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: 12640
Title: Overexpression of High-mobility Group Box 1 (HMGB1) Correlates with Lymph Node Metastasis and Poor Prognosis in Intrahepatic Cholangiocarcinoma
Reviewer code: 02944839
Science editor: Yuan Qi
Date sent for review: 2014-07-20 09:55
Date reviewed: 2014-07-21 17:04

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

COMMENTS TO AUTHORS

The authors present a nicely written paper on an interesting topic: Evaluation of prognostic factors in cholangiocarcinoma. Despite the methodologically well performed study some weaknesses remain: 1. The number of patients is quite small, making it difficult to draw the conclusions hinted at by the authors. 2. The turning point of 12.7 for LMVD becoming a relevant prognostic Parameter seems rather deliberately constructed. 3. The DISCUSSION section lacks critical evaluation of the presented data, weak points of the study as well as potential bias factors should be discussed. 4. Some minor language flaws persist.

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: 12640
Title: Overexpression of High-mobility Group Box 1 (HMGB1) Correlates with Lymph Node Metastasis and Poor Prognosis in Intrahepatic Cholangiocarcinoma
Reviewer code: 02861223
Science editor: Yuan Qi
Date sent for review: 2014-07-20 09:55
Date reviewed: 2014-07-22 16:08

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A: Excellent	[Y] 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	[ ] Grade C: A great deal of language polishing	[ ] No records	
[ ] Grade D: Fair		BPG Search:	[ ] Rejection
[ ] Grade E: Poor	[ ] Grade D: Rejected	[ ] Existing	[ ] Minor revision
		[ ] No records	[Y] Major revision

COMMENTS TO AUTHORS

The authors in this submitted paper have evaluated high-mobility group box 1 (HMBG1) as a possible novel prognostic marker for intrahepatic cholangiocarcinoma (IHCC). Additionally, mechanistic studies were performed investigating a presumed functional link between HMBG1 and epithelial-mesenchymal transition (EMT) and vascular endothelial growth factor C (VEGF-C)-dependent lymphangiogenesis. This study deals with an interesting topic; some of the findings herein have not been reported in this particular setting and may indeed give some new insights. Nevertheless, there remain certain issues and open questions. Although a prognostic role of HMGB1 with functional implications in EMT and tumor progress have not been investigated for IHCC, comparable results have been reported for other tumor entities. Further, some of the authors' conclusions are based on correlations and therefore remain speculative. Critique and concerns: 1. Whether the "results define an important role of HMGB1 in the progression of cholangiocarcinoma", as proposed by the authors, remains uncertain. In vivo tumor models would be needed to strengthen the conclusions. The authors might either wish to expand functional studies to in vivo models or put drawn conclusions into perspective throughout the paper. 2. Using immunohistochemistry (IHC) for the expression of HMGB1 and others, did the authors differentiate between the center of the tumor and the invasion front? 3. Please indicate whether the used antibodies were monoclonal or polyclonal! If polyclonal antibodies were used, where there

non-specific bands in western blotting or unspecific staining in IHC? 4. As indicated under "Materials & Methods", the semiquantitative IHC scoring system was based the intensity and distribution of cells. The authors might wish to refer to published papers using this score system. 5. IHC slides with scores of 8 or higher were classified as "overexpression" – why 8 was the cutoff? Does a score of 8 or higher really define samples with an "overexpression"? What is the reference tissue? The authors might wish to better distinguish between "low expression" and "high expression"? Further, tumors above 12.7 were classified as "high" LMVD group – why 12.7 was the cutoff? For the sake of consistency, the authors might wish to define groups according to "lower cutoff" and "cutoff or higher". 6. The authors evaluated a possible link between HMGB1 and VEGF-C. It remains unclear, why they did not check for VEGF-D! 7. In table 1 "*" indicates values being analyzed by Fisher's exact test. This symbol could be misleading, as it is usually used for levels of significance. Please change! 8. Figure 2 shows box blots for groups "HMGB1 Positive" and "HMGB1 Negative". Indeed, the groups the authors refer to might be "HMGB1 high" and "HMGB1 low". 9. Figure 3 shows Kaplan Meier curves. By accident, group HMGB1+VEGF-C+ is missing in the legend.