Reviewer’s report

Title: Association of mutation patterns in gyrA/B genes and ofloxacin resistance levels in Mycobacterium tuberculosis isolates from East China in 2009.

Version: 1 Date: 24 December 2010

Reviewer: Paolo Miotto

Reviewer’s report:

This manuscript by Cui et al reports the association of ofloxacin (OFX) resistance levels with different mutations in gyrA and gyrB genes related to fluoroquinolone (FQ) resistance in Mycobacterium tuberculosis isolates from East China.

The Authors characterized the gene sequence of gyrA and gyrB in 192 M. tuberculosis clinical isolates (95 OFX-resistant, 97 OFX-susceptible) and then compared mutations with MIC levels. The Authors found that there were not statistical significant correlations between MIC levels and mutation at specific codons nor specific aminoacidic changes.

Methods and results are clearly written; however the discussion and conclusions sections should be further deepen and revised.

Discretionary revisions

Comment 1

Along the manuscript drug concentrations are reported sometimes as µg/mL whereas some other as mg/L. To help the reader I suggest using always the same concentration unit.

Comment 2

Materials and Methods
Paragraph “Drug susceptibility test”: I suggest “The drug susceptibility test (DST) of selected strains was…”.

Comment 3

Acknowledgements
“This work was supported by the grant 10QA11405800 from the Shanghai Rising-Star Program to [PI]”.

Minor essential revisions

Comment 4

Carefully check text format (apex, spaces…). Abbreviations should be described at the first time of use; once introduced, abbreviations should be used along the all manuscript.
Comment 5

Materials and Methods
Paragraph “MIC determination”: replace “according to the reference manual [20]” with “as described by Kumar and colleagues [20]”.

Comment 6

Results
Paragraph 1: I suggest “S95T mutation in gyrA is a natural polymorphism”; please provide appropriate reference.

Comment 7

Results
Paragraph 2: please report percentages using only one decimal, as along all the manuscript.

Comment 8

Discussion
Carefully check for the use of abbreviations (e.g. M. tuberculosis, fluoroquinolone, ofloxacin…all these have been already introduced in the manuscript; please use abbreviations also in the discussion section).

Comment 9

Discussion
Paragraph 3: I suggest “amino acid modification at codons 90, …”.

Comment 10

Discussion
Paragraph 4, statement 2: eliminate “But”.

Comment 11

Discussion
Paragraph 4: add “[according to] several published studies”.

Comment 12

Tables
I suggest to provide data as follow:

<table>
<thead>
<tr>
<th>Codon mutation</th>
<th>Nucleotidic change</th>
<th>MIC (Value 1) (Value 2) …</th>
</tr>
</thead>
<tbody>
<tr>
<td>… … n of strains</td>
<td>(n of strains) …</td>
<td>…</td>
</tr>
</tbody>
</table>
and then report range and median values in the text (results section) or in the
table on other columns.

Major compulsory revisions

Comment 13

Materials and Methods
Paragraph “Selection of strains”: the Authors state that clinical isolates were
collected from epidemiologically unlinked cases. Please report how did you
performed epidemiological selection (e.g. based on genotyping techniques such
as IS6110 or similar).

Comment 14

Materials and Methods
Paragraph “PCR”: please report GenBank accession numbers for each gene.

Comment 15

Materials and Methods
Paragraph 3: please explicitly state why D94F mutation has been excluded from
the ANOVA analysis.

Comment 16

Discussion
The discussion section could be further deepen and modified in order to be more
exhaustive.
The Authors refer to the paper by Yin; since the paper was about levofloxacin, I
suggest to made some appropriate comments.
I suggest to refer and compare your results with those obtained by Sun Z. et al in

Comment 17

Discussion
Paragraph 4: the Authors state that some mutations found are not related to OFX
resistance. Even though, in principle, these statements may be acceptable,
because the lack of an experimental proof-of-principle (e.g. cloning mutations in
well characterized/reference strains) I suggest to better clarify that these
statements are hypotheses/inferences.

Comment 18

Conclusions
Last statement: please better clarify the statement “Furthermore, our findings
indicate that the association of the extent of drug resistance and corresponding
gene mutations varied due to different anti-TB drugs”.

**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:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests