Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: office@baishideng.com
https://www.wjgnet.com

PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Oncology*

Manuscript NO: 89022

Title: Identification of immune cell-related prognostic genes characterized by a distinct microenvironment in hepatocellular carcinoma (HCC)

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05348255
Position: Peer Reviewer
Academic degree: MD

Professional title: Professor

Reviewer's Country/Territory: Egypt

Author's Country/Territory: China

Manuscript submission date: 2023-10-18

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-11-03 08:21

Reviewer performed review: 2023-11-03 08:27

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Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish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

Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: office@baishideng.com
https://www.wjgnet.com

Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [Y] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[ ] Grade A: Priority publishing [ ] Grade B: Minor language polishing [Y] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

-the study is in need of major language editing -the clinical significance is lacking

Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: office@baishideng.com
https://www.wjgnet.com

PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Oncology*

Manuscript NO: 89022

Title: Identification of immune cell-related prognostic genes characterized by a distinct microenvironment in hepatocellular carcinoma (HCC)

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00503448
Position: Peer Reviewer
Academic degree: MD

Professional title: Associate Professor, Research Assistant Professor

Reviewer's Country/Territory: Italy

Author's Country/Territory: China

Manuscript submission date: 2023-10-18

Reviewer chosen by: Yu-Lu Chen

Reviewer accepted review: 2023-11-08 12:01

Reviewer performed review: 2023-11-09 08:03

Review time: 20 Hours

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

Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: office@baishideng.com
https://www.wjgnet.com

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, the authors aimed to establishing a prognostic survival model with 7 prognostic genes able to predict overall survival in patients of hepatocellular carcinoma (HCC) and revealing the immune profile of tumor microenvironment (TME). They extracted data from TCGA and ICGC datasets for screening prognostic genes along with developing and validating a 7-gene prognostic survival model by method of weighted gene co-expression network analysis (WGCNA) and LASSO with cox regression. They found 7 prognostic genes for signature construction. Survival receiver operating characteristic (ROC) analysis demonstrated the good performance of survival prediction. TBM could be considered as an independent factor in HCC survival prediction. Of interest, several immune checkpoints including VTCN1 and TNFSF9 were found to be associated with the 7 genes and risk scores. Different combinations of checkpoint blockade targeting inhibitory CTLA4 and PD1 receptors, and potential chemotherapy drug held great promise for specific HCC therapy. The authors concluded that their novel 7 genes (CYTH3, ENG, HTRA3, PDZD4, SAMD14, PGF, PLN) prognostic model shows high predictive efficiency thus supporting the TBM analysis based on the 7 genes

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: office@baishideng.com
https://www.wjgnet.com

as a predictive marker of the immune response in HCC for clinical application The study is of interest, however, in my opinion, the authors should tried to focus their research on the topic now of major clinical impact. Genetic studies exploring and searching for genetic influences in HCC development as well as treatment response/resistance, have been extensively studied. However, with the recent increasing development of systemic treatments, the authors should discuss the recent evidence supporting the higher anti-tumor efficacy of combination treatment strategy based on the combination of tyrosine kinase inhibitor plus immune checkpoint inhibitors as well-described in a recent comprehensive review addressing the improved efficacy and overall survival and safety profile of combination (TKI plus ICI) treatments, as recently reported (TKIs in combination with immunotherapy for hepatocellular carcinoma. Expert Rev Anticancer Ther. 2023 Mar;23(3):279-291). -To improve the clinical significance I would suggest to recall and discuss the following 2 topics both related to the genetic impact in HCC development and immune cells pattern: 1) recent studies suggested a genetic role in hepatocarcinogenesis according to the underlying liver disease which are now changing in the changing scenarion of HCC as recently demonstrated in a largen cohort of HCC patients (The changing scenario of hepatocellular carcinoma in Italy: an update. Liver Int. 2021 Mar;41(3):585-597.). This important epidemiological issue should be recalled and discussed. 2) one of the most abundant immunosuppressive cell population in the tumor microenvironment is the CD4+ CD25+ FOXP3 T cell population which also amply express CTLA4 and PD1 thus representing a direct target of ICIs, as recently described in a comprehensive review addressing the role of Tregs according to etiology of underlying liver diseases (Hepatocellular carcinoma in viral and autoimmune liver diseases: Role of CD4+ CD25+ Foxp3+ regulatory T cells in the immune microenvironment. World J Gastroenterol. 2021 Jun 14;27(22):2994-3009.). 3) the last point worth mentioning is the impact of immune cell profile also in the treatment reponse to locoregional treatments

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: office@baishideng.com
https://www.wjgnet.com

such as transarterial chemoembolization (TACE). It has been demonstrated that CT-radiomics signature could effectively predict the prognosis and treatment response of HCC, which is also associated with the tumor microenvironment heterogeneity (A radiomics signature associated with underlying gene expression pattern for the prediction of prognosis and treatment response in hepatocellular carcinoma. Eur J Radiol. 2023 Oct;167:111086.). On the contrary, the authors should recall and discuss that previous suggested prognostic score such as the ART score are not able to predict the outcomes of HCC patients who underwent TACE as previously demonstrated (The ART score is not effective to select patients for transarterial chemoembolization retreatment in an Italian series. Dig Dis. 2014;32(6):711-6.).