TIGR are still trying to make sense of the sequence. *P. falciparum* appears to have about 5300 genes. The researchers are not yet able to identify the function of some 60% of these genes, they report. In addition, genes with related functions appear to be clustered on the genome, suggesting that they might share the same regulatory DNA.

Even with unanswered questions, researchers are using the sequence to build a catalog of *Plasmodium* proteins and to make gene chips for molecular studies of different points in *P. falciparum*'s life cycle. In the proteomics arena, at least two research groups report in *Nature* that they are using sophisticated mass spectrometry techniques to look at thousands of proteins and determine when in the parasite's life cycle they are active. For vaccine developers, who want to create defenses against all of the parasite's alter egos, "that's very valuable information," says Gardner.

In one proteomics study, Laurence Florens and John Yates of the Scripps Research Institute in La Jolla, California, and their colleagues examined more than 2400 proteins. They found that the protein complement of the sporozoite—the form of the parasite a mosquito injects when it feeds on human blood—was quite different from that of other stages of the life cycle. Almost half of the sporozoite's proteins were found nowhere else, they report. But there were also a few unexpected genes in common. Researchers had thought that the parasite made var proteins—used to evade the immune system—only while in human blood, but these studies have now shown that "they are expressed before it even gets to the host," says Carucci.

And in a separate evaluation of 1289 proteins, Edwin Lasonder and Matthias Mann of the University of Southern Denmark in Odense found 315 that are unique to the immature male and female gametes that enter the mosquito and 226 in the asexual stages. "Intellectually, it's very exciting to think we have a total catalog of the relevant genes for all the parts of the life cycle," says Roos, who has set up a database (PlasmoDB.org) to compile the onslaught of genomic data on *Plasmodium*.

Harvard's Sarah Volkman and her colleagues, among others, are using the *P. falciparum* sequence to expand studies of drug resistance. As described on page 216, working with Elizabeth Winzeler of the Genomics Institute of the Novartis Research Foundation in La Jolla, California, Volkman's team built gene chips to detect genetic changes—or polymorphisms—between *P. falciparum* strains. "Drug resistance is bred by polymorphisms," Winzeler explains. "So being able to actually determine where [the polymorphisms] exist allows you to study the spread of drug resistance."

Whether with more gene chips, proteomic studies, gene searches, or comparative genomics, other malaria experts are eager to make use of the newly sequenced mosquito and *Plasmodium* genomes. "There are going to be fantastic strides in the years to come," says Thomas Wellems, a malaria expert at the National Institute of Allergy and Infectious Diseases in Bethesda, Maryland. "I have no doubt that a deeper understanding of the biology of the parasite is going to lead us to better therapies." **–ELIZABETH PENNISI**

CLINICAL RESEARCH

## Gene Therapy a Suspect In Leukemia-like Disease

A French gene-therapy team that was hailed in 2000 for its breakthrough in curing children of a lethal immune deficiency reported a serious adverse event this week. One of 10 children they treated has developed a blood disorder resembling leukemia. Concerned that the therapy might have caused the problem, researchers Alain Fischer and Marina Cavazzana-Calvo of the Necker Hospital in Paris have halted the trial and urged others who use similar methods to hold off until the risks are assessed. At press time, French regulatory officials were preparing a public advisory.

**Setback.** Alain Fischer and Marina Cavazzana-Calvo announcing successful gene-therapy treatment in April 2000.

CREDIT: FRANÇOIS GUILLOT/AFP/CORBIS

Fischer says he and his group recognized the importance of the case "exactly 1 month ago" but decided to study it and explain it to their patients before going public. The French team quickly sent advisory letters to investigators in charge of similar gene therapy trials using gene transfer "vectors" made from a retrovirus called the mouse Moloney leukemia virus. When the warning reached the U.S. National Institutes of Health (NIH) in Bethesda, Maryland, a clinical group immediately cancelled a six-patient trial due to begin in September.

This French trial was designed to identify children with a type of severe combined immunodeficiency (SCID) caused by a mutation on the X chromosome and to treat them early (*Science,* 28 April 2000, p. 669). So far, the team has treated nine infants and one teenager. All faced the prospect of lethal infections or harsh therapy such as bone marrow transplantation, which itself often has fatal consequences. Gene therapy offered a way out; in most cases it restored the immune system without toxicity.

