Author's response to reviews

Title: Genetic Polymorphisms of Nampt Related with the Susceptibility to Esophageal Squamous Cell Carcinoma

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Author's response to reviews: see over
Reviewer: Lin Zhang
Reviewer's report:
Major Compulsory Revisions
1. In the abstract, the authors should include the 95%CI.
2. The investigators failed to describe how their chose these SNPs.
3. The authors did not provide pictures of the three SNPs PCR-RFLP result and sequencing analysis. This problem should be addressed by submitting representative pictures.
4. The potential function of these SNPs should be addressed in the manuscript.
Level of interest: An article of importance in its field
Quality of written English: Needs some language corrections before being published
Statistical review: No, the manuscript does not need to be seen by a statistician.

Responses to Pro. Lin Zhang:

Thank you for your comments on our paper. We have revised it according to your suggestions.

1. We have added 95% CI of every statistical result in the abstract.
2. Three SNPs of NAMPT, including rs61330082 in the promoter region, rs2505568 and rs9034 in the 3’untranslated region, were selected because of their potential effects on the influence of Nampt expression, which were related with the development of ESCC. We have added the reason in the background.
3. To reduce the size of this manuscript, we omitted the pictures of the three SNPs PCR-RFLP results and sequencing analysis. These were added in Supplementary Figure 1.
4. Genetic mutation at the rs61330082 loci in the promoter region might influence the structure or function of the Nampt protein. Rs2505568 or rs9034 at the 3’ untranslated region are important for the regulation of gene expression. These potential functions of the three SNPs were separately stated in the background in two paragraphs regarding each SNP’s effects on ESCC.
5. This manuscript has now been edited by a native English speaker with scientific expertise.

I hope these changes will make this paper more acceptable for publication.

Yours sincerely,
Ziping Chen
Reviewer: Enrica Rumiato
Reviewer's report:
The authors described the impact of three selected genetic polymorphisms in <italics>NAMPT<italics> gene on the risk to develop esophageal cancer carcinoma, studying 405 ESCC patients and 405 matched controls. They found that the rs61330082 polymorphism is associated with the risk to develop ESCC and it could be also a risk factor in haplotype with the two other <italics>NAMPT<italics> variants. The aim of the study is original, however, there are several major limitations.

Major revisions
English needs a deep revision (tenses, sentence structure, acronyms, grammatical errors, etc.). It is unpleasant to read and difficult to judge the scientific content of the manuscript in this form.
Furthermore:
1. In the Abstract there are several discrepancies between the Results and Conclusion as concern genotypes (lines 42 and 50). Many contradictions are also present in the text. The authors should be consistent throughout their article.
2. The gene <italics>NAMPT<italics> is cited as “Nampt” all over the manuscript and in the Title. The authors should follow the Human Genome Organization Gene Nomenclature (capital/italics for genes and only capital for proteins).
3. The Discussion must be improved and better structured, and the authors should also clearly state the limitations of their work.

Minor revisions
1. The study is technically sound: there are more recent methods than the RFLP-PCR. A validation set is desirable.
2. The authors should also include a correction for multiple tests.
3. All the percent values should be approximated in the same way (in the Abstract, Tables and text).

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests: I declare that I have no competing interests
Response to Pro. Enrica Rumiato:

Thank you for your attention and critical suggestions regarding our manuscript. Overall, the comments were fair, encouraging and constructive, and as such, we have learned much from them. We are therefore glad to have made the changes you have suggested. Our responses to your comments are enclosed.

Major revisions
1. The manuscript has now been copyedited by a native English speaker.
2. Our results demonstrated that genotypes CT and TT and allele T at rs61330082 of NAMPT were significantly decreased in the ESCC cases compared with the controls. In other words, genotype CC and allele C were significantly increased in the ESCC cases compared with the controls. It was suggested that genotype CC or allele C at rs61330082 could increase carrier susceptibility to ESCC. Therefore, I think that it was reasonable.
3. Thank you for your comment regarding the correct written format for genes and proteins. This have now been corrected throughout the manuscript.
4. The Discussion has been edited as you suggested, and the limitations were stated.

Minor revisions
1. There are many more novel and convenient methods than PCR-RFLP. However, as our lab was limited in its capabilities, PCR-RFLP was our only feasible option. In the future, we wish to use those methods for new and similar work.
2. We have corrected some multiple tests.
3. The percent values have been approximated in the same way.

I hope these changes will make this manuscript more acceptable for publication.

Yours sincerely,
Ziping Chen