Reviewer's report

Title: CD4 lymphocyte dynamics in Tanzanian pulmonary tuberculosis patients with and without HIV co-infection

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Reviewer: G C Cooke

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Review of Andersen et al

General Comments

This is a quite detailed piece of work that has tried to make good use of the opportunity to carry out a large study of TB (incl HIV). The strengths of it are the relatively large numbers, the study of well matched controls and the investigation of CD4 in HIV negative TB patients.

I do have some significant concerns over the data presented, mainly about the message the reader is supposed to take away beyond straightforward documentation of changes. It may be that the manuscript was finished some months ago, but to say the evidence of timing ART is “moderate” suggests that authors had not read several recent high profile clinical trials on this question (NEJM and CID 2011). Reference to these studies and presentation of data in context of these studies would greatly increase its relevance and might go some way to explaining the phenomena seen in those studies.

Some questions seem particularly relevant give those findings

How do CD4 counts change when analysis is stratified by baseline CD4?
Why do CD4 counts apparently rise in the first two months and then fall?

The clear finding of significant rises in CD4 counts in HIV neg patients is potentially interesting and not well recognised. Discussion of the its potential role in paradoxical TB reactions is important to discuss. I assume there is no clinical data on paradox, paradoxical TB-IRIS or unmasking TB-IRIS where the T Cell dynamics could all shed light.

The paper would be strengthened by a discussion of mechanisms (compartmental shifts in CD4?)

Minor comments that would strengthen the paper

- It would benefit from being read through for sense, some ideas are not clearly presented
- Abbreviations should be standardised (MTB, etc)
- More detail on what way previous results are conflicting – is there a hypothesis
to be tested?
- Ten cell leader (clarify what this means?)
- PTB +ve/-ve terminology is unusual and confusing (they are all assumed to have PTB but some are sm-ve/cult-ve)
- CD4 percentages would be helpful to understand the dynamics
- Graphs would benefit from CIs to help interpretation
- More detailed on the nutritional intervention – what was being used? Could it include anything with potential immunomodulatory effects e.g. Vit D