Reviewer's report

Title: Utility of the REBA MTB-Rifa(R) Assay for early detection of rifampicin resistant Mycobacterium tuberculosis and correlation with multi-drug resistance

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Reviewer: Howard Takiff

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Review Cho REBA BMC Inf Dis August 2013

The manuscript from Cho et al describes the use of the REBA Mtb Rifa line probe assay to detect rifampicin resistance in clinical isolates and sputum samples. The work was well done and the study is interesting and perhaps relevant, especially in light of the many MDR and XDR cases in South Korea. The REBA assay seems to perform well with isolates and AFB positive sputa.

Major Compulsory Revisions

1. The only serious deficiency is that there is no real comparison with the Xpert system, which has been widely accepted for detecting Rif resistance. The authors mention that the GeneXpert system is expensive and that the incorporation of new rpoB targets is complicated, but don't provide adequate information to show the advantages of the REBA assay. If the authors are proposing the REBA system as a viable alternative technique, they need to give accurate estimates of the cost, labor involved and overall time to obtain a result with the REBA system, and describe how it might be employed in the daily workload in a setting with a TB and resistance burden similar to that of South Korea, and perhaps also its usage in other settings.

2. In the discussion the authors try to indirectly address the XPERT's lauded ability to detect M. tb and RIF resistance in AFB negative sputa, but if this point is included, it should be more directly addressed in a comparison of XPERT to REBA. The XPERT system has been so widely praised and advocated that it is now incumbent upon studies with other techniques to demonstrate their relevance, beyond simply a catalogue of the rpoB mutations found.

3. The inclusion in the title of RIF resistance correlating with MDR-TB is perhaps unnecessary, as this correlation has been well established. The inclusion of the new rpoB loci that are present in 1% of isolates from South Korea may not be justified for kits used in other parts of the world, but perhaps these regions of the gene have not been systematically examined in studies from other countries and may be more prevalent than thought.

4. It would be worth reviewing the literature to see how many previous studies would have identified this mutation in Rif resistant isolates, but that is not essential for this publication.

5. The manuscript is generally well written, although a number of minor problems
with the writing are listed below, in detail, as BMC has no copy editor. The main
problems are in the Discussion and Conclusions, which seems to have been less
carefully edited than the other sections. It is somewhat long and rambling, with
occasional run-on and confusing sentences that don’t clearly explain the points
the authors wish to make.

6. The 2 novel mutations don’t seem to be included in Table 2.

Minor compulsory and discretionary points:

7. Background line 109: this intro is a bit too long with a repetition of things that
have been stated in many articles.
8. Line 111 “like GeneXpert COMMA
9. Line 113 - 4 The phrasing is awkward, and pricing details on XPERT might
help make the argument for the REBA technique.
10. Line 127- 130 This sentence is long and awkward and slightly confusing.
11. Line 172 WAS used
12. Line 174 – omit one “of”
13. Line 199 “deposited” seems inappropriate here if it means affixed to the
membrane
14. Discussion:
15. Line 273 than “in” other reports
16. Line 282 maybe eliminate “tendencies”
17. Line 264-5 was higher than in Europe, Africa and the United States, and the
mutation frequency of His-526...
18. Line 289 How would geological differences affect mutation selection? M. tb
strain differences might.
19. Line 292 high level phenotypic resistance (eliminate “of”)
20. Line 292 – 3 The sentence is awkward; how about something like, “frequency
and distribution of mutations was similar in both sputum samples and RIF
resistant isolates, however some mutations and most of the double mutations
seen in the isolates were not found in the sputum samples.”
21. Line 295-97 Unclear what the authors wish to assert.
22. Line 299 – 310 This paragraph is awkward and confusing and should be
rewritten.
23. Line 317-8 Please rewrite this sentence with only one “previously”, and if
preserving the current form please change to … but “it” has been noted.
24. Line 321 – Consider adding “sterically” preclude

25. Conclusions:The second sentence is long, complicated and confusing. It
should be broken up and rewritten.
**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:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.