Point-by-point response to the review comments.

We express our sincere thanks to the reviewers for careful and thorough reading of this manuscript and for the constructive suggestions, which help to improve the quality of this review manuscript.

Our response follows (the reviewer's comments are underlined).

Reviewer #1:

The manuscript gives a broad overview of cellular senescence and its implications to liver diseases. This review gives a brief summary of the current status of senescence research in hepatocytes, cholangiocytes and stellate cells. The manuscript is clearly written and is highly readable. A few spelling mistakes need to be corrected:

(1) Abstract: Change to: Once becoming senescent, the cell stops dividing permanently but remains metabolically active.

Reply: Corrected

(2) Page 8: …CxCL1, CxCL2, CxCL3 ect. Change to: CXCL1, CXCL2, CXCL3 etc.

Reply: Corrected

(3) Page 9: Change to: The NOTCH1 was shown to be upregulated in cells undergoing oncogene-induced senescence (OIS), …

Reply: Corrected

(4) change to: But there are key questions that remain to be addressed: 1) which factor(s)… The integrity of the nuclear envelope is disrupted… ….and upregulate SASP expression via inducing type-I interferons (IFN-I).

Reply: Corrected

(5) Page 18: change to: Hepatocellular fibrosis often results from the excessive deposition of ECM… Change to: …ROS, which may lead to senescence in HSC but the underlying mechanism…

Reply: Corrected

(6) Page 19: change to … important insight to fight against hepatic inflammation, fibrosis or cancer…

Reply: Corrected

Reviewer #2:

Overall this is a well written review, and the title is interesting and attracting. However the authors use a large amount of space to address the characteristics of senescence and associated signaling pathways, which have been reviewed multiple times elsewhere. The article will be better if it can be arranged reasonably.

The manuscript is designed for both readers that are interested in the comprehensive discussion about hepatic senescence and readers who are only interested in subsections. The current form of the review manuscript fulfils both of these needs and we are concerned that if we delete out some parts of the senescence characteristics and the signaling pathways then the subsections will not be understandable to the reader who is only interested in one or a few sections or only those particular sections. Every section of the manuscript has both general discussions on global senescence and specific emphasis on hepatic senescence. If we cut some parts, there will be a disconnection, and difficult to read and comprehend. Additionally, despite the senescence topic has been the frequent subject of review, our emphasis has been on the signaling pathways of SASP, which has not been well reviewed with recent advances. This is particularly important of hepatic senescence where SASP could play important pathological roles. Therefore we would like to keep the manuscript largely in its current form. However, we express our sincere thanks to the reviewer for the comments.