

June 22, 2023

Li Ma

Science Editor, Editorial Office Director, Company Editor-in-Chief, Editorial Office  
Baishideng Publishing Group Inc

Dear Editor:

We would like to thank you for your response and for giving us the opportunity to improve and resubmit our manuscript (ID: 86091) entitled “**Integrin beta 3-overexpressing mesenchymal stromal cells display enhanced homing and can reduce atherosclerotic plaque.**” We are pleased that the reviewers and the editor had made many constructive suggestions, which have helped us significantly improve our manuscript. We are hereby resubmitting a revised manuscript conforming to all of the reviewers’ comments. In particular, we have addressed all the reviewer's comments in a point-by-point manner and revisions are indicated highlighted in the revised manuscript. We feel that our manuscript is significantly strengthened, and hope that our manuscript may now fulfill the criteria for publication in *World Journal of Stem Cells*.

Thank you for your consideration. We look forward to hearing from you.

Sincerely,

Wei Cui, MD

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**Reviewer #1:**

**Scientific Quality:** Grade A (Excellent)

**Language Quality:** Grade A (Priority publishing)

**Conclusion:** Accept (High priority)

**Specific Comments to Authors:** In this study, the Authors aimed at enhancing the migratory activity and homing of human umbilical cord-derived mesenchymal stem cells (MSCs) towards atherosclerotic vascular sites in apolipoprotein E<sup>-/-</sup> (ApoE<sup>-/-</sup>) mice fed a high-fat diet (HFD). For this purpose, they transduced hMSCs with a lentiviral vector encoding the integrin beta 3 receptor (ITGB3), and/or GFP. The Authors provided compelling evidence that the genetically modified MSCs targeted atherosclerotic plaques in vivo following intravenous injection in HFD ApoE<sup>-/-</sup> mice, significantly reducing, and counteracting the progression of the plaque area. This strategy also led to a decrease in the local inflammatory response, while eliciting an anti-inflammatory associated tissue rescue. The in vivo data were corroborated by in vitro evidence that MSC-ITGB3 remarkably enhanced their migration towards inflammatory sites in vitro, as shown by in vitro transwell-based cell chemotaxis assay, containing in the bottom chamber either TNF-alpha-treated mouse macrophages, or mouse atherosclerotic aorta samples. The presented results entail remarkable novelty and biomedical implication. The methods used are rigorous, and the Discussion section is in keeping with the experimental findings, also highlighting the study limitations, and specifying the needs for subsequent steps aimed at tracing the target location and lifespan of MSCs-ITGB3 through in vivo imaging technology.

