

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

Specific Comments to Authors: Zou et al. investigated the role of invariant natural killer T (iNKT) cells in cholestatic liver injury caused by ethinylestradiol (EE) by using mouse model. They found that EE increased intrahepatic iNKT cells along with biased Th1 cytokine production. They also investigated the mechanism of iNKT cell-mediated cholestatic liver injury caused by EE in the mouse model. The experimental design is valid and its results are clear. The interpretation is appropriate and the text is easy to read. This is a well-done study. I list up some minor points.

1. Histopathological results: The meaning of pathological score is not clear. Please specify. In addition, the authors only describe portal/periportal inflammation, such as piecemeal necrosis and proliferation of pseudocholeangiolar duct. How about lobular inflammation? By the way, “bile duct hyperplasia” that the authors say is not right. Correctly, it is proliferation of pseudocholeangiolar duct.

Response:

We thank the reviewer for pointing out this. We described the methods as follows: “Slides were coded, randomized, and assessed by pathologists who during the evaluation of the slides were blinded to the treatment groups. Scoring for liver injury was conducted according to the following criteria: no hepatocellular necrosis, proliferation of pseudocholeangiolar duct, or inflammatory cell infiltration, 0; mild, 1; moderate, 2; severe, 3.” (Paragraph3, Page 7). We observed portal inflammation rather than lobular inflammation. We edited Figure 2, the results and corrected the “bile duct hyperplasia” to “proliferation of pseudocholeangiolar duct”.

2. Why does the fold change of control C57BL/6J in Fig. 3A and Fig. 5A, B, C not distribute around 1.0?

Response:

We thank the reviewer for pointing out this. We re-calculated the PCR results and the fold change of control C57BL/6J mice in Fig. 3A and Fig. 5A, B, C distribute around 1.0.

3. (p.16, ll.15-17) CD1d knockout mice (lacking NKT cells) exhibit enhanced (>4-fold) proinflammatory cytokine secretion and higher mRNA levels of TLR4 in a NAFLD model[44].: This should be “CD1d knockout mice (lacking NKT cells) exhibit enhanced (>4-fold) proinflammatory cytokine secretion and higher mRNA levels of TLR4 in kidney of a NAFLD model.”

Response:

We thank the reviewer for pointing out this. We corrected this sentence.

4. LPS is not defined in the text.

Response:

We are sorry for the mistake. We corrected this and other abbreviations.