Author's response to reviews

Title: An association between hOGG1 Ser326Cys polymorphism and the risk of bladder cancer in non-smokers: a meta-analysis

Authors:

Changwei Ji (dr.jichangwei@gmail.com)
Zhao Liu (dr.zhliu@hotmail.com)
Huimei Chen (chenhuimei@nju.edu.cn)
Hongqian Guo (dr.guohongqian@gmail.com)
Changjian Liu (dr.cjliu@hotmail.com)

Version: 3 Date: 5 June 2012

Author's response to reviews:

June 5, 2012

Dr. Christna Chap
Senior Executive Editor
BMC-series

Dear Dr. Chap,

Thank you very much for your kind support and advice. We have revised the manuscript, and would like to re-submit it for your consideration. We have addressed all the comments made by the reviewers and attached them to this letter. The manuscript has been carefully revised by a professional editor to make the English easy to read and understand. All the amendments are highlighted in red in the revised manuscript.

Looking forward to your reply.

Yours sincerely,

Changjian Liu, M.D.

321 Zhongshan Road
Department of Vascular Surgery
Medical School Affiliated Drum Tower Hospital
Nanjing University, Nanjing 210008, China
The authors performed a meta-analysis on a single functional SNP for risk of bladder cancer. A total of 7 case-control studies were identified which included 2474 patients and 2408 controls. There was no overall association with bladder cancer risk. However, when the data were stratified by smoking, the 326Cys allele significantly increased the risk for bladder cancer and the ORs in the additive model, homozygote contrast, and recessive genetic models. There are no substantial concerns regarding this manuscript. Although the authors have improved the writing, the grammar and English still needs to be polished a bit more.

Response: We would like to express our sincere thanks to the reviewer for the constructive and positive comments. We have carefully revised the language of the manuscript with the help of a professional technical editor who is a native English speaker.

Specific Comments

1. Page 6. What do the authors mean by “relatively nearer”?
Response: We apologize for this typo error. It has been deleted in the revised version (page 6, paragraph 1).

2. Page 6. The authors state, “Thus, a total of 7 published studies met the inclusion criteria, having case–control designs and being available genotype frequencies.” “Having” is misspelled. Moreover, the sentence is poorly written. Here is a suggestion: “Thus, a total of 7 published studies met the inclusion criteria which included a case–control study design and published genotype frequencies.”
Response: We greatly appreciate this suggestion, and have made the corrections as suggested (page 6, paragraph 1).

3. The authors use “non-smokers” which is an ambiguous definition since it could include never smokers and former smokers. Please clarify the definition. If the authors are defining “non-smokers” as never smokers, be sure to define “smokers” as ever smokers (current smokers and former smokers combined).
Response: We appreciate this insightful suggestion. We define “smokers” as current smokers and former smokers, and “non-smokers” as never smokers. We have revised the manuscript accordingly in the Materials and Methods section.
4. In Tables 4 and 5 please include either in a footnote or modify the table to indicate which genotype(s) is (are) the referent group(s) so the reader knows which group is associated with an increased risk.

Response: We have added the footnotes in Table 4 and Table 5 in the revised manuscript.

5. Figures 1 and 2. It’s unclear what is represented in the “Total” group.

Response: The “Total” in Figures 1 and 2 represents the sum of the column. The mistakes in Figure 2 which made this misunderstanding have been corrected in the revised version.

Replies to Reviewer 2

1. The conclusion from this study may not be generalized to other studies, because 6 out of the 7 studies included in this meta-analysis are hospital-based and only 1 is population-based. There are many population-based studies of bladder cancer that have collected genome-wide genetic data. Without including data from those population-based studies limits the implication of the findings from this study.

Response: We agree with the reviewer that the conclusion made from population-based studies is more solid than from hospital-based studies. However, in our defined topics and criteria, most of the available data obtained from the literatures are hospital based. We analyzed these data and made a primary conclusion in current study. With more population-based data available in the future, we will be able to make a more solid conclusion on this topic.

2. Publication bias may exist for the analysis stratified by smoking status. Only 4 out of 7 studies provided stratified data, and 3 studies contributed to the dominant / recessive model analysis, and two studies contributed to the additive model. It is very likely that these published studies provided such stratified analysis only when there were significant heterogeneity observed between smokers and non-smokers.

Response: It is true that the heterogeneity and publication bias may exist, mainly due to the limited number of studies discussing the topic. We have tried to avoid these problems by using random-effects models and Funnel plots methods. Nevertheless, as suggested by the reviewer, further studies are needed to systemically evaluate these problems and draw more accurate conclusions.