HIV Alters DNA, Causing Rare Cancer

A few years ago, a man walked into a San Francisco health clinic complaining of a cough and shortness of breath. For 10 years, he had lived alone, avoided sexual activity, and shown no sign of AIDS, despite having been infected with the AIDS virus, HIV, years earlier.

But 10 days after his visit, this man died, succumbing to an unusual cancer, says Michael S. McGrath, a cancer biologist at the University of California, San Francisco (UCSF).

Analysis of the genetic makeup of the man's tumor, as well as a similar investigation of tumors from six other men with this cancer, has for the first time demonstrated a direct link between HIV and tumor growth. UCSF's Bruce Shiramizu, McGrath, and their colleagues discovered that a piece of HIV genetic material had inserted itself into human DNA near a particular cancer-causing gene. Presumably, that added material turned on this oncogene, which is associated with several other types of tumors, they report in the April 15 CANCER RESEARCH.

"It's the first time this has been seen in a human cancer," says Michael Emerman, a virologist at the Fred Hutchinson Cancer Research Center in Seattle.

"[The finding] highlights the fact that retroviruses can cause tumors and can do so by a variety of mechanisms," adds Robert Yarchoan at the National Cancer Institute in Bethesda, Md.

In these seven San Francisco patients, white blood cells — including T cells, B cells, and macrophages — had multiplied and spread out of control, creating a lymphoma with a mixed cell type. Until now, most lymphomas seen in AIDS patients derived from a single white cell type, often B cells. B-cell lymphoma, as well as other cancers associated with AIDS, seems to arise because the virus weakens the immune system.

In contrast, these seven patients tended not to show signs of immune suppression. Instead, "most of them had this [cancer] as their [first AIDS] symptom," McGrath notes.

Scientists have long known that HIV and other retroviruses randomly stick their genetic material into the host cell's DNA, leaving open the possibility that the insertion could cause genes nearby to go awry. Indeed, McGrath and several other research groups had searched for evidence that HIV can cause cancer this way for about a decade, with no luck until now, he says.

He hypothesizes two explanations for the sudden appearance of this cancer in HIV-infected people. On the one hand, HIV may be evolving and may have developed different ways of acting inside white blood cells. This suggestion presents the possibility that HIV may also change the way it infects people, he notes.

On the other hand, these cancers may be an unwelcome outcome of patients living longer with their HIV infections, perhaps because of medications that slow HIV's spread in the body and battle opportunistic infections. The longer the infection persists, the greater the likelihood that HIV genetic material will insert itself into a cell's DNA.

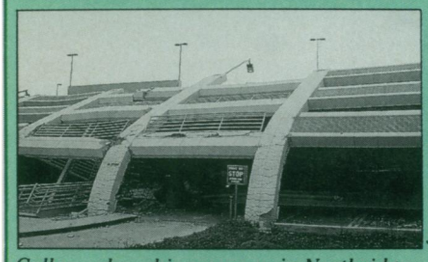
These results suggest a downside to another report released this week. For this study, UCSF's Dennis Osmond and his colleagues tracked white-blood-cell counts of 761 HIV-infected men. From 1983 to 1986, the median survival after these counts dropped below a certain level was 28.4 months. From 1986 to 1988, the time lengthened to 40.1 months, and from 1988 to 1993, it hovered around 38.1 months, they report in the April 13 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION.

Further analysis revealed that these men lived longer primarily because of better treatments for the pneumonia commonly associated with AIDS, Osmond adds. — *E. Pennisi*

Can Los Angeles ride out a stronger quake?

A giant lurking beyond the Los Angeles horizon, the San Andreas fault has long loomed in the fears of southern Californians, who wonder when the expected "Big One" will strike. But seismologists in recent years have also urged the city to consider the threat from lesser quakes on hidden faults directly beneath Los Angeles, a point punctuated by the Northridge quake that struck on Jan. 17.

