

## **Responses to Reviewers**

### **Reviewer #1 (code 03477256)**

1. Please present recent data on microbiome and NASH.
2. What about bariatric surgery in morbidly obese with NASH and its resolution ?
3. Please present the crosstalk between adipose tissue and NASH.
4. More international and actual references should be included.

### **Response**

Thank you for your valuable indications.

1. We added the related statements, Table 4, and three references (ref. #94-96).
2. We added the report from von Schönfels W et al. (#76) and the related statement to the text.
3. We described this point in more detail and added 2 references (#23, 24).
4. We added above international references.

### **Reviewer #2 (code 00035033)**

This is a very well performed, comprehensive, complete and updated review on the current status and perspectives of the approach to the management and to research in the field of non alcoholic fatty liver disease. The Authors have covered all the areas of NAFLD management and research, from diagnosis to treatment. My only suggestion refers to the chapter 1. Mechanisms of steatogenesis where "very-long-chain lipoprotein particles" should be changed in "very-low-density lipoprotein particles (VLDL)".

### **Response**

Thank you for your suggestion. We corrected full term of VLDL.

### **Reviewer #3 (code 00011429)**

This is a review manuscript of non-alcoholic fatty liver disease. The paper is clearly written and well presented.

Major points: The title of the paper is "Current status, problems, and perspectives of non-alcoholic fatty liver disease research". However, the content of the paper is mostly a comprehensive review of non-alcoholic fatty liver disease. It gives a summary of NAFLD/NASH pathogenesis, diagnosis and treatment.

### **Response**

Thank you for your important comments. We summarized current

understanding of NAFLD/NASH pathogenesis, diagnosis, and treatment, and discussed problems and perspectives.

Minor points. 1. There are some writing errors such as “individials” 2. The subtitle 3 is Mechanisms of fibrogenesis and hepatocarcinogenesis The subtitle 4 is Mechanism of hepatocarcinogenesis 3. “NAFL at the first liver biopsy, which gradually regressed to cirrhosis and HCC over 20 years”. I think the word regressed should be ‘progressed’. 4. Vilar-Gomez et al. analyzed NASH patients who received repeated biopsy to reveal weight loss, the absence of diabetes, ALT normalization, young age, and baseline NAS < 5 as independent predictors of NASH resolution without fibrosis worsening after 1-year of lifestyle intervention [71] I could not understand this sentence. It needs to clarify.

### Response

We appreciate your indication.

1. We carefully checked and corrected typographical errors.
2. We changed subtitle 3 to “Mechanism of fibrogenesis”.
3. We corrected this point.
4. We corrected this sentence.