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PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

Manuscript NO: 39458

Title: Aberrant expression of alternative isoforms of transcription factors in hepatocellular carcinoma

Reviewer's code: 03259512

Reviewer's country: Australia

Science editor: Fang-Fang Ji

Date sent for review: 2018-04-23

Date reviewed: 2018-04-23

Review time: 1 Hour

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection	Peer-Review: [Y] Anonymous [ ] Onymous Peer-reviewer's expertise on the topic of the manuscript: [Y] Advanced [ ] General [ ] No expertise Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors /current study reviewed experimental data and identified biological effects of liver-specific TFs implicated in carcinogenesis, tumor progression, and clinical outcome. The study reviewed/ assessed the ratio of TFs isoforms and suggests that

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targeting specific TF variants may be beneficial for the prognosis and treatment of Hepatocellular carcinoma (HCC). The review is well-written and comprehensive, although not overloaded with details. There are some points to be addressed. Authors should revise and improve the manuscript. Minor points to address. 1. The abstract should state that this is a review and what was reviewed (Include something similar to this sentence: "This study reviewed …" etc). The reviewed transcription factors should be listed shortly in the abstract and some of them included as key words. 2. The sub-heading should be descriptive. It is not enough to write "p53 family". It is necessary to clarify the following/explored role of p53 signaling in regulation of hepatic genome etc. The sub-headings for each sub-chapter should be improved. 3. Table 1 should be mentioned earlier in the text (cite it several times at the appropriate places); not only in the Conclusion part. 4. A Diagram should be drawn to represent the network of TFs involved in regulation of HCC (hypothetical). 5. Limitations of the in vitro studies conducted to reveal the role of TFs in HCC should be also presented at the end of some chapters as conclusive remarks. 6. In vivo /clinical studies (of any available) should be also included at least shortly.

INITIAL REVIEW OF THE MANUSCRIPT

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PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

Manuscript NO: 39458

Title: Aberrant expression of alternative isoforms of transcription factors in hepatocellular carcinoma

Reviewer's code: 02444752

Reviewer's country: China

Science editor: Fang-Fang Ji

Date sent for review: 2018-04-23

Date reviewed: 2018-04-28

Review time: 5 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection	Peer-Review: [Y] Anonymous [ ] Onymous Peer-reviewer's expertise on the topic of the manuscript: [ ] Advanced [Y] General [ ] No expertise Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

This review manuscript is well written and suitable for publication in World Journal of Hepatology.

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PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

Manuscript NO: 39458

Title: Aberrant expression of alternative isoforms of transcription factors in hepatocellular carcinoma

Reviewer's code: 02529007

Reviewer's country: Iran

Science editor: Fang-Fang Ji

Date sent for review: 2018-04-23

Date reviewed: 2018-04-29

Review time: 6 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection	Peer-Review: [Y] Anonymous [ ] Onymous Peer-reviewer's expertise on the topic of the manuscript: [ ] Advanced [Y] General [ ] No expertise Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The manuscript # 39458 entitled, "Aberrant Expression of Alternative Isoforms of Transcription Factors in Hepatocellular Carcinoma" reviews the state of the art for structural properties, biological effects and clinical impact of the most investigated TF

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isoforms specific to liver and HCC and provides future prospects on further expansion of the knowledge on the functions of TF variants for discovering new clinically relevant prognostic markers and therapeutic targets for HCC. Comments: Taken together the manuscript is well-arranged and written and the provided information might be of interest of the audience of the World Journal of Hepatology. The following comments might help to further improve the manuscript. - Manuscript needs to be edited by an English scientific editor for required English corrections. In specific, many long sentences need to be split. Forexample the following single sentence from Introduction: Multiple sources of evidence suggest that this amount may be underestimated due to the existence of protein isoforms that arise from the usage of alternative promoters or translation start sites (TSSs), alternative splicing regulated by ubiquitous and tissue-specific splicing factors, which affects transcripts of 92–94 % of genes, and alternative cleavage and polyadenylation[3-5]. - A number of words in the manuscript need to be replaced with proper/correct ones. For example in the following sentence: “druggable” and “yet” might be changed to “Treatment/therapeutic” and “to date”, respectively. Although recurrent driver genes and somatic mutations have been identified in HCC, most of them cannot be considered as druggable targets for therapy yet[20]. - There are several new 2018 reviews and articles related to TFs in HCC and some of which might be pointed and quoted at least in the introductory part even if they are not directly related to isoforms. Some examples are as following: TFCP2/TFCP2L1/UBP1 transcription factors in cancer. Kotarba G, Krzywinska E, Grabowska AI, Taracha A, Wilanowski T. Cancer Lett. 2018 Apr 28;420:72-79. doi: 10.1016/j.canlet.2018.01.078. Epub 2018 Feb 7. Regulation and role of nuclear factor-E2-related factor 2 (Nrf2) in multidrug resistance of hepatocellular carcinoma. Tian B, Lu ZN, Guo XL. Chem Biol Interact. 2018 Jan 25;280:70-76. doi: 10.1016/j.cbi.2017.12.014. Epub 2017 Dec 6. Review. Key signaling pathways, genes

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and transcription factors associated with hepatocellular carcinoma. Wang J, Tian Y, Chen H, Li H, Zheng S. Mol Med Rep. 2018 Apr 12. doi: 10.3892/mmr.2018.8871. [Epub ahead of print] T-box transcription factor Tbx3 contributes to human hepatocellular carcinoma cell migration and invasion by repressing E-cadherin expression. Feng X, Yao W, Zhang Z, Yuan F, Liang L, Zhou J, Liu S, Song J. Oncol Res. 2018 Jan 2. doi: 10.3727/096504017X15145624664031. [Epub ahead of print] High MYBL2 expression and transcription regulatory activity is associated with poor overall survival in patients with hepatocellular carcinoma. Guan Z, Cheng W, Huang D, Wei A. Curr Res Transl Med. 2018 Mar;66(1):27-32. doi: 10.1016/j.retram.2017.11.002. Epub 2017 Dec 21. Regulation and role of nuclear factor-E2-related factor 2 (Nrf2) in multidrug resistance ofhepatocellular carcinoma. Tian B, Lu ZN, Guo XL. Chem Biol Interact. 2018 Jan 25;280:70-76. doi: 10.1016/j.cbi.2017.12.014. Epub 2017 Dec 6. Review p.Q511L mutation of HNF1α in hepatocellular carcinoma suppresses the transcriptional activity and the anti-tumor effect of HNF1α. Ding CH, Deng LF, Chen F, Ding K, Chen WS, Xie WF, Zhang X. Biochem Biophys Res Commun. 2018 Jan 1;495(1):86-91. doi: 10.1016/j.bbrc.2017.10.174. Epub 2017 Nov 1. NFκB mediated elevation of KCNJ11 promotes tumor progression of hepatocellular carcinomathrough interaction of lactate dehydrogenase A. Zhang K, Mu L, Ding MC, Xu R, Ding ZJ, Liang J. Biochem Biophys Res Commun. 2018 Jan 1;495(1):246-253. doi: 10.1016/j.bbrc.2017.11.011. Epub 2017 Nov 3

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