Reviewer's report

Title: MicroRNA regulation and its effects on cellular transcriptome in Human Immunodeficiency Virus-1 (HIV-1) infected individuals with distinct viral load and CD4 cell counts

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Reviewer: Steven Bosinger

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Review of revised manuscript by Duskova et al

The authors have provided a manuscript highly revised in the text, however many of my previous concerns regarding validation were not addressed. While the authors did perform qRT-PCR on miRNAs as shown in Fig. 2A – I would argue that in Fig 2A only 1 out of 6 miRNAs actually behaved concordantly between the qRT-PCR and the miRNA profiling data – while miR-18b, miR-938 and miR-1260 are in the same direction – within the scale provided it doesn't look like there was much fold-change. Even more strikingly discordant is miR-1262 – in which the PCR data showed upregulation despite the profiling data showing down-regulation of over 1200-fold.

Regarding validation of the miRNA-mRNA interactions – as noted before – there is no wet-lab validation studies of the in silico prediction models that are employed. Of course no two algorithms will provide the same output, but running multiple algorithms on the same dataset is not enough for validation. While this author will concede that more publications are emerging in which functional demonstration that a given miRNA is influencing a set of genes directly (ie. by transfection or siRNA studies) is not being provided (eg. Chang et al 2013), in this case the authors have performed the transcriptional profiling and can estimate the concordance of their model without any additional experiments. Put another way: in Figure 5 the authors show a complex network of 3 miRNA influencing about 50 genes based on GroupMir prediction. They also performed expression microarray on these samples - where is the data showing what actually happened to these 50 genes? (or as many that are available on the array). We are shown a handful of genes in Table 4 – but those are presumably handpicked. This would allow an understanding of how accurate the model is.

Given the low concordance between the qPCR and miRNA profiling data, and the lack of wet-lab validation of their models, it is not possible to get an idea of the accuracy of the data, which is the major weakness of this study.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I have no competing interests.