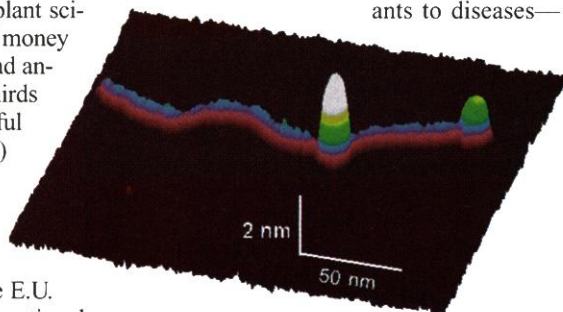


DNA IMAGING

Getting a Feel for Genetic Variations

Even before last week's news of the near-completion of the human genome sequence, researchers had set about the arduous task of figuring out just how the sequence differs among individuals—and how those variations may predispose people to various illnesses. Current genetics technologies make it relatively straightforward to determine where such differences lie on a given chromosome, say, chromosome 11. But determining which of the two copies of that chromosome the change resides on—a necessary first step toward linking those variants to diseases—



Fingered. A microscope easily spots a specially tagged site along DNA.

has proved challenging indeed. Now a team of researchers at Harvard University and the Massachusetts Institute of Technology (MIT) has come up with a novel atomic imaging microscope that may dramatically speed this task.

The microscope is a modification of the popular atomic force microscope (AFM), which uses an ultrasharp tip to map surfaces of everything from computer chips to DNA at the atomic level. The new version caps a conventional silicon tip with a carbon nanotube, an ultrathin, strawlike network of carbon atoms a mere nanometer or so across. By using this molecule-sized tip, the researchers—led by Harvard chemist Charles Lieber and MIT geneticist David Housman—were able to get their AFM to march down a strand of DNA and identify uniquely shaped reporter molecules engineered to tag the genetic variations. In this case, these variations are sites along a chromosome that harbor a one-letter difference in spelling called a single-nucleotide polymorphism (SNP).

As they describe in the July issue of *Nature Biotechnology*, the Harvard/MIT group—which includes postdoc Adam Woolley, then-postdoc Chantal Guillemette, and grad student Chin Li Cheung—was able to feel its way around one of the most vexing problems in genetics: haplotyping. Haplotyping is the task of figuring out exactly

ScienceScope

Preventive Medicine Top U.S. research universities can do a far better job of protecting human subjects, says a new report by the Association of American Universities (AAU). The report (www.tulane.edu/~aau) urges the AAU's 61 member schools to beef up their Institutional Review Boards, which oversee clinical studies, by seeking outside accreditation and enrolling more nonscientists. AAU President Nils Hasselmo says that such changes could make redundant proposed legislation that would broaden federal oversight of clinical research (*Science*, 16 June, p. 1949). The report also proposes that the government help foot the bill.

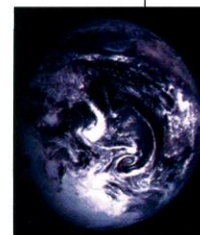
Space Squabble Relations between the Administration and Representative James Sensenbrenner (R-WI), who chairs the House Science Committee, are strained on a good day. But his NASA authorization bill has added a new layer of stress.

The bill, H.R. 1654, would kill Triana, a pet project of Vice President Al Gore to beam satellite images of Earth (below). It also orders NASA to get a refund from the Russians for any space station delays and blocks the agency's ability to keep revenue from commercial deals. After the Administration threatened a veto, Sensenbrenner offered a "grand compromise" that would save Triana. But last week, at an inconclusive conference between House and Senate members, Democrats complained that some of Sensenbrenner's demands were not in the original bill approved by the House and that their suggestions were ignored.

Capitol Hill observers say that the way Sensenbrenner handles the squabble could affect his bid to chair the Judiciary Committee in the next session. "If he wants to show that he can be conciliatory, this is not the way to do it," harrumphs one Democratic aide.

Short Leash Energy Secretary Bill Richardson has given new security czar James Gordon until 5 September to work out a new arrangement with the University of California (UC) for its management of the nation's nuclear weapons labs. The UC contract runs until 2002, but Richardson says its performance "is unacceptable and must be addressed immediately." UC officials say they "welcome the opportunity to work with [the Department of Energy]."

