Dear Dr. Tarnawski:

We appreciate you giving us the opportunity to revise our manuscript. We also appreciate the reviewers and associate editors for your constructive comments and suggestions on our manuscript entitled “Abdominal paracentesis drainage ameliorates severe acute pancreatitis in rats by regulating the polarization of peritoneal macrophages” (Manuscript NO: 42515).

We have studied your comments very carefully and tried our best to revise our manuscript accordingly. The changes are highlighted by using the track changes mode in MS Word. We hope the revised version could meet with approval, we also would be glad to respond to any further questions and comments that you may have.

Our point-by-point responses to the comments and suggestions are listed below.

Yours, sincerely

Lijun Tang

Answering Reviewers

Reviewer #1

[Comments 1.] In humans the impact that leads to pancreatitis and the result (the disease) have a gap of time between them. In your experimental model the abdominal tube is inserted immediately after the injection of the agent that creates the pancreatic insult. Is the time interval between these two events enough to establish the pancreatitis?

[Answer 1.] The animal model induced by sodium taurocholate retrograde injection is a well-established severe acute pancreatitis(SAP) model which doesn’t suffer a mild to severe progress and is characterized by significant injuries in pancreas and remote organs including liver[1], lung[2], kidney[3] and even in heart[4]. The hyperemia of pancreas and pancreatitis associated ascitic fluids (PAAF) can be seen immediately after the injection. The biomarkers of remote organ injuries can be detected in 3-6 hours after the injection[5]. In another hand,

our previous studies demonstrated that the 12-hour mortality rate for this SAP animal model reaches 57.1%[6]. We believe any invasive manipulation after the induce of SAP model may increase the risk of death. Take all these into consideration, we chose the current protocol to perform APD treatment in SAP rat model and this protocol has been used in our serial studies[6-8].

[Comments 2.] A chart comparing the measurements of each of the 3 groups (pancreatitis, abdominal tube, sham), side by side, may present the same information you give with the Fig 1 and 3 in a more condense way. Never the less this is totally up to your choice.

[Answer 2.] Thank you for your advice. It do present these information concisely by using chart, however, histogram may well reflect the difference between each group. So, we prefer the histograms in Fig.1 and Fig.3.

[Comments 3.] Minor corrections: page 5, line 9 (INTRODUCTION): "pathogenesis of SAP ... " the article "the" could be removed. page 8, line 8 before the end (before ELISA):"slides every pancreas" reads better as "slides for every pancreas"

[Answer 3.] All these expressions have been corrected.

Reviewer #2

[Comments 1.] The prognosis of SAP can be mortal"(DOI: 10.31832/smj.376327) and (Turkiye Klinikleri J Gen Surg-Special Topics 2018;11(2):112-4). I suggest both of these uptodate studies.

[Answer 2.] Thank you for your comments, related paper has been cited in the revised version.

Thank you again for your comments and we look forward to hearing from you regarding our submission as well as any further questions and comments that you may have.

Reference:

1 Zhao YF, Zhai WL, Zhang SJ, Chen XP. Protection effect of triptolide to liver injury in rats with severe acute pancreatitis. Hepatobiliary Pancreat Dis Int 2005; 4: 604-608 [PMID:16286273]

2 **Zhu R, Zhao Y, Li X, Bai T, Wang S, Wang W, Sun Y**. Effects of penehyclidine hydrochloride on severe acute pancreatitis-associated acute lung injury in rats. Biomed Pharmacother 2018; 97: 1689-1693 [PMID:29793332 DOI: 10.1016/j.biopha.2017.12.025]

3 **Zhang XH, Li ML, Wang B, Guo MX, Zhu RM**. Caspase-1 inhibition alleviates acute renal injury in rats with severe acute pancreatitis. World J Gastroenterol 2014; 20: 10457-10463 [PMID:25132762 DOI: 10.3748/wjg.v20.i30.10457]

4 **Li L, Sun Z, Xu C, Wu J, Liu G, Cui H, Chen H**. Adenovirus-mediated overexpression of sst2 attenuates cardiac injury in the rat with severe acute pancreatitis. Life Sci 2018; 202: 167-174 [PMID:29653119 DOI: 10.1016/j.lfs.2018.04.008]

5 **Liang HY, Chen T, Wang T, Huang Z, Yan HT, Tang LJ**. Time course of intestinal barrier function injury in a sodium taurocholate-induced severe acute pancreatitis in rat model. Journal of digestive diseases 2014; 15: 386-393]

6 **Zhou J, Huang Z, Lin N, Liu W, Yang G, Wu D, Xiao H, Sun H, Tang L**. Abdominal paracentesis drainage protects rats against severe acute pancreatitis-associated lung injury by reducing the mobilization of intestinal xdh/xod. Free Radical Biology & Medicine 2016; 99: 374-384 [PMID:27585949 DOI: 10.1016/j.freeradbiomed.2016.08.029]

7 **Yang G, Wu D, Liang H, Zhao Y, Zhou J, Xiao H, Huang M, Ning, Lin, Huang Z**. Abdominal paracentesis drainage attenuates intestinal barrier dysfunction via upregulating zo-1 expression in rats with severe acute pancreatitis. Int J Clin Exp Med 2017; 10: 11585-11595]

8 **Chen GY, Dai RW, Luo H, Liu WH, Chen T, Lin N, Wang T, Luo GD, Tang LJ**. Effect of percutaneous catheter drainage on pancreatic injury in rats with severe acute pancreatitis induced by sodium taurocholate. Pancreatology 2015; 15: 71-77 [PMID:25455348 DOI: 10.1016/j.pan.2014.10.005]