



# BAISHIDENG PUBLISHING GROUP INC

7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

http://www.wjgnet.com

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Stem Cells

**Manuscript NO:** 34591

**Title:** Murine hepatocellular carcinoma derived stem cells reveal epithelial-to-mesenchymal plasticity

**Reviewer's code:** 02446280

**Reviewer's country:** Russia

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2017-05-10

**Date reviewed:** 2017-05-18

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<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"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		[Y] No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

### COMMENTS TO AUTHORS

The manuscript entitled "Murine Hepatocellular carcinoma derived stem cells reveal epithelial-to mesenchymal plasticity" addresses very intriguing issue of tumor initiating cells on particular model of hepatocellular cancer. They applied well known sphere formation assay to access whether it is applicable for investigation of hepatic cells stemness and epithelial to mesenchymal transition. Using qRT-PCR they proved that their model maybe a valuable tool to investigate tumor initiating cells that have much common with stem cells.

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Stem Cells

**Manuscript NO:** 34591

**Title:** Murine hepatocellular carcinoma derived stem cells reveal epithelial-to-mesenchymal plasticity

**Reviewer's code:** 03370303

**Reviewer's country:** Japan

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2017-05-31

**Date reviewed:** 2017-06-01

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	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"/> The same title	<input checked="" 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"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

### COMMENTS TO AUTHORS

This manuscript is interesting, presenting a feasible method for concentrating a stem-like population from hepatic cancer cells by extending their previously reported technique for enriching a cancer-initiating population from lung cancer cell lines (Morrison BJ et al., PLoS One 2012; 7: e49752). They also showed that the concentrated population bears mesenchymal characteristics, suggesting that epithelial-to-mesenchymal transition (EMT) has taken place in that population. I hope that their technique will contribute to an advanced understanding of cancer stem cells. Although the content of the manuscript is clear and solid, there is one concern regarding the use of the term "sphere". As is well known, E-cadherin is expressed in immature stem cells (e.g. morula cells and pluripotent stem cells) and is suggested to play an indispensable role for an implementation of compaction. As authors showed in Figure 3A, E-cadherin expression levels were considerably low in Hepa 1-6 CSCs compared to AML12 CSCs. This finding is consistent with the morphological observation (Figure 1), where Hepa 1-6 CSCs



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<http://www.wjgnet.com>

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created irregularly shaped aggregates without compaction while AML12 CSCs created typical and compact sphere-like structures. Therefore, it would be appropriate for authors to use the term “aggregates” instead of “spheres” throughout the manuscript.