Dear editor and reviewer,

On behalf of the co-authors, we thank you for offering us an opportunity to revise our manuscript and re-submit to ***World Journal of Gastroenterology***. Thank you for your insightful comments concerning our manuscript entitled "Fibrinogen-like protein 2 deficiency inhibits virus-induced fulminant hepatitis through abrogating inflammatory macrophage activation" (Manuscript ID: 70678), and your input has greatly improved our manuscript. We have carefully gone through the comments and revised the manuscript accordingly. We hope these efforts in revised version of the manuscript will clarify your main concerns and meet the criteria for publishing in your journal. A more detailed, point-by-point response to various comments and questions is provided below.

Reviewer's comments:

In this manuscript, the authors examined the role of macrophage Fgl2 in a mouse model of virus-induced fulminant hepatitis. Fgl2 expression was increased in Kupffer cells and MoMFs with proinflammatory phenotypes after viral infection. Fgl2 deletion in bone marrow cells attenuated virus-induced hepatitis, associated with decreased inflammation. In addition, Fgl2 deletion increased M2 phenotypes in macrophages. This is a well-written paper. I have minor comments.

1. The effect of Fgl2 deletion on antibacterial immunity was examined. How about that on antiviral immunity? Please examine the effect of Fgl2 deletion on cellular antiviral responses and viral loads.

Response: Thank you for your insightful comments. As revealed in Fig.8C, Bone marrow-derived macrophages (BMDMs) with Fgl2 deletion expressed decreased IRF3 and IRF7 in response to MHV-3 infection, which are core transcription factors for interferons transcription for antiviral immunity. Please see page 16, lines 323-325 and Fig. 8C. At the meantime, viral loads were decreased significantly in Fgl2-/- mice. Please see page 12, lines 245-246 and Supplementary Fig. S3B.

2. The authors used a mouse model of fulminant hepatitis. Does Fgl2 deletion

prolong mouse survival?

Response: Thanks for the reviewer's comment. Over 20% of mice with Fgl2 deletion survived after MHV-3 infection, while none wild type mice survived following MHV-3 infection (Ref #14 of the main text). Such experiments was repeated with so many times with the similar result.

Editorial office's comments:

(1) Science editor:

Specific Comments to Authors: The manuscript elaborated the role of macrophages in viral severe hepatitis. I find it a well-structured interesting study, which can be considered for further review in this journal, however, there are several concerns to be clarified prior for the further review. **Please provide the bar chart of WB in Figure 7. I want to see if there is any statistical difference.** Scientific Quality: Grade B (Very good) Language Quality: Grade B (Very good) Recommendation: Conditional acceptance.

Response: Thanks for the science editor's comment. We provide WB picture in figure 8 and bar charts of that in supplemental figure 5 to address that the induction of Fgl2 in macrophages regulates inflammatory signaling by modulating NF-kB, IRF3, IRF7, and p38 phosphorylation. There are no statistical difference in MyD88, TRIF, phosphorylated JNK, phosphorylated ERK, phosphorylated BTK. Please see supplemental figure 5.

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Gastroenterology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Before final acceptance, **uniform presentation should be used for figures showing the same or similar contents**; for example, "Figure 1Pathological

changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...". **Please provide decomposable Figures** (in which all components are movable and editable), **organize them into a single PowerPoint file.** Please authors are required to **provide standard three-line tables**, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

Response: Thanks for arranging the revision of the manuscript. Decomposable figures are organized in the power point file (70678-Figures.pptx) with uniform presentation and the table is provided as requested in the word file (70678-Tables.docx) in the revised files.