

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 74989

Title: Intracellular alpha-fetoprotein mitigates hepatocyte apoptosis and necroptosis by inhibiting endoplasmic reticulum stress

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00722239

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Associate Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: China

Manuscript submission date: 2022-01-13

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-02-04 03:12

Reviewer performed review: 2022-02-08 09:40

Review time: 4 Days and 6 Hours

Scientific quality	<input checked="" type="radio"/> Grade A: Excellent <input type="radio"/> Grade B: Very good <input type="radio"/> Grade C: Good <input type="radio"/> Grade D: Fair <input type="radio"/> Grade E: Do not publish
Language quality	<input checked="" type="radio"/> Grade A: Priority publishing <input type="radio"/> Grade B: Minor language polishing <input type="radio"/> Grade C: A great deal of language polishing <input type="radio"/> Grade D: Rejection
Conclusion	<input type="radio"/> Accept (High priority) <input type="radio"/> Accept (General priority) <input checked="" type="radio"/> Minor revision <input type="radio"/> Major revision <input type="radio"/> Rejection
Re-review	<input checked="" type="radio"/> Yes <input type="radio"/> No

Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
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SPECIFIC COMMENTS TO AUTHORS

The authors have investigated the intracellular AFP expression in hepatocyte under the condition of liver injury in vivo and in vitro experiments. Their results indicated that intracellular AFP expression induced by ER stress-mediated hepatocyte injury. The AFP expression was attenuated by ATF6 silencing meanwhile AFP silencing deteriorated the ER stress and hepatocyte apoptosis and necroptosis. Although correlation of AFP expression and liver injury/fibrosis has been reported, the findings regarding regulatory relationships of AFP and ER stress are interesting and distinct. In addition, the study is well conducted, experiments are appropriately performed, and the manuscript is well-written. I consider this paper has enough potential for publication. I have following comments. 1. In Figure 3, why AFP which induced by ER stress do not secrete to serum or supernatant? How about fraction of AFP (especially L3 fraction), and the fraction of AFP is the same or different between HepG2 cells and injured hepatocytes? 2. In Figure 1, the images of immunohistochemistry of AFP, positive staining of AFP seems to be found at cytoplasm and nuclear. How assess the positivity of AFP stain, cytoplasm only or including nuclear expression? 3. In Figure 3G, is it "TG" (is it TM)? Please confirm.

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Reviewer's code: 06190980

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: United States

Author's Country/Territory: China

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Reviewer chosen by: AI Technique

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
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Peer-reviewer statements	Peer-Review: [<input checked="" type="radio"/>] Anonymous [<input type="radio"/>] Onymous Conflicts-of-Interest: [<input type="radio"/>] Yes [<input checked="" type="radio"/>] No
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SPECIFIC COMMENTS TO AUTHORS

I would like to suggest that the figures legend need to be more descriptive and better label pointing out the findings in the immunohistochemistry sections/pictures. How “hepatocyte apoptosis and necroptosis” were identified?