

Answering Reviewers Letter (MS No: 42952)

Response for the comments of the editor and referee

Dear respected chief editor and reviewers,

With greatest and heart-felt appreciation, we are glad to resubmit our manuscript with revision as advice, and the response for the comments are shown as following:

Academic Editor comments:

1” ...The review of your manuscript, which you submitted to the World Journal of Stem Cells, is now completed and the first decision for publication is available. We request that you submit your revision in no more than 7 days. ...”

Response: Thanks a lot for this great and encouraging news, with the professional comment of the editor and referee, and the grace of God. It’s our greatest pleasure to follow up the advice of academic editor and the referee to do the revision on our manuscript, accordingly.

2. “Please provide language a certificate letter from a professional English language editing company.”

Response: Noticed and thanks a lot for the loving reminder about the request of the journal for the non-native speakers of English. As the advice, we have already sent to the suggested professional English language editing company-American Journal Expert for this. The Certificate will be submitted too. Note that the changes by the Language Editing Company have been highlighted as the way of track changes.

3. “Please add the content of “Conflict-of-interest statement” and “Biostatistics review certificate...”

Response: Yes, it has added as advice, as shown in page 3 and 4, respectively. Thanks a lot for the loving reminder and sorry for our careless missing.

4. “Please write a summary of no more than 100 words to present the core content of your manuscript, highlighting the most innovative and important findings and/or arguments. ...”

Response: Thanks a lot for the thoughtful reminding, and we have rewrite the whole section in a more attractive and summary way, as shown in page 8.

5. “Please read the core tip then provide the audio core tip: ...”

Response: OK, and it has been done. Thanks a lot for the professional guidance.

6. Please add “ARTICLE HIGHLIGHTS... The guidelines for writing and...”

Response: OK, and it has been done, as shown in page 35. Thanks a lot for the loving guidance.

7. “Please add PubMed citation numbers and DOI citation to the reference list and list all authors. Please revise throughout. The author should provide the first page of the paper without PMID and DOI...”

Response: OK, and it has been done. Thanks a lot for the helpful guidance

Reviewer's comments:

Reviewer No 1.

1. “This article is very interesting, showing the intracellular pH of hiPSC is higher than that of differentiated cells. Authors also showed the suggested molecular mechanism of the higher pHi of undifferentiated hiPSC. Although the data shown here are limited to one line of hiPSC (HPS0077), the finding is rational and impressive. I believe that this article will contribute to an advanced understanding of the mystery of pluripotent stem cells in general.

Response: Thanks a lot for the positive, encouraging and loving comment of the reviewer for our submitted manuscript. Yes, on behalf of all authors, I would like extend our heat-felt appreciation for the valued comments, and will do the revision accordingly.

2. Minor concerns:

- 1) The order of the appearance of Figures is rather complicated. For example, the description regarding Figure 7 appears before that of Figure 3. In addition, the description regarding Figure 1A and 1B appears in M&M (Measurements of intracellular pH) while that of Figure 1C appears in Results. Please rearrange the order of the appearance of the descriptions regarding these Figures. For example, Figure 7 can be mentioned in Discussion. Figure 1C can be included in M&M. Alternatively, Figure 1A and Figure 1B can be mentioned in Results, but not in M&M.

Response: Thanks a lot for the thoughtful and professional comment about this. To avoid the possible confusion to readers, the Figure 1A and Figure 1B have been mentioned in the Section of Results, as advice.

- 2) In page 21, line 2, the phrase “...may inhibited...” should be corrected as “...may inhibit...” or “...might inhibit...”.

Response: OK, has been changed and double checking the English Language Editing Company assigned by the journal, i.e. AJE. The change has also been highlighted with red color in the text (page 25, line 7).

- 3) In page 23, line 2, the phrase “Regard to ...” should be corrected as “Regarding to ...”.

Response: OK. As the whole section has been rewritten, as advised by 2nd reviewer. It has been changed and double checked by the English Language Editing Company assigned by the journal, i.e. AJE. The change has also been highlighted with red color in the text.

- 4) In page 23, line 5, the phrase “...a decrease of pHi...” should be corrected as “...a decrease in pHi...”.

Response: OK. As the whole section has been rewritten, as advised by 2nd reviewer. It has been changed and double checked by the English Language Editing Company assigned by the journal, i.e. AJE. The change has also been highlighted with red color in the text.

5) In page 25, line 6, the phrase "... were substantially existed for..." should be corrected as "... were substantially existing for..." or "... substantially existed for..."

Response: OK. As the whole section has been rewritten, as advised by 2nd reviewer. It has been changed and double checked by the English Language Editing Company assigned by the journal, i.e. AJE. The change has also been highlighted with red color in the text.

6) In page 27, line 1, please delete the word "also".

Response: OK. As the whole section has been rewritten, as advised by 2nd reviewer. It has been changed and double checked by the English Language Editing Company assigned by the journal, i.e. AJE. The change has also been highlighted with red color in the text.

7) In page 27, line 2, the words "pluripotent markers" should be corrected as "expressions of pluripotent markers".

Response: OK. As the whole section has been rewritten, as advised by 2nd reviewer. It has been changed and double checked by the English Language Editing Company assigned by the journal, i.e. AJE. The change has also been highlighted with red color in the text.

Reviewer No 2.

1. This article describes about the mechanism of intracellular pH regulation in human iPSCs. The change of expression of pHi regulators in Figure 6 may be described more in detail. The symbols for error bars may be re-checked carefully.

Response: Thanks a lot for the thoughtful and professional comment about this. To make sure the reader can follow up the whole story of manuscript, we have described the Figure 6 in more detail and logic way, including the both Sections of Result and Legend, which highlighted with red colour.