

RESPONSE TO REVIEWERS

Point by point response

The authors wish to thank the Reviewers for their valuable suggestions and constructive criticism. Here we provide a point-by-point response to each query raised.

Reviewer #1

Specific Comment 1: Introduction, first paragraph. Suggest to discuss the pathomechanism of NAFLD (unclear), the current multi-hit hypothesis, and its association with dormant lifestyle. One recent article could be cited: Okekunle AP, Youn J, Song S, Chung GE, Yang SY, Kim YS, Lee JE. Predicted pro-inflammatory hs-CRP score and non-alcoholic fatty liver disease. Gastroenterol Rep (Oxf). 2023 Oct 11;11:goad059. doi: 10.1093/gastro/goad059. PMID: 37842198; PMCID: PMC10568523.

Response: We wish to thank the reviewer for the suggestion. As suggested, we have discussed discuss the patho-mechanism of NAFLD (unclear), the current multi-hit hypothesis, and its association with dormant lifestyle in the Introduction, first paragraph. The added part is highlighted in yellow. Also, we have now cited the above study in our article [See Reference No. 6].

Specific Comment 2: Section 3.3: what are the similarities and differences in autophagy between mouse models and human NAFLD?

Response: The authors wish to thank the Reviewer for raising that concern. The defects in autophagy observed in human NAFLD are similar to that observed in murine models of NAFLD wherein early increase in autophagic flux is followed by late block in autophagic flux and concomitant increase in ER-stress. We have now discussed this in the manuscript in Section 3.3 (text highlighted in yellow).

Specific Comment 3: The second "4.1" should be "4.2".

Response: The authors wish to thank the Reviewer for pointing that out. We have now corrected this.

Specific Comment 4: Suggest to discuss the prominent questions/future directions in autophagy research in four individual liver cell types.

Response: The authors wish to thank the Reviewers for the insight. We have now discussed the future perspectives of cell-type specific autophagy research in four major liver cell types in Section 8 and highlighted the text in yellow.

Reviewer #2

Specific comment 1: There are three types of autophagy: microautophagy, chaperone-mediated autophagy, and macroautophagy, which type of autophagy does the author focus in this article and why?

Response: The authors wish to thank the Reviewer for the concern. As already mentioned in Section 2 (text highlighted in yellow for reference), we have focussed on macro-autophagy (which we refer to as autophagy in the text) as macro-autophagy is the major type of autophagy that is perturbed in human NAFLD/NASH.

Specific comment 2: Why are two 4.1 in part 4?

Response: The authors wish to thank the Reviewer for pointing that out. It was a typing error and we have now corrected this in the manuscript.

Specific comment 3: Maybe section 4 -7 could be summed up into a big one with several subheadings.

Response: We wish to thank the reviewer for the suggestion. However, our review focuses on the specific role of autophagy in four major (yet distinct) liver cell types which have been exclusively discussed and form the essence of our study. We believe that merging of these sections will dissolve the uniqueness of each section and may add to ambiguity.

Specific comment 4: There are many irregular writings in the manuscript.

Response: To the best of our ability, we have tried to improve the writing in the manuscript at several instances.