Author's response to reviews

Title: Interaction of functional NPC1 gene Polymorphism with smoking on coronary heart disease

Authors:

Weiwei Ma (maweiw82@gmail.com)
Jing Xu (xujinggnijux@yahoo.com)
Qianqian Wang (wangqiangian84@gmail.com)
Ying Xin (xinyin20081115@163.com)
Lin Zhang (EPUSKY@sina.com)
Xinxin Zheng (zhengxxfuwai@gmail.com)
Kai Sun (sunkai@sglab.org)
Hu Wang (whcqq@yahoo.com)
Rutai Hui (huirutai@sglab.org)
Xiaohong Huang (huangxhong12@gmail.com)

Version: 4 Date: 13 July 2010

Author's response to reviews: see over
Dear Biomed Central Editorial,

Enclosed you could find the revised version of the manuscript MS: 1931598682359280 “Interaction of functional NPC1 gene Polymorphism with smoking on coronary heart disease” by Weiwei Ma, Jing Xu, Qianqian Wang, Ying Xin, Lin Zhang, Kai Sun, Hu Wang, Rutai Hui and Xiaohong Huang. The editor’s and the reviewers’ comments have been responded point by point in the attachment. We hope that this will be to your satisfaction.

Thank you very much for your consideration and looking forward to hearing from you at your earliest convenience. Please do not hesitate to contact me if you need any further information.

Yours Sincerely,

Xiaohong Huang

We thank the reviewer Pawel Niemiec’s time and the comments were very helpful in improving our manuscript.

1). The quality of English is still unsatisfactory (e.g. see results section, NPC1 gene polymorphism and cigarette smoking subsection).
Response: Thank you very much for your comments. We have improved the quality of English in the whole text. We have highlighted all changes.

2). The Authors did not give a references to recommendations and standards used in the classification of CAD, MI or risk factors. The references 16 and 17 are inadequate.
Response: Thank you very much for your comments. We have revised our manuscript as you suggested. See reference 17 (about hypertonction) and 19 (about DM) in re-revised manuscript. See page 4, line 96 and 104.

3) There are the results of comparison of AG/AA, GG/AG and GG/AA in the table 3, but not AA/AG, AG/AA, AA/GG, and this is a fundamental difference > protective/predisposing effect (univariate ORs are: 1.08, p=0.47 for AA/AG, 1.46, p=0.65 for AG/GG, 1.57, p=0.023 for AA/GG).
I do not understand why the authors presented these results. This analysis does not take into account the presence of three genotypes in the population and the authors consequently eliminated from the analysis one genotype (e.g. in AA/AG comparison, the GG genotype is ignored). 

Response: Thank you very much for your comments. We have corrected the error and merged the table 3 and table 4, by only presenting two by two genotype comparisons. See table 3 in page 13.

4) Once again, I suggest to substitute the models of inheritance by concrete genotypes comparisons (e.g. GG vs AA+AG) in whole text. This will improve the readability of the Paper.

Response: Thank you very much for your comments. We have revised our manuscript as you suggested. We have substituted the models of inheritance by concrete genotypes comparisons (GG vs AG+AA, GG vs AG vs AA, GG+AG vs AA) in whole text.

5) Results section, NPC1 gene polymorphism and cigarette smoking subsection.
   a) convert “table 4” to “table 5” in the text
   b) I’m not sure that the results of this subsection and subsequent conclusions (also title) are correct, because there is still no numerical data (N of smokers with concrete genotypes), but only ORs and P values in the table 5.

Response: Thank you very much for your comments. We have converted table 4 in the text. Moreover we have checked against the results of NPC1 gene polymorphism and cigarette smoking subsection and we promise that ORs and P values in the table 5 are accurate. However we don’t know how to merge the numerical data in the table 5, because that will make the table more complex. We have presented the numerical data (N of smokers with concrete genotypes) in this letter.

<table>
<thead>
<tr>
<th>genotype</th>
<th>n%</th>
<th>AA</th>
<th>AG</th>
<th>GG</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>nonsmoking</td>
<td>438(54.89)</td>
<td>299(37.47)</td>
<td>61(7.64)</td>
<td>798</td>
<td></td>
</tr>
<tr>
<td>smoking</td>
<td>547(58.63)</td>
<td>331(35.48)</td>
<td>55(5.89)</td>
<td>933</td>
<td></td>
</tr>
</tbody>
</table>

Six subjects were absent.
We thank the reviewer Fakhredin Sayed Tabatabaei’s time and the comments were very helpful in improving our manuscript.

1. The results are presented in dominant, additive, and recessive models. These models are only appropriate for Mendelian diseases. Multifactorial and polygenic (complex) disorders do not usually follow such genetic models. Instead we may only consider two by two comparisons between genotypes, as well as the trend. The authors should merge table 3 and 4, by removing those genetic models and only presenting two by two comparisons. Table 5 should also present two by two comparisons between the genotypes instead of the models. I suppose what the authors mean by "additive model" is actually the trend between the three genotypes. In this case, those results may remain. Table 6, and the text should also be amended accordingly.

Response: Thank you very much for your comments. We have revised our manuscript as you suggested. We have substituted the models of inheritance by concrete genotypes comparisons (GG vs AG+AA, GG vs AG vs AA, GG+AG vs AA) in whole text.

2. The authors claim in conclusion: "...in smokers, NPC1 variants seem to confer protection to coronary heart disease onset." The word "onset" should be removed, because this study is based on prevalence and not the incidence of the disease.

Response: Thank you very much for your comments. We have removed the word onset in conclusion as you suggested. See page 7, line 246.

3. There are multiple spelling/gramatical mistakes in the manuscript that has to be corrected before publication.

Response: Thank you very much for your comments. We have improved the quality of English in the whole text. We have highlighted all changes.