

Responses to the Comments of Editor and Reviewers

Dear Editor,

Thank you so much for your kind advice for our manuscript entitled "Reactive oxygen species-induced activation of YAP-1 through the c-Myc pathway is a therapeutic target in hepatocellular carcinoma". We also appreciate the constructive comments from the reviewers. These comments are most valuable for us in preparing a more valuable manuscript. We have revised the manuscript according to the reviewers' suggestions. The changes within the revised manuscript were highlighted (underlined and in blue). Specific responses to reviewer's comments are described below:

Reviewer #1 comments: Authors have showed a connection between YAP-1 and the UPR through the c-Myc pathway during oxidative stress in HCC. Although the Hippo pathway and c-Myc pathway share many important functions, including the regulation of growth, death and survival in cells and the regulation of stress resistance and life spans in organisms. However, you should confirm some biological functions between YAP-1 and c-Myc?

Author's response: We completely understand the reviewer's concern. It is an important and valuable suggestion. We have performed additional experiments to confirm the biological functions between YAP-1 and c-Myc. We described the results on the Result section of the revised manuscript on page 13, line 20–page 14, lines 3.

Reviewer #2 comment: Very interesting study and well performed. Worth to be published in our journal.

Author's response: We sincerely appreciate the reviewer's comment.

Science Editor's comments: Format:

The CrossCheck results showed the similarity to be high. According to our policy, the overall similarity index should be less than 30%, and the single source similarity should be less than 5%. Please rephrase these repeated sentences.

Author's response: It is an important and valuable suggestion. We have revised the

whole manuscript reducing the overall similarity index less than 30%, and the single source similarity less than 5%.

Supplementary comments:

I found no “Author contribution” section. Please provide the author contributions.

Author’s response: We have described the author contributions on the Title page of the revised manuscript on page 2, lines 16–20.

I found the authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s).

Author’s response: We have uploaded the approved grant application forms of National Research Foundation of Korea grant; and The Research Supporting Program of The Korean Association for the Study of the Liver and The Korean Liver Foundation .

I found the authors did not provide the original figures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor

Author’s response: We have uploaded the original figure documents using PowerPoint

I found the authors did not add the PMID and DOI in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout.

Author’s response: We have revised the reference list adding the PMID and DOI.

I found the authors did not write the “article highlight” section. Please write the “article highlights” section at the end of the main text.

Author’s response: We have additionally described the “article highlights” section at the end of the main text of the revised manuscript on page 19–20.

We hope that we have adequately responded to all the comments from the editor and

reviewers, and the revised manuscript will meet the editorial requirements. We look forward to your expert advice and comments.

Sincerely yours,

Yuri Cho, MD, PhD

Assistant Professor

Department of Internal Medicine

CHA Gangnam Medical Center

CHA University School of Medicine

569, Nonhyon-ro, Gangnam-gu, Seoul, 06135, Republic of Korea

Tel: +82-2-3468-3281, Fax: +82-2-558-1119

E-mail: presh_yuri@hanmail.net