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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 5324
Title: Role of endoplasmic reticulum stress in the pathogenesis of nonalcoholic fatty liver disease
Reviewer code: 00224478
Science editor: Ma, Ya-Juan
Date sent for review: 2013-08-30 13:34
Date reviewed: 2013-09-06 23:52

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[Y] Grade C (Good)	[Y] Grade C: a great deal of language polishing	[ ] No records	
[ ] Grade D (Fair)		BPG Search:	[ ]Rejection
[ ] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[Y] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS

This review could be published before the following questions should be resolved: 1) A signaling diagram should be provided; 2) The English language should be polished. For example, some changes are set below: Tile: Roles of endoplasmic reticulum stress in the pathogenesis of nonalcoholic fatty liver disease Abstract Nonalcoholic fatty liver disease (NAFLD) has emerged as a common public health problem in the past decades. The underlying mechanisms leading to the development of NAFLD are not fully understood. Recently, the endoplasmic reticulum (ER) stress response has been proposed to play a crucial role in the development of steatosis and progression to nonalcoholic steatohepatitis (NASH). The accumulation of unfolded or malfolded proteins within the ER can enable activation of the stress response signaling to restore the equilibrium of protein synthesis into the physiological homeostatic states. Conversely, delayed or insufficient responses to ER stress is likely to result in pathogenesis of NAFLD, including fatty acid accumulation, insulin resistance, inflammation and apoptosis. Therefore, understanding the role(s) of ER stress in the pathology of NAFLD has become a topic of intense investigation. This mini-review highlights the recent findings on the ER stress signal pathways involved in the pathogenesis of NAFLD. Core tip: NAFLD is a progressive disorder leading to the liver dysfunction and ultimate failure. The pathological keystones of NAFLD include steatosis, systemic inflammation and cell death, along with chronic ER stress-induced signaling pathways being involved in. This review highlights the recent findings of the ER stress response pathways in the pathogenesis of NAFLD; this may be identified as a novel therapeutic target for the prevention and treatment of NAFLD. Therefore, the text should be modified using the standard English language.

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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 5324
Title: Role of endoplasmic reticulum stress in the pathogenesis of nonalcoholic fatty liver disease
Reviewer code: 00051402
Science editor: Ma, Ya-Juan
Date sent for review: 2013-08-30 13:34
Date reviewed: 2013-09-10 18:40

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[Y] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[Y] Accept
[ ] 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 manuscript by XQ Zhang et al., titled Role of endoplasmic reticulum stress in the pathogenesis of nonalcoholic fatty liver disease was reviewed. Comments: 1. Well written, there are only a few grammatical / spelling errors which can be easily remedied. 2. Consider the addition of figures / flow charts to complement the text; the text gets a bit overwhelming to follow due to the nature of the complexities of the information being presented. 3. Consider a table for easy reference of the myriad of abbreviations used in the manuscript. 4. Settle on one convention of presenting abbreviations in the body of the manuscript. Sometimes the name is used and the abbreviation follows in parentheses; other times the abbreviation is used first and the full name in parentheses.

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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 5324
Title: Role of endoplasmic reticulum stress in the pathogenesis of nonalcoholic fatty liver disease
Reviewer code: 00225256
Science editor: Ma, Ya-Juan
Date sent for review: 2013-08-30 13:34
Date reviewed: 2013-09-13 18:25

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[Y] Grade C (Good)	[Y] Grade C: a great deal of language polishing	[ ] No records	
[ ] Grade D (Fair)		BPG Search:	[ ]Rejection
[ ] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[Y] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS

? It will be more helpful if an illustration/diagrammatic representation of UPR linking to lipid metabolism, IR, inflammation and apoptosis will be represented. It will be more clear and easy to understand. ? More focus of the reader should be drawn to the recent advances in the field of ER Stress/UPR related to NAFLD. ? Conclusion seems like too general in scope; conclusion based on recent advances in the field as well as information regarding new potential therapeutic options (if any) should be focused along with generally drawn conclusion. ? Minor formatting errors should be addressed as well especially addressing the full names of protein molecules.

