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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 47875

Title: MiR-194 inactivates hepatic stellate cells and alleviates liver fibrosis by inhibiting AKT2

Reviewer's code: 03699961

Reviewer's country: Japan

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-05-14 09:51

Reviewer performed review: 2019-05-19 23:25

Review time: 5 Days and 13 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection	Peer-Review: [Y] Anonymous [ ] Onymous Peer-reviewer's expertise on the topic of the manuscript: [ ] Advanced [Y] General [ ] No expertise Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Title: MiR-194 inactivates hepatic stellate cells and alleviates liver fibrosis by inhibiting AKT2 Jun-Cheng Wu, Rong Chen, Xin Luo, et al. 1) General Comments In this manuscript, the authors at first reported that miR-194 down-regulated AKT2/cyclin D1

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expression, which in turn suppressed G1/S transition in hepatic stellate cells leading to the reduction of α-smooth muscle actin and type I collagen expressions. After that, it was revealed that the introduction of miR-194 agomir through the tail vein diminished liver fibrosis in CCl4-treated mice in association with the reduction of AKT2/cyclin D1 expression. The strategy is straightforward, and the results are clear. However, most of the results are simply followed the observations that has been reported and expectable. The authors should focus the presentation on their original observations. The following are concerns that the authors may wish to consider: 2) Specific comments Major concerns: 1. The story that was traced throughout this report is readily presumable. Hepatic stellate cells are widely accepted as a central player in liver fibrosis. MiR-194, which suppresses the proliferation of cancer cells via targeting AKT2 pathway, was down-regulated in hepatic stellate cells that was isolated from the rats with fibrous liver due to bile duct ligation. AKT positively regulates cyclin D1 expression, which promotes G1/S transition, and leads to cell proliferation. Therefore, miR-194 will exert a protective action against liver fibrosis by suppressing AKT2/cyclin D1 pathway in hepatic stellate cells. The results that are emphasized in this report should be the observations that the introduction of miR-194 agomir through the tail vein diminished liver fibrosis in CCl4-treated mice in association with the reduction of AKT2/cyclin D1 expression. The authors should summarize the story described above based on the literature in detail in the introduction section and focused in the results and discussion sections on in vivo study using miR-194 agomir. 2. Please describe the sequences used in mrR-194 and AKT targeting studies to specify OV-miR-NC, si-NC, respective controls, and so on. Minor concerns: 1. English should be revised. 2. Liver cirrhosis is not an irreversible situation. 3. Do not use an abbreviation from the first description.

INITIAL REVIEW OF THE MANUSCRIPT

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 47875

Title: MiR-194 inactivates hepatic stellate cells and alleviates liver fibrosis by inhibiting AKT2

Reviewer's code: 03412688

Reviewer's country: Brazil

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-05-16 14:06

Reviewer performed review: 2019-05-20 17:49

Review time: 4 Days and 3 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection	[Y] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection	Peer-Review: [Y] Anonymous [ ] Onymous Peer-reviewer's expertise on the topic of the manuscript: [ ] Advanced [Y] General [ ] No expertise Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

In this paper, the authors demonstrated the role and, at least partially, the mechanism of action of miR-194 as an inhibitor/control of liver fibrosis. The designs of all experiments were very elegant. The data demonstrated in this paper could be a promising new

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therapeutic approach of hepatic fibrosis. I have just a few minor comments: 1) At Abstract (Results line 3): "suppressed cell viability" or "suppressed cell proliferation"? 2) The text was written very objectively and in some parts it could a little hard to understand.

INITIAL REVIEW OF THE MANUSCRIPT

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 47875

Title: MiR-194 inactivates hepatic stellate cells and alleviates liver fibrosis by inhibiting AKT2

Reviewer's code: 00503048

Reviewer's country: Italy

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-05-14 11:33

Reviewer performed review: 2019-05-29 13:09

Review time: 15 Days and 1 Hour

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish	[ ] Grade A: Priority publishing [ ] Grade B: Minor language polishing [Y] Grade C: A great deal of language polishing [ ] Grade D: Rejection	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection	Peer-Review: [Y] Anonymous [ ] Onymous Peer-reviewer's expertise on the topic of the manuscript: [Y] Advanced [ ] General [ ] No expertise Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

This work provides data about the protective role of miR-194 in liver fibrosis. The authors demonstrate its involvement in the development of liver fibrosis and a potential therapeutic role for the treatment of this pathology. Overall, the results support the

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conclusions, but sometimes it is not clear the understanding of the phrases. English revision is mandatory. The final phrase "In conclusion, miR-194 was essential in the development of liver fibrosis" is wrong. The correct version could be "In conclusion, miR-194 deregulation was essential in the development of liver fibrosis". Minor points -Figure 1E, the q-pHSC image is shown at a magnification that is different from the others -Figure 3B, cell cycle graph, the legend of colours is lacking (e.g. what does red refer about?)

INITIAL REVIEW OF THE MANUSCRIPT

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