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PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Cases*

Manuscript NO: 74064

Title: Effects of Targeted-edited Oncogenic IGF-1R with Specific-sgRNA on Biological Behaviors of HepG2 Cells

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02719046
Position: Peer Reviewer
Academic degree: PhD
Professional title: Associate Professor
Reviewer's Country/Territory: Tunisia
Author's Country/Territory: China

Manuscript submission date: 2021-12-13

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-12-14 20:04

Reviewer performed review: 2021-12-14 20:08

Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No

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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

In this manuscipt, the authors report the "Effects of Targeted-edited Oncogenic IGF-1R with Specific-sgRNA on Biological Behaviors of HepG2 Cells". This is a very interesting study which represents a useful contrbution to the medical literature It deserves to be published after minor English language editing

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Reviewer's code: 03699961
Position: Associate Editor
Academic degree: MD, PhD

Professional title: Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: China

Manuscript submission date: 2021-12-13

Reviewer chosen by: Qi-Gu Yao

Reviewer accepted review: 2022-03-20 13:18

Reviewer performed review: 2022-03-26 08:07

Review time: 5 Days and 18 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Title: Effects of Targeted-edited Oncogenic IGF-1R with Specific-sgRNA on Biological Behaviors of HepG2 Cells. Min Yao, Yin Cai, Zhi-Jun Wu, et al. 1) General Comments In this manuscript, the authors explored the expressions of insulin-like growth factor-1 receptor (IGF-1R) and P-glycoprotein (P-gp) in hepatocellular carcinoma (HCC), surrounding liver tissues, and sera to show the important biological roles in hepatocarcinogenesis, HCC progression, and therapeutic managements. After editing the target sequence using Crispr/Cas9 system, cell proliferation, apoptosis, cell cycle arrest, migration, and invasion were quantitatively evaluated in a hepatoma cell line. Furthermore, the synergistic effects on cell growth of the IGF-1R editing and anti-cancer agents were investigated. Although the strategies were straightforward, data presentation is insufficient. Novel evidence is scarce. There is no direct evidence suggesting the conclusion that IGF-1R gene is a potential modulator to reverse multidrug resistance (MDR) in HCC cells. The followings are several concerns that the authors may wish to consider: 2) Specific comments Major concerns: 1. Because the crucial roles of IGF-1R in hepatocarcinogenesis, HCC progression, and therapeutic managements have been reported as the authors mentioned, all the results presented in this manuscript are similar with the evidence that have been reported in the literature except for the synergistic effects on cell growth of the IGF-1R editing and anti-cancer agents. Although the authors expected that the synergistic growth inhibitory effects are achieved by reversing MDR character of HCC specifically through the function of P-gp, there is no direct evidence suggesting a molecular link neither between IGF-1R and MDR nor between IGF-1R and P-gp. Without the direct evidence suggesting two

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molecules, it is difficult to draw the conclusion. 2. In comparisons among three or more groups, I believe the authors would perform statistics using ANOVA first and follow post hoc tests to see the probabilities in a specific combination. Unfortunately, however, there are no explanation for post hoc test. Only one probability is presented and is unclear if it is for ANOVA or for one of specific combinations. Furthermore, the chi-square values and probabilities are not consistent with my calculation. For example, "Differentiation Group" of IGF-1R in Table 2 shows chi-square value of 4.699 and probability of 0.030, which are calculated as 7.131 and 0.0076, respectively, using GraphPad Prism 8 software. In addition, TNM stage and other factors such as tumor size and number are confounding each other. They should not be analyzed together. In summary, statistical methods and results should be checked again and presented more precisely. Minor concerns: 1. Many typos, poor English expressions, careless mistakes of referencing, and so on. Carefully rewrite and edit English. 2. In "Editing IGF-IR with cell proliferation inhibition" paragraph of Result section, the relative ratio of IGF-1R to β-actin expression of Western bolting in the control group was reported as 31.22 ± 0.13. Is it correct? 3. In "Effects of edited IGF-IR on the biological features of HepG2 cells" paragraph of Result section, the actual numbers of apoptotic cells should be described. 4. There is not description for Figure 3C at all. 5. In "Synergistic effect of sgRNA with anti-cancer drugs" paragraph of Result section, the corresponding table should not be Table 3. It should be Table 4.

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Reviewer's code: 04152258
Position: Editorial Board
Academic degree: MD

Professional title: Assistant Professor, Staff Physician

Reviewer's Country/Territory: United States

Author's Country/Territory: China

Manuscript submission date: 2021-12-13

Reviewer chosen by: Qi-Gu Yao

Reviewer accepted review: 2022-03-20 12:12

Reviewer performed review: 2022-03-27 19:35

Review time: 7 Days and 7 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [ ] Grade B: Minor language polishing [Y] Grade C: A great deal of language polishing [ ] Grade D: Rejection
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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Thank you for submission of the article. The topic is very interesting and the result are very encouraging. However, major revisions are needed before acceptance. Please see my revisions attached.