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315-321 Lockhart Road,
Wan Chai, Hong Kong, China

ESPS Peer-review Report

Name of Journal: World Journal of Diabetes

ESPS Manuscript NO: 7232

Title: Hepatitis C virus infection and insulin resistance

Reviewer code: 00506347

Science editor: Zhai, Huan-Huan

Date sent for review: 2013-11-09 17:45

Date reviewed: 2013-11-12 05:08

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

interesting topic. well thought out review



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ESPS Peer-review Report

Name of Journal: World Journal of Diabetes

ESPS Manuscript NO: 7232

Title: Hepatitis C virus infection and insulin resistance

Reviewer code: 00495228

Science editor: Zhai, Huan-Huan

Date sent for review: 2013-11-09 17:45

Date reviewed: 2013-11-19 04:11

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

The review by S. Bose and R. Ray provide a good and extensive description of modulation of hepatic metabolic pathways under pathological conditions of hepatitis C virus infection. The paper is well written and contains up to date information on the topic.



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ESPS Peer-review Report

Name of Journal: World Journal of Diabetes

ESPS Manuscript NO: 7232

Title: Hepatitis C virus infection and insulin resistance

Reviewer code: 00433336

Science editor: Zhai, Huan-Huan

Date sent for review: 2013-11-09 17:45

Date reviewed: 2013-11-19 23:01

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

Major revisions: 1. Manuscript organization. Recommended to introduce figure 1 as the lead into section "MODULATION OF INSULIN RECEPTOR SUBSTRATE BY HCV" of the manuscript as an overall "road map" to the discussion. Would recommend organizing the discussion further as follows: 1. mechanisms underlying increased glucose production and 2. mechanisms underlying insulin resistance. 2. Clinical translation: recommend adding a section of the clinical implications of HCV-mediated insulin resistance including discussions of 1. the impact of HCV treatment on insulin resistance and glucose homeostasis and 2. implications for glucose lowering agents, i.e., is there a rationale, based on the earlier discussion in the manuscript, that an insulin sensitizer approach like metformin or TZD, would be preferable to other approaches.



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ESPS Peer-review Report

Name of Journal: World Journal of Diabetes

ESPS Manuscript NO: 7232

Title: Hepatitis C virus infection and insulin resistance

Reviewer code: 00496285

Science editor: Zhai, Huan-Huan

Date sent for review: 2013-11-09 17:45

Date reviewed: 2013-11-21 21:29

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
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<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

This manuscript by Dr. Bose and Dr. Ray reviews the existing literature on insulin resistance in hepatitis C virus infection. General comments: This review is timely and its subject is of great interest when considering the large number of patients with hepatitis C virus infection worldwide and the diabetes epidemic. In general, the authors should spell out the conditions followed by an abbreviation when first appearing and afterwards the authors should use the abbreviation consistently. Specific comments: Introduction: -I suggest moving "Currently HCV vaccine is not available." Line 2 page 4 to line 15 page 3 after "...currently infected with HCV(6)." because this would be a more logic place to highlight that there's no immunological methods to prevent the high number of infected individuals. -The aim of the review should be stated in the Introduction. Glucose uptake & insulin resistance: -The paragraph is highly relevant, but could be significantly improved: The authors should focus on T2DM only and not T1DM, which is completely irrelevant to this review. The content of the paragraph should be presented more straightforward and redundancies should be removed. - "In type II diabetes mellitus (T2DM), sufficient insulin is produced": This is simply, by definition, incorrect. -Last sentence page 4: Why is only one of the major complications to T2DM mentioned? -Be consistent: Signaling or signalling? -The liver plays a major role in T2DM (the 2nd most important tissue following skeletal muscle) and this should be acknowledged and mentioned in this paragraph (including references). Otherwise, it is not clear to the reader why this review is so important. Chronic HCV infection and insulin resistance: -I suggest changing the headline to "Chronic HCV infection & insulin resistance" to continue the use of "&" from the previous paragraph. Modulation of insulin receptor substrate by HCV: -"...phosphorylation, marking its for degradation via...": I doesn't make sense to me. Impaired



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lipid and glucose metabolism by HCV: -“...and more blood sugar...”: Please rephrase to “...increased plasma glucose...” -“...leading to insulin resistance (Fig. 1).” Please add “is presented in” before (Fig. 1). Therapeutic approaches and future goals: -To my opinion this paragraph is not ambitious enough when it comes to the treatment of impaired insulin resistance and overt T2DM. E.g. what is the specific treatment goal with regards to glucose homeostasis? How do we evaluate patients with HCV and impaired glucose tolerance? What upper limit for HbA1c is acceptable? When lifestyle interventions fail when is pharmaceutical means needed and what drugs are first and second choice? When it comes to T2DM in HCV infection, is the diabetes treated as usual or is there documentation for using other first line drugs?