Reviewer's report

Title: IL-10+ NK and TGF-β+ NK cells play negative regulatory roles in HIV infection

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Reviewer: Ezequiel Ruiz- Mateos

Reviewer's report:

In this manuscript Jiang et al. found by flow cytometry higher levels of IL-10+NK and TGF-beta+NK cells in untreated HIV-infected individuals compared to healthy controls. In addition, the authors assayed the effect of IL-10 and TGFbeta in vitro on NK function showing that IL-10 and TGFbeta inhibited the degranulation and secretion of IFN-gamma by NK cells.

Major comments

- The authors showed no data in subjects on suppressive antiretroviral treatment and the differences found were not corrected by potential confounders as at least age. Where HIV-infected patients age- and sex- matched with healthy donors? Where are the characteristics of the healthy donors? At least sex- and age- should be shown.

- Figure 1. What is the point of dividing the subjects in high and low CD4 T-cell counts and viral load? Since there are not striking differences in total NK cell and subset levels dividing by these thresholds may be these groups should be avoided. Alternatively, have the authors try to correlate CD4 T cell and viral load with NK cell levels?

- Authors may clearly state that IL10+NK cell levels were previously measured in HIV-infected patients in Brockman et al. Blood 2009 (ref. 16 in the manuscript)

- Table 1. Please represent as median [IQR] the different variables in the whole group of subjects and not by individual subjects.

- Figure 4. Again, as suggested for figure 1, I do not see the point of dividing the groups by CD4 and VL levels.
- Figure 5 and 6 have no error bars how many times were these experiments repeated and in how many donors? No statistical contrasts are shown.

- The statement in lines 29-32 in the discussion is not supported by the results. Authors must temper this statement. Reference 16 should be cited in the discussion and contrasted with the results.

Minor comments

- Line 19. "the" is innecesary

- Please avoid using "normal" controls and please use "healthy" controls or donors.

- Figure 2. Authors may show the gating strategy of NK cells and subsets.

- Figure 3. It would have been interested to test the simultaneous production of both cytokines.

- Line 17 after (p=0.034, p=0.076) may be followed by (Figure 4A). Line 21 after (p=0.028) may be followed by (Figure 4B)

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes
Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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