Although it racked up $15 billion in damages and killed 61 people, the magnitude 6.7 quake spared tall buildings. But the city cannot count on such luck next time, say engineers, seismologists, and emergency-response officials, who met last week in Pasadena, Calif., to discuss the effects of a magnitude 7 quake beneath downtown Los Angeles.



R. Monastersky

Collapsed parking garage in Northridge.

This type of shock would apparently shift the ground enough to topple some 20-story buildings built to current safety standards, says John Hall, an engineer at the California Institute of Technology in Pasadena.

The hypothetical-earthquake exercise, planned long before January's disaster, addressed a shock occurring on the Elysian Park fault, a fracture that produced a magnitude 5.9 quake in 1989. A magnitude 7 jolt would release three times the energy of the Northridge shock but only 3 percent of the energy of a magnitude 8 San Andreas quake.

Although not huge, the modeled quake destroyed some tall buildings in Hall's study because they could not withstand the large, fast ground shifts that occur close to a fault. Such pulses of motion travel wavelike up tall buildings, causing them to lean. If the period of the pulses matches the building's height, the tilting gets amplified and the structure can fall over.

Unlike shaking, which spreads far from a quake's epicenter, severe ground shifts happen only near a fault in a large shock. Seismologists have warned of fast displacements in the past, but they have lacked any direct evidence of them. As a result, construction codes have not taken this motion into account. "These near-fault pulses are what's missing in the code. We really haven't had much experience with them," says Hall.

Last week, Caltech researchers reported measurements from the 1992 Landers earthquake proving that land nearby does shift rapidly. At a site only 2 kilometers from the fault, the ground moved 2.5 meters in 4 seconds.

Besides the new findings about ground movements, engineers must also grapple with unanticipated problems in steel-frame buildings that surfaced during the Northridge quake. So far, inspectors have found cracked joints between beams and columns in at least 50 buildings.

No steel-frame buildings collapsed during the January jolt. But the fractured joints have weakened some structures, reducing their safety in future shocks. In light of the joint problem, Hall wonders whether even undamaged steel buildings would survive a stronger quake. He notes, however, that most

deaths probably would occur in smaller buildings already known to be seismically unsafe.

Highway bridges should ride out a magnitude 7 shaker without major damage, says James E. Roberts of the California Department of Transportation in Sacramento. Although several freeway bridges collapsed in January, strengthened bridges survived and should withstand stronger jolts, he says.

Officials have less optimism about the city's ability to fight quake-sparked fires, which traditionally cause much of the damage during such disasters. Robert Canfield, emergency preparedness coordinator for Los Angeles, noted that the city devoted half its fire-fighting resources to save one burning high-rise in 1987. Should several such blazes break out, the city could rescue people, but it could not save those buildings. "We are going to have to walk away from them and devote our first efforts to saving lives," Canfield says.

He and others stressed that Northridge claimed so few lives in part because it struck at 4:30 a.m. on a holiday, a time when the garages and freeways that collapsed were nearly empty.

Although the scenario involved a hypothetical earthquake, seismologists say Los Angeles sits on several faults that could produce quakes of magnitude 7 or greater. What's more, the city has not had enough Northridge-size quakes in its history to relieve the strain building underground, says James F. Dolan from Caltech. Magnitude 7 shocks, if they occurred every few hundred years, could release this pressure. But the city has not seen such a killer in at least 2 centuries, a fact that sets seismologists on edge. *—R. Monastersky*

Asian link proposed for primate evolution

Excavations in southeastern China have yielded an array of fossils suggesting that Asia played an important role in the early evolution of primates, according to a report in the April 14 NATURE.

Annual fieldwork since 1992 in caves along the face of a limestone quarry near the village of Shanghuang has unearthed about 75 primate fossils, mainly teeth and jaw fragments, and thousands of other mammal bones. Chinese investigators discovered the fossil deposits in 1987.

No volcanic rock for dating exists at the site, but comparisons to North American fossil mammals dated in this way place the Chinese finds at 45 million years old, assert paleontologists K. Christopher Beard and Mary R. Dawson of the Carnegie Museum of Natural History in Pittsburgh and Tao Qi and his coworkers of the Academia Sinica in Beijing.

