Bush. It also contains several hundred million dollars for improving science and math teaching as part of a successor to the Education Department's Eisenhower program.

A report accompanying the bill urges NIH to move ahead quickly to fund controversial research on human stem cells derived from embryos and adults. In doing so, it sidesteps a potentially bruising fight over existing language that instructs NIH not to fund research involving the destruction of human embryos by explaining that it does not conflict with recent White House rules restricting federally funded researchers to using stem cell lines created before 9 August (*Science*, 17 August, p. 1242). "The language and logic are tortured, but the message is clear: Get on with stem cell research," says one aide to a House Democrat.

Panel members also rejected a White House effort to trim CDC by adding more than $380 million to the Administration's request. That amount would boost CDC's budget by 5.5%, to $4 billion. In particular, lawmakers restored nearly $150 million to the CDC's health promotion budget, which sponsors education and advertising campaigns aimed at preventing disease.

The panel also added $50 million to a small increase requested by the White House for antibioterrorism programs within the Department of Health and Human Services, for an overall 25% boost to $300 million. Associated research and public preparedness efforts are expected to get more funds from the $40 billion emergency spending package that Congress approved in the wake of the 11 September terrorist attacks.

The full House is expected to sign its version of the NIH spending bill within a few weeks, shifting attention to the Senate. Biomedical researchers were hoping for even better news as early as this week from the Senate spending panel that oversees NIH, because its leaders, Senators Tom Harkin (D–IA) and Arlen Specter (R–PA), have already promised a $3.4 billion increase. Differences between the House and Senate bills will be worked out by negotiators from each body, perhaps before the end of the month.

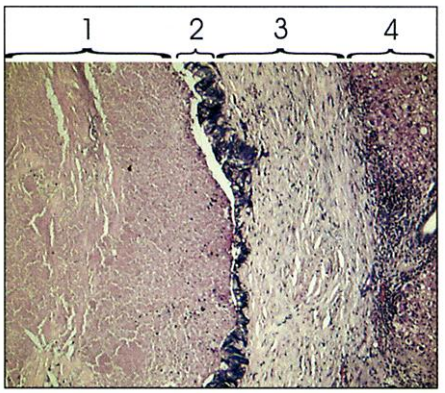
–DAVID MALAKOFF

CANCER RESEARCH

New Insights Into Metastasis

The metastatic cell is a tumor's stealth invader: able to slip into foreign territory, set up a beachhead, and grow until it kills. Indeed, it's the metastases, not the primary cancer, that usually defeat oncologists' efforts to cure their patients. Results published online today by *Science* (www.sciencexpress.org) now pinpoint a genetic change that may help colon cancer cells metastasize to the liver—information that could help researchers develop drugs to stanch the invasion.

The work, which comes from Kenneth Kinzler, Bert Vogelstein, and their colleagues at the Johns Hopkins Medical Institutions in Baltimore, Maryland, shows that a tyrosine phosphatase enzyme called PRL-3 is expressed at higher levels in colon cancer cells that have metastasized to the liver than in nonmetastatic colon tumors and normal colon epithelial cells. In at least some cases, this was because of a genetic change, an amplification of the *PRL-3* gene. The finding suggests that an excess of the enzyme, which may normally help control cellular activities, somehow fosters the spread of colon cancer to the liver, its principal site of metastasis.



Mixed bag. In addition to living cancer cells (2), this liver metastasis contains dead and dying cancer cells (1) and a capsule of connective tissue (3), all surrounded by liver and inflammatory cells (4).

Although the Johns Hopkins workers do not yet know how *PRL-3* might spur colon cancer metastasis, other researchers are already enthusiastic. They note that although many gene changes have been tied to the early stages of cancer development, few have been linked to metastasis. There's "still remarkably little known about the molecular genetics and signaling pathways responsible for metastasis … and that's the most lethal aspect of cancer," says Jeffrey Trent of the National Human Genome Research Institute in Bethesda, Maryland. The *PRL-3* discovery may provide an entrée to tracing one of those pathways, Trent and others say.

"Very exciting," is how cancer biologist Lance Liotta of the National Cancer Institute, also in Bethesda, describes the finding. Not only could the enzyme provide a good target for chemotherapeutic drugs, but it may also provide a molecular marker to help clinicians assess tumor aggressiveness.

