

ANSWERING REVIEWERS

March 19, 2015

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: ESPS Manuscript NO: 16396-edited.doc).

Title: Understanding the pathophysiological mechanisms in the pediatric NAFLD: The role of genetics

Authors: Pierluigi Marzuillo, Anna Grandone, Laura Perrone, Emanuele Miraglia del Giudice.

Name of Journal: *World Journal of Hepatology*

ESPS Manuscript NO: 16936

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

- (1) We introduced the multiple hit hypothesis instead of the two hit hypothesis.
- (2) We added data of a very recent publication about one of the topics of the Editorial
- (3) We performed minor English corrections.

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 'Pierluigi Marzuillo'.

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We thank the reviewers for taking the time to read and comment on our manuscript. All the changes have been highlighted in the text. We added data of a very recent publication about one of the topics of the Editorial (see lines 168-176 of the new version of the manuscript)

Reviewer 00187937

Comments: Dear Editor, in this editorial, Marzuillo et al. have reviewed the pathophysiological mechanisms in the pediatric NAFLD dealing with the role of genetics. This is well prepared article, but I can offer the authors to focus on multiple hit hypothesis instead of the two hit hypothesis. Regards.

Answer: thank you for your comments. We introduced the concept of the "multiple hit hypothesis", as you suggested (see lines 188-192 of the new version of the manuscript).

Reviewer 00742006

Comments: This is very interesting and high quality paper to be published after minor English correction.

Answer: thank you for your comment. We performed English corrections all over the manuscript.

Reviewer 02445616

Comments: The manuscript entitled "Understanding the pathophysiological mechanisms in the pediatric NAFLD: The role of genetics" highlighted an important area in hepatology. Although two hits hypothesis explains some causes of NAFLD, gene polymorphisms also play an important role. In this editorial, three genes polymorphisms (PNPLA3, GPR120, and TM6SF2) have been reviewed. Their physiology and pathophysiology are discussed. The updated two hits hypothesis is clearly shown in Figure 1. It is a good editorial and deserves to be published as it is written right now.

Answer: Thank you for your comments.