Reviewer's report

**Title:** Response to M. tuberculosis RD1 selected peptides in Ugandan HIV-infected patients with tuberculosis

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**Reviewer:** Philippe Henri LAGRANGE

**Reviewer's report:**

**General**
This preliminary report deals with the TB diagnosis accuracy of the ex vivo immune response to RD1 selected peptides, measured with an ELISPOT technique, in 20 HIV infected patients with sputum positive TB pulmonary disease. It compared this accuracy with an other ELISPOT test using 2 intact RD1 proteins. These immunological data are also evaluated in relation to the CD4+ counts and the HIV viral load in the patients at the time of TB diagnosis. Moreover, a part of these patients (9 and 12, respectively) were retested at 3 and 6 months after starting specific anti-TB treatment. At the time of TB diagnosis, similar accuracy was found using the 2 groups of antigens, even if statistics showed some differences when applied to absolute sum ESAT-/CFP10 spot counts. However, due to the fact that these 2 responses were shown to be CD4+ related, the AUC of the spots/CD4+ counts did not differ significantly. The same is also indicated in Table 2. Thus, the statement that the RD1 selected peptides response is associated with active TB disease in HIV-infected individuals, but not the RD1 proteins (in the discussion) has to be changed.

Since, this preliminary study, as discussed by the authors, presents limitations, the principal being the small number of patients and mostly the controls, the statements comparing the 2 tests (in the abstract and in the conclusion) should to be more accurate. Individual small or major discordance between the 2 tests should be indicated.

**Specific comments:**
- **Title:** it should be more specific indicating that the HIV-infected patients are patients with smear positive pulmonary tuberculosis, as described in M&M and results. Such HIV-TB co infected patients are not really difficult to diagnose as compared to smear negative HIV-TB co infected patients that represent the most difficult group to be diagnosed as early as possible.
- **Abstract:** the exact number of evaluated HIV-TB coinfected patients needs to be indicated.
- **Results:** The correlation between the RD1 selected responses and the clinical, microbiological radiological data, being indicated in the subtitle (page9) are not given in the text, apart the fact that the culture were negative after 6 months of therapy. Since, the authors did wrote in the M&M that the sputum examination was performed monthly, if would be interesting to describe the microbiological
follow-up (either as the semiquantitative smear test or the time of culture positivity) at different time points. It would be also interesting to evaluate such individual microbiological follow up with the individual spots follow up (at 3 and 6 months). Relative to the significant, decrease of the RD1 selected peptides spots, it is shown that the levels reached at 6 months of therapy was not complete for several patients. The same seems to be occur when the authors used the RD1 proteins. This is not discussed later. Why? Did these patients being followed after stopping the treatment? Are they more prone to develop relapse? The Figure 4AB is not indicated in the text.

- Table: in the table 2 the reference to Rangaka should be indicated as a reference number.

- Discussion: The inverse correlation between the individual HIV load and the number of spots could be associated with the same inverse correlation with the individual CD4+ counts. The reference (28) indicated in page 12 (line 17 and 20) is not appropriate.

- References: There are two references 29. All references beyond the number 29 need to be adjusted in the text and in the reference list.

In conclusion, minor essential revisions need to be done before this report could be accepted.

What next?: Accept after minor essential revisions

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 interest's"