Reviewer’s report

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

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Reviewer: Claudio Casoli

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Major Compulsory Revisions

The efforts to systematically examine miRNA profiles in PBMCs of HIV-1 infected subjects for new HIV-1 “biomarkers” discovery is of clinical/scientific relevance. Biomarkers are urgently needed for HIV management to distinguish between active and asymptomatic latent HIV infection. The current study proposes to determine the feasibility of detection of the differentially miRNAs expressed in PBMCs between control, LVL- and HVL-HIV-1 positive subjects and, analyzing the transcriptome profile and predicted target gene, to construct the miRNA-mRNA regulatory networks. The authors indicate that gene expression is significantly altered in PBMCs in response to virus replication; interestingly the infected individuals, with low or undetectable viral load, exhibit a gene expression profile very similar to control or uninfected subjects. As regards this point, the authors should better explain the status of the uninfected subjects. Are these subjects HIV-1 exposed uninfected?

The greatest weakness in this proposal is the lack of substantial data on PBMCs subpopulations. Although the use of miRNA signature in PBMCs for HIV-1 infection prognosis is an intuitive approach, the authors show complex data that largely involve various cell subtypes with different function vs. correlation with miRNA profile. The PBMCs composition is misleading regarding miRNA expression profiles (see CD4 number which resulted 1/10 in HVL respect to control or LVL) since sample processing and data collection resulted inadequately addressed. The authors should plan to study miRNAs in a single cellular subtype of PBMCs, now.

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.