

## **HIV protease inhibitors: immunological insights.**

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Regimens of highly active antiretroviral therapy (HAART), including those containing one or more of the potent HIV protease inhibitors, often cause large increases in CD4 cell count as well as large decreases in plasma HIV RNA that persist over time. Patients improve clinically, and the occurrence (or recurrence) of opportunistic diseases appears to be reduced. This raises issues about the source and functional capacity of the CD4 cells seen in patients receiving HAART. This article briefly summarizes the current information about the recirculation of T cells from lymphoid tissue to blood after HAART, increases in the number of naive (CD45RA+, CD62L+) and memory (CD45RO+) CD4 cells, changes in the T cell repertoire (Vbeta), and the possible role of selected cytokines that may be useful in facilitating immune reconstitution in patients receiving HAART. Preliminary data from some studies have revealed that, after several months of therapy, the number of memory CD4 cells increased, followed by increases in naive CD4 cells. Other studies have found that the number of naive CD4 cells increases only if these cells were present before initiation of therapy and that disruptions of the Vbeta subsets are not immediately corrected. Studies concerning the relations of various cytokines to immune reconstitution are also ongoing. On the basis of the limited results available in late 1997, there is good reason to hope for at least partial immune reconstitution in HIV patients treated with HAART, especially if therapy is initiated before severe damage to the immune system has occurred. In the future, cytokines such as interleukin-2, vaccinations, cellular replacement or stem cell transfer, or bone marrow transplants may play important roles in therapy.

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