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PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 43173

Title: Regenerative potential of mouse embryonic stem cell-derived PDGFRα+ cardiac lineage committed cells in infarcted myocardium

Reviewer's code: 01851506

Reviewer's country: Japan

Science editor: Fang-Fang Ji

Date sent for review: 2018-10-29

Date reviewed: 2018-11-01

Review time: 3 Days

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[ ] Grade E: Do not publish		[ ] Rejection	[ ] Advanced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

SPECIFIC COMMENTS TO AUTHORS

Comments to the authors. Major points. In this paper Hong et al have evaluated the regenerative potential of PDGFRα+ cardiac lineage committed cells (PDGFRα+CLCs) and αMHC+ cardiac myocytes (CMs) in a murine model of infarcted myocardium (MI).

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The authors found that these cells have improved the contractile function and structure of the infarcted heart upon implantation. It is appreciable that the authors have developed a unique method to induce PDGFRα+CLCs with chemicals (CsAYTE). They also have made the PDGFRα+CLCs and αMHC+ CMs tangible with td-Tomato and GFP, respectively. Although the present findings are interesting in terms of MI therapy, it remains unclear whether the implanted cells could survive and function more than two weeks. While the authors mention that "Both types of implanted cells persisted up to 60 days after implantation (Figure 4C)", they did not address whether the implanted cells function properly. Besides these critiques, the paper did not address whether the use of reporter genes such as td-Tomato and GFP in ES cells would compromise the proper function of PDGFRα+CLCs and αMHC+ CMs in vivo. Minor points The text can be more succinct. When use %, please precise whether it is (v/v), (w/v), or (v/w). There are some typographical errors and the word "antigen recovery" is uncomprehensible.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

[ ] The same title

[ ] Duplicate publication

[ ] Plagiarism

[Y] No

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[Y] No

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PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 43173

Title: Regenerative potential of mouse embryonic stem cell-derived PDGFRα+ cardiac lineage committed cells in infarcted myocardium

Reviewer's code: 02566952

Reviewer's country: Romania

Science editor: Fang-Fang Ji

Date sent for review: 2018-10-29

Date reviewed: 2018-11-03

Review time: 5 Days

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

SPECIFIC COMMENTS TO AUTHORS

The manuscript reports about the role of cardiac progenitor cells derived from ESC (embryonic stem cells) in restoring cardiac function in a small animal (mice) model of cardiac infraction. The study is well designed, results correctly presented and

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interpreted. Below are point by point comments Title No mention here about the type of pluripotent stem cells used to obtaining cardiac progenitor. Is this because ESC are not obligatory fashionable nor ethically easy compared to IPSCs or is just in order to incite the reader to discover him/her self the origin of such cells? Abstract Structured and well organized, same mention here about keeping to denomination of PSCs derived cardiac progenitors. The reviewer does not pretend it is incorrect but rather that this denomination is nonspecific as they are more than one types of pluripotent stem cells out there. Do the authors have a specific reason not to mention the actual origin of these cardiac progenitor (here ESCs?) or do they consider their results apply to ALL types of pluripotent stem cell sources (including IPSCs?) Introduction Is concise and relevant to the topic . Do the authors consider their method of obtaining still proliferating but cardimyocyte committed cells is useful somehow in deriving an algorithm for sorting other cell population ? What would be the meaning of introducing a paragraph about nonexistent cardiac progenitor markers? Material and methods Very well and thoroughly described Results Correctly presented and interpreted , an elegant proof of cardiac progenitor implantation within infarcted area and assessment of their morphological and functional significance compared to nontreated hearts. Can the authors consider in the future to quantitatively asses and compare engraftment and/or differentiation rate of cardiac progenitors after implantation? Discussion A very thorough argumentation on the benefits of using precommited cardiac progenitor cells that retain expansion potential and apparently differentiate in vivo preferentially to cardiomyocytes and not to other lineages. However without an quantitative assessment of comparative survival and engraftment rate it is really difficult to argue about such cell superiority for serving as therapeutic cells especially given the fact their morphological and functional effects compared to committed cells are similar. As very well presented in the discussion, long term cell survival is an issue (it is meritory authors have an

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extended observation period up to 60 days) therefore combined direct and paracrine effects are desirable. Maybe it would be good to asses as well endogenous cardiac progenitor recruitment (if any) . The cell therapy delivery route in this study was direct myocardial injection immediately after infarctation, very difficult to reproduce in clinical settings. How do the authors consider a regional (intra arterial delivery) and delayed (hours to days after infarctation) are going to influence the results? Extremely good observation about the potential arhytmogenic effect of injecting cells that retain their proliferative capability , this would be definitely a topic for further investigation.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

[ ] The same title

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PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 43173

Title: Regenerative potential of mouse embryonic stem cell-derived PDGFRα+ cardiac lineage committed cells in infarcted myocardium

Reviewer's code: 02446054

Reviewer's country: United States

Science editor: Fang-Fang Ji

Date sent for review: 2018-11-19

Date reviewed: 2018-11-25

Review time: 6 Days

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

SPECIFIC COMMENTS TO AUTHORS

Regenerative potential of pluripotent stem cell-derived PDGFR + cardiac lineage committed cells in infarcted myocardium This is an excellent paper describing in vivo utility of the authors earlier isolated progenitor population derived from embryonic

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stem cells. The authors provide extensive delineation of reparation derived from the progenitor population in an immunodeficient animal model of myocardial infarction.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

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[Y] No

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[Y] No