37063-Response to Reviewers

Reviewer #1*: İt might solve the problem and meanwhile treatment strategy for many diseases that have the same background.*

Response: We thank the reviewers for their comments.

Reviewer #2*: The manuscript entitled The role of inflammatory response in liver diseases: therapeutic strategies by Jos éA Del Campo, Paloma Gallego, Lourdes Grande is well-written and presented. It is timely and explains the role of inflammation in NAFLD.*

Response: We truly thank the reviewers for their comments.

Reviewer #3*: Of interest, authors reviewed the inflammasome and liver diseases.*

Response: We thank the reviewers for their useful comments that will improve our manuscript. We have followed all reviewer suggestions accordingly.

1. In Introduction section, authors mentioned "..... bile diseases of NAFLD, or NASH." But NAFLD and NASH are not bile diseases.

Response: We apologize for this mistake and we thank the reviewer for his/her comments. We have modified this sentence in the revised manuscript (page 4). This point has been also addressed by reviewer #4.

2. In page 10, authors mentioned "..... which finally triggers the production of proinflammatory cytokines and interferon type 1(IFN-type1)." Interferon-alpha? Interferon-beta? Authors should describe them according to the proper references: Kanda T, Steele R, Ray R, Ray RB. Hepatitis C virus infection induces the beta interferon signaling pathway in immortalized human hepatocytes. J Virol. 2007 Nov;81(22):12375-81.

Response: We have modified the manuscript according to reviewer suggestion. The reference by *Kanda et al* has been included in the reference list.

3. In page 12, "In 1876, Karl Kupffer discovered a group of cells with prolongations when he tried to look for nerve fibers in the liver, which he called stellate cells of the liver." Authors should explain them according to proper references.

Response: We have modified the manuscript (page 12) according to reviewer suggestion and included the proper references.

4. In Figure 1, letters are too small to read. Authors should fix them.

Response: We have modified the figure according to reviewer suggestion.

Reviewer #4*: This review reports an update on the role of the inflammasome in the aggravation of liver disease, and how selective blockade of this main pathway may be a useful strategy to delay fibrosis progression in liver diseases. In the section Introduction the sentence "The diseases usually occur in response to chronic hepatocellular injury caused mainly by the abuse of alcoholic intake, chronic infections such as those caused by the HCV, bile diseases of NAFLD, or NASH.." should be better ".....such as those caused by the HCV, bile duct damage, NAFLD or NASH.."*

Response: We thank the reviewer for his/her comments that would allow us to improve the manuscript. We have modified the sentence in Introduction according to reviewer suggestion (page 4). This point has been also addressed by reviewer #3.

In the text, after the first report, hepatocellular carcinoma should be always reported as HCC, please verify. Are the authors sure that this work is in press? Brunt, E.M., Wong, V.W.-S., Nobili, V., Day, CP., Sookoian, S., Maher, J.J., Sirlin, C., Neuschwander-Tetri, B.A., Rinella, M.E. (2015) Noalcoholic fatty liver disease. Nat.Rev.Prim. in press. I think that should be added a short paragraph to specify that the control (management) of inflammatory patterns is crucial also in case of potential treatment of liver diseases

with stem cells. In the last years, an increasing amount of works is dedicated to the research in the field of stem cells and in, this case, in restoring liver functionality (see the recent review by Fagoonee t al. Stem Cells Dev. Stem Cells Dev 2016;25:1471-82.

Response: We completely agree with the reviewer comments and we apologize for the mistake in the reference list. We have modified the manuscript in the revised version according to reviewer suggestion, including the reference by Fagoonee et al.