections of experimental animals

Technological Innovations, $88 million (¥10.6 billion)
Develop bioimaging technologies and bioinformatics; support the translation of basic results into medical treatments

Other genetic research, $21 million (¥2.6 billion)
Analyze SNPs, with goal of developing tailor-made medical treatments

Research into immunity and allergies, $42 million (¥5.0 billion)
Support for applying genetic techniques to understanding conditions affecting immunity and allergic reactions

* Budgets do not include salaries of permanent staff but do cover the salaries of temporary employees such as postdocs.

SOURCE: MINISTRY OF EDUCATION, CULTURE, SPORTS, SCIENCE, AND TECHNOLOGY BUDGET REQUEST FOR FY 2002