

## OPEN PEER REVIEW REPORT 2

**Name of journal:** Neural Regeneration Research

**Manuscript NO:** NRR-D-22-00079

**Title:** Erythropoietin mitigates ferroptosis following spinal cord injury and ameliorates neurological function recovery via activating xCT/Gpx4 pathway

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### COMMENTS TO AUTHORS

This an interesting research which investigated whether ferroptosis was involved in the neuroprotective effect mediated by erythropoietin in cases of spinal cord injury. Ferroptosis opposes neural regeneration, Erythropoietin can increase neuroprotection and decrease PCD. However its effect on ferroptosis is not known. The authors found that, erythropoietin activating xCT/Gpx4 pathway to regulate ferroptosis

Minor comments.

1. It is not clear why initially, there was no difference between high dose and low dose EPO.
2. Was it known before that EPO has a neuroprotective role in spinal cord injury. If yes, then, there is no novelty in the results section "EPO promotes regeneration of spinal cord injury"
3. If RSL3 which is an activator of Ferroptosis, diminishes EPO effect does not that mean that Ferroptosis regulate EPO as well. I wonder if the authors can clarify the bidirectional relationship between Ferroptosis and EPO more.
4. The discussion section might need more in depth analysis of the results.