Fine with them. Human reproductive cloning advocates (left to right) Panos Zavos, Avi Ben Abraham, and Brigitte Boisselier won't be slowed by any U.N. resolutions this year.

several countries, including the United Kingdom, Singapore, and the Netherlands. Indeed, Scottish researcher Ian Wilmut, one of the creators of Dolly the cloned sheep, has said he plans to proceed with human cloning experiments with the goal of producing ES cell lines (*Science*, 4 October, p. 37).

The United States has no national legislation governing cloning, and several privately funded U.S. groups are proceeding with research cloning experiments. A similar disagreement in the U.S. Senate earlier this year foiled efforts to pass either a ban on reproductive cloning or a ban on all human cloning research (*Science*, 21 June, p. 2117). However, that situation might change now that Republicans have regained control of the Senate (see p. 1313). **–GRETCHEN VOGEL**

TROPICAL DISEASE

Misspelled Gene Tames Malaria

Malaria kills about a million people each year. But even in countries where the disease takes a heavy toll, the risk is not the same for everyone: Some people have a remarkable ability to suppress the malaria parasite's debilitating effects. Now, researchers have tied that resistance to a subtle variation in a single gene that can cut by nearly 90% the risk that an infection will become life-threatening.

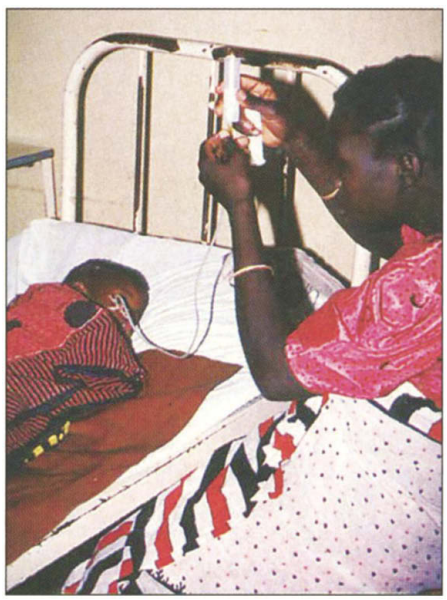
The gene mutation causes people to ratchet up production of nitric oxide (NO), a gas that plays a role in a diverse range of physiological processes. Previous studies with rodents had found that NO can protect against malaria and a variety of other diseases, says microbiologist Ferric Fang of the University of Washington, Seattle. But the new study provides some of the best evidence to date that NO plays an important role in disease protection in humans, says Fang, who calls the study a "significant contribution."

The study was led by hematologist Brice Weinberg of the Veterans Affairs and Duke University Medical Centers in Durham, North Carolina. Weinberg's team sampled DNA from 185 Tanzanian children—47 of whom had been infected by the malaria parasite but remained healthy, and 138 who were sick with the disease. The researchers looked for mutations in and around the gene that encodes inducible nitric oxide synthase (*NOS2*), the enzyme that makes NO. They found that a single mutation in which a cytosine replaces a thymine in the *NOS2* gene's promoter region—its DNA on-switch—turned up more often in the healthy children. Children with the mutation had higher than normal NO levels in their blood and urine, suggesting that the gas could be protecting them.

The team then analyzed DNA samples and clinical data from a 5-year study of 1106 children in Kenya run by the Centers for Disease Control and Prevention. They again found that the mutation in the *NOS2* promoter had a protective effect. "Overall, the mutation lowered the risk of severe malaria by 88% in Tanzania and 75% in Kenya," says molecular geneticist Maurine Hobbs of the University of Utah in Salt Lake City, a co-author of the study, which appears in the 9 November issue of *The Lancet*.

This isn't the first mutation thought to protect against malaria, but "this study is one of the most compelling because they have demonstrated a connection between genetics, NO production, and clinical status," says clinical immunologist Brian Greenwood of the London School of Hygiene & Tropical Medicine in the United Kingdom. "The story told by this study is very appealing and logical."

Exactly how NO protects is still unclear, however. Researchers have hypothesized



Unlucky. A chance twist in the genetic code can protect against malaria.

