

Format for ANSWERING REVIEWERS

February 28, 2014

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 6438-edited.doc).

Title: Pediatric Non-Alcoholic Fatty Liver Disease: new insights and future directions.

Authors: Pierluigi Marzuillo, Emanuele Miraglia del Giudice, Nicola Santoro.

Name of Journal: *World Journal of Hepatology*

ESPS Manuscript NO: 6438

The manuscript has been improved according to the suggestions of reviewers:

- (1) we created a figure summarizing the risk factors of NAFLD development in whom we summarized all the SNPs.
- (2) we also created a Table summarizing the current and future treatment strategies.
- (3) we added a conclusion to the review
- (4) we modified "the gold standard" terms in the introduction section.
- (5) we shortened the manuscript.

In the next page there are the detailed answers to reviewers.

We hope that our manuscript will be of interest for the readers of the *World Journal of Hepatology*

Sincerely yours,

A handwritten signature in black ink that reads 'Nicola Santoro'.

Nicola Santoro, M.D., PhD. Yale University School of

Medicine, Department of Pediatrics,

330 Cedar Street, P.O. Box 208064, New Haven, CT 06520.

Telephone number: (203) 737-6356, Fax Number: (203) 785-

6421; e-mail: nicola.santoro@yale.edu

We thank the reviewers for taking the time to read and comment on our manuscript. All the changes have been highlighted in the text.

Reviewer 00004431

Comment: There are several important SNPs and the SNPs should be summarized in a Table

Answer: We created a figure summarizing the risk factors of NAFLD development in whom we summarized all the SNPs (see figure 1).

Reviewer 02860814

Comment: 1. The authors must provide some figures and/or tables in order to make their publication more illustrative. I suggest to provide a figure for the SNPs implicated in the pathogenesis and a table with the summary of current and future treatment strategies. 2. A conclusion with the most important finding in the era of pediatric NAFLD should be added at the end of the manuscript.

Answer: 1. We provided a figure summarizing the NAFLD risk factors in whom we listed the SNPs implicated in the pathogenesis. We also created a Table summarizing the current and future treatment strategies (see figure 1 and table 1). 2. As suggested, at the end of the paper, we wrote a conclusion (see the conclusion section at the end of the manuscript).

Reviewer 00071717

Comment: Modify “the gold standart” terms in the introduction section. Liver biopsy is the gold standart for evaluating liver histology in patients with NAFLD, but not for diagnosing NAFLD.

Answer: As suggested, we modified “the gold standard” terms in the introduction section (see line 18, page 4).

Reviewer 02526287

We reviewed with interest the paper entitled “ Pediatric non-alcoholic fatty liver disease: new insights and future directions” by Marzuillo et al. The paper is an updated and meaningful review on NAFLD in children covering a topic deeply addressed in adults but only sporadically addressed in pediatic population. All the most relevant issues are exhaustively discussed. In particular, the authors emphasized epidemiologic aspects connected with NAFLD in children which is a steadily increasing clinical condition ranking among the most common forms of liver disease in this setting. The most relevant risk factors connected with NAFLD occurrence as obesity, insulin resistence, Type 2 Diabetes and dietetic disorders as well as genetic predispositions including PNPLA3 and GCKr variants are fully discussed. Current and future treatment options are reported and discussed. To our opinion however, the paper seems too long and a shortening work should be advisable. In particular some paragraphs dealing with pathophysiology of NAFLD and NASH should be condensed or even deleted. The language is fairly good and references updated.

Answer: as required, we performed a shortening work of the manuscript.

