Author's response to reviews

Title: Genetic variant I148M in PNPLA3 is associated with the ultrasonography-determined steatosis degree in a Chinese population

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

I am pleased to submit the revised manuscript, “Genetic variant I148M in PNPLA3 is associated with the ultrasonography-determined steatosis degree in a Chinese population” to BMC Medical Genetics for review and possible publication.

In the revision, per reviewer 2’s suggestion we use “the ultrasonography-determined steatosis degree” throughout the paper to accurately reflect the content of the paper. All the changes are marked in red ink. Please find enclosed our point-by-point responses to the concerns raised by the reviewers.

We thank you and reviewers’ energy and time on our manuscript, and look forward to your favorable reply.

Sincerely,

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Reviewer 1:
Minor compulsory revisions:
There are several typos that should be corrected in the revised sections of the manuscript.

We corrected typos we were able to identify and asked a scientist, who is a native speaker, to proofread the manuscript. The changes include:

1) In the Abstract Methods: we changed “were” to “was”.
2) The second paragraph of Background: we changed “suggest” to “suggests”.
3) The last paragraph of Method: we inserted “by” between “and” and “a proportion test”.
4) The second last paragraph of Results: we changed “increasing” and “decreasing” to “increase” and “decrease”, respectively.
5) The last paragraph of Results: we changed “detected” to “detect”.
6) The second last paragraph of Discussion: we corrected the misspelled “association”.
7) The second last paragraph of Discussion: we rephrased the use of suggest: “… suggested that PNPLA3 be involved …”.
8) The last paragraph of Discussion: we rephrased a sentence “however, their interaction towards NAFLD susceptibility was insignificant by either a case-only or a case-control study”.


Reviewer 2
The manuscript has been improved. This reviewer still thinks that a major limitation of this study is that the same population has been used and published with a very similar outcome.

Using the same sample, we previously published a one-paper letter (reference 17) simply replicating the association between the PNPLA3 I148M variant and NAFLD affection status (203 cases and 202 controls). In the current report, we investigated two other topics: 1) association between I148M and the ultrasonography-determined steatosis degree, and 2) the interaction between I148M variation and body mass index towards NAFLD susceptibility and plasma alanine aminotransferase levels. Therefore, we are really reporting different though related research topics in this paper.

The second is the assessment of degree of steatosis by ultrasonography. The used of the word severity is misleading for the liver community. Then, the phrase "ultrasonography-determined severity of steatosis" and should be replaced throughout the manuscript by the phrase used by the own authors "ultrasonography-determined steatosis degree". This is particularly important in the title.

We admit a major limitation of the study is that the steatosis grade was assessed based on ultrasonography instead of liver biopsy, as we put in the discussion session. However, we are afraid it reflected a major restriction of liver study in developing countries, at least in China. For the same reason, there were still guidelines published on using ultrasonography for the diagnosis of NAFLD (reference 26) in the 21st century. Fortunately, in the literature there was study showing an accuracy of 88% in the diagnosis and staging of fatty liver from a direct comparison between the pathological and ultrasonographic findings (references 38).

To be accurate, we use the term “ultrasonography-determined steatosis degree” throughout the paper. We thank the reviewer for the suggestion.