Author's response to reviews

Title: Targeting mTOR/p70S6K/glycolysis signaling pathway restores glucocorticoid sensitivity to 4E-BP1 null Burkitt Lymphoma

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Author's response to reviews: see over
Dear Editor,

On behalf of my co-authors, we thank you very much for giving us an opportunity to revise our manuscript, we appreciate Dr. Gregory B Carey and Dr. Melba Jaramillo very much for their positive and constructive comments and suggestions on our manuscript entitled "Targeting the mTOR/p70S6K/glycolysis signaling pathway restores glucocorticoid sensitivity to 4E-BP1 null Burkitt lymphoma cells" (ID: 1851984681437080).

We have studied the comments and suggestions carefully and have made revisions which were highlighted in yellow in the paper.

We would like to express our great appreciation to you and reviewers for comments and suggestions on our paper.

Thank you very much for your attention and consideration.

Sincerely,
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Response to Reviewers’ Comments

Response to Dr. Gregory B Carey

1. We have corrected the MTT assay as a cell viability assay.

2. We have rewritten the sentence. It is now “These effects were achieved by the inhibition of mTOR/p70S6K signaling pathway, which led to the inhibition of glycolysis and the induction of autophagy. Pretreatment with pan-caspase inhibitor z-VAD-fmk or autophagy inhibitor 3-MA failed to protect the cells from combined treatment-induced death”.

3. We have rewritten those sentences.

4. Yes, we have corrected it.

5. We have corrected it.

6. We have removed the section on SS and accompanying figures.

7. Fig 2C was removed from the article.

8. Because our work on Karpas 299 model has not been published yet, we removed the sentence.

9. Because Fig 3B can show the result of Fig 3A, we removed Fig 3A.

10. Thank you very much for the suggestion. We reanalyzed the results by gating on the amount of annexin V binding to PI negative cells and indicated the gating in the figure legends.

11. Bcl-2 family members play an important role in GC-induced apoptosis and may play an important role in GC resistance in lymphoid tumor. In different cell lines, different changes occurred in the members of Bcl-2 family. The molecular mechanisms of GC resistance remain unclear in Burkitt lymphoma. Those changes on bcl-2 related proteins may correlate with GC resistance in Raji cells, which need confirmation by further research.

12. We have redrawn Fig 4D and 4E to show the result more clearly. In combined group, pre-treatment with z-VAD-fmk induced the cell viability slightly and reduced the cell apoptosis rate obviously (p<0.05). But z-VAD-fmk did not full protect the cells from cell death induced by combined treatment. And we draw a graph to show the relationship between apoptosis and autophagy under the combined treatment in Raji cells.
13. Yes, Rap used alone can induce autophagy. Combined with Dex increased 1.323-fold in LC3-II/LC3-I compared with Rap used alone.

14. Yes, maybe, but we have not found it out.

15. These are *Annexin V-FLUOS* positive/PI negative cells.

16. Raji cells are null of 4E-BP1. To show the blot of 4E-BP1 need a positive control cell line, so we did not show it in the draft.

17. We have corrected it. According to your valuable suggestion, we have added the results of lactic acid production (Fig 5B and 5D).

18. We have rewritten it.

19. Sorry, we made a mistake. We have corrected it.

20. We have rewritten it.

21. We have corrected it.

Special thanks to you for your good comments.
Response to Dr. Melba Jaramillo

Thank you very much for your positive and constructive comments and suggestions.

The manuscript has been carefully read through and all the grammar errors we could find in the text have been corrected. And the english quality of the manuscript was improved by native speakers.

We have redrawn the figures to make them more clearly and corrected the manuscript carefully according to your comments.