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PEER-REVIEW REPORT

Name of journal: *World Journal of Hepatology*

Manuscript NO: 74670

Title: The functions of three ubiquitin-conjugating enzyme 2 genes in hepatocellular carcinoma diagnosis and prognosis

Provenance and peer review: Invited manuscript; externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03674268

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Chief Doctor, Professor

Reviewer's Country/Territory: China

Author's Country/Territory: United States

Manuscript submission date: 2021-12-31

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-01-02 05:25

Reviewer performed review: 2022-01-03 09:31

Review time: 1 Day and 4 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish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) [ ] Minor revision [ ] Major revision [Y] 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

In this study, the authors analyzed TCGA database and found diagnostic and prognostic roles of UBE2C, UBE2T, UBE2S in HCC. My major concern is the study lack of novelty. Data digging in TCGA database is far from convincing. First, UBE2 is a large enzyme family contained many proteins. The authors did not show the reason to choose UBE2C, UBE2T, and UBE2S (ranked as top 4, top 8, and top 31) rather than the top3 proteins. Second, several previous studies have revealed the function and mechanism of UBE2 in HCC. This paper presented the same conclusions that upregulation of UBE2T, UBE2S, UBE2C, UBE2I in HCC predicted poor prognosis and promoted HCC progression. Third, the study should includes not only analysis from the databases but also data from clinical samples. In addition, relationship between p53 mutation and UBE2 overexpression was interesting, but not convincing.

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Reviewer's code: 06190776

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Associate Professor, Chief Physician, Deputy Director, Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: United States

Manuscript submission date: 2021-12-31

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-01-31 15:28

Reviewer performed review: 2022-02-10 13:22

Review time: 9 Days and 21 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] 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
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SPECIFIC COMMENTS TO AUTHORS

In this work, the authors demonstrated Ubiquitination plays an essential role in the biochemical processes of cells, tried to illustrate overexpression of UBE2C, UBE2T, and UBE2S was negatively associated with prognostic outcomes and overall survival times, indicating an association between UBE2 expression with p53 function, which could be a diagnostic and prognostic biomarkers for HCC. However, there are major specific points in this manuscript as shown in following comments: 1. The range of title is too large, the research of function for a gene should include proliferation, apoptosis, invasion and metastasis in HCC cells level. Please explain it. 2. It is recommended that immunofluorescence double-labeling experiments demonstrate subcellular localization of UBE2 protein. 3.Please highlight what are the major functions of UBE2 in HCC in the discussion of the manuscript.