Peer Review File

Article information: https://dx.doi.org/10.21037/tgh-23-93

Reviewer A

The authors found a phenotype in which PIM1 inhibitor suppresses ConA hepatitis. Although the suppressive effects of SMI-4a are considered to be certain, mechanistic analysis is insufficient and investigation is needed.

Major:
Comment 1: The analysis of hepatic immune cells should be detailed. Macrophages in blood are mentioned in Figure 3I, but what about the liver? Whether the number is decreased or the activation is suppressed? Are there no effects of PIM1 inhibitors on other cells? Staining the number of macrophages in serum is not common. PBMCs should be used for FACS examination.
Reply 1: Thanks for your suggestion, we supplemented the experiment on the changes of macrophages in liver tissue and detected the content of macrophages by flow cytometry. We found that the number of macrophages in liver issue is decreased. Following your suggestion, we tested other immune cells including Neutrophils and T cells in liver issue.PIM1 inhibitors also have effects on other immune cells including Neutrophils and T cells.
Change in the text: We add some data about the effect of SMI-4a on Con A-stimulated immune cells (macrophages,Neutrophils and T cells)in liver tissue(see Page 9 line 240-244).We have deleted the number of macrophages in serum.

Comment 2: The effect of SMI-4a on Con A-stimulated T cells should also be investigated.
Reply 2: We have supplemented the experiment on the effect of SMI-4a on Con A-stimulated T cells.We found that SMI-4a can decrease the count of T cells in Figure 4C and D.
Change in the text: We add some data about the effect of SMI-4a on Con A-stimulated T cells in liver tissue(see Page 9 line 242-244).

Comment 3: Expression of various cytokines and PIM1 target genes in liver tissue should be investigated to reinforce the hypothesis of the mechanism.
Reply 3: Thank you for your suggestion.Expression of various cytokines in liver tissue were tested by qPCR in Figure 4G,H and I.PIM1 target genes P-p65 in liver tissue cannot detect by qPCR only by WB, so we didn't add data. PIM1 target genes c-casepase in liver tissue cannot detect by qPCR only by WB,so we didn't add data.
Change in the text: We add some data about expression of various cytokines in liver tissue(see Page 9 line 244-246)

Comment 4: SMI-4 has been studied at only one dose. Dose-dependency should be established up to lower doses. At present, the possibility of nonspecific effects cannot be ruled out. Was kinase selectivity of SMI-4a confirmed?
Reply 4: In my manuscript, only one concentration dose of SMI-4a is determined based on previous literature references. In the article of Pim-1 inhibitor SMI-4a suppresses tumor growth in non-small cell lung cancer via PI3K/AKT/mTOR pathway,it use the certain concentration dose of SMI-4a.Also in the article of PIM1 inhibition attenuated endotoxin-induced acute lung injury

through modulating ELK3/ICAM1 axis on pulmonary microvascular endothelial cells,it used this same dose.Therefore, We didn't do a dose gradient
of SMI-4a, and the dosage in the literature was directly referred to the experiment. The kinase selectivity of SMI-4a has been detailed in the instructions for the selectivity of PIM1.SMI-4a is an ATP competitive inhibitor of Pim1 with an IC50 of 17 nM according to the specification.
Change in the text: We have modified our text as advised (see Page 5, line 125-126.)

Minor:
Comment 1: The impact of clinical application to autoimmune hepatitis, etc. should be discussed.
Reply 1: We have discussed the impact of clinical application to autoimmune hepatitis.There is no special treatment for acute autoimmune hepatitis in clinical practice, and it is treated by immunosuppressants and hormones. Our study could provide a drug that could be considered for autoimmune acute hepatitis. To provide new ideas for treatment.
Change in the text:We have modified our text as advised (see Page 9, line 259-262.)We add the content about autoimmune hepatitis.

Comment 2: Spacing between words is often imprecise and should be corrected.
Reply 2: We have carefully changed the spacing between words in the manuscript.
Change in the text:We have modified our text as advised (see Page 7, line 188-193),(see Page 9 line268-269). Totally in the whole manuscript.

Reviewer B

1. ”in vivo/in vitro/gene” in the entire article should be italicized.
Rely: I change the in vivo/in vitro/gene to be italicized.

2. The abbreviations should be defined upon first use in the Abstract and Main Text.
Rely: I add all the abbreviations in the Abstract in Page 2.

3. “All applicable international, national, and/or institutional guidelines for the care and use of animals were followed.”

We do not suggest saying that “All” guidelines are followed. Please edit the statement and add it to the Methods section.
Rely: I change the sentence “All applicable international, national, and/or institutional guidelines for the care and use of animals were followed.” in the text.

4. The main text of an original article should include a Conclusions section.
Rely: I add the conclusion in Page 11 line 297-301.

5. The PCRprimers in Section 2.13 are suggested to be organized in a table.
Rely: I add the table about PCRprimers.

6. All the abbreviations in the figure(s) and table(s) should be defined in the explanatory legend.
Rely: I add the abbreviations in the figure and table.

7. All the figures have two summary legend. We would suggest to use one only or combine them into one.

Rely: The summary legend was modified in the text.

8. We suggest to be clear on **which group** is n=X for in each legend.
Rely: I add the n=X in each legend,so it will be clear.