Contributors: Wayne Kondro, Michael Balter, Eliot Marshall, Andrew Lawler



ordinating research activities on both national and E.U. levels. The fundamental studies would eventually translate into new ways to raise yields and slash pesticide use. "If science is to tackle these challenges, there is a dire need for more integration," says plant geneticist Michael Bevan of the United Kingdom's John Innes Center. Zabeau sees parallel national initiatives in plant genomics in Germany and France as examples of unnecessary competition for scarce resources. At the same time, he acknowledges that collaborative research also faces many obstacles. "We have networks in place, but we need significant funding and an infrastructure that allows us to come together in practice," says Zabeau.

Under Framework 5—the E.U.'s research portfolio for 1999 through 2003—plant science no longer has its own pot of money but must compete with microbial and animal research. One result is a two-thirds reduction in the number of successful proposals (seven in the first round) compared with the previous Framework program. Among the casualties is a plan to complete work on the well-studied mustard, *Arabidopsis thaliana*. After the E.U. put up \$20 million toward an international sequencing effort, "all funding was denied for the final phase," says EPSO coordinator Karin Metzlaff.

National funding for plant research has also declined, with Denmark and the Netherlands particularly hard hit. Dutch authorities are in the midst of implementing a 30% cut over 5 years and have ended funding for all collaborative projects. All Danish programs in plant biotechnology will expire by 2002, and no new initiatives are planned.

That alarms industry, which relies upon a strong public-sector commitment to basic research, says Georges Freyssinet, head of global genomics research at Aventis CropScience in Lyons, France. "The next 5 to 10 years will be essential," he says, warning that now is the worst possible time to be reducing government support for plant research. European companies may need to move research operations elsewhere if the political culture surrounding genetically modified foods does not improve, he adds.

E.U. officials have already begun to plan for the sixth Framework Program, which starts in 2004. And although Busquin confesses that the plant science community has his ear, he says that "risk assessment and ethical aspects are important issues that have to be addressed." The research chief also doesn't want to be seen as catering to a particular discipline: It is "impossible at this point to promise more funds for individual fields," he says.

—LONE FRANK

Lone Frank writes from Copenhagen.

which of several possible gene variants occurs on a given chromosome. The difficulty arises because each cell contains two copies of each chromosome, one from the mother and one from the father. At any location along the chromosome, geneticists can tell whether the two chromosome copies are identical—that is, whether they contain the same chemical letter—or different. But when the chromosomes differ—that is, contain a SNP—the researchers can't readily tell which letter belongs on which chromosome. And the exact spelling of each chromosome is essential information, because it may change a gene into a disease-causing form, says Housman.

Currently, explains Andrew Collins, a geneticist at Southampton University in the United Kingdom, researchers do family studies to look for disease genes. If they can't find suitable families, they look at the frequency with which different SNPs pop up in many individuals and then resort to statistical methods to infer the likely exact spelling of each chromosome. But this process is "prone to error," he says.

The nanotube-based AFM may change that by enabling researchers to forgo statistics and observe the SNPs on a chromosome directly. The researchers borrowed an idea from the standard sequencing method, which reveals the DNA's four chemical letters in living color by linking a different fluorescent dye molecule to each of them. But here, instead of using a fluorescent signal, the researchers added an oligonucleotide—a short strand of DNA designed to bind to a single complementary DNA fragment, in this case one surrounding a known SNP location. Each oligo was engineered to stick only when the SNP harbored a particular genetic letter—G, for example. To this oligo they hitched a reporter compound. As the AFM marched along the atomic hills and valleys of the DNA, when it hit the reporter compound the researchers knew they had found their G SNP. By adding several oligo-reporter combinations, then simply reading down a section of a gene of interest, they could readily decipher whether a series of SNPs of interest were present on the same chromosome. Says Collins: "That's a very useful thing to have."

