

July 15, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 11553-review.doc).

Title: Experimental infection of Z: ZCLA Mongolian Gerbils with human Hepatitis E virus

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Name of Journal: *World Journal of Gastroenterology*

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

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

- (1) In the clinical setting, the value of ALT elevates very high in acute E type hepatitis. Concerning the elevation of ALT value in the inoculated group, the value is not so high. How do the authors think about that?

Response: It is really true as reviewer described that the value of ALT elevates very high in human acute HEV infection. The aim of this paper was to investigate if Z: ZCLA Mongolian gerbils were readily susceptible to infection with human HEV. But the value of ALT in the inoculated Z: ZCLA Mongolian gerbils is not so high, as it in the Balb/c nude mice which inoculated with swine HEV. That could represent the difference between human and rat, and the ALT value probably is not the optimal index for evaluating the HEV infection in Z: ZCLA Mongolian gerbils.

- (2) Concerning the value of ALT in figure 1, is it the average of the inoculated group or is it the value of ALT of the representative case? The authors should clarify that point and the number of cases showing the value of ALT in the inoculated group. After that, the authors should make table 2 according to the analysis.

Response: We have made correction according to the reviewer's comments. In the Materials and Methods, we had described that 2 gerbils of the infection group and 1 gerbil of the control group were humanely euthanized weekly post-inoculation and serum was collected weekly for ALT assay. So the values of ALT in figure 1, are the average of 2 inoculated gerbils and the only 1 control gerbils in every 7 day. Because the number of detected gerbils was not changed in every 7 day, so we did not make table 2.

- (3) The authors should describe the nucleic acid sequence of the patient's serum and the inoculated group's serum. After that, the authors should confirm the concordance of the nucleic acid sequence between the patient's serum and the inoculated group's serum.

Response: As reviewer suggested that the nRT-PCR products from the HEV patient's fecal sample and inoculated gerbils' fecal sample were identified by sequencing(data not shown). According to the sequencing result, the nucleic acid sequence of the patient virus as same as the inoculated gerbil virus. Other differences between the two kinds of virus are remain in studying. We are planning to publish it as soon as possible.

- (4) The authors should analyze the titer of IgA type antibodies of HEV and IgM type antibodies of HEV in addition to IgG type antibodies of HEV.

Response: It is really true as reviewer suggested that we should analyze the titer of IgA and

IgM type antibodies of HEV. However, Z: ZCLA Mongolian gerbil is a new laboratory stock. It is difficult to get commercial kits to analyze the IgA and IgM type antibodies of Z: ZCLA Mongolian gerbil HEV. So we are very sorry that we could not detect the IgA and IgM type antibodies of gerbil HEV.

- (5) The authors should describe the value of another liver function such as ASL, ALP and Bil in the inoculated group.

Response: We are very sorry for our negligence that we hadn't detected the values of ASL, ALP and Bil. The infection of Z: ZCLA Mongolian gerbils with human HEV was primarily studied. We wished to investigate if Z: ZCLA Mongolian gerbils could be the model organism for infection with human HEV. So we detected the ALT value which was very high in human acute E type hepatitis infection, and missed other liver function indexes. Now we had used up all the gerbil's serum and the HEV patient's fecal sample, it is difficult to detect ASL, ALP and Bil using the same serum. It is really true as reviewer suggested that the values ASL, ALP and Bil should be described, so we will detect these indexes by following study.

Special thanks to you for your good comments.

3 References and typesetting were corrected

We tried our best to improve the manuscript and made some changes in the manuscript. These changes will not influence the content and framework of the paper. And here we did not list the changes but marked in red in revised paper.

We appreciate for Editors/Reviewers' warm work earnestly, and hope that the correction will meet with approval.

Once again, thank you very much for your comments and suggestions.

Sincerely yours,

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