Could herpes speed up AIDS?

Phyllida Brown

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 necesary 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, as 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 cloned 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 immunofluorescence and fluorocytometry. 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 increase production.

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 if 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 on mature T cells, but as the immature 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." □

Long tails—a hard act for swallows

IF YOU are a male swallow, you stand a better chance of being chosen by a female if your tail is long and symmetrical rather than stunted and lopsided. But this is not merely because females consider such tails attractive. According to a Swedish biologist, there is a more important reason: a long, symmetrical tail is a reliable indication that a male will make a father and provide his offspring with good genes.

Anders Moller of Uppsala University has investigated tail symmetry in the male swallow (*Hirundo rustica*). He measured the long outer tail feathers of 96 male swallows, and noted whether they were symmetrical or uneven. He found that the shorter tails were also more uneven (*Animal Behaviour*, vol 40, p 1185).

Hugh Clarke/Frank Lane

Tail with a happy ending: male swallows with symmetric feathers always get their girl

Biologists believe that if physical characteristics arise from the plan set out in genes, then they should be symmetrical. But if an animal lives in a difficult environment which makes growing a struggle, it may fail to develop a trait equally on both sides of its body, and so become asymmetric.

According to Moller, the asymmetry of short-tailed males shows that for them the strain of growing feathers has been greater than for their long-tailed rivals. They have not been able to shoulder the energy cost of growing long feathers, and so have shown themselves to be less robust than their long-tailed rivals.

Moller also carried out experiments in which he lengthened the tails of male swallows artificially. He found that long tails can make catching prey more difficult. Moller says that males with long, symmetrical tails are also actively demonstrating that they are strong enough to overcome even these costs as well. Moller concludes that female swallows that don't just pick long-tailed males on a sexual whim: they are choosing their mates because long tails reflect genuine quality.

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