

Dear editor Xue-jiao Wang,

Thank you for giving us a chance to revise our article. The editor and reviewer gave valuable and precious suggestions and reminding. We answered the suggestions point by point as follows and ticked the revision in the blue color. And if there is any question, please do not hesitate to connect us.

Yours sincerely,

Yuan Yuan

Editor's comments:

1. Page 1, for example: Koji Takeuchi, Department of Pharmacology and Experimental Therapeutics, Division of Pathological Sciences, Kyoto Pharmaceutical University, Misasagi, Yamashina, Kyoto 607-8414, Japan

Answering: The author's addresses had added as direction.

2. Page 2, A copy of the full approved grant application form(s), consisting of the information section and body section, should be provided to the BPG in PDF format.

Answering: The copy of the approved grant application form, is provided in PDF attachment which uploaded in the system.

3. Page 5, please provide all authors abbreviation names and manuscript title here.

Answering: All authors abbreviation names and manuscript title are added.

4. Page 6, Should be "cancer[1,2]". No blank. Please check throughout the article.

Answering: We revised all the reference and words and made them "No blank".

5. Page 17, Please finish this part following the below reminders(highlight)

Answering: The highlight has added in Page 17-18.

6. Page 25, some request about Tables.

Answering: We revised as the direction. The tables submitted are longer than two pages are published as online-only supplementary material.

7. Page 27, some request about notes in illustrations and tables.

Answering: We revised as the direction. Data with statistical significance in a table was denoted using superscripted alphabetical lettering, such as ^a $P < 0.05$. Other notes in tables or under illustrations were expressed as F1, F2, F3.

Reviewers' comments:

1. Reviewer 1(02861175): Dear authors. after read your manuscript, I have same advises and minor corrections. please see file reviewer comment. I think your study is a basic to clinical study (translation study), so the result can be implicated in the clinical in HCC management.

(1). Page 4, According to the title ... Prognosis: A Case-control Study; these statement have to note in the methods and who or what is the case and or the control subject (sample)?

Answering: Thank you for your kind advice. We added the information about the case and control subject in the abstract in Page 4. “.....in a total of 1338 samples including 521 HCC patients and frequency-matched 817 controls.”

(2). Page 4:What are samples gotten? When was the study done? Where was the study done?

Answering: Thank you for your valuable suggestion. The samples were gotten from unrelated Chinese population. This study was done from 2012 – 2015 at the First Hospital of China Medical University. We have added these information in the abstract in Page 4.

(3). Page 7: Are there any criteria inclusion and exclusion?

Answering: Thank you for your suggestion. The criteria inclusion and exclusion are as follow: 1). The participants who underwent surgical operation were diagnosed with HCC by pathological confirmation, in accordance with the WHO classification; 2). Removal the other pathological type of liver cancer (gallbladder cell carcinoma, mix-type liver cancer and hepatosarcoma). We have added them in Page 7.

(4). In fig 1, there are 2 studies. I need your confirmation about this, I think the second study (study prognosis) is the sub analysis of the main study (study risk). Please make the exact study design

Answering: Thank you for your suggestion. We have revised the fig 1.

(5). Page 23, Placed the sentence like the title of paragraph (above).

Answering: Thank you for your suggestion. We have revised it.

(6). The statement in conclusion must be simple (1 or 2 sentences) without any suggestions.

Conclusion is the answer of hypothesis. If any statement was related with the study limitation and suggestion for next study, please noted in the end of discussion.

Answering: Thank you for advice. We revised it and made the conclusion simply.

2. Reviewer 1(03104092): It is a well written manuscript that adds to the knowledge of the impact of polymorphisms in lncRNA on HCC risk and prognosis. For such reasons, even if the number of patients analyzed was small for a statistical study, it is worth reporting and will open the opportunity to expand the analysis in a larger population as well as other races. One spelling mistake in the Introduction section was noticed: the HOTAIR gene was misspelled HOTH AIR in one occasion. I would also consider modifying slightly the title to include the gene ID, making it more specific.

Answering: Thank you for advice. We revised the misspelled HOTH AIR in Page 6. And we also include the gene ID which following the gene names in Page 6, to make it more specific.

3. Reviewer 1 (03067188): This is an interesting study aiming to investigate the association of 12 tagSNPs in 3 onco- lncRNAs with hepatocellular cancer in Chinese population. Authors concluded that 3 SNPs in HOTTIP, one promoter SNP in MALAT1 and one haplotype of HOTTIP gene were associated with hepatocellular cancer risk. Additionally, the two-way interaction of HOTTIP rs17501292-MALAT1 rs619586 polymorphisms showed a decreased effect on hepatocellular cancer risk. The study is well-designed. The topic of the study is original. Sample size is large. The manuscript is well-written, methodology is sufficient, including a multivariate approach and results are presented in a suitable fashion. This is a manuscript that deserves to be published.

Answering: Thank you for your professional comments.