

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Hepatology

**Manuscript NO:** 57325

**Title:** Circulating miR-21-5p level has limited prognostic value in patients with hepatocellular carcinoma and is influenced by renal function

**Reviewer's code:** 05068976

**Position:** Peer Reviewer

**Academic degree:** PhD

**Professional title:** Professor

**Reviewer's Country/Territory:** Spain

**Author's Country/Territory:** Germany

**Manuscript submission date:** 2020-06-12

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2020-06-14 21:20

**Reviewer performed review:** 2020-07-15 03:15

**Review time:** 30 Days and 5 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## **SPECIFIC COMMENTS TO AUTHORS**

The work by Franck et al. was focused on the evaluation of the prognostic value of circulating miR-21 levels in HCC. Using an European cohort of patients (n=91) with HCC, the authors found that there was no association between serum miR-21 levels and disease etiology, BCLC stage and/or Child-Pugh score. However, a positive correlation of miR-21 levels and AST or miR-122 levels was evident, while serum mir-21 levels negatively correlated with kidney function. Regarding survival, miR-21 serum levels were not found to be correlated with worse survival. Most of the results presented here pinpoint that serum miR-21 levels might not have a prognostic role for HCC. Still, there are some important points that should be addressed in order to confirm these findings.

1 – Please revise the manuscript to correct some grammatical errors and typos; 2 – Since the authors were not able to reproduce some of the previous findings from other groups (mostly obtained in Asian cohorts), it would be important in figure 1 to include also healthy controls, in order to confirm if miR-21 serum levels are increased in HCC, thus recapitulating the findings from other groups. 3 – How were the patients diagnosed? Was the diagnosis confirmed by histology? 4 – In methods, the authors mention that miR-21 expression was measured by SYBR Green while miR-122 by the Taqman methodology (which is the most widely used). What is the rationale behind this? Probably measuring miR-21 expression with the Taqman technology would be more reliable. 5 – In Figures 2-5, please include the r and p values (instead of presenting them in the tables). It is easier to follow when they are accompanied by the figure. 6 – Was there any correlation between miR-21 serum levels and albumin (hepatocyte function)? 7 – Regarding survival, considering that patients with high AFP display higher levels of miR-21, do patients with high AFP and high miR-21 display worse survival? 8 – Throughout all the manuscript, in order to follow the most recent

guidelines for mentioning miRNAs, the authors should include the species and the strand of the miRNA being evaluated (e.g. has-miR-21-3p). 9 – The authors only evaluated overall survival. What about relapse-free survival (RFS)? Do patients with higher miR-21 levels present more recurrence? Please repeat all the survival analysis for RFS. 10 – Are the serum levels of miR-21 correlated with the development of metastasis? 11 – In table 1, please replace <50% and >50% percentile by Low and High. It is easier to follow. Furthermore, regarding pre-treatment of patients, what was the regimen in this case?

## RE-REVIEW REPORT OF REVISED MANUSCRIPT

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**Author's Country/Territory:** Germany

**Manuscript submission date:** 2020-06-12

**Reviewer chosen by:** Jia-Ping Yan

**Reviewer accepted review:** 2020-08-19 07:17

**Reviewer performed review:** 2020-08-19 07:31

**Review time:** 1 Hour

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## SPECIFIC COMMENTS TO AUTHORS



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The authors addressed all my concerns and the manuscript was improved and now suitable for publication. Congratulations on this great work.