During a routine check of their fourth patient last spring, however, the French researchers noted that the child had a high number of γδ T cells in his blood. The import didn't hit home until late August, Fischer says, when the T cell count climbed "very high"—to 200,000 cells per microliter. Other symptoms also appeared, including mild anemia, and the child was hospitalized.

Molecular studies revealed that the T cells were monoclonal: All had come from a single cell. Furthermore, Fischer explains, all the cells contained the same DNA signature, a sequence reflecting the site where the retrovirus vector had integrated itself into the host's genome. "Unfortunately," Fischer says, that site is in the coding region of a gene on chromosome 11 that's "aberrantly expressed" in a form of childhood acute lymphoblastic leukemia.

Fischer believes that the vector triggered "an insertional mutagenesis event"—splicing itself into a dangerous gene and stepping up its production. "Everyone was aware" of a theoretical risk that retrovirus vectors might do this, he says, but the risk seemed very small. The phenomenon did not turn up in animal experiments or in other clinical data.

Although gene therapy probably contributed to the patient's T cell response, Fischer says, other factors probably played a role, too. For example, the child might have been predisposed to disease, as other members of his family have had childhood cancers. And an infection might have been important as well; the child got chickenpox shortly before his T cell count spun out of control. But at the moment, Fischer acknowledges, it's not clear whether this was a "very unlucky" random event or a sign that the risk of using retrovirus vectors has been "underestimated" in the past.

Researchers at the Necker Hospital are collaborating with Christof von Kalle of the Institute for Molecular Medicine in Freiburg, Germany, to try to create a map of all known human DNA integration sites for this retrovirus vector. They hope this will enable them to estimate the risks better. Meanwhile, the

child is receiving chemotherapy.

Few gene-therapy researchers were available to comment on the case at press time. But Jennifer Puck, a leader of the planned SCID therapy trial at NIH, knows of four other groups that are using or were planning to use similar gene-therapy techniques. At the moment, she says, "we don't know whether the risks [of insertional mutagenesis] are one in 80 or one in 10 million."

U.S. regulatory officials declined to comment on the case. But NIH's Recombinant DNA Advisory Committee is reported to be preparing a broad review of the case at its next meeting, scheduled tentatively for 4 to 6 December. **–ELIOT MARSHALL**

SCIENCE TEACHING

## Georgia County Opens Door to Creationism

The forces of creationism gained ground in Georgia last week when a local school board unanimously adopted a policy that opens the door to creationist-inspired critiques of evolution in biology classes. The policy follows the board's decision in March to insert "disclaimers" into new elementary and high school biology textbooks saying that evolution is only a "theory." The action directly affects only 95,000 students in Cobb County, a suburb of Atlanta and the 28th largest school district in the country. But many science educators say it is part of a national campaign to teach creationist ideas alongside evolution for the sake of "balance."

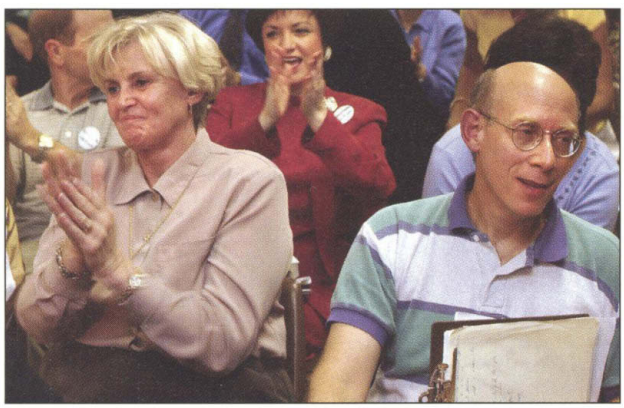
The new policy, approved 27 September by a 7–0 vote, asserts that "discussion of disputed views of academic subjects is a necessary element of providing a balanced education, including the study of the origin of the species." It goes on to say that the policy is intended "to foster critical thinking among students [and not] to restrict the teaching of evolution [or] to promote or require the teaching of creationism." It supersedes a 1995 policy stating that instruction relating to the origin of life should be conducted with "respect" for the "family teachings" of Cobb County citizens.