**Response:** We would like to thank the reviewer for the positive evaluation of our manuscript.

**Reviewer #2:**

**Scientific Quality:** Grade D (Fair)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Rejection

**Specific Comments to Authors:** Some experiments are not conducted correctly.

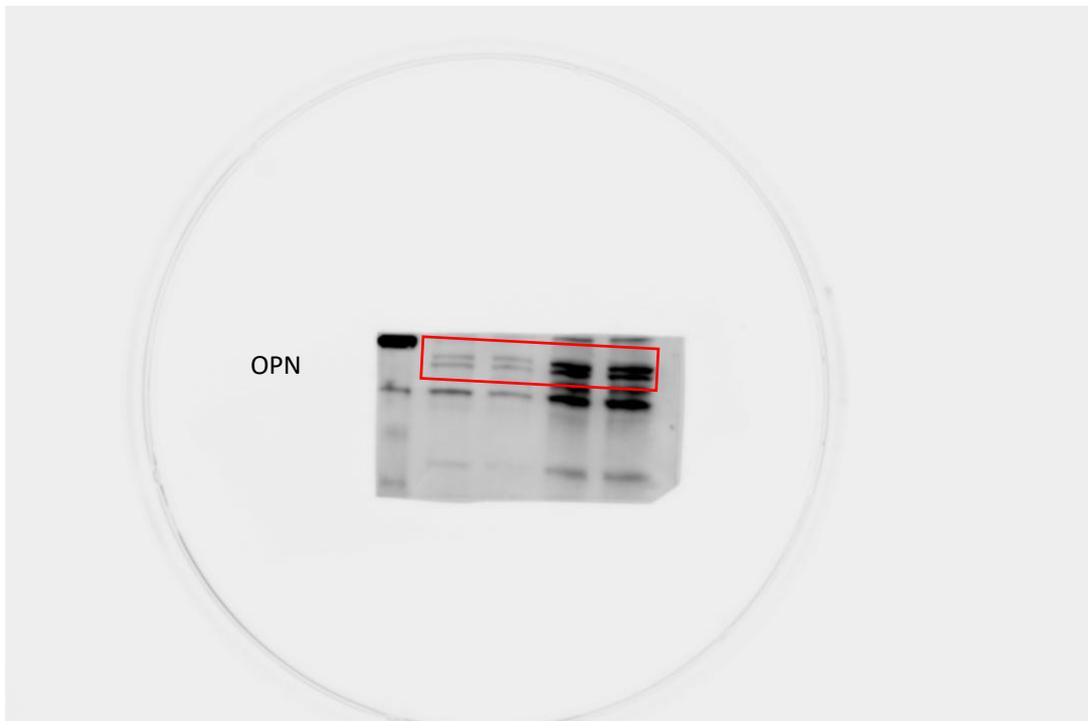
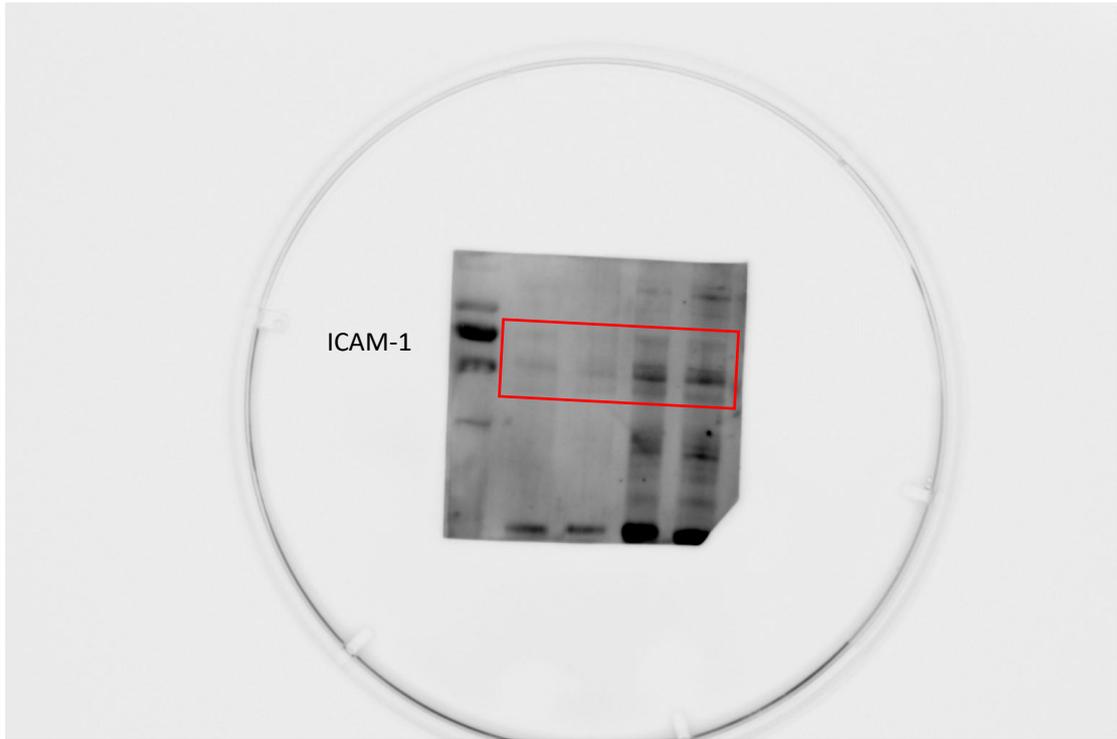
Please provide raw western blot images for the reviewers to check.

**Response:** We would like to thank the reviewer for evaluating our manuscript and for the suggestion. We have carefully checked the procedures of all the experiments and made the appropriate corrections. The original western blot images are shown below.