"The site at Shanghuang has, at a stroke, revolutionized our appreciation of the involvement of Asia in the early evolution of primates," comments anthropologist Robert D. Martin of the University of Zurich in the same NATURE.

Other researchers view the new finds as too fragmentary to support any sweeping revisions of how primates evolved.

Beard and his colleagues identify five new fossil primate species at the Chinese site. These belong either to the lemurlike adapids, the tarsierlike omomyids, or the early simians, forerunners of monkeys, apes, and humans.

Only adapids and omomyids have turned up at North American and European sites of comparable age; several African simians dating to about 40 million years ago have been discovered since 1988.

The proposed Chinese simian, dubbed *Eosimias sinensis,* displays several jaw and tooth features that distinguish it from adapids and omomyids, Beard argues.

"*Eosimias* shows that early relatives of monkeys lived in Asia about the same time that they lived in Africa," the Pittsburgh researcher maintains. "Whether monkeys first evolved in Africa or Asia cannot be established now."

Various investigators have promoted either omomyids or adapids living between 55 million and 36 million years ago as simian ancestors (SN: 1/12/91, p.20). Beard's group argues that, given the new Chinese evidence, the first simians had appeared by 55 million years ago and derived neither from omomyids nor from adapids.

Dawson notes that some scientists who study fossil primates doubt that the *Eosimias* specimens come from a monkeylike higher primate. In the absence of a more complete skull, the evolutionary identity of *Eosimias* remains unclear, asserts Elwyn L. Simons, an anthropologist at Duke University in Durham, N.C.

"Beard will have a difficult time gaining widespread acceptance of his argument for an important radiation of early [higher primates] in Asia based on such fragmentary evidence," contends Simons, who directs excavations at an Egyptian primate site.

N.J. Perkins, M. McNaugher/Carnegie Museum

Preliminary reconstruction of Eosimias.

In another controversial assessment, Beard's group assigns several fossil teeth from Shanghuang to *Tarsius,* the genus that includes living tarsiers. No other modern primate genus is even half as old as the age proposed for *Tarsius* by the U.S.-Chinese team.

Ancient Chinese tarsiers lived in tropical forests much like those inhabited by modern tarsiers, Dawson holds. "They apparently found a habitat they liked and stuck with it," she says.

But to claim such an ancient age for *Tarsius* based only on fossil teeth "is going way out on a limb," Simons argues. Comparisons with the distinctive faces and limbs of modern tarsiers must also be made, he notes.

Beard and his coworkers assign some Shanghuang fossils to an adapid that resembled an extinct European primate and identify others as an omomyid with anatomical ties to a North American primate of comparable age. Early primates migrated between Asia and other continents 45 million years ago, they suggest.

Early simians may have originated more than 65 million years ago, Martin concludes. But Simons disagrees, noting that the oldest well-established higher primates lived about 40 million years ago. *—B. Bower*

Sizing up a smoker's risk of lung cancer

Black smokers run a greater risk of developing lung cancer than white smokers. Although the mechanism underlying that racial difference remains a mystery, scientists now suggest that black smokers may have a greater metabolic predisposition to the malignancy.

The new research may also provide more ammunition for those battling the tobacco industry. Many scientists believe that cigarette manufacturers aggressively target blacks in advertising campaigns designed to draw in new smokers.

John Richie Jr., a biochemist at the American Health Foundation in Valhalla, N.Y., and his colleagues knew that tobacco contains NNK, a nicotine-derived compound that causes lung cancer in mice. The team wanted to find out whether they could detect any differences in the way smokers metabolize this chemical.

They started their investigation by recruiting 25 white and 31 black smokers. The researchers analyzed urine samples from each smoker, homing in on two breakdown products of NNK: NNAL and NNAL-Gluc. NNAL also causes lung cancer in mice. When the body detoxifies NNAL, NNAL-Gluc results.

The researchers hypothesized that smokers whose bodies transformed NNAL into NNAL-Gluc more efficiently