

Response letter

Reviewer's code: 05079464

Reviewer's country: Mexico

SPECIFIC COMMENTS TO AUTHORS

1. The discussion made by the authors provides important information about new therapies against pancreatic cancer, they discuss in appropriately form their results. However, they do not compare their results with other studies in pancreatic cancer cells and other Disintegrin Metalloproteases. I recommend to the authors to review the interaction of the metalloproteases family with other malignant tumors and their therapies. Furthermore, as possible, review the metalloproteases and their interaction in treatment with pancreatic cancer cells, in order to compare the results with other studies.

Reply: We thank the reviewer for pointing out this, and in the revised manuscript, the discussion of ADAM28 and its associated molecules was included in the discussion section. We believe that the revised manuscript could enhance the importance of ADAM28 in the cancer study.

2. The authors showed the English certificate of the manuscript. However, they send the main text without the suggested corrections by the experts in the language. Thus, I recommend to review this point.

Reply: We thank the reviewer's suggestion, and in revised manuscript, we have corrected the minor language problem, and marked as red. Please allow me to show appreciate to the reviewer's suggestion.

3. The authors presented correct research methods and they provided the approval number of ethics for the study in animals, but they did not present the ARRIVE guidelines

Reply: We thank the reviewer's suggestion, and the ARRIVE guideline

statement was included in the revised manuscript. Also, this study does not include the animal experiments, so the institutional animal care use statement is not applicable to this manuscript. However, the human tumor tissues were included in this study to study the expression of ADAM28, and this study was approved by the ethical committee of the third affiliated hospital of Sun Yat-Sen University. And we uploaded the PDF document and the ARRIVE statement.

Reviewer's code: 03004570

Reviewer's country: Turkey

SPECIFIC COMMENTS TO AUTHORS

1. This manuscript is a comprehensive basic study that is focused on gemcitabine (GEM) resistance. Authors found that ADAM28 is involved in the GEM resistance and should be a novel target to overcome this resistance. This finding may be clinically important in the future. Materials and methods are adequate. Results are clear. Figures are excellent.

Reply: We thank for the positive comments from the reviewer. In the revised manuscript, we completed the language polishing, and we believed that the manuscript has been greatly improved with the help of reviewers.

2. There are some small typing errors. First in the line 11 and line 24 of pp#18; the word "expression" is duplicated and one of them should be deleted, and then the word "reveled" should be "revealed".

Reply: We thank the reviewer's careful review, and in the revised manuscript, the errors were corrected according to the reviewer's suggestion.

3. Secondly, in the line 6 of pp#14, correct sentence should be continued such as "... cancer therapy, in SW1990 cells...". Similarly, in the line 14 of pp#15,

correct sentence should be continued as “....molecules, the correlation between....”. I recommend this article for publication after these minor corrections.

Reply: We appreciated the reviewer’s careful review, and in the revised manuscript, these minor language problems have been corrected, and we thank the reviewer’s suggestion again.

Reviewer’s code: 02734287

Reviewer’s country: Croatia

SPECIFIC COMMENTS TO AUTHORS

Genetic analysis of drug resistant pancreatic cancer is an area of great interest and the results of the study are promising. However, the language of the manuscript is very poor and the paper needs to be completely rewritten in order for the authors to be able to convey their messages and conclusions.

Reply: We thank the reviewer’s suggestion, and we polish the language of our revised manuscript with the help of English native speaker.