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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 81309

Title: Stress granules inhibit endoplasmic reticulum stress-mediated apoptosis during hypoxia-induced injury in acute liver failure

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06399425
Position: Peer Reviewer
Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: China

Manuscript submission date: 2022-11-03

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-11-04 06:53

Reviewer performed review: 2022-11-04 08:44

Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish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

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

SPECIFIC COMMENTS TO AUTHORS

Brief summary: The paper entitled "Stress granules inhibit endoplasmic reticulum stress-mediated apoptosis during hypoxia-induced injury in acute liver failure" confirmed that SGs could protect hepatocytes from hypoxia-induced damage during ALF by reducing ERS mediated apoptosis. The research was done really well, however, there are still some problems in the manuscript. I think the manuscript will be given further consideration after revision. Comments: 1) There are some writing errors in the manuscript that need to be corrected. For example: in "Cell culture and treatment" section, "The Hypoxia + Ars group was first treated with Hypoxia for 12 h, followed by hypoxia treatment for 12 h". And then, "min" and "minutes" should be unified. "in vivo" should be italicized. 2) The immunofluorescence results should be listed in the statistical chart, rather than just visual observation 3) In the text, Ars is described as a agonist for SGs, but in figure legends, Ars appears to have become an inhibitor. 4) The color of some histograms is very similar, which is not conducive to readers' judgment. 5) The immunofluorescence diagrams in figure 4 have no scale bar.

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Title: Stress granules inhibit endoplasmic reticulum stress-mediated apoptosis during hypoxia-induced injury in acute liver failure

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05199192
Position: Peer Reviewer
Academic degree: MD

Professional title: Attending Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: China

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Reviewer accepted review: 2022-11-03 09:42

Reviewer performed review: 2022-11-09 07:01

Review time: 5 Days and 21 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
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	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

1. The discussion part of the manuscript needs to be further concluded on its scientific value and clinical significance should be analyzed in depth, based on the experimental results and references, rather than simply summarizing previous research and repeating the experimental results. And there is lots of Typo's error don't meet the standard of this journal, such as: the reference [3] in the first paragraph of page 4 repeated marks（Page 4, line 13, and Page 4, line 17）; Figure 4 Effect of SGs on G3BP1 and ERS related molecules in heterocyte hypoxia model through ERS (Page 22, line 2) etc. 2. The specific experimental groups were not introduced in detail, which was difficult to understand. For example, the experimental groups presented in the results were not specifically described in the method section. No hypoxia+anisodamine group presented in Figure 3. 3. The color resolution of the histogram was not high enough to tell, such as Figure 1G and 1H, Figure 2G and 2H, Figure 4D and 4C, Figure 6E and 6F. 4. The criteria to determine the successful establishment of ALF mouse model was no introduction in the manuscript. Acute liver failure has a high mortality rate, and a large number of hepatocytes died, which was unfortunately not mentioned the cumulative mortality of mice in the relevant experimental groups in the manuscript. Secondly, the pathological changes of liver tissues in the three groups shown in Figure 5A are little different, and no significant liver cell damage is found in the model group, which is inconsistent with the pathological changes of high level ALT, TBIL and TUNEL shown later. 5. This paper focuses on the role of stress granules in acute liver failure. Stress particles are composed of mRNA and ribosomal proteins. Typical stress particles include TIA-1, G3BP, HuR, TTP, poly(A)mRNA, 40S ribosome subunit, eIF4E, eIF4G, eIF4A, eIF4B,

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poly(A) binding protein (PABP), eIF3 and eIF2 (PMID:29129640, PMID:34670846). In the experiment, only immunofluorescence detection of G3BP1 was used to label the stress particles. It is recommended to use more than two detection methods to detect the level of stress particles, such as laser confocal, western blotting, etc., to reduce the deviation of experimental results and increase the persuasion. In addition, despite the use of Ars and anisomycin in the intervention of stress granules, there is still no direct evidence to prove the influence of SGs on hepatocyte apoptosis. 6. In this manuscript, SGs were used to reduce hypoxia induced liver injury, while arsenite (Ars), as the agonist of SGs, plays a protective role in liver injury. However, in other research reports, arsenite can damage liver cells (PMID: 35998476, 19733843）. How to explain the contradictory results of arsenite's influence on liver injury in your research and others' researches?