He and others pointed out that it is difficult for viral particles in blood to penetrate the nuclei of sperm, although they may more easily enter seminal fluid. And he noted that risks can be reduced easily by requiring subjects to use barrier contraception methods until all traces of the vector have disappeared. Other officials commented privately after the meeting that the Food and Drug Administration (FDA), which ordered the experiment to be put on hold, seems ready now to let it resume. But FDA almost certainly will ask the investigators to run more tests of germ line effects.

Kay interpreted the review as "reasonably favorable." So did Grossbard. But Grossbard noted a potentially big logistical problem. The first volunteer was given a low dose of the vector, and future volunteers who receive higher doses may take longer to clear the vector. If so, and if the FDA continues to insist that each patient be free of vector DNA for 3 months before the next is treated, Grossbard estimated that the time to complete a basic safety trial "may approach or exceed 5 years." He suggested that this was a heavy price to pay for "a very small theoretical risk."

Presenting FDA's concerns, agency scientist Stephanie Simek agreed that the risk was low but insisted that it is real. She also pointed out that the risk had not been flagged by preclinical animal studies and warned that there's a possibility that "all treated subjects" may test positive, at least initially. She then asked a provocative question: "Does the potential benefit of a [gene therapy] product outweigh the potential risk of developing a transgenic human?"

The most likely compromise, according to one observer who did not want to speak for attribution, may be to have the hemophilia B trial go forward as planned, but with a requirement that investigators collect additional sperm samples and analyze them "in a more timely fashion" than in the past.

–ELIOT MARSHALL

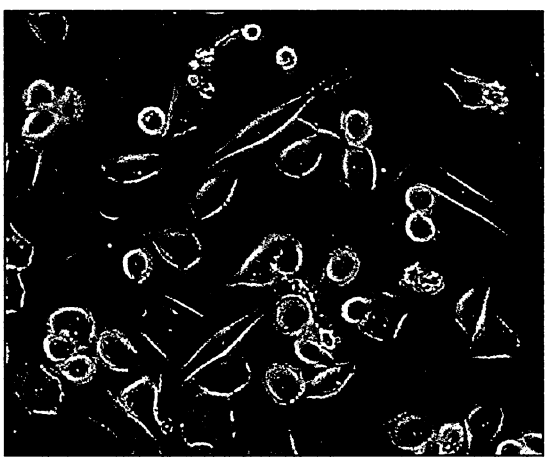
CARCINOGENIC BACTERIA

Cracking Gut Bugs' Cell-Skewing Strategy

Most of the bacteria that cause disease were tracked down long ago, but for decades one microbe got away with murder. Discovered in 1982, *Helicobacter pylori* infects two-thirds of the world's population; it causes ulcers and cancer that kill 7 million people each year (*Science*, 21 May 1999, p. 1328). Researchers have learned a lot about how the microbe digs into the wall of the stomach to cause ulcers, but they knew little about how the bug makes cells malignant—until now.

In a study published online by *Science* this week (www.sciencexpress.org), molecular oncologist Masanori Hatakeyama of Hokkaido University in Sapporo, Japan, and his colleagues have shown exactly how one of the bacterium's proteins hijacks a signaling pathway in stomach cells, pushing them to change shape and allowing them to move—an early step toward turning cells cancerous. "It's a major step forward," says cellular microbiologist Brett Finlay of the University of British Columbia in Vancouver.

H. pylori infections are about half as carcinogenic as smoking cigarettes: People infected with the bacterium are two to six times as likely as uninfected people to develop either gastric cancer, which is derived from cells in the lining of the stomach, or mucosal-associated lymphoid tissue (MALT) lymphoma, which is derived from immune cells that move to the stomach to battle the *H. pylori* infection. Researchers knew that when virulent strains of *H. pylori* infect the stomach lining, they cause stomach cells to elongate until they resemble hummingbird beaks. And virulent, but not benign, strains of the microbe inject a protein called CagA into the stomach cells, which then tag CagA with phosphate groups. Because tumor-causing viruses trigger cancer in part by spurring cells to add or remove phosphates from proteins, "I was wondering if such things also happen in bacterial infection," Hatakeyama says.



CREDIT: M. HATAKEYAMA

Haywire. By commandeering a signaling pathway, *H. pylori* causes cells to malform.

