

Comments of the Reviewers, authors' answers and consequent modifications.

Dear Editor, dear Reviewers.

We are re-submitting our invited manuscript, modified according to the peers' reviews and the Editorial rules.

Please, consider our point-to-point answers to your criticisms, comments and suggestions which were all very appropriate and that we appreciated greatly.

Our answer is relatively fast since most of the information needed are already available in the published articles which are quoted in our review, and, after having received the last comment - 2013-12-26th– we completed our work:

Reviewer 1 – 00068250 – commenting: 2013-12-05 12:59

- a) In this manuscript, authors stated, by reviewing publications and combining themselves research, that the environmental infections, and notably Adipogenic Adenoviruses ADV36 and ADV37 infections in Humans, are associated with obesity, and allied conditions, such as fatty liver, being causative factors of obesity and consequent disease in humans and animals.

R. Correct, and we address as much as possible limitations and bias of our studies (we do not consider limitations of the study of other, few Authors, which report different results.

- b) The contents are significant for readers.

R. Thank you, this is the reason of our job.

- c) The format style should be edited according to the request of the journal.

R. we modified the draft along the recommendations and requirements of the WJG.

- d) Abbreviations should be given their whole-names when they appeared first.

R. Abbreviation are now preceded by the whole-names when quoted for the first time in the text.

- e) In figures we cannot recognize what the lines stand for, respectively.

R. This is a general very appropriate comment. We apologize. Now figures are – hopefully – better focused to the theme of the article and better explained: legends describe now more accurately what is written in the body of the manuscript.

- f) In the part of OBESITY, the author referred a model MLR, how to compare it with other two BMI and HOMA?

R. The complete model is now presented, a little more synthetically in comparison with the published table.

- g) As stated in the paper, Ad36 seropositive NAFLD patients have greater adiposity. Therefore, it is not difficult to consider nutritional intervention may have more effect on weight loss. But its effect on fatty liver severity and insulin resistance need more explanation.

R. Yes, correct. The point is that a greater weight loss independently from the body weight at the beginning of the intervention. We demonstrated it using a MLR model BMI-weighted, i.e. balanced, for excluding the initial weight as a possible confounding factor.

- h) How to exclude the interference of other factors such as Adv37? Is there no any synergic effect of Adv36 and Adv37 on human liver diseases?

R. This is a very good question. We have not yet a definite answer. Published data were based on ADV36 seropositivity for neutralizing antibodies and, limited to the study on ADV37, also to the compound ADV36/ADV37 seropositivity. We are trying, with about one thousand ADV36/37 assays available at moment, to ascertain the actual effects of the serological status, lone or double.

Literature is currently focused to ADV36, as also the title of the present review is.

- i) In the part of MECHANISMS, a systematic diagram may be better supplementary for the part.

R. This is not exactly our field of investigation-speculation: nonetheless, we are including a scheme derived from the most comprehensive one already available.

Reviewer 2. 00188649. commenting: 2013-12-14 22:05

- A. Characteristics and biological significance of ADV36/ADV37 needs to be described briefly. More clinical manifestations are to be presented for the causation of hepatitis by these viruses.

R. Thanks for this comment: we actually are not writing of hepatitis, but we describe something of the biological significance of these adenoviruses.

- B. Bright echo pattern of the liver, increase or decrease of echo pattern of the liver should be elaborated for association of the adenoviruses and fatty liver disease.

R. some further detail is given regarding the association of US findings with US guided liver FNAB

- C. Prevalence and anti-virus strategies should be mentioned.

R. It is more clearly, now, and briefly discussed.

- D. Please correct numerous grammar errors including verb tense and use of symbols.

R. This was, hopefully, done, also by the help of a professional British translator

- E. I suggest the authors to have professional counsel fix English writing and organization problem throughout the rest of the article.

R. We agree. Thanks for the suggestion and I apologize.

Best regards to the Editor and the best wishes for an happy new year.

Yours sincerely

Guglielmo Trovato.