AIDS Virus Coat Activates T Cells

Gp120 is not simply an inert protein that forms the outer coat of the AIDS virus. The molecule, which is being used as the basis for several experimental AIDS vaccines, appears to have biological activity of its own. New information on the behavior of gp120 may help researchers understand more about the complex biology of T lymphocytes.

Gp120 stands for the coat glycoprotein of the AIDS virus, which has a molecular weight of 120 kilodaltons. When it binds to its receptor—the CD4 antigen on the surface of normal T4 lymphocytes—it triggers a rise in intracellular calcium and stimulates resting T cells to enter the cell cycle, according to David Center and Hardy Kornfeld of Boston University School of Medicine and their colleagues. Other researchers who have attempted similar studies do not obtain the same responses, however. The new data appear in the 29 September issue of *Nature*.

It is not clear whether the new information will help to explain how the AIDS virus, called human immunodeficiency virus type 1 (HIV-1), kills T4 lymphocytes or causes disease. Rather, it supports a previous finding that the CD4 molecule may act as a receptor for a naturally occurring growth factor, possibly a lymphokine secreted by T8 lymphocytes, says Center. Gp120 mimics the action of the lymphokine because it induces fresh, uninfected T4 cells to become motile and it stimulates more of them to express the interleukin-2 growth factor receptor on their surface—an indication that the cells are activated from the G_0 or resting phase of the cell cycle to the G_{1a} phase.

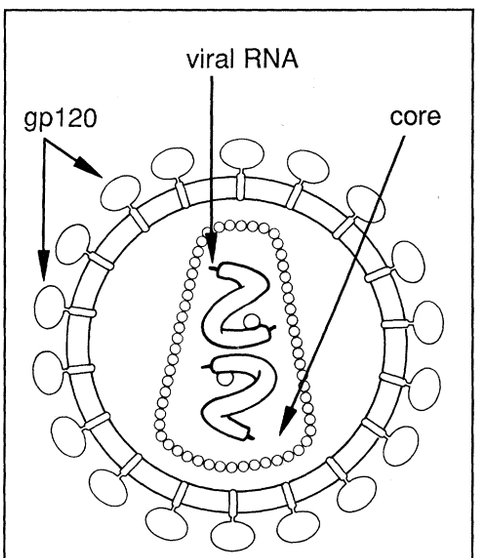
Center does not yet know the amino acid sequence of the lymphokine, which he calls lymphocyte chemoattractant factor, nor does he know how closely it might resemble gp120. But both molecules bind to CD4 and stimulate the breakdown of phosphatidyl inositol, a membrane lipid, to form inositol trisphosphate. They also induce about a twofold rise in intracellular calcium ions, largely from intracellular sources. Contrary to data from other experimental systems, the calcium concentration in the lymphocytes increases before the concentration of inositol trisphosphate reaches its peak.

Not everyone sees the same T cell responses to gp120. "We have tried similar experiments and found no changes in intracellular calcium," says Carl June of the Naval Medical Research Institute in Bethesda, Maryland. June used a different preparation of gp120, which might account for the different results. He and his colleagues reported previously that HIV infection of T cells causes a calcium-signaling defect (*Science*, 29 July, page 573). It is not clear how or whether this relates to the new work.

Scott Koenig of the National Institute of Allergy and Infectious Diseases wonders what the results from Center and his coworkers might mean in a person infected with HIV-1. "If their finding has relevance in vivo—and I say that with a big 'if'—it could be a mechanism for suppressing immune function," he says. "That is, if T cells are constantly being turned on by gp120, they could be less receptive to normal biological signals."

Center says that experiments to investigate this are in progress. Meanwhile, he will use gp120 as a tool to probe the functions of the CD4 receptor.

■ DEBORAH M. BARNES



Model of the AIDS virus

Adapted from *Scientific American*, October, 1988, page 55

A Shallower Ozone Hole, As Expected

The depletion of stratospheric ozone over Antarctica this September and October was a modest 15% compared to last year's 50%. The moderation of the ozone loss "is something we expected," says Mark Schoeberl of the Goddard Space Flight Center in Greenbelt, Maryland. "The hole is perhaps even shallower than expected, so we don't have all the possible interactions nailed down, but I'm certainly convinced that the hole is not going away."

The difference this year was that the stratosphere of the Southern Hemisphere was more strongly stirred than usual. The more active circulation distorted and weakened the vortex of polar winds that encircles and contains the hole and increased the transport of air from lower, warmer latitudes. As a result, the stratosphere over Antarctica was 10°C warmer than last year. A warmer stratosphere would mean fewer ice clouds, whose particles seem to be essential to the ozone-destroying reactions involving chlorofluorocarbons. The fewer the polar stratospheric clouds, the less ozone destruction.

The more dynamic atmosphere would also tend to dilute the denitrified, dehydrated air created by the ice clouds that is essential to ozone destruction. From balloon observations at McMurdo Station, the stronger winds even appeared to be bringing in ozone-rich air at altitudes above the depletion zone, compensating in part for ozone losses. The dynamics of the atmosphere have an important effect on the amount of stratospheric ozone, notes Schoeberl.

Researchers are not particularly surprised that there was a turnaround this year. As soon as the winds in the lower stratosphere near the equator reversed from westerly to easterly in about July, the presumption was that the 1988 hole would not be as deep as 1987's. These links among the alternating winds over the equator, called the quasi-biennial oscillation (QBO), Antarctic stratospheric temperatures, and Antarctic ozone were first noted about a year ago.

Controversy continues over the exact mechanisms that might link the equatorial and polar stratospheres. The debate has been complicated by the discovery that sunspots as well as the QBO are a factor in determining polar temperatures (*Science*, 23 October 1987, p. 479). Last year's record high depletions in the hole occurred during the westerly phase near the sunspot minimum, optimum conditions for an unusually cold polar stratosphere and thus for large ozone depletions.

Researchers are now looking toward the Arctic stratosphere, which tends to be warmer than the Antarctic's, and a major airborne expedition planned for this January and February. If the Arctic follows suit and is warmer than normal or even not unusually cold, finding patches of polar stratospheric clouds and flying instrumented aircraft into them could prove difficult.

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