

technological envelope. "Compared with the U.S. and Europe, there is still a large technology gap," says Shouxian Fang, director of the Beijing Electron Positron Collider National Laboratory and a former director of China's Institute of High Energy Physics. Asian countries are less interested in high-energy particle colliders for cutting-edge physics, he says, and more interested in lower energy synchrotron light sources and proton accelerators for basic research in commercially important areas, such as materials science, medicine, and the transmutation of nuclear waste.

Last week's meeting featured updates on more than a dozen accelerator programs, with participants presenting the latest designs for components and diagnostic devices and swapping ideas to squeeze the best performance out of their machines. It also allowed researchers from more advanced programs to share their knowledge with colleagues at emerging facilities, continuing what until now has been an informal tradition. For example, Richard Sah, a physicist at Taiwan's Synchrotron Radiation Research Center, whose center has already gotten help from KEK on boosting machine performance, aided Thai physicists designing a new control system for the Siam Photon Project.

Cooperation within Asia could also enable those without an accelerator program to keep up with the field. "We have no plans for any large-scale accelerator facilities in Malaysia," says Swee Ping Chia, a physicist at the University of Malaya and current president of the Malaysian Institute of Physics. But he says many of Malaysia's researchers would benefit from exposure to the experimental uses of accelerators: "We want to send people to participate in accelerator experiments and bring that knowledge back home." Indeed, scientists from Taiwan, South Korea, China, the Philippines, and India are part of the team working on the KEK B-meson facility, which will come on line next year.

At present, North American accelerator scientists meet in odd-numbered years and their European counterparts host a similar meeting in even-numbered years. KEK's Sugawara says he would like to see a 3-year cycle, with one major international accelerator conference each year. But Robert Jameson, an accelerator physicist at New Mexico's Los Alamos National Laboratory who served on the organizing committee for the Tsukuba meeting, says European and U.S. groups might not want to reduce the frequency of their own conferences. "Two years is about the right timing," Jameson says.

Regardless of scheduling obstacles, the Asian group plans to forge ahead. "We should promote this movement toward greater cooperation," says conference planner Makoto Inoue of Kyoto University. The next Asian meeting is scheduled for Beijing in 2001.

—Dennis Normile

## GENE SEQUENCING

# France's Sequencers Aim to Join the Big League

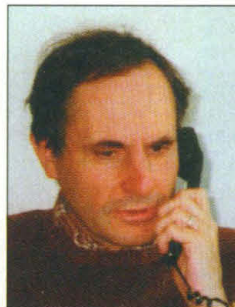
**EVRY, FRANCE**—As the worldwide effort to sequence the human genome moves into high gear, gene researchers are welcoming the latest member of the team: France's Genoscope, a major gene sequencing center in this industrial suburb just outside Paris. Genoscope, also known as the National Sequencing Center, plans to tackle between 5% and 10% of the human genome, which would put it in the same league as such major players as the Sanger Centre near Cambridge, U.K., Washington University in St. Louis, and The Institute for Genomic Research in Rockville, Maryland. As part of its preparation for this daunting task, the French center—which has been quietly tooling up since last summer—will soon complete its inaugural project: the sequencing of the genome of *Pyrococcus abyssi*, an archaebacterium that lives at high temperatures and whose sequence may help resolve controversies about the nature of early life forms (see sidebar).

Genoscope's director, genetic researcher Jean Weissenbach, says the center will eventually churn out 300 million nucleotide base pairs per year of raw data. Just how much of this capacity will be devoted to sequencing the human genome has yet to be determined; like most other gene sequencing centers around the world, Genoscope will work on DNA from a wide variety of organisms, including plants and fish as well as humans. Weissenbach is also grappling with the difficult question of how quickly sequence data should be publicly released once it is generated—an issue that has been the subject of international debate for a number of years. This is a particularly sticky point because the French research ministry wants its biomedical research activities to pay off its public investment by generating patents (*Science*, 6 March, p. 1442).

