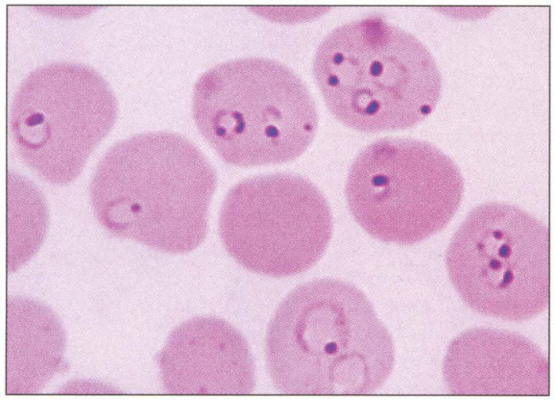
MALARIA RESEARCH

Parasite Genome Sequenced, Scrutinized

Plasmodium falciparum packs a powerful punch. The protozoan parasite causes malaria in hundreds of millions of people, most living in Africa. Thus far it has ducked every vaccine attempt and shaken off most of the drugs developed to knock out the disease. But now *P. falciparum*'s opponents have three new genome sequences in their corner, making them hopeful that they will put up a better fight in the next round. (See The Mosquito Genome, a special section that begins on page 77.)

This week, an almost complete DNA sequence of *P. falciparum*, as well as a draft of the genome sequence of a related *Plasmodium* species that infects rodents and is used to learn more about its human counterpart, appears in *Nature*. And on page 129 of this issue of *Science*, other researchers are reporting the DNA sequence of *Anopheles gambiae*, the mosquito that most efficiently transmits *P. falciparum* to humans in Africa. Together with the human genome sequence, researchers now have in hand the genetic blueprints for the parasite, its vector, and its victim. This "will provide the ability to take a holistic approach in understanding how the parasite interacts with the human host," says Alan Cowman, a molecular parasitologist at the Walter and Eliza Hall Institute of Medical Research in Melbourne, Australia. With that approach, researchers say, new antimalarial strategies should be possible.



Malarial menace. Researchers have sequenced the genome of *Plasmodium falciparum* (dark spots inside red blood cells).

CREDIT: CDC

Just as *P. falciparum* has shown no mercy in its long association with people, it also proved a tough opponent for researchers trying to decipher its 23-million-base genome. They encountered "surprisingly difficult problems," says David Roos, a malaria expert at the University of Pennsylvania in Philadelphia. Indeed, it took dozens of people from four organizations—the Sanger Centre in Hinxton, U.K. (now called the Wellcome Trust Sanger Institute), The Institute for Genomic Research (TIGR) in Rockville, Maryland, the Naval Medical Research Center (NMRC) in Silver Spring, Maryland, and the Stanford Genome Technology Center in California—to get the job done.

When the project began in 1996, the sequencers were immediately stymied by the parasite's unusually high proportion of adenine and thymine, two of the bases that make up the DNA code. The chemical nature of these bases hindered efforts to chop the DNA into large snippets that make wholesale sequencing and reassembling of each chromosome easier. Early on, the preponderance of adenine and thymine clogged up the computer programs designed to evaluate data quality and piece the DNA back together. And in another complication, the researchers were able to isolate the DNA for just 11 of the parasite's 14 chromosomes. They eventually treated the three remaining chromosomes as a "blob" that proved even more difficult to decipher.

Chromosomes 2 and 3 were finished in 1998, and now another eight are complete, with four more—6, 7, 8, and 13—in the final stages. Even the incomplete code provided ammunition for malaria fighters. Now, with the sequence essentially known, as well as a draft of the *P. yoelii* genome sequence by a team led by TIGR, whole-genome analyses are providing a "much better appreciation for the complexity [of *P. falciparum*] and also its Achilles' heels," says NMRC molecular biologist Daniel Carucci, a physician who helped coordinate the project.

