Reviewer’s report

Title: The roles of tumor necrosis factor-alpha in colon tight junction protein expression and intestinal mucosa structure in a mouse model of acute liver failure

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Reviewer: Hiroyasu Ito

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Comments:

In this manuscript, the authors have investigated the effects of TNF-# on the ultrastructure of the intestinal mucosa using acute liver failure murine model. They demonstrated that TNF-# damages TJs and affects the expression of ZO-1 protein in vivo, and may participate in the pathological mechanism of SBP complicated to ALF. Although the present data are potentially easily understandable and very interesting, there are several issues that should be addressed as noted below.

Major:

1. Authors demonstrated that TNF-# damages TJs and decreases the expression of ZO-1 protein in vivo. However, in the group in which only mice was administrated with recombinant TNF-#, there was no damage on TJs and the expression of ZO-1 was not decrease. If high dose of recombinant TNF-# was injected to mice, is it observed the damage of TJs and the decrease of the expression of ZO-1?

Authors should discuss on these issues.

2. In Western blot analysis of tissue ZO-1 content, the author should show the internal control protein expression (e.g. #-actin, GAPDH etc.) to normalize for protein loading. (Fig. 5)

3. In Fig.1, the concentration of TNF-# level was elevated at 9 hour after GaIN/LPS injection again. Why are observed these bimodal peaks of the concentration of TNF-# level after GaIN/LPS injection?

Authors should address this issues in Discussion.

Minor:

1. In Table 1, number of mice in the groups of anti-TNF-#-IgG+GalN/LPS and anti-TNF-#R-IgG+GalN/LPS might be wrong.

2. The description `TNF-a` at line 32 in Discussion might be wrong.

Level of interest: An article whose findings are important to those with closely
related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.