OPEN PEER REVIEW REPORT 1

Reviewer 1: Xavier d'Anglemont de Tassigny, Hospital Universitario Virgen del Rocio, Spain.

Comments to the authors:

This is a relatively simplistic model of neurodegeneration and the protective effect of the GRb1 compound would require further effort with different models to evaluate the overall benefit of testing it as a therapy for Parkinsons's disease (or other neurodegenerative disorder). Nevertheless, the work is worth publication after some amendments.

This paper provides data regarding the neuroprotective effect of Ginsenoside Rb1 in a model of lipopolysaccharide-induced nigral inflammation in the adult rat.

The effect of this ginseng-derived bioactive molecule provides important neuroprotection in the region of the substantia nigra at the time of which LPS inflammation is induced, and severely impairs the nigrostriatal dopaminergic system. The authors provide convincing results suggesting that their GRb1 molecule protect the dopamine neuron loss by preventing excessive inflammation induced by LPS. This results in a diminution of the LPS-associated dopamine loss in the striatum and a decrease of the NFkB pathway activation in the nigral region. These results are accompanied with convincing behaviour data. In overall, the data presented here are sound and well presented. However, redaction of the manuscript should be more carefully done (see my comments below).

Major comments:

Ethical concern: Chloral Hydrate is not a suitable anesthetic drug for animal surgery. See the correspondence from Mark G. Baxter in Anesthesiology 7 2009, Vol.111, 209. doi:10.1097/ALN.0b013e3181a8617e. The authors are invited to replace chloral hydrate anesthesia for other drugs (ketamine/xylasine, isoflurane for example) in the future.

In Figure 4A, it is quite surprising not observing any sign of inflammation in the SN region even after sham injection, at least along the line where the needle was inserted. Could the authors explain this?

Would Grb1 treatment prevent inflammation in other brain regions? Is this property specific of the sole SN region (which I doubt of)? Have the authors tested this? It would be worth discussing this point.

Western blot analyses of phosphorylated IkB and IKK require additional total IkB and IKK protein blot. This is a mandatory control in this type of assay.

Minor comments

Page 6, line 14: "Cell Signaling Biotechnology" is "Cell Signaling Technology"

Page 6, line 58: What is "NS" ? Please define.

Page 8, line 60: replace "weighted" with "weighed".

Page 11, Line 34: "The survival ratio of TH-positive neurons in the lesioned side was reserved to 57.8%." This sentence does not make much sense. Please rephrase.

The molecular weight of each protein analyzed by western blot should be indicated in the respective figures.