

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 87122

Title: Combined TIM-3 and PD-1 blockade restrains hepatocellular carcinoma development by facilitating CD4⁺ and CD8⁺ T cell-mediated antitumor immune responses

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 07746241

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Assistant Professor

Reviewer's Country/Territory: Greece

Author's Country/Territory: China

Manuscript submission date: 2023-09-05

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-09-07 00:24

Reviewer performed review: 2023-09-12 10:16

Review time: 5 Days and 9 Hours

Scientific quality	<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 Grade E: Do not publish
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
Scientific significance of the conclusion in 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 scientific significance
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
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> 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

SPECIFIC COMMENTS TO AUTHORS

Title: Combined TIM-3 and PD-1 blockade restrains hepatocellular carcinoma development by facilitating CD4⁺ and CD8⁺ T cell-mediated antitumor immune responses. 1- TITLE reflected the main subject of the manuscript. 2- The ABSTRACT summarized and reflect the described in the manuscript. 3- KEY WORDS reflected the focus of the manuscript. 4- The manuscript adequately described the background and presented treatments of hepatocellular carcinoma, and the general information of immune checkpoint inhibitors targeting PD-1 and TIM-3. 5- The manuscript described methods (acquisition of clinical specimens, animals, and relevant cells, cell processing, and detection of immunohistochemistry and cytokine levels, Statistical analysis, etc.) in adequate detail. 6- The research objectives are achieved by the experiments used in this study. Authors determined the levels of PD-1 and TIM-3 on CD4⁺ and CD8⁺ T cells from tumor tissues, ascites, and matched adjacent tissues of HCC patients with flow



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cytometry. They also treated HCC xenograft mouse model with anti-TIM-3 mAb and/or anti-PD-1 mAb. 7- The manuscript interpreted the findings adequately and appropriately, highlighting the key points concisely, clearly and logically. 8- Manuscript included sufficient, good quality Tables and Figures. Overall, the manuscript is well, concisely and coherently organized and presented and the style, language and grammar are accurate and appropriated. The data are rich and logical, so I recommend that the manuscript can be published.

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Peer-review model: Single blind

Reviewer's code: 07746928

Position: Peer Reviewer

Academic degree: PhD

Professional title: Doctor

Reviewer's Country/Territory: Spain

Author's Country/Territory: China

Manuscript submission date: 2023-09-05

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-09-10 13:18

Reviewer performed review: 2023-09-13 08:16

Review time: 2 Days and 18 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 type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty

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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
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> 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

SPECIFIC COMMENTS TO AUTHORS

Thank you for a useful and important synopsis of this important topic. Due to the complex pathological mechanisms of HCC, ICIs with a single target exhibit poor overall response rate in HCC patients. I'm really appreciate that you investigated the effects of combined blockade of TIM-3 and PD-1 on T cell immunological function and cancer development in HCC mouse model. As you have found, combined blockade of TIM-3 and PD-1 has additive antitumor effects in a mouse model of HCC compared to treatment alone. Your findings will benefit the clinical treatment of HCC. Overall, your study is well conducted with good methodology and intelligible English. The material studied allows to draw the conclusions. SPECIFIC COMMENTS: What does the special symbol SS, **, ##, && represent in Figure 2 and Figure 3 mean? Please specify. The legend of some figures is not clearly described. It should have a detailed figure legend that provides a clear and comprehensive description of the information presented in the

figure, so that I can understand without having to refer back to any other portion of the manuscript.