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PEER-REVIEW REPORT

Name of journal: *World Journal of Hepatology*

Manuscript NO: 83908

Title: Tumor budding as a potential prognostic marker in determining the behavior of primary liver cancers

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06286468

Position: Peer Reviewer

Academic degree: PhD

Professional title: Associate Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Turkey

Manuscript submission date: 2023-02-15

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-02-15 12:07

Reviewer performed review: 2023-02-25 16:47

Review time: 10 Days and 4 Hours

Scientific quality	<input checked="" type="checkbox"/> Grade A: Excellent <input 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 Grade E: Do not publish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 checked="" type="checkbox"/> Grade A: Priority publishing <input 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 checked="" type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input 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

I think more work is needed in the Conclusion section. Detailed description of Figure1 in the manuscript is necessary. Is the Figure1 from the authors' own experiment or not? Plotting scale should also be added in Figure1. The concept of EMT was first reported in embryology area. EMT is a biological process which is of great importance in embryogenesis and organ development. I suggest that the research process and some discoveries of EMT could be added in the discussion or introduction section. Some references could be cited, "EMT Transition States during Tumor Progression and Metastasis", "Exosomes Regulate the Epithelial-Mesenchymal Transition in Cancer" for example, or any other similar references.

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Reviewer's code: 05775678

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Doctor

Reviewer's Country/Territory: Italy

Author's Country/Territory: Turkey

Manuscript submission date: 2023-02-15

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-02-27 14:23

Reviewer performed review: 2023-03-07 20:49

Review time: 8 Days and 6 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

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
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Conclusion	<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
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

In their manuscript Unal and colleagues produced a brief review about TB in primary liver carcinomas, i.e. HCC and CCC. This type of manuscript is original in primary liver cancer and TB is a highly discussed topic in the recent literature in many tumor types. For this reasons, the manuscript is interesting. The tables and the figure are well organized and useful. This kind of review summarize the actual knowledge and therefor could be a valid starting point for new studies. Some questions and suggestions for the authors: - all the published papers on the topic are reviewed in the manuscript? or did you perform a selection of them, and which were the criteria? - the authors repeated several times that there are not so much papers in the literature about the topic, and I suggest to highlight instead that the literature suggest to further investigate the potential prognostic role of TB in these tumor types, which is a conclusion that could be stated more clearly. - do you believe that there is a need for a TB scoring method dedicated to primary liver cancer? I suggest to discuss more that the assessing and scoring method are fundamental also to compare results from different studies. Anyway, despite different scoring methods TB seems to be a negative prognostic marker in these tumors. -



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I suggest to consider the recent paper in which TB0 has been proposed as new category for TB assessment in CRC. - I suggest to consider that intratumoral and peripheral assessment are not necessarily the same, despite this has been considered in CRC. Is there any paper on this topic in the liver? - there is no discussion about the limitation on the paper reviewed despite their low number, which are other limitations? small number of cases? ethnicity? scoring method? etc.... - which are the potential therapeutic implication of TB assessment and inclusion in pathology report?

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Doctor

Reviewer's Country/Territory: Italy

Author's Country/Territory: Turkey

Manuscript submission date: 2023-02-15

Reviewer chosen by: Yu-Jie Ma

Reviewer accepted review: 2023-04-07 07:06

Reviewer performed review: 2023-04-07 07:21

Review time: 1 Hour

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 checked="" type="radio"/>] Accept (High priority) [<input type="radio"/>] Accept (General priority) [<input type="radio"/>] Minor revision [<input type="radio"/>] Major revision [<input type="radio"/>] Rejection
Peer-reviewer	Peer-Review: [<input checked="" type="radio"/>] Anonymous [<input type="radio"/>] Onymous



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statements

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

SPECIFIC COMMENTS TO AUTHORS

The authors modified their manuscript according to the suggestions of the reviewer. The manuscript is ready for publication.