Author’s response to reviews

Title: Membrane protein Nav1.7 contributes to the persistent post-surgical pain regulated by p-p65 in dorsal root ganglion (DRG) of SMIR rats model.

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Dear Editors and Reviewers:

Thank you for your letter and for the reviewers’ comments concerning our manuscript entitled “Membrane protein Nav1.7 contributes to the persistent post-surgical pain regulated by p-p65 in dorsal root ganglion (DRG) of SMIR rats model” (BANE-D-17-00166). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. Revised portion are marked in red in the paper. The main corrections in the paper and the responds to the reviewer’s comments are as flowing:

Responds to the reviewer’s comments:

Reviewer 1:

1. Response to comment: However the English is poor and needs to be rewritten. Many run on sentences, frequent use of the presence very tense rather than the past tense.

Response: I am very sorry for my poor English. My manuscript have been reviewed by my friend who is fluent in English.
2. Response to comment: Page 3. How many rats were used in the study. How determined.

Response: At least 134 rats were included in the study. No less than 6 rats in each group and no less than 3 rats in each group for western blot. Rats were randomly assigned to each group.

3. Response to comment: What is your power analysis in the statistical section on page 6? Please expand the discussion of your statistics.

Response: We use statistical software and statistical methods in this study, One-way ANOVA for western blotting data and Two-way ANOVA for behavior data, P < 0.05 would be considered significant. The specific statistical analysis is described in the results and discussion. We have re-written this data in detail according to the suggestion.

4. Response to comment: In your discussion section, can you give an insight as to how your study results could possibly be applied to the clinical situation. In what way does your result "provide a novel way for PPP therapy?"

Response: Thank you very much. Considering the reviewer’s suggestion, We have re-written this part of the discussion. Based on these results, we think that Nav1.7 as well as NF-kb may become the target of clinical analgesic drugs.

Reviewer #2:

1. Response to comment: To my knowledge, persistent postsurgical pain has been defined as pain persisting for 3 months after surgery. In the manuscript, the authors state that PPP is defined as pain 1 month after surgery. Please clarify.

Response: Thank you for your question. In humans, which lasted for more than three months after surgery was called PPP, whereas in rat animal models, Rats only can live for 30 months, So 2 week enough long for PPP.

2. Response to comment: In figure 3, the distribution of NaV1.7 is reported in small and medium diameter neurons as well as in CGRP, NeuN, and IB4 cells, Can the authors comment on whether and how the distribution of NaV1.7 differs between baseline and 10 day post-surgery?

Response: This is a good suggestion, but we only detect the cell type of NaV1.7 expression, and we will conduct in-depth research on the following research.

3. Response to comment: The authors should examine whether p-P65 and NaV1.7 co-localize in DRGs. An analysis of the cell-type(s) wherein these proteins co-localize would be valuable.
Response: Thanks very much for so good suggestion, this result is very important for the research. We have add new results of p-P65 and NaV1.7 co-localize in DRGs.

4. Response to comment: The ChIP assay results show weak band intensities after PCR. Does this reflect low occupancy of the NaV1.7 promoter by P65?

Response: Thanks very much for the question. We think that this weak band intensities after PCR can explain low occupancy of the NaV1.7 promoter by P65.

5. Response to comment: The amount of protein loaded appears to differ between the conditions in Figure 4C. The authors should repeat this experiment and provide data with more equivalent loading controls.

Response: Thank you very much. This experiment has been repeated.

6. Response to comment: In the methods, please list the antibody catalog numbers and/or RRIDs.

Response: Thank you very much. We have made correction according to the Reviewer’s comments.

Special thanks to you for your good comments.

We tried our best to improve the manuscript and made some changes in the manuscript. These changes will not influence the content and framework of the paper. And here we did not list the changes but marked in red in revised paper.

We appreciate for Editors’ warm work earnestly, and hope that the correction will meet with approval.

Once again, thank you very much for your comments and suggestions.