OPEN PEER REVIEW REPORT 1

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Title: TMEM16A contributes to persistent hyperalgesia in neuropathic pain of chronic constriction injury rats
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COMMENTS TO AUTHORS

In this manuscript, the authors mainly explore the function of "TMEM16A" in the mechanism of neuropathic pain. They carried out the study by the systematic testing such as construction of CCI model, implantation of intrathecal catheter, experimental design, evaluation of thermal hyperalgesia, immunofluorescence, intact DRG preparation and electrophysiological recording, and western blot analysis, finding that T16Ainh-A01 blockade increases in CCI-induced TMEM16A expression. The results demonstrated that intrathecal administration of selective CaCCs inhibitors caused antiallodynic and antihyperalgesic effects in spinal nerve injured rats. In the end, the study revealed that TMEM16A protein expression in DRG neurons was up-regulated after chronic constriction injury but selective TMEM16A inhibitor T16Ainh-A01 reversed this increase. In the future, TMEM16A may become a potential analgesic target for preventing chronic pain measures, and TMEM16A and neuropathic pain. This manuscript is further exploring based on the article of "The association between the expression of PAR2" published before. The experimental design and illustration were meaningful. However, there are still a few issues to be clarified prior to the publication of this manuscript.

1. The difference between this study and the published article "The association between the expression of PAR2 and TMEM16A and neuropathic pain" should be clarified.
2. In the "Introduction" section, the incidence rate of the disease should be supplemented, for example, neuropathic pain.
3. The references and the mechanisms about "Inhibition of CCI-induced hyperexcitable state of DRG neurons by T16Ainh-A01, a selective antagonist of TMEM16A" and "Intrathecal injection of T16Ainh-A01 could recover resting potential, reverse the lowered rheobase value and inhibit the firing rate" should be added.
4. Some of the references should be updated. It would be better to be replaced by more references of the latest three years.
5. How many animals have you used in the "Animals" section?