Reviewer's report

Title: MicroRNA-21 promotes hepatocellular carcinoma HepG2 cell proliferation through repression of mitogen-activated protein kinase-kinase 3

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Reviewer: Mayuko Furuta

Reviewer's report:

In this manuscript, the authors have identified MAP2K3 as a novel target of oncomiR, miR-21. Besides the importance of miR-21 in cancer and the impact of their novel target gene, some indispensable data was missing. Several points need clarifying.

Major Compulsory Revisions

1. The authors described the repression of MAP2K3 was inversely correlated with miR-21 (in the Abstract, page 2 line 7.). Although, there are no results of miR-21 expression status using the corresponding tumor and non-tumor samples. While it is well known that miR-21 is overexpressed in tumor samples, the conclusion that these are correlated is unclear. In addition, the authors used qRT-PCR for miRNA expression analysis. How does the miRNA with only 22nt small RNA could be amplified with the primer? The authors should mentioned the reference or show detailed methods if they don’t use widely used materials such as TaqMan probe.

2. The authors used only HepG2 cells for the entire experiments as they presented in the title. It is not sure that using HepG2 cell for overexpression experiment is appropriate and reasonable while HepG2 are previously reported to overexpress miR-21 compared with normal liver tissues (Zhu et al., Oncol Rep. 2012). The authors also should mention the expression status of HepG2 in the main text by showing data or adding some references.

3. Some of the control experiments were missing in the Luciferase reporter assay in Fig.2B and C. First of all, the authors should add the results of co-transfection of pMIR-Report empty vector with pAd/con or pAd/pri-miR-21 for Fig.2B and pAd/con or pAd/miR-21/inhibitor for Fig.2C to exclude the possibility of off-target effect. In addition, the asterisk should show which is the pair to be compared.

4. The sentence on page 12 line 8, describe the repression of MAP2K3 in HCC is a evidence to show MAP2K3 as a target of miR-21 is misreading. The authors should describe why they focused on MAP2K3 while they are plenty of predicted targets for miR-21.

Level of interest: An article of limited interest

Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
'I declare that I have no competing interests