

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Hepatology

**Manuscript NO:** 57567

**Title:** Inhibition of VAP-1 modifies hepatic steatosis in vitro and in vivo

**Reviewer's code:** 03011764

**Position:** Editorial Board

**Academic degree:** MD

**Professional title:** Assistant Professor

**Reviewer's Country/Territory:** Italy

**Author's Country/Territory:** United Kingdom

**Manuscript submission date:** 2020-06-15

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2020-06-16 05:35

**Reviewer performed review:** 2020-06-16 06:13

**Review time:** 1 Hour

<b>Scientific quality</b>	<input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input checked="" type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

#### **SPECIFIC COMMENTS TO AUTHORS**

Very interesting work. Experimental part conducted with attention to each step, animal management, tissue processing and analysis of the results. The work has a significant translational impact so I find it absolutely suitable for publication.

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Hepatology

**Manuscript NO:** 57567

**Title:** Inhibition of VAP-1 modifies hepatic steatosis in vitro and in vivo

**Reviewer's code:** 00198170

**Position:** Peer Reviewer

**Academic degree:** PhD

**Professional title:** Associate Professor

**Reviewer's Country/Territory:** Singapore

**Author's Country/Territory:** United Kingdom

**Manuscript submission date:** 2020-06-15

**Reviewer chosen by:** AI Technique

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**Review time:** 2 Days and 5 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## **SPECIFIC COMMENTS TO AUTHORS**

The findings that VAP-1 deficiency reduced lipid accumulation in the hepatocytes is interesting. The authors also showed corresponding expression changes in lipid transporter and key metabolic response gene expression. However, the underlying mechanism remains unknown. Major 1) Figure 1A. Better quality figures at lower magnification are necessary to reveal more features, so that they can be clearly evaluated. Nuclear staining in H&E is not clear. The staining for Picrosirius Red is not correct, cytoplasm should be stained yellow and collagen red. The collagen staining in NASH sample is not convincing. Please include scale bar. 2) Figure 4 and Supplemental Figure 4. Except for a few genes, the fold change in most genes appeared to be rather marginal. Please provide the fold change either in a separate table or in the figure. Statistical analysis should be provided. As hepatic steatosis is primarily excessive lipid accumulation in hepatocytes, it will be important to measure triglycerides level in the tissues instead of triglyceride secretion (Figure 3A). It will also be important to know if there is a reduction in fatty acid beta-oxidation which is related to PPARA expression (Figure 3A and B). "Bromoethylamine (VAP-1 inhibitor) reduced accumulation to control levels, whilst inhibitors of other amine oxidases (MAOA and MAOB and LOX) did not reduce the uptake seen in the presence of VAP-1 plus substrate." This is not consistent with the data shown. e.g LOX inhibitor, less MOA A/B inhibitors, similarly reduced lipid accumulation. Please explain this outcome. A statistical analysis should be done comparing values with VAP-1 and LOX inhibitors, and with VAP-1 and MOA A/B inhibitors. Figure 3C. As VAP-1 has been implicated to play a role in immune cell trafficking, which can affect lipid accumulation. It will be important to show H&E stain of the WT and KO livers, and changes in lipid transporter and key metabolic response gene expression, before HFD and after 12 weeks of diet. What is the protein expression of VAP-1 in WT liver before and after 12 weeks of HFD? Please include scale bar for the



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figures. The mechanism is unknown. The changes in lipid transporter and key metabolic response gene expression, is at best, associated/correlated with the pathology. They do not reveal the mechanism. In the first instance, it is unclear if VAP-1 is involved in their expression. It will be important to extend the finding from Figure 4 to include treatment with VAP-1 inhibitor. How does VAP-1 alter the expression of these genes? Please discuss about the limitations of this study. Minor Figure 2A. Please include scale bar. Page 11, tryglyceride should be triglycerides