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315-321 Lockhart Road,
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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 7269
Title: Insulin-like growth factor binding protein-related protein 1 induces liver fibrosis by Smad2/3 signaling: effect on hepatic stellate cell activation and hepatocyte apoptosis
Reviewer code: 00006459
Science editor: Gou, Su-Xin
Date sent for review: 2013-11-13 09:16
Date reviewed: 2013-12-15 14:43

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	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[Y] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS
This paper on rat liver and a rat HSC cell line presents interesting data. The graphs all need to be changed to scatter plots; this is now the general standard plot to display all data as well as mean and SD. I prefer SD to SE. Many experiments are n=3 and this is a concern. In the 4th para of results, "similar results for RNA" is not appropriate; the data needs to be disclosed. The next page has a "data not shown" statement; the data needs to be disclosed. The English and writing are good except for the need for minor English edits in a few places. In the abstract please define AdshSmad3. Western blotting needs to be written with a capital W every time. Do not use the term "medicating"; you probably intend to say "stimulated" or "treated". Please provide page numbers in the ms.

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ESPS Manuscript NO: 7269
Title: Insulin-like growth factor binding protein-related protein 1 induces liver fibrosis by Smad2/3 signaling: effect on hepatic stellate cell activation and hepatocyte apoptosis
Reviewer code: 00069371
Science editor: Gou, Su-Xin
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Date reviewed: 2013-12-16 19:28

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[Y] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[Y] 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
Comments on WJG 184653 This study described the role and mechanism of IGFBPrP1 in liver fibrosis. Although, not actually the new knowledge, the studies support the current concept of liver cirrhosis. They were well-designed and up to date by covering an in vivo study. The authors conclude that IGFBPrP1 induces liver fibrosis by hepatic stellate cells activation and heptocyte apoptosis, both signaling is via Smad3 pathway. The specific comments 1. words & abreviation: please check and correct in full western or Western medicated or mediated hepatic steatosis or hepatocyteic steatosis SMA= smooth muscle action AdrP1 or AdIGFBPrP1 cAd or Cad AdshNC or shNC AdSmad or AdshSmad3, 2. Methods: cell culture model – should show hepatocyte culture as well Quantitative real-time PCR should be read by copy number- relative results in fig 1, did not show what related to ? Sirius Red stains collagen - should be mentioned in the method % positive staining cells and TUNEL assay – whether measurement is per area/ field or total number? Immunohistochem - results read by image-Pro Plus based on intensity or % positive cells - (whether measurement is per area/ field or total number?) 3. Results & Figures Detail described in texts that included numbers/digits are confusing. Please find the better way to express the numbers How the numbered are derived, different groups and times should be rewritten to made clearer interpretation eg. Fig3 Western blotting of phosphor-Smad32/3, band density should be grouping in the same figure. The decreased approximately 3 folds in the figure, at different time (48, 72 h) were not got along well with 0.6 and 1.5 folds in the text. What do you mean by the transfection efficiency? Fig 3 did not show positive cells after varied MOI transfection. The higher magnification is suggested. Although the figures showed the representative results, measurement methods must be declared.

The knock down result showed abrogated of SMA, but the figures in parenthesis were reversed (0.196-0.723) Fig 4 Since you are localizing GFP positive cells, Smad3 and p-Smad3 cells, please use arrows / arrowheads to point whether they are HSC or hepatocyte. Higher magnification should give a better viewing. The observed time 14d or 28 d was lacking in the text. Also, clarify the percent positive area or intensity? Fig 5 –mistaken of detail in the text, AdShmad3 and AdSmad3 made confusion. Also, missing legend and labeling of figures A and B. 4. Discussion the clinical applicability should be elucidate a little more concrete

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ESPS Manuscript NO: 7269
Title: Insulin-like growth factor binding protein-related protein 1 induces liver fibrosis by Smad2/3 signaling: effect on hepatic stellate cell activation and hepatocyte apoptosis
Reviewer code: 02444774
Science editor: Gou, Su-Xin
Date sent for review: 2013-11-13 09:16
Date reviewed: 2013-12-19 00:13

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

COMMENTS TO AUTHORS
This was a nicely written paper with good experimental approach and data. Some minor comments for considerations: 1. Is it pathway etiology dependent? Is it only applicable in NASH but not viral hepatitis? 2. The authors should elaborate more in details about the clinical implications of the results.

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Title: Insulin-like growth factor binding protein-related protein 1 induces liver fibrosis by Smad2/3 signaling: effect on hepatic stellate cell activation and hepatocyte apoptosis
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[Y] Accept
[Y] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
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COMMENTS TO AUTHORS
This is a very interesting and well performed study evaluating the role and mechanism of insulin-lile growth factor binding protein-related protein-1 (IGFBPrP1) in the development of liver fibrosis. The authors used in vitro and in vivo models to demonstrate that overexpression of IGFBPrP1 induces liver fibrosis by mediating hepatocyte apoptosis and HSC activation. Moreover, they identified the IGFBPrP1-mediated pathway involved in liver fibrosis development. The interesting conlcusion of the study was that this pathway could be a potential therapeutic target for liver fibrosis. The study is well designed and well written with clinical relevant conclusions and appropiate data supporting the results.