Reviewer's report

Title: IP-10 response to RD1 antigens might be a useful biomarker for monitoring tuberculosis therapy

Version: 2 Date: 27 February 2011

Reviewer: Payam Nahid

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The authors have addressed my concerns from the first review. Even with a smaller, more refined set of 17 patients (16 of whom are culture confirmed), the changes in RD1-selected peptide stimulated IP10 and IFNg are significant. Interestingly, despite all patients being treated successfully at 6 months, some still have stimulated IP10/IFNg levels go up or stay unchanged, tempering any conclusions that one might wish to draw. As an exploratory study, these findings are interesting, but should be viewed as hypothesis generating and in need of a larger, better characterized cohort for confirmation. In light of these issues, I'd suggest that the authors further temper their conclusions (particularly in the abstract) by reiterating that these findings are hypothesis generating and need to be confirmed in a larger, well-characterized cohort of treated TB patients (much as they have stated at the end of the discussion).

I highlight a few minor residual issues in the revision:

1) Methods, page 6 - middle of page: My read is that cases were defined microbiologically, either with sputum smears or culture, however, later on in the manuscript, the authors state that one case was a clinical diagnosis. Please clarify how a case was defined in the methods. Either include clinical diagnosis (without bacteriologic confirmation), or exclude the patient that was not culture or smear positive from analyses.

2) Methods, page 6 - bottom of page: Please check spelling of rifampicin and pyrazinamide.

3) Methods, page 7: In the response to reviewers, the authors state that IP10 was measured using a R&D kit, however, the methods continue to say a BD sciences kit was used. Please clarify.

4) Results, page 10 - top of page: It would be more accurate to state that of 41 HIV-uninfected individuals previously described, 17 subjects met eligibility criteria for the study, and to state more clearly what the eligibility criteria were in the methods.

5) Results, page 10 - top of page: Please provide the mean duration and range for treatment to be completed in the 17 patients. I understand that each patient was initiated on a standard short course regimen, but how long did it take to complete?

6) Results, page 12- top of page: "When considering the highest IP-10 response
to either ESAT-6 or CFP-10 selected peptides per single patient, the median IP-10 secretion was significantly higher at the time of diagnosis (median: 5116 pg/ml; IQR: 2207-7063) than at the end of treatment (T6) (median: 73 pg/ml; IQR: 0-5222) (p=0.0060)". Does this mean you compared highest IP10 response to either ESAT6 or CFP10 to the same antigen at T6, or did you compare the highest IP10 response to either ESAT6 or CFP10 at T0 to the lowest IP10 response to either ESAT6 or CFP10 at T6? Please clarify.

**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 declare that I have no competing interests