Dear reviewers,

Thank you very much for your letter and for the reviewers' comment concerning out manuscript "Differences of core genes in liver fibrosis and hepatocellular carcinoma: evidence from integrated bioinformatics and immunohistochemical analysis" (No. 75071). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researchers. We have studied comments carefully and have made correction which we hope meet with approval. The main corrections in the paper and the responds to the reviewers' comments are as flowing:

1. Reviewer #1

1) Patient liver samples collection "Patients who were tested positive for hepatitis B surface antigen, chronic hepatitis C, drug-induced liver disease, non-alcoholic liver disease, alcoholic liver disease, autoimmune liver disease, cholestatic liver disease, or hereditary metabolic liver disease were excluded". Please, could the authors explain why patients who were tested positive for hepatitis B surface antigen? The authors included patients with CHB (n=28) and CHB-associated HCC (n=12). Chronic HBV infection is defined as persistence of HBsAg in serum for at least 6 months after acute infection. Clarification should be provided on this issue.

   Response: We thank you for pointing out the important issue. Yes, you are correct. It is our mistake. Indeed, as you mentioned, "Patients who were tested positive for hepatitis B surface antigen" isn't the one of the Exclusion criteria. We have corrected the comments in the article and added the diagnostic criteria for chronic hepatitis B as "the persistence of HBsAg in blood serum for at least 6 months".

2) Statistical analysis Were the data distributed normally? The statistical analysis

section is poor; please, the authors should describe this section with enough detail to enable readers to understand your results.

Response: Thank you very much. We have added the details about "Statistical analyses" in Method section.

Statistical analyses

GraphPad Prism 8.0 (GraphPad Software Inc. La Jolla, CA, USA) and SPSS 23.0 software (SPSS Inc. Chicago, IL, USA) were used for statistical analyses. Data are presented as mean ± SEM (for normally distributed data) or median with interquartile range (for non-normally distributed data). Statistically significant differences were determined using a two-tailed Student's *t*-test or analysis of variance (ANOVA). Statistical significance was set and marked as * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, and **** $p < 0.0001$. Replicates are indicated in the figure legends, and (n) represents the number of experimental replicates.

3) The Results Section and the material and methods section are conflated. Results should be reported in the Results Section and the methods should be previously explained in the Material and Methods Section.

Response: Thank you for your thoughtful suggestion. We rewrote the part of Result Section and Method Section to reduce repetition. Please kindly review the details in the two sections.

4) It is difficult to follow what the author(s) demonstrated in the tables. Authors should be more careful of tables details.

Response: Thank you for your thoughtful suggestion. We have written up the content of tables details in the results section.

The clinical profile of the patients enrolled in the study is summarized in Table 4. The results showed that males were the majority in S3-4 and HCC groups. The age, TBil, ALB, and CHE values in all groups and the AFP value in non-HCC group were in normal distribution, and the median

AFP value in the HCC group was higher than the upper limit of normal value. In patients with CHB, HBV DNA was detected as positive, and most ALT and AST levels were elevated, which was consistent with the inflammatory activity of the liver. Most patients with HCC were detected negative for HBV DNA, which is related to antiviral treatment.

2. Reviewer #2

1) Make abstract results more concise.

Response: According to your comment, we have re-written the abstract in the correct format of WJGO.

2) Mention the limitations of bioinformatics also in discussion.

Response: Thank you for your good question. We have added the limitation of bioinformatics in the discussion section.

Our current study has some limitations. First, we only analyzed the transcriptome, and many studies have shown that epigenetic modifications and non-coding RNAs also play an important role in the progression of liver disease[33, 49].

3. Reviewer #3

Reviewer #3 had no comments about this article.

4. Science Editor

English needs to be improved by native speakers further.

Response: We carefully read the complete manuscript and further asked the professional editing company to make a second round of language editing.

editage

Editing Certificate

This document certifies that the manuscript listed below has been edited to ensure language and grammar accuracy and is error free in these aspects. The logical presentation of ideas and the structure of the paper were also checked during the editing process. The edit was performed by professional editors at Editage, a division of Cactus Communications. The author's core research ideas were not altered in any way during the editing process. The quality of the edit has been guaranteed, with the assumption that our suggested changes have been accepted and the text has not been further altered without the knowledge of our editors.

MANUSCRIPT TITLE

Differential expression of core genes in liver fibrosis and hepatocellular carcinoma: evidence from integrated bioinformatics and immunohistochemical analysis

AUTHORS

王琦

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THE EDITAGE Promise QUALITY GUARANTEE

Vikas Narang

Vikas Narang
Chief Operating Officer - Editage

We hope that the revision is acceptable for the publication in your journal.

Looking forward to hearing from you soon.

Yours Sincerely

Qi Wang