Author's response to reviews

Title: Association of polymorphisms in survivin gene with the risk of hepatocellular carcinoma in Chinese han population: a case control study

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Author's response to reviews: see over
Dear Dr. Tim Sands,

Thank you very much for your letter and advice. We have revised the paper, and would like to re-submit it for your consideration. We have addressed the comments raised by the reviewers, and the amendments are highlighted in red in the revised manuscript. We hope that the revision is acceptable, and I look forward to hearing from you soon.

With best wishes,

Yours sincerely,

Li Yuhua
2011.5.5
We would like to express our sincere thanks to the reviewers for the constructive and positive comments.

We rearranges and reanalyzes our data, correcting our errors about the results in the revised version.

Replies to Reviewer 1

Specific Comments

1. The authors need to shorten the manuscript significantly and focus it solely on the “negative association”. The proposed “protective” genotype combination might be mentioned, but should not discussed in details, since data are simply too weak to draw any conclusion on this finding. The usage of “might perhaps” by the authors reflects the very low confidence of their finding. The shortening should be done in all parts. The working hypothesis at the end of the introduction includes statements about the potential functional role of the investigated polymorphisms in relation to HCC. Since no functional aspect is studied, the authors should clarify that they simply studied the prevalence of these polymorphisms in context to HCC.

The manuscript has been shortened in all parts, especially in the discussion. The discussion has been changed as required in the revised version. The use of “might perhaps” is avoided as much as possible. In addition, our hypothesis and aim are revised (page 5, paragraph 2 ) in the revised version.

2. There are numerous mistakes in style, grammar and format (different letter type, sizes, missing spaces after dots or commas, before parenthesis). Furthermore, there are typos like Ppulation, genetypes, moreover, hepatitis, thranslation. The authors have to correct these issues throughout the complete manuscript.

Correction has been made in the revised version.

3. The presentation of odd ratios needs always the corresponding 95% -confidence interval throughout the complete manuscript.

95% CIs for haplotype analysis have been added in the revised version.
4. The number of the ethical vote for the study should be included. 
The number of the ethical vote has been added in the ‘Study Population and Samples’ (page 6, paragraph 1, line 5) to address this issue.

5. Data within the text are not always the same as those presented in tables (e.g. OR of hepatitis B or history of hepatitis. 
The data has been analyzed and checked once again, corrections have been made in the results in the revised version.

6. The discussion is mostly redundant to the introduction and results. The authors should focus on the interpretation/comparison of their data with other studies. Functional speculations without having investigated these issues should be omitted. 
Corrections have been made in the discussion in the revised version.

7. The authors might also consider presenting a figure with the PCR products before and after restriction to strengthen their data. 
Figure 1-6 has been added in the revised version.

8. Table 6 contains identical ORs for HBSAg+ and Ha for all three genetic models. This is not possible. 
Since different genetic models are for haplotypes, while environmental factors are identical in different genetic models, so environmental factor’s parameters might be identical for different models. In addition, we estimates their parameters several times, ORs for HBSAg+ or Ha’s are identical for different genetic models.

Replies to Reviewer 2

1. In introduction, the authors sayed that "to date, the relationship between survivin gene polymorphisms and the risk of HCC has not been studied yet worldwide" there is a study published recently the Bayram S et al. / Cancer Epidemiology 2011 Feb 4. [Epub ahead of print] PMID: 21296634, doi:10.1016/j.canep.2011.01.004 entiteld “The association between
the surviving #31G/C promoter polymorphism and hepatocellular carcinoma risk in a Turkish population " and the term of not been studied must be reviewed in the section of introduction and discussion. It would be useful to use the data of Bayram S et al. / Cancer Epidemiology 2011.

The reference 28 has been added in the introduction and discussion in the revised version.

2. Sample size is small in present study and statistical power is low in analyses. Considerable explanation should be given on power of study.

Correction has been made about the discussion in the revised version, small sample size is a possible cause for the negative results in present study, while due to the lack of power calculation in our study, we don’t discuss the study power in details. Nonetheless, we pointed that “further large sample studies are required to clarify our results”.

3. The expression level of survivin in different rs8073069, rs9904341 and rs1042489 genotypes should be examined in normal liver as well as HCC tumors.

We don’t investigation the SNP’s function in the present study, while four references (Reference 24,25,26,30) were introduced in the background or discussion. Two (24,26) were in-vitro studies on cells, the other two studies (25,30) investigated the expression level of survivin with different SNP genotypes in the population. Yang (25) examined tumors and adjacent non-tumor liver tissues, the survivin were very low in non-tumor liver tissues, he only studied the association of SNP with survivin expression in tumor tissues, while Maria (30) only examined the tumor tissues.

4. The English style of the paper should be revised and numerous typing errors should be corrected.

Correction has been made in the revised version.

5. Discussion is too long; it should be shorter and crisp

Correction has been made in the revised version.