

## ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 26383

**Title:** Mitochondrial DNA from hepatocytes as a ligand for TLR9: Drivers of NASH?

**Reviewer's code:** 03357364

**Reviewer's country:** United States

**Science editor:** Yuan Qi

**Date sent for review:** 2016-04-07 10:10

**Date reviewed:** 2016-04-15 22:25

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 checked="" 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 type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	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

In this Editorial, the authors gave a brief background of nonalcoholic steatohepatitis (NASH) and summarized a recent JCI paper. It is recommended to publish with minor language polishing. Also, I feel too much emphases on describing the results, most of which could be found in the original paper. I suggest expending the discussion and providing more insights in the future research and clinical directions.

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

**ESPS manuscript NO:** 26383

**Title:** Mitochondrial DNA from hepatocytes as a ligand for TLR9: Drivers of NASH?

**Reviewer's code:** 03269739

**Reviewer's country:** China

**Science editor:** Yuan Qi

**Date sent for review:** 2016-04-07 10:10

**Date reviewed:** 2016-04-18 14:33

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 checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input checked="" type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	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

In this Editorial, the authors summarized a recent JCI paper about hepatocyte mitochondrial DNA serves as DAMP activating a hepatic PRR, TLR9, in mice and in the plasma of NASH patients leading to NASH. The description of the paper was clear, but the opinion of the authors was few. It's better to provide more insights about the trend of NASH or what's need to do in future work.

## ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 26383

**Title:** Mitochondrial DNA from hepatocytes as a ligand for TLR9: Drivers of NASH?

**Reviewer's code:** 02811953

**Reviewer's country:** United States

**Science editor:** Yuan Qi

**Date sent for review:** 2016-04-07 10:10

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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
<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 manuscript (ESPS NO: 26383) entitled "Mitochondrial DNA from hepatocytes as a ligand for TLR9: Drivers of NASH?" is an editorial by Priya Handa et al. The authors of this manuscript try to indicate that hepatocyte mitochondrial DNA activates hepatic PRR, TLR9 and acts as an inducer for NASH. They suggest that blocking TLR9 may be a potential therapy for NASH. Major comments 1. Some editing is needed. For example, in lines 14-15 on page 4, "...which contribute to the increased serum free fatty acids in the liver" probably means "...increase uptake or entry...". It should be revised. 2. The description of fatty acids sources in hepatocytes is not complete. The fatty acids in hepatocytes can be from de novo lipogenesis, adipocytes and lipoproteins. Please include this in the revision. 3. The manuscript talked about mtDNA and its effects on TLR9. Please try to elaborate more about how mtDNA is shipped out of the cells and is taken into the cells. 4. In the figure, it seems that authors only indicated that IRS954 works in Kupffer cells, but not hepatocytes and stellate cells. Please elaborate the reason. Minor comments 1. In line 8 on page 6, should be "TNF $\alpha$  mRNA".