



PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 51080

Title: Comparison between the Therapeutic Effects of Differentiated and Undifferentiated Wharton's Jelly Mesenchymal Stem Cells in Rats with Streptozotocin-induced Diabetes

Reviewer's code: 02540650

Position: Editorial Board

Academic degree: MD

Professional title: Professor

Reviewer's country: Egypt

Author's country: Taiwan

Reviewer chosen by: Le Zhang

Reviewer accepted review: 2019-09-17 09:51

Reviewer performed review: 2019-09-17 10:34

Review time: 1 Hour

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 checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input checked="" 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 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



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SPECIFIC COMMENTS TO AUTHORS

Although Frequently studied topic, but it was well designed and written. Please explain the following? 1. Very few data is provided for characteristics, recognition and function of hWJ-MSCs 2. Cite your experiment especially culture and separation of stem cells to a known and adjusted method 3. Adjust your dose of injected stem cells into the rat (dose is different from other studies) 4. Quality of figure 1 D-G that demonstrating immunofluorescence staining with anti-insulin antibodies is bad, I think it is nit working 5. Many spelling and grammar mistakes are found that necessitates strong deal with language

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

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BPG Search:

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- No



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Manuscript NO: 51080

Title: Comparison between the Therapeutic Effects of Differentiated and Undifferentiated Wharton's Jelly Mesenchymal Stem Cells in Rats with Streptozotocin-induced Diabetes

Reviewer's code: 00058696

Position: Editor-in-Chief

Academic degree: MD

Professional title: Doctor, Professor

Reviewer's country: United States

Author's country: Taiwan

Reviewer chosen by: Le Zhang

Reviewer accepted review: 2019-10-04 12:43

Reviewer performed review: 2019-10-09 00:57

Review time: 4 Days and 12 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 type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input checked="" type="checkbox"/> Accept	<input checked="" 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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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



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SPECIFIC COMMENTS TO AUTHORS

I have carefully read this new manuscript. My major questions are summarized below: 1) Several times the authors discuss an absence of a cure for diabetes mellitus. The authors should either specify that they are referring to Type 1 diabetes, or remove these statements (since there is ample evidence with regards to weight loss as a treatment option for obese individuals with Type 2 diabetes). 2) There are no p values presented in the Abstract and there is a lack of p values presented in the Results Section. Authors, please include p values. 3) The very first sentence in RESULTS is the validation for the method being used. This sentence must be within the first 2 paragraphs of MATERIALS AND METHODS. 4) Methods, "Immunofluorescence ... pancreas in rats": degree of the insulinitis was scored. Authors: either provide a reference for the scoring, or define/validate your scoring method. For example, did the authors count in a set number of islets or in a set number of sections? 5) Insulin ELISA kit "detect not only human insulin but also rat insulin". Authors: either provide a reference or demonstrate validation of this statement. 6) Discussion; Line 10: "hyperglycemic state in diabetic rats". Authors: please provide a reference for this statement. 7) Page 16, line 2: "Other scholars believe". I believe the authors mean "Other investigators believe". Page 16, Line 6: "could indeed home to the pancreas of"; I do not know what the word "home" means in this sentence. Page 16, Line 7: "diabetic rats and repair the insulinitis". I believe that the authors need a different work for "repair" such as "reduce" or "suppress". Page 16, lines 12-13: "the effects declined gradually afterwards". Authors: was this change caused by inflammatory damage? Page 16, last sentence: "C-peptide ELISA kit ... was specific for the (can omit the) human C-peptide". Authors: please either include a reference for this statement or results of validation experiments should be included in the RESULTS. 8) Page 18, paragraph 2:



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“the insulin produced by the rat pancreatic B cells had a higher resistance”. I do not know what is meant by a “higher resistance”. Page 18, paragraph 3: “studies are needed to improve the survival of cells”. Authors: do you mean “studies are needed to develop methods to improve the survival of cells”? 9) Figure 6: “severe insulinitis” should either be defined in the text in MATERIALS AND METHODS, or a reference should be provided. Since there is no definition, it is less likely that another research group could replicate the authors’ research study. Figure 6 Legend: p values are provided, but the method of quantitation used to obtain the percentages being tested is not well defined; it is not clear what statistical testing was utilized to obtain these p values. Minor Issues: 1) The authors use the phrase “got significantly” when I believe that they mean “are significantly”. 2) Figure 2 Legend: Authors: please remove the “coulds”.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

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BPG Search:

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Manuscript NO: 51080

Title: Comparison between the Therapeutic Effects of Differentiated and Undifferentiated Wharton's Jelly Mesenchymal Stem Cells in Rats with Streptozotocin-induced Diabetes

Reviewer's code: 00052339

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Professor

Reviewer's country: Japan

Author's country: Taiwan

Reviewer chosen by: Le Zhang

Reviewer accepted review: 2019-10-07 02:15

Reviewer performed review: 2019-10-17 02:05

Review time: 9 Days and 23 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
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SPECIFIC COMMENTS TO AUTHORS

Comparison between the Therapeutic Effects of Differentiated and Undifferentiated Wharton's Jelly Mesenchymal Stem Cells in Rats with Streptozotocin-induced Diabetes
Chen-Yuan Hsiao et al Reviewer's comments: This manuscript reported the in vivo treatment for DM using differentiated Wharton's Jelly Mesenchymal Stem Cells (hWJ-MSCs). Although the results here may be promising, the mechanisms and conclusion should be precisely analyzed. Major points: #1 In Fig.2 the undifferentiated hWJ-MSCs produced neither insulin nor C-peptide, but in vivo hyperglycemia was improved in Fig.3A and C. What is the mechanism for this discrepancy? Did the undifferentiated hWJ-MSCs were differentiated to insulin-producing cells (IPCs) in pancreatic tissues? #2 The undifferentiated hWJ-MSCs improved the insulinitis in Fig.6 better than differentiated insulin-producing cells (IPCs). The treatment with hWJ-MSCs gave rise to the up-regulation of serum IL-4 and TGF- β in Fig.4C and D. I think both IL-4 and TGF- β are inflammatory cytokines. How do the authors explain the mechanisms of decreased inflammation in pancreas treated by hWJ-MSCs better than IPCs treatment? #3 How many hWJ-MSCs and IPCs transplanted via portal vein were remained in the liver? The transplanted IPCs into liver might be functional to produce insulin and improve DM. Minor points #1 I Fig.3B, the undifferentiated hWJ-MSCs produced insulin but not C-peptide. The authors can explain the mechanisms. #2 In Fig.3B, the undifferentiated hWJ-MSCs could be produce insulin, however, the immunostaining could not identify insulin in the cells in Fig.5B. What is the explanation for this?

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