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.

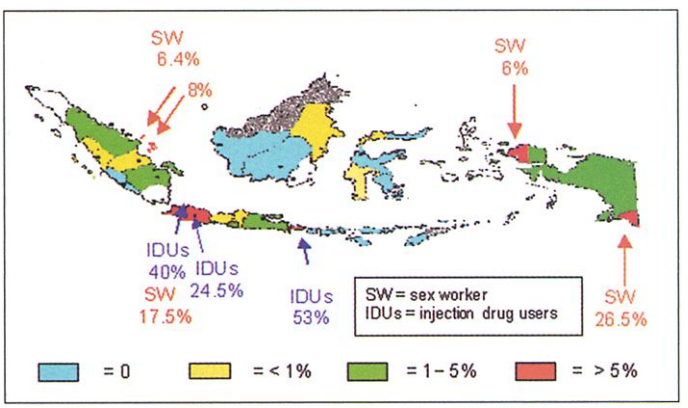
What that advantage might be, and how it might contribute to colon cancer metastasis, is not yet known. As Fidler points out, metastasis is complex, involving some 10 steps from the time a metastatic cell escapes the primary tumor until it settles down in a site where it can grow. Researchers will want 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

CREDIT: MAP

"disturbing regularity," the report states, migrant laborers who frequent sex workers take HIV back to their home states.

Chris Beyrer, an epidemiologist at Johns Hopkins University who specializes in the spread of HIV in Asia, says he applauds the MAP report for emphasizing the connection between injection drug use and sexual risk groups. "They've got it exactly right," says Beyrer, who in 1998 published *War in the Blood: Sex, Politics, and AIDS in Southeast Asia*.

The news, however, isn't all bad. "The MAP network doesn't want to be alarmist ... we see a window of opportunity," says Stanecki. The MAP report emphasizes, for example, that Thailand has used aggressive condom campaigns and education of high-risk groups to curb an epidemic that could have been much worse. According to MAP modelers, if Thailand had not intervened, 10% to 15% of its adult population might now be infected; the actual prevalence is 1% to 2%. That shows what can be accomplished—if the warning signals are heeded. **–JON COHEN**

MAGNETORECEPTION

Animal Magnetism Guides Migration

Animals are the ultimate commuters. From butterflies to newts, many creatures roam the neighborhood—or globe—and still manage to find their way home. In this issue, two studies reveal how sea turtles and mole rats tap a basic navigational tool: Earth's magnetic field.

Loggerhead sea turtles migrate around the North Atlantic, encountering different magnetic fields en route. A team led by marine biologist Kenneth Lohmann of the University of North Carolina (UNC), Chapel Hill, reports on page 364 that the turtles detect these fields, like boundaries, and use them to stay on course. The study suggests a strategy that may guide one of nature's longest migrations.

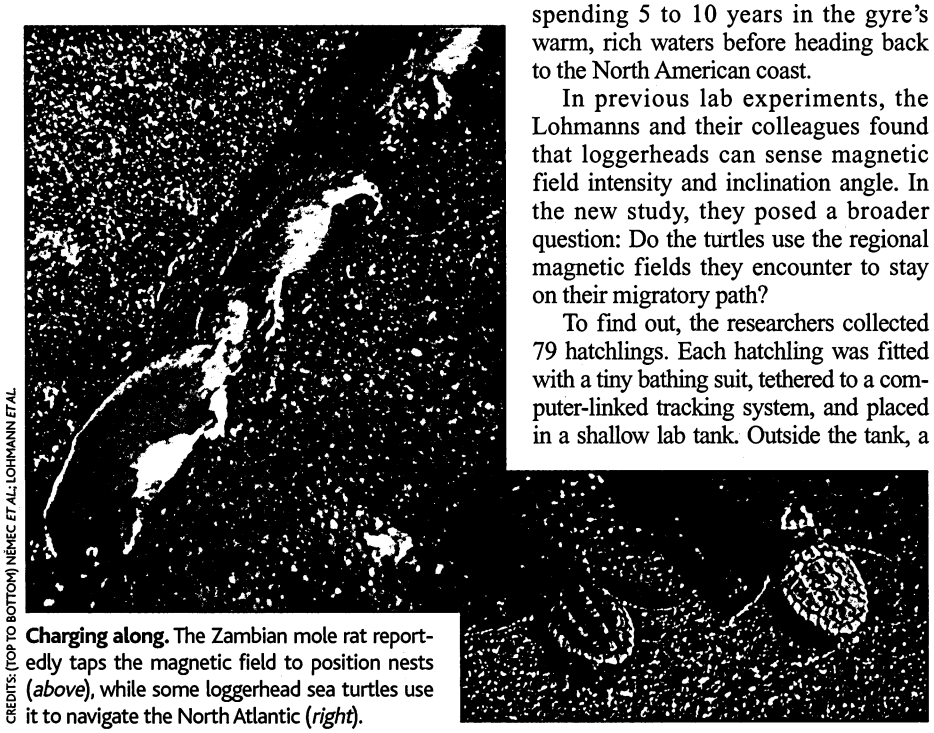
And on page 366, a team led by neuroanatomist Pavel Němec of Charles University in Prague identifies for the first time an area of the mammalian brain that apparently processes magnetic field information. "This opens up a whole new area of research in magnetic sense," says biologist Michael Walker of the University of Auckland in New Zealand.

