Elite controllers block integration of HIV DNA into host genome

September 19 2011

Alone among those infected with HIV-1, so-called elite controllers spontaneously maintain undetectable levels of viral replication even absent the benefit of anti-retroviral therapy. Now Mathias Lichterfeld of the Massachusetts General Hospital, Boston, and Xu Yu of the Ragon Institute show that in elite controllers, integration of HIV-1 DNA into the host chromosomes of CD4 T cells—the main target cells of HIV-1 -- is markedly reduced in comparison to those whose infection has run a more normal course. “[Elite controllers] behave like people who get effective antiretroviral treatment, despite the fact that they don’t,” says Lichterfeld.

In the study, the researchers removed CD4 T cells from elite controllers, from random HIV-1 negative persons, and from HIV-1 infected persons with progressive disease, and infected those cells with HIV-1 in the laboratory. While HIV-1 successfully integrated into both reference populations’ CD4 T cells far more effectively than into those of elite controllers, the researchers found higher levels of unintegrated, extrachromosomal HIV-1 DNA floating around in the elite controllers’ CD4 T cells.

“Overall, this suggests that the process of chromosomal integration of HIV-1 is somehow inhibited in elite controllers,” says Lichterfeld. Now poorly understood, the mechanism likely involves a synergistic interplay between multiple innate and adaptive immune defenses, he says.

“We think that these subjects can really teach us a lot about how immune-

mediated control can work under real-life circumstances," says Lichterfeld. "If we were to understand in detail what's going on in these patients, we might be able to develop some sort of intervention that could protect people against HIV-1."

This report is consistent with a paper published earlier this year which showed that elite controllers have low levels of chromosomally integrated HIV-1 DNA, and higher levels of extrachromosomal, 2-LTR circular HIV DNA, as compared to patients on highly active anti-retroviral therapy (HAART) (*PLoS Pathog*. 7:e1001300).

The research is published in the September 2011 issue of the *Journal of Virology*.

More information: M.J. Buzon, et al., 2011. Inhibition of HIV-1 integration in ex vivo-infected CD4 T cells from elite controllers. J. Virol. 85:9646-9650

Provided by American Society for Microbiology