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PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Oncology*

Manuscript NO: 89167

Title: What are the changes in the hotspots and frontiers of microRNAs in hepatocellular carcinoma over the past decade?

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: 2023-10-22

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-10-29 06:17

Reviewer performed review: 2023-11-08 22:32

Review time: 10 Days and 16 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Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish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	[ ] Grade A: Excellent [Y] 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 manuscript, the authors aimed to perform a comprehensive analysis of recent research concerning miRNAs in hepatocellular carcinoma (HCC). All relevant publications were retrieved and, overall, a total of 9,426 publications on this topic were selected. According to the keywords analysis, the researches of miRNAs focused on their expression level, the effects and mechanisms on the biological behavior of HCC. Keywords bursting analysis showed that in the early years (2013–2017), “microRNA expression”, “gene expression”, “expression profile”, “functional polymorphism”, “circulating microRNA”, “susceptibility” and “mir 21” et al. started to raise attention. In the latest phase (2018–2022), the hot topics were “sorafenib resistance”, “tumor microenvironment” and so on. They thus concluded that the study would provide a comprehensive overview for the researches of miRNAs in HCC based on bibliometric analysis ranging from miRNAs expression level, the effects, and mechanisms on the biological behavior of HCC, to sorafenib resistance, tumor microenvironment and so on. 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. miRNA in HCC development as well

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as treatment response/resistance, have been extensively studied. However, with the recent increasing development of systemic treatments, the authors should disucss 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 miRNA: 1) recent studies addressed the different miRNA profile 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 (). This important epidemiological issue should be recalled and discussed. 2) regarding the resistance to sorafenib and the safety profile, the authors should discuss the clinically relevant topic related to the need of predicitve marker able to identify patients responding to sorafenib and other systemic therapies as well as marker able to predict treatment-related adverse events since it has been recently demonstrated that optimal management od adverse events and improvements of theri managment translates into longer patient overall survival, as recently demonstrated (Management of adverse events with tailored sorafenib dosing prolongs survival of hepatocellular carcinoma patients. J Hepatol. 2019 Dec;71(6):1175-1183.).