

PEER-REVIEW REPORT

Name of journal: *World Journal of Stem Cells*

Manuscript NO: 76421

Title: Stem cell therapy for insulin-dependent diabetes: are we still on the road?

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06179533

Position: Peer Reviewer

Academic degree: MSc

Professional title: Associate Professor

Reviewer's Country/Territory: Turkey

Author's Country/Territory: China

Manuscript submission date: 2022-03-17

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-03-17 09:22

Reviewer performed review: 2022-03-24 08:42

Review time: 6 Days and 23 Hours

Scientific quality	[<input checked="" type="radio"/>] Grade A: Excellent [<input type="radio"/>] Grade B: Very good [<input type="radio"/>] Grade C: Good [<input type="radio"/>] Grade D: Fair [<input type="radio"/>] Grade E: Do not publish
Language quality	[<input checked="" type="radio"/>] Grade A: Priority publishing [<input type="radio"/>] Grade B: Minor language polishing [<input type="radio"/>] Grade C: A great deal of language polishing [<input type="radio"/>] Grade D: Rejection
Conclusion	[<input checked="" type="radio"/>] Accept (High priority) [<input type="radio"/>] Accept (General priority) [<input type="radio"/>] Minor revision [<input type="radio"/>] Major revision [<input type="radio"/>] Rejection
Re-review	[<input checked="" type="radio"/>] Yes [<input type="radio"/>] No
Peer-reviewer	Peer-Review: [<input checked="" type="radio"/>] Anonymous [<input type="radio"/>] Onymous



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statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

I very much likes the manuscript, the English language is adequate, the information is brief and up-to-date.

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Name of journal: *World Journal of Stem Cells*

Manuscript NO: 76421

Title: Stem cell therapy for insulin-dependent diabetes: are we still on the road?

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03673990

Position: Peer Reviewer

Academic degree: MD

Professional title: Professor

Reviewer's Country/Territory: Poland

Author's Country/Territory: China

Manuscript submission date: 2022-03-17

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-03-18 06:42

Reviewer performed review: 2022-03-27 11:49

Review time: 9 Days and 5 Hours

Scientific quality	[<input checked="" type="radio"/>] Grade A: Excellent [<input type="radio"/>] Grade B: Very good [<input type="radio"/>] Grade C: Good [<input type="radio"/>] Grade D: Fair [<input type="radio"/>] Grade E: Do not publish
Language quality	[<input checked="" type="radio"/>] Grade A: Priority publishing [<input type="radio"/>] Grade B: Minor language polishing [<input type="radio"/>] Grade C: A great deal of language polishing [<input type="radio"/>] Grade D: Rejection
Conclusion	[<input checked="" type="radio"/>] Accept (High priority) [<input type="radio"/>] Accept (General priority) [<input type="radio"/>] Minor revision [<input type="radio"/>] Major revision [<input type="radio"/>] Rejection
Re-review	[<input checked="" type="radio"/>] Yes [<input type="radio"/>] No
Peer-reviewer	Peer-Review: [<input checked="" type="radio"/>] Anonymous [<input type="radio"/>] Onymous

statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The manuscript titled “Stem cell therapy – dependent diabetes: are we still on the road?” sent to the World Journal of Stem Cells is a review of the current state of the use of stem cells as a replacement therapy in patients with insulin depletion, especially type 1 diabetics. The authors take up a very interesting topic, which, due to the rapid development of various therapeutic technologies in diabetes type 1, may result in real and effective way of its treatment soon. The strong advantage of the paper is presentation of stem cell therapy from different perspectives. The authors first widely describe the embryonic development of endocrine cells starting from its progenitors showing the differences of human and mouse models in this process, what could counteract the simple translation into the human being. The authors describe different sources of stem cells being studied in the described indication, starting from embryonic, via induced pluripotent stem cells, ending in adult stem cells. Then they show the advantages and disadvantages of different type of stem cells for diabetes documenting their effectiveness and safety on the newest studies. Taken into consideration that the present progress of stem cell therapy in different indications is being not only studied, but also applicated, its usage in diabetes seems to be very close for reality. The FDA approved in 2021 for clinical trial the new drug with stem cells has been a proof of such a concept. The authors indicate the present state of authorization and legacy of stem cell therapy and other limitations enabling its official presence in the clinical practice. The authors in a clear way in the form of figures and tables show the application of induced pluripotent stem cells, the differences between human and mouse pancreatic embryogenesis, advantages and disadvantages of different types of stem cell therapy for diabetes. The authors could present the embryonic development of endocrine cells in the



