Author's response to reviews

Title: Genetic polymorphisms of MDM2 and TP53 genes are associated with risk of nasopharyngeal carcinoma in a Chinese population

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Author's response to reviews: see over
Dear Editor,

Thank you very much for your letter and advice. We have revised the paper, according to reviewers, and the amendments are highlighted in RED in the revised manuscript. We also responded point by point to the comments as listed below. We hope that the revised manuscript is acceptable for publication.

Thank you.

With best wishes,

Sincerely yours,

Yuehui Liu

Replies to Reviewers

We would like to thank the reviews for the constructive and positive comments.

Replies to Reviewer 1

1. I should be good to present some figures from PCR and direct sequencing analyses with appropriate legends and fragments, nucleotides description.

--We added two figures for genotyping and DNA sequencing.

2. It is not necessary to show the TNM, EBV and MTS data in Table 1. The data are not directly linked to the aims, as the paper does not inform (was not aimed) to NPC biologic variability and aggressively. Furthermore, these data are mentioned in the results paragraph in the main text.

--Although our stratified analysis did not found significant different between these clinical characteristics and TP53 and MDM2 polymorphisms, we consider these data may help the reader to grasp our case population. Therefore, we’d like to maintain them in Table 1.

Replies to Reviewer 2

1. The official gene symbol for the gene encoding p53 protein is TP53.

--We have corrected as suggested.

2. Based on the associations presented this reviewer suggests to avoid the term “supermultiplicative” as it is also used in mathematics and genetics. The term “more than multiplicative”, as used in methods and in the cited paper, seems
adequate at this stage of the analysis which must be confirmed in further studies.

-- We have corrected as suggested.

3. Methods: The DNA amount of 100 ug for p53 PCR seems to be high. For the p53 genotypes, the restriction pattern should be given.

-- It is 100ng.

4. The authors should compare allele frequencies with already published ones.

-- I added one sentence to describe this question in discussion.

5. mRNA quantification: β actin does not seem to be the ideal reference gene as expression levels of β actin are much higher.

-- Although β-actin was not very ideal reference gene, so far we can not find another gene to replace it. Moreover, its ct value was also acceptable, around 15-17. Therefore, we’d like to maintain this reference gene.

6. Are data available on smoking and alcohol consumption and do these risk factors affect NPC risk?

-- Smoking and alcohol are very important factor for NPC development, but our clinical data for these section are not available. Smoking data of 236 cases were miss and 358 cases missed alcohol data. Since over half cases have not data, it will get a big bias result by using these data to do the stratified analysis.

7. Discussion, line 4: increased levels of MDM2 expression in human bone marrow: reference?

-- It is NPC tissue but not bone marrow.

8. The authors must urgently revise the references. They are not presented as they appear in the manuscript and some of the references listed are not present in the manuscript. It is not sufficient to copy the reference list from another manuscript.

-- I am sorry to make these mistake, we have corrected as suggested.

9. The manuscript is rather well written but at some positions difficult to understand and should therefore be revised (examples are: discussion, paragraph 3, line 5: “Moreover, another meta-analysis studies …. were significantly increase susceptibility”; or Results, Gene-gene interaction, line 6: what is the meaning of mentioning the second OR at this position?)
--I change the sentence: Moreover, another meta-analysis study reported that the TP53 Pro/Pro polymorphisms was significantly increase susceptibility to NPC. And I delete the second OR in paper.