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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 29638
Title: Understanding the role of PIN1 in hepatocellular carcinoma
Reviewer's code: 00068723
Reviewer's country: Japan
Science editor: Ze-Mao Gong
Date sent for review: 2016-08-25 15:16
Date reviewed: 2016-08-26 09:22

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] The same title	[Y] High priority for publication
[Y] 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

This manuscript introduced PIN1 in HCC. The manuscript was relatively well-organized, and informative. Introduction on PIN1 with surgical specimens or clinical data should be propagated with more literatures. This part would show the rationale for the investigation of PIN1 aiming at treatment of HCC. Table would present the drugs targeting PIN1 for the treatment of HCC.

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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 29638
Title: Understanding the role of PIN1 in hepatocellular carcinoma
Reviewer's code: 00503516
Reviewer's country: Italy
Science editor: Ze-Mao Gong
Date sent for review: 2016-08-25 15:16
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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[Y] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

Chi-Wai Cheng et al have described the role of the peptidyl-prolyl cis/trans isomerase PIN1 in hepatocellular carcinoma. The review is well written and organized. Minor comments 1) I suggest the authors to include in the introduction a schematic cartoon of PIN1 protein showing the different parts and the relative functions. 2) In the section: "Roles of PIN1 in hepatocarcinogenesis" I suggest to briefly explain the role of Rb in relation to E2F. 3) In the section: "PIN1 as a new drug target for hepatocellular carcinoma treatment" the author write: "Therefore, it remains uncertain whether PIN1 inhibitors would have any adverse effect on normal tissues. Preclinical or clinical studies are necessary to examine the safety and effectiveness of the PIN1 inhibitors in cancer treatment". It may be useful to write a sentence reminding the readers that the use of HCC targeted delivery systems may overcome the detrimental effects on normal cells. 4) In the section: "PIN1 as a new drug target for hepatocellular carcinoma treatment" the author mention the fact that sorafenib may exert its therapeutic effects in HCC also via indirect impairment of PIN1. I recommend the author to mention another examples of drug able to down regulate HCC growth via direct/indirect impairment of PIN1, namely bortezomib (Farra et al, Biochimie. 2015 May;112:85-95).

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ESPS PEER-REVIEW REPORT

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[Y] Grade A: Priority publishing	Google Search:	[ ] Accept
[Y] Grade B: Very good	[ ] 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	[Y] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

The review article by Chi-Wai Cheng, et al. is well-written. They reviewed the precise mechanisms of PIN1 in HCC progression and proposed that PIN1 should be a potential therapeutic target in the treatment of HCC. The review article suggests a new vision for HCC progression and treatment. The review article provides many important findings; therefore, the study is meaningful for publication. However, several issues are pointed out to improve this review article. (Comments) 1) In the Introduction Section, the authors demonstrated that 'PIN1 is mainly localized in the nucleus.' In my understanding, PIN1 ubiquitously exists in both nucleus and cytoplasm. Is the sentence true? If yes, please provide the reference which mentioned about that. 2) In the Introduction Section, the authors introduce NF-?B as one of the PIN1-interacting partners. It is better to change 'NF-kB' to 'NF-kB-p65'. 3) In the section about 'Regulation of PIN1 expression and activity', they explained E2F, NOTCH1, miRNAs, as important factors to regulate PIN1 expression. A previous report by Wang J, et al. have demonstrated that FOXC1 negatively regulates PIN1 expression and function of human basal-like breast cancer cell. Why don't you add the explanation about FOXC1. 4) In the section about 'PIN1 and ?-catenin/ cyclin D1 signaling pathway', the author demonstrated the

following sentence 'In the presence of TNF-a, PIN1 binds the phosphorylated ~ ' for the explanation of the reference 20. I believe that TNF-a is not necessary for PIN1 to bind to NF-kB-p65. Therefore, the words 'In the presence of TNF-a' should be deleted. Moreover, it might be better to add the fact that Ser276 of NF-kB-p65 is phosphorylated after binding of PIN1. 5) EMT is reported to promote tumor cell invasion and metastasis in many cancers including HCC. Several reports have shown that Pin1 might be involved in the increase of EMT-mediated tumor invasiveness in several cancers including HCC. Therefore, I recommend to add the section about 'Roles of PIN1 in EMT-mediated tumor invasiveness'.