



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

Scientific quality	<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 Grade E: Do not publish
Language quality	<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
Conclusion	<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
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



**Baishideng
Publishing
Group**

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

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



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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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Reviewer's Country/Territory: Spain

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

Scientific quality	<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
Language quality	<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
Conclusion	<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
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https://www.wjgnet.com

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