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PEER-REVIEW REPORT

Name of journal: *World Journal of Stem Cells*

Manuscript NO: 98693

Title: Stem cell therapy: A promising therapeutic approach for skeletal muscle atrophy

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 08192009
Position: Editorial Board
Academic degree: MD, PhD, Assistant Professor
Professional title: N/A
Reviewer's Country/Territory: China
Author's Country/Territory: China

Manuscript submission date: 2024-07-04
Reviewer chosen by: Yu-Fei Wei
Reviewer accepted review: 2024-08-02 06:29
Reviewer performed review: 2024-08-07 01:08
Review time: 4 Days and 18 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No creativity or innovation

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Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

This paper aims to offer a comprehensive overview of the current understanding of stem cells in treating skeletal muscle atrophy. The authors provide background information on muscle atrophy and its correlation with specific diseases, while briefly addressing the underlying mechanisms of muscle atrophy development, as the focus of the review is primarily on treatment options. The technical aspects of the paper, particularly the figures, are commendable, offering clear visual representations of the molecular mechanisms and therapeutic approaches discussed. The timing of this review is opportune, and I have several recommendations to enhance its impact. 1. The mechanisms of muscle atrophy resulting from denervation, including reduced neurotrophic factor availability and decreased activity levels, should also be considered. 2. The authors have not presented any evidence to support the use of hematopoietic stem cells in the treatment of muscle atrophy. Please include this section. 3. The cited references are insufficient. Bodine SC, Sinha I, Sweeney HL. Mechanisms of Skeletal Muscle Atrophy and Molecular Circuitry of Stem Cell Fate in Skeletal Muscle Regeneration and Aging. J Gerontol A Biol Sci Med Sci. 2023;78(Suppl 1):14-18. 4. Has

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stem cell therapy for skeletal muscle atrophy been applied in preclinical research?Are there any ongoing clinical trials involving the application of stem cell treatments? If so, please provide a list to facilitate assessment of translational progress. 5. Table 1 should provide more comprehensive information, encompassing animal models and types of muscle wasting diseases. 6. "Although the use of MSCs has some advantages over conventional treatments in clinical trials, most of them fail to achieve the expected therapeutic effects" If the author intends to draw such a conclusion, it is imperative to incorporate relevant literature in support of this perspective. 7. "Cell-free therapies based on stem cell derivatives have better prospects compared to conventional cell transplantation therapy" This conclusion also requires additional evidence for substantiation. 8. There are still some errors in the manuscript writing. Please revise the grammar and other aspects of the manuscript. It is recommended to choose a native speaker to write the manuscript for better quality.

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Peer-review model: Single blind

Reviewer's code: 07831482
Position: Peer Reviewer
Academic degree: PhD, Postdoctoral Fellow

Professional title: N/A

Reviewer's Country/Territory: China

Author's Country/Territory: China

Manuscript submission date: 2024-07-04

Reviewer chosen by: Shang Wu

Reviewer accepted review: 2024-11-08 06:41

Reviewer performed review: 2024-11-17 06:46

Review time: 9 Days

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No creativity or innovation

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Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [Y] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The review of Wang et al. entitled 'The role of stem cells in the treatment of skeletal muscle atrophy' aims to address stem cell-based cell therapy and stem cell derivative therapy to treat muscle atrophy. It would be beneficial to provide a more detailed summary of progress in intricate molecular mechanisms underlying skeletal muscle atrophy and provides an overview of current therapeutic approaches, with particular emphasis on mesenchymal stem cells, induced pluripotent stem cells, and their derivatives for treating skeletal muscle atrophy. This review is nicely designed and written clearly. However, this is my advice to fix some points in the manuscript: 1 In Section 1, the author provides a comprehensive review of the current molecular mechanisms and associated signaling pathways that lead to muscle atrophy. It is suggested that the author summarize these molecules through a cartoon diagram, which would allow readers to more clearly understand the molecular mechanisms underlying muscle atrophy. 2 In Section 2, there appears to be a logical issue: the text first discusses pharmacological treatment and then addresses rehabilitation therapy. Is there a relationship between these two approaches in the context of treating muscle atrophy?

