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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Surgery*

Manuscript NO: 88581

Title: Construction and validation of somatic mutation-derived LncRNA signatures of genomic instability to predict prognosis of hepatocellular carcinoma

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06195974
Position: Editorial Board
Academic degree: MD, PhD
Professional title: Assistant Professor
Reviewer's Country/Territory: United States
Author's Country/Territory: China

Manuscript submission date: 2023-10-02

Reviewer chosen by: Yu-Lu Chen

Reviewer accepted review: 2023-11-16 21:49

Reviewer performed review: 2023-11-16 22:16

Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[Y] Grade A: Excellent [ ] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No creativity or innovation

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Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No scientific significance
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
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

In this study, Duan and colleagues attempted to establish a genomic instability-derived Long non-coding RNAs (LncRNAs) signature (GILncSig) able to predict the prognosis of HCC patients by combining LncRNA expression profile with somatic mutation profile. GI-LncRNAs were identified by combining LncRNA expression and somatic mutation profiles. GILncSig was established in the training set by Cox regression analysis, and its predictive ability was verified in testing set and TCGA set. In addition, we explored the effects of GILncSig and TP53 on the prognosis. A total of 88 GI-LncRNAs were found and GILncSig was constructed by 5 LncRNAs (MIR210HG, AC016735.1, AC116351.1, AC010643.1, LUCAT1). Multivariate Cox regression analysis and stratified analysis confirmed that GILncSig could be used as an independent prognostic factor The ROC curve analysis of GILncSig showed that its AUC (0.773) was higher than the two LncRNA signatures published recently. Furthermore, GILncSig may have a better predictive performance than TP53 mutation status alone. The study is of interest since identification of prognostic scores to be used as independent biomarker to predict the clinical outcome of HCC patients and for prognosis assessment and further clinical

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decision making in HCC patients is of current major clinical relevance. I have only minor comments to further improve the clinical impact of the study: 1) in the introduction, the authors should recall the changing scenario of HCC in the last years. In particular, the last 20 years several aspects of HCC scenario have changed, as well as its management as well as the etiology due to the increased rate of non-viral etiology of underlying liver disease such as metabolic liver disease, the improvement of surveillance leading to the higher rate of early stage of HCC as recently demonstrated (DOI: 10.1111/liv.14735), and, importantly, the improved overall survival obtained with evolved systemic treatments based on the combination treatments based on TKI plus immune checkpoint inhibitors as recently well-described (DOI: 10.1080/14737140.2023.2181162). At the light of these important literature data, the authors should further discuss the importance of prognostic markers of HCC invasivness as well as markers able to predict response to systemic treatments.