Author's response to reviews

Title: Protective effects of heme oxygenase-1 against severe acute pancreatitis via inhibition of tumor necrosis factor-α and augmentation of interleukin-10

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Author’s response to reviews:

Editor Comments:

Point: The language should be edited by an native English-speaker.

Response: Thanks for your comment. The language has been modified in the original.

Reviewer reports:

Reviewer 1:

The authors have choosen an interesting subject and performed an elaborated animal experiment. They used sophisticated molecular determinations to provide evidence that induction of Heme Oxygenase-1 might be protective in severe acute pancreatitis.

I have some concerns.

Major

Abstract
Point: It should be mentioned in the abstract which species of animals were used.

Response: Thanks for your comment. It’s has been modified in the original. (Abstract section, line 18, page 1)

“Four groups of Sprague-Dawley (SD) rats were used……”

Methods

Point: Effects of hemin and ZnPP on rats without induction of acute pancreatitis were not tested as control. This should be commented on.

Response: Thanks for your nice and precious advice and allow me to do some explanation. The main object of this research is the protective effect of HO-1 on rats with SAP, on the basis of which we designed the protocol, grouped the animals and testified our viewpoint.

There were some other researches on HO-1, which are similar to our designs. For example:


Results

Point: The authors refer to "hemin pretreatment", but hemin was administered 30 minutes after induction of pancreatitis.

Response: Thanks for your comment. This is a writing mistake, and the mistake has been modified in the original. (Abstract section, line 28, page 1)

“Hemin treatment significantly decreased……”

Point: Availability of data and material

"The work described was original research that has not been published previously, and not under consideration for publication elsewhere, in whole or in part. All the authors listed have approved the manuscript that is enclosed."
“AP is a common disease which the mortality is up to 30% in severe cases.”

Point: If this inflammation is marked, it would lead to inappropriate activation of immune system demonstrating as systemic inflammatory response syndrome(SIRS) and eventually result in multiple organs dysfunction syndrome(MODS) [3].

Grammar: it will lead

Response: Thanks for your comment. This mistake has been modified in the original. (Background section, line 14, page 2)

“it will lead to……”

Point: In this procession, the therapy targeting…

Wording: In this process

Response: Thanks for your comment. This mistake has been modified in the original. (Background section, line 17, page 2)

“In this process, the therapy targeting to……”

Point: are highly conserved

are a highly conserved

Response: Thanks for your comment. The sentence has been modified in the original. (Background section, line 21, page 2)

“Heat shock proteins (HSPs) belong to a proteins family which are highly conserved.”

Point: these proteins perform a variety of cells

Is this what you mean? these proteins induce a variety of cells

Response: Thanks for your comment. This is a writing mistake, and the sentence has been modified in the original. (Background section, line 22, page 2)

“These proteins widely express in a variety of cells against stress and injury inciting stimulis.”

Point: catalyzea
catalyzes

Response: Thanks for your comment. This mistake has been modified in the original. (Background section, line 29, page 2)
“which catalyzes the……”

Methods

Point: was retrograde injected

Grammar: was retrogradely injected

Response: Thanks for your comment. This mistake has been modified in the original. (Methods section, line 31, page 3)

“……was retrogradely injected……”

Point: Promrga A3500, Madison, WI

Spelling: Promega A3500, Madison, WI

Response: Thanks for your comment. This mistake has been modified in the original. (Methods section, line 25, page 4)

“Promega A3500”

Results

Point: increased significantly

were significantly increased

Response: Thanks for your comment. This mistake has been modified in the original. (Results section, line 21, page 5; line 2, 16 and 20, page 6)

Point: decreased significantly

were significantly decreased

Response: Thanks for your comment. This mistake has been modified in the original. (Results section, line 6, 10 and 18, page 6)

Point: The pathological scores is significantly

The pathological scores were significantly

Response: Thanks for your comment. This mistake has been modified in the original. (Results section, line 1 and 10, page 7)
“The pathological scores were significantly……”

