Reviewer's report

Title: Association between KIF1B rs17401966 genetic polymorphism and hepatocellular carcinoma susceptibility: an updated meta-analysis

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Reviewer: Adrià Aterido

Reviewer's report:

The authors of the present manuscript have performed a meta-analysis to investigate the association between genetic variation at KIF1B gene (SNP rs17401966) and HCC risk using 18 case-control studies. In this analysis, the SNP rs17401966 has shown a nominal association with HCC risk and two subgroups of patients.

After careful examination of the present manuscript, I have the following concerns:

1. There is a previous study that has meta-analyzed the association between rs17401966 and HCC risk (Su M. et al, Clin Mol, Hepatol, 2017). The studies included in the present meta-analysis are roughly the same. This article includes also a stratified analysis like the one performed in the present manuscript. Surprisingly, this previous work of reference is not cited neither in the introduction nor in the discussion. Comparing the results of the present study with meta-analyses previously performed for HCC risk is essential to contextualize the genetic association findings.

2. The stratified meta-analysis is performed on two subgroups of HCC patients, including HBV-positive and Chinese patients. Importantly, it has been previously reported that chronic HBV infection contributes to ≥80% of HCC patients from China (Chen CJ et al, J Gastroenterol Hepatol, 1997). The two stratified analyses here performed are therefore likely to be redundant. Knowing the number of HBV-positive patients from each study included in the meta-analysis would help to rule out this possibility. This could also help to discard that HBV-patients included in the meta-analysis are taken from only one or a very few studies (in such a case, the concept meta-analysis would be strongly compromised). However, these data are hidden in Table 1.

3. In addition to the previous meta-analysis, there is a GWAS that has already found a strong association between the candidate SNP and the risk of developing HCC (P=1.7e-18, Zhang H et al., Nat Genet, 2010). Therefore, the interest and novelty of the present work is quite doubtful.
4. In the methods section, it should be written down the range of years used as a threshold to select the studies for meta-analysis. In such a case, the similarity between the present study and the previous meta-analysis would be clearly shown (Su M. et al, Clin Mol, Hepatol, 2017).

5. In the discussion section, the authors state that the present analysis has been performed because the conclusions of the previous studies are controversial. In my opinion, it would be more informative for the reader if a more detailed explanation of the controversies was described. The addition of this explanation is also necessary to visualize both the novelty and interest of the present meta-analysis.

6. The present work can have an added value. The meta-analysis stratified by ethnicity could be further performed on Japanese patients. The results of this analysis could be contrasted to the findings obtained in Chinese patients and, hopefully, it could provide new insights into the ethnic-specific associations of the candidate SNP with the risk of developing HCC.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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