

Format for ANSWERING REVIEWERS



March 12, 2017

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 29796-review.doc).

Title: Potential application of neogalactosylalbumin in positron emission tomography evaluation of liver function

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Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 29796

Point-by-Point Response

If you choose to revise your manuscript for resubmission, please follow the steps listed below:

Answer: Yes, we revised the manuscript with tracked and clean versions for resubmission. Our responses point-by-point in italics and bolds listed below.

Step 1. Please revise your manuscript according to the reviewers' comments. To access the reviewers' comments, please log into the Express Submission and Peer-review System (ESPS) by entering your registered e-mail: jinbao0820@163.com and user password: baojin0228.. under the "Author Track Manuscripts" heading at <http://www.wjnet.com/esps/trackmanuscript.aspx>. You are expected to

address each of the points raised by the reviewers in a response letter that is to accompany your resubmission. Please download the manuscript file edited by the editor, located in the “Manuscript” column, by clicking the link and the title line. You will find the editor’s suggestions in the edited manuscript file, which have been added using the Track Changes function.

Answer: Yes, each of the points raised by the reviewers in a response letter has been addressed. And, we have downloaded the edited manuscript file and revised the manuscript in accordance with the suggestions.

All of the revisions that you make to the revised manuscript should be cited in the response letter and highlighted in the updated version of the manuscript. In order to continually improve the quality of peer-review for our journals, we urge authors to carefully revise their manuscripts according to the peer-reviewers’ comments and we promote productive academic interactions between the peer-reviewers, the authors, and our readers. To this end, we include each of the reviewers’ comments, in an anonymized manner, as well as the authors’ responses along with the manuscript’s publication online.

Answer: Yes, we have revised the manuscripts according to the peer-reviewer’s comments carefully. All of the revisions that we made in the revised manuscript have been cited in this response letter and highlighted in the updated tracked version of the manuscript.

Step 2. Please update the manuscript according to the Guidelines and Requirements for Manuscript Revision-Clinical Trials Study. You can find the Guidelines and Requirements for Manuscript Revision-Clinical Trials Study, which includes the detailed writing requirements for the Title, Running Title, Authorship, Abstract, Keywords, Core Tip, Academic Rules and Norms, Tables and Illustrations, Comments and References, as an attachment.

Answer: Yes, we have updated the manuscript according to the Guidelines and Requirements for Manuscript Revision-Clinical Trials Study in the tracked version of the manuscript.

Step 3. Please provide the scientific research process. The authors are asked to submit a report that describes the entire scientific research process that was used to obtain the data and findings presented therein. Once the manuscript is accepted for publication, this report will be released together with the manuscript to promote further in-depth reading by the article's attracted audience, ultimately improving the academic influence of the article. This report should answer the following questions:

- 1 What did this study explore?
- 2 How did the authors perform all experiments?
- 3 How did the authors process all experimental data?
- 4 How did the authors deal with the pre-study hypothesis?
- 5 What are the novel findings of this study?

