



Fast Lane T Cells

May 1, 2002

Could solving the prickly mystery of how CD4 cells are lost lead to new approaches to therapy?

Researchers think so, and here's why. The long-held theory that HIV depletes its primary target, CD4 cells, by blocking new T-cell production was dealt a blow -- make that a one-two punch -- by a duo of recent studies that reached a new conclusion: The virus actually accelerates the division (proliferation) of existing T cells (both CD4s and CD8s) and increases their rate of death. So the eventual loss of CD4 cells that brings on immune deficiency and disease results from *increased cell death*, rather than *decreased cell production*.

These breakthrough findings were reported independently in December's *Journal of Experimental Medicine* by two top teams -- one led by virologist Joseph Kovacs, MD, at the National Institute of Allergy and Infectious Diseases (NIAID) and the other by Hiroshi Mori, MD, and David Ho, MD, both of the Aaron Diamond AIDS Research Center. More specifically, the Kovacs team found that HIV is causing a very rapid expansion of one subset of CD4 cells, while there is a much slower increase in a different subset. The cells in the fast-building group also die at a much quicker rate than the ones in the slow group. Interestingly, viral loads only seem to correlate with the size of the rapid proliferator group, not the slowbies. And alas, the current drugs only target the speedsters.

That means that even HAART-takers with nondetectable viral loads may still experience a decline in CD4 cells over time because of what's happening to the untouched slow group. However, if drugs could be developed to target those more slowly proliferating cells, that might help put the brakes on immune decline. For Ho, a "hit early and hit hard" advocate, the discovery supports aggressive treatment to blunt T-cell loss as soon as possible. He cautions that individuals still need to weigh the benefits and risks of HAART, but says, "If we are draining [CD4 cells] from a finite source while allowing HIV replication to occur, there is wear and tear on the immune system. I'd rather preserve the immune system than repair it -- because there are no tools to repair it right now."