

August 1st , 2013

Prof. Lian-Sheng Ma, President and Company Editor-in-Chief
World J Gastroenterology
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My ID is **00503536**

Dear Editor,

We have revised our invited Editorial entitled “Liver physiology and liver diseases in the elderly” according to the reviewer.

Please find enclosed the edited manuscript in Word format (file name: 4057-Editorial.doc)

Title: Liver physiology and liver diseases in the elderly

Author: Kazuto Tajiri, Yukihiro Shimizu

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 4057

We have listed the answers below (underlined), and revised portions in the manuscripts are also underlined. We believe that those revisions are satisfactory for the reviewers.

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Reviewer #.*00506363*

SPECIFIC COMMENTS MAY CONSIST OF THE FOLLOWING POINTS

Abstract: Gives a clear delineation of the research background, objectives, and conclusions

We have added sentences of background, objectives, and conclusions in the abstract section as suggested..

Please make sure all acronyms are written out in their first usage (i.e. Treg on page 7).

We have checked all acronyms. Regarding Treg, it is first shown on page 6.

Page 9, line 5-6: the phrase “should be avoided” does not make sense at the end of that sentence, omit.

We have omitted the phrase “should be avoided” as indicated.

Page 11, line 2: Omit the word “Therefore”. It was just used in the prior sentence.

We have corrected according to the reviewer’s suggestion.

Page 11, line 18: I believe the sentence should read “while 25.5% **were positive** in those...”

We have added “were positive” as suggested.

Page 12, last sentence: If advancing age is a poor prognostic factor in PBC, then shouldn’t patients after 65 years of age be **more likely** to have advanced disease (not less likely)??? Please check this reference.

We have revised the sentences to make them clear descriptions.

Page 17, last sentence of Summary: should say “hepatic function or **function** of other organs”

We have extensively revised the sentences of Summary.

References: Appropriate

Figure1: Gives a nice summary of discussion

We have added sentences of summary in the figure legend for Fig. 1 as suggested by the reviewer.

Reviewer # 00505151

1. Abstract: "cells are reduced" should be "cells diminish"
- 2 Introduction: liver as well as other organs change with aging, and understanding these changes is
- 3.Introduction: Hepatocytes contain denser body..
- 3 Introduction: levels may decline
4. Introduction: in the elderly than in younger subjects
- 5 Introduction: There are a lot of repeats in paper
- 5 6. Introduction: may be another contributing factor
- 7 Introduction: binds EGF
- 8 Introduction Another mechanism underlying
- 9 Introduction: may be the inhibition
- 10 Introduction: while CD8 T cells
- 11 Introduction: delete with aging.
- 12 Introduction: syringes, shaving blades, and sexual contact.
- 13 too many repeated "in elderly"
- 14 Introduction: reorganize page 11 and 12
- 15 page 14: Old age is a risk factor of DILI because the elderly are susceptible to adverse drug reactions; Delete however associate with a cholestatic type of
- 16 The authors have to fix the flow from one topic to another. The writing is random.
- 17 Being over 60 years of age

We revised above portions according to the reviewer's suggestions. We deleted "with aging" and "elderly" as much as possible to avoid the redundancy. We also revised the flow of the sentences to make logical descriptions.

Reviewer # 00504308

In this manuscript, the authors highlighted liver physiology and liver diseases in the elderly. Reviewer and readers are interested in the field. Attention to the following points would be required to strengthen the impact. The followings are comments for the improvement of manuscript. 1. Cellular senescence is recently reported to be involved in the pathophysiology of various chronic liver diseases and hepatocarcinogenesis. The authors should review it. 2. It is kind to

readers to summarize various liver diseases in the elderly. The authors should make a comprehensive table of them.

1. We added the descriptions regarding the recent reports on hepatocyte senescence in association with liver diseases or hepatocarcinogenesis in the section titled “Morphology of aged liver and microscopic or molecular characteristics of senescent hepatocytes”. We also describes a close association between aging and NAFLD in the “Nonalcoholic fatty liver disease” section (p15).
2. We made a table (Table 1) showing summary of characteristics in liver diseases in the elderly as indicated.

We hope the manuscript is now acceptable for publication in your Journal. We are looking forward to hearing from you soon.

Best regards,

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