Other participants in the human genome project say that Genoscope's contribution will be sorely needed if the goal of completing the entire sequence by 2005 is to be reached; only a little more than 3% of the 3 billion total base pairs has been completed so far. "The more effort we can muster in Europe, the better," says John Sulston, direc-

tor of the Sanger Centre. Indeed, many French researchers believe that Genoscope's contributions might have come much earlier if French politics had not slowed the country's genome project down. "Our successive changes of government—left, right, left—have made a mess of genome policy in this country," says Bertrand Jordan, a molecular biologist at the Center for Immunology in Marseilles. Although the idea of a sequencing center was first proposed in 1990 under the Socialists, the project languished until 1996 when the conservatives revived it, but they spent many months agonizing over its location and funding. Fortunately the Socialists, who returned to power in June 1997, have stuck to their predecessors' commitment to budget \$13 million a year over 10 years for Genoscope.

These funds have allowed Weissenbach to purchase 50 gene-sequencing machines as well as assemble more than 100 scientists, technicians, and computer experts. And to help turn this investment into marketable therapies, the French government, in co-



GENOSCOPE



GENOSCOPE

**Pitching in.** Jean Weissenbach (inset) will devote some of Genoscope's 50 sequencers to the human genome effort.

operation with local governments and the French muscular dystrophy association, is making Genoscope the nucleus of a new genetic research park that will accommodate industrial partners as well as a publicly funded genotyping center—devoted to studying genetic diseases—that will be led by Mark Lathrop, currently director of the Wellcome Trust Centre for Human Genetics in Oxford, U.K.

The goal for Genoscope "is not necessarily to be the fourth or fifth center in the world and do exactly what all the others are doing," says André Capron, director-general of the Pasteur Institute of Lille and

## Did Life Begin in Hot Water?

Patrick Forterre, a molecular biologist at the University of Paris's campus in Orsay, cannot believe his good luck. For much of his career, Forterre has been studying a strange group of microbes known as the Archaea, many of which are hyperthermophiles—bugs that live at temperatures sometimes exceeding the boiling point of water. Despite the modest resources available for Archaea research in France, Forterre and other French colleagues have painstakingly unraveled the biochemistry of several archaean hyperthermophiles, identifying a number of new genes and proteins. But now Forterre and his colleagues have been handed a very welcome gift: Their proposal to sequence the entire genome of *Pyrococcus abyssi*, an archaean that lives in undersea hydrothermal vents, was accepted as the first project of Genoscope, France's new gene sequencing center (see main text).

When the sequence is completed later this spring, Forterre will no longer have to search out archaean genes one at a time. "Now we will be able to concentrate our efforts on more interesting things," he says. In particular, Forterre hopes to accumulate more evidence for his somewhat iconoclastic views about the early history of life. Forterre was an early disciple of evolutionist Carl Woese, of the University of Illinois, Urbana-Champaign, who proposed in the early 1980s that the Archaea formed a third kingdom of life alongside bacteria and eukaryotes. Woese and other researchers later concluded from genetic and biochemical comparisons of modern organisms that the earliest ancestor of all present-day life probably arose in high-temperature conditions. Forterre, however, argues that the evolutionary evidence could also support a "cold" origin for the earliest ancestor, and that the heat-loving lifestyle might have been a later adaptation.

Forterre's reservations are shared by some well-known researchers, including origins-of-life pioneer Stanley Miller of the University of California, San Diego, and evolutionary biologist Antonio

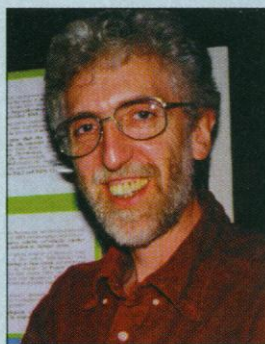
Lazcano of the National University of Mexico in Mexico City. "Most people doing prebiotic chemistry are convinced that a hot origin of life is unlikely," says Lazcano, pointing out that the amino acids, nucleic acids, and other molecular building blocks of early organisms would have been chemically unstable at high temperatures. Modern hyperthermophiles have evolved sophisticated biochemical tricks to adapt to high temperatures.