Discussion

Point: was associated with a marked increase HO-1 gene expression in

Response: Thanks for your comment. The sentence has been modified in the original. (Discussion section, line 19, page 7)

“……with a significant increase of HO-1 gene expression in……”

Point: it can inhibit the synthetize

it can inhibit the synthesis

Response: Thanks for your comment. The sentence has been modified in the original. (Discussion section, line 4, page 8)

“IL-10 can inhibit the synthesis of……”

Point: have demonstrated a major anti-inflammatory effect

have demonstrated a major of anti-inflammatory effect

Response: Thanks for your comment. This mistake has been modified in the original. (Discussion section, line 14-15, page 8)

“Some studies have demonstrated a major of anti-inflammatory effect of CO……”

Point: HO-1 is the stress-inducible from which is known to…

Is this what you mean? HO-1 is the stress-inducible isoform of heme oxygenase which is known to…

Response: Thanks for your comment. This is a writing mistake, and the sentence has been modified in the original. (Discussion section, line 23, page 8)

“HO-1 is the stress-inducible enzyme which is known to……”

Reviewer 2:

Specific Comments
Point: 1. Grammar should be checked throughout the manuscript.

Response: Thanks for your comment. The language has been modified in the original.

Point: 2. Abstract, line 32: do you mean examine or analyze the role of HO-1 on systemic inflammation? The word "improve" does not fit here.

Response: Thanks for your comment. This is a writing mistake, and the sentence has been modified in the original. (Abstract section, line 16, page 1)

“The objective of this study was to investigate the role of……”

Point: 3. Second page of Abstract, line 4: How do you know this is the main mechanism? HO-1 could also effect other pathways.

Response: Thanks for your comment. This is a writing mistake, and the mistake has been modified in the original. (Abstract section, line 2-4, page 2)

“Early HO-1 expression may modulate systemic inflammatory response and prevent end-organ injury in SAP model through inhibition of TNF-α and augmentation of IL-10.”

Point: 4. Background line 20-22: this sentence (It is clear … in severe cases) is a little confusing. Maybe reword.

Response: Thanks for your comment. The sentence has been modified in the original. (Background section, line 11-12, page 2)

“AP is a common disease which the mortality is up to 30% in severe cases.”

Point: 5. Background line 43: add "activities to protect" to the sentence. For example, "perform a variety of activities to protect cells against stressful"

Response: Thanks for your comment. The sentence has been modified in the original. (Background section, line 21-22, page 2)

“Heat shock proteins (HSPs) belong to a proteins family which are highly conserved. These proteins widely express in a variety of cells against stress and injury inciting stimuli.”

Point: 6. Background lines 49-56, state HO-1 plays an important role SAP, while the next page, lines 7-9 indicate the role is unknown. How can it be important and unknown at the same time.

Response: Thanks for your comment. This is a writing mistake, and the mistake has been modified in the original. (Background section, line 3-5, page 3)

“However, the role of HO-1 in the exocrine pancreas and its potential modulation role in pancreatic injury are still not fully elucidated.”
Point: 7. Results, line 54, pancreatic histology: should this be the pancreas not the pancreatic duct? The duct is not shown in the images or described in the SAP group. Also, this sentence should be split into 3 sentences rather than describing all of the treatments in one run on sentence.

Response: Thanks for your comment. This is a writing mistake, and the mistake has been modified in the original. (Results section, line 24-26, page 6)

“The structure of pancreas in control group showed morphologically normal, while the pancreas in SAP group displayed partly hemorrhage, necrosis and infiltration of neutrophile granulocyte.”

Point: 8. Figure 3: the treatments are not labeled in the figure or indicated in the figure legend. This should be added. Also, the image resolution is too low to confirm the description in the text. Higher resolution images should be included.

Response: Thanks for your comment. It`s has been modified in the original.

The treatments have been indicated in the figure legend. (Page 16)