Response Letter

Dear editor and all reviewers,

Hope all is well. We sincerely appreciate you for spending time on our manuscript and all your useful comments and suggestions. Our responses to each of your concerns are provided below (blue characters).

Reviewers' comments:

Reviewer #1:

In brief In HCC tissues, CDKN2B-AS1 was upregulated. Depletion of CDKN2B-AS1 inhibited the proliferation of HCC cells, and the depletion of CDKN2B-AS1 also induced cell cycle arrest and apoptosis. CDKN2B-AS1 could interact with E2F1. Depletion of CDKN2B-AS1 inhibited the binding of E2F1 to GNAZ promoter region. Overexpression of E2F1 reversed the biological effects of depletion of CDKN2B-AS1 on the malignant behaviors of HCC cells. The study was excıtıng to read. he authors performed the Koch's postulates perfectly. I believe the current form of the mansucrıpt is suitable for publication.

Authors' response:

Thank you for the positive comments on our work. We will continue to investigate on it and dig deeper in the mechanisms behind, and we hope our work can provide insights for other researchers in this field.

Reviewer #2:

In this manuscript, Tao et al. report an original research to investigate the role of lncRNA CDKN2B-AS1 in HCC. They concluded that CDKN2B-AS1 overexpression facilitates malignant biological behaviors of HCC cells, such as enhanced viability, proliferation, cell cycle progression and anti-apoptosis ability. This study is very well designed and the findings are very interesting, and within the scope of World Journal of Gastrointestinal Oncology. The methods are clearly described and results are reasonable. However, the following points need to be addressed: 1. There are some grammar errors to be checked and corrected. 2 The reference type needs to be revised

according to journal guideline. 3. More detailed figure legends and high-resolution images should be provided, which contribute to a more comprehensive understanding for readers.

Authors' response:

We appreciate your recognition and your suggestions. We have made amendments to our manuscript according to your comments: 1. We have carefully checked and corrected grammar mistakes in the manuscript. 2. We have added the PMID and DOI to the references we cited. 3. We have revised and add more details in our figure legends and provided high-resolution figures. Thanks.

Reviewer #3:

I had trouble viewing some of the details. However, overall, I think this is a reasonable manuscript and may be considered for publication. The authors may rewrite their conclusions and the lacunae of their results/experiments. An in-vivo experiment cannot be conclusive any way considering the evolutionary distance and the fact that many many of these such as LncRNA CDKN2B-AS1 may not have the same function/effect in mice. A knock-out in cell lines or knock out iPSC derived hepatocytes may be a solution-which may be difficult for the authors to carry out. There are several ways the current strategies employed by the authors may lead to wrong conclusions.

Authors' response:

We really appreciate your constructive suggestions. We have revised our discussion part of our manuscript according to your comments. Indeed, we currently do not have the technique to perform such knockout experiment, so we have mentioned as one of the shortcomings of our study:

'*In addition, knockout rather than knockdown of the CDKN2B-AS1 in HCC cell lines or iPSC derived hepatocytes should be performed to validate the functions of this gene as a more authentic and objective evidence*.' Thank you.

Best regards,

Guowei Wang