

Format for ANSWERING REVIEWERS

May 4th 2016

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 26094-edited.doc).

Title: Genetics of Non-alcoholic fatty liver disease: from susceptibility and nutrient interactions to management

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Name of Journal: *World Journal of Hepatology*

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We thank all the reviewers for their comments on the manuscript. The manuscript has been improved according to the suggestions of reviewers:

Reviewer 1:

Comment 1: It is not sufficiently clear that loci influencing liver enzymes do not necessarily represent influences in NAFLD (see recent discussion in Int J Obes (Lond). 2015 Feb;39(2):279-87.

Response: We agree with the reviewer and the reprint quoted, that it is not clear that loci influencing liver enzymes do not necessarily influence the risk of NAFLD. Further, we also agree that neither obesity nor NAFLD are simple monogenic disorders.

Comment 2: Equally important, discussion on the role of obesity and/or insulin resistance is not sufficient.

Response: The review has focused on the genetics of obesity and insulin resistance in the context of NAFLD.

Comment 3: Ancestries prevent strong conclusions, and consequently, this section should be completely rewritten.

Response: Various studies have consistently associated variants in PNPLA3 gene with NAFLD across ancestries. Although limited data are available on TM6SF2 gene, it is well studied including the functional aspects. We have deleted TM6SF2 gene from the conclusions and based on the data available on PNPLA3 retained the gene.

Reviewer 2

Comment 1: Figure 2 is too simple. I suggest including some mechanisms to make it more attractive.

Response: We have modified the figure as suggested by the reviewer by adding mechanism.

Comment 2: About TM6SF2, authors should include some information about the parallel risk of cardiovascular disease.

Response: Paragraph added

Comment 3: -Before Conclusions, authors should include a new section with future trends.

Response: Paragraph added

Reviewer 3

Comment 1: Review grammar and language polishing

Response: We thoroughly checked for Grammar and language.

Thank you again for publishing our manuscript in the *World Journal of Hepatology*.

Sincerely yours,



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