

Format for ANSWERING REVIEWERS

March 12, 2015

Dear Editor,



Please find enclosed the edited manuscript in Word format (Editorial manuscript 16368 NASH-(revised): 16368-review.doc).

Title: IS THERE A ROLE FOR ADAPTIVE IMMUNITY IN NONALCOHOLIC STEATOHEPATITIS (NASH)?

Author: Salvatore Sutti, Aastha Jindal, Stefania Bruzzi, Irene Locatelli, Cristina Bozzola, Emanuele Albano

Name of Journal: *World Journal of Hepatology*

ESPS Manuscript NO: 16368

The manuscript has been modified according to the suggestions of reviewers introducing the following changes:

Reviewer 291808

1) We are well aware that non alcoholic steatohepatitis (NASH) induced by feeding mice with methionine choline deficient (MCD) diet does not reproduce all the features characterizing the human disease. However, the use of MCD diet is useful in the study of liver immune responses as steatohepatitis in this model is associated with an appreciable activation of humoral and cellular immune response that reproduce some of the features of the human disease. To our knowledge, no data is available concerning the role of liver adaptive immune responses in genetic model of obesity. In the revised version of the paper we have included the discussion of a recent paper (see ref. 34) showing a role of CD8+ T and NKT-lymphocytes in the pathogenesis of NASH induced by mice feeding with a choline deficient high fat diet that also cause overweight and insulin resistance. Interestingly, in this latter model immune reactions appears to be involved in promoting hepatocellular carcinoma.

2) Unfortunately, most of the data pointing on the role of adaptive immunity in the pathogenesis and progression of (NASH) are still at an early stage and from the experimental findings available at the moment it is not yet possible to speculate about future therapeutic opportunities. We have mentioned this point in the conclusion. However, on the basis of ongoing experiments I am confident that in a short time we might propose some therapeutic approach based on the interference with immune mechanisms.

3) The title has been corrected as: IS THERE A ROLE FOR ADAPTIVE IMMUNITY IN NON ALCOHOLIC STEATOHEPATITIS (NASH)?

4) The references 16 and 17 have been rearranged.

Reviewer 503062

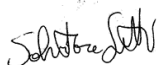
- 1) The body text has been subdivided in different paragraphs according to the reviewer suggestion.
- 2) The title has been corrected as: IS THERE A ROLE FOR ADAPTIVE IMMUNITY IN NON ALCOHOLIC STEATOHEPATITIS (NASH)?
- 3) In the abstract, the sentence “their possible involvement mechanisms by which in sustaining hepatic inflammation in NASH” has been changed as “their possible mechanisms involved in sustaining hepatic inflammation in NASH”.

Overall, the manuscript has been improved taking in account the reviewers as well as the editor comments. The mistakes evidenced during the revision process have been corrected and all the modifications made in the body text have been marked in yellow.

References and typesetting have been corrected.

Thank you again for publishing our manuscript in the *World Journal of Hepatology*.

Sincerely yours,



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