Figure 1A

GAPDH, ICAM1, OPN, and VCAM1





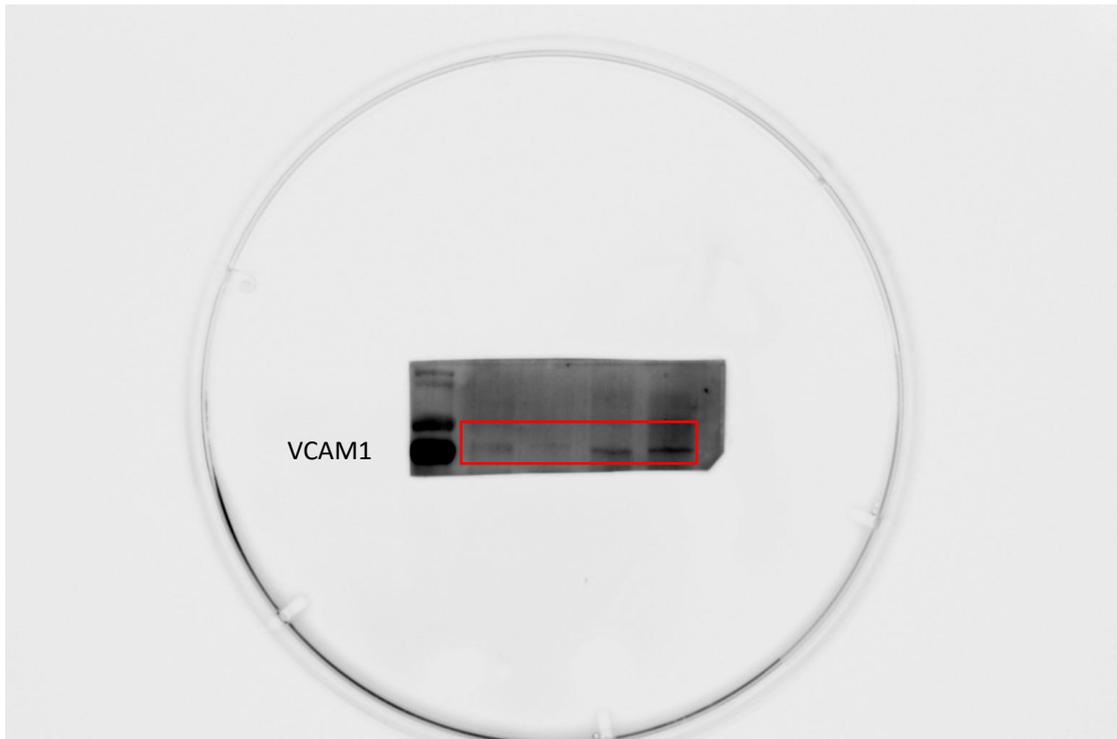
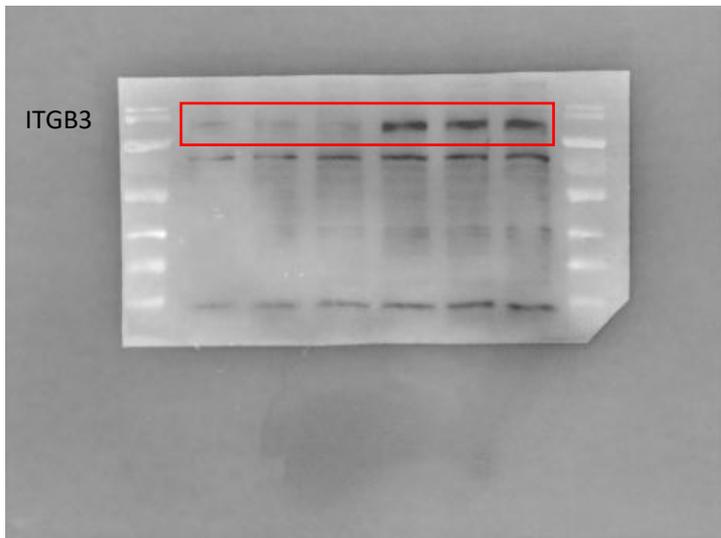
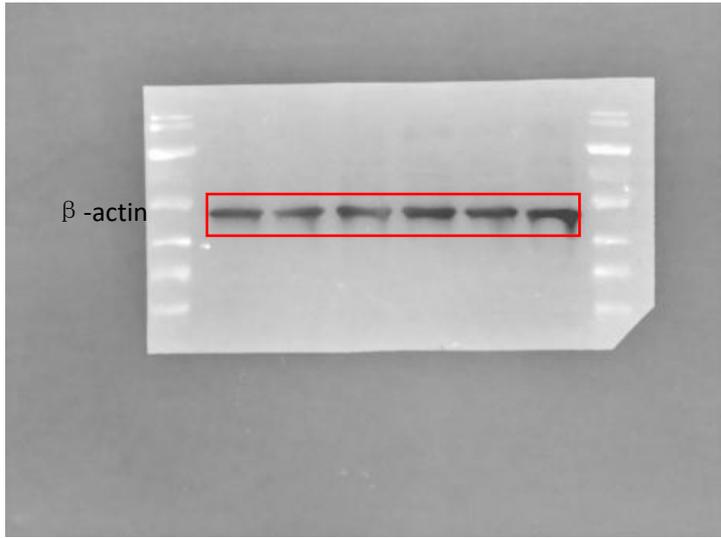


