Mutant gene explains some HIV resistance

Building upon recent discoveries of how the AIDS virus enters cells, scientists have now found that some people, perhaps 1 percent of the white population, harbor genetic mutations that make them resistant to HIV infection.

The defects occur in a gene for an immune cell protein known as CC-CKR-5. The most common strains of HIV commandeer that protein in order to infect cells (SN: 6/22/96, p. 390).

The mutations appear to explain some puzzling cases in which people exposed to the deadly virus remain uninfected. The discovery also strengthens the hypothesis that drugs which interfere with the interaction between HIV and CC-CKR-5 can safely slow the spread of the virus in infected individuals.

One research group, headed by Nathaniel R. Landau of the Aaron Diamond AIDS Research Center in New York, uncovered the mutant genes while studying HIV-negative people who had been repeatedly exposed to the virus. In test-tube experiments, the investigators found that the immune cells of two such people resisted infection with the HIV strains often transmitted sexually.

The two people have a mutation in each of their two copies of the CC-CKR-5 gene, the researchers report in the Aug. 9 CELL. The defect, the same in both instances, is a large gap in the gene's DNA sequence. It results in a shortened protein that the virus can't use. The investigators speculate that the two people inherited one mutant copy of the gene from each parent.

When the scientists examined 144 people of Western European origin, they found that 24 had one copy of the mutant gene. Of 44 Venezuelans tested, however, none did.

The mutation "is common in some human populations but rarer in others. These findings suggest a rather recent evolutionary origin of the mutation," concludes Landau's team.

A research group headed by Marc Parmentier of the Free University of Brussels found the same CC-CKR-5 gene mutation when they screened 704 white people from France and Belgium. The investigators will report in the Aug. 22 NATURE that 8 of the people have two copies of the mutant gene and 114 have one copy. Among more than 350 people from Africa and Japan, none has the mutation, the group found.

While it seems reasonable that having mutations in both copies of the CC-CKR-5 gene offers considerable protection from infection with HIV, scientists caution that several HIV strains use molecules other than CC-CKR-5 to infect cells.

Investigators do not yet know whether heterozygotes, people with one mutant copy and one normal copy, also have a lowered risk of infection. Some preliminary evidence suggests that they do, says Robert W. Doms of the University of Pennsylvania in Philadelphia, a coauthor of the NATURE report.

Even if heterozygotes do not enjoy resistance to infection, HIV may spread more slowly in their bodies. "It is conceivable that one might get infected and not progress as rapidly [to AIDS]," notes Doms.

Researchers are increasingly excited about preventing or treating many HIV infections with compounds that bind to CC-CKR-5 and thus stop the virus from using the protein to infect cells. Since CC-CKR-5 normally helps immune cells respond to infections, investigators have worried that drugs interfering with it would cause harmful side effects. Such drugs may be safe, however, since people lacking a functional CC-CKR-5 protein seem to be healthy.

"The body doesn't appear to need [CC-CKR-5], but the virus does need it to infect cells. This tips the balance in favor of being able to interfere with that interaction without harming the host," says Anthony S. Fauci of the National Institute of Allergy and Infectious Diseases in Bethesda, Md. *— J. Travis*

Earth matured early in its adolescence

Geoscientists, the biographers of the planet, struggle to chronicle a reluctant 4.5-billion-year-old subject that jealously guards all secrets about its distant youth. By slowly chipping away at the rock record, however, researchers are starting to develop a portrait of Earth in its tumultuous first 2 billion years, the Archean era.

Evidence culled from South Africa now reveals that the planet had a flip-flopping magnetic field as far back as 3.2 billion years ago, reports a trio of geophysicists this week.

"We feel we have an example of the oldest known reversal of Earth's magnetic field. It looks like the magnetic field has behaved similarly since that time," says Paul W. Layer of the University of Alaska, Fairbanks.

Generated by currents of molten iron alloy within Earth's core, the geomagnetic field has a habit of reversing its direction every few hundred thousand years. Although evidence of the field's existence reaches back 3.45 billion years, scientists could not tell when the field had matured to the point of flipping its polarity. Prior to the South African discovery, the oldest reversal record had hailed from rocks about 2.7 billion years old.

Layer and his coauthors, Alfred Kröner of the Johannes Gutenberg University in Mainz, Germany, and Michael McWilliams of Stanford University, report their find in the Aug. 16 SCIENCE.

The team uncovered signs of the reversal in northeast South Africa within a pluton—a deposit of once-molten volcanic rock that forced its way up through the crust and then hardened while still underground. Over billions of years, erosion stripped away rock layers above and exposed the innards of the 30-kilometer-wide pluton.

The pluton stores ancient magnetic information because it contains iron-rich particles that aligned themselves with the orientation of Earth's field when the rock was molten. As the deposit gradually cooled 3.2 billion years ago, these particles became locked in place, recording the field's direction.

Layer and his colleagues discovered that rock toward the edge of the pluton showed a magnetic orientation almost directly opposite to that of material in its interior. They reasoned that the magnetic field must have reversed during the several million years it took the entire pluton to cool. Because the outer layer of the pluton cooled first, it locked in the field direction prior to the reversal. Later, the interior recorded the postreversal orientation.

If subsequent volcanic activity had reheated the pluton, it would have reset the magnetic orientation to that of a younger age. But Layer and his colleagues say that they have ruled out this possibility by studying the radioactive decay of elements within the rock. The data indicate that the pluton has escaped severe heat since the time it first cooled, in Earth's adolescence.

Not all geomagnetists share this certainty. Rob Van Der Voo of the University of Michigan in Ann Arbor says that "one has to disprove remagnetization, and that is hard to do. I've looked at hundreds of rock formations and about half of them are probably remagnetized."

Layer's tests get a better reception from Joseph G. Meert of Indiana State University in Terre Haute, who has documented a later Archean reversal in Kenya. "I and others will approach this with caution. But the authors have demonstrated the case against resetting as best they could."

Meert says he would like to see confirming evidence of the reversal from another site, although he holds out little hope of finding other relatively undisturbed rocks from this age.

— R. Monastersky