To find out, the researchers first made an educated guess about which human protein CagA interacts with once inside stomach cells. Others had shown that human cells treated with hepatocyte growth factor (HGF) also resemble a hummingbird beak and that HGF-treated cells tag a receptor protein with phosphates, much as occurs with CagA. The HGF receptor alters a signaling protein called SHP-2. Suspecting that this might be one more similarity between HGF and CagA, "we decided to examine if SHP-2 was involved with *Helicobacter*-induced morphological change," Hatakeyama says.

It was. Antibodies to CagA fished out SHP-2 and vice versa, suggesting that the two proteins team up inside the cell. What's more, cells infected with a mutated version of CagA that didn't bind SHP-2 no longer elongated into their characteristic shape.

Next, Hatakeyama's team asked whether CagA boosts SHP-2's ability to pass on signals. Ordinarily, cells send messages using a molecular bucket brigade. In HGF-induced signaling, SHP-2 is one of the recruits; it joins the HGF receptor and clips phosphates off other proteins. SHP-2 and CagA appear to form a similar complex: They team up only when CagA is phosphorylated, and SHP-2 clips phosphates from other proteins only when joined to CagA. That means CagA plugs into the normal cellular signaling system, Hatakeyama says, leading the cell astray and making it vulnerable to becoming cancerous.

Bacteriologist Stanley Falkow of Stanford University says the work "speaks to what must be an important event that predisposes [cells] to malignancy." But cell biologist Michael Naumann of the Max Planck Institute for Infection Biology in Berlin cautions that other signaling molecules probably help pass along the signal to elongate. Indeed, in work in press in *Molecular Microbiology*, microbiologists Rino Rappuoli, Antonello Covacci, and their colleagues at Chiron Corp. in Siena, Italy, identified two enzymes, c-Src and Lyn, that tag CagA with phosphates inside stomach cells. Many of the molecular links between *H. pylori* and cancer still remain to be discovered, Falkow emphasizes—but *H. pylori* investigators are closing in on their quarry.

–DAN FERBER

INDIA

New Report Tackles Wealth of Problems

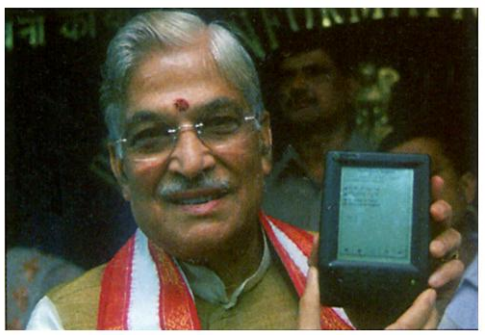
NEW DELHI—The Indian government last week produced a harsh assessment of the state of science as part of a new draft statement on what's needed to help the country compete in a global economy.

"There is an urgent need to revitalize the scientific enterprise," declares the government's long-awaited draft of the Millennium Science and Technology Policy,* the first document of its kind since the country's independence in 1947. But its analysis should

* www.insa-india.org/newsdesk/sc-tc-pl.htm

come as no surprise to the Indian scientific community. "The situation is very alarming," says Goverdhan Mehta, an organic chemist and president of the Indian National Science Academy. "Science in India is not in a healthy condition."

The document affirms the government's role in supporting research and repeats its pledge to more than double spending, to 2% of the country's gross national product, over the next 5 years. It also highlights 12 areas where the government needs to focus its attention, from rebuilding a tattered academic system and rekindling public interest in science to speeding the transfer of technology from the laboratory to the market. Among the suggested mechanisms are creating bodies to fund basic science and foster innovation, and paying more attention to outside organizations that offer scientific and technical advice to the government. Another strategy would pour additional resources into 50 or more model universities and technical institutions.



Get connected. Science minister Murli Manohar Joshi holds the Indian-made Simputer, an inexpensive digital tool for the masses.

The draft statement stresses the importance of public understanding of science, with an emphasis on improved instruction from the primary grades through the undergraduate years. "We appear to have lost an entire generation of scientists," the document declares, "and strategic departments like space, defense, and atomic energy find it increasingly difficult to attract the best of human resources." It suggests that the government pay more attention to indigenous knowledge, covering everything from medicine to sustainable development. It also points to the need for better technologies to mitigate natural disasters, as well as stronger laws to protect intellectual property.

