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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 32048
Title: Notch mediated by TGF-β/Smad pathway in Concanavalin A-induced liver fibrosis rats
Reviewer's code: 02937521
Reviewer's country: Egypt
Science editor: Yuan Qi
Date sent for review: 2016-12-23 15:07
Date reviewed: 2017-01-04 19:46

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[Y] Accept
[Y] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[ ] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

Comments to the authors Dear authors I read with great interest your manuscript entitled: Notch mediated by TGF-β/Smad pathway in Concanavalin A-induced liver fibrosis rats I find the topic interesting , the manuscript is well structured, and the results and conclusion are important and may have a good impact on the liver fibrosis patients and their outcome. I find the manuscript only needs some revision and editing of the English language, and changing the title into more informative and interesting one. Regards

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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
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Title: Notch mediated by TGF-β/Smad pathway in Concanavalin A-induced liver fibrosis rats
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Reviewer's country: Hungary
Science editor: Yuan Qi
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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[Y] Grade C: Good	[Y] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[ ] Minor revision
[ ] Grade E: Poor		[Y] No	[Y] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

The authors aimed to investigate the relation between Notch and TGF-beta pathways. These two pathways have crucial roles in hepatic fibrogenesis, in the activation of hepatic stellate cells (HSC) and a fraction of macrophages activated classically. Therefore, the interaction between the two pathways is in the interest of recent hepatic fibrogenesis-related research. In the presented article, the authors investigated this issue in relation to peripheral blood mononuclear cells (PBMC) isolated from Concanavalin A-treated fibrotic rats. The respective inhibitors were investigated in a maintained cell culture of these PBMC cells. Therefore, this article provides a particular answer only that is associated with the white blood cells being present in the circulation of the hepatic fibrosis-induced rats, presuming that the PBMC fraction is characteristic and indicative of the fibrotic state, and that the PBMC fraction may have a role in hepatic fibrogenesis. A crucial issue here is the association of increased Notch and TGF-beta in PBMC with the development of hepatic fibrosis in the respective rat. Did the author monitor this association on a weekly basis and correlate this in the course of fibrogenesis? The second issue is the important role of HSC fraction in liver fibrosis.

Since it is possible to isolate HSC fraction from liver or there are HSC cell lines available, did the author perform (does the author plan to perform) similar inhibition experiment on HSCs? In addition, did the author check whether rat fibroblast or macrophage cell lines are available? The third issue regards the found inhibitory effects and the drawn conclusions. The authors observed downregulation of the same members of Notch and TGF-beta pathways irrespective of the inhibition of either Notch or TGF-beta. This does not necessarily indicate the direct interplay between the two pathways. Therefore, it would be necessary to study this process in liver and monitor other targets of the two pathways, such as alfa-SMA, COL1alfa1. In addition, overexpression studies are needed with Notch and TGF-beta pathway members and targets. Furthermore, the sentence "Our study demonstrated that Notch signaling mediated by TGF-β/Smad signaling pathway, resulting in liver fibrosis" is in my view an exaggeration. The fourth issue is associated with the presentation of the topic and the rational of the study regarding the investigation of PBMC in relation to hepatic fibrosis and the presentation of Notch and TGF-beta interplay, which are not thorough in my view. The fifth issue is the English language polishing throughout of the text. Further comments: - Role of Notch signaling in Introduction: what is pattern formation??? - Authors used only rats; however, mice also appears in the Materials and methods - DMSO was the control group but the authors did not mention that the inhibitors were dissolved in which percent of DMSO - Jagged1 is listed in Table 1, but it is missing from the text in Materials and methods - The PCR profile is not mentioned. Did the authors use the one recommended by the manufacturer? - A possible way to indicate the degree of Celsius sign by using a small o letter in superscript followed by a capital C letter - "gel electrophoresis (SDS-PAGE) gel" – the gel word after the parenthesis is not needed - Did the author use variable amount of proteins as indicated (30-100 ug)? How did the author normalize the western blot data? - I was very pleased to see densitometry charts in the article, but what program was used for this? - The ECL system provided by GE Healthcare is not for alkaline phosphatase-conjugated secondary antibodies as it is stated in the text but for HRP-conjugated antibodies. - Standard deviation is abbreviated as S.D. - The used statistical tests are missing from the Figure legends.

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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
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		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

The authors aim to explore the exact interaction between Notch and Transforming growth factor β(TGF-β) signaling in liver fibrosis. They established liver fibrotic rats model by concanavalin A (ConA) and isolated peripheral blood mononuclear cells (PBMCs) from model rats. It is meaningful, the design is reasonable, and the methods are appropriate. Several points need to be clarified. Major: 1. Since the topic is liver fibrosis, it is better that if data of the collagen fiber stain such as masson or sirius red is provided to confirm the formation of fibrosis, as well as serum ALT and AST levels which can reflect the liver function. 2. The number of each experiment of PCR, Western Blot should be displayed in the figure legends. 3. Recent research about TGF-β signaling and fibrosis, as well as the relationship between Notch1, Hes1, Hes 5, TGF-β1, Smad3, need to be more illustrated in the "Discussion" part. Minor: 1. In conclusion of "abstract", "up-regulation" should be changed into "up-regulate". 2. In the first paragraph of INTRODUCTION, the final sentence is incomplete. "However, whether similar regulator occurs in liver fibrosis, and what happened between the two signaling during the restore stage of liver fibrosis" can be changed into "However, whether similar

regulator occurs in liver fibrosis, and what happened between the two signaling during the restore stage of liver fibrosis, still need to be further clarified."