

OPEN PEER REVIEW REPORT 1

Name of journal: Neural Regeneration Research Manuscript NO: NRR-D-20-00164 Title: The therapeutic potential of targeting exchange protein directly activated by cyclic adenosine 3', 5'-monophosphate (Epac) for central nervous system trauma Reviewer's Name: Ernesto Doncel-Pérez Reviewer's country: Spain Date sent for review: 2020-3-15

COMMENTS TO AUTHORS

Your manuscript deals about an important player in CNS injury like cAMP. The ubiquitous propriety of this second messenger makes difficult their use in specific treatment for traumatic SCI. However, your proposal of modulating cAMP through Epac2 brings some new cues on this sense. In your manuscript we can find a good compilation of studies in cAMP signaling and regulation, and its influence in neural cells. I'm enjoyed reading your manuscript and I recommend their acceptance.

Anyway, I have some minor observations that could help readers to follow your exposition, these are:

_ In page 2, line 30. Define Epac2 in abstract, please.

_ In page 3, line 7. A more recent reference about global incidence of TSCI could be necessary.

_ In Table 1; Pages 8-9. The molecules mentioned in activity column are not defined, it'll avoid to reader searching in text.

_ In page 10, lane 24. Some explanation for NF-200 marker could be useful in order to a better comprehension of their use on this context.

I hope you can go ahead with this work in SCI field.