Could herpes speed up AIDS?

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A COMMON herpes virus could hasten the onset of AIDS in HIV-positive people by helping HIV to attack the immune system. The claim comes from a group of American researchers led by Robert Gallo, the co-discoverer of HIV.

The findings do not change our picture of HIV as the cause of AIDS. Recently, some researchers have claimed that HIV alone does not cause AIDS and that another agent is necessary for the virus to harm the body (This Week, 16 June 1990). Such claims have been widely discounted by evidence from animal studies, and no one in Gallo's laboratory supports them.

We still believe HIV is the necessary factor for AIDS, it is still the cause of AIDS," says Paolo Lusso, a senior member of the team from the National Cancer Institute at Bethesda, Maryland. "But it may be that in some people the acceleration of the disease could be caused by co-factors." He stressed that the research is at an early stage.

Scientists have often suggested that the human herpes virus 6 might be such a co-factor, but there has been no proof of the claim. HHV-6, a member of the family of herpes viruses that includes herpes simplex type 1 and Epstein-Barr, is very common: at least 70 per cent of the population have antibodies to it. This has made it impossible to tell whether it affects the course of disease in HIV-positive people, because "you find it everywhere", says Lusso.

Now, the researchers in Maryland have shown that cultured T cells infected with HHV-6 (but not HIV) produce "dramatically" larger amounts of CD4 than normal. CD4 is the molecule that is the main receptor for HIV on cells. More importantly, they have also found that HHV-6 seems to induce certain other T cells, which normally lack CD4, to make the molecule. This increases the number of cells that are susceptible to infection with HIV (Nature, 7 February, p 533).

"This seems to be a new and peculiar virus-to-virus reaction," says Lusso. "One virus is regulating the expression of the receptor for the other." HHV-6 seemed to be inducing genes in the T cells to switch on, he said, probably at an early stage in infection. The team tested other herpes viruses and found no such effect, which suggests that it is specific to HHV-6.

So far, the only evidence comes from the behaviour of cells in the laboratory. Lusso accepts that studies in people and in animals will be necessary to confirm the importance of the results. "We are trying to get evidence in vivo," he says.

HIV's main targets in the immune system are a type of T cell, often known as T-helpers but more accurately described as CD4-positive cells, because they have the receptor on their surface. Another family of T cells, sometimes called "cytotoxic T" or "killer T" cells, lack CD4 and have another molecule, CD8, which distinguishes them. These are not normally susceptible to HIV.

The team found that clodod and purified CD8-positive cells, which produce no CD4, began to produce CD4 in the presence of HHV-6. They measured the amount of the molecule using standard techniques of immuno-fluorescence and fluorometry. The number of CD4-positive cells in the culture correlated well with the number expressing antigens to HHV-6.

In control cultures, the researchers exposed cells to inactivated HHV-6: the CD8-positive cells did not produce CD4, nor did the CD4-positive cells inactivated by infection.

As a second test, the team compared the CD8-positive cells before and after infection with HHV-6, to see whether they produced messenger RNA for CD4. Uninfected cells produced no mRNA for the molecule, as measured by comparing bands on a gel. Infected cells produced large amounts.

Finally, the team exposed CD8-positive cells infected with HHV-6 to HIV. As a control, cells uninfected with HHV-6 were also exposed to HIV. After repeated washing, the team detected genetic material from HIV in the infected cells but not in the uninfected cells. However, they sought the DNA by means of the polymerase chain reaction—a technique notorious for its risks of contamination.

To find out how important HHV-6 really is in people with HIV, the scientists will need to study its effects in humans. One way would be to look for T cells that carry both CD4 and CD8 in HIV-positive people.

No one is suggesting that the minority of people without antibodies to HHV-6 would not eventually develop AIDS. They were exposed to HIV. "In the long term, HIV alone is sufficient to cause AIDS," says Lusso.

The team would also need to perform animal studies, but, says Lusso, "that is still a dream". Ideally, researchers would take two groups of animals, one infected with herpes, the other not, and then infect them with an HIV-like virus, such as one of the simian immune deficiency viruses that cause diseases in animals. The two groups' progress to disease could then be compared.

Lusso says the team had considered using chimpanzees but there are ethical arguments against this and, in any case, HIV does not make chimpanzees ill.

No one knows exactly how genes govern the expression of CD4 and CD8 in mature T cells, but at the very least, mature T cells in the thymus possess both receptors, all cells must have the genetic potential to produce both CD4 and CD8. "We are trying to identify any gene on HHV-6 that is responsible for this regulation [of CD4]," says Lusso. "If we can clone it, it will be a precious tool for studying how CD4 is regulated."