Reviewer's report

Title: Identification of tuberculosis-associated proteins in whole blood supernatant

Version: 1 Date: 3 November 2010

Reviewer: Marc Jacobsen

Reviewer's report:

The authors identified tuberculosis-associated proteins in whole blood supernatants of in vitro cultured unstimulated and antigen stimulated samples. The results are confirmed in tuberculosis patients and control study groups with distinct ethnical background using different methods.

Major Compulsory Revisions:

Although the study is well performed and the results are plausible I have concerns with regard to the usability of the protein markers identified. The retinol binding protein-4 and fetuin-A may be differentially expressed for different reasons (e.g. other infections, nutrition, genetic background) independent of tuberculosis. This hypothesis is supported by the finding that concentrations of fetuin-A in tuberculosis patients from Vietnam (p. 16, line 4, median 210µg/ml) and healthy controls from Japan (p. 15, line 6, median 211µg/ml) are similar and also retinol binding protein-4 concentrations between these two groups are likely not significant. The authors must discuss this and should also show both results from Japan and Vietnam study groups in one figure.

These heterogeneity candidate protein levels in study groups from different countries questions the usability of these markers as biomarkers in tuberculosis. To verify a role of these proteins as markers of active tuberculosis and/or recovery under chemotherapy one would need analyses during the course of chemotherapy from individual tuberculosis patients.

Minor Essential Revisions

The analyses of supernatants after M. tuberculosis specific stimulations are less informative since very small numbers of T cells respond to in vitro restimulation. Therefore the protein results should be correlated with the IFN# concentrations detected in individual donors.

Discretionary Revisions:

The numbers of samples used for each analysis should be clearly stated in the Methods section and in all legends to figures.

P. 17, line 22, the term 'post-treatment' is unclear since no patients post treatment have been included.

Please use line numbers for the review process.
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 interests.