Author's response to reviews

Title: Lack of association between Fas -670A/G polymorphism and risk of cervical cancer: an Update by meta-analysis

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Version: 4 Date: 31 March 2013

Author's response to reviews: see over
Dear Atienza,
Thank you very much for your letter and advice. We have revised the manuscript, and would like to re-submit it for your consideration. We have addressed the comments raised by the reviewers, and the amendments are highlighted in red to Professor Sousa and in blue to Professor Viatte in the revised manuscript. Point by point responses to the reviewers’ comments are listed below this letter. We hope that the revised version of the manuscript is now acceptable for publication in your journal.
I look forward to hearing from you soon.
With best wishes,
Yours sincerely,
Wuning Mo
Corresponding author
Dear Professor Sousa,

Thank you very much for your letter. I am very grateful to your comments for our manuscript. We would like to express our sincere thanks to the reviewers for the constructive and positive comments.

Based on your comment and request, we have made extensive modification on our original manuscript. Here, we attached revised manuscript with the correction sections red marked, which was attached in the formats of MS word for your approval. A Cover letter answering every question from you was also summarized and enclosed.

Major Comments
- Authors must completely revise the manuscript since there are several English language and grammar errors in the manuscript that should be corrected. Authors should request the help of a native English speaker to help then to rewrite the manuscript all over.

  About the English writing of the manuscript, we ask for native English speaker to revise the paper before it was submitted to the magazine and this time. I don’t know whether it has reached to your magazine’s standard.

- Title: it is not necessary to refer the number of subjects in the study in the title, moreover, this number is the sum of cases and controls, therefore readers could be influenced by the title.

  Answer: “the number of subjects” in the study in the title has been cancelled. Correction has been made in the revised version.

- Introduction: It is not clear why the authors have chosen the -670A/G Fas polymorphism. Is there a plausible biological role? Were there many studies performed? What were the main results from previous studies? Are there any other important SNPs on this gene?

  Answer: Several sentences have been added in the Background (page 3, paragraph 3 and page 3, paragraph 4, line 6) in the revised version to address this issue.

- Methodology: Authors did not used a correct methodology for meta-analysis design: 1) authors have not used a true QUERY for search publications, the use of specific words is not always correlated with the MESH terms and therefore it is probable that the number of articles to be included can be higher; 2) in inclusion and exclusion criteria authors have used unspecific terms that did not provide a specific significance to the criteria (e.g. "genotypes or other information that could help us infer the results");

  Answer: 1) Several sentences have been changed in the Methods (page 3, paragraph 5, line 4) in the revised version to address this issue. Although the search strategy makes a little change, the literatures included in our meta-analysis consequently do not change.

  2) The sentence has been changed in the Methods (page 4, paragraph 2, line 3) in the revised version to address this issue.
- Results and Discussion: Authors should separate these two parts, since in results it is only important to summarize the results from the risk analysis, sensitivity analysis and heterogeneity tests.

Answer: Correction has been made in the revised version.

- Discussion: 1) Authors should start by summarizing the biological role for this polymorphism and relevance for either clinical or epidemiological studies; 2) biases to the study should be addressed (e.g. number of studies, search criteria, type of population, number of cases in each study, etc...); 3) since the number of manuscripts is very short (n=6) authors, should be more prone to discuss the results and make critics to them individually or grouped by result.

Answer: 1) The biological role for this polymorphism and relevance has been stated in Discussion (page 6, paragraph 4).

2) Some biases to the study have been addressed in our revised manuscript. The number of cases and types of population was shown in Table 1. The number of studies was shown in Table 2.

3) Several sentences have been added in the Discussion (page 7, paragraph 4, line 1) in the revised version to address this issue. We have tried our best to discuss the results and made critics to them grouped by result.

- Conclusions: Conclusions are usually a summary of the major results of the study and not a description of data and studies... this is more likely to be used in conclusion.

Answer: Correction has been made in the revised version.

Minor Comments:
- Article does not fill completely the style of the manuscript for this journal (e.g. missing the page number, etc.). Please see the template in http://www.biomedcentral.com/bmcmedgenet/authors/instructions/researcharticle

Answer: We have made amendments in journal style of BMC medical genetic in the whole manuscript and corrections have been made in the revised version to address the issue.
Dear Professor Viatte,

Thank you very much for your letter. I am very grateful to your comments for our manuscript. Based on your comment and request, we have made extensive modification on our original manuscript. Here, we attached revised manuscript with the correction sections blue marked, which was attached in the formats of MS word for your approval. A Cover letter answering every question from you was also summarized and enclosed.

Minor Essential Revisions:

1) The analysis in “White” (as defined by the authors) is presented as a meta-analysis in this particular subgroup in the abstract and main text body, but is not, since there is only one study considered “for analysis”. Therefore, no meta-analysis could be performed in “White”. This point should be made clearer in the abstract and manuscript.

   Answer: The meta-analysis concerned with “White” has been cancelled in the revised manuscript.

2) No references to studies on the role of Fas polymorphisms in cervical cancer are mentioned in the introduction. Though references are provided later in the manuscript and are the subject of the meta-analysis performed by the authors, the subject should be better referenced in the introduction.

   Answer: The relevant reference which conducted on Fas polymorphism with cervical cancer has been added in the Background (page 3, paragraph 4, line 6) in the revised version to address this issue.

3) Extensive language editing will be eventually required at some places for the reader to better understand the authors. As an example, the beginning of the “Conclusions” (“Although previous meta-analysis maybe involve some parts of the relationship between Fas -670A/G polymorphism and cervical cancer risk, its eligible studies are not quite comprehensive.”) is not clear and requires editing. Do the authors refer to a previously published meta-analysis? If yes, why is it not mentioned in the introduction and why are the references not cited after the above-mentioned statement?

   Answer: We have discussed the shortage of previous meta-analysis in the Background and Discussion (page 3, paragraph 4, line 9 and page 6, paragraph 5, line 1). The relevant reference has also been added in the revised manuscript. About the English writing of the manuscript, we ask for native English speaker to revise the paper before it was submitted to the magazine and this time. I don’t know whether it has reached to your magazine’s standard.

4) Conclusions: “When stratifying for race, significant association was detected in neither Asian populations nor African populations, suggesting there were no difference in genetic background and the environment they live in.” This statement seems to be too broad. The genetic distance between different ethnicities considered
together by the authors for analysis could be substantial. It is not excluded that true effects are present in one specific sub-population, but undetected due to lack of statistical power (as they mention it later in the same chapter), or diluted / cancelled out by population stratification issues when different study populations are grouped together for analysis.

Answer: Several sentences have been changed in the Discussion (page 7, paragraph 4, line 3) in the revised version to address this issue.

5) Ref. 25 is from “J. Exp. Med.” not “Exp. Med.”
Answer: Correction has been made in the references in the revised manuscript (Ref.24).

Discretionary Revisions:
1) Abstract: All results as presented in the main results table 2 are included in the abstract. The authors might consider shortening the abstract.
Answer: New version of abstract has been made in the revised manuscript

2) Author might consider replacing the term “race” by “ethnicities”; “human race” is unclearly and controversially defined in biology.
Answer: All the term of “race” has been replaced by “ethnicities” in the revised manuscript.