CREDITS: (TOP TO BOTTOM) STEPHEN J. BOITANO/AP; THE WELLCOME TRUST; ANDY CRUMP/WHO/TDR

ScienceScope

Finally Wellcome The United Kingdom's premier genomics lab is set to grow. After 5 years of intense negotiations, local authorities have approved a plan by the Wellcome Trust to add 27,000 square meters of academic and commercial space to its Genome Campus in Hinxton, near Cambridge. The trust's initial plan for a larger expansion was rejected in 1997.

The Genome Campus is already home to the Sanger Institute, a prominent player in the Human Genome Project. Next week, workers will break ground on an additional 10,000 square meters of labs, along with mouse and computing facilities. Future additions will include an Innovation Centre for start-up companies and additional space for firms growing as a result of progress in related fields. The project is expected to be finished by 2007, at a cost of $150 million.

All Together Now Look for the Bush Administration to kick off a math and science education initiative next month with a high-profile gathering at the Smithsonian Institution.

The initiative, part of the "No Child Left Behind" presidential campaign, is intended to meld the myriad federal and private-sector efforts aimed at improving student achievement, teacher preparation, and community involvement in math and science at the elementary and secondary school levels. "We're going to start off with what we know works in math because, frankly, we know so little about how children learn science," says Susan Sclafani, counselor to Education Secretary Rodney Paige.

Sclafani's office will spearhead the effort, which she hopes will attract professional societies and high-tech companies as well as other federal agencies funding research on teaching and learning. If so, the initiative has a ways to go. "It's news to me," says one federal official about next month's get-together, echoing the comments of an executive at one association long involved in the subject. "But it sounds like a good idea."

Contributors: Govert Schilling, Jeffrey Mervis, Adam Bostanci

that high levels of NO might kill *Plasmodium falciparum* parasites in the liver, where the parasite first gets a foothold and begins to multiply. But somewhat surprisingly, the new mutation mitigates the severity of the disease without reducing the number of parasites in the bloodstream: Children with the mutation had parasite levels comparable to those of children without it.

NO might play a variety of other protective roles. Animal experiments have shown that NO reduces expression of adhesion molecules on cell surfaces, which prevents infected red blood cells from sticking to blood vessel walls and causing the restricted blood flow associated with deadly cerebral malaria. NO also limits production of cytokines—proteins that stimulate immune responses and might contribute to tissue damage in malaria.

Still, although researchers welcome the new finding as a basic insight into human immune defenses, they say it probably won't lead to immediate improvements in malaria treatment. "NO won't be the panacea for malaria; it's just one piece of the puzzle," says study co-author Nicholas Anstey, an infectious disease specialist at the Menzies School of Health Research in Darwin, Australia.

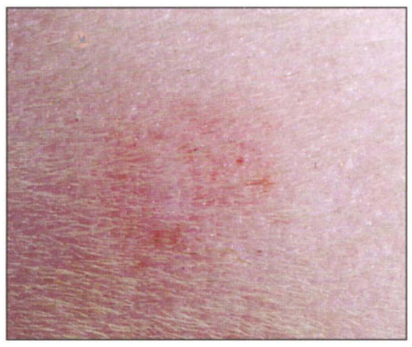
–DEBORAH HILL

Deborah Hill is a science writer in Idaho Falls, Idaho.

IMMUNOLOGY

Antibodies Kill by Producing Ozone

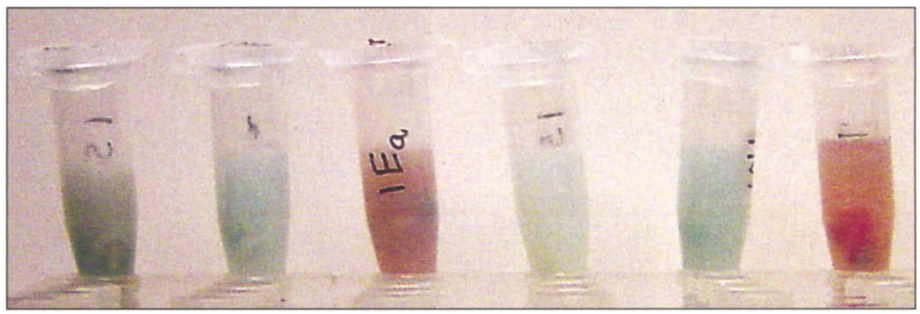
Antibodies have long been known as the immune system's reconnaissance forces: scouts that seek out foreign antigens and summon up the big guns to wipe them out. But evidence now indicates that antibodies may also be killers in their own right.



In work published online today by *Science* (www.sciencemag.org/cgi/content/abstract/1077642), Paul Wentworth, Richard Lerner, and their colleagues at the Scripps Research Institute in La Jolla, California, report evidence that antibodies, when provided with appropriate starting materials, catalyze the production of highly active forms of oxygen, likely including ozone. This can not only kill bacterial pathogens directly but might also promote inflammatory and other immune responses. The work puts antibodies in a whole new light, says immunologist Carl Nathan of the Weill Cornell Medical Center in New York City. Because they weren't supposed to have such direct effects, "it will be hard to think of antibodies in the same way [as before]."

Hints of antibodies' lethal nature began surfacing about 2 years ago. Thanks partly to early work from Lerner's lab, antibodies are known to have catalytic activities. And Wentworth, Lerner, and their colleagues showed that when they are supplied with a reactive form of oxygen known as singlet oxygen, antibodies can generate hydrogen peroxide from water (*Science*, 7 September 2001, pp. 1749 and 1806). Hydrogen peroxide is a well-known bacteria killer; it's often used as an antiseptic. But because the Scripps team generated singlet oxygen in a highly nonphysiological way and didn't show directly that bacteria die from the hydrogen peroxide produced, "people said, 'What does this have to do with biology?' " recalls Lerner.

The new work addresses that issue and suggests a surprising new twist to antibodies' modus operandi. First, the Scripps researchers demonstrated that antibodies can kill bacteria without help from any other immune system forces. In one set of test tube experiments, they showed that antibodies, in conjunction with a singlet oxygen-generating system that could not kill bacteria on its own, wiped out more than 95% of *Escherichia coli* bacteria.



Ozone indicator. In the Arthus reaction, skin becomes inflamed at the site of antibody injection (*lower left*). Biopsies of such inflamed sites (tubes 3 and 6 from left), but not of normal skin (tubes 1, 2, 4, and 5), contain ozone as indicated by their reaction with the dye indigo carmine.

But the experiments turned up a puzzle: The antibodies weren't generating enough hydrogen peroxide to account for all the cell killing. That suggested that some other, more powerful bactericidal agent was also being formed.

Evidence from a series of experiments pointed to ozone as the most likely suspect. For example, the researchers found that antibodies provided with singlet oxygen produce an oxidizing agent that splits the dye indigo carmine, just as ozone does. Ozone hadn't previously been implicated in immune responses. "We're now in brand-new territory," Nathan says.

The work still left one big question hanging: Is there a plausible physiological source of singlet oxygen? (The Scripps team had again used a nonphysiological source.) Wentworth, Lerner, and their colleagues believe they have an answer. They report evidence that immune cells called neutrophils, which help destroy invading bacteria, can generate singlet oxygen.

In addition to showing that antibodies can produce hydrogen peroxide and ozone, the team has linked this activity to an inflammatory response called the Arthus reaction in living rats. In this system, inflammation is induced by injecting an antigen—the researchers used bovine serum albumin—into the animals' bloodstream and simultaneously injecting antibodies to it into their skin; the skin becomes inflamed at the injection sites. Analysis of the inflamed skin tissue showed that it, too, contained an oxidizing agent that behaves just like ozone.

Chemist Chris Foote of the University of California, Los Angeles, describes the work as "amazing." It shows, he says, that "there's a powerful oxidant there that no one suspected." He cautions, however, that the current experiments don't totally prove that the oxidant is ozone. Lerner concedes the point but says that other work now under way, including studies of atherosclerosis, will provide definitive proof.

Meanwhile, Nathan suggests that antibody-mediated ozone production could contribute to a variety of inflammatory conditions, including rheumatoid arthritis and inflammatory bowel disease. He notes, for example, that the inflamed joints of arthritis patients contain something called rheumatoid factor, which is actually an antibody directed against other antibodies, as well as neutrophils. If this leads to antibody-catalyzed production of hydrogen peroxide and ozone, the result could be a double whammy, causing damage to the joint directly and also indirectly by enhancing the activity of neutrophil products. More work will be needed to test these ideas, but antibodies now appear to have more tricks up their sleeves than anyone expected.

–JEAN MARX

CREDITS: P. WENTWORTH ET AL.