Reviewer's report

Title: MicroRNA-29 family expression and its relation to antiviral immune response and viro-immunological markers in untreated HIV-1-infected patients

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Reviewer: Sanjay Swaminathan

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The aim of this paper is to explore the role of the miR-29 members (29a, 29b and 29c) in HIV infection. Whilst there were few positive findings, one of the main findings was that miR-29b levels were higher in PBMCs from HIV-1 infected individuals compared to healthy donors. However, there was no correlation noted between miR-29 and either HIV viral load or CD4+ T cell counts.

Major Compulsory Revisions:

There has been a number of papers which have shown that distinct cellular subsets harbour unique miRNA profiles. The reliance of looking at PBMCs ignores the fact that key subsets are altered in HIV-1 infection, such as CD4+ T cell subsets. The claim, for example that miR-29c levels were higher in HIV-1 infected individuals with low viral loads (Fig 2A) may have been true but it is very likely that these patients also had an elevated T cell count which may have accounted for this.

I also had difficulty understanding how the relative gene expression was calculated. The usual method is to use relative quantification (RQ = 2^-##Ct) for each miRNA using the ##Ct method as suggested by the manufacturer. I could not figure out why there was such a huge dynamic range of miRNA expression noted for each of the groups that were shown in each of the figures.

I also found the link between miR-29b and IL-32 (and MxA) less than convincing. Whist the link between miR-29b potentially modulating IL-32 may have been published, the weak correlation observed in this cohort was not that impressive.

Minor Essential Revisions:

The way that data was presented in the Table (Table 1 for example) was difficult to interpret. Was the T cell count the mean or median? I found the legend confusing in this table. Also, how many years post diagnosis were the samples taken (or are all of these patients newly diagnosed?). Do any of the patients have Hepatitis B/C co-infection and what is the primary mode of acquisition of HIV in these patients? Some of this information would have been useful.

RNA quality is very important in miRNA studies. There is no description of the quality control that was used to assess whether high quality RNA was being used in this study or not (such as the use of Bioanalyzer, 260/230 or 260/280 ratios) etc. Were the PBMC pellets stored for any extended period of time before RNA
extraction?

Also there is no description of how HIV viral load or CD4+ T cell count was measured.

Discretionary Revisions:
The language is somewhat loose at times. For example, on page 6, line 167, the sentence begins, "MiRNA levels of IL-32#, IL-32non#...." when surely the authors mean mRNA levels of IL-32#, IL-32non#....".

Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being published

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

Declaration of competing interests:

I have no competing interests with regard to this paper.