ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 7306

Title: Hepatitis C Virus Non Structural Protein 5A Induces Insulin Resistance by Serine Phosphorylation of Insulin Receptor Substrate-1 and Increased Gluconeogenesis: a step towards Type 2 Diabetes Mellitus

Reviewer code: 00503187

Science editor: Gou, Su-Xin

Date sent for review: 2013-11-14 09:37

Date reviewed: 2013-11-22 23:52

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[Y] Grade C: a great deal of language polishing	[ ] No records	[Y]Rejection
[ ] Grade D (Fair)		BPG Search:	[ ] Minor revision
[Y] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

The manuscript by Parvaiz et al studies the involvement of hepatitis C virus infection in the development of insulin resistance. The authors show increased phosphorylation of IRS-1 Ser307, and increased phosphorylation of Akt Ser473, and suggest that this impairs insulin signaling and leads to the development of insulin resistance.   It has previously been published in a more thorough study on patients with hepatitis C virus infection that impaired IRS-1/PI3K signaling could provide a mechanism for increased prevalence of type 2 diabetes in these patients (Aytug S et al.:Impaired IRS-1/PI-3-kinase signaling in patients with HCV: a mechanism for in- creased prevalence of type 2 diabetes. Hepatology. 2003;38:1384–92). These authors show a reduction in IRS-1 tyrosine phosphorylation accompanied by a decrease in IRS-1/p85 PI3-kinase association, and a decrease in IRS-1–associated PI3-kinase enzymatic activity. They also show a marked reduction in insulin-stimulated Akt phosphorylation. The results by Parvaiz et al are contradictory to these previously published data.   The manuscript by Parvaiz et al is rather a preliminary report than a full story, and contradicts what has been published before in human patients. Data is wrongly interpreted, as Akt activation does not lead to inslin resistance. The data is of poor quality, the figures are not convincing, and the text requires rewriting. Based on this I can not recommend publishing the manuscript.

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Title: Hepatitis C Virus Non Structural Protein 5A Induces Insulin Resistance by Serine Phosphorylation of Insulin Receptor Substrate-1 and Increased Gluconeogenesis: a step towards Type 2 Diabetes Mellitus

Reviewer code: 00036874

Science editor: Gou, Su-Xin

Date sent for review: 2013-11-14 09:37

Date reviewed: 2013-12-02 19:34

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[Y] Accept
[Y] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	
[ ] Grade D (Fair)		BPG Search:	[ ]Rejection
[ ] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[ ] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS

minor corrections: is there an author from Rosalind Franklin University of medicine and Science?

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Title: Hepatitis C Virus Non Structural Protein 5A Induces Insulin Resistance by Serine Phosphorylation of Insulin Receptor Substrate-1 and Increased Gluconeogenesis: a step towards Type 2 Diabetes Mellitus
Reviewer code: 02445708
Science editor: Gou, Su-Xin
Date sent for review: 2013-11-14 09:37
Date reviewed: 2013-12-03 18:14

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[Y] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[ ] Grade D (Fair)		BPG Search:	[ ] Minor revision
[ ] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[Y] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

This paper describes the influence of Hepatitis C Virus (HCV) non structural protein 5A (NS5A) on serine phosphorylation of: a) insulin receptor substrate-1; b) Fox01 and c) GSK-3β and key gluconeogenic enzyme genes mRNA level. The main thrust of the paper is that the authors claim to have demonstrated   that HCV NS5A induce insulin resistance by modulating the pohosphorylation of proteins involved in insulin signaling pathway and up-regulation of gluconeogenesis. Although the paper reports a potentially interesting and an important study, there are several issue that need attention. Specific comments: 1. There is a lot of redundant description in the manuscript, especially in Introduction, Results and Discussion sections. These sections could be significantly shorter and easier read if redundancies in description are avoided.   2. The quality of data presented in Figs. 1-4 is very low, and consequently difficult or even impossible to interpretation. The most bands presented in Figs. 1-4   must be replaced by better one.   3. What does mean   the sentence "(…) The 18s was used as an internal control (…)" (page 5)? or "(…) 18S was used as housekeeping gene (…)" legend to Fig. 5   4. It is stated several times in text and in Fig 5 that HCV NS5a increases   gluconeogenic gene expression.   This is not shown. It seems to me that Fig. 5 shows the effect of HCV NS5a on PEPCK, G 6-P, CREB and TNFα mRNA levels. Increase of mRNA levels does not necessarily mean that mRNA synthesis is stimulated. It could be a post-transcriptional mechanism. This must be corrected (use mRNA level instead gene expression) 5. Diacylglycerols and ceramides are two different groups of lipids. Thus what does mean the sentence "(…) the

accumulation of diacylglycerols (ceramides)" (…) page 3).   6. There are few errors in the text.

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Title: Hepatitis C Virus Non Structural Protein 5A Induces Insulin Resistance by Serine Phosphorylation of Insulin Receptor Substrate-1 and Increased Gluconeogenesis: a step towards Type 2 Diabetes Mellitus
Reviewer code: 00503474
Science editor: Gou, Su-Xin
Date sent for review: 2013-11-14 09:37
Date reviewed: 2013-12-10 20:19

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[Y] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	
[ ] Grade D (Fair)		BPG Search:	[ ]Rejection
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COMMENTS TO AUTHORS

Title of the article :   Hepatitis C Virus Non Structural Protein 5A Induces Insulin Resistance by Serine Phosphorylation of Insulin Receptor Substrate-1 and Increased Gluconeogenesis: a step towards Type 2 Diabetes Mellitus Manuscript category   :   Original article Journal   :WJG   Overall publication value of the article: 1. Is the subject an important one?:   Yes   2. Does the article possess scientific value?: Yes   3.Title: Does the title bring the main massage of the study?: Yes   4.Abstract: Is the abstract presented in structured form?: Yes. However, methodology is not clear of the authors did. 5.Does the abstract give an adequate picture of the entire article?: Yes   6.Introduction: Is the background of the study made clear and helpful to readers unfamiliar with the subject? a. Abbreviation when mentioned   for the first time should be written in full. Eg   PGC-1α ,CREB, PEPCK and G6P , GSK and so on. b. can't : should be cannot in the text. c. Fox01 is written as such in   the text many times , at the end of introduction differently : FOX01. Pl unify. d. The aim of the work should be written in clear way such as :   The aim of the present work is to ------ so on.   7. Is the purpose of the article clearly stated?: Yes   8. Material and Methods: Is the research design appropriate and the methods clearly explained?: Yes   9. Are the criteria for selecting the sample clearly explained and justified?: Yes   10.Are the essential characteristics of the sample adequately described?: Details of methodology should be checked by a specialist in molecular biology .   11. Is the sample size adequate and representative?: Not mentioned   12.Has the data been collected in a

systematic and comprehensive manner?: Yes　　13.Is the statistical methodology appropriate?: author should explain why he used SEM rather than SD　　14.Are there any ethical concerns about this study?: Yes ,There is no mention of ethial committee approval .This is vital for researchers work with such dangeros virus like virus C　　15.Results:　Is the analysis of the data systematic.: Yes　16.Are the results important?: Yes　　　17.Discussion:　Is the interpretation of the results clearly presented and adequately supported by the evidence adduced?: Yes　18.Conclusions:　Are the conclusions logically valid and justified by the evidence adduced?: Yes　19.Graphics:　Are all the figures and tables adequate and necessary?: Yes　　20.References:　-Are the references up-to-date?: Yes　- Have the most important previous studies been cited?: Yes