The study by Smith et al. focuses on the activation status of CD4+ T cells in HIV-1 infected patients, which is key in the HIV pathogenesis. Specifically, the authors report on the frequency and activation levels of CD4+ T cells specific for herpesviruses (CMV, EBV, HSV, VZV) compared to CD4+ T cells specific for the non-persistent antigen tetanus toxoid (TT) in HIV-1 infected patients. Of note, the authors show that HIV infection is associated with increased activation (CD38 expression) of herpesvirus specific CD4+ T cells. Their results indicate that the activation of these cells participates to the overall immune activation in HIV-1 infected patients, associated with disease progression. The data are clear and convincing.

The authors’ conclusion is in line with evidence showing a similar phenomenon for CD8+ T cells. This is, to my knowledge, the first report of increased activation (CD38 expression) of herpesvirus specific CD4+ T cells in HIV infected patients. The results are relevant for our understanding of HIV pathogenesis.

Discretionary Revisions:
The supplementary figure, which is not necessary, could be left apart.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests