

ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 7657

Title: Smad3 phospho-isoform signaling in HCV-related chronic liver diseases

Reviewer code: 00054187

Science editor: Ling-Ling Wen

Date sent for review: 2013-11-28 10:56

Date reviewed: 2014-01-06 03:22

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existed	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

This is an excellent review about molecular and cellular mechanisms of hepatic carcinogenesis related to chronic HCV infection. The authors use many self-citations and references. The text is clearly presented (Introduction) and conducted. Concerns that should be accessed: 1. Section "JNK dependent Smad3 signaling through linker phosphorylation" – in the last paragraph the authors wrote "To address this problem, we....", but there is no reference – a reference should be included, or a major explanation regarding this research should be presented. 2. Section "Smad3 phospho-isoform signaling: tumor suppressive TGF- β type 1 receptor....." and Figure 1 – the authors describe molecular activation in uninfected and infected hepatocytes. It seems that this is a result of self-research – this should be clearer in the text and figure legend, as well as some more detail regarding this research could be presented (an in vitro study? what kind of sample was used? How were samples selected?) 3. Figure 2 – which sources of these information? Also self-research? Some aspects seem hypothesis.

ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 7657

Title: Smad3 phospho-isoform signaling in HCV-related chronic liver diseases

Reviewer code: 02860875

Science editor: Ling-Ling Wen

Date sent for review: 2013-11-28 10:56

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existed	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input checked="" type="checkbox"/> Minor revision
		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

Yamaguchi et al have produced a short review article exploring the relationship between TGF- β and JNK signaling in chronic liver disease. They have revealed an interesting cross-talk between these 2 pathways underpinned by mutually exclusive phosphorylation events of Smad3 and the respective downstream signaling pathways. The article is focused, but rather brief in places. The English is good and concise. I have the following comments. 1. Page 6, para 2. "HCV triggers an immune-mediated inflammatory response that promotes neoplastic transformation of damaged hepatocytes." I am not sure how strong the evidence is to make this kind of assertion. Whilst there is certainly an association with viraemia and level of viraemia in HBV, there is relatively little evidence of direct causation that immune cells drive transformation. 2. Page 7, perhaps some example photomicrographs could be included to demonstrate the effect the authors have previously demonstrated. Their pictures from the 2007 Hepatology paper looked really good, perhaps some examples could be used here. 3. There needs to be a brief discussion about the mutually inhibitory nature of the SMAD3 phosphorylation events and some discussion of the evidence about how this is achieved in vitro. Then further discussion about how this might occur in the progression to cirrhosis and HCC, with a frank discussion of the current uncertainties. The current speculation about how this occurs (p8, para 2) is rather unconvincing. 4. Page 8, para 3, "After successful antiviral therapy, patients with chronic hepatitis C have less HCC risk because hepatocytic Smad3 phospho-isoform signaling has shifted from carcinogenesis to tumor suppression...". Again their evidence is purely associative rather than causal. Whilst this effect is interesting, to suggest that it underpins the reduction in HCC risk is not supported by evidence.

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 7657

Title: Smad3 phospho-isoform signaling in HCV-related chronic liver diseases

Reviewer code: 02538717

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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 type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input checked="" type="checkbox"/> Grade E (Poor)	<input checked="" type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

Manuscript entitled "Smad3 phospho-isoform signaling in HCV-related chronic liver diseases", it has been reviewed completed. The authors might have obtained the interesting data. However, it is unfortunate that the manuscript is not well prepared for readers. Some comments are listed below. References are too old, majority are over 3 years ago, the author should refer the new publish article.