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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Pathophysiology

ESPS manuscript NO: 21139

Title: Alcoholic pancreatitis: New insights into the pathogenesis and treatment

Reviewer's code: 03081313

Reviewer's country: Spain

Science editor: Fang-Fang Ji

Date sent for review: 2015-07-02 22:11

Date reviewed: 2015-07-16 17:46

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 type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
		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

This is a very comprehensive review about new insights related to alcoholic pancreatitis. A figure/table could improve the understanding of such a dense text; other minor details (indicated in the attached pdf) need to be revised.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Pathophysiology

ESPS manuscript NO: 21139

Title: Alcoholic pancreatitis: New insights into the pathogenesis and treatment

Reviewer's code: 00947129

Reviewer's country: Hungary

Science editor: Fang-Fang Ji

Date sent for review: 2015-07-02 22:11

Date reviewed: 2015-07-12 01:38

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input 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 checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input checked="" type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
		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

Clemens et al. review the pathogenesis and possible therapeutic targets in alcoholic pancreatitis. Unfortunately, this paper is very similar to that already published in World Journal of Gastrointestinal Pathophysiology (2014; 5:147-57) by the same group. In fact, some paragraphs are identical which is completely inappropriate. Other major points: 1. The abstract should be more specific and should at least list the covered topics. 2. The titles of some of the sections are odd, e.g. on page 2 nothing is written about alcoholic pancreatitis, most of the section on the "Effects of Ethanol on the Inappropriate Activation of Pancreatic Enzymes" is about description of calcium signaling. 3. References are completely missing from some paragraphs (e.g. on page 2, paragraph 1; page 5, paragraphs 4 and 5; page 9, paragraphs 3 and 4). 4. Page 2, paragraph 1: pancreatic ductal cells not only form a framework for the pancreas, but also secrete bicarbonate. Page 2, paragraph 3: The mortality rate of severe acute pancreatitis can be much higher than 10% (see Pandolfi et al., Gastroenterology 2007). 5. The roles of pancreatic acinar and stellate cells are discussed in the pathogenesis of alcoholic pancreatitis, but the possible role of ductal cells is completely ignored (see Maleth J et al., Gastroenterology 2015). 6. There is a lot of redundancy in the paper. The roles of



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NF- κ B and AP-1 in mediating the proinflammatory response or the function of stellate cells are mentioned mentioned in numerous places. On page 5: "Intracellular calcium has a critical role in both normal and pathologic actions of acinar cells." ... "Thus, intracellular calcium is involved both in the normal and the pathologic process of acinar cells." On page 3: "The NF- κ B-mediated inflammatory response appears to be responsible for up to half of the pancreatic tissue damage that is associated with acute pancreatitis, as well as the potentially fatal severe systemic inflammatory response 10." and page 14: "In fact the NF- κ B-mediated inflammatory response is responsible for up to half of the pancreatic tissue damage that is associated with acute pancreatitis, as well as the potentially fatal severe systemic inflammatory response 10." 7. Sarcoendoplasmic reticulum Ca²⁺ ATPase pump (SERCA) is a very important regulator of intracellular Ca²⁺ signaling (which is discussed in great detail on pages 5-6), yet it is only mentioned in the mitochondrial dysfunction section. 8. On page 13: "The fact that pancreatic stellate cells express alcohol dehydrogenase may have an important role in the development of alcoholic pancreatitis." does not make sense. On page 15 what do you mean by general and alcoholic acute pancreatitis? 9. There is no need to abbreviate words that only appear once in the paper (e.g. uPA, PDI, IRE1, TGF- β). 10. The conclusions state that "It has been demonstrated that inhibiting fatty acid ethyl ester synthase attenuates experimental acute pancreatitis.", but this is not discussed in the review. 11. References are missing the PMID, some journal names are not abbreviated (according to the requested format). 12. The paper would definitely benefit from some Figures. Some typos: Page 10: up regulation (upregulation), page 10: wild type (wild-type), page 15: Lieber-DeCarli (Lieber-DeCarli).



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Pathophysiology

ESPS manuscript NO: 21139

Title: Alcoholic pancreatitis: New insights into the pathogenesis and treatment

Reviewer's code: 00053888

Reviewer's country: United Kingdom

Science editor: Fang-Fang Ji

Date sent for review: 2015-07-02 22:11

Date reviewed: 2015-07-03 22:35

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 type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
		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

I think that is an excellent review paper that brings together some important scientific mechanisms in the aetiology of alcohol induced pancreatitis. I think that the manuscript is very worthy of publication my only criticism is that it is a complex and rather 'wordy' manuscript and would benefit from breaking up a little with some tables &/or figures.



