Response to review comments

Response to Editor

Dear Editor,

Thank you for your careful review of my manuscript! I apologize for some mistakes in the manuscript. This was due to our carelessness, but I promise that this does not affect the final scientific results of this study. Based on your and the reviewers' suggestions, we have carefully reviewed and revised the manuscript to ensure that this manuscript conforms to the journal's publication requirements. If you have any questions, please don't hesitate to contact me!

Best wishes!
Mingyue Tang

Response to reviewers

Reviewer 1

Dear Reviewer 1,

Thank you for taking the time to review my manuscript and giving me many valuable suggestions to make us recognize the deficiencies in our research. I apologize for some errors in the manuscript! Now, I have corrected the manuscript as you suggested and answered some questions. Looking forward to your further corrections!

Best wishes!
Mingyue Tang

Comment 1: Reviewer #1:

Scientific Quality: Grade C (Good)
Language Quality: Grade C (A great deal of language polishing)
Conclusion: Major revision
Specific Comments to Authors:

The results of the manuscript entitled “PLXDC1 may be a biomarker of poor prognosis in hepatocellular carcinoma and mediates immune evasion” and authored by Tang et al demonstrated that
This study analyzed PLXDC1 from multiple biological perspectives and found that PLXDC1 is a biomarker of poor prognosis and mediates the immune evasion status of HCC. Before focusing on HCC, it would be beneficial to include a broader overview of targeted pathways and their impacts on enhancing human health. The following studies investigate pathways that have been targeted to treat/prevent different diseases and should be integrated: PMID: 37450997, https://doi.org/10.1186/s41936-020-00177-9, PMID: 34662244, PMID: 33782460, https://www.scirp.org/journal/paperinformation.aspx?paperid=7085 and PMID: 28879232 (specifically for bioinformatics methodology). Relevant patents for pathways targeted to treat/prevent HCC should also be discussed. Detailed comments • Careful proofreading is REQUIRED. • Abbreviation list should be carefully reviewed. • More in-depth discussion is needed. • The following studies should be considered to enrich the discussion and update the references list: https://patents.google.com/patent/US10912741B2/en, PMID: 37568716, PMID: 36139719, https://patents.google.com/patent/US10568873B1/en, PMID: 37627094, PMID: 36120345, and PMID: 26641660.

Reply 1: Thank you for our reminder! We have made changes based on your suggestions.

Changes in the text: “In the past, targeting cancer characteristics has been effective in treating various types of cancer. These traditional anticancer drugs have shown remarkable therapeutic effects but still have adverse side effects for patients. Cisplatin (CIS) is a broad-spectrum anticancer drug that has cytotoxic effects on both normal and cancer cells. Hibiscus extract reduced cis-induced hepatotoxicity in mice, and its use in combination therapy could improve the efficacy of CIS for cancer treatment. Several studies have reported that steroidal saponin is also effective at inhibiting tumor markers, but its poor bioavailability and insufficient preclinical studies limit its application(18-19). With the continuous development of proteomics and bioinformatics fields, screening new anticancer peptides may become a promising strategy for the future treatment and/or prevention of different types of cancer. The high accuracy of DyCluster in detecting protein complexes is a valid argument in support of this method. DyCluster is also able to detect biologically meaningful protein groups(20-21).” “Combination therapy with different anticancer drugs remains a core practice for overcoming the shortcomings of conventional cancer therapy. Combination therapy allows the use of multiple drugs at dose reduction, thereby increasing efficacy and reducing the likelihood of serious adverse events. Recently, a new cancer treatment option has emerged that combines conventional chemotherapy with a naturally
derived chemical that is cytotoxic to cancer cells and causes limited damage to normal cells. The current findings suggest that crocin and sorafenib treatment regimens reduce hepatotoxicity, hinder the development of HCC, and improve liver function. Here, the overexpression of PLXDC1 was shown to be associated with cirrhosis, and some studies have shown that dandelion may prevent liver fibrosis, the inflammatory response and oxidative stress in rats(26-29). “

Reviewer 2

Dear Reviewer 2,

Thank you for taking your valuable time to review our manuscript and for your high approval of this research. If you have any questions, please don't hesitate to contact me!

Best wishes!
Mingyue Tang

Comment 2: Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors:

Tang et al. investigated PLXDC1 expression in HCC patients who were primarily HBV-infected. The format of this manuscript does not follow the guidelines. There are many analyses and results; however, clinical variables are too few to conclude. ALBI score and APRI score should be included in the analysis. Otherwise, ALBIPLXDC1 expression may correlate with reduced survival rates and indicate a risk factor for HCC progression. The implication of immune evasion is interesting.

Reply2: Thank you for our advice! We have made changes based on your suggestions.(Table 1, Table 2)
Specific Comments to Authors: Congratulations on finding additional prognostic factors. However, the text has no statement regarding these novel findings, including methods, results, and discussion. It would be interesting to confirm it by applying survival ROC with four independent prognostic factors. Survival analysis should use cirrhosis, ALBI score, APRI score, and riskScore rather than age, gender, and grade.

Reply:
Thank you for your careful review of my manuscript (Manuscript NO: 90651)! I apologize for some mistakes in the manuscript. About reviewers 1 the latest reply about we did not add recommended literature, we explain here, due to the article after upload format change, modify the part of the red has disappeared, may lead to the misunderstanding, we feel sorry, now we download the article and the red mark in the article). Literature section is 17-21 and 26-29. Now the article is uploaded together in the email. If you have any questions, please don't hesitate to contact me!