Author's response to reviews

Title: Association between novel PLCE1 variants identified in published esophageal cancer genome-wide association studies and risk of squamous cell carcinoma of the head and neck

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Author's response to reviews: see over
May 23, 2011

Dear Dr Renske Steenbergen:

Thank you for your email of May. 19, 2011, in which you encouraged us to further revise our manuscript (MS: 8472926144986010) entitled "Association between novel PLCE1 variants identified in published esophageal cancer genome-wide association studies and risk of squamous cell carcinoma of the head and neck."

Here we submit the revision of our manuscript that was revised, point by point, according to reviewers’ comments. We would like to thank the editors and the reviewers for their valuable comments and recommendations that have greatly improved the quality of this paper. We hope our responses are satisfactory.

Sincerely,

Qingyi Wei, M.D., Ph.D.
Professor of Epidemiology

Enclosures
Response to the reviewers’ comments and suggestions on “Association between novel PLCE1 variants identified in published esophageal cancer genome-wide association studies and risk of squamous cell carcinoma of the head and neck” (MS: 8472926144986010) submitted to BMC Cancer by Ma et al.

Reviewer: Balraj Mittal

Reviewer's report:
Major Compulsory Revisions
None.

Response: Thanks for the comments.

Minor compulsory revision

1) In Material and Method section, author should mention the cutoff value of P value.

Response: As suggested, we have added a sentence in the revision to state the cut off value of P as following:

“All statistical analyses were two sided, and P <0.05 was considered statistically significant.” (Page 8)

2) P value of most of the association observed are either marginally significant or did not remain significant after Bonferroni’s correction in subgroup analysis except the association of rs11599672 with non-oropharyngeal SCCHN and association of rs2274223 with alcohol habits at non-orpharyngeal sites. Considering the high significance observed at genome wide levels, the findings of present manuscript are interesting. Author should discuss this discrepancy in the text.

Response: Thanks for the suggestions. In the revision, we have discussed the results as following:

“Even after Bonferroni corrections, the association of rs11599672 with non-oropharyngeal SCCHN and association of rs2274223 with drinking at non-orpharyngeal sites remained significant, suggesting different roles of these polymorphisms in the etiology of two different tumor subsites… The findings from GWASs and our study implied that polymorphisms of PLCE1 are likely to be associated with the development of cancers related to tobacco and alcohol exposure, which will need further validation from large-studies on different cancers…”(Page 14)

3) The frequency of smokers and alcohol users were significantly higher on patients compared to controls. The possibility is that association of genetic variants with these environmental factors observed in present study may also be due to this difference rather being due to effect of genetic factors alone.
Response: We understand the reviewer’s concern. The distributions of smoking and drinking were significantly different between cases and controls, which might be the confounding factors for the association of genetic factors with SCCHN risk. However, we have adjusted these two factors in our data analysis and conducted the stratification analysis by smoking and drinking. We think these methods may reduce the confounding effect of these two factors on our results.