

## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Gastroenterology*

**Manuscript NO:** 80399

**Title:** Impact of endothelial nitric oxide synthase activation on accelerated liver regeneration in a rat ALPPS model

**Provenance and peer review:** Unsolicited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 05152215

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

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

**Author's Country/Territory:** Japan

**Manuscript submission date:** 2022-11-04

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2022-11-05 10:50

**Reviewer performed review:** 2022-11-08 14:32

**Review time:** 3 Days and 3 Hours

Scientific quality	<input checked="" type="radio"/> Grade A: Excellent <input type="radio"/> Grade B: Very good <input type="radio"/> Grade C: Good <input type="radio"/> Grade D: Fair <input type="radio"/> Grade E: Do not publish
Language quality	<input checked="" type="radio"/> Grade A: Priority publishing <input type="radio"/> Grade B: Minor language polishing <input type="radio"/> Grade C: A great deal of language polishing <input type="radio"/> Grade D: Rejection
Conclusion	<input checked="" type="radio"/> Accept (High priority) <input type="radio"/> Accept (General priority) <input type="radio"/> Minor revision <input type="radio"/> Major revision <input type="radio"/> Rejection
Re-review	<input checked="" type="radio"/> Yes <input type="radio"/> 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 manuscript entitled "Impact of Endothelial Nitric Oxide Synthase Activation on Accelerated Liver Regeneration in a Rat ALPPS Model" by Dr. Hitoshi Masuo, et al. uses an interesting APPLS model to explore the mechanism of liver regeneration. Although the effect of endothelial nitric oxide synthase on liver hyperplasia was previously discussed in papers, but the authors focused on "Associating Liver Partition and Portal vein Ligation for staged hepatectomy (ALPPS)", which has certain academic value. In addition, the author's conclusion, that is "Early introduction of inflammatory cyclines might not be positive for accelerated FLR regeneration after ALPPS, where as Akt eNOS path activation may contribute to accelerated regeneration of the FLR", is somewhat innovative.

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**Peer-review model:** Single blind

**Reviewer's code:** 05378552

**Position:** Peer Reviewer

**Academic degree:** MD, MSc

**Professional title:** Doctor

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

**Author's Country/Territory:** Japan

**Manuscript submission date:** 2022-11-04

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2022-11-17 13:44

**Reviewer performed review:** 2022-11-17 14:59

**Review time:** 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" 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
Language quality	<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
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<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

First of all, this is a very interesting study, starting from clinical problems and using animal models as research objects, to profoundly explain the factors related to liver regeneration of ALPPS and PVE. The research idea of the manuscript is clear, the result is reliable and the conclusion is appropriate. However, I have some questions which need to be answered by the author. The details are as follows: 1. In the Surgical Procedures and Study Design section, the authors divided the rats into two groups. Should a control group be set up? The control group only received open and closed abdomen. Is it necessary? 2. The process of liver regeneration is a complex process, never a single factor or a single pathway plays a key role. So the discussion section and the conclusion don't have to be too absolute. In a word, this manuscript is novel, full of content and correct in research methods, and can be published after revision.

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**Peer-review model:** Single blind

**Reviewer's code:** 06417922

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

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

**Author's Country/Territory:** Japan

**Manuscript submission date:** 2022-11-04

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2022-11-14 01:23

**Reviewer performed review:** 2022-11-24 09:25

**Review time:** 10 Days and 8 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" 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
Language quality	<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
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

<b>Peer-reviewer statements</b>	Peer-Review: [ <input type="checkbox"/> ] Anonymous [ <input checked="" type="checkbox"/> ] Onymous
	Conflicts-of-Interest: [ <input type="checkbox"/> ] Yes [ <input checked="" type="checkbox"/> ] No

### **SPECIFIC COMMENTS TO AUTHORS**

As we all know, ALPPS is an effective method to grow the future liver remnant before performing extended hepatectomy. However, its mechanism remains unclear. Hitoshi et al. presented an interesting manuscript on the mechanism of promoting liver regeneration by ALPPS. The results indicate that activation of the Akt-eNOS signaling pathway may contribute to accelerated regeneration of the FLR after ALPPS. The authors make a good description of the mechanism. It is a useful and interesting work for hepatobiliary surgeons.

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**Peer-review model:** Single blind

**Reviewer's code:** 03294368

**Position:** Editorial Board

**Academic degree:** DSc, MD, PhD

**Professional title:** Dean, Professor

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

**Author's Country/Territory:** Japan

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**Reviewer chosen by:** AI Technique

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**Review time:** 9 Days and 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" 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
Language quality	<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
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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<b>Peer-reviewer statements</b>	Peer-Review: [ <input type="checkbox"/> ] Anonymous [ <input checked="" type="checkbox"/> ] Onymous
	Conflicts-of-Interest: [ <input type="checkbox"/> ] Yes [ <input checked="" type="checkbox"/> ] No

### **SPECIFIC COMMENTS TO AUTHORS**

The subject of the paper is actual and exists in the focus of liver surgeons. The title reflects the main subject/hypothesis of the manuscript. Abstract is well written and reflects well the work described in the manuscript. The background is provided clearly and is based on the data of modern literature. The used methods are well selected and the animals number is adequate to the aim and objective of the study. The main result showing that in case of portal vein branch occlusion, if it will be supplemented by the activator of Akt-eNOS pathway, might give the same results similar to ALPPS, have to be considered as important and interesting. The figures, illustrations and tables are clear and well designed. Statistical analysis is done correctly. The paper is written with correct English and organized in accordance with journal requirements.