OPEN PEER REVIEW REPORT 1

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Title: HMGB1 mediates inflammatory response of astrocytes via OX2/PGE2 signaling following spinal cord injury
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Reviewer's country: USA
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COMMENTS TO AUTHORS

Overall very interesting study with somewhat unexpected results. Would consider including a sketch describing the biochemical mechanism you described, and a flowchart describing the methods in your research. And finally the question remains: How do your results fit into the puzzle we are trying solve in regards to immunodulation and secondary injury after SCI? What would be your next step in trying to determine the mechanism behind the release of TNF-α and IL-1β in astrocytes (since HMGB1 did not demonstrate)? What would be the overall next step in further investigating mechanisms of secondary injury and effective ways to prevent them?

There has been a multitude of molecular and pharmaceutical research that investigates different targets to prevent secondary injury following SCI. Despite all of it, there remains no effective way (in-vivo) to treat and prevent secondary injury, other than blood pressure augmentation and surgical spinal cord decompression. Steroids have remained controversial. There has been a number of various anti-inflammatory and immunomodulator trials for SCI, but so far none of them have been truly promising in-vivo. While your research findings are significant, it remains unclear how we can reliably translate it into an effective treatment to improve neurologic recovery after SCI. Although targeting a specific immune response and mechanism may be part of the answer.

Also I prefer the first title "HMGB1 mediates inflammatory response of astrocytes via COX2/PGE2 signaling following spinal cord injury". It gives a better understanding of the anticipated read. Also gives more familiarity since most clinicians have more insight on COX2/PGE2, rather than HMGB1