Author's response to reviews

Title: Cytotoxic response persists in subjects treated for tuberculosis decades ago

Authors:
Laura E Savolainen (laura.e.savolainen@helsinki.fi)
Pekka Koskivirta (pkoskivirta@gmail.com)
Anu Kantele (anu.kantele@hus.fi)
Heikki Valleala (heikki.valleala@hus.fi)
Liana Pusa (liana.pusa@hus.fi)
Riitta Tuompo (riitta.tuompo@hus.fi)
Benita Westerlund-Wikström (benita.westerlund@helsinki.fi)
Tamara Tuuminen (tamara.tuuminen@helsinki.fi)

Version: 3 Date: 2 December 2013

Author's response to reviews: see over
Dear Editor Dr. Dalia Goletti

Thank you for your suggestion to accept our revised manuscript. We have now concerned your request and included a section discussing the limitations of the study.

Limitations concerned by referee Thomas Scriba:

3. The sample sizes in the different analyses shown in Figures 1 and 2 are different. For example, in figure 1 the “mod” group shows 7 datapoints for GrB expressing cells and 5 for IFN-# expressing cells. What is the reason behind this? This should be stated in the manuscript. These sample sizes of 5-7 for some groups are also very small – likely too small to perform robust statistical tests and draw meaningful conclusions about differences in specific immune responses, which are notoriously heterogenous.

RESPONSE: Next section has been added to discussion rows: 256-262.
Relatively small cohorts of patients with active TB and LTBI which were not matched for gender or age is a limitation of our study. Another limitation of ours as of many similar studies is our current inability to stratify TB infection into categories compatible with recently accepted notion that TB infection is in fact a continuum of infection severity starting from real latency through subclinical infection and ending with active disease [Barry CE 3rd et al. 2009]. From the point of view of the today’s knowledge the dichotomous division of infection into active TB and LTBI seems too simplistic.

We hope that our paper will be now acceptable for the publication in BMC Infectious diseases.

Sincerely yours
Laura Savolainen, MSc
Tamara Tuuminen, MD, PhD, specialist in clinical microbiology