**Peer Review File**

Article information: https://dx.doi.org/10.21037/tcr-24-110

**Reviewer A**

The paper titled "The Role of IQCB1 in Liver Cancer: A Bioinformatics Analysis" is interesting. IQCB1 has the potential to function as a diagnostic and prognostic molecular marker, and its association with immune infiltration and checkpoint mechanisms has been observed. However, there are several minor issues that if addressed would significantly improve the manuscript.

1) What are the correlations between IQCB1 and the tumor microenvironment? How valuable are IQCB1 in predicting survival and drug sensitivity in LIHC patients? It is recommended to add relevant content.
**Reply:** Thank you for your professional advice. In our original article, we provided a brief description. Based on your suggestions, we have added and revised the relevant content to elaborate on the relationship between IQCB1 and the tumor microenvironment(See Page12, line256-264). As described in the article, IQCB1 is a risk factor and has certain prognostic value in LIHC as described in this article. However, predicting survival and drug sensitivity in LIHC patients is a complex problem involving multiple factors, including other molecules, signaling pathways, and more. So how valuable are IQCB1 in these processes? We cannot specify it clearly, but I believe that future research or our upcoming studies will have the opportunity to elucidate it(See Page13, line277-281).

2): There have been many studies on LIHC. What is the difference between this study and previous studies? What is the innovation? These need to be described in the introduction.
**Reply:** We appreciate your professional comments on our article. Yes, there are many studies on LIHC, however, no one has studied the IQCB1 molecule in LIHC. If you search for LIHC and IQCB1 on PubMed, you will not find any related literature. This study is the first to investigate the role of IQCB1 in LIHC. We have already described the related content in the introduction(See Page4, line78-82).

3): It is necessary to clearly indicate the correlation between IQCB1 in LIHC and disease characteristics and gene expression patterns among immune pathways.
**Reply:** Thanks to the reviewers' valuable comments, we have our analysis to explicitly detail the correlation between IQCB1 expression and various clinical and pathological features of LIHC(See Page7-8, line148-164). Additionally, we have examined the expression patterns of IQCB1 in relation to key immune pathways and markers(See Page11, line226-234).

4): It is recommended to add experiments to study the biological function of IQCBI.
**Reply:** While our study primarily focuses on bioinformatics analyses, we acknowledge the importance of experimental validation. We have discussed the potential biological functions of IQCB1 based on our bioinformatics findings and suggested future experimental directions. Due

to unforeseen circumstances, we have encountered obstacles in conducting experimental verification of biological functions, despite receiving valuable advice from experts. Moving forward, we intend to collaborate with other research units to further investigate the relevant mechanisms.

5): It is suggested that the internal mechanism of IQCBI and immune cells should be added to the discussion.
**Reply:** We thank the reviewers for their valuable questions. We added some content (See Page16, line341-348).

6): How to judge the prognostic characteristics of LIHC based on the results of this study? How to provide candidate targets for the treatment of LIHC? It is recommended to include relevant descriptions in the discussion.
**Reply:** Thanks to the reviewers' valuable comments.we added some relevant descriptions in the discussion(See Page13, Line277-281).

7)Please analyze the potential molecular mechanism and pathobiology of IQCBI in LIHC based on the existing results and literature.
**Reply:** We appreciate your professional comments on our article. As there is no research on IQCB1 in liver cancer, based on this study, we analyzed the correlation between IQCB1 and immune cells and immune checkpoints, which may promote immune escape and cause the occurrence and development of liver cancer(See Page16, Line337-348. Page13,Line285-286).

**Reviewer B**

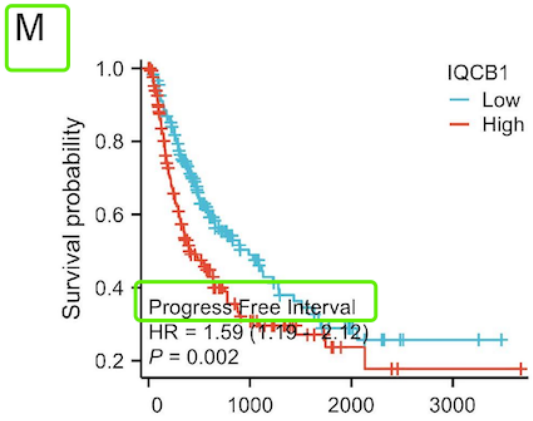
1. Figures and table
   1) Please indicate the meaning of "*" "**" "***" "ns" in Figure 1, 2, 6.

   Reply: We have modified the content.

   2) Please add units to Age and BMI in Figure 2I and 2J.

   Reply: We have modified the Figure2.
   3) Figure 2M-N legends don't match with Figure 2M-N.

   "Impact of IQCB1 expression on OS (L), DSS (M), PFI (N)."



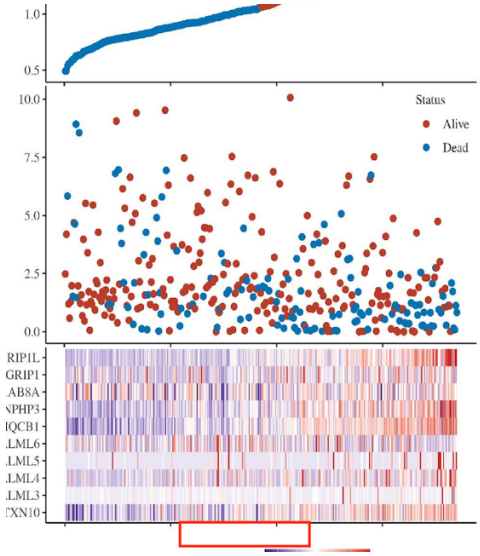

Reply: We have modified the content.

4) There are two “hormone AR, hormone ER” in one sentence, please check if it should remove one.

- The pathway activity of hub genes were illustrated in the Figure4D. IQCB1 activited pathways including apoptosis, cell cycle, DNA damage response, hormone AR, hormone ER, PI3K/AKT and inhibited apoptosis, cell cycle, EMT, hormone AR, hormone ER, RAS/MAPK, RTK, TSC/mTOR.

Reply: In Figure 4D, we can see that IQCBI has both activation and inhibition effects in these two signaling pathways, so the description in the original text is not problematic and should not be deleted.

5) Please add descriptions to X axes in Figure 5C.




Reply: We have modified the content.

6) Please indicate two median time refer to which groups respectively in Figure 5D.


Reply: We have modified the content (Page 11, Line 229-231).