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form of a table and show the critical points for the use of stem cells in this process
There is also no more up-to-date literature or a description on the subject recently.
Finally the paper is extremely worth to be published in the World Journal of Stem Cells.

PEER-REVIEW REPORT

Name of journal: *World Journal of Stem Cells*

Manuscript NO: 76421

Title: Stem cell therapy for insulin-dependent diabetes: are we still on the road?

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00503243

Position: Editor-in-Chief

Academic degree: MD

Professional title: Professor

Reviewer's Country/Territory: Italy

Author's Country/Territory: China

Manuscript submission date: 2022-03-17

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-03-17 09:16

Reviewer performed review: 2022-03-29 10:10

Review time: 12 Days

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous



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Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Excellent and complete manuscript on the state of art of stem cell treatment for patients with diabetes mellitus due to insulin shortage. the references are complete and the discussion is also wide and complete. In my opinion the authors should more mention on pancreas transplantation that is still now the best option for such patients

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Manuscript NO: 76421

Title: Stem cell therapy for insulin-dependent diabetes: are we still on the road?

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06191957

Position: Editorial Board

Academic degree: PhD

Professional title: Associate Professor

Reviewer's Country/Territory: South Korea

Author's Country/Territory: China

Manuscript submission date: 2022-03-17

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-03-18 06:28

Reviewer performed review: 2022-04-02 01:51

Review time: 14 Days and 19 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous

SPECIFIC COMMENTS TO AUTHORS

The authors demonstrated about cell therapy by inducing beta cell differentiation from various stem cell types. In manuscript, the authors explained development of embryonic stem cells and differentiation of stem cells into beta cells to improve diabetes. It is considered to be a paper that well classifies the advantages and disadvantages of stem cell types and uses. However, the data analysis between of the papers related to embryonic cell development (page 3-4) and stem cell differentiation techniques (page 5-8) seems very weak. In addition, it is considered that the following direct/indirect issues need to be resolved. 1. The purpose of the author's statement is unclear. Is the author explaining the stem cell differentiation method for the treatment of diabetes? Or does it explain the outcomes of treatment? The authors should clearly set goals of review paper. 2. In introduction, cited data from IDF Diabetes Atlas by the authors is ambiguous. On the basis of Atlas, the exact timing and number of patients with diabetes onset should be presented. 3. In page 3, the sentence "The limitations of human donor-derived β cells alternatives, availability of insulin-secreting β cells from pluripotent stem cells (PSCs)" is not complete, and the meaning does not fit the context of the paragraph related to insulin-secreting beta cell differentiated from stem cells. 4. In fact, after the chapter discussing pancreas development, research examples using development factors should explain in induction of pancreas differentiation using various stem cells. However, the relationship of chapters between the pancreas development and the differentiation of PSCs into insulin-secreting beta cells has not been clearly described. 5. The full names of the first abbreviations used in the sentence, such as FGF, MPP, and PTF1A, were not mentioned. And, what is 6-7 'wpc'? Is this 'weeks post conception'? 6. Name of this paper is stem cell therapy for insulin-'dependent' diabetes. But, the author focused on



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independent diabetes treatment in the chapter <the progression in stem cell therapy for insulin-'independent' diabetes>. The subject and content are contradictory. 7. In addition, it does not clearly distinguish diabetes treatment by cell source of ESC, iPSC, and MSC, so the readability is poor.