The Johns Hopkins team looked for the molecular changes underlying colon cancer metastasis by using a technique called serial

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ScienceScope

EPA Science Bill Moving A plan to beef up science at the Environmental Protection Agency (EPA) is wending its way through Congress. Last week, the House Science Committee approved HR 64, which would direct the agency to appoint a new deputy administrator for science and technology to oversee all EPA research (*Science*, 21 July 2000, p. 371). The bill would also extend to 5 years the term of the assistant administrator of EPA's Office of Research and Development. (The term is currently undefined.)

The bill's sponsor, Representative Vernon Ehlers (R–MI), hopes for a vote on the House floor before Congress recesses this fall. Eventually he wants to merge his proposal with a companion Senate bill sponsored by Senator George V. Voinovich (R–OH). EPA has not yet officially weighed in on the legislation, but agency officials have reportedly expressed some concerns. Ehlers says he doesn't see that as an obstacle, because he is hearing "favorable signals from the White House."

Is Proximity Power? Physicist John Marburger (right), President George W. Bush's pick to be his science adviser and head of the White House Office of Science and Technology Policy (OSTP), had an easy confirmation hearing this week before a Senate committee. And science lobbyists predict that his nomination will sail through the full Senate by the end of the month. But once officially in place, Marburger may find his office arrangements in flux.

The Secret Service last week confirmed that, due to security concerns, OSTP staff have been moved out of their longtime offices in the Old Executive Office Building next to the White House and into offices outside the White House fence a few blocks away. The ouster apparently is part of a plan to make workers less vulnerable to truck bombs.

Marburger will reportedly retain a workspace near the corridors of power and told senators that he will have access to the president. But lower level OSTP staffers have heard that their transfer could be permanent. The separation, says one former OSTP staffer, will make it harder for science policy advocates to "cultivate the kind of water-cooler contacts that can make a big difference in getting your voice heard in policy debates."

analysis of gene expression (SAGE). They developed the system about 6 years ago for performing wholesale analysis of the genes expressed in cells (*Science*, 20 October 1995, p. 484). In this study, they wanted to compare levels of gene expression in colon cancers that had metastasized to the liver with those in primary colon tumors and normal colon cells. But the researchers' original efforts ran into trouble. "Tumors are composed of lots of different cell types, and most of the genes expressed at different levels were actually coming from nontumor cells," Vogelstein says.

The team had to painstakingly separate the cancer cells from all the other cell types in their tumor samples before comparing gene expression patterns. But this, says metastasis researcher Isaiah Fidler of the M. D. Anderson Cancer Center in Houston, Texas, is one of the strengths of the work: "They did it the right way, comparing [isolated] metastatic cells with primary tumor cells."

This analysis identified 144 genes expressed at higher levels in the metastatic tumor cells and 79 expressed at lower levels. The researchers decided to focus on *PRL-3*, Vogelstein says, because it was up-regulated in all the metastases they looked at—"its consistency was striking," he notes—and because its structure suggests that it is a tyrosine phosphatase.

These enzymes, which remove phosphate groups from the amino acid tyrosine, are involved in regulating cell activities. Not much is known about the function of PRL-3, which was identified just 3 years ago, but there are indications that it and its relatives, PRL-1 and -2, foster cell growth. Further work by the Johns Hopkins team confirmed that PRL-3 levels reflect a cell's menace. Its expression increased from little or none in normal colon epithelia to intermediate in advanced but nonmetastatic primary tumors to high in the metastases. But perhaps the best evidence that the enzyme is involved in metastasis was the finding that extra copies of the gene were present in three of 12 metastases examined. Such gene amplifications were unstable and tend to be lost, Vogelstein says, unless they provide some selective advantage.

