



## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Gastroenterology*

**Manuscript NO:** 82092

**Title:** Ferroptosis inhibition attenuates inflammatory response in mice with acute hypertriglyceridemic pancreatitis

**Provenance and peer review:** Unsolicited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 05118373

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** China

**Manuscript submission date:** 2022-12-06

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2022-12-06 01:46

**Reviewer performed review:** 2022-12-14 16:50

**Review time:** 8 Days and 15 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No



<b>Peer-reviewer statements</b>	Peer-Review: [ <input type="checkbox"/> ] Anonymous [ <input checked="" type="checkbox"/> ] Onymous
	Conflicts-of-Interest: [ <input type="checkbox"/> ] Yes [ <input checked="" type="checkbox"/> ] No

### SPECIFIC COMMENTS TO AUTHORS

In this straightforward study, the authors indicated that ferroptosis is involved in the process of hypertriglyceridemic pancreatitis (HTGP) and that NOX2 is a key point in the regulation of ferroptosis. However, there are some important issues that detract from the manuscript's overall impact.

1. The materials and methods section doesn't describe clearly in Animal model processing and treatment. - The weight changes of experimental animals should also be described. - Any mortality or other exclusions should be fully documented. This should include a description of the procedure for replacing any animals that might have been lost from a group during the prolonged survival intervals. - It still should indicate the animal numbers used in each Figure. - There is lack of rational for using the protocols of P-407 and caerulein treatment. Are those treatment based on pilot experiments or previous reports?
2. The bioinformatics tools that have been used for the proteome sequencing analysis. The produced raw data should also be outlined and compared with other already published references.
3. How about the changes of TG、TC and a-AMY between P-407 group and P-407+CAE group in Figure 1?
4. The quantification criteria by HE images (Figure 1, Figure 4 and Figure 5) were assessed should be clearly stated.
5. It was confused with the groups shown in Figure 3 (A and B) and Figure 5 (B and D). The four groups in each diagram should be clearly arranged.
6. The authors indicates that X-ct is SLC7A11 (line 443), and the protein names should be consistent with the manuscript, Figure and legends.
7. It is difficult to estimate the changes of X-ct and GPS4 without statistical graphs of X-ct and GPX4. In addition, only the IHC of X-ct, GPX4 and MDA content could not draw a convincing conclusion that HTGP specifically induces mouse pancreatic ferroptosis.
8. There are



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some grammatical and syntax errors in the manuscript, and should need more editing from this point of view.



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**Peer-review model:** Single blind

**Reviewer's code:** 06481804

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

**Reviewer's Country/Territory:** Australia

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**Review time:** 10 Days and 11 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Novelty of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
<b>Creativity or innovation of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation



<b>Scientific significance of the conclusion in this manuscript</b>	<input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

This study by Meng et al. has investigated the role of ferroptosis in hypertriglyceridemic pancreatitis (HTGP) and showed that inhibition ferroptosis using Fer-1 attenuate inflammatory and serum MDA level and consequently decrease organ injury in mice. Authors also demonstrate that NOX2 axis modulate initiation of ferroptosis and subsequent the pathological consequences in multiple organ dysfunction. Pathological injury on multiple organs of mice with HTGP diminishes following NOX2 inhibitor administration. Hypertriglyceridemic pancreatitis is poorly treated in clinic and the incidence rate alarmingly increase worldwide. There is badly need of insight which may reveal new therapeutic approaches and therefore this is an area of research importance. The data is adequate, well organized, and convincing. There are a few comments/suggestions from the reviewer to improve the study further. Specific comments are listed below

1. Although the data is sufficient to support the conclusions, the logic and readability of the manuscript is suffered by terminology usage and inadequate data description. I would suggest expanding some of the text in the result section.
2. Authors assessed injury of pancreas, lung, and kidney following



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P407+CAE administration. As liver is a key organ in regulating lipid metabolism. It will be helpful to examine the effect of P407+CAE administration on liver function and insulin resistance. 3. How does the proteomic analysis performed, there is no information in method part. What was the data base used to identify the protein? 3. Using proteomic data (in figure 2), authors showed that ferroptosis is a key biological process differentially regulated in pair-wise comparisons of 'AP vs WT' and 'HTGP vs AP'. However, there is lack of information regarding number and identity of ferroptosis -related protein in the study. 4. There is no information indicated on the Volcano plot (Fig 2D), where does NOS2 sit on the volcano plot. What are other proteins upregulated and downregulated. 5. Hypertriglyceridemic pancreatitis (HTGP) and P407+CAE used interchangeably, should be conspicuously used, otherwise, it may cause misunderstanding. Minor comments (words used improperly) - Line 83, word "predict" - Line 128, word "screening" - Line 179, "proteome sequencing", suggestion proteomic profiling - Line 207, "rebounded" - Line 308, "significant evidence" - Line 443, "Calculation"