Reviewer's report

Title: T-cell and serological responses to Erp, an exported Mycobacterium tuberculosis protein, in tuberculosis patients and healthy individuals

Version: 1 Date: 29 May 2007

Reviewer: Pascal Meylan

Reviewer's report:

General
In the present paper, the authors characterize in quite exquisite details the immune response against a recently described protein, with the awowed goal of developing a test able to differentiate latent from active Tb.

The major problem in this respect is that neither the patient number (especially as not all patients had samples available for each test modality; see for instance patient number in table 1) in the different groups, nor the statistical evaluation are appropriate to accurately determine the potential of anti-Erp responses to differentially diagnose latent from active Tb.

For instance, small groups of patients with results which are not obviously normally distributed require non parametric tests and descriptors (e.g. median instead of means). In addition, the question is not so much as to whether groups have statistically different results, but rather whether the different groups are recognized by the test, i.e. given a chosen threshold, the test will accurately classify the patient as sick with Tb or latent infected, defining a sensibility and specificity indeed subjectable to a ROC analysis.

The study falls short of this and thus can only be considered as a pilot study suggesting that anti-Erp responses should be studied in an appropriate fashion to this end.

The definition of the patients groups is also debatable. Indeed, a group of BCG vaccinated individuals were divided, according to ESAT tests into "healthy BCG+" and "latently Tb BCG+". This is confusing. On one hand, BCG vaccination is confounding groups that should be formed with Tb-exposed individuals with any testing supporting infection, but with a negative work up for tb disease. I feel like the current definition by ESAT-6 response is not the state of the art of defining patients categories.

In fact the proper denomination of the current groups should rather be "BCG vaccinated, M. tb-non infected" and "BCG-vaccinated, M. tb-infected"

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

The two tables are very difficult to grasp; there should be a way of expressing these results in a way that makes them easier to understand. The text is of little help to this end

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

The manuscript should have the pages numbered!

There are numerous locutions that are inappropriate or indeed francisisms. I propose to have the text edited by a English native or at least someone with a good command of English: some examples

Abstract, end of conclusions: should read "do not"

Introduction: a gene encodes a protein, but a protein is a cell surface component.

p4 top: This antigen might offer a useful approach in the diagnosis (not management) of tuberculosis disease versus latent infection

Subjects and methods

p5: patients who (not that, they are not things)

next paragraph: this group was further divided (not divised) into 2 ...

non infected (instead of no infected)

Antigens: were dilutions tested for each assay? " and the optimal concentration was chosen for each antigen", but what are the criteria for optimal?

Lymphoproliferation, either quote a paper for that standard method, or if describing, mention the incorporated label

Elispot: the fact that the cell preparation does not matter might arguably be moved into a first paragraph of the results.

Methods last paragraph: the title should mention that this is an ELISA

Results.

If there were disseminated infections, those may have to be analysed separately as they may be anergic
third paragraph: according (not regarding) to their responses to ESAT-6.

Lymphoproliferation: there are no negative controls. To give percents in a group of three is somewhat misleading. As there are many statistical comparisons between groups, I wonder whether a Bonferonni’s adjustment should be applied, which may change the conclusions.

T cell responses: here the argument of overlap between the groups particularly applies. See figure Erp for instance

Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions.

Level of interest: An article whose findings are important to those with closely related research interests.

Quality of written English: Needs some language corrections before being published.

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests.