Altered States

Can removing, tweaking and reinfusing your CD4 cells allow your immune system to control HIV? **Anne-christine d'Adesky** on some science friction

April 1, 2002 By Anne-christine d'Adesky

Lately there's so much gloomy news of HIV drug side effects and resistance that you may have missed one exciting bright spot on the treatment front: progress in not only bolstering battered immune defenses in HAART-takers but also making their new T cells resistant to future infection.

In the January 17 issue of *Nature Medicine*, Bruce Levine, MD, of the University of Pennsylvania Cancer Center, and colleagues at the Walter Read Army Institute of Research in Rockville, Maryland, published the results of a small but groundbreaking study in which they extracted T cells from 10 HIVers on HAART, tweaked them and then reinfused them. The volunteers were all healthy current or former Navy servicemen with an average of 350 to 500 CD4s and undetectable or low viral loads. While in the lab, the immune cells were exposed to tiny magnetic beads coated with antibodies and a plant lectin, plus immune-booster IL-2, and then allowed to grow. Two weeks later, the beads were washed off, and the cells put back into the sailors.

The bead-treating process increased the percentage of a subset of CD4 helper cells that secrete chemical messengers, which can stimulate the production of neighboring immune cells. The infusions also decreased the percentage of a subset of CD4 cells whose surface has a CCR5 gene receptor, which acts as a doorway for HIV. Through re-infusion, then, the HIVers' immune balance is shifted -- more HIV-fighting cells, fewer HIV-vulnerable ones.

After the third infusion, at around week 28, the group had an average increase of more than 200 CD4s as well as a bump in CD8, B cell and natural killer cells. These numbers persisted between transfusions and remained stable after one year. (One man had a peak gain of 750 CD4s.)

Levine's team concluded that this improved T-cell ratio was "independent of HAART" and that "an HIV-resistant state was conferred on the cellular system and is consistent with a prolonged survival of the infused cells." He also has unpublished viral-load data that supports the claim of newly developed resistance to HIV -- the "good" kind.

The trial ended last July. Today, Levine says, all 10 HIVers are still doing well -- their higher CD4 levels are stable and viral loads undetectable. Still, no one is shouting victory. It's too early to say whether the T-cell rise is due to the reproduction of transfused cells or to some stimulation of neighboring immune cells.

And while a higher T-cell count looks good on paper, there’s no guarantee that the new cells work as well as the old ones. Until Levine’s team digs deeper, it won’t know which types of immune cells have been replenished or whether these will replace lost cells that were already primed to fight opportunistic infections, such as PCP or CMV.

The scientists, jazzed by their data, are doing a follow-up HIV trial to measure how well the transfused cells respond to a battery of recall antigens, from tetanus to CMV -- and, of course, HIV. In the coming months, Levine plans to pair this T-cell-boosting approach with trials of structured treatment interruptions (STIs) to better answer the cosmic question: Can a re-primed immune system maintain long-term control of HIV? Enough to consider a HAART-free future? Levine refuses to speculate -- but the genie is out of the bottle.
