OPEN PEER REVIEW REPORT 1

Name of journal: Neural Regeneration Research
Manuscript NO: NRR-D-21-00856
Title: High-throughput RNA-sequencing reveals the mechanisms underlying neuroprotection of lamotrigine against Alzheimer's disease neuropathology
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COMMENTS TO AUTHORS

The authors of the present work performed high-throughput RNA-sequencing and revealed that these were beneficial effects of LTG on AD16 related neuropathologies and may be reagulated the expression of Ptgds, Cd74, 17 Map3k1, Fosb, and Spp1 in the brain of five-month-old APP/PS1 mice. The findings are really interesting and promising towards a potential clinical application in AD. This is also supported in the work by Zhang et al 2014, pusblished in Neurobiology of Aging.
My comments and suggestions: Did the authors performed any study in relevant human cell models, (neuroblastoma lines, neurons or iPS-derived neurons)?, this will support the hypotesis based on the animal AD model and therefore make more robust your prelimimar data, thinking towards a clinical application of Lamotrigine in AD patients in the future. This is higly relevant, due to the enormous amount of evidence of the failure of all the promising therapeutics for AD, due to the lacking human disease context. Is there any immunocytochemical (ICC) analysis that support the Western blot results from the Iba1 expression in Figure 5?