Peer Review File

Article information: https://dx.doi.org/10.21037/tp-23-189

Reviewer A:

Comment 1: First, the abstract needs some revisions. The background did not indicate the potential clinical significance of this research focus and clearly indicate the knowledge gap on this research topic. The methods need to be detailed enough including the experimental procedures and how the animal model of HIBD was established. The results need to quantify the finding by reporting main statistics such as expression levels and accurate P values. The conclusion needs comments for the unaddressed research questions of this study.

Reply 1: We have modified our text as advised.

Changes in the text: **See Pages 2, lines 31-60.**

Comment 2: Second, in the introduction of the main text, the authors need to review what has been known on the pathological and molecular mechanisms of HIBD, in particular the authors' previous work on this, and have comments on the potential clinical significance of this research focus. In last paragraph, please describe the hypotheses of this study, not to describe what the work was done in this study.

Reply 2: We have modified our text as advised.

Changes in the text: **See Page 4, lines 94-104; Page 6, lines 152-153.**

Comment 3: Third, in the methodology, please first have a brief overview of the experimental procedures and the research questions to be answered by these procedures. In statistics, please ensure $P<0.05$ is two-sided. T test is not appropriate for the pairwise comparisons if there are three groups to be compared. Please consider ANOVA and SNK or LSD for pairwise comparisons.

Reply 3: We have modified our text as advised.

Changes in the text: **See Page 13, lines 358-364.**

Reviewer B

The paper titled “Ferrostatin-1 attenuates hypoxic-ischemic brain damage in neonatal rats by inhibiting ferroptosis” is interesting. The results suggest that both hypoxic-ischemic brain damage and Erastin can cause changes in GPX4/ACSL3/ACSL4 axis expression to induce ferroptosis, while Fer-1 can inhibit ferroptosis and reduce HIBD injury, indicating that GPX4/ACSL3/ACSL4 axis is an important therapeutic target in HIBD, and Fer-1 has the potential in the clinical treatment of HIBD. However, there are several minor issues that if addressed would significantly improve the manuscript.

Comment 1: What are the various functions of ferroptosis in the pathological processes of hypoxic-ischemic brain damage? It is suggested to increase the latest progress of apoptosis, necroptosis, autophagy, ferroptosis, and pyroptosis in hypoxic-ischemic brain damage.

Reply 1: We have modified our text as advised.

Changes in the text: **See Pages 5-6, lines 117-151.**

Comment 2: What is the basis for selecting the dosage concentration for this study? Suggest adding relevant literature support.

Reply 2: We added some relevant literature support.

Changes in the text: **See Page 7, lines 200-201, line 204-205.**

Comment 3: The pathophysiological mechanism and research progress of hypoxic-ischemic brain damage should be added to the discussion.

Reply 3: We have modified our text as advised.

Changes in the text: **See Pages 17-18, lines 493-507.**

Comment 4: The introduction part of this paper is not comprehensive enough, and the similar papers have not been cited, such as "Vitamin D suppresses ferroptosis and protects against neonatal hypoxic-ischemic encephalopathy by activating the Nrf2/HO-1 pathway, Transl Pediatr, PMID: 36345441". It is recommended to quote this article.

Reply 4: We have modified our text as advised.

Changes in the text: **See Page 4, lines 94-98.**

Comment 5: How to ensure that samples used for TEM are sampled in the same way in different groups?

Reply 5: We have modified our text as advised.

Changes in the text: **See Page 9, lines 251-255.**

Comment 6: What is the impact of this study on the further treatment of hypoxic-ischemic brain damage? It is recommended to include relevant content in the discussion.

Reply 6: We have modified our text as advised.

Changes in the text: **See Pages 20-21, lines 585-604.**