One Achilles' heel could be an odd subcellular component, called the apicoplast, found only in *Plasmodium* and its relatives. It seems to be derived from a chloroplast that had been appropriated from algae consumed by the parasite's ancestor. Ever since the apicoplast's discovery by Roos in 1997, malaria experts have been eyeing its proteins as possible drug targets. Researchers knew that the apicoplast was involved in lipid metabolism, "but we didn't know how," says Roos.

Now, thanks to the genome sequence, "we've been able to put together a complete metabolic pathway," he says, and show that about 12% of all the parasite's proteins, once made, head for the apicoplast. This structure also appears to be the only place where the parasite makes the fatty acids it needs to survive. Thus, Carucci explains, "if one [could] target this biochemical pathway, one would have a drug-target strategy that would be highly effective against the parasite and would not affect humans."

Malcolm Gardner and his colleagues at

ScienceScope

Caught Plagiarizing Indian physicists are demanding an inquiry into a case of plagiarism involving a paper co-authored by the vice chancellor of a prominent regional university. Balwant Singh Rajput, a particle physicist and vice chancellor of Kumaun University in the Himalayan state of Uttaranchal, has acknowledged that he failed to properly oversee a student—S. C. Joshi—who has admitted that he plagiarized a 6-year-old paper (www.geocities.com/physics_plagiarism). Joshi's tainted paper was published in the March 2002 issue of *Europhysics Letters*; it borrowed extensively from an article on the properties of black holes published in *Physical Review D* by Renata Kallosh of Stanford University.

Rajput says that Joshi never told him about the paper and that he has asked the journal editor to delete his name from it. An apologetic Joshi admits to having erred but says that it is the university's "usual practice" to credit superiors as co-authors.

The Society for Scientific Values, an independent think tank in New Delhi that monitors scientific misconduct, is asking authorities to investigate. Indira Nath, an immunologist and past secretary of the group, says Rajput's response "is too flimsy."

North Korean Glasnost? Western experts might soon get a glimpse of North Korea's shadowy network of defense research labs. Speaking at a nuclear security meeting in London this week, Representative Curt Weldon (R–PA), a senior member of the House Armed Services Committee, revealed that U.S. and North Korean officials are discussing how to redirect North Korean weapons scientists to peaceful, commercially oriented projects. The potential U.S.-sponsored effort could be modeled on the Department of Energy's Initiatives for Proliferation Prevention program, which now retrains defense scientists in the former Soviet Union.

The possibility of working with North Korean researchers is intriguing, say some scientists. The nation's science community is a "black box," says Abel Julio Gonzalez, a nonproliferation specialist at the International Atomic Energy Agency in Vienna, Austria. Weldon says he hopes to lead a congressional delegation to Pyongyang later this year.

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."

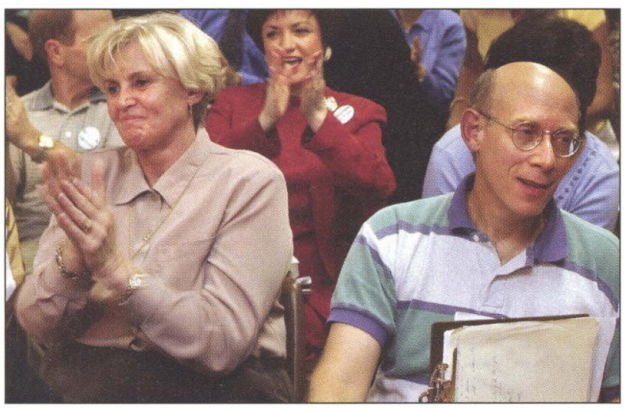
The new policy, approved 27 September by a 7–0 vote, asserts that "discussion of disputed views of academic subjects is a necessary element of providing a balanced education, including the study of the origin of the species." It goes on to say that the policy is intended "to foster critical thinking 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



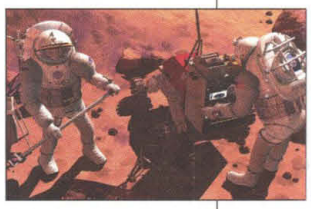
Going critical. Jeffrey Selman, who has sued the board for adding disclaimers to textbooks, refrains from joining applause for the board's latest attempt to provide a "balanced education."

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