Figure 2A

ITGB3 and  $\beta$ -actin





**Reviewer #3:**

**Scientific Quality:** Grade B (Very good)

**Language Quality:** Grade A (Priority publishing)

**Conclusion:** Accept (General priority)

**Specific Comments to Authors:** This interesting study is about finding new directions for the therapy of atherosclerosis. The study has a reasonable and understandable design and is performed using adequate research methods. The article is well illustrated with figures, which increases the clarity of the findings. The discussion covers the study well and contains sufficient references to the literature.

**Response:** We would like to thank the reviewer for the positive evaluation of our manuscript.

**Reviewer #4:**

**Scientific Quality:** Grade B (Very good)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Accept (General priority)

**Specific Comments to Authors:** 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 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. MATERIALS AND METHODS: - The variables selected for the study are described clearly and are appropriate, given the nature of the question asked. [SEP]- The research design is described in detail. [SEP]- The research design is appropriate and does not contain particular weaknesses. [SEP]- The measurement instrument, including its psychometric qualities, is described clearly. [SEP]- The population of interest and the sampling procedure are defined clearly. [SEP]- The data collection procedure is clearly described. [SEP]- The setting in which the study took place is described. [SEP]- The data analysis procedures are stated in precise terms. [SEP]- The data analysis procedures are appropriate. Results: the results are presented clearly, the authors provide accurate research results, and there is sufficient evidence for each result, Specific data accompany the result statement, and Tables and figures are used efficiently. Conclusion: in general: Good and the research provides sample data for the authors to make their conclusion. Grammar: There are a lot of grammatical errors. This must be taken care of and addressed. 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.

**Response:** We would like to thank the reviewer for evaluating our manuscript and for his/her comment. To address any language-related and grammatical errors, we sent our manuscript to an English editing company (Editage) for English proofreading. We

hope that the level of English has been significantly improved in the revised manuscript and that the manuscript is now suitable for publication in the *World Journal of Stem Cells*.

Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

**(1) Science editor:**

The manuscript has been peer-reviewed, and it's ready for the first decision.

**Response:** We would like to thank the Science Editor for evaluating our manuscript.

**(2) Company Editor-in-Chief:**

I have reviewed the Peer-Review Report and the full text of the manuscript, all of which have met the basic publishing requirements of the World Journal of Stem Cells, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. The quality of the English language of the manuscript does not meet the requirements of the journal. Before final acceptance, the author(s) must provide the English Language Certificate issued by a professional English language editing company. Please visit the following website for the professional English language editing companies we recommend: <https://www.wjgnet.com/bpg/gerinfo/240>. Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the Reference Citation Analysis (RCA). RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for

more information at: <https://www.referencecitationanalysis.com/>. Uniform presentation should be used for figures showing the same or similar contents; for example, “Figure 1 Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...”. Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is ‘original’, the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2023.

**Response:** We would like to thank the Editor for evaluating our manuscript and for his/her comment. As suggested, we sent our manuscript to an English editing company (Editage) for English proofreading. We hope that the level of English has been significantly improved in the revised manuscript.

Regarding figures, we have used uniform presentation for figures showing the same or similar contents. Decomposable Figures were provided in a single PowerPoint file as requested. All the figures are original. Thus, we have added the following copyright information to the bottom right-hand side of the picture in the PowerPoint (PPT) file: Copyright ©The Author(s) 2023.