

## OPEN PEER REVIEW REPORT 1

**Name of journal:** Neural Regeneration Research

**Manuscript NO:** NRR-D-18-00487

**Title:** Repositioning of dipeptidyl peptidase-4 inhibitors and glucagon like peptide-1 agonists as potential neuroprotective agents

**Reviewer's Name:** Alessandro Castorina

**Reviewer's country:** Australia

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**Review time:** 5 days

### COMMENTS TO AUTHORS

The paper entitled 'Repositioning of DPP-4 inhibitors & GLP-1 agonists as potential neuroprotective agents' is a perspective article reporting some valuable insights on the efficacy of dipeptidyl peptidase-4 (DPP-4) inhibitors and glucagon-like peptides for the treatment of neurological disorders. These insights mainly arise from the neuroprotective effects elicited by this class of compounds. In general, the paper offers a fresh view on the potential neuroprotective role of these anti-diabetic drugs that could benefit the treatment of neurodegenerative conditions. Out of surprise, there is no reference to a very recent systematic review published by Neural Regeneration Research (Ref. Tackling dipeptidyl peptidase IV in neurological disorders. Al-Badri G, Leggio GM, Musumeci G, Marzagalli R, Drago F, Castorina A. Neural Regen Res. 2018 Jan;13(1):26-34.), where other direct substrates of DPP-4 that are worth mentioning are illustrated (PACAP, GIP) and the disease-modifying effect of both DPP-4 inhibition and/or GLP-1 are contextualised to neurological disorders. Other than than, this reviewer has some minor concerns/comments on the paper. These are shown below for the authors' convenience.

(Page 1, line 16) I would recommend removing 'recent' from this sentence. Alternatively the author might consider rephrasing with 'a relatively recent addition...'. DPP-4 inhibitors have been documented since 2004 (Reference below) and may no longer be considered recent.

Inhibition of dipeptidyl peptidase-4 reduces glycemia, sustains insulin levels, and reduces glucagon levels in type 2 diabetes. Ahrén B, Landin-Olsson M, Jansson PA, Svensson M, Holmes D, Schweizer A. J Clin Endocrinol Metab. 2004 May;89(5):2078-84.

(Page 3, line 12-15) Please rephrase the following sentence: 'Conclusion: repurposing of DPP-4 inhibitors & GLP-1RA for NDD is a breakthrough in the field of neural regeneration research due to two reasons. The first reason is that the first developed gliptins showed a reported neuroprotective effects in animal models.' with 'Conclusion: repurposing DPP-4 inhibitors and GLP-1RA for NDD is a breakthrough in the field of neural regeneration research for two main reasons: (1) The reported neuroprotective effects of the firstly developed gliptins in animal models; (2) their mechanisms of action involve increasing GLP-1 bioavailability, hence its neuroprotective activities.'