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Pathophysiology

ESPS manuscript NO: 21139

Title: Alcoholic pancreatitis: New insights into the pathogenesis and treatment

Reviewer's code: 02462595

Reviewer's country: Germany

Science editor: Fang-Fang Ji

Date sent for review: 2015-07-02 22:11

Date reviewed: 2015-07-05 18:30

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input checked="" type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input 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"/> 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 checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		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

Dear Professor Clemens, you and your colleagues present a very sound review on the current knowledge of the pathophysiology of alcoholic pancreatitis. I don't have suggestions and don't see necessity for improvement of this article. I only found one needless punctuation mark (semicolon) on page 14 (Treatment of isolated acini with ethanol or acetaldehyde decreases the activity of these two factors, whereas; treatment with FAEs increases their activity.)



ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Pathophysiology

ESPS manuscript NO: 21139

Title: Alcoholic pancreatitis: New insights into the pathogenesis and treatment

Reviewer's code: 02526196

Reviewer's country: Denmark

Science editor: Fang-Fang Ji

Date sent for review: 2015-07-02 22:11

Date reviewed: 2015-07-07 19:35

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"/> 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 type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
		BPG Search:	<input checked="" 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

GENERAL COMMENTS: The topic of alcoholic pancreatitis is very important as the alcohol abuse is one of the most common factors associated with pancreatitis. In this review, authors described the new development related to the pathogenesis and treatment in relation to alcoholic pancreatitis. The knowledge in this review is very important for the readership of World Journal of Gastrointestinal Pathophysiology. However, the manuscript is needed to improve before accepting for publication in World Journal of Gastrointestinal Pathophysiology. 1, The structure of the review could be better and it is suggested to structure the review as following: ? Abstract ? Introduction ? Outline of pancreatitis ? Alcoholic pancreatitis ? Pathogenesis of alcoholic pancreatitis Subtitle 1 Subtitle 2 ? Treatment of alcoholic pancreatitis Subtitle 1 Subtitle 2 ? Conclusions and future perspectives ? References 2, There are no any figures, tables and flowcharts in the review. If authors can use some of these in the review, that will be help the readers to easy and better understand the contents of review. **SPECIFIC COMMENTS:** Title page and title: The title accurately reflect the major topic and contents of the review. However, the title page is needed to revise according to the request of WJGP. The running title is missing, please add. Abstract: It is



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missing, please add. Introduction: It is missing, please add. Main text: It is suggested to modify the format according to my comments above. The paragraph 1 to 5 should add another subtitle "Outline of pancreatitis". The subtitle "Alcoholic pancreatitis" moves down to the beginning of paragraph 6. The authors described the pathogenesis of alcoholic pancreatitis in detail in the main text, however the treatment of alcoholic pancreatitis is only briefly introduced. More detail about the treatment is suggested to add into the review. References: The references are appropriate, relevant, and updated. However the format of the references is needed to revise according to the request of WJGP. CLASSIFICATION OF THE MANUSCRIPT grades C. LANGUAGE EVALUATION Grade B CONCLUSION: It is suggested authors to make revision according to the comments before accepting publication in WJGP.



ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Pathophysiology

ESPS manuscript NO: 21139

Title: Alcoholic pancreatitis: New insights into the pathogenesis and treatment

Reviewer’s code: 03002252

Reviewer’s country: Belgium

Science editor: Fang-Fang Ji

Date sent for review: 2015-07-02 22:11

Date reviewed: 2015-07-06 21:42

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input 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"/> 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 checked="" type="checkbox"/> Plagiarism	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		[Y] No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

In this review manuscript the authors focus on the pathogenesis of alcoholic pancreatitis. They describe the effects of ethanol on the inappropriate activation of pancreatic enzymes, mitochondrial dysfunction, endoplasmic reticulum-stress, impaired autophagy, the involvement of pancreatic stellate cells, the effects of ethanol on pancreatic repair and the role of the inflammatory response. The manuscript is generally well written and provides the reader with a good overview of the current knowledge. I only have one remark: the manuscript would gain readability by the inclusion of a couple of schematic representations.