

Dear Editor,

Thank you very much for your working on our manuscript. We appreciate this positive feedback from the reviewer. As suggested, we now revised the manuscript based on the suggestions and the amendments are highlighted in red. Point by point responses are listed below. All the references with PMID and DOI information have been updated. Duplicated or error references have been removed. The image was revised according to the editorial suggestions, and an editable PPT version has been updated.

We hope this new version of manuscript would be more readable. We look forward to hearing from you soon. Thank you again for your time and consideration.

Respectfully,

Zhigang Chen

Point to Point Responses

1. Although the authors have briefly discussed the therapeutic strategies for CSCs, it is not clear how inhibition of glycolysis or glucose deprivation lead to the death of non-CSCs. The authors need to expand on this issue.

Response: Thanks for the reviewer's valuable suggestions. According to the reviewer's suggestion, we have revised our manuscript in the Clinical Implications part. It has been reported that inhibition of glycolysis or glucose deprivation could cause G0-G1 phase arrest or induce apoptosis, thus leading to cells death.

2. Although the current review article provides considerable information about energy metabolism by CSCs and non-CSCs, the authors failed to interpret the data.

Response: We appreciate the positive feedback. We have added interpretation of the energy metabolism in the main text which is highlighted in red. Also we explain the clinical value of energy metabolism in CSCs in the Clinical Implications part.

3. Lastly, the authors need to add a section on "Future Direction".

Response: Thanks for the editor's valuable suggestions. We apologize for our mistakes. We have added the section "Future Direction" at the end of the article.