OPEN PEER REVIEW REPORT 1

Name of journal: Neural Regeneration Research

Manuscript NO: NRR-D-22-00802

Title: Bone marrow mesenchymal stem cells-derived exosomes alleviate ischemic brain injury

through IL-33/ST2 signaling pathway Reviewer's Name: Creed Stary Reviewer's country: USA

COMMENTS TO AUTHORS

In the present study the Authors extend prior work identifying a neuroprotective effect against experimental stroke with exosomes derived from human bone marrow mesenchymal cells by identifying a role for astrocyte IL-33 and ST2 in protection. The study employs in vivo mouse middle cerebral artery occlusion stroke model and *in vitro* ischemia in primary neuronal and astrocyte cultures using up and down regulation approaches. The study is sufficiently novel and clinically relevant, however lacks methodological details as described below. In general all major methodological approaches require references unless specifically developed by the authors in the present study.

- 1. Please provide reference for MCAO and all behavioral tests.
- 2. Please specify timing for animal sacrifice and tissue analysis.
- 3. Please specify "human' BM-MSCs and provide reference for harvesting.
- 4. Please provide references for exosome isolation, purification, identification, and labeling.
- 5. Please provide additional detail and references for primary brain cell cultures.
- 6. Please specify what age cultures were when utilized (day-in-vitro) and please provide details for transfection protocol
- 7. Please indicate what instrument or equipment was used for cell viability assays.
- 8. Please indicate whether measurements were performed blinded.
- 9. All reagents require catalogue numbers.
- 10. Fig 3 legend please clarify what the colors represent for the heat map PKH26.
- 11. Fig 6 legend please define CM as astrocyte conditioned medium.