Newfound genetic clue to HIV rate in blacks

Sabin Russell, Chronicle Medical Writer
Thursday, July 17, 2008

(07-16) 09:04 PDT SAN FRANCISCO -- An international team of AIDS scientists has discovered that a gene variant common in blacks protects against certain types of malaria but increases susceptibility to HIV infection by 40 percent.

Researchers, keen to find some biological clues to explain why people of African descent are bearing a disproportionate share of the world's AIDS cases, suspect this subtle genetic trait - found in 60 percent of American blacks and 90 percent of Africans - might partly explain the difference.

Ten percent of the world's population lives in sub-Saharan Africa, but that region accounts for 70 percent of the men, women and children living with HIV infection. In the United States, African Americans make up 12 percent of the population but account for half of newly diagnosed HIV infections.

"The cause of this imbalance is not necessarily driven by behavior," said Phill Wilson, founder of the Black AIDS Institute in Los Angeles. "Gay black men do not engage in riskier behavior than gay white men, for example. African people with this gene may have a higher vulnerability."

Based on their analysis, the researchers estimated that this gene variant alone may account for 11 percent of the estimated 25 million HIV infections that have occurred in sub-Saharan Africa - roughly 2.7 million cases.

The gene study was led by Dr. Sunil Ahuja, a professor of infectious diseases at the University of Texas Health Science Center at San Antonio, and published Wednesday in the journal Cell Host & Microbe.

Finding the duffy protein

Working in collaboration with renowned virologist Robin Weiss of University College in London, the group zeroed in on a protein found on the surface of red blood cells. It is known in laboratory circles as the "Duffy antigen."

Certain species of malaria parasites latch on to the Duffy protein and use it as a gateway to enter red blood cells. Africans overwhelmingly carry a gene that disables this gateway - and Weiss believes this may have been the result of an evolutionary battle between humans and malaria. The genetic trait is

also prevalent among African Americans, who typically carry a mixture of African and European bloodlines.

"If there is no Duffy there, the malaria parasite can't get in," said Weiss.

In the 20th century, however, the Duffy protein appears to have taken on another role, seeming to absorb HIV particles, like a sponge, the researchers said. By sopping up the virus, the protein hampers the virus' chances of invading vulnerable white blood cells - the first step in HIV infection.

People with a disabled Duffy protein - most Africans, for example - may therefore be more vulnerable to infection.

Ahuja's team compared 814 African American military personnel who were HIV negative with 470 who were infected with HIV. Out of this comparison, the researchers found a 40 percent higher risk of HIV among those whose genes suppressed the Duffy protein.

The researchers also made another remarkable finding - once a person with the African gene becomes infected, the same genetic trait appears to prolong survival. One of the Duffy protein's natural roles appears to be to ramp up the immune system. It attracts a number of chemical signals that promote inflammation - a defensive mechanism that normally protects the body, but lays out a banquet of white blood cells for HIV to infect and destroy.

So the same genetic mutation that raises the risk of HIV infection provides some protection to those who become infected. Similarly, those who carry the normal Duffy protein may be somewhat shielded from HIV infection, but once infected may sicken and die sooner without treatment. "There is a high order of complexity here," Ahuja conceded.

Although Ahuja and his team are highly respected researchers, some scientists in the field cautioned that the conclusions may be premature. "I'm a little skeptical about it," said Cheryl Winkler, head of the Laboratory of Genomic Diversity at the National Cancer Institute, in Frederick, Md.

More study urged

Winkler, an expert in genetic factors that cause disease, said the differences in infection rates between soldiers who carried the gene variant and those who did not was statistically significant, but barely so. "They have a model here, but they don't have enough evidence," she said. "This definitely requires more study and replication of results before you can make these assumptions."

UCSF Professor Dr. Warner Greene, director of the Gladstone Institute of Virology in San Francisco, said the new study is intriguing and presents a portrait of the evolutionary struggle between humans and pathogens. "In response to the threat of malaria, you may be set up to become more susceptible to HIV," he said.

At a deeper level, he said, the study opens doors for new research into the complex relationship between blood cells and the chemical signals that turn the immune system on and off.

"They've done a real good job of trying to explain their results," said UCSF virologist Dr. Jay Levy, who was among the first to isolate HIV as the cause of AIDS. "It poses a nice challenge to researchers trying to understand how HIV causes disease."

How the study was done

To find out if people carrying the malaria-protective gene might be more vulnerable to HIV, researchers drew on a unique cohort of experimental subjects - U.S. Air Force personnel whose blood has been collected and stored for 25 years.

The Wilford Hall Medical Center cohort is a valuable resource for genetic research because military personnel live in similar environments (military bases), work for the same employer (the Air Force), have similar incomes and the same health care. Those similarities make it easier for researchers to pinpoint differences unlikely to be caused by social or environmental factors.

In this study, researchers compared 814 African American military personnel who were HIV-negative with 470 who were infected with HIV.

They also screened those airmen to find if they carried the Duffy protein. Out of this comparison popped the surprising number: A 40 percent higher risk of HIV among those whose genes suppressed the Duffy protein - a trait that presumably evolved in Africa as a defense against malaria.

By the numbers

The AIDS epidemic disproportionately affects people of African descent.

49%

of new HIV cases in the United States are diagnosed in African Americans, who make up 12 percent of the population.

10%

of the world's population lives in sub-Saharan Africa.

70%

of the world's HIV/AIDS cases are in sub-Saharan Africa.

Sources: Centers for Disease Control and Prevention; UNAIDS

E-mail Sabin Russell at srussell@sfchronicle.com.

http://sfgate.com/cgi-bin/article.cgi?f=/c/a/2008/07/17/MNRI11PM03.DTL

This article appeared on page **A - 1** of the San Francisco Chronicle