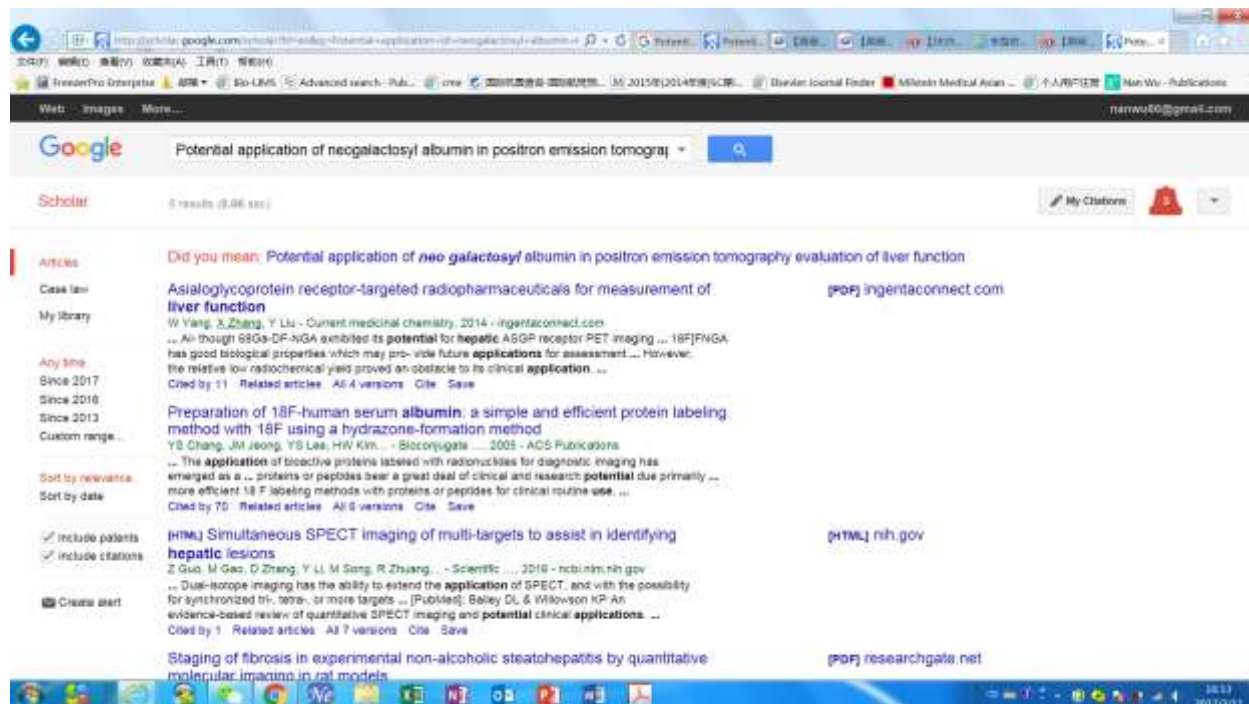
Answer: Yes, we have submitted a document called 29796-Scientific research process which answered all of the questions listed above.

Step 4. Please provide an Audio Core Tip. In order to attract readers to read your full-text article, we request that the author make an audio file describing the final core tip of the manuscript. This audio file will be published online, along with your article. **Acceptable file formats** are .mp3, .wav, or .aiff.

Answer: Yes, we have submitted an audio file called 29796-Audio Core Tip.

Step 5. Please subject the final title of the manuscript to Google Scholar search, and store screenshot images of the results. We strongly suggest that you check the final title of the manuscript using Google Scholar at <http://scholar.google.com/>.

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Step 6. Please provide the files related to academic rules and norms. The files related to academic rules and norms include the Institutional Review Board statement, clinical trial registration statement, informed consent statement, biostatistics statement, conflict-of-interest statement, and data sharing statement. You can find the detailed requirements in the Guidelines and Requirements for Manuscript Revision-Clinical Trials Study and in the Format for Manuscript Revision-Clinical Trials Study, both of which are provided as attachments.

Answer: All related materials except the clinical trial registration statement and informed consent statement have been submitted.

Step 7. Please provide the approved grant application form(s) or funding agency copy of any approval document(s)/letter(s). For manuscripts supported by various foundations (*i.e.*, charitable, not-for-profit organizations), the authors should provide a copy of the full approved grant application form(s) or

funding agency copy of any approval document(s)/letter(s), consisting of the information section and body section in PDF format. The approved grant application form(s) or funding agency copy of any approval document(s)/letter(s) will be released online together with the manuscript in order for readers to obtain more information about the study and to increase the likelihood of subsequent citation.

Answer: The approved grant application forms called 29796-Grant application forms in PDF format have been submitted.

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Answer: Yes, we have revised the language of the manuscript by a biomedical document translation named LSCRC. A language editing certificate has been provided. If need, we will revise it again by the biomedical editing companies suggested in the guidelines for high quality.

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Answer: Yes, we submitted the revised manuscript and all related documents listed below.

- 1 29796-Revised manuscript*
- 2 29796-Answering reviewers*
- 3 29796-Copyright assignment*
- 4 29796-Scientific research process*
- 5 29796-Audio core tip*
- 6 29796-Institutional review board statement*
- 7 29796-Biostatistics statement*
- 8 29796-Conflict-of-interest statement*
- 9 29796-Data sharing statement*
- 10 29796-Google Scholar*
- 11 29796-Grant application form(s)*
- 12 29796-Language certificate*

A FINAL REMINDER: The following is a list of all required documents that authors have to submit. Please confirm that all these documents are properly prepared before submitting the revision. The documents should be named as

manuscript No.-documents category, such as 29796-Revised manuscript.

