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: Damien Masson

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The manuscript “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” by Hong-li Song et al. demonstrate with a mouse model of acute liver failure that the TNFa induces an intestinal epithelial barrier disruption and a bacterial peritonitis.

- This study with eight groups of mice (n=8 mice per group) is well designed.
- The choice of the target ZO-1 gene used is pertinent.
- The authors investigate strong histopathological parameters of this acute liver failure mouse model.
- The time points of 2h, 6h, 9h for the histological and transcriptional analysis are justified.

Minor Essential Revisions

The manuscript and particularly the experimental design on mouse model is well written, and this study has exciting implication for early pharmacological intervention by targeting TNF or TNFR1. Indeed, the efficiency and protective effects of 2 mAb (anti-TNFa and anti-TNFa-R1) were demonstrated. This last point could be discussed.

The authors suggest that TNFa induces tight junction disruption and ZO-1 expression down-regulation. However, the chronology of events could be discussed. The first TNFa peak 2h post injection may induced the ZO-1 down expression and the tight junction disruption observed at 9h. Effectively, only the GalN/LPS treatment induces an high serum TNFa level increased and they found that major alteration of the intestinal epithelial barrier occurred 9h after GalN/LPS treatment. In fact, at 9h post treatment, the multi-visceral decompensation was evident (liver necrosis, intestinal epithelial barrier disruption …) and the second TNFa peak 9h post injection was perhaps the result of the bacterial invasion. This last point could be discussed.

The reference following the sentence “Among the pro-inflammatory mediators, the TNFa and TNFaR1 systems …” 24 is not appropriate and could be replaced by the references 25 and 26.
In the legend (Figure 2): “Transmission electron microscopy of mousse …., the GalN/LPS group (D, E and F), and groups …” must be corrected by “Transmission electron microscopy of mousse …., the GalN/LPS group (D), and groups …” (E) and (F) are respectively LPS control group and galN control group.

The figure 3 legend could be more concise without repetition.

A good correlation was found between mRNA and protein ZO-1 expression at 2h, 6h, 9h after GalN/LPS treatment. So The figures 5 and 6 could be associated. However The membranes could be reprobed with anti b-actin antibodies to control the protein electrophoresed amount.

**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