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## PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 67468

Title: Transforming growth factor beta-1 upregulates glucose transporter 1 and

glycolysis through canonical and noncanonical pathways in hepatic stellate cells

Reviewer's code: 05915822 Position: Peer Reviewer Academic degree: MD

**Professional title:** Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: China

**Manuscript submission date:** 2021-04-30

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-04-30 04:12

Reviewer performed review: 2021-05-08 09:12

**Review time:** 8 Days and 5 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish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



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# SPECIFIC COMMENTS TO AUTHORS

This work presented by Ming-yu Zhou, et al. is clear and has a well-funded reasoning. The manuscript is well written. I have only some minor comments. 1. Figure 1E. quantifying the changes with software. 2. Figure 7. add Figure legends; change "Figur7" to "Figure 7". 3. Materials and methods: provide sequences of siRNAs and primers used in this study.



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Name of journal: World Journal of Gastroenterology

Manuscript NO: 67468

Title: Transforming growth factor beta-1 upregulates glucose transporter 1 and

glycolysis through canonical and noncanonical pathways in hepatic stellate cells

Reviewer's code: 00504362 Position: Editorial Board Academic degree: PhD

**Professional title:** Professor

Reviewer's Country/Territory: Chile

Author's Country/Territory: China

Manuscript submission date: 2021-04-30

Reviewer chosen by: Man Liu

Reviewer accepted review: 2021-06-17 20:09

Reviewer performed review: 2021-06-18 19:38

Review time: 23 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish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
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y]Yes []No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous  Conflicts-of-Interest: [ ] Yes [Y] No



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### SPECIFIC COMMENTS TO AUTHORS

This is a very interesting manuscript aimed to clarify the contribution of glucose transporter 1 in the TGF-beta1 fibrogenic pathway that drives the activation of HSCs. However, this reviewer has some concerns. 1.-This reviewer missed a toxicity analysis to support that RNA interference does not produce any effects on cell viability and proliferation rates, as well as the expression of relevant targets (TGF-beta receptors). 2.-This reviewer missed a more detailed explanation about the procedure used to verify the purity of isolated HSCs. 3.-The rationale for the selection of the TGF- $\beta$ 1 dose (3 ng/ml) is missed. 4.-Please checked out all the Supplier' names, to get a uniform form throughout the text. 5.- Despite the relevance of the topic, the number of references corresponding to the last three years did not exceed 25%. 6.-Please check out the text for grammar.



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Name of journal: World Journal of Gastroenterology

Manuscript NO: 67468

Title: Transforming growth factor beta-1 upregulates glucose transporter 1 and

glycolysis through canonical and noncanonical pathways in hepatic stellate cells

Reviewer's code: 03782335 Position: Peer Reviewer Academic degree: MD, PhD

**Professional title:** Assistant Professor

Reviewer's Country/Territory: Kosovo

Author's Country/Territory: China

Manuscript submission date: 2021-04-30

Reviewer chosen by: Man Liu

Reviewer accepted review: 2021-06-16 13:57

Reviewer performed review: 2021-07-08 01:11

**Review time:** 21 Days and 11 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] 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
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ]Yes [Y]No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous  Conflicts-of-Interest: [ ] Yes [Y] No



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### SPECIFIC COMMENTS TO AUTHORS

Authors of this work have done a good job to relate TGFβ1 pathway and GLUT1 expression in liver fibrosis. This paper reveals new mechanisms involved in liver fibrosis which are mediated through nonparenchymal liver cells. Cannonical TGFβ1 pathway includes the targeting of SMAD4 by SMAD2 and SMAD3 proteins to form the the SMAD complex. This is not mentioned in the manuscript, please correct. The sentence "However, the expression pattern and underlying mechanism of GLUT1 remain unclear " and "This study first demonstrated that the GLUT1 expression was significantly increased in human and mouse liver fibrosis " are partly true. The role of GLUT1 transportation through exosomes in HSCs has been studied. Wan et al. study (2019) entitled "Exosomes from activated hepatic stellate cells contain GLUT1 and PKM2: a role for exosomes in metabolic switch of liver nonparenchymal cells" has revealed that activated HSCs by Hif-1 release exosomes which contain GLUT1. This mechanism is responsible for the metabolic switch of HSCs and other liver nonparenchymal cells. Please discuss. Indicate which version of SPSS has been used during the statistical analysis. In statistical analysis section, mean±square error was used to express mean tendencies between groups, but in figures one sees that mean±SD was used. Please clarify! Final recommendation is minor revision.