TCR TRANSLATIONAL CANCER RESEARCH
ADVANCES CLINICAL MEDICINE TOWARD THE GOAL OF IMPROVING PATIENTS' QUALITY OF LIFE
IMPACT FACTOR 1.241

Peer Review File

Article information: https://dx.doi.org/10.21037/tcr-21-1389

Reviewer A

The manuscript by Li and co-authors describes a novel protein potentially involved in carboplatin resistance in ovarian cancer. The authors created carboplatin-resistant cell lines and used sequencing technology to identify PSMD4 as one of the potential players in chemoresistance.

Critique.

Comment 1: Tumors were generated using a subcutaneous model, which does not replicate how ovarian cancer metastasizes. The authors should indicate in the manuscript that the treatment regimen may not result in tumor reduction in patients, as their metastases develop intraperitoneally.

Reply 1: Thank you for your valuable comments. This is a shortcoming of our study, and we have discussed it in our revised manuscript.

Changes in the text: We have modified our text as advised (see Page 24, line 3-6).

Comment 2: The manuscript is difficult to read, as there are numerous stylistic errors throughout the manuscript in addition to typos and incorrectly used words. Professional editing is recommended.

Reply 2: Thank you for your advice. We have tried our best to improve the English expression. Our manuscript was edited for proper English language, grammar, punctuation, spelling, and overall style by one or more of the highly qualified native English speaking editors at Editideas. We also provide the certification of Editideas as an attached file. Once again, thank you very much for your kind advice.

Changes in the text: We have modified our text as advised (see Revised Manuscript).

Comment 3: Minor critique. The title needs to be rephrased and one of the words - “accumulation" needs to be removed.

Reply 3: Thank you for your comments, we have revised the title.

Changes in the text: We have modified our text as advised (see Page 1, line 2-4).

Reviewer B

This is very comprehensive study investigating the role of PSMD4 in epithelial

ovarian cancer. Overall the the experiments have been conducted well

Comment 1: Abstract line 9, please replace normal with parental or carboplatin sensitive.

Reply: Thank you for your valuable comments. We have revised it.

Changes in the text: We have modified our text as advised (see Page 3, line 10).

Comment 2: Page 7 line 15-17. Please add information re the stability of the carboplatin resistance in the ovarian cancer cell lines.

Reply: Thank you so much for your comments. We have added relevant information about the stability of carboplatin-resistant cell lines in this study. The content we added is "Two weeks after the withdrawal of the carboplatin treatment, the biological characteristics of the resistant strains were observed. One month after the withdrawal of the carboplatin, the carboplatin-resistant cell lines can still maintain drug resistance. Compared with the IC50 when the carboplatin was withdrawn, there was no statistical difference in the IC50 change at 1 month after the carboplatin was withdrawn (P>0.05), indicating that the carboplatin-resistant cell lines have better drug resistance stability.".

Changes in the text: We have modified our text as advised (see Page 8, line 11-17).

Comment 3: Page 11. Line 15. Please add details of the antibody dilution used for this study and information on the positive and negative controls used for the immunohistochemistry.

Reply: Thanks for your comments. We have added the antibody dilution used for this study and the positive/negative controls of immunohistochemistry in Supplementary Figure 1.

Changes in the text: We have modified our text as advised (see Page 13, line 12-20, and Supplementary Figure 1).

Comment 4: Page 12 Line 10. Please add information to the methods for the shPSMDA vectors used and how cells were generated

Reply: Thank you for your valuable comments. We gave a detailed description of the construction of OV-PSMDA and shPSMD4 plasmids.

Changes in the text: We have modified our text as advised (see Page 7, line 20 - Page 8, line 7).

Comment 5: Page 13 line 19. Is the carboplatin resistance stable after many passages.

Reply: Thank you so much for your comments. We have added relevant information about the stability of carboplatin-resistant cell lines in this study. The content we

added is "Two weeks after the withdrawal of the carboplatin treatment, the biological characteristics of the resistant strains were observed. One month after the withdrawal of the carboplatin, the carboplatin-resistant cell lines can still maintain drug resistance. Compared with the IC50 when the carboplatin was withdrawn, there was no statistical difference in the IC50 change at 1 month after the carboplatin was withdrawn (P>0.05), indicating that the carboplatin-resistant cell lines have better drug resistance stability.".
Changes in the text: We have modified our text as advised (see Page 8, line 11-17).

Comment 6: page 14 line 13. no explanation for fig 2D provided.
Reply: Thanks for your comments. We have added the results and explanations for Figure 2D to the revised manuscript.
Changes in the text: We have modified our text as advised (see Page 17, line 3-5).

Comment 7: page 14 line 14. should explain that GSE33482 database was used for this analysis.
Reply: Thanks for your comments. We have carried out the usage instructions of GSE33482 database in the revised manuscript.
Changes in the text: We have modified our text as advised (see Page 17, line 6-8).

Comment 8: page 15. no details provided in the methods for the generation of OV-PSMDA and shPSMD4.
Reply: Thank you for your valuable comments. We gave a detailed description of the construction of OV-PSMDA and shPSMD4 plasmids.
Changes in the text: We have modified our text as advised (see Page 7, line 20 - Page 8, line 7).

Comment 9: page 14 line 17. diagnostic is incorrect term. prognostic should be used.
Reply: Thank you for your valuable comments. We have revised it.
Changes in the text: We have modified our text as advised (see Page 17, line 12).

Comment 10: page 18 line 3. please confirm that measurements have been performed on cancer areas. Some images in Figure 8 B do not appear to contain any cancer cells.
Reply: Thank you very much for your valuable comments. Through consultation with pathologists, we have corrected and accurately checked the Revised Figure 8B.
Changes in the text: We have modified our text as advised (see Revised Figure 8B).

Comment 11: Figure 1
Add IC50 values to graphs for Figure 1E and 1F.

Reply: We have added the IC50 values in Figure 1E and 1F, respectively.
Changes in the text: We have modified our text as advised (see Revised Figure 1E and 1F).

Comment 12: Figure 1C images are poor quality.
Reply: Thanks for your comments. We have improved the quality of Figure 1C.
Changes in the text: We have modified our text as advised (see Revised Figure 1C).

Comment 13: Please add scale bar rather than magnification for Fig 1C and 1D.
Reply: Thank you for your valuable comments. We have revised it.
Changes in the text: We have modified our text as advised (see Revised Figure 1C and 1D).

Comment 14: Figure 2. The explanation of the colors for Fig 2A is misplaced with Fig Fig 2C. There are circles but not squares in Fig 2. What groups BP CC and MF indicate?
Reply: Thank you for your valuable comments. We have revised it. BP: biological process; CC: cell components; MF: molecular function.
Changes in the text: We have modified our text as advised (see Page 32, line 15- Page 16, and the legend of Figure 2).

Comment 15: Figure 3 Please define CR and NCR
Reply: Thank you for your valuable comments. We have added the concepts of abbreviations CR and NCR in the legend of Figure 3. CR: complete response; NCR: non-complete response.
Changes in the text: We have modified our text as advised (see the legend of Figure 3).

Comment 16: Figure 8. Please check images included in 8B with a pathologist. Some of these do not appear to contain any cancer cells
Reply: Thank you very much for your valuable comments. Through consultation with pathologists, we have corrected and accurately checked the Revised Figure 8B.
Changes in the text: We have modified our text as advised (see Revised Figure 8B).