Please use this rule to name all the documents as listed below.

- 1 29796-Revised manuscript
- 2 29796-Answering reviewers
- 3 29796-Copyright assignment
- 4 29796-Scientific research process
- 5 29796-Audio core tip
- 6 29796-Institutional review board statement
- 7 29796-Clinical trial registration statement
- 8 29796-Informed consent statement
- 9 29796-Biostatistics statement
- 10 29796-Conflict-of-interest statement
- 11 29796-Data sharing statement
- 12 29796-Google Scholar
- 13 29796-Grant application form(s)
- 14 29796-Language certificate

As your manuscript is a Clinical Trials Study, you are required to provide documents No. 1 to No. 12 above, according to the Committee on Publication Ethics.

If the manuscript supported by foundations, then the No. 13 document must be provided as well.

If the authors are non-native speakers of English, then the No. 14 document must be provided as well.

If the authors cannot provide all of the documents required, the editorial office will not be able to accept the manuscript for publication. We apologize if this regulation poses any inconvenience, and thank you for your understanding!

If you have any questions that arise during the revision of your manuscript, please feel free to contact me *via* e-mail at: y.j.ma@wignet.com. Furthermore, if you have any complaints or suggestions, you may contact Director Yuan

Qi via e-mail at: y.qi@wjgnet.com or telephone at: +86-10-5908-0036 or +86-10-5908-0038.

Answer: Thank you very much. We have submitted the documents depend on the lists.

Reviewer A

This is a very interesting application of the PET/CT technique to the analysis of liver pathophysiology. The data are convincing and the specificity of the labeling is adequate. I only suggest the use of the approach to be applied to different hepatic pathologies or dysfunctions, such as fibrosis and/or the implementation of the evaluation of the fibrotic response with conventional devices. Also I consider that it would be important to contrast in the experimental model the fed/fasted status, just to see if there are better consistency in any of these conditions.

Answer: Thank you very much for your valuable suggestions. The study in this manuscript is one of the serial research. We will do more trials in different models in the further research.

Reviewer B

In material and Methods the Authors should clearly specify the number of enrolled animals in the two groups (fibrosis versus control).

Answer: Thank you very much. We specified the number of enrolled animals in the two groups in Material and Methods.

Reviewer C

Important topic of high potential interest for hepatology community. However, several criticisms may be raised against the design of the study. Some of them are already discussed by the authors in the manuscript but this is not enough to do not consider what I listed below: 1- How many days from the stop of carbon tetrachloride (CCl₄) exposure was the functional test performed? This

can influence the test since the liver damage induced by CCl₄ is at least in part reversible. 2-Fibrosis does not necessarily mean liver dysfunction. However, it can parallel the degree of liver dysfunction. Therefore, it is mandatory adding new experiments to test the performance of the neogalactosylalbumin (NGA) measurement by positron emission tomography at different degree of fibrosis (e.g. different time of exposition to CCl₄). This, with an additional parallel comparison with biochemical data, would be more coherent with the aim of the study. 3-In order to give a consistency to their results, authors should confirm the performance of NGA measurement in another model of cirrhosis such as thioacetamide exposure or bile duct ligation. 4-Shapiro-Wilk is a “normal” distribution test, not “formal”. It may be a typos mistake.

Answer: Thank you for your comments and suggestions. 1, Animal was sacrificed at the second day after the fibrotic liver model was harvested for 42 days of carbon tetrachloride (CCl₄) exposure. 2, Yes, fibrosis does not mean liver dysfunction. But in our study, the functionally impaired liver model has been successful established. The manuscript of the method has been published in Basic & Clinical Medicine^[1]. It maybe true that difference degree of fibrosis can be established suffered from different time of exposition to CCl₄. And in this study, the parameters from the pharmacokinetics curve of NGA are significantly different between control and fibrosis mice. For more important, they have significant correlations with the major traditional serological tests. 3, It's a good suggestion. We will do more experiments in different model. 4, Thank you again. We have revised in the updated manuscript.

Reference:

1, Li Shaohua, Qiu Ling, Cheng Xinqi, Li Ji, Du Shunda, Mao Yilei. The establishment of hepatic fibrosis model in mice through intraperitoneal injection with low concentration carbon tetrachloride. Basic & Clinical Med. 2014;34(12):1694-95.