

OPEN PEER REVIEW REPORT 1

Name of journal: Neural Regeneration Research

Manuscript NO: NRR-D-20-01038

Title: Alpha-synuclein preformed fibrils – a tool to understand Parkinson's disease and develop disease modifying therapy

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Reviewer's country: Austria

COMMENTS TO AUTHORS

The review written by Chmielarz P. and Domanskyi A. highlights the role of alpha-synuclein PFFs in PD and is interesting and informative. However, I do have some major concerns regarding the manuscript:

The authors write about different studies and findings. However, they do not cite the original papers (only 2 or 3). Actually, they do not mention any citation after the single findings. The authors cite some reviews; however this is not state of the art to cite 5-10 reviews for all findings that are described. The authors should include the citations of the original papers for findings they mention.

The authors list a lot of therapeutic approaches, yet they only give one more detailed example. Why did the authors mention prasinezumab, yet no other approaches e.g. Anle138b NPT200-11 etc (only mentioned briefly afterwards and no citations of original papers.)

The authors write about PD, however they also mention ALS, AD and MSA. The order how they mention the different diseases is a little bit confusing. I would put more emphasis on PD and not mention AD and other diseases first... Maybe the other disease even can be omitted (ALS, AD) as it is not really clear what the authors really want to say with this list of disease? Just mentioning that there are other diseases with protein aggregations?

Page 5: The authors mention that it is not clear how PFFs are released into the extracellular space. Maybe they could mention the probable mechanism of alpha-synuclein release through exosomes here.

The authors should mention/introduce what ASOs and PROTACs are in the text, for readers that are not familiar with these abbreviations (not only in the figure legend).

The figure is quite nice and informative. However, coloring the individual components would probably improve the understanding of the figure (e.g. for soluble and misfolded alpha-synuclein, proteasome etc)

The authors should proof read their manuscript. There are a lot of minor errors (see below), but there are also some sentences that are hard to read/understand (e.g. page 6 line 47-51).

Page 4, Line 56: remove "a"

Page 5, line 15: "inhibit their growth by to avoid formation" remove by or to

Page 5, line 55: "induced deposits through of neuronal connections", remove of

Page 6, line 35: remove one "also"