

RESPONSES TO REVIEWERS' CONCERNS

Sep 5, 2013

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name:4892-review.doc).

Title: Potential Role of *Helicobacter pylori* Infection in Nonalcoholic Fatty Liver Disease

Author: Meng Li, Zhe Shen, You-ming Li

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 4892

The manuscript has been improved according to the suggestions of reviewers and editors:

1 Format has been updated. We've changed the order of the key words, putting "Nonalcoholic fatty liver disease" in the second. We've put the figure 1 legend at the end of the text. Besides, Dr. Shen has provided much help in the revised procedure, and thus he is now added into the author list. Our revised manuscript was also supported by a grant from Zhejiang Provincial Laboratory Animal Science Technology Program of China (No. 2011C37088) and the National Natural Science Foundation of China (No. 81300303). And we have now added this information into the context on the title page.

2 Revision has been made according to the suggestions of the reviewers. And all the revisions in the text are shown using red highlight.

Reviewer(1) 01136482

Comment:

The present review is updated and well written. However, to better understand the review and the data here reported, it is necessary to add a paragraph and to update the references, on the changes of intestinal permeability in patients with NAFLD (Abenavoli et al. Endocrine. 2013). In addition it is necessary to report the role in the liver disease progression of the bacterial toxins, that coming out from the gastrointestinal area via portal blood (Abenavoli et al. Int J Immunopathol Pharmacol. 2010).

Response:

We sincerely believe that the comments of the reviewer were highly insightful and enabled us to greatly improve the quality of our manuscript. Accordingly, we have added a section (later in this manuscript, on pages 10 and 11, highlighted in red) focusing on the possible link between increased intestinal permeability and *H. pylori* toxins. After perusing the references provided by the reviewer, we broaden our reading concerning this point as added references 89-97. We made the assumption that the liver may be damaged by *H. pylori* toxins and constituents circulating in blood coming out from the gastroduodenal area. And it is probably linked with the increased intestinal permeability in patients with NAFLD. In view of the association between *H. pylori* and PBC or CD, the immune response especially cross-reactive antibody response may be involved in the progression. But this concept remains obscure. The current studies are limited. Accordingly, we add a sentence about this part in the core tip (on page 2, highlighted in red). We sincerely thank the reviewer for pondering this aspect to let us update the references and better

understand the role of *H. pylori* infection in NAFLD.

Reviewer(2) 02540714

Comment:

The paper I have received for review raises an extremely relevant clinical problem, i.e. the role of *H. pylori* infection in the pathogenesis of non-alcoholic fatty liver disease (NAFLD). This review article is based on meticulously selected and current literature including 73 studies. The manuscript was divided into sub-sections, which facilitates the understanding of the issues addressed to. In the introduction, the authors discuss the role of infection in the pathogenesis of gastrointestinal diseases, liver diseases, including NAFLD. The figure provided presents the potential mechanism of *H.pylori* effects on NAFLD. The part regarding the results of experimental studies is of great importance. The sub-section devoted to the role of fetuin A in the pathogenesis of NAFLD is noteworthy. To sum up, the paper brings us closer to understanding the role of *H.pylori* infection in the pathogenesis of NAFLD and should be accepted for publication in the WJG.

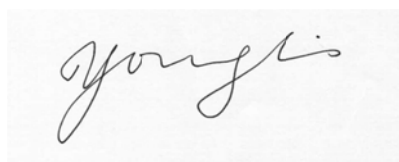
Response:

We are grateful to the reviewer for his/her appreciation regarding the quality of our work and sincerely thank the reviewer for the kind words.

3 References and typesetting were corrected. To have a deeper understanding of this topic, we've inserted several sentences concerning sub-sections in the text as highlighted in red. And we've added 28 new references to make the review more comprehensive. In addition, we've polished our manuscript carefully to make it suitable for publication in the *World Journal of Gastroenterology*.

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

Sincerely yours,

A handwritten signature in black ink, appearing to read 'You-ming Li', is shown on a light gray background.

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