The vote was preceded by an intense publicity and lobbying blitz from scientists, including a letter from National Academy of Sciences president Bruce Alberts urging the academy's Georgia members to speak out against the measure. Scientists from most of the state's colleges and universities also submitted petitions. The Seattle-based Discovery Institute, creationism's main think tank, has been recirculating a year-old statement signed by 130 scientists nationwide, as well as a new one signed by 28 Georgia scientists, expressing "skepticism toward the Darwinian claim that 'random mutation and natural selection account for the complexity of life.' "

It's not clear what the practical impact of the new policy will be. School board chairperson Curtis Johnston Jr. could not be reached for comment, but last month he told the *Atlanta Journal-Constitution* that the board proposed a revision to "clarify things" for teachers who are "nervous about what they can talk about." Cobb County's high school science supervisor George Stickel is even more opaque. Until school officials draw up regulations to implement the new policy, he says, "your guess is as good as mine" about how it will affect students. But he hopes that teachers will use the issue as "an educative moment."

Those who oppose the new policy see it as a signal to district parents who are sympathetic to creationism or "intelligent design." Ronald Matson, a biologist at Kennesaw State University in Marietta, says that the resolution "fails to discriminate between science and nonscience ways of knowing … [thus] opening the doors to those with a creationist view to demand equal time." Wes McCoy, a science teacher at North Cobb High School, says that many regard it as a "nod" to creationists, one that says, "even though we cannot teach it, we kind of wish we could."

The Supreme Court ruled in 1987 that creationism has no place in science classes; since then, evolution foes have taken the tack that students need to be informed of the "scientific" controversies surrounding evolution. Jeffrey Selman, a Cobb County parent who is challenging the board's textbook disclaimers as a violation of the constitutional separation of church and state, says that he plans to add the new policy to his



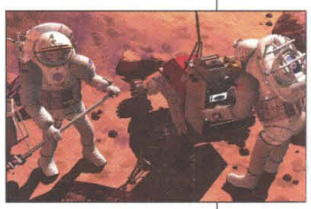
**Going critical.** Jeffrey Selman, who has sued the board for adding disclaimers to textbooks, refrains from joining applause for the board's latest attempt to provide a "balanced education."

CREDITS: (LEFT TO RIGHT) RICH ADDICKS; NASA

## ScienceScope

**Good Librations** Advocates for human space flight have bickered for decades—mostly among themselves—over whether people should return to the moon or go directly to Mars. Now some NASA officials are urging a middle path: Create a small human and advanced robotics outpost at the point where the gravity of Earth and the moon cancel each other out.

An outpost at that stable "libration point"—just 100,000 kilometers from the lunar surface—could serve as a "gateway" for robotic and eventually human missions to the moon and Mars, says Harley Thronson, NASA's chief of space science technology and co-author of a paper to be presented next week in Houston, Texas. More immediately, the outpost could fine-tune or fix instruments—such as a planned new telescope—that will hover just beyond Earth's orbit.



NASA is funding a $5 million study to flesh out future uses of such human and robotic platforms. An informal planning effort begun under the Clinton Administration has already borne fruit: It helped launch the space agency's push for 2003 funding for nuclear propulsion and electric technologies. Now, insiders predict that NASA's next budget request will include support for other new technologies, as a way to build up NASA's technical arsenal.

**Strike Three?** France is once again on the warpath against U.S. firm Myriad Genetics, based in Salt Lake City, Utah. The Institut Curie in Paris, along with other institutes from 12 European countries, is asking the European Patent Office (EPO) to overturn a third Myriad patent on the *BRCA1* gene, which is used to test for a predisposition to breast and ovarian cancer. Some of the same groups have already challenged two other related Myriad patents (*Science*, 14 September 2001, p. 1971); they say the claims are part of Myriad's plan for a monopoly on the tests.

EPO is unlikely to rule before 2005, says a spokesperson. Opponents of the patent feel they need help from the European Commission in Brussels. "Being numerous doesn't necessarily mean we will win," says Claude Huriet, Institut Curie's president. Myriad officials have consistently defended the patents as valid.

**Contributors: Pallava Bagla, Richard Stone, Andrew Lawler, Barbara Casassus**