



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 37890

Title: NASH severity is defined by a failure in compensatory antioxidant capacity in the setting of mitochondrial dysfunction

Reviewer’s code: 01047326

Reviewer’s country: Spain

Science editor: Ya-Juan Ma

Date sent for review: 2018-01-17

Date reviewed: 2018-01-29

Review time: 12 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	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"/> 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 type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

1.- If nonalcoholic steatohepatitis (NASH) is a disorder included within the Non-alcoholic fatty liver disease (NAFLD) the following sentence is not clear: " Hepatic mitochondrial function and oxidative stress in metabolically-relevant, pre-clinical models of NAFLD vs. NASH have not been fully assessed." maybe the authors would be write "two preclinical models of NAFLD, simple steatosis vs NASH" or "less severe vs more severe preclinical models of NAFLD" 2.- Why is the NASH core between Ob / ob and FAZto different? 3.- Brand and Nichols (ref 22) do not describe leak control ratio (LCR) LCR . It is Koliaki C et al in Cell Metabolism 21, 5: 739-746 4.-Brand and Nicholls describe Sate3 adp plus 1 μM oligomycin as state 4o not state 3o 5.-Non fasting levels of glucose and insulin really is not the best indicative for the diabete indicator. In fact SD of Terminal non-fasting plasma insulin levels is too higher 6.- he author do



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not show the mouse serum levels of the leptin. 7.- Figure 4D selected by the authors does not reflect the differences shown in the graph "mitochondrial number by cytoplasmic area". What methodology/software have you used to quantify Mitochondrial length and number per total cytoplasmic area? 8.- "Maximal mitochondrial respiratory capacity was significantly increased in ob/ob LFD compared to lean hepatocytes (+45%, $p < 0.05$; Figure 3B)" is not Figure 3B 9.- Why do not the authors perform the electron microscopy studies in mouse FAZTO? GPx enzyme is responsible for the detoxification of H_2O_2 (when it is present in low concentration but the authors are not considered the GPX.



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 37890

Title: NASH severity is defined by a failure in compensatory antioxidant capacity in the setting of mitochondrial dysfunction

Reviewer's code: 02547503

Reviewer's country: Italy

Science editor: Ya-Juan Ma

Date sent for review: 2018-01-17

Date reviewed: 2018-02-03

Review time: 17 Days

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 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"/> 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"/> No	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		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

1) Authors must increase the number of mice in experimental groups since 5 or 6 mice are not sufficient for a correct statistical analysis; 2) Authors should provide new and better images of type I collagen IHC: in the session of result they state that "hepatic fibrosis assessed by quantification of type 1 collagen stained area was significantly greater in ob/ob LFD vs. lean livers..." page 12, but the relative figure, panel E do not allow the reader to appreciate this difference. The staining of collagen type 1 is the same for ob/ob LFD and lean mice; 3) In figure 4D both immunofluorescence that graph do not show a significant difference between the number of mitochondria, also in relation with the panel C in which they showed the mitochondria area. Which method has been used to quantify mitochondrial length and the number for total cytoplasmic area? The same observation for FATZO mice (figure 9). 4) Since mitochondria are related to oxidative



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stress, it could be interesting to analyze the role and the quantification of glutathione peroxidase and its activity.



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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 37890

Title: NASH severity is defined by a failure in compensatory antioxidant capacity in the setting of mitochondrial dysfunction

Reviewer's code: 02541391

Reviewer's country: Romania

Science editor: Ya-Juan Ma

Date sent for review: 2018-01-28

Date reviewed: 2018-02-04

Review time: 7 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	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"/> The same title	<input type="checkbox"/> High priority for publication
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		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

I have read with great interest the study by Boland et al. and consider it to be a significant contribution to the field of NAFLD study. I have no significant comments regarding the manuscript, different from the other reviewers, and consider it fit for publication once they resolve the issues already raised. I'd like to commend the authors for their diligence and expect further developments of their work.