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PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Cases*

Manuscript NO: 71574

Title: Glycolytic and fatty acid oxidation genes affect the treatment and prognosis of liver cancer

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03882844
Position: Editorial Board
Academic degree: FACG, MBBS, MD
Professional title: Associate Professor
Reviewer's Country/Territory: United States
Author's Country/Territory: China

Manuscript submission date: 2021-09-13
Reviewer chosen by: AI Technique
Reviewer accepted review: 2021-09-22 10:32
Reviewer performed review: 2021-09-30 23:42
Review time: 8 Days and 13 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish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

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

SPECIFIC COMMENTS TO AUTHORS

I congratulate author for advancing the field of liver cancer

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PEER-REVIEW REPORT

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Manuscript NO: 71574

Title: Glycolytic and fatty acid oxidation genes affect the treatment and prognosis of liver cancer

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02451447
Position: Editorial Board
Academic degree: MD, PhD
Professional title: Associate Professor
Reviewer's Country/Territory: United States
Author's Country/Territory: China

Manuscript submission date: 2021-09-13

Reviewer chosen by: Qi-Gu Yao (Online Science Editor)

Reviewer accepted review: 2022-01-02 16:04

Reviewer performed review: 2022-01-02 17:14

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Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish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

SPECIFIC COMMENTS TO AUTHORS

The authors divided liver cancer samples into four subgroups and compared survival and molecular biological differences between different subtypes by using cluster analysis. The paper is well written. Comments: 1. Among them, the Glycolytis group has significantly more immune cell infiltration: NK cells, CD4 T cells, Treg cells, mast cells, etc. But glycolysis was seen to have the shortest median survival time of tumours. The authors discussed the possibilities of Treg and ROS in this glycolytic group HCCs. Studies have shown higher intratumoral inflammatory infiltrate is associated with better prognosis and response to ICB (PMID: 28624577 and PMID: 29603348). The authors may need to analyze more details of infiltrating immune cell types such as CD4 and CD8, since these are closely related to ICB treatment response and survival. 2. The current does not consider etiologies of HCC. Are there any difference in the metabolic pathways between viral hepatitis and non-alcoholic liver disease associated HCCs? Recent study has shown HCC arising from non-alcoholic liver disease does not benefit from the ICB treatment. Patients with NASH-driven HCC who received ICB treatment showed reduced overall survival compared to patients with other etiologies (PMID: 33762733). If the authors can further analyze the proposed 4 groups in viral or non-viral (NASH) will be very helpful. The etiologies of the HCCs can also be found from the database the authors used for this study. 3. Page 7: “In terms of SNP, the most frequent mutation gene of the Glycolysis group is TP5”: The TP5 should be TP53, right? 4. Page 8: “The low-risk group and FAO group were more sensitive to ICB treatment”. It is unclear what is the low-risk group? 5. Page 8: “We used this method to compare the high- and low-risk groups of the prediction model and found that the low-risk group could benefit,

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regardless of ICB treatment or common chemotherapy drugs". Same question as above, how the low and high-risk groups were defined? Please describe it clearly in the methods section.

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PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Cases*

Manuscript NO: 71574

Title: Glycolytic and fatty acid oxidation genes affect the treatment and prognosis of liver cancer

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02954382
Position: Editorial Board
Academic degree: MSc, PhD
Professional title: Assistant Professor, Surgeon
Reviewer's Country/Territory: Kosovo
Author's Country/Territory: China

Manuscript submission date: 2021-09-13
Reviewer chosen by: Qi-Gu Yao (Online Science Editor)
Reviewer accepted review: 2022-01-03 17:30
Reviewer performed review: 2022-01-09 17:24
Review time: 5 Days and 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) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No

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

SPECIFIC COMMENTS TO AUTHORS

Reviewer's report Title: Glycolytic and fatty acid oxidation genes affect the treatment and prognosis of liver cancer Date: January 9, 2022 Reviewer's report: 1 Title. Does the title reflect the main subject/hypothesis of the manuscript? Yes, the title of the manuscript is concise, informative and reflect the main subject of the manuscript 2 Abstract. Does the abstract summarize and reflect the work described in the manuscript? Yes, and that was done concisely, and very clearly 3. Key words. Do the key words reflect the focus of the manuscript? Yes 4. Introduction. Does the manuscript adequately describe the background, present status and significance of the study? Yes. This manuscript shortly, and clearly describe the background, present status, and what authors aimed by this study 5. Methods: This section is clearly written by authors, and is OK, including all subsections 6. Results This section is concisely written by authors, including all subsections 7. Discussion Is OK 8. References. Does the manuscript cite appropriately the latest, important and authoritative references in the introduction and discussion sections? Does the author self-cite, omit, incorrectly cite and/or over-cite references? In this manuscript are cited important and authoritative references 9. Quality of manuscript organization and presentation. Is the manuscript well, concisely and coherently organized and presented? Is the style, language and grammar accurate and appropriate? Yes, the manuscript is clearly, concisely, and coherently presented. Language and grammar are appropriate 10. Illustrations and tables. Are the figures, diagrams and tables sufficient, good quality and appropriately illustrative of the paper contents? Do figures require labeling with arrows, asterisks etc., better legends? Tables and Diagrams are of good quality, illustrative, and reflect the paper contents

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RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Clinical Cases*

Manuscript NO: 71574

Title: Glycolytic and fatty acid oxidation genes affect the treatment and prognosis of liver cancer

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02451447
Position: Editorial Board
Academic degree: MD, PhD
Professional title: Associate Professor
Reviewer's Country/Territory: United States
Author's Country/Territory: China

Manuscript submission date: 2021-09-13

Reviewer chosen by: Han Zhang (Online Science Editor)

Reviewer accepted review: 2022-02-13 15:12

Reviewer performed review: 2022-02-13 15:36

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
Peer-reviewer	Peer-Review: [Y] Anonymous [ ] Onymous

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statements	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors have made significant improvement in this revised version. I only have a minor suggestion for the authors which was my second comment in last version. Although the authors did not find anything in the so far available database, please briefly discuss that these genes discussed in this paper might be etiologically different, based on the reference I gave last time (Here I am copying my original comment and the author's reply for your reference). Otherwise, I have no more comments. 2. The current does not consider etiologies of HCC. Are there any difference in the metabolic pathways between viral hepatitis and non-alcoholic liver disease associated HCCs? Recent study has shown HCC arising from non-alcoholic liver disease does not benefit from the ICB treatment. Patients with NASH-driven HCC who received ICB treatment showed reduced overall survival compared to patients with other etiologies (PMID: 33762733). If the authors can further analyze the proposed 4 groups in viral or non-viral (NASH) will be very helpful. The etiologies of the HCCs can also be found from the database the authors used for this study. 2.Answer: Dear reviewer, your proposal is very novel and topical. Unfortunately, we were not able to find required clinical data in the TCGA and ICGC databases. We have tried to conduct the study in the GEO database but could not get the desired results due to the lack of data. We also hope to find ways to include this variable for analysis in subsequent studies. Thank you very much for your suggestions, which have broadened our horizon greatly.