Reviewer's report

Title: Effects of infection and disease with Mycobacterium tuberculosis on serum antibody to glucan and arabinomannan: two surface polysaccharides of this pathogen

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Reviewer: Anali Conesa-Botella

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The authors describe serum antibodies levels against 2 capsular polysaccharides (arabinomannan and Glucan) extracted from Mycobacterium tuberculosis. They demonstrated that patients with active TB or history/treated TB had higher antibody levels against those 2 polysaccharides compared to unexposed PPD-negative individuals.

Unfortunately, as commented by the authors, the sample size was small and despite interesting findings, the discussion lacks nuances in the interpretation and the authors are too enthusiastic about the possible implication of their results.

Discretionary Revisions
- Results: L 130: “the date of the positive 130 PPD ranged from 1959 (retested positive subsequent to sample donation) to 1998.” Confusing: rather give the delay between the last PPD+ test and the enrolment date.

Minor Essential Revisions

Introduction:
- L 51: (epidemiology of TB), please add reference.
- Mtb is not a Gram-positive organism, but an acid-fast organism.

Material and methods:
- When were the sample collected (Jan-Dec 1999?), and tested (in 1999 or recently)? Were the patients retrospectively selected?
- Group 2 would be latent TB?
- The authors might increase understandability of their results by indicating the p-values on the figure 1.
- It would be easier for the reader to follow the explanations if the authors would give names to the 4 groups instead of numbers. For example: PPD-negative, exposed, latent TB, active/past TB.

Major Compulsory Revisions
- Were the arabinomannan and glucans were specific to Mtb? Was lipoarabinomannan also recognized? Were the antibodies monoclonal or
polyclonal? Do they recognize those structures from other bacteria or non-tuberculous mycobacteria?

- Conclusion of abstract: “These data suggests that antibody responses to the CP of Mtb may be useful for serodiagnosis, and that vaccines based on these CPs may stimulate protective responses.” The conclusion of the abstract should be more nuanced.

- “What could be the origin of CP antibodies in group 0?” Please rephrase. Suggestion: Interestingly, antibodies were also detected in the PPD-negative group…

This is an interesting question which I would like to be answered. I’m not convinced at all by the answer from the authors (lack of clarity and flow of idea in that paragraph. Please use adequate terminology (infection: latent?)

According to the authors, TB would result from latent and reinfection of TB in “less resistant” people. No place for new infection (I guess that in US the prevalence of latent TB not so high)?

- “Similar to other capsulated pathogens, cross-reactive anti-polysaccharide antibodies were probably generated by exposure to environmental mycobacteria or non-pathogenic enteric or pulmonary bacteria [13-15].”

Are the authors talking of cross-reactivity (lack of sensitivity: one antibody against an antigen which is able to recognize another antigen of very similar configuration) or that the antibody detection was targeting tuberculous and non-tuberculous Mtb (lack of specificity of the antigen selected for the antibody detection)?

- I was expected some discussion about:
  o Are the antibodies protective against Mtb (exposed and latent TB would have higher levels; good for vaccine) or are they present during disease? In this paper, instead authors suggest that antibodies present in patients with active or past TB are good target for vaccine. But those antibodies might also result from a past contact with TB. Discussion on this would be interesting.
  o The interpretation of the significance in different type of antibodies (IgA= mucosal defense; IgG/M=> serological defense).

**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