Reviewer's report

Title: Rv1985c, a promising novel antigen for diagnosis of tuberculosis infection from BCG vaccinated controls

Version: 1 Date: 4 February 2010

Reviewer: Kazue Higuchi

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Major Compulsory Revisions
1) Although the cut-off value of Rv1985c-ELISPOT appear to be set as the same as T-SPOT.TB, the appropriate cut-off value of Rv1985c-ELISPOT should be determined based on obtained data in this study using ROC analysis. Therefore, authors should analyze the data using ROC to determine the appropriate cut-off value of Rv1985c-ELISPOT, and show the sensitivity and specificity of this assay.

2) The combination of Rv1985c and PATHOZYME-MYCO IgG yielded the promising sensitivity, which is similar to TST. Since the specificity of the combination was superior to TST even in BCG-vaccinated population, this system could be replaced with TST. However authors did not discuss on this point. I would like authors to discuss on this point.

3) Although authors concluded that Rv1985c can be used to immunologically diagnose TB infection, Rv1985c alone cannot be used to immunologically diagnose TB infection based on the data in this study. Thus, authors should alter their conclusion, such as “Rv1985c can be used to immunologically diagnose TB infection along with ESAT-6 and CFP-10”.

Minor Essential Revisions
1) RD expresses the region of difference, not the region of deletion (page 2, line 10 and page 4, line 6).
2) In background of abstract, insert (TB) (page 2, line 14) after tuberculosis, and use TB afterward in abstract (i.e. page 2, lines 17 and 18).
3) Insert a hyphen between BCG and vaccinated (page 2, line 14 and page 5, line 1).
4) Add a reference for the sentence “Among people infected with TB bacilli, .... Time during their life” (page 3, line 17).
5) Add “by TST” between “BCG-vaccinated individuals” and “is difficult” (page 4, line 3).
6) Delete a period before reference (page 4, line 8).
7) Once LTBI is used in page 4, line 2, use LTBI after ward (i.e. page 4, lines 17 and 21; page 5 line 13; page 13, line 6; page 14, lines 8 and 12).
8) Move the full names of ESAT-6 and CFP-10 in page 6 lines 7-8 to page 5 line
16.

9) In the methods, please add the strain of M. tuberculosis and how M. tuberculosis was grown for cloning and expression of Rv1985c (page 6).

10) In line 17 of page 7, a degree seems to be a square.

11) Please add the full name of SFUs in line 20 of page 7.

12) Please describe a type of an automated ELISPOT Reader (page 8, line 2).

13) Add (data not shown) after the sentence “……Rv1985c was expressed during the growth in vitro” (page9, line 14).

14) Insert a hyphen between T and cell (page 10, lines 1 and 3).

15) Add p-value after the sentence “ However, no statistic ………and LTBI groups” (page 10, line 8).

16) In the legend of Figure 3, change “latent TB infection” and “healthy control” to LTBI and HC, respectively. Also change “P-values of SFU…..” To “P-value of absorbance…..”.

17) In Table 1, change “Healthy, BCG” to “healthy, BCG-“.

18) In Table 3, change healthy controls in the title to HC.

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.