

RESPONSE TO REVIEWERS

We truly thank the reviewers and the Editor for their useful comments. Following, we have addressed each of the points raised by the reviewers:

Reviewer #1:

Specific comments: 1. Page 4 line 13 – define “FASN” as listed here and its effect on lipid metabolism. 2. Page 4 line 4 from bottom – start a new paragraph with the sentence starting “Adiponutrin or patatin-like...” 3. The review could be improved by the addition of a table or diagram that lists the lipid enzymes, lipoproteins, and genetic polymorphisms that are involved or modulated during HCV infection. 4. Page 7 line 2 from bottom. The issue of how statins may be used clinically to improve HCV treatment is potentially important. Could the authors perhaps expand on this and include a discussion of Rao et al. Gastroenterology 2011;140:144-152.

Reply: 1. FASN has been properly identified in the revised manuscript (page 5).
2. OK, done.
3. A new figure has been included in the revised manuscript.
4. This statement has been included in the revised manuscript (page 9) and a new reference (#61) has been added.

Reviewer #2:

About hepatitis C viral infection and the lipid metabolism of the host, authors gather it up well. In real treatment, how is the treatment result? When fatty liver, hyperlipemia, obesity are complicated, how long do results change in the ratio of? I think that this point should increase.

Reply: This is a very interesting point to be considered in the future. It seems that with the new therapeutic options (sofosbuvir, daclatasvir, etc) the former problem raised with fatty liver and obesity has been solved, although little information is found in the literature regarding this point. Data from a recent paper published by Meissner et al. (Hepatology 2015; 61:790-801) dealing with this issue has been included in the manuscript.

Reviewer #3:

Jose A del Campo and Manuel Romero-Gomez have presented an updated overview of the role of HCV in the modulation of the host lipid metabolism. The paper is well-written and structured. It clearly explains the involvement of the viral and host factors that participate in this interaction and the effect of new antiviral therapies. My comments: Please revise the English language for some misspelled words and wordiness (too long sentences). Please add one or two figures to enhance

your work Thank you

Reply: Thank you. We have revised English spelling and grammar to facilitate understanding for readers. A new figure has been included in the text.

Reviewer #4:

The review manuscript written by Del Campo et al. summarizes the association of lipid metabolism and HCV replication. They further suggest the contribution of lipid metabolism to the effect of DAA therapy. The review is well written and provides important information on the role of lipid metabolism in the treatment of HCV infection. It would be much better to show a summarized figure.

Reply: Thank you. We have included a new figure in the manuscript to summarize the point of view.

Reviewer #5:

The authors present a short review on modulation of lipid metabolism in HCV infection. The review is not over burdened with detailed information and this enhances the readability of the manuscript. However, there are a few areas that would benefit from further information. Some figures are necessary and will benefit the manuscript. A figure on lipid metabolism and the engagement with HCV proteins is one such figure required. The authors are advised to be wary of using "cure". While the new DAAs are very efficacious, there is a failure rate, small, but it exists. The term cure, really awaits more prospective studies. Page 5, references 36-38, expand on this information. References are needed for several statements throughout the manuscript. This is a worthwhile manuscript in that it describes some of the relevant literature in an uncluttered manner. It could be enhanced by detailing a section on viral replication and the intimate involvement of lipid.

Reply: We thank the reviewers for their useful comments. We agree that with a summarizing figure the story can be better understood. This figure has been included in the revised manuscript.

We also agree that 100% of cure is not achieved with any current therapy for HCV, and in fact, is lower for HCV genotype 3, which still need further options to obtain SVR similar that genotype 1a or 1b. Additional references have been included.