HIV attack destroys immune innocence

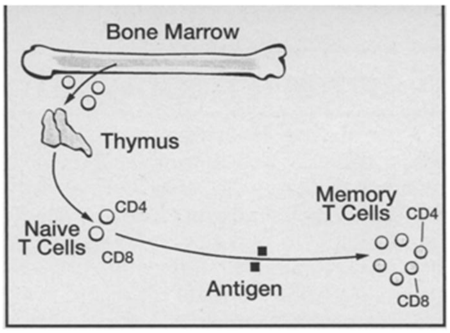
In a world where it is best to "know thine enemy," naiveté should be a fatal flaw. But cells of the immune system need a certain innocence in order to fight new invaders. After the battle, they carry a "memory" of their bacterial or viral foe and remain alert for its next attack.

While HIV infection is marked by a general decline in the number of immune cells, new evidence indicates that the virus may scuttle the immune system by destroying naive immune cells that have yet to taste battle. The findings, reported by Stanford University Medical Center researchers in the May Journal of Clinical Investigation, may help doctors track the progression of AIDS but could have ominous implications for therapies.

All immune cells originate in bone marrow. A subset, the T cells, migrates to the thymus and develops into a variety of naive helper (CD4) and killer (CD8) cells — two kinds of immune cells that work in concert to fight infection. Released from the thymus and exposed to the antigens of invaders, T cells become memory cells and respond only to future attacks by the same invader.

All T cells carry characteristic protein markers on their surfaces. HIV, the AIDS-causing virus, infects them by recognizing the marker for CD4 cells.

Currently, physicians track the progress of HIV infection by measuring the decline of CD4 cells. But some patients with very low CD4 counts remain well, while others with relatively high counts die quickly. Stanford immunologist Mario Roederer says that although CD4 counts may predict a mean time to death, they represent "a very poor marker of the disease for an individual."



Formed in bone marrow, immature T cells migrate to the thymus. Naive T cells emerge, meet antigen, and develop into memory cells.

The Stanford researchers, led by Leonard A. Herzenberg and Leonore A. Herzenberg, decided to focus only on naive T cells. They marked T cells with fluorescent antibodies specific to three surface protein markers — either CD4 or CD8, plus two markers specific to naive cells. The combination of markers distinguishes naive helper and killer T cells from their memory counterparts.

The group compared the numbers of naive T cells in 266 HIV-infected adults with the counts for 44 uninfected adults. Fifty percent of the T cells in normal adults were naive, as opposed to only 10 percent in HIV-infected participants. Roederer claims he saw a "pronounced effect" with the first few patients.

The Stanford team found similar numbers of CD8 cells in the two groups. Strikingly, however, less than 15 percent of the CD8 cells in HIV-infected individuals were naive, compared to 50 percent for the control group. The team also reports similar results in children.

Roederer and Leonard Herzenberg speculate that HIV disrupts the balance between naive and memory CD8 cells by infecting them in the thymus before they have fully matured. They suggest that counting naive cells could better predict the course of AIDS for individuals.

However, because the body needs naive cells in order to mount an immune response to new bacterial and viral threats, current therapies designed to stimulate immune responses against HIV could be doomed to failure. "We may have to rethink our approaches to HIV," says Herzenberg.

Though encouraged by the Stanford group's finding, Jonathan M. Kagan of the National Institute of Allergy and Infectious Diseases in Bethesda, Md., warns that they may be "observing the result of an overall activation of the immune system" due to HIV infection rather than destruction of naive T cells.

Herzenberg hopes to continue the work to determine whether decreases in naive T cells correspond closely to disease progression. *— L. Seachrist*

Probing high-energy physics inside an atom

High-energy particle accelerators are not the only tools available to physicists to test their theories of the fundamental particles and forces of nature. Lasers also help them study subtle details of the way electrons behave in certain types of atoms.

Such tabletop experiments probe the elementary particle physics frontier, says E. Norval Fortson of the University of Washington in Seattle.

Precision measurements on an atomic scale can test various aspects of the standard model of particle physics, which describes the interactions of quarks, electrons, and other components of matter, he notes. They may even provide glimpses of new physics beyond the standard model.

One such test involves the weak force, one of the particle interactions in the standard model. This force is responsible for radioactivity and plays a central role in the decay of an isolated neutron into a proton, electron, and antineutrino.

According to the standard model, the weak force acts on particles in a way that distinguishes left from right. This effect is known as parity violation.

For example, when a cobalt-60 nucleus having a particular orientation decays to create a nickel-60 nucleus, an electron, and an antineutrino, the electron is ejected preferentially in one direction. The existence of this favored direction in weak interactions makes the universe left-handed.

Fortson, Washington colleague Paul A. Vetter, and their coworkers looked for parity violation in the behavior of the outermost electron of a thallium atom. The researchers carefully observed what happens when polarized laser light passes through thallium vapor.

A slight rotation in the angle of polarization provides a direct measure of parity violation in the interaction between an electron and the quarks of the thallium nucleus. Combining the experimental measurements with theoretical calculations of the distribution of electrons in a thallium atom, the Washington team obtained a result in good agreement with the standard model.

Fortson and Vetter reported their findings at last month's American Physical Society meeting, held in Washington, D.C.

Using a similar strategy but working independently, N.H. Edwards of the Clarendon Laboratory in Oxford, England, and his collaborators have made comparable measurements of parity nonconservation in thallium.

Certain aspects of the results hint that "there may be new physics here, but at this point, one can't say," Fortson says. "We need to do better."

By refining the electron distribution calculations and working with a single atomic ion rather than a vapor, the researchers hope to approach the precision achieved in particle accelerators.

At the same time, M. Scott Dewey and Geoffrey Greene of the National Institute of Standards and Technology (NIST) in Gaithersburg, Md., and their collaborators are investigating the details of parity violation by making precise measurements of the neutron lifetime. Such determinations offer additional insights into the nature of the weak interaction.

The researchers use neutrons generated in a research reactor at NIST. Slowed down, these neutrons are guided to a magnetic trap. If the neutron happens to decay, the resulting proton gets caged by the trap's magnetic field. An electric field around the trap then nudges the proton to a detector.

The NIST team expects to contribute a new value to the world average for the neutron lifetime — which currently stands at 887 seconds — within the next few months. *— I. Peterson*