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PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 47708

Title: Induced pluripotent stem cells for therapy personalization in pediatric patients: Focus on drug induced adverse events

Reviewer's code: 00503952
Position: Editorial Board
Academic degree: MD, MSc
Professional title: Senior Scientist
Reviewer's country: Canada
Author's country: Italy
Reviewer chosen by: Ying Dou
Reviewer accepted review: 2019-03-26 14:14
Reviewer performed review: 2019-03-28 04:56
Review time: 1 Day and 14 Hours

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[Y] Grade E: Do not publish		[Y] Rejection	[Y] Advanced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

SPECIFIC COMMENTS TO AUTHORS

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The so-called induced pluripotent stem cells are not same as real stem cells, they are unlikely to be used as stem cells for gene therapy or any medical research. It is now too late to stop spending time and money on these garbage cells- the so-called Induced pluripotent stem cells {J Biomed Res. 2015 Jan; 29(1): 1–2}.

INITIAL REVIEW OF THE MANUSCRIPT

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PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 47708

Title: Induced pluripotent stem cells for therapy personalization in pediatric patients: Focus on drug induced adverse events

Reviewer's code: 03372822
Position: Editorial Board
Academic degree: PhD

Professional title: Assistant Professor

Reviewer's country: Portugal

Author's country: Italy

Reviewer chosen by: Ying Dou

Reviewer accepted review: 2019-07-19 13:25

Reviewer performed review: 2019-07-29 09:45

Review time: 9 Days and 20 Hours

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

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In this review, the authors present the multiple possibilities to address Adverse drug reactions (ADR) in a patient personalized manner using induced pluripotents stem cells (iPSC). The use of organoids and organ-in-a-chip are also presented. However, there is little emphasis in the use of these cells to address pedriatric specific problems. The organs discussed and modelized are very relevant for ADR. The authors often give too much information about the differentiation protocols used to differentiate the cells of interest from iPSC. However, this review is not a technical review and the authors do not point out the critical reagents or parameters in the protocols necessary to achieve the cells of interest. Thus, these descriptions appear like an overload of information. iPSC have been reprogrammed from centenarian persons and have acquired the same level of reprogramming as iPSC a derived from cells of juvenile subjects. Thus, the age of the original donor, may no longer be reflected after reprogramming. Please discuss this point as the cells derived from iPSC originated from adults or young subjects may respond in a same way to drugs. Page 12, the authors address the "interindividual difference" reflected in the iPSC. However, iPSC clones from the same patient may display differences. These intraindividual differences, which may be a foe to test drugs to ADRS are not mentioned in the review. Please discuss this point. The possibility to make direct conversions from somatic cells to cells of interest described in this manuscript exist, but this technology has not been presented here. Could this conversion approach present some advantages to iPSC for testing ADR? Please discuss

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PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 47708

Title: Induced pluripotent stem cells for therapy personalization in pediatric patients: Focus on drug induced adverse events

Reviewer's code: 00546602
Position: Peer Reviewer
Academic degree: PhD

Professional title: Associate Professor

Reviewer's country: Australia

Author's country: Italy

Reviewer chosen by: Ying Dou

Reviewer accepted review: 2019-07-18 22:59

Reviewer performed review: 2019-07-30 23:00

Review time: 12 Days

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

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The iPSC technology is emerging as a new concept for diagnostics, drug development, bio-marker discovery and potential for therapeutics. In the present review, authors have summarised the use of such cellular technology to identify drug induced adverse events vis-a-vis developing personalised medicine. Authors have described and reviewed the potential use of iPSC technology in evaluating drug toxicity in various ailments. The review does provide a critical analysis of various pathological conditions where iPSC technology could make a difference in assessment and identifying the adverse events. However, there are number of limitations in the use of iPSC technology to achieve those goals at the moment because of the clonal variability, erasing of epigenetic memory of the parent cells, complexities of organ culture and faithfully gauging the outcomes etc and this review completely fails in addressing those issues. If authors are ready to incorporate a separate section of reviewing such limitations in using iPSC technology, this MS may be considered for re-review and publication

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