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ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 10806

Title: High expression of CCL20 is a poor prognosis factor by enhancing proliferation and migration of hepatocellular carcinoma cells through epithelial-mesenchymal transition

Reviewer code: 00069630

Science editor: Ya-Juan Ma

Date sent for review: 2014-04-21 14:00

Date reviewed: 2014-04-29 23:21

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 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 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"/> 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

In this manuscript, the authors detected expression of CCL20 in HCC tissues and analyzed its prognostic significance for HCC patients, further analyzed the possible mechanisms underlying CCL20 might promote EMT-like phenotype via PI3K-AKT and Wnt pathway. The article was organized well and the data were presented clearly. However, either the clinic significance or the molecular mechanism of CCL20 is worth more comprehensive experiments to draw a convincing conclusion. Major Points: 1. It has been reported previously that high expression of CCL20 is associated with poor prognosis in patients with hepatocellular carcinoma after curative resection (PMID: 22072303) 2. The experiments conducted to explore the mechanism of CCL20 were using a recombinant protein rather than an expression vector. Without the product information or the catalog number, it's hard to evaluate whether this recombinant CCL20 could represent the actual functions in vivo/vitro. More importantly, since these products usually provided together with a carrier protein or in special solution, acutely this experiment was not designed strictly due to the lack of a proper control experiment. Accordingly, the conclusion would be suspicious. 3. The authors tried to demonstrate that CCL20 could promote EMT phenotype via PI3K-AKT and Wnt pathway, but this conclusion was only drew from the correlation analysis between the CCL20 and PI3K/Wnt-related protein expression by immunohistochemistry assay. Actually, PI3K and Wnt pathways themselves are frequently activated in the advanced or metastatic HCC, so the coincidence that the high expression of CCL20 and those pathway proteins can not give confirmative evidence of their regulation relationship. Minor Points: 1. EMT-like phenotype is a very tricky trait during the cell



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culture; it could appear transiently or with cell passages in practice. A stable transition could be confirmed by wound healing experiment and the switch between E-cadherin and N-cadherin.



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ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 10806

Title: High expression of CCL20 is a poor prognosis factor by enhancing proliferation and migration of hepatocellular carcinoma cells through epithelial-mesenchymal transition

Reviewer code: 02528139

Science editor: Ya-Juan Ma

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

COMMENTS TO AUTHORS

In this paper Dr. Hou et al. studied biological roles of CCL20 in HCC. This study focused on the CCL20 as a candidate biomarker for the RFS and OS. Moreover, they analyzed the biological effect of CCL20 for HCC proliferation and migration through EMT. However, several points require improvements.

1. In fig 1, they should show the almost same lesion of HCC tissue. Therefore, the reader can easily compare the expression of these proteins in the same tumor.
2. In fig2, they should find the HCC cell lines that highly expressed CCL20. Moreover, the knock down analysis should be carried out since the importance of CCL20 expression for the proliferation and migration activity of HCC were not clear.
3. The other chemokines might also contribute to the proliferation and migration activity of HCC. They should analyze or discuss the importance of CCL20 in comparison to other chemokines.



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ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 10806

Title: High expression of CCL20 is a poor prognosis factor by enhancing proliferation and migration of hepatocellular carcinoma cells through epithelial-mesenchymal transition

Reviewer code: 00068443

Science editor: Ya-Juan Ma

Date sent for review: 2014-04-21 14:00

Date reviewed: 2014-05-03 10:13

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

COMMENTS TO AUTHORS

In their present manuscript, the authors detected CCL20 expression in HCC tissues and analyzed the association of CCL20 with OS and RSF. Moreover, they analyzed the effect of CCL20 through EMT and showed that CCL20 could induce EMT that promoting HCC cells proliferation and migration. Major comments: 1. The Kaplan-Meier is for estimating the survival function from lifetime data. It is often used to measure the fraction of patients living for a certain amount of time. Cox regression results in estimates of how much the predictor increases or decreases the odds of the event occurring and whether time to event is increased or decreased. Cox regression may be suitable for estimating the relationship of the OS or RSF and the clinicopathologic characteristics. 2. Describe the information and the titer of antibody product used in every experiment. 3. the knock-down analysis and gene transduction should be carried out to clarify the importance of CCL20 expression for the proliferation and migration in HCC.