Forterre and other researchers in the field are hoping that by comparing the genome sequences of *P. abyssi* and other recently sequenced Archaea, scientists will eventually be able to resolve the hot-cold origins controversy—for example, by tracing the evolutionary history of reverse gyrase, an enzyme that stabilizes DNA molecules against high temperatures. To this end, Forterre and Gary Olsen, who collaborates with Woese at the University of Illinois, are considering teaming up to propose that Genoscope sequence another archaean microbe, *Methanococcus maripaludis*, a so-called

mesophile that lives optimally at a more moderate temperature of about 37 degrees Celsius. Another member of this genus, the hyperthermophile *Methanococcus jannaschii*, whose optimum temperature is about 80°C, was sequenced in 1996. Forterre and Olsen agree that comparing these two closely related Archaea—one heat-adapted and one not—with each other and with other Archaea and bacteria might provide clues about whether hyperthermophilia was an early characteristic of life or a habit acquired later.

"This should help us to understand the mechanism of thermoadaptation," says Forterre, "and also the direction of evolution, whether from cold to hot or from hot to cold." And although Forterre says he cannot predict the result, he is confident that "we will have a greater chance to discover some relevant information." After years of chipping away at archaean genomes, that is a chance Forterre is very glad to have.

—M.B.



**Iconoclast.** Archaea expert Patrick Forterre.

president of the steering committee appointed by the research ministry to oversee both Genoscope and the genotyping center. Capron says that the two centers will target genomes, as well as individual genes, whose sequences "can lead to important applications," particularly in the area of human, plant, or animal diseases.

Genoscope can also be "a fantastic tool" to further fundamental knowledge, adds Capron. One of its first projects, for example, will be to sequence part of the genome of *Tetraodon fluviatilis*, a freshwater puffer fish whose unusually small genome—only about 400 million base pairs—makes it a model organism for genetic studies of vertebrates. And the center has already joined an international consortium that is sequencing the weed *Arabidopsis thaliana*—whose 120-million-base-pair genome is a model for thousands of other plant species.

These projects, along with the human genome effort, will be treated as internal

Genoscope programs, and the center will follow a policy of posting its data on the Internet as soon as it is available, in line with a growing international consensus on data release. But Weissenbach says that according to guidelines adopted by the research ministry, publicly funded joint projects with other French labs, such as the sequencing of *Pyrococcus abyssi*, will not necessarily release their data immediately, to allow researchers time to patent their discoveries first. The center does not have the clout, he says, to force a policy of immediate release on outside researchers: "We are not as strong as the Sanger Centre, which can impose its own rules on its collaborators." Indeed, Sanger director Sulston, as well as the U.K.'s Wellcome Trust, which provides most of the Sanger Centre's funds, are strong advocates of immediate release. A February meeting of top gene researchers in Bermuda, convened by the Wellcome Trust, called on sequencers to follow a policy of immediate release for all

sequenced organisms.

French authorities are now set for a showdown with gene researchers around the world on data release. Germany faced a similar situation last year when it attempted to force labs involved in its new genome program to withhold data to allow industry to apply for patents, but in the end it dropped the condition (*Science*, 30 May 1997, p. 1323). "The French government is out of line on this one. ... We would like to put pressure on France" to change its policy, Sulston says, adding, "we all know the pressure Jean is under on this point."

Clearly, France will have to resolve its policy on data release before Genoscope can take its proper place at the table of the world's leading gene sequencing centers. But the completion of the *Pyrococcus abyssi* genome, due later this spring, is an important first step. Says Weissenbach: "This puts us on the map."

—Michael Balter