

Format for ANSWERING REVIEWERS

December 8, 2014

Professor Oscar Kuang-Sheng Lee,
Editors in Chief
World Journal of Stem Cells



Dear Professor Lee,

Please find enclosed the edited manuscript in Word format (file name: 14383-edited).

Title: Utility of tricalcium phosphate and osteogenic matrix cell sheet constructs for bone defect reconstruction

Authors: Tomoyuki Ueha, Manabu Akahane, Takamasa Shimizu, Yoshinobu Uchihara, Yusuke Morita, Naoya Nitta, Akira Kido, Yusuke Inagaki, Kenji Kawate, Yasuhito Tanaka

Name of Journal: *World Journal of Stem Cells*

ESPS Manuscript No: 14383

The manuscript has been improved in accordance with the suggestions from the reviewers. Revisions have been made as described below.

Reviewer A.

General comments

- (1) The importance of the research and the significance of the research findings
This research is important since it indicates the possibility in which cell sheet constructs in combination with MSCs are useful as materials for bone defect treatment.
- (2) The novelty and innovative nature of the research
It is innovative in terms of indicating the sheet efficacy in BMSCs and beta-tricalcium phosphate constructs.
- (3) The quality of the manuscript's presentation and readability
Please carefully check references again.
- (4) The ethics-related aspects of the research
N/A

Response

Thank you for these comments. We have revised our manuscript including the reference numbers in accordance with your specific comments. Please see our revisions highlighted in yellow.

Specific comments

Title: It reflects the major topic and contents of the study.

Abstract: It describes about the aim of the research to investigate the possibility of osteogenic matrix cell sheets and beta-tricalcium phosphate. The explanation for current methods may be added around line 58.

Response

We have added an explanation of the current methods to line 57 of the Abstract.

Introduction: Please explain the differences between previous matrix cell sheet technique and current bone tissue engineering more clearly in the second paragraph (line 91-106). Description about ceramics or surgical procedure comparing with reference 9, Maurilio M et al Tissue Eng (2007) may be added.

Response

We have added some sentences to the second paragraph of the Introduction section (lines 99–107). In these sentences, we have explained the differences between the previous technique and the current method, and the differences between our experiment and the report by Marcacci *et al.*

Material and methods: It is well described.

Results: The precise explanation in Results section may be added. The differences between continuous and segmental bone formation, the detailed explanation of compressive stiffness may be added.

Response

We have added the precise results of the biomechanical compression testing to the Results section (lines 253–257).

Discussion: The interesting technique using bone and cultured mesenchymal stem cells focusing on immunosuppressive effect and osteogenic or chondrogenic differentiation of MSCs may be discussed more deeply.

Response

We have added a paragraph to the Discussion section (lines 327–338). We have also added some references according to the revision of the Discussion section.

References: Please check Reference numbers especially between 21 and 22.

Tables and figures: It seems okay.

Response

We have corrected the reference numbers. Thank you for pointing out this issue.

Reviewer B.

The article describes about the application of tricalcium phosphate and osteogenic matrix cell sheet for bone defect reconstruction. The efficacy of bone formation with matrix cell sheets, BMSC, and beta-tricalcium phosphate has been examined. Although the result section should be described more in detail, this study provides helpful insights for understating overall regenerative medicine technique.

Overall classification

B: very good

Scientific writing
B: minor language polishing
Conclusion
Minor revision

Response

The revised manuscript has been proofread by a native English speaker.

Thank you again for reviewing our manuscript for publication in the *World Journal of Stem Cells*.

Sincerely yours,

A handwritten signature in black ink, appearing to read 'Manabu Akahane', with a small dot at the end.

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