

OPEN PEER REVIEW REPORT 1

Name of journal: Neural Regeneration Research

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Title: MAP4K4 Induced Rapid Blood-Brain Barrier Damage after Subarachnoid Hemorrhage in Mice

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COMMENTS TO AUTHORS

This study first demonstrated the involvement of MAP4K4 in blood-brain barrier disruption after subarachnoid hemorrhage (SAH) in mice. The authors performed 3 kinds of interventions (recombinant MAP4K4 protein, MAP4K4 siRNA and PF-06260933) to confirm the findings, which become convincing. However, there are some concerns as follows.

1. How many mice were excluded due to SAH grade <8. In addition, some mice died due to severe SAH. I think that the number of animals in each group in each figure legend is not correct. Please recheck all figure legends.
2. In experiment 1, the authors described 2 peaks of MAP4K4 induction. However, as the authors evaluated the time course by 72 hours, it is unknown if the second peak is at 72 hours or later. Expression levels of MAP4K4 should be assessed at later time points than 72 hours.
3. Immunostaining: please describe which part of brain was evaluated. How is the relationship with bregma?
4. Immunostaining: please describe the method for DAPI.
5. Western blotting: Please describe the method to get nuclear and cytoplasmic fractions. For proteins other than p-p65, the cytoplasmic fraction was used for Western blotting?
6. There are many wrong descriptions. For example,
Results: In the section of "Pharmacological MAP4K4 inhibition...", the second line, was PF administered at 24 and 72 hours post-SAH?
Discussion: In the second line, "peak at 24h and 48h" is wrong.
Please check all descriptions through the paper.
7. Please add the number of page through the paper.
8. Fig 1A: tublin→tubulin
Fig 5F: 24h-post SAH→24h post-SAH