



PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 46522

Title: Derivation and applications of human hepatocyte-like cells

Reviewer's code: 02728252

Reviewer's country: Egypt

Science editor: Jin-Lei Wang

Reviewer accepted review: 2019-02-18 02:49

Reviewer performed review: 2019-02-18 21:03

Review time: 18 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

High quality review, no further comments.

INITIAL REVIEW OF THE MANUSCRIPT

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PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 46522

Title: Derivation and applications of human hepatocyte-like cells

Reviewer’s code: 02446120

Reviewer’s country: Argentina

Science editor: Jin-Lei Wang

Reviewer accepted review: 2019-03-27 13:18

Reviewer performed review: 2019-04-03 08:49

Review time: 6 Days and 19 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer’s expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Comments to the Authors The manuscript “Derivation and applications of human hepatocyte-like cells” by Li S et al., is a comprehensive description of the latest advances and potential applications of Human hepatocyte-like cells (HLCs). Since HLCs usually exhibit immature features and great heterogeneity, the authors review the main recent



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advances to improve cell culture conditions and genome editing, which are necessary before translation to the clinic. The authors emphasize the derivation of HLCs from hPSCs, and possible uses of these cells in the study of rare diseases and population genetics, among other applications. The authors' work is relevant since there is an increase in prevalence of liver diseases which requires both: more effective treatments, and the improvement of cell yielding for transplantation. Also, the manuscript describes the current available differentiation protocols and their consecutive steps: endoderm differentiation, hepatic induction, and liver maturation and it provides different optimization strategies to improve maturation and decrease HLCs heterogeneity. Major point The manuscript is relevant, interesting and well written, however, one of the most critical aspects related with translation of stem cells to the clinic, is that these cells frequently acquire cancer cell properties. Even when the authors state that the cell source for transplantation should have no tumorigenic risk, they don't analyze this very important problem. Therefore, I would strongly recommend adding a paragraph which includes the relevance of this issue and the improvements and difficulties in this area.

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