OPEN PEER REVIEW REPORT 1

Name of journal: Neural Regeneration Research
Manuscript NO: NRR-D-20-00792
Title: Lineage tracing of direct astrocyte-to-neuron conversion in the mouse cortex
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Reviewer's country: China
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COMMENTS TO AUTHORS

In vivo reprogramming is of great significance and the process is complicated. Various discussions will benefit the development of this field. This manuscript has great guiding significance for the reprogramming of astrocytes into neurons in vivo. It provides several basic principles for the research in this field.

This manuscript report that reducing AAV dosage to safe level will avoid artifacts caused by toxic dosage. The author recommend that the AAV results are further verified with retroviruses. These findings are interesting and the quality of the data is overall high. The manuscript should be improved on the following points prior to publications.

1. In figure 1, how about the expression specificity of the virus infection for a longer period (such as 30 or 60 days)?
2. Make sure if figure 3C is consistent with the region of Box 2 in figure 3A.
3. In different viral systems (including lentivirus), how long does NeuroD1-mediated reprogramming take for neurons to mature and express NeuN?
4. What is the difference in the conversion efficiency of different virus systems at the same time?
5. Is there any evidence to prove that high virus dosing may cause neuron damage or even death? Whether the expression of GFAP in neurons will be up-regulated, leading to virus infecting neurons?
6. Will neurons be labeled after Aldh1l1-CreERT2 mice and Ai14 mice be crossed? If so, what is the percentage?
7. Is it possible to prove that astrocytes divide continuously using BrdU, maintain a balance, and the number of converted neurons remains relative constant?
8. P15, line 7: C56BL/6J mice should be C57.....