

OPEN PEER REVIEW REPORT 1

Name of journal: Neural Regeneration Research

Manuscript NO: NRR-D-19-00348

Title: Neurodegenerative Diseases as Proteinopathies-driven Immune Disorders

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COMMENTS TO AUTHORS

According to the latest data in addition to the deposition of misfolded proteins an important role in the development of neurodegenerative disorders and proteinopathies is played by innate immune activation, chronic inflammation and adaptive immunity. The authors discuss association between the innate and the adaptive immune system and the deposition of misfolded proteins as a clue to the understanding of mechanism of proteinopathies. This is an important field of investigation which has a potential for the development of immunotherapeutic strategies for the treatment of neurodegenerative diseases. The manuscript is well written, contains new data and hypothesis and will be interesting for the readers of "Neural Regeneration Research".

The following corrections should be done.

Page 2. Background. Lines 8-10. The authors should add a citation of a recent paper : " Protein misfolding, aggregation, and conformational strains in neurodegenerative diseases" by Claudio Soto & Sandra Pritzkow, published in 2018 in Nature Neuroscience, v 21, pages1332-1340 (2018).

Page 2, lines 45-47: "It is well known that the most frequent neurodegenerative proteinopathies are AD, LBD and PD are ones" This is a clumsy sentence. What does it mean "are ones"? Should be deleted.

Page 3, lines 43-45 "It particular, Parkinson Disease is characterized by the deposition of α -synuclein aggregates in the brainstem..." The authors should cite here a recent review on PD: "Emamzadeh et al., Parkinson's disease: Biomarkers, Treatment, and Risk Factors. Front. Neurosci., 2018". The correct spelling of PD is Parkinson's disease

Page 3, lines 53-55. "... γ -synuclein is a member of a protein family with pleiotropic effects, including β - and γ -synuclein (Clayton and George, 1998)...". The authors should add here a citation of a more recent review on synucleins: "Intracellular dynamics of synucleins: Here, there and everywhere. International Review of Cell Molecular Biology, 2015; 320:103-169.

Page 4, lines 5-7: "The major component of amyloid plaques is a peptide containing the amino acid residues 39-43". This is a wrong statement; pentapeptide 39-43 cannot form amyloid. The two important A β peptides involved are A β 1-40 and A β 1-42.

Page 4, lines 9-10: "Such a peptide is proteolytically cleaved by large glycoproteins, known as "amyloid precursor proteins...". A wrong statement again. Peptides are cleaved not by amyloid precursor protein, but from amyloid precursor protein. Should be written:"Amyloid precursor protein (APP) is split by the β -secretase complex, giving rise to different A β peptides".

Page 8, line 1. "a-synuclein. Those antibodies exerted neuroprotective effects on α -synuclein-induced nigral cell"

The authors should be consistent using either latin or greek letters for α -synuclein throughout the whole manuscript.