IL-7—a potential immune booster makes its debut in Montreal

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One of the hallmarks of HIV infection is that levels in the blood of a group of important immune system cells—CD4+ T cells—can decrease over time, reaching their lowest levels when AIDS develops.

Additionally, several studies have found that relatively high numbers of another T cell—CD8+ cells—are associated with a decreased risk of death.

One of the goals of highly active antiretroviral therapy (HAART) is to suppress production of HIV and raise CD4+ cell counts. However, despite the use of HAART and good adherence, some people with HIV/AIDS (PHAs) do not have a large increase in CD4+ count. The reasons for this are not clear but may be related to unresolved immune system damage and dysfunction caused by HIV.

Understanding how HIV damages the immune system is important if scientists are to find ways of reversing this damage and healing the immune system. The precise pathways through which HIV causes AIDS are not clear, despite 20 years of research. This is because scientists have found that understanding the interaction between HIV and the immune system is not easy. Sometimes, immunologic events that seem so clear and easy-to-understand in a test-tube become less so when studied in monkeys and people. Still, researchers toil away in their labs, and slowly increase their understanding of the immune system. And they are aware that their gains and insight could be fleeting and may one day be eclipsed by other findings.

Two teams of researchers in Canada—at McGill University and the University of Ottawa—have been studying HIV’s interaction with the immune system. In particular, they have focused their work on the activities of CD8+ cells. These cells are the immune system’s chief defenders against viruses and tumours.

In PHAs, CD8+ cells generally seem to be unable to control or contain HIV effectively. If a way could be found to remedy this situation, perhaps better control of HIV could be achieved, thus increasing the effectiveness of HAART.

In studying CD8+ cells, the Canadian teams have found that a signal called IL-7, or interleukin 7, used by the immune system to send messages, seems to have gone awry.

About IL-7

This molecule is made by the immune system and helps T-cells to mature and maintain their numbers. IL-7 belongs to a group of signals called cytokines. In laboratory experiments with cells and mice, IL-7 can have the following effects on CD4+ and CD8+ cells:

- prolong their survival
- stimulate their growth and development
- enhance their antiviral activity

Working together

In order for IL-7 to work, it needs to bind, or attach, to a specialized receptor (called CD127) on T cells. In untreated HIV infection, it seems that CD4+ and CD8+ cells do not have enough receptors for IL-7. Because there are not enough receptors for IL-7, this cytokine may not find and bind to the small number of IL-7 receptors. Perhaps one way to compensate for this shortfall in receptors is to administer relatively high doses of IL-7 so that all CD127
receptors can be reached by IL-7.

**IL-7 in monkeys**

Some monkeys can develop an AIDS-like illness when infected with simian immunodeficiency virus (SIV). In experiments with SIV positive monkeys, researchers have found that a combination of HAART and IL-7 can increase CD4+ and CD8+ cell counts, at least over the short-term. Exposure to IL-7 did not increase levels of SIV replication.

**IL-7 in people**

Short-term experiments in HIV negative people who were terminally ill with cancer showed that IL-7 significantly increased CD4+ and CD8+ cell counts.

Preliminary results from experiments in France suggest that repeated doses of IL-7, given as injections under the skin, can significantly raise CD4+ and CD8+ cell counts in some PHAs. To further understand the effect of IL-7 in PHAs, clinical trials are planned for Canada, France, Italy and the United States.

**IL-7 in Montreal**

Researchers at Montreal's Royal Victoria Hospital intend to conduct a placebo-controlled trial of IL-7. The results of this trial will help decide which doses of IL-7 should be used in future long-term studies. The Royal Victoria team will be seeking potential volunteers with several characteristics, including the following:

- they are HIV positive
- they have been taking HAART for at least 12 months and have been virologically stable and suppressed for the past three months

The study is now open for recruitment. Physicians interested in referring potential volunteers for this study may contact the trial nurse, Lina, at 514.934.1934 extension 32186.

If this initial Canadian trial of IL-7 is successful and the cytokine is found to be safe, then longer studies are likely, not just in Montreal but perhaps in other centres in Canada as well. Another potential use for IL-7 might be to increase the effectiveness of treatments for hepatitis C virus infection.

Long-term studies of IL-7 are essential because researchers need to know if the increased levels of CD4+ and CD8+ cells have antiviral activity and improve the health of PHAs.

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