

# 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.

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



Collapsed parking garage in Northridge.

R. Monastersky