"A concerted plan of action is necessary to infuse dynamism into our science and technology policy," declares the policy, which grew out of a yearlong exercise led by science minister Murli Manohar Joshi. The document is expected to be submitted to Parliament after its approval by the Cabinet.

–PALLAVA BAGLA

CREDITS: (TOP TO BOTTOM) P. BAGLA; CHARLES HANLEY/AP

INFECTIOUS DISEASES

Bed Nets Prove Their Mettle Against Malaria

ATLANTA—Most scientists announce their results at conferences or in scholarly journals. But late last August a team of researchers presented new data at a celebration in the town of Asembo Bay in western Kenya, complete with food, drinks, dancing, singing, and boat races on Lake Victoria. The reason, say the researchers from the Kenya Medical Research Institute in Nairobi and the U.S. Centers for Disease Control and Prevention (CDC) in Atlanta, is that they wanted to tell the people who had participated in their study the good news first.

Last month, the researchers presented their results to their colleagues, during a meeting* in downtown Atlanta. Although the occasion was far more subdued, the talk engendered almost as much excitement. The 2-year study showed that the use of insecticide-impregnated bed nets saves many lives, even in areas with intense malaria transmission year-round. A set of 18 papers about the trial will appear in the *American Journal of Tropical Medicine and Hygiene* next spring.

The study provides the missing piece in a series of trials. Previous studies—held in Ghana, The Gambia, Burkina Faso, and coastal Kenya—had shown that bed nets could save the lives of children, malaria's main victims. But none of them took place in areas with extremely high, year-round transmission, such as western Kenya, where a person receives hundreds of bites from infected mosquitoes each year. Would it even be worth trying to distribute bed nets in equatorial Africa? "We were quite skeptical ourselves," says Bernard Nahlen, one of the investigators.

Under wraps. Bed nets work—even in places with intense malaria transmission.

The new study puts that question to rest, says Christian Lengeler of the Swiss Tropical Institute in Basel. "We can now make a blanket recommendation: Everywhere there is malaria, you should use treated bed nets," he says. The study also shows that a remarkably low-tech and relatively cheap intervention can have more impact than many snazzy scientific advances. "About $10 million has been sunk into showing that bed nets work," says Lengeler. "That's peanuts compared to what you put into a new vaccine or new drugs."

For the trial, researchers randomly divided each of 221 villages and their combined 125,000 inhabitants into two groups. One group received enough bed nets to cover each and every sleeping space, and the nets were treated with permethrin over the next 2 years. The second group did not receive nets, although they were given them at the end of the trial. The use of nets reduced deaths among children under 1 year of age—when most of the mortality due to malaria occurs—by about 22%, according to the CDC's Penny Phillips-Howard.

The nets also reduced cases of placental malaria among pregnant women by about 23%, and 28% fewer had low-birth-weight babies. Bed nets even protected people who did not use them, as long as they were in the vicinity of people who did. The researchers believe this "herd effect" stems from a reduction in the number of infected mosquitoes—just like broad vaccine coverage can reduce the incidence of a disease by reducing the number of carriers, protecting even those who are not vaccinated.

The introduction of bed nets is already one of the pillars of Roll Back Malaria, an ambitious program to reduce malaria deaths worldwide by 50% from 2000 levels by 2010, spearheaded by the World Health Organization. At the moment, bed nets are just beginning to be introduced in many African countries, however, and opinions vary on how to speed their distribution. To a great extent, the market can take care of it, says Brian Greenwood of the London School of Hygiene and Tropical Medicine. Bed nets are increasingly popular in Africa, despite their $3 to $4 price tag. "Having 200 to 300 mosquitoes in your bedroom makes it go up on your priority list," Greenwood says. And commerce can distribute the nets into even the smallest villages, he adds—as it has done with Coca-Cola.

But that approach is of little use to the poorest 20% of the population who cannot afford a net—which is why some of the nets will have to be given out for free, says Lengeler. One way to boost coverage further would be to remove taxes and tariffs that many countries now charge on textile imports, including bed nets. According to Lengeler, "That's perhaps the single most important thing that needs to happen now."

–MARTIN ENSERINK

* 50th Annual Meeting of the American Society of Tropical Medicine and Hygiene. Atlanta, 11–15 November.