

March 13th, 2017

World Journal of Gastroenterology Editorial Office  
Science editor, Dr. Yuan Qi

RE: Manuscript number: 32840 entitled "**Treatment with the Nrf2 activator, Dimethyl Fumarate, ameliorates Liver Ischemia/Reperfusion Injury in Rats**"

Please find enclosed a revised version of our manuscript (manuscript number: 32840) entitled "**Treatment with the Nrf2 activator, Dimethyl Fumarate, ameliorates Liver Ischemia/Reperfusion Injury in Rats**" by Chie Takasu et al., that we are resubmitting for consideration for publication on World Journal of Gastroenterology.

We are grateful to the editor and the reviewers for the positive overall feed-back and for the helpful criticism. Our revised paper is much improved, and we are hopeful that it now fulfils the quality standards needed for publication in World Journal of Gastroenterology.

We are herein enclosing a point-by-point rebuttal to reviewers' comments. Thank you for your kind considerations in advance on our manuscript and I look forward to hearing a positive reply from you very soon.

Respectfully yours,

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### **Response to review comments**

(Manuscript number: 32840)

The authors would like to thank reviewers for careful review of our manuscript and providing us with their comments and suggestion to improve the quality of the manuscript. According to the comments, the manuscript was revised carefully. The major changes in the revised manuscript are highlighted by yellow. We hope our revision has improved the paper to a level of satisfaction. The following responses have been prepared to address all of the reviewers' comments in a point-by-point fashion.

1) The main weakness of the paper is the lack of images and measurements of parameters in the control rats that are un-treated with I/RI. The images of livers of un-treated rats should be shown in Fig 1 (H&E and TUNEL staining). In Figs 2-4, levels of the parameters examined in I/RI treated rats should be compared with those in

rats un-treated with I/RI. Without these data, it is not clear to what degree DMF corrects/protects liver biology and functions.

We strongly appreciate the reviewer's comment on this point. We have added the images of livers of sham group (H.E and TUNEL staining). As shown in Figure 1, there were remarkable liver damages by our I/RI model, whereas the H.E and TUNEL staining in the sham group showed completely normal as we expected. We therefore decided not to perform further experiment in the sham group.

2) Figure 3 shows levels of several proteins by Western blotting. Although these data look convincing, it would be important to measure and include levels of corresponding mRNAs.

The comment is well taken and we share the reviewers comment about importance of mRNAs. However, we didn't check mRNA expressions in this study.

3) Presentation of experimental data in section "Results" is extremely brief and it is

not sufficient. This section needs to be re-written with clear statements why this particular experiment was done and it should also include connections between different sections.

The comment is well taken and the conclusion is revised accordingly.

4) The legends to figures are very brief. Some details for the experiments in the legends would help readers to understand the data.

The comment is well taken and the figure legend is revised accordingly.