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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 3847
Title: The Splanchnic-Aortic Inflammatory Axis in Experimental Portal Hypertension
Reviewer code: 00006683
Science editor: Wang, Jin-Lei
Date sent for review: 2013-05-31 15:45
Date reviewed: 2013-06-18 00:08

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[Y] Accept
[Y] Grade B (Very good)	[Y] 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

The paper by Aller, et al. is an interesting review on the systemic and hepatic inflammatory effects of experimental portal hypertension. There some issues that should be addressed: 1) What is the reason for using the triple stenosis for PVL? Why the authors postulate it is better than the normal PVL? What evidences do they have? Have they compared both models in terms of hemodynamic parameters, liver function, etc? 2) What is the exact reason for studying animals with long-term PVL at 22 months??? Why not at 12, 20 or 30? Please provide a sound reason. 3) Do the authors know of any evidences that relate portal hypertension without cirrhosis (portal thrombosis for example) to increased cardiovascular risk in humans? Please explain and provide information 4) The paper needs a critical review by an English expert. Examples of errors might be: 1) abstract: line 12: produced in; 2) line 14: model to study; 3) pag 7, 2nd para, line 3 and 6: there is; 4) pag 8, 2nd para, line 6: including toxins; 5) 3rd para, line 5: can affect; 5) pag 11, 3rd para, line 5: could regulate.

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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
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Title: The Splanchnic-Aortic Inflammatory Axis in Experimental Portal Hypertension
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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
[ ] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[ ] Minor revision
		[ ] No records	[Y] Major revision

COMMENTS TO AUTHORS

In the present review, Authors provide a comprehensive interpretation of the phenomena which, in the experimental model of portal vein ligated-rat, link pre-hepatic portal hypertension to metabolic disturbances, splanchnic and systemic inflammation, and inflammatory aortopathy. Some mechanisms highlighted in this model, i.e., alteration of the gut microbiome, intestinal wall inflammation and permeability, could be partially translated to any kind of portal hypertension, including that observed in liver cirrhosis, and can add in the understanding of this field. Some other mechanisms, i.e., systemic and vascular inflammation as final consequences of portal hypertension leading to increased vascular disease, are difficult to be extrapolated to the human setting, where portal hypertension has not been associated with any increase of cardiovascular events, and should be at the moment considered model-specific. Major comments 1) In Figure 1, it is clear that dysbiosis and bacterial overgrowth are the first results of portal hypertension, leading to intestinal inflammation, liver steatosis and the other secondary consequences. However, in the text (Paragraph: "Inflammatory response related to portal hypertension"), it seems that intestinal inflammation occurs per se, as a first step, and that it is "splanchnic inflammation" -to- "alter the gut microbiota composition". Could the author clarify this point in the text? What Authors suggest to be the sequence of events? 2) It could be very interesting trying to connect the mechanisms observed in this animal model to what is observed portal hypertension in humans, and comment on these points: 1) Could some of these mechanisms contribute to the liver damage which, after a certain threshold (of portal hypertension?), seems to progress in the cirrhotic patient independently from the removal of the offending agent (alcohol, virus, etc)? 2) Why human portal hypertension, cirrhotic or noncirrhotic, has not been consistently associated with increased vascular disease? Minor comments All the

paper should be edited with particular attention. Concerning only the abstract, for example: 6th line: "…the existence of a (rather than an) portal hypertensive…"; 11th line: "that is produced (rather than produce)…"; 13th line: "…model for (rather than for to) study…". The entire paper is full of this kind of mistakes.