April 13, 2021

Editor-In-Chief World Journal of Gastrointestinal Oncology

Editor-in-Chief

Lian-Sheng Ma

Dear Professor Lian-Sheng Ma

We are pleased to submit the revisions to our invited review

"The Gut Microbiome in Non-Alcoholic Fatty Liver Disease associated Hepatocellular Carcinoma: Current Knowledge and Potential for Therapeutics"

Manuscript NO.: 65491, Review

Manuscript Type: Review, revisions submitted

ID (00029287)

We appreciate the thoughtful comments of the reviewers and have made the suggested edits. The changes are highlighted in the manuscript in red font and the pages referenced here.

Reviewer #1:

- The relationship between FXR and EGFR dependent pathways and microbiome in liver diseases is further elucidated – page 13 and 14 in section "Bile Acids and interaction with gut microbiome, role in liver disease"
- The exploratory role of SCFA in microbiome and NAFLD is clarified and the section shortened (page 15 and 16)
- 3. The association of obesity associated gut microbiome in NAFLD is clarified with reduced diversity and the specific impact high fat diet on liver diseases through microbiome is highlighted on page 19 in therapeutics section

Reviewer #2:

- 1, The first paragraph in the section "Bile Acids and Interaction with gut microbiome, role in liver disease" is improved improved. (page 11,12 and parts of page 13,14)
- 2. The senescence associated secretory phenotype (SASP) of hepatic stellate cells is more intensively described (page 10)

3. The intestinal microbiota has some effects on diurnal rhythms in host metabolism. This important point is addressed in the review and the work of Kuang (Science 2019; 365:1428) is cited (page 14 and 15).

We hope the manuscript is now acceptable for publication in World Journal of Gastrointestinal Oncology. All of the authors were involved in the writing of the manuscript and approve it in its current form. None of us is aware of any potential conflict of interest regarding the issues we have raised.

Communications regarding this article may be sent to:

Sincerely,

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