



**PEER-REVIEW REPORT**

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

**Manuscript NO:** 106272

**Title:** Human umbilical cord mesenchymal stem cells reduce platelet  $\alpha$ -granule release in rats via the AKT/MEK/ERK pathway during acute exposure to high-altitude hypoxia

**Provenance and peer review:** Unsolicited manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 08386045

**Position:** Peer Reviewer

**Academic degree and professional title:** PhD

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** China

**Manuscript submission date:** 2025-02-20

**Reviewer chosen by:** Hong-Xin Jiang

**Reviewer accepted review:** 2025-03-20 02:39

**Reviewer performed review:** 2025-03-20 08:49

**Review time:** 6 Hours

<b>Content to be reviewed</b>	<p>Does the manuscript's content fall within the scope of the journal? <b>Yes</b></p> <p>Is there any Key Word that is not included in the manuscript title? <b>Yes</b></p> <p>Do authors' affiliations correspond to the content of the manuscript? <b>Yes</b></p> <p>Does the Abstract contain the contents of each part of the manuscript (IMRaD)? <b>Yes</b></p> <p>Are the Key Words complete? <b>Yes</b></p>
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**https://www.wjgnet.com**

Is the content of the Introduction adequate? **Yes**

Is the content of the Materials and Methods complete?

**Yes**

Is the description of the experiments clear and complete? **Yes**

Are the experimental data presented in the manuscript's biostatistics content reliable? **Yes**

Are the experimental data of the Results true and reliable? **Yes**

Are the quality and resolution of the images up to standard? **Yes**

Do the selection and design of the figures and tables follow the principles of necessity and clarity? **Yes**

Is there any duplication between various parts of the manuscript and between the main text and the content presented in the figures and tables? **No**

Are the figures and tables numbered consecutively in the order in which they appear in the manuscript? **Yes**

Is the Conclusion reasonable? **Yes**

Are all references necessary and reasonable? **Yes**

Is the content of the Discussion reasonable? **Yes**

Do authors omit important references? **Yes**

Are all references related to the topic of the manuscript? **Yes**

Do authors only cite their own earlier publications? **Yes**

Is the manuscript's text correct, concise, and clear? **Yes**

Will the manuscript's content be of interest to readers?  
**Yes**

Are additional experiments needed for the study? **No**

Does the research scope comply with ethics? **No**



Scientific quality	Grade A (Excellent)
Novelty of this manuscript	Grade B (Very Good)
Creativity or innovation of this manuscript	Grade B (Very Good)
Scientific significance of the conclusion in this manuscript	Grade A (Excellent)
Language quality	Grade A (Excellent)
Does this manuscript describe a study of the existing knowledge system?	Yes
Does this manuscript report a revolutionary innovation?	Yes
Does this manuscript report an unconventional innovation?	Yes
Conclusion	Minor revision
Re-review	Yes
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No

### SPECIFIC COMMENTS TO AUTHORS

Minor revision: 1. In lines 281 to 286, the labeling order of Figure B and C is reversed. 2. The A, B, C in Figure 4 should be enlarged to ensure sufficient clarity. 3. Please upload the ethics approval form again. Acute exposure to high-altitude hypoxic environments is associated with an increased risk of thrombosis; however, current preventive measures remain inadequate. Recent studies have demonstrated promising therapeutic effects of human umbilical cord mesenchymal stem cell (hUC-MSC) transplantation on the prevention and treatment of various clinical conditions, including thrombotic diseases. Platelets are crucial for thrombus formation, with their  $\alpha$ -granules serving as key



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determinants of platelet function. However, little is known of the influence of hUC-MSCs on platelet  $\alpha$ -granules. This study investigated the influence of hUC-MSCs on platelet  $\alpha$ -granules in rats during acute exposure to high-altitude hypoxia. Acute exposure to high-altitude hypoxia increased the platelet count, altered platelet morphology, and increased  $\alpha$ -granule density and release. These effects were reversed by hUC-MSC treatment, mediated by the AKT/MEK/ERK pathway. The findings demonstrate that acute exposure to high-altitude hypoxia increases the platelet count, alters platelet morphology, increases  $\alpha$ -granule density, and promotes the release of  $\alpha$ -granule contents in rats. Treatment with hUC-MSCs can reverse these changes, possibly through the AKT/MEK/ERK signaling pathway. These results provide novel insights into the prevention of acute high-altitude-associated thrombosis using hUC-MSCs. Nevertheless, given the complexity of thrombosis formation involving multiple factors and mechanisms, further investigation is needed to verify the role of hUC-MSCs in preventing acute high-altitude-associated thrombosis. These findings provide new insight into the application of hUC-MSCs for the prevention and treatment of thrombosis. The content of this study is detailed and innovative. The content is logical and clear. The language expression standard in the text. The reference introduction is reasonable and appropriate. This article can be accepted after minor revisions. There is no need to review the manuscript again.



