



**PEER-REVIEW REPORT**

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

**Manuscript NO:** 45932

**Title:** Tonsil-derived stem cells as a new source of adult stem cells

**Reviewer's code:** 02446101

**Reviewer's country:** China

**Science editor:** Jin-Lei Wang

**Date sent for review:** 2019-02-15

**Date reviewed:** 2019-02-15

**Review time:** 11 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 checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" 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 checked="" type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

In this review, the authors summarize the details of T-SC isolation and identification and provide an overview of their application in cell therapy and regenerative medicine. The content of this paper is systematic, which has obvious reference value for increasing the understanding of tonsil stem cells. I'm sure that the manuscript really provides some



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new ideas to the readers. However, there're still some issued which should be addressed.

1. The limits and shortcomings of T-SC should be added. 2. The first paragraph of 6.3 is too long and meaningless, which should be reduced. 3. A table of conditions for inducing differentiation of tonsil stem cells should be added to facilitate readers' understanding. 4. The molecular mechanism of tonsil stem cell differentiation should be discussed and added. So, major revision should be recommended for this manuscript.

#### INITIAL REVIEW OF THE MANUSCRIPT

##### *Google Search:*

- The same title
- Duplicate publication
- Plagiarism
- No

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- Duplicate publication
- Plagiarism
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**PEER-REVIEW REPORT**

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

**Manuscript NO:** 45932

**Title:** Tonsil-derived stem cells as a new source of adult stem cells

**Reviewer's code:** 01851506

**Reviewer's country:** Japan

**Science editor:** Jin-Lei Wang

**Date sent for review:** 2019-02-15

**Date reviewed:** 2019-02-18

**Review time:** 1 Hour, 3 Days

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 checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" 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**

In this manuscript the authors discuss the potential of the tonsil-derived stem cells (T-SCs) as an alternative source for mesenchymal stem cells (MSCs) in clinical application. As a proof of T-SCs being useful, they cited the literatures demonstrating that T-SCs indeed possess a potential to differentiate into mesoderm such as osteogenic,



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chondrogenic, adiogenic, and myogenic lineage. Furthermore, T-SCs have a potential to differentiate into ectoderm such as neurogenic and gliogenic, and also into endoderm such as hepatocyte, pancreatic, and parathyroid lineages. The review is intriguing and well written. However, the reviewer has several concerns. 1. While the authors described the method to isolate the T-SCs in detail in "Isolating and identifying tonsil-derived mesenchymal stem cells" section, it should be kept in mind that this is a review but not a regular article. Therefore, this part should be revised appropriately. 2. It is helpful for a wide range of readers to discuss the potential contaminating cells in T-SCs defined by the cell surface markers CD73, CD90, CD105, CD29, CD44, CD166, CD58, and CD49e (also negative for CD11b, CD21, CD23, CD35, and CD54). Readers not expert in the field would understand the advantage and limitation of above surface molecules as stem cell markers. 3. It is not appropriate to mention that The reason why Tonsil derived stem cells has more differentiation potency than other adult mesenchymal stem cells (Title for Figure 1), as Tonsil tissues consist of two different origin tissues; epithelial cells from endoderm origin and lymphoid tissues from mesoderm origin. The mechanisms underlying the peculiar differentiation potential of T-SCs are much more complicated than the fact that Tonsil tissues consist of two different origin tissues. It is helpful to show in the Figure 1 where CD73, CD90, CD105, CD29, CD44, CD166, CD58, and CD49e-positive T-SCs reside. Do T-SCs stem from the endoderm and/or the mesodermal (lymphoid) part of the tonsil?

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[ Y ] No

*BPG Search:*

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**PEER-REVIEW REPORT**

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

**Manuscript NO:** 45932

**Title:** Tonsil-derived stem cells as a new source of adult stem cells

**Reviewer's code:** 03370303

**Reviewer's country:** Japan

**Science editor:** Jin-Lei Wang

**Date sent for review:** 2019-02-15

**Date reviewed:** 2019-02-18

**Review time:** 2 Hours, 3 Days

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**

This review is excellent, showing detailed information regarding how to prepare T-SCs and how to induce their differentiation into various cell lineages. It also gives us useful information regarding the optimal scaffold condition for the differentiation into each cell lineage. This review, which covers broad areas from cell culture technique, tissue



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engineering and pre-clinical/clinical studies, will contribute to the development and expansion of T-SC-based regenerative medicine. There are a few minor concerns. Before publication in World Journal of Stem Cells, they should be properly addressed. Minor concerns: 1) In page 6, line 12, the words “70-uM cell strainer” should be corrected as “70- $\mu$ m cell strainer”. 2) In page 6, lines 14-15, the words “at a density of 108 cells” should be corrected as “at the density of 108 cells”. 3) In page 15, lines 1-2, please show the non-abbreviated form for the word “BLiM-MSCs”. Is it the abbreviation for “Liver from BM-MSCs”? 4) In page 18, lines 20-21, please show the reference for the description “T-SCs can also differentiate into various tissue types, such as embryonic stem cells.”. I am afraid that T-SCs could not be differentiate into embryonic stem cells. If there are no appropriate papers to be referred, the sentence should be replaced by, for example, “T-SCs can also differentiate into cells from all three germ layers.”.

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**PEER-REVIEW REPORT**

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

**Manuscript NO:** 45932

**Title:** Tonsil-derived stem cells as a new source of adult stem cells

**Reviewer's code:** 03478635

**Reviewer's country:** Japan

**Science editor:** Jin-Lei Wang

**Date sent for review:** 2019-02-15

**Date reviewed:** 2019-02-18

**Review time:** 5 Hours, 3 Days

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:
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<input type="checkbox"/> Grade C: Good	polishing	<input checked="" 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
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		<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**

This review article describes about the new role of tonsil-derived stem cells as the source of adult stem cells. The figures are illustrated very well, although the origin of tonsil in figure 2 is a little bit consuming.



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