

## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Clinical Cases*

**Manuscript NO:** 85867

**Title:** Recent progress in understanding mitokines as diagnostic and therapeutic targets in hepatocellular carcinoma

**Provenance and peer review:** Invited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 03478911

**Position:** Associate Editor

**Academic degree:** PhD

**Professional title:** Chief Technician, Executive Vice President, Research Assistant Professor

**Reviewer's Country/Territory:** South Korea

**Author's Country/Territory:** China

**Manuscript submission date:** 2023-05-18

**Reviewer chosen by:** Geng-Long Liu

**Reviewer accepted review:** 2023-06-04 02:22

**Reviewer performed review:** 2023-06-06 03:51

**Review time:** 2 Days and 1 Hour

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 Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty

<b>Creativity or innovation of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation
<b>Scientific significance of the conclusion in this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
<b>Language quality</b>	<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
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## SPECIFIC COMMENTS TO AUTHORS

This is a well-organized review, but the following two points are very critical issues. 1. As described, mitochondrial stress elicits the production of stress response molecules indicated as mitokines. However, the contents described that most mitokines are only expressed in the nucleus. The theoretical background and research that mitokines is secreted directly from mitochondria and related to HCC growth and differentiation is lacking. The factors are already known as biomarkers of HCC, even if not related to mitochondria stress. It is wondering whether all expression factors in the nucleus can be defined as mitokines. 2. There have been no investigations into clinical trials targeting mitokines (eg. NCT04725474). 3. It is strongly recommended that several mitokines presented by the authors be summarized in a separate table related to molecular biological features or as the role of prognostic factors.

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**Reviewer's code:** 05393454

**Position:** Peer Reviewer

**Academic degree:** PhD

**Professional title:** Professor

**Reviewer's Country/Territory:** India

**Author's Country/Territory:** China

**Manuscript submission date:** 2023-05-18

**Reviewer chosen by:** Geng-Long Liu

**Reviewer accepted review:** 2023-06-25 10:35

**Reviewer performed review:** 2023-06-26 06:10

**Review time:** 19 Hours

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
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

<b>Scientific significance of the conclusion in this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
<b>Language quality</b>	<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
<b>Conclusion</b>	<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
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

#### SPECIFIC COMMENTS TO AUTHORS

1. The English need improvement since there are some grammatical and syntax errors in the manuscript. For example, the words “abnormal” may be as “an abnormal”; “the endoplasmic” as “endoplasmic”; “the "ER stress."” as “"ER stress."”; “Binding” as “The binding”. The grammar mistakes which are not mentioned here are also to be checked and corrected properly.

2. There are some typing mistakes as well, and authors are advised to carefully proof-read the text. For example, the words “school” may be as “School”; “ethic” as “ethics”; “Diagnosistic” as “Diagnostic”; “intertissue” as “inter tissue”. The typos not mentioned here are also to be checked and corrected properly.

3. Check the abbreviations throughout the manuscript and introduce the abbreviation when the full word appears the first time in the abstract and the remaining for the text and then use only the abbreviation (For example, reactive oxygen species (ROS), damage-associated molecular patterns (DAMPs), etc.,). Make a word abbreviated in the article that is repeated at least three times in the text, not all words to be abbreviated.

4. The introduction part appears less informative about the Hepatocellular Carcinoma, thus this section should be indicated as detailed to understand the manuscript in clear.



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5. The literature search should be described in detail. The authors are encouraged to include the database, search engines (like PubMed, ScienceDirect, Google scholar etc.), the keywords used etc., which may be included since it is a review article. 6. The authors are encouraged to include one table for better outcome of the manuscript since it is a review article.

## RE-REVIEW REPORT OF REVISED MANUSCRIPT

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**Reviewer's Country/Territory:** South Korea

**Author's Country/Territory:** China

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**Reviewer chosen by:** Jia-Ping Yan

**Reviewer accepted review:** 2023-07-18 00:19

**Reviewer performed review:** 2023-07-18 00:22

**Review time:** 1 Hour

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<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
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection



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<b>Peer-reviewer statements</b>	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**

All concerns have been well addressed. There is no additional issue to raise.