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**Peer-review model:** Single blind

**Reviewer's code:** 03618516

**Position:** Peer Reviewer

**Academic degree and professional title:** Associate Professor, PhD

**Reviewer's Country/Territory:** India

**Author's Country/Territory:** China

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**Reviewer chosen by:** Hong-Xin Jiang

**Reviewer accepted review:** 2025-03-20 04:43

**Reviewer performed review:** 2025-03-21 06:28

**Review time:** 1 Day and 1 Hour

<b>Content to be reviewed</b>	Does the manuscript's content fall within the scope of the journal? <b>Yes</b> Is there any Key Word that is not included in the manuscript title? <b>Yes</b> Do authors' affiliations correspond to the content of the manuscript? <b>Yes</b> Does the Abstract contain the contents of each part of the manuscript (IMRaD)? <b>Yes</b> Are the Key Words complete? <b>Yes</b>
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**Yes**

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Are the experimental data of the Results true and reliable? **Yes**

Are the quality and resolution of the images up to standard? **Yes**

Do the selection and design of the figures and tables follow the principles of necessity and clarity? **Yes**

Is there any duplication between various parts of the manuscript and between the main text and the content presented in the figures and tables? **Yes**

Are the figures and tables numbered consecutively in the order in which they appear in the manuscript? **Yes**

Is the content of the Discussion reasonable? **Yes**

Is the Conclusion reasonable? **Yes**

Are all references necessary and reasonable? **Yes**

Do authors omit important references? **No**

Are all references related to the topic of the manuscript? **Yes**

Do authors only cite their own earlier publications? **No**

Is the manuscript's text correct, concise, and clear? **Yes**

Will the manuscript's content be of interest to readers?  
**Yes**

Are additional experiments needed for the study? **No**

Does the research scope comply with ethics? **Yes**



Scientific quality	Grade C (Good)
Novelty of this manuscript	Grade B (Very Good)
Creativity or innovation of this manuscript	Grade C (Good)
Scientific significance of the conclusion in this manuscript	Grade B (Very Good)
Language quality	Grade C (Good)
Does this manuscript describe a study of the existing knowledge system?	Yes
Does this manuscript report a revolutionary innovation?	Yes
Does this manuscript report an unconventional innovation?	No
Conclusion	Minor revision
Re-review	Yes
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No

### SPECIFIC COMMENTS TO AUTHORS

The article titled "hUC-MSCs reduce platelet  $\alpha$ -granule release in rats via the AKT/MEK/ERK pathway during acute exposure to high-altitude hypoxia" is good work but I have few queries/comments that need to be resolved before final recommendation of the article. 1. Title & Abstract: 1.1. The title is clear but could be more concise while retaining key elements. 1.2. The abstract is well-structured but should briefly highlight the potential clinical applications of the findings. 1.3. Some minor grammatical issues need correction, e.g., "as also as the expression of" should be "as well as the expression of." 2. Introduction: 2.1. The introduction provides a strong rationale



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but could emphasize the novelty of the study more. 2.2. The discussion on high-altitude thrombosis is good but could reference more recent studies. 2.3. Some claims, such as "Recent studies have demonstrated promising therapeutic effects," need specific citations. 3. Methods: 3.1. The methodology is detailed, but the selection criteria for animals should be clearer. 3.2. A separate subheading for statistical methods would improve readability. 3.3. Justification for using CD62p as an activation marker in flow cytometry should be included. 3.4. The preparation of hUC-MSCs needs more details on culture conditions and passage numbers. 3.5. ELISA and Western blot methods should specify the number of independent experiments performed. 4. Results: 4.1. The results are well-presented, but some sections contain redundant information. 4.2. Figure legends should explain comparisons more clearly. 4.3. The discussion on platelet activation should be better linked to clinical relevance. 4.4. Individual variability in response to hypoxia should be acknowledged. 5. Discussion: 5.1 The discussion effectively explains results but could relate findings more to prior studies. 5.2 Limitations should be expanded, especially regarding sample size and generalizability. 5.3 Alternative pathways to AKT/MEK/ERK activation should be briefly discussed. 5.4 A final paragraph summarizing the translational relevance of findings would strengthen the discussion. 6. Language & Style: 6.1. The manuscript contains minor grammatical errors and awkward phrasing. Examples include: • "as also as the expression of" → "as well as the expression of." • "was found to reverse these changes" → "was found to mitigate these changes." 6.2. Passive voice is frequently used; active voice may enhance readability in some sections. 7. Conclusion: 7.1. The conclusion restates findings well but should highlight future directions, such as human trials.



## RE-REVIEW REPORT OF REVISED MANUSCRIPT

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**Peer-review model:** Single blind

**Reviewer's code:** 08386045

**Position:** Peer Reviewer

**Academic degree and professional title:** PhD

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** China

**Manuscript submission date:** 2025-02-20

**Reviewer chosen by:** Jing-Jie Wang

**Reviewer accepted review:** 2025-04-11 03:07

**Reviewer performed review:** 2025-04-11 03:09

**Review time:** 1 Hour

<b>Content to be reviewed</b>	Does the research scope comply with ethics? <b>Yes</b> Are additional experiments needed for the study? <b>Yes</b> Will the manuscript's content be of interest to readers? <b>Yes</b> Is the manuscript's text correct, concise, and clear? <b>Yes</b> Do authors only cite their own earlier publications? <b>Yes</b> Are all references related to the topic of the manuscript? <b>Yes</b> Do authors omit important references? <b>Yes</b>
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Is the content of the Discussion reasonable? **Yes**

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Are the quality and resolution of the images up to standard? **Yes**

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Are the Key Words complete? **Yes**

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Novelty of this manuscript	Grade A (Excellent)
Creativity or innovation of this manuscript	Grade A (Excellent)
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Language quality	Grade A (Excellent)
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Does this manuscript report a revolutionary innovation?	Yes
Does this manuscript report an unconventional innovation?	Yes
Conclusion	Accept
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No

**SPECIFIC COMMENTS TO AUTHORS**

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