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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

ESPS manuscript NO: 28058

Title: Linagliptin alleviates fatty liver disease in diabetic db/db mice

Reviewer's code: 00506298

Reviewer's country: Spain

Science editor: Fang-Fang Ji

Date sent for review: 2016-06-28 19:19

Date reviewed: 2016-07-11 18:46

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

The investigation by Michurina et al aimed to study the effects of Linagliptin on the structural signs of non-alcoholic fatty liver disease in db/db mice. This is an interesting work from a basic science point of view, that may have clinical practice consequences. I think the manuscript is suitable to be published in WJD.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

ESPS manuscript NO: 28058

Title: Linagliptin alleviates fatty liver disease in diabetic db/db mice

Reviewer's code: 02446208

Reviewer's country: United States

Science editor: Fang-Fang Ji

Date sent for review: 2016-06-28 19:19

Date reviewed: 2016-07-18 22:04

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
		BPG Search:	<input checked="" type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This manuscript describes a study using the DPP4 inhibitor Linagliptin to treat db/db diabetic and obese mice and identifying its effects on the structural signs of non-alcoholic fatty liver disease (NAFLD) in the mouse model. Authors found that linagliptin alleviates liver steatosis and ultrastructural changes in hepatocytes in db/db diabetic mice without commitment blood glucose-lowering in the mice. This is an interesting and current topic. This study is likely to contribute to the better understanding of Linagliptin and its use in the treatment of non-alcoholic fatty liver disease, which is a serious health problem for many obese T2D patients. In general, the study was well designed, well performed, and well analyzed and summarized. But it is not ideally presented and discussed. In addition, the study was primarily on the characterization of structural / morphological changes without addressing mechanism of action of the drug. Authors should address this reviewer's major and minor concerns and revised manuscript accordingly before it can be considered for acceptance and publication in this journal. Major concerns 1. Linagliptin is known to reduce blood glucose levels in T2D patients? Why this study does not show the hypoglycemic effect of the drug? If it does not, would it call for concern on the animal model used? What is the



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explanation for this discrepancy? If blood glucose is not reduced by linagliptin, A1c should have been measured instead. 2. Page 11, line 15, "linagliptin potently affects the enhanced expression of LYVE-1 in the endothelial cells". Would it be more correct to say "linagliptin potently enhanced expression of LYVE-1 in the endothelial cells". The enhanced expression of LYVE-1 is a result of linagliptin, right? 3. Figures 7 and 8. The figures are not drawn in the standard format. The X- and Y-axes should have labels on the graphs, not just in the figure legends. 4. For Table 1, it looks that the major reason that the two treated groups do not show any statistical differences was that there were some mice in the placebo group never got very obese during the treatment period (they had near-normal weight). It might be better to exclude these mice, which may be considered as outliers, in the study using some criteria. Standard deviations of the data should be included. If these can be done, some new conclusions may be drawn. Based on the data shown, linagliptin-treated mice always have narrower ranges on all the parameters. 5. The statement of "The improvement in the structural parameters of the liver in linagliptin-treated mice was not related to changes in the plasma glucose levels." may be somewhat questionable. It may be more correct to say "The improvement in the structural parameters of the liver in linagliptin-treated mice was not correlated to changes in the plasma glucose levels." Or "The improvement in the structural parameters of the liver in linagliptin-treated mice was not accompanied with changes in the plasma glucose levels." Or "The improvement in the structural parameters of the liver in linagliptin-treated mice was independent to changes in the plasma glucose levels. Minors Figure 1. These two pictures were made using the same staining method. Then why they have such different colors? Figures 1-6. It would be much better if these sub-cellular pictures show rulers so that readers of the manuscript know the dimensions of the cellular structures without having to do calculations by themselves.



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes

ESPS manuscript NO: 28058

Title: Linagliptin alleviates fatty liver disease in diabetic db/db mice

Reviewer's code: 02446593

Reviewer's country: United States

Science editor: Fang-Fang Ji

Date sent for review: 2016-06-28 19:19

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	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"/> The same title	<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"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		[Y] No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

Minchurina et al report the results of a controlled trial of the use of DPP-IV inhibitor linagliptin in db/db mice and its effect on liver histology and metabolic parameters. The study appears to have been conducted very professionally and the results are presented appropriately. The introduction and discussion are relevant and the conclusions drawn are in line with the evidence presented. Overall, this is a very well written paper that is appropriate for publication and should be of interest to your readers.