

Dear Editor,

here we submit the revised version of our manuscript (ID 00036624) entitled: **“Promoting genetics in NAFLD: combined risk score through polymorphisms and clinical variables?”**.

We are really glad the reviewer found our manuscript of value and we greatly appreciated their comments, which have permitted us to revise and improve the quality of the work.

We think our manuscript is now significantly improved and hope you will find it suitable for publication in your journal.

Best regards,

Umberto Vespasiani Gentilucci, M.D., Ph.D.

**Reviewer 1).** This reviews summarized the previous studies which conducted the risk score system for the diagnosing of NAFLD. It is an interesting topic and the contents were attractive. It is acceptable to publish this article in the World Journal of Gastroenterology, but some issues should be clarified and corrected. 1. The authors declared that “they expect that combined genetic/clinical scores, derived from longitudinal studies and built on a few strong genetic variants and relevant clinical variables, will reach a significant predictive power...”. I wonder that whether the authors had applied an effective risk score system to predict the risk of NAFLD or NASH? 2. There are 10 keywords, I do not know if the keywords had exceeded the maximum number limitation of this Journal? 3. In the table 2, the variables included of Donati et al [28], 2017 should include the age, sex, obesity, T2DM, severe fibrosis, not just the risk allele. 4. Some sentences should be reorganized with the clear expression.

**Answer to Reviewer 1).** We are glad the reviewer appreciated our work and we thank him/her for the comments.

We agree with the reviewer that the mentioned sentence was a little bit too speculative. Although, at the moment, we don't have personal data able to support the absolute certainty of this view, we think that our interpretation is consistent with all the evidence produced so far on this topic and comprehensively reported in this Editorial. However, in agreement with the suggestion of the reviewer, the sentence has now been mitigated both in the abstract and in the text.

We have verified that the number of keywords is up to 10.

We have corrected and integrated the pertinent part of Table 2), as suggested.

The manuscript has been completely revised with the aid of an English native speaker.

**Reviewer 2).** Very well done work.

**Answer to Reviewer 2).** We are really glad and honored of such a comment!

**Reviewer 3).** The review by Vespasiani-Gentilucci et al, “Promoting genetics in NAFLD: combined risk score through polymorphisms and clinical variables?”, is very well written, and timely. However, I felt somewhat lost while reviewing the manuscript with the wealth of information. The manuscript will benefit with a Table that summarizes, particularly the combined (genetic/clinical) risk scores in the assessment of NAFLD patients. Additionally, a figure that summarizes the various genetic polymorphisms and its sites of action in the NASH pathogenesis will be beneficial to the readers.

**Answer to Reviewer 3).** We are glad the reviewer appreciated our work. We understand that the wealth of information may make reading more demanding and we have therefore tried to solve this problem by dividing the text in themed paragraphs as well as to summarize pertinent studies in

Tables. Actually, Table 1) and 2) summarized both pure genetic and combined risk score which has been proposed so far for their association with NAFLD and/or with its evolution. We agree with the reviewer that a figure summarizing the polymorphisms more consistently associated with NAFLD and their site of action would have been of aid, and it has therefore now been introduced as Figure 1).