

Peer Review File

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Reviewer A

In the first part of this manuscript, the authors give a comprehensive review of the process of cancer cell survival including ferroptosis, autophagy, and apoptosis in that the Hippo-YAP pathway is involved. Subsequently, they summarize the recent findings of the Hippo-YAP pathway-dependent regulation of cancer immunosuppression. The authors have successfully summarized huge and diverse information of recent findings around the Hippo-YAP pathway's field. In case of arguing the controversial reports, they carefully dictate both results and adequately handle the topic.

After mending several points, I recommend this manuscript to be published in Translational Cancer Research.

Comment 1. The figure has not been fully revised. Font sizes are too small. Almost all figure elements/sentences are out of alignment (the label 'MP4Ks' and 'TAOK' are the most extreme examples). The cartoon of figure 2 should include more information about the glutathione synthesis by adding the drawing of system xc-. The design of figure 3 is difficult to grasp its meaning immediately.

Reply 1: We are sorry for the inconvenience caused by our figure presentation. We started by adjusting the font size in each image to make them larger and more visible

than before. We appreciate that the reviewers pointed out the mismatch between the drawings and the text. We adjusted the individual elements to get each label within the corresponding range. We acknowledge that the absence of system X_C⁻ in Figure 2 makes the relationship between erastin and GSH unclear, therefore we added the drawing of system X_C⁻ and a description of system X_C⁻ in the figure legend. In view of the issues raised by the reviewers regarding the design of Figure 3, we decided to partially redraw Figure 3 after careful analysis, in order to remove reading barriers. Accordingly, the figure legend has also been slightly revised.

Changes in the text: We have modified in Figure1-4 and in the figure legends of Figure2 and Figure3.

Comment 2. Please use the same terminology throughout the manuscript (e.g., 'YAP' and 'YAP1', 'MDA231' and 'MDA-MB-231').

Reply 2: Thanks for your suggestions. To unify and simplify the different terminology, we have corrected all 'YAP1' into 'YAP' and 'MDA-MB-231' into 'MDA231'.

Changes in the text: 'YAP1' has been replaced by 'YAP' in the revised manuscript (Page 12, line 233; page 12 line 235; page 14, line 273; page 14, line 276; page 14, line 280), and 'MDA-MB-231' has been replaced by 'MDA231' in the revised manuscript (Page 6, line 113).

Comment 3. In page 4 line 71, Zhang et al. (2009) Nat. Cell Biol. 11:1444-50 seems to be more appropriate as a reference for AREG.

Reply 3: Your suggestion really means a lot to us. Yes, it would be more understandable if we adopt Zhang et al. (2009) Nat. Cell Biol. 11:1444-50.

Changes in the text: We have deleted the original thirteenth citation and replaced it with this recommended one in the revised manuscript (Page 4, line 72).

Comment 4. In page 4 line 72, there is no reference paper in the dictation of VGLL4.

Please cite Zhang et al. (2014) Cell Res. 24:331-43.

Reply 4: We thank the reviewer's scrupulous correction. Indeed, the description of VGLL4 is incomplete and the recommended paper supplements it.

Changes in the text: The citation has been added in the revised manuscript (Page 4, line 75).

Comment 5. In page 5, the word 'system XC-' should be written in a form that 'C' is subscript and '-' is superscript.

Reply 5: We feel sorry for the improper format. We have used 'system X_C⁻' as you suggested.

Changes in the text: The word 'system XC-' has been transformed into 'system X_C⁻' in the revised manuscript (Page 5, line 87; page 5, line 89; page 8, line 151).

Comment 6. In page 6 line 115, the abbreviation 'OVCA' is firstly appeared without its full form.

Reply 6: We agree that this issue should be addressed. We adopted its full form 'ovarian cancer'.

Changes in the text: We have deleted the abbreviation and added the full form in the revised manuscript (Page 6, line 117).

Comment 7. In page 7 line 140, the phosphorylation of Ser109 is mentioned in ref. 32, and the phosphorylation of Thr241 is mentioned in ref. 33.

Reply 7: Thanks for your careful check. We are sorry for our carelessness. We switched the position of the two so that they corresponded to the citations.

Changes in the text: We have modified that in the revised manuscript (Page 8, line 142).

Comment 8. In page 9 line 165, the referenced paper does not fully support the content of this sentence. Please cite additional papers (e.g., Li et al. (2019) Biomedicine & Pharmacotherapy 119:109415).

Reply 8: We agree with the reviewer. Only one paper seems to be lack of rationality and stringency, and the recommended paper makes the logic more complete.

Changes in the text: The citation has been added in the revised manuscript (Page 9, line 168).

Comment 9. In page 13 line 244, the reference number 70 is mistakenly placed as a superscript.

Reply 9: We are sorry for the careless mistake. Thanks for your reminding.

Changes in the text: The superscript format of the reference number 73 has been removed in the revised manuscript (Page 13, line 248).

Comment 10. In page 23 line 442, this reference lacks the information of issue number and specific article number. Please add '507:112-123'.

Reply 10: Thanks for your nice suggestion. We have updated the reference.

Changes in the text: The information of issue number and specific article number have been added in the revised manuscript (Page 3, line 41; Page 23, line 447-449).

Comment 11. In page 30 line 647, this reference lacks the information of specific article number. Please add 'eaaj1757'.

Reply 11: Thanks again for your nice suggestion. We have removed the original citation and added its fuller version.

Changes in the text: We have modified that in the revised manuscript (Page 17, line 340; page 28, line 680-682).

Reviewer B

Good review, well done.

However, figures need better definition.

Reply: Thank you for your kind comments on our manuscript. We acknowledge that better figures would help authors interpret the results and readers clarify the structures. According to your suggestions, we have beautified our images, such as by unifying the elements of Figure 1, enriching the content of Figure 2, simplifying the structure of Figure 3, etc. Hope revised figures would be easier to understand.

Changes in the text: We have modified in Figure1-4 and in the figure legends of Figure 2 and Figure 3.