

COVER LETTER

Dear Editor,

We are submitting revised "Early immune response in post-ERCP pancreatitis as a model for acute pancreatitis". Manuscript No. 46350.

Answer to the reviewers' comments:

1. " In this opinion review entitled "Early immune response in post-ERCP pancreatitis as a model for acute pancreatitis", the authors summarized some interesting information of ERCP-induced acute pancreatitis by comparing the studies of clinical presentations and immune response of acute pancreatitis induced by ERCP and other risk factors. However, as a opinion review, the authors' opinions of immune response in post-ERCP pancreatitis is not clear, possible due to limited research on this topic. In addition, the abstract seems to be a part of the introduction, but not an abstract. "

We added an abstract.

As author states there is a limited research on this topic, therefore we conclude that further research, especially of innate immunity cells and their function in PEP is important.

2. "The Opinion paper of Plavsic et al. entitled "Early immune response in post-ERCP pancreatitis as a model for acute pancreatitis" supports the hypothesis that post-ERCP pancreatitis may be a different clinical entity from Acute Pancreatitis and the difference may be sustained by innate immunity stigmata. Some remarks need to be moved: • Abbreviations appear in the text without the related extensive definition at the first mention • Abstract is lacking and, presumably, Introduction is reported as Abstract • A clear aim of the paper is not reported • The literature data reported in the paper are not adequately discussed and this is

mandatory in an Opinion paper • Concepts of translational medicine are almost confusing.”

We corrected abbreviations in text and tables.

Abstract was added and we also tried to summarize the aim of the paper.

3. “In this article, the role of immune cells in patients with PEP is not well reviewed. It is necessary to describe not only the dynamics of cytokines in PEP development but also the mechanism of immune cells in PEP development.”

We wrote in conclusion that “As table 2 shows, most of the studies that researched the role of immune cells in innate immunity, used patients with AP as the research subjects. Answers about the role of immune cells in patients with PEP are still insufficient.

On the contrary, the role of different cytokines in both groups of patients was extensively studied. “

Research of different cytokines did not result with adequate biomarker for disease severity, and thanks to discovered role of innate immune cells in pathogenesis of sepsis we proposed that the next research should focus on the role of innate immune cells in pathogenesis of pancreatitis.