Reviewer's report

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

**Version:** 1  **Date:** 14 September 2007

**Reviewer:** Hazel Dockrell

**Reviewer's report:**

**General**

This interesting pilot study describes the response to selected RD1 region peptides from M. tuberculosis in Ugandan HIV patients coinfected with HIV. The results indicate that obtaining a ratio of spot forming cells to the CD4 count may provide a sensitive and specific test for tuberculosis.

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**Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)**

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**Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)**

1. Methods. The HIV infected subjects without TB were recruited as control subjects “to assess changes in spot forming cells over time”. This statement is confusing as the longitudinal data shown is only from the TB – HIV coinfected group.

2. There is no statement concerning whether the HIV infected subjects (± active TB) were receiving anti retroviral therapy. This information is necessary in order to interpret the changes in responses over time. How did the CD4 counts change over this six month period?

3. Two of the “non TB” controls had high ESAT6 / CFP10 peptide responses, and three gave good responses to the ESAT6 and CFP10 proteins. Have any of these subjects subsequently developed TB?

4. Some statement could be added about whether combined ELISPOT/CD4 count ratios are likely to be used as a research tool, or as a routine diagnostic test in the settings where coinfection with TYB and HIV are common.

5. I do not think a lack of response to two RD1 proteins/peptides can really be used to define anergy, in the absence of an antigen such as PPD or a non-mycobacterial antigen such as Candida. (p8)

6. Discussion, lines 1 – 4. The results presented show a better association of
ELISPOT responses to the RD1 peptides with active disease than of responses to the RD1 antigens, but the results on pages 8 – 9 and in Figure 1 seem to show a similar trend for the protein responses, and it would be better to say these responses did not change significantly (p9). The exact p values should be shown for the RD1 protein differences in Figures 1b and 2b.

7. Table 1. A statement should be included that the groups with/without active TB were not matched for extent of HIV infection.

8. Table 2. This needs to be labelled more clearly as a ratio rather than as a frequency of SFCs.

9. The control group is inconsistently labelled as no active TB, no TB patients, and referred to as the group without TB; also the Figure legends say 1 A-B but 2AB etc.

10. The English requires some editing; for example, I would prefer “selected RD1 peptides”; overtime should be “over time” throughout, p12; line 3 of second paragraph, “only one patient gave and indeterminate result”; lines 6 – 7, “thus an impairment is expected in the presence of severe immunosuppression”.

Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after minor essential revisions

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 declare that I have no competing interests.