For now the Harvard researchers are looking at DNA strands around 1000 genetic letters long. That's on the short side for many geneticists trying to associate combinations of SNPs with disease. But Lieber says there's no reason the technique shouldn't work with sequences perhaps as long as 100,000 letters. Furthermore, by borrowing data-storage techniques, geneticists may be able to create arrays of hundreds of AFM tips working in parallel to carry out ultrafast haplotyping. If so, says Robert Waterston, a

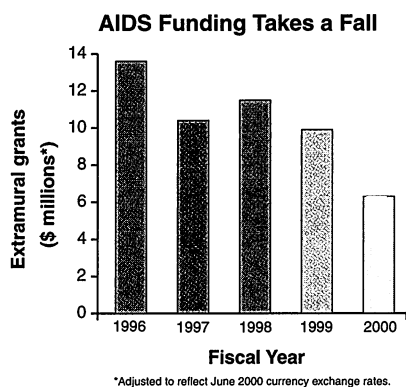
geneticist who heads the genome sequencing center at Washington University in St. Louis, Missouri, "[this] could be the start of something impressive."

—ROBERT F. SERVICE

AIDS RESEARCH

Italian Scientists Seek To Reverse Budget Cuts

PARIS—The closing session of the XIII International AIDS Conference in Durban, South Africa, next week will be a proud moment for Italy. That's when Italian researcher Stefano Vella becomes president of the International AIDS Society (IAS), which organizes these biennial conferences. But even



Reduced effort. New cuts continue downward slide of AIDS funding.

as the Durban meeting highlights Italy's prominence in the AIDS community, the Italian government is gutting the country's national AIDS program.

The cuts, for the 2000 fiscal year beginning 1 July, mean a 36% reduction in funding for extramural grants from the current year. They continue a trend begun in 1997 (see chart). Italian AIDS researchers have known about the latest round of cuts for several months. But it is only after the appointment in late April of a cancer researcher, Umberto Veronesi, as Italy's new health minister and in the run-up to the Durban meeting that they have begun to speak out about their harmful effect.

"The national AIDS program is one of Italy's big success stories," says Vella, who directs the AIDS clinical research program at the Istituto Superiore de Sanità (ISS) in Rome, the agency that provides nearly all extramural funds for AIDS research. "We don't want everything we have accomplished to be lost." Their pleas have attracted international support. "Italian scientists are very important players in the global AIDS research effort," says Antho-

ny Fauci, director of the U.S. National Institute of Allergy and Infectious Diseases in Bethesda, Maryland.

The 13-year-old Italian AIDS program first ran into trouble in 1997, when then-health minister Rosy Bindi froze AIDS funding for several months. The freeze was part of a government reordering of priorities that placed more emphasis on applied research (*Science*, 11 April 1997, p. 191). When the dust settled, the \$13.6 million extramural program had been reduced to just over \$10 million. And the decline has continued: The proposed budget for 2000–01 is only \$6.3 million. "This will have a major impact," says AIDS researcher Guido Poli of the San Raffaele Scientific Institute in Milan, who depends on ISS grants for about 80% of his lab's funding. "I will have to severely reduce many of my current projects, and it will affect our ability to pay young researchers and to participate in meetings."

Italian AIDS researchers are now hoping that Veronesi, who replaced Bindi when a new Italian government took office this spring (*Science*, 5 May, p. 791), will be more sympathetic to their cause. Now that Veronesi has had time to get settled into his job, Vella and his colleagues say they are hoping to meet with the minister to discuss how to reverse the funding cuts. Veronesi was unavailable for comment.

If the cuts are not restored, the election of an Italian as IAS president may turn out to be a hollow reward. Says Fauci: "If [Italian researchers] are unable to pursue their scientific activities at full speed because of a lack of resources, the entire global AIDS research effort will suffer."

—MICHAEL BALTER

ASTRONOMY

Radio Galaxies Return From the Dead

Even for deep-space objects, radio galaxies are odd beasts—so odd that scientists have trouble explaining why they exist at all. Now astronomers in the Netherlands have deepened the mystery by discovering that some radio galaxies live twice.

The hallmark of a typical radio galaxy is a double blaze of radio energy, which erupts when thin jets of ionized matter shooting in opposite directions slam into intergalactic atoms at enormous speed, millions of light-years from the galactic core. The origin of the jets is still unknown. Most astronomers suspect that they stream from the poles of a whirling supermassive black hole, which sucks in nearby gases and spews part of them out again as plasma. But just how the black hole's engine