OPEN PEER REVIEW REPORT 1

Reviewer 1: Olga Chechneva, University of California Davis, USA.

Comments to authors:

The manuscript: "Soluble Nogo Receptor 1 Fusion Protein Augments the Protective Effects of Neural Progenitor Cells in Stroke" investigates the effect of NgR1 inhibition on proliferation and differentiation of endogenous and transplanted neural stem cells in animal model of ischemic injury, photothrombotic ischemia. The data demonstrate that inhibition of NgR1 by NgR-Fc treatment promotes neural stem cell proliferation and differentiation and improves neurological outcome after ischemic injury.

1. The authors previously reported the increase in proliferation in NPC after treatment with antagonist of NgR1 (NgR-Fc) in vitro. No effect on proliferation of NPC by NgR-Fc was found in the present study. The discrepancies in the effect of NgR-Fc between studies need to be addressed.
2. Figure2C shows increase in NgR1+ and BrdU+ cells in the SVZ after PCI. SVZ area can not be visually detected in the presented images. Therefore, it is difficult to see whether representative images compare the same areas between two animal groups. No scale bar is indicated for the enlargements. Moreover, NgR1 seems to be a cytoplasmic protein. However, in Figure 2C is has nuclear appearance.
3. Make the correction for the panel labeling in Figure 5. The quality of images in Figure5 a-b is not convenient. Labeling of the areas in the image may help to define the exact location. It looks like the infarcted area is lost and transplanted cells present mostly in the penumbra that contradict the statement in the Results section: "NPCs were observed to migrate into the infarcted area or even infiltrate the infarct core in the sNgR-Fc+NPCs group". Using another marker, such as GAP43 or Synaptophysis or even GFAP (astrocytes) can help to clear define the border between penumbra and core.
4. Magnification in Figure 6A does not match magnification in Figure 6B.
5. Figure 6D-E: need quantification to make a statement regarding differences in cell number between groups.
6. Discussion: The statement: "First, NgR1 is an endogenous NPC-expressed ligand that is up-regulated in cortex ischemia" is not supported by the presented data. Present study shows increase in NgR1 only in SVZ and hippocampus.
7. Discussion of the paper mostly provides citations on other related studies instead of focusing on discussing the findings of the study.