BAISHIDENG PUBLISHING GROUP INC
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242 Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com http://www.wjgnet.com

ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 12334
Title: FoxM1 Overexpression Correlates with Hepatocellular Carcinoma Metastasis through Induction of Epithelial-Mesenchymal Transition
Reviewer code: 01197938
Science editor: Su-Xin Gou
Date sent for review: 2014-07-03 15:32
Date reviewed: 2014-07-15 09:53

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

COMMENTS TO AUTHORS

Overview: The authors described the roles of FOXM1 in epithelial-mesenchimal transition (EMT) in hepatocellular carcinoma. They also noted that FOXM1-SNAL1 axis facilitates EMT in the cells, althogh the FOXM1-dependent EMT has been already reported in other cancer cells, eg. gastric cancer cells and breast cancer cells. The manuscript is well written; however, following concerns should be addressed: Major concerns: 1. Additional siRNA sequence against Foxm1 should be tested in order to avoid unexpected off-target effects (Figure 4). 2. Authours craimed that FOXM1-SNAl1 axis is necessary for EMT. However, I am wondering that other factors is associated with this process, since expression analysis displayed that forced over-expression of FOXM1 up-regulated Snal2, Zeb1 and so on. Thus, the dominance of FOXM1-SNAL1 is currently uncertain, even considering that Snal1 silencing down-regulated EMT. SNAL1 must be compared at least with SNAL2 (or perhaps others) in Figure 5, eg. promoter affinity, siRNA-based knockdown experiments. Minor concerns: 1. Concentrations of plasmid or siRNA is missing. The authors must mention how to ensure negligible off-target effects in siRNA experiment. In addition, control siRNA should be defined. 2. Morphological changes is needed to be defined in results sections (Figure 3C, 4C and 5E). What is 'typical morphology'? 3. In the present immunobrot experiments, FOXM1 usually detected as double bands (Figure 1C, 4E and 5F). However, in Figure 4A, FOXM1 was detected as single bands even in the same cell lines. Is this correct? 4. This manuscript contains many typographical errors; eg.

lever instead of level, further more insteed of furthermore. 5. Multiple comparison should be conducted in Figure 1A-1D, 2C-2D, 5B-5D 6. Statistical analysis in Figure 1E, Figure 2B shoud be mentioned.

BAISHIDENG PUBLISHING GROUP INC
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242 Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com http://www.wjgnet.com

ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 12334
Title: FoxM1 Overexpression Correlates with Hepatocellular Carcinoma Metastasis through Induction of Epithelial-Mesenchymal Transition
Reviewer code: 02533610
Science editor: Su-Xin Gou
Date sent for review: 2014-07-03 15:32
Date reviewed: 2014-07-07 13:25

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

COMMENTS TO AUTHORS

The manuscript "FoxM1 Overexpression Correlates with Hepatocellular Carcinoma Metastasis through Induction of Epithelial-Mesenchymal Transition" sought to determine the role of FoxM1 in EMT in hepatocellular carcinoma and metastasis and regulatory function of FoxM1 in SNAIL expression and function. They discovered that the novel FoxM1-SNAIL signaling pathway critically regulates hepatocellular carcinoma EMT, invasion, and metastasis. In general the paper is fine. The relationship between FoxM1 and clinical features of HCC, and FoxM1 may mediate HCC cell invasion have been revealed before. The novelty of this paper is FOXM1 may regulate the activation of Snai1 then decrease the expression of CDH1. Minor comments: 1. The Western images of Figure 1C is not clear, please provide better pictures. 2. The author did not mention how much time they needed to detect CDH1, FoxM1 and Vimentin expression. They also did not mention how much time did the HGF need to induce the typical morphology changes. 3. Avoid strong language: example is the title where "may contribute" or "likely contributes" rather then "affected" should be used. 4. Since EMT does not just induce cell motility and invasion, but also mediate drug-resistant in cancer cells. Does FoxM1 factor have any drug-resistant effect on the HCC patients or cells? 5. In the Figure 5A, I can not find the why the snai1 should be the most significant changed gene in response to FOXM1 overexpression. The real time PCR data also revealed the Snai2, ZEB1 and Twist1 may also be upregulated after enforced FOXM1 expression.