

## ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 24455

**Title:** Steatotic livers are more susceptible to normothermic ischemia-reperfusion injury due to impaired mitochondrial Complex-I function

**Reviewer's code:** 00053727

**Reviewer's country:** India

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2016-01-25 09:55

**Date reviewed:** 2016-02-01 14:43

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

## COMMENTS TO AUTHORS

The authors evaluated the mitochondrial function analysis on steatotic livers and tried to find the effect of protective role IPC on steatotic livers .The Paper is interesting and continuing the work by the same groups 'Mitochondrial dysfunction in steatotic rat livers occurs because a defect in complex i makes the liver susceptible to prolonged cold ischemia' published in Liver Transplantation in 2015. The following additional work needs to be done to confirm the effect. 1. NAS score among various groups needs to be quantified 2. The authors needs to measure (MDA) level, total superoxide dismutase (SOD) activity, and nitricoxide synthase (NOS) in tissue. 3. In addition the level of NO, NOS in serum and in liver tissues needs to be evaluated. 4. Immunohistochemistry/q Rt PCR for TNF alpha and nuclear factor kappa B (NFkB) needs to be done . Minor changes: It has been mentioned the rats were enrolled at 3 weeks old .Please clarify whether the animals are weaned are kept with mother. In abstract it has been mentioned 3 gps and in materials and methods it has been 6 Gps .Please clarify.

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**Title:** Steatotic livers are more susceptible to normothermic ischemia-reperfusion injury due to impaired mitochondrial Complex-I function

**Reviewer's code:** 00004425

**Reviewer's country:** United States

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2016-01-25 09:55

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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 checked="" 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
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<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

It is well known that hepatic steatosis increased susceptibility to ischemia-reperfusion (I/R) injury and this effect is linked to mitochondrial dysfunction. This study explored alterations of mitochondrial Complexes I and II in lean and high-fat, high sucrose diet-induced steatotic rat livers after 1 h-warm ischemia plus 4 h reperfusion. The authors showed that there was a significant decrease in Complex I in steatotic livers compared to lean livers but there was no difference in Complex II between these two groups. Ischemic preconditioning (IPC) decreased ALT release and histological changes after I/R but did not blunt decreases in Complex I in steatotic livers. This study obtained some interesting data; however, there are a few issues to be addressed. 1. Please describe the fat and carbohydrate contents in the control diet. What is the fat in high fat diet (saturated or unsaturated fat, etc.)? 2. The histology of necrosis (Fig. 2) is not very convincing. Moreover, Fig. 2D has much less fat than B and F. 3. This study measured respiration using liver homogenates but not isolated mitochondria. Some of the oxygen consumption may be not completely related to mitochondrial respiration but linked to other pathways (e.g. proxisomal oxidation of fatty acids).



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What percentage of the respiration is cyanide inhibitable? 4. How IPC decreased I/R injury in steatotic livers? Did IPC decrease reactive oxygen species formation in this study?