OPEN PEER REVIEW REPORT 1

Name of journal: Neural Regeneration Research
Manuscript NO: NRR-D-22-00035
Title: TMEM16F knockdown mitigates neuroinflammation by microglia polarization towards M2 phenotype via inhibiting NLRP3 inflammasomes in Alzheimer's disease
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Reviewer's country: Sweden

COMMENTS TO AUTHORS

This is an interesting article. I have provided some comments below:
1: The results of the statistical analyses should be more thoroughly reported. It is stated that the results will be presented as mean and SD, yet they are generally presented as mean and SEM. SD would be preferable to SEM. However, when the study samples are very small, it may be even more informative to report individual data points rather than a measure of spread. Further, actual p values should be reported, instead of stating <0.05 or <0.01. I also think it would be good if the actual sizes of important differences were reported in the text when possible.
2: I understand that it is rather common to use ANOVA when running statistical analyses on data from, for example, western blots. However, it may be difficult to establish whether the conditions of using a parametric test are met (such as normal distribution and similar variance in all groups), especially when the groups are very small. Did you consider using non-parametric tests such as Kruskal-Wallis and/or Mann-Whitney?
3: The abstract would benefit from containing additional information. The different groups of mice should be specified as well as the sample size and method for statistical analysis. I understand that there is a word limit to adhere to, but I think some more information could be included with efficient writing.
4: In the introduction, there is a sentence stating that M1-like microglia are anti-inflammatory and M2-like microglia pro-inflammatory. It should be the other way around.
5: I believe the introduction could be improved by being somewhat shorter and more focused on the background relevant to your study. For example, some general facts about AD could be omitted.
6: Some text under Materials and Methods is almost identical to previous works and should be cited accordingly.
7: I suggest that you specify under the relevant section of Materials and Methods that the mice were 9 months old when they received the injections into hippocampus, to make the text easier to follow. Likewise, I think it would be good if you specified here the time from injection to Morris water maze test, and to sacrifice. How many mice were excluded from the Morris water maze test?
8: How did you select which brains to collect for the different analyses?
9: Did you use ANOVA for all statistical analyses? Some comparisons (for example the comparison of TMEM16F expression between APP/PS1 and WT) seem to be between only two groups?
10: Under Results, you report some experiments/comparisons that were not mentioned under Materials and Methods. I think it would be preferable to mention them under Materials and Methods instead. An example is the comparison of TMEM16F expression between APP/PS1 and WT. I also recommend that you report actual differences under Results rather than using subjective terms such as 'obviously elevated'.
11: In Figure Legend 1: What does n>3 mean?
12: Some sentences are very long. I recommend splitting them into shorter sentences to make the text easier to follow.