

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Orthopedics

**Manuscript NO:** 64688

**Title:** Effects of sclerostin antibody on bone healing

**Reviewer's code:** 03122873

**Position:** Peer Reviewer

**Academic degree:** DSc, FRCS (Ed), MBBS

**Professional title:** Academic Research, Director, Doctor, Professor

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

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

**Manuscript submission date:** 2021-03-08

**Reviewer chosen by:** Man Liu

**Reviewer accepted review:** 2021-03-10 03:49

**Reviewer performed review:** 2021-03-15 08:35

**Review time:** 5 Days and 4 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<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
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

#### **SPECIFIC COMMENTS TO AUTHORS**

Authors could discuss why Sel-Ab apparently worked well in animal models of fracture healing and not in clinical cases.

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Orthopedics

**Manuscript NO:** 64688

**Title:** Effects of sclerostin antibody on bone healing

**Reviewer's code:** 05685371

**Position:** Peer Reviewer

**Academic degree:** MD, PhD

**Professional title:** Assistant Professor, Doctor

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

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

**Manuscript submission date:** 2021-03-08

**Reviewer chosen by:** Man Liu

**Reviewer accepted review:** 2021-03-10 08:44

**Reviewer performed review:** 2021-03-20 03:26

**Review time:** 9 Days and 18 Hours

<b>Scientific quality</b>	<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
<b>Language quality</b>	<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
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## **SPECIFIC COMMENTS TO AUTHORS**

This manuscript focuses on the effects of the sclerostin antibody on bone healing. This paper presented that Scl-Ab stimulates bone formation via canonical wnt- $\beta$ -catenin pathway, and then discussed the current experimental and clinical evidence of Scl-Ab in bone healing. Then it presented that Scl-Ab has shown positive effects on bone healing in several animal models, whereas in two clinical studies, Scl-Ab failed to show positive effects in the femur and tibia. Overall the study presents that the effect of Scl-Ab on osteoporosis and fractures are different. In the future, research is required to better understand the timing and localization of the appearance of sclerostin-expressing cells according to this pathogenesis, as well as to identify the timing and intervals of drug administration. Comment: 1.The abstract did not summarize and reflect the work described in the manuscript and it should be organized better. 2.As to the mechanisms of action, some researches have showed that low density lipoprotein receptor-related protein 4 (LRP4) can also associate with sclerostin, which enhances the suppressive effect of sclerostin on Wnt signaling[1]. The author need to pull this information together in the context. (Line 111-122) 3.There were some inconsistencies in this paragraph as listed below. In additon, the author need to add a few sentences, which would make it easy to understand the difference between Scl-Ab and PTH in this paragraph. Line 172: The osteoprogenitors increased to similar levels in both groups at week 4. Line 177: These results suggest that Scl-Ab increases the differentiation induction of osteoprogenitors to osteoblasts only, while PTH1-34 increases both the differentiation induction of osteoprogenitors to osteoblasts and the number of osteoprogenitors, although the level of bone formation was similar or even higher in Scl-Ab than in PTH1-34 Reference 1. Leupin Olivier,Piters Elke,Halleux Christine et al. Bone overgrowth-associated mutations in the LRP4 gene impair sclerostin facilitator function.[J] .J Biol Chem, 2011, 286: 19489-500.

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Orthopedics

**Manuscript NO:** 64688

**Title:** Effects of sclerostin antibody on bone healing

**Reviewer's code:** 02910538

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor, Senior Scientist

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

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

**Manuscript submission date:** 2021-03-08

**Reviewer chosen by:** Man Liu

**Reviewer accepted review:** 2021-03-09 14:49

**Reviewer performed review:** 2021-03-22 11:12

**Review time:** 12 Days and 20 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

#### **SPECIFIC COMMENTS TO AUTHORS**

In this paper the effect of sclerostin antibody on bone healing is analysed. Besides a robust literature on osteoporosis, only two papers are available on this topic in humans and the results of these two studies do not support the use of romosozumab to accelerate bone healing. Consequently, in this 10-page paper, just one page is sufficient to analyse the specific topic: in my opinion the amount of available data are inappropriate for a review. Accordingly, the specific topic of the paper could be a paragraph of a more general review on the effect of romosozumab on osteoporosis, which I suggest to prepare.

## RE-REVIEW REPORT OF REVISED MANUSCRIPT

**Name of journal:** World Journal of Orthopedics

**Manuscript NO:** 64688

**Title:** Effects of sclerostin antibody on bone healing

**Reviewer's code:** 02910538

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor, Senior Scientist

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

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

**Manuscript submission date:** 2021-03-08

**Reviewer chosen by:** Jia-Ru Fan

**Reviewer accepted review:** 2021-04-13 11:31

**Reviewer performed review:** 2021-04-13 11:46

**Review time:** 1 Hour

<b>Scientific quality</b>	<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
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## SPECIFIC COMMENTS TO AUTHORS

The authors made the requested modifications and the paper was improved. I have no



**Baishideng  
Publishing  
Group**

7041 Koll Center Parkway, Suite  
160, Pleasanton, CA 94566, USA  
**Telephone:** +1-925-399-1568  
**E-mail:** [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
**https://**[www.wjgnet.com](http://www.wjgnet.com)

further comments.