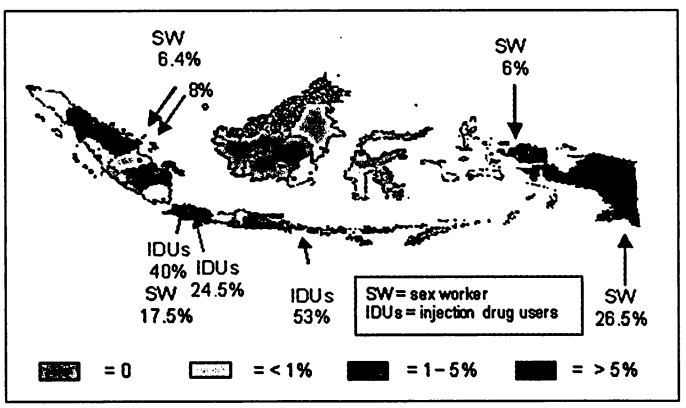
What that advantage might be, and how it might contribute to colon cancer metastasis, is not yet known. As Fidler points out, metastasis is complex, involving some 10 steps from the time a metastatic cell escapes the primary tumor until it settles down in a site where it can grow. Researchers will want to know where *PRL-3* comes into play and whether it's involved in the metastasis of other cancers as well. Given that cancer cells succeed all too often in metastasizing, any clues to how they do that are welcome.

–JEAN MARX

EPIDEMIOLOGY

HIV Gains Foothold in Key Asian Groups

A few years ago, Indonesia was scarcely a blip on the radar screens of epidemiologists who track the AIDS epidemic. Now, it's sending a strong warning signal. A new report that analyzes the spread of HIV and AIDS through Asia and the Pacific says that Indonesia, the world's fourth most populous nation, has an "exploding" rate of new infections among injection drug users, as well as "steep rises" among sex workers. And the authors stress that what's happening in Indonesia is being repeated in several other Asian countries. "We have new epidemics breaking out after many years of silence," says Bernhard Schwartländer, an epidemiologist at the Joint United Nations Programme on HIV/AIDS (UNAIDS), which helped finance the report.



Warning signals. HIV prevalence among sex workers and injection drug users in Indonesia, 1999–2000.

The 33-page analysis, written by Modeling the AIDS Pandemic (MAP), an international network of epidemiologists, public health experts, and modelers, notes that China and Vietnam are already beginning to see a dramatic spread of the virus through sex workers and injection drug users. And the authors urge the leaders of Bangladesh and the Philippines—two countries that still have strikingly low levels of HIV—to learn from the problems their neighbors are facing. "No society is immune," says Karen Stanecki, an epidemiologist at the U.S. Census Bureau who chairs MAP.

The report doesn't offer estimates of national HIV prevalence, because the authors contend that aggregate numbers can be misleading in this part of the world. As the report states, "national figures are meaningless in huge countries such as China, India, and Indonesia, where some states and provinces have more inhabitants than most nations of the world." Instead, the authors argue that what is happening at the local level offers "a more realistic basis for assessing the future course of the region's epidemics."

Much of the report analyzes how HIV gets a foothold in different populations. It notes that in Asia, injection drug users, sex workers, and migrant laborers often provide the early connections.

Take Indonesia, for example. In 1999, UNAIDS estimated that only 0.05% of Indonesia's population was infected. But surveillance data from 1999–2000 show that as many as 53% of injection drug users in some Indonesian provinces are now HIV-positive (see map). Until recently, the report says, "the very phenomenon of drug injection was little known" in Indonesia, but injection drug users are now the epicenter of an HIV outbreak that could become widespread. Although some AIDS researchers have contended that injection drug users represent a "self-contained" epidemic, the MAP report says that data from Indonesia suggest that many drug injectors are likely to infect sex workers—who now have infection rates as high as 26.5%—and other sex partners.

The same is happening in Vietnam. HIV prevalence among injection drug users in Vietnam tops 60% in some cities, the report says, and surveys have found that more than 20% of drug users bought sex in the past year—and most did not use condoms. Since 1994, infection rates among sex workers have jumped from 0.5% to 3.5%.

A similar confluence of factors has begun to accelerate the spread of HIV through many of Asia's largest countries. In China, HIV at first was confined largely to injection drug users and people who donated blood in clinics where needles were contaminated. Now the MAP report warns of "rapid rises" in infection rates among sex workers, who rarely use condoms. "As millions of men frequent sex workers every year, it is inevitable that HIV infection [rates] among these men will rise and that the fatal virus will eventually get passed on to their wives and regular girlfriends," the report predicts.

India has an estimated 3.9 million HIV-infected people, more than any other country in the region. Although the prevalence of HIV is still low compared with most of sub-Saharan Africa, states that attract large numbers of migrant workers have dramatically higher infection rates, the report notes. With

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