

PEER-REVIEW REPORT

Name of journal: *World Journal of Diabetes*

Manuscript NO: 80473

Title: Mesenchymal stem cell-derived exosomes: the dawn of diabetic wound healing

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03372482

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Academic Research, Assistant Professor, Associate Professor

Reviewer's Country/Territory: Egypt

Author's Country/Territory: China

Manuscript submission date: 2022-09-29

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-09-29 08:17

Reviewer performed review: 2022-09-29 08:32

Review time: 1 Hour

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 Grade E: Do not publish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 checked="" type="checkbox"/> Accept (High priority) <input 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

statements

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

SPECIFIC COMMENTS TO AUTHORS

Chronic wound healing has long been an unmet medical need in the field of wound repair, with diabetes being one of its major etiologies. Diabetic chronic wounds, especially diabetic foot ulcers, are one of the most frightening chronic complications of diabetes. Although the treatment strategies, drugs, and dressings for diabetic chronic wounds have made great progress, it is still ineffective for some patients who have refractory wounds. Stem cell-based therapies have achieved specific efficacy in the treatment of chronic wounds, with mesenchymal stem cells being the most widely used. However, the preparation process of cell therapy is cumbersome, and there are problems of malignant differentiation, immune rejection, and embolization after transplantation, making clinical implementation difficult. Recent studies have found that stem cells mainly exert their trauma repair effects through paracrine secretion, as their main bioactive component, exosomes play an important role in intercellular communication. Mesenchymal stem cell-derived exosomes inherit the powerful inflammation and immune modulation, angiogenesis, cell proliferation, and migration promotion, oxidative stress alleviation, collagen remodeling imbalances regulation of their parent cells, and avoid the risks of direct stem cell transplantation, showing promising performance as novel "cell-free" therapies in chronic wounds. This review aims to elucidate the potential mechanism and update the progress of mesenchymal stem cell-derived exosomes in diabetic chronic wound healing, thereby providing new therapeutic directions for diabetic chronic wounds that are difficult to be cured by conventional therapy. In General: it's a good paper and the subject of the manuscript is applicable and useful. Title: the title properly explains the purpose and objective of the article Abstract: abstract contains an appropriate summary for the article, the language



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used in the abstract is easy to read and understand, and there are no suggestions for improvement. Introduction: authors do provide adequate background on the topic and reason for this article and describe what the authors hoped to achieve. Results: the results are presented clearly, the authors provide accurate research results, and there is sufficient evidence for each result. Conclusion: in general: Good and the research provides sample data for the authors to make their conclusion. Grammar: Need Some revision. (Check The Paper Comments). Please provide and edit the following information in the Paper 1. Conflict of Interest. 2. Source of Funding. 3. Some references without DOI. 4. Writing references according to the terms of the journal. 5. The result and discussion must be in one paragraph. Finally, this was an attractive article. In its current state, it adds much new insightful information to the field. Therefore, I accept that paper to be published in your journal.

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Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Professor

Reviewer's Country/Territory: France

Author's Country/Territory: China

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Reviewer accepted review: 2022-09-30 14:26

Reviewer performed review: 2022-10-08 16:50

Review time: 8 Days and 2 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
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Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

This review article investigated diabetic chronic wounds (DCWs) healing treated by mesenchymal stem cell-derived exosomes (MSC-Exos). The authors focused on the mechanisms and treatment strategy for DCWs, exosomes' biological characteristics, and the role of MSC-Exos in various stages of DCWs healing. The authors also referred to the translation from the preclinical research to the clinical application. This review paper elucidated the progress of MSC-Exos treatment for DCWs and provided new therapeutic directions for DCWs, as the author mentioned. The manuscript is interesting but I have some specific comments below that I recommend the authors should address before consideration for publication. Specific points 1. Figure 1 is untidy and has too much information. Although schemas representing the cutaneous wound healing on the lower side of the figure are well drawn and easy to understand, signaling pathways on the upper side of the figure should be better reorganized and likely split in new figures to improve the reading. 2. The author should mention more specific barrier for clinical application of MSC-Exos in the section of "Current status and prospects of clinical applications of exosomes in diabetic chronic wounds". 3. The author should modify and soften the expression that stem cell-based therapies have risks and that exosome-based therapies are replacement for them. Various types of stem cell have been already applied for the clinical phase in other areas without any adverse events. 4. In the abstract section authors also should soften their comments "However, the preparation process of cell therapy is cumbersome, and there are problems of malignant differentiation, immune rejection, and embolization after transplantation, making clinical implementation difficult" since it is not right and the safety of cell therapy is not at risk. The exosomes are parts of new biotherapies in addition to cell-bases ones

however, nothing yet demonstrated that this is a better treatment. 5. The preparation process of exosomes is difficult due to the large heterogeneity of their components. This point should be better highlighted for future clinical trials and routine practice. 6. Check syntaxes and errors