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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 5324
Title: Role of endoplasmic reticulum stress in the pathogenesis of nonalcoholic fatty liver disease
Reviewer code: 00024434
Science editor: Ma, Ya-Juan
Date sent for review: 2013-08-30 13:34
Date reviewed: 2013-10-14 16:42

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
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[Y]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[ ] Minor revision
[Y] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

This review article is worse than the 2 review articles published in 2011 and 2012. (Endoplasmic reticulum stress in nonalcoholic fatty liver disease. Annu Rev Nutr. 2012 Aug 21;32:17-33; Endoplasmic reticulum stress and the unfolded protein response innonalcoholic fatty liver disease.Antioxid Redox Signal. 2011 Jul 15;15(2):505-21.) They are similar in many aspects and this article does not seem to provide new findings. (Of course, this is because all of them are review articles) # It is not easy for readers to get a whole view of "role of endoplasmic reticulum stress in the pathogenesis of NAFLD" from this paper. As mentioned by the authors, NAFLD encompasses a spectrum of liver damage ranging from steatosis to nonalcoholic steatohepatitis (NASH), which can progress to fibrosis and cirrhosis. It is better to describe the role of endoplasmic reticulum stress in each stage of NAFLD separately. In addition, figures to illustrate the four possible mechanisms (lipid metabolism, IR, inflammation and apoptosis) are recommended for the readers to understand these complex mechanisms more quickly

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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 5324
Title: Role of endoplasmic reticulum stress in the pathogenesis of nonalcoholic fatty liver disease
Reviewer code: 00227507
Science editor: Ma, Ya-Juan
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[Y] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[Y] Accept
[ ] Grade B (Very good)	[ ] 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
This is a concise and object review of mechanistic studies for understanding NAFLD and NASH. It is a timely review on the rise of fatty liver disease around the world. The review is well written. There is only a minor point to be clarified about the two-hit hypothesis in the Introduction section: "Although the "two-hit" hypothesis has become a widely accepted framework to guide current studies in this area, the pathogenesis of NAFLD remains largely unknown". What is the two-hit hypothesis? Please define this term here.

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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 5324
Title: Role of endoplasmic reticulum stress in the pathogenesis of nonalcoholic fatty liver disease
Reviewer code: 00009225
Science editor: Ma, Ya-Juan
Date sent for review: 2013-08-30 13:34
Date reviewed: 2013-11-07 18:11

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] 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	[Y] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS
This review highlights the recent findings linking the ER stress signal pathways and the pathogenesis of NAFLD. the review help to identify novel therapeutic targets for the prevention and treatment of NAFLD please elaborate on the role of glucophage OR metformine and autophagy and patients with NAFLD

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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
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Reviewer code: 00184525
Science editor: Ma, Ya-Juan
Date sent for review: 2013-08-30 13:34
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[Y] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[Y] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

This is a concise review on the role of ER stress in NAFLD pathogenesis. The authors should pay attention to the following: 1. The "two-hit hypothesis" is no longer central for NAFLD pathogenesis as "one-hit" and "multiple-hit" hypotheses seem more plausible. The text should be revised accordingly. 2. The notions that "first step in the progression of NAfLD is steatosis" is not correct. Steatosis is the first step in the development of NAFLD. NASH is the progressive form of NAFLD and in addition to steatosis, inflammation, and hepatocyte injury in the form of ballooning are the minimal diagnostic criteria. 3. Intracytoplasmic fat in NAFLD could be mixed as both macro- and microvesicular steatosis may be seen on histology 4. NASH is characterised by steatosis, inflammation and hepatocellular injury, as mentioned in comment 2. Fibrosis is not needed for NASH diagnosis 5. In the Conclusion the notion that all NAFLD are progressive is not correct. NASH is the progressive form of NAFLD. 6. Figure 2 should be placed in the main text (ER stress and NAFLD chapter) not in the conclusion.