OPEN PEER REVIEW REPORT 1

Name of journal: Neural Regeneration Research
Manuscript NO: NRR-D-20-00130
Title: Novel Galectin-3 interactions involved in oligodendroglial differentiation make inroads into therapeutic strategies for demyelinating diseases
Reviewer's Name: Wensheng Lin
Reviewer's country: USA
Date sent for review: 2020-2-24

COMMENTS TO AUTHORS

The authors summarize the roles of Gal-3 in oligodendrocyte differentiation and myelination as well as in demyelinating diseases. The manuscript is well written, and the topic is important. There is a minor concern. One Figure and two tables are merged together as a Figure. It could be better to separate them. Moreover, there is no legend for the Figure.

OPEN PEER REVIEW REPORT 2

Name of journal: Neural Regeneration Research
Manuscript NO: NRR-D-20-00130
Title: Novel Galectin-3 interactions involved in oligodendroglial differentiation make inroads into therapeutic strategies for demyelinating diseases
Reviewer's Name: Tianci Chu
Reviewer's country: USA
Date sent for review: 2020-2-29

COMMENTS TO AUTHORS

This is a well-written perspective on novel findings of Galectin-3 in OLG differentiation at different maturation stages. The knowledge in molecules and mechanisms that determine OLG response is essential to identify interventions that drive OLG differentiation, through which to promote the onset of remyelination and regenerative process.

Minor points to improve:

1. This perspective talks little about further research directions (both basic and translational research), and lacks details in developing potential therapies. Considering that the title is about Gal-3 in making inroads into therapeutic strategies for demyelinating diseases, the authors are recommended to make emphasis and to put more comments on this part.
2. Please briefly describe the expression and changes of Gal-3 in MS and other demyelinating diseases. This will improve the understanding of its clinical significance and relevance to demyelinating diseases when discussing potential therapeutic strategies.
3. The words in Figure 1 are hard to read. Please increase its resolution for prints.
4. The information of the last reference is incomplete (Reference section).

OPEN PEER REVIEW REPORT 3

Name of journal: Neural Regeneration Research
Manuscript NO: NRR-D-20-00130
Title: Novel Galectin-3 interactions involved in oligodendroglial differentiation make inroads into therapeutic strategies for demyelinating diseases
Reviewer's Name: Yi Pang
Reviewer's country: USA
Date sent for review: 2020-2-29

COMMENTS TO AUTHORS

A number of studies (mostly from the authors' own work) show that Gal-3 promote OPC differentiation and microglial phagocytic phenotype, this lead to the conclusion that Gal-3 could be a therapeutic target for remyelination. While the evidence to support this notion is quite strong, it needs to point out that other studies suggest that Gal-3 may play a deleterious role in MS model. For example, Gal-3 deficiency reduces neuroinflammation and attenuate EAE severity in a EAE model (J Immunol 2009;182:1167-73) or Theiler's murine encephalomyelitis virus model (Glia 2016;64:105-21). Gal-3 knockdown suppresses neuroinflammation and microglia-mediated pathogenesis in Huntington's model (Nat Commun 2019;10:3473). In a recent study, it was demonstrated that overexpression of Gal-3 does not induce neuroinflammation but reduces oligodendrocytes in healthy neonatal mice (Glia 2020;68:435-450). It seems that Gal-3 plays a complex role in oligodendrocyte biology/myelination, depending on the level of Gal-3 expressed (physiological vs pathological) and also context of tissue environment. I think further elaborating on this topic would strengthen the manuscript.

Minor:

1. Many abbreviations are not defined in the text: PDGFRa, NG2, CNPase, Olig1, APC, MBP, etc.
2. Page 4, line 34: "Given that unsuccessful remyelination may respond to inefficient removal of myelin-debris by microglia", not clear what "respond" really mean.