Earth's churning liquid core casts a magnetic field across the planet's surface. Birds, fish, crustaceans, and a host of other animals appear to use regional variations in the magnetic field, along with sensory cues such as sight and sound, to navigate. "We're faced with all these animals who go from place to place, sometimes over thousands of miles, with remarkable precision," says marine biologist Michael Salmon of Florida Atlantic University in Boca Raton. "But very few people have been able to figure out just how they do it."

Lohmann and his spouse, UNC biologist Catherine Lohmann, study loggerhead sea turtles that hatch on the eastern coast of Florida and immediately crawl into the moonlit ocean. The hatchlings head into the North Atlantic gyre: a circular ocean current that flows clockwise around the Sargasso Sea. Loggerheads loop the gyre, heading northeast toward Europe and then south, spending 5 to 10 years in the gyre's warm, rich waters before heading back to the North American coast.

In previous lab experiments, the Lohmanns and their colleagues found that loggerheads can sense magnetic field intensity and inclination angle. In the new study, they posed a broader question: Do the turtles use the regional magnetic fields they encounter to stay on their migratory path?

To find out, the researchers collected 79 hatchlings. Each hatchling was fitted with a tiny bathing suit, tethered to a computer-linked tracking system, and placed in a shallow lab tank. Outside the tank, a



CREDITS: (TOP TO BOTTOM) NĚMEC *ET AL.*; LOHMANN *ET AL.*

Charging along. The Zambian mole rat reportedly taps the magnetic field to position nests (*above*), while some loggerhead sea turtles use it to navigate the North Atlantic (*right*).

ScienceScope

Patent Challenge Grows The battle against a European patent for a breast cancer test went continent-wide this week. As *Science* went to press, researchers and clinicians from six European countries were poised to file formal opposition to a patent awarded last January to Myriad Genetics of Salt Lake City, Utah. It covers a test that detects mutations in the *BRCA1* gene that researchers believe are responsible for more than half of all hereditary breast cancers. Opponents say the patent gives Myriad an unfair monopoly on breast cancer testing.

The Institut Curie in Paris had already announced that it would oppose the patent (*Science*, 14 September, p. 1971). Now weighing in are human and medical genetics societies from five other European countries: Belgium, Denmark, Germany, the Netherlands, and the United Kingdom. In addition, on 4 October the European Parliament adopted a resolution opposing the patent.

Patent opponents, says human geneticist Gert Matthijs of the University of Leuven in Belgium, want to "make sure ... that the social medicine we practice [in Europe] does not become exceedingly expensive because of patent rights." Myriad officials predict that their patent will stand.

Howling at Earmarks Critics and supporters of congressional pork-barrel spending on academic science projects found little common ground at a 1-day workshop on the issue in Washington, D.C., last week. Lawmakers last year "earmarked" a record $1.7 billion to universities for buildings and research projects that had not been requested by the White House. The meeting was held in the wake of a White House effort to persuade university and science groups to publicly oppose such practices (*Science*, 28 September, p. 2364).

Critics, including House Science Committee aide Dan Pearson, said that earmarking leads to taxpayer funding for questionable science. But one prominent ex-earmarker, former Louisiana Senator J. Bennett Johnston—now a lobbyist—noted that earmarks account for just a few percent of the government's $43 billion civilian R&D budget. He advised earmarking opponents to "put your efforts elsewhere, because you are not going to win." He also accused some universities of hypocrisy, publicly decrying earmarks but privately hiring lobbyists—such as himself—to win cash from Congress. Some schools, he charged, "want to bark with the dogs *and* howl with the coons."