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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 18437
Title: Chronic hepatitis C virus infection and lipoprotein metabolism
Reviewer's code: 00039634
Reviewer's country: Italy
Science editor: Ya-Juan Ma
Date sent for review: 2015-04-21 16:32
Date reviewed: 2015-05-13 21:33

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[Y] Grade C: Good	[Y] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[ ] Minor revision
[ ] Grade E: Poor		[Y] No	[Y] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

The interesting review by Aizawa et al, assessed the closely interactions between HCV and lipids, and further the possibility that lipid metabolism could be a potential target for antiviral therapy. In fact, altered lipid metabolism have a role in chronic liver disease and hepatocarcinogenesis HCV-related. Authors, firstly review the metabolism of lipoprotein to understand the interaction with HCV. Then, they highlight the processes of HCV assembly, secretion, and entry into hepatocytes, focusing on the association with lipoproteins; finally, they discuss the significance of dyslipoproteinemia in chronic HCV infection. The idea seems to be very good, but the paper is confusing and too long. The clinical aspect of dyslipoproteinemia in patients with chronic hepatitis are missing. Further the paper by Rojas A et, published on J Viral Hepat. 2014 Jan;21(1):19-24 need to be discuss. I suggest to divide the review in three part; the fir regarding basic mechanism of lipid metabolism and HCV interaction; the second regarding the clinical aspect of dyslipoproteinemia in patients with HCV related disease (chronic hepatitis, cirrhosis and hepatocellular carcinoma); third the possible therapeutic aspect of lipid lowering drug in patients with HCV infection. The english need to be revised.

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ESPS PEER-REVIEW REPORT

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[Y] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

Aizawa et al. reviewed the association between HCV infection and altered lipoprotein metabolism. Although well-written, the following points will help to improve this review. 1. The authors found increased VLDL remnant in HCV G1b patients. Moriya et al. reported decreased CII and CIII in HCV-positive patients (Hep Res 2013). It is important to show how HCV itself can modulate systemic or hepatic lipoprotein metabolism. Or, will specifically HCV-induced hepatitis or steatosis, but not HBV, lead to dyslipoproteinemia? If the authors mention the possible mechanism and the effect of confounding factors of chronic HCV infection (HCV-specific inflammation, iron deposition, steatosis, etc.), this review is more informative. 2. Showing proposed mechanisms on how HCV (or HCV-related hepatitis) disturbs lipoprotein metabolism as Fig. 5 will help readers' understanding.

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ESPS PEER-REVIEW REPORT

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[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[Y] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

The article is very interesting and didactic designed. I fully agree with the authors that direct-acting antivirals are not affordable for most patients infected with HCV and the study of the correlation between lipid metabolism and infection with HCV should be continued for better understanding of the pathophysiology and for find novel (and, perhaps, cheaper) therapeutic solutions. It is useful that the authors mention that in hepatocytes infected with HCV there is a significant increase of geranyl-geranyl-phyrophosphate synthesis and a host geranyl-geranylated protein is suspected to be involved in HCV replication. The inhibition of the enzyme regulating cholesterol synthesis (HMG-CoA reductase) also decreases some farnesylated and geralylated products. Geranyl-geranyol inhibition could represent a therapeutic strategy against the infection with HCV. In addition, a host cell depletion of cholesterol can inhibit the replication of HCV. Many authors, including some Japanese ones, studied the effectiveness of statins as adjuvant therapy against HCV infection. Statins added to the standard treatment of chronic hepatitis C with pegylated interferon and ribavirin helped to improve early, rapid and sustained virologic response in many studies. In addition, eicosapentaenoic acid can suppress the expression of low-density lipoprotein receptor, that is

necessary for the HCV entry in hepatocyte (Statins in Chronic Hepatitis C: Stage result. Biomedical Research 2014; 25 (4): 463-469). It would be interesting to study whether by reducing the levels of proinflammatory cytokines (IL-6, IL-8, TNF-alpha) interferon used in chronic hepatitis C can help to the reduction of atherogenesis. Table 1 should be rebuilt (the upper part is not readable). There are some minor grammatical mistakes that must be corrected (e.g. hepatotrophic virus, SDR-BI). I agree to the publication of the article, after making the suggested small corrections.