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Since the author mentions that rehabilitation therapy is the major clinical treatment for muscle atrophy, and anti-inflammatory and antioxidant drugs have been mostly used in pre-clinical studies, their efficacy and safety in humans need further investigation. Given this, why not discuss rehabilitation therapy first? 3 In section3, ". Due to their excellent properties such as unlimited proliferation and directed differentiation," Unlimited proliferation is not the rationale behind the suitability of stem cells for the treatment of muscle atrophy. For instance, the UC-MSCs at lower passages demonstrate superior therapeutic efficacy in vivo on mice with acute graft-versus-host disease, suggesting that excessive proliferation of MSCs may impair their therapeutic outcomes (PMID: 31779707). 4 In the section 3.1, the author has provided a detailed description of the advancements in the treatment of muscle atrophy using MSCs derived from three different tissue sources. MSCs from these sources can effectively alleviate the symptoms of muscle atrophy and maintain muscle homeostasis by regulating local inflammation, promoting muscle regeneration, and protecting the nerves that innervate muscles. Current literature indicates that MSCs from different origins exhibit heterogeneity, and these differences may impact their therapeutic efficacy in treating muscle atrophy. It is recommended that the author discusses the potential influence of these heterogeneities on the treatment of muscle atrophy with MSCs (PMID: 38124129).

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Peer-review model: Single blind

Reviewer's code: 08396937
Position: Peer Reviewer
Academic degree: PhD
Professional title: N/A
Reviewer's Country/Territory: China
Author's Country/Territory: China

Manuscript submission date: 2024-07-04
Reviewer chosen by: Shang Wu
Reviewer accepted review: 2024-11-11 00:31
Reviewer performed review: 2024-11-19 08:27
Review time: 8 Days and 7 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No creativity or innovation

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Scientific significance of the conclusion in this manuscript	[Y] Grade A: Excellent [ ] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Reviewer : The manuscript focuses on the potential of stem cell therapy for treating skeletal muscle atrophy, a condition characterized by the loss of muscle mass due to various physiological and pathological factors, including aging, injury, disuse, or diseases like amyotrophic lateral sclerosis (ALS) and muscular dystrophies. The article emphasizes the current lack of effective treatments for muscle atrophy and explores how stem cell-based therapies could fill this gap. I would like to recommend its publication pending the address of the following comments: 1.The current title is somewhat generic. Consider making it more specific to reflect the core focus of the paper. 2.The introduction covers various aspects of muscle atrophy, but the flow is somewhat disjointed. Consider reorganizing the content to ensure a logical sequence: start with the significance of muscle atrophy, introduce existing challenges, and then transition into the potential of stem cell therapies. This will provide a smoother flow of information. 3.The transitions between sections are somewhat abrupt. For instance, after discussing muscle atrophy mechanisms, the manuscript directly moves into treatment strategies. Consider adding transitional sentences or paragraphs to connect topics smoothly,

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perhaps using rhetorical questions or summary statements to guide the reader. 4.The discussion section currently lacks depth, particularly regarding the limitations of stem cell therapy (such as immune rejection, ethical concerns, and clinical challenges). Expanding this section with a critical analysis of these issues and proposing actionable future research directions will strengthen the manuscript's impact. 5.The formatting of references is inconsistent and adding references to recent studies in the field will also enhance the manuscript's credibility. 6.Ensure that every significant claim is supported by a specific reference. Additionally, updating the references to include more recent studies (2023-2024) will increase the manuscript's relevance. 7.The discussion section currently lacks depth, particularly regarding the limitations of stem cell therapy (such as immune rejection, ethical concerns, and clinical challenges). Expanding this section with a critical analysis of these issues and proposing actionable future research directions will strengthen the manuscript's impact.

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RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Stem Cells*

Manuscript NO: 98693

Title: Stem cell therapy: A promising therapeutic approach for skeletal muscle atrophy

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 07831482
Position: Peer Reviewer
Academic degree: PhD, Postdoctoral Fellow
Professional title: N/A
Reviewer's Country/Territory: China
Author's Country/Territory: China

Manuscript submission date: 2024-07-04
Reviewer chosen by: Jing-Jie Wang
Reviewer accepted review: 2024-12-13 01:58
Reviewer performed review: 2024-12-13 02:19
Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No creativity or innovation

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Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

I have no additional comments; the article is deemed suitable for publication. Congratulations.