

OPEN PEER REVIEW REPORT 1

Name of journal: Neural Regeneration Research

Manuscript NO: NRR-D-21-00370

Title: Retinal regeneration requires dynamic Notch signaling

Reviewer's Name: Mariana S. Silveira

Reviewer's country: Brazil

COMMENTS TO AUTHORS

The article will be of a great significance to the field. It is extremely relevant as it provides an overview of the current knowledge, including recent advances. The authors address in detail Notch signaling in the context of Müller glia-dependent retinal regeneration in zebrafish, highlighting relevant parallels and differences with mammals and other organisms, and aspects which demand further investigation. Small changes are suggested below to increase the clarity of the text.

The organization of the review could change to stress better the message in each section. After the Abstract, the first Section could be Introduction, as it is, but I suggest that the sections which were numbered could all be subsections (with no numbers) of a second section called (for example) Notch signaling elements and regeneration in zebrafish. Some changes to the titles of these subsections are recommended, for example: Notch receptors: synthesis and activation instead of Notch receptor production.

The final section would then be Implications for mammalian retina regeneration.

The review would also benefit from an additional figure summarizing the evidence on how Notch signaling impacts regeneration from Muller glia in zebrafish prior to the last Section.

Specific comments

- On page 4, lines 8-11, the authors state that "The NPC continues to proliferate to produce a cluster of multipotent progenitors that differentiate primarily into the neurons lost to damage and, at a lower frequency, all other retinal cell types"

The authors cite the relevant study from Lahne et al (2021), however, Powell et al, 2016 (DOI: 10.1038/srep24851) also addressed this and reached different conclusions. Could the authors discuss the results which support the statement that neurons other than the ones lost to damage differentiate at a lower frequency?

-On page 6, line 56: The sentence "The mib1 mutant was first discovered in zebrafish and found to bind and ubiquitylate Delta ligands (Itoh et al, 2003)" should be corrected to: The mib1 mutants were first discovered in zebrafish and led to the description that Mib1 bind and ubiquitylate Delta ligands (Itoh et al, 2003).

- Page 8, line 48: In the sentence "...indicating that induced and increased Müller glia proliferation was mediated by Notch signaling. ", I suggest the following change: ...indicating that induced and increased Müller glia proliferation was mediated by the inhibition of Notch signaling.

OPEN PEER REVIEW REPORT 2

Name of journal: Neural Regeneration Research

Manuscript NO: NRR-D-21-00370

Title: Retinal regeneration requires dynamic Notch signaling

Reviewer's Name: Lucia Poggi

Reviewer's country: Italy

COMMENTS TO AUTHORS

I find this review entitled "Retinal regeneration requires dynamic Notch signaling" very exhaustive and informative on what is known so far about the very complex Notch signalling in neural development and regeneration.

This review will therefore be very useful for the researchers inside and outside the field.

I only have one suggestion:

The authors did outline very nicely acquired knowledges on Notch signalling both in development and regeneration. Perhaps it would be also useful to implement the manuscript with a table similar to table 1, in which the authors briefly outline the key findings, at the same time as highlighting the gaps to be filled, for example indicating known developmental processes that need to be still translated to the regenerative ones.