

October 27<sup>th</sup>, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 22240 Scarfi revision.docx).

**Title:** The use of BMPs in mesenchymal stem cell stimulation of cartilage and bone repair

**Author:** Sonia Scarfi

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

**ESPS Manuscript NO:** 22240

The manuscript has been improved according to the suggestions and requests:

1. Requests from the Editor in the "edited manuscript" have been fulfilled and all additions are highlighted in red.
2. A deep revision has been made according to the suggestions given by the four reviewers. All additions and corrections are highlighted in red in the text as requested.
3. The writing style in the manuscript was very carefully revised, long sentences have been shortened for clarity and grammatical errors and typos attentively corrected throughout the manuscript as suggested by the reviewers.

The following is a point-by-point reply to the Reviewers' comments.

Reply to Reviewer 02446041

1-2-3: the grammatical errors have been corrected as suggested

4: the core tip has been modified according to the reviewer's suggestion

5: a scheme has been added illustrating BMP signaling pathways (Scheme 1), both canonical (Scheme 1A) and non canonical (Scheme 1B)

6: a table illustrating BMP functions in MSC differentiation has been added (Table 1) as suggested by the reviewer

7: the grammatical error has been corrected as suggested

8: a table illustrating the use of BMPs and MSCs in bone tissue repair has been added (Table 2) as suggested by the reviewer

9: a paragraph (highlighted in red at page 9 lines 27-30 and page 10 lines 1-11) has been added discussing the adverse effects of BMP use in clinics as suggested by the reviewer

10: the conclusion has been revised and modified as suggested by the reviewer

Reply to Reviewer 02904760

- 1: a paragraph describing the diseases occurring with BMP mutations has been added as suggested by the reviewer in the Introduction (highlighted in red page 5, lines 9-23)
- 2: the error has been corrected as suggested by the reviewer
- 3: a new paragraph with the classification of BMPs has been added (highlighted in red page 6, lines 15-21) as suggested by the reviewer
- 4: the mistake in the expression has been corrected as suggested
- 5: the roles of the various BMPs listed have been described as suggested by the reviewer (highlighted in red page 8 lines 22-29 and page 9 lines 1-8)
- 6: the non canonical BMP signaling pathways have been described as suggested by the reviewer (highlighted in red page 7 lines 21-28 and page 8 lines 1-5) and also a scheme (1B) has been added for clarity
- 7: mistakes have been corrected as suggested by the reviewer
- 8 and 16: the different experimental settings in which BMP stimulate alternative osteoinductive or chondrocytic differentiation pathways in MSCs and the possible mechanisms of action have been described as suggested by the reviewer (page 11 lines 12-23; page 11 lines 26-28 and page 12 lines 1-4)
- 9 to 15: all the mistakes listed by the reviewer have been corrected and long sentences have been shortened throughout the manuscript as suggested

Thank you very much for all the corrections suggested throughout the text, they have all been included in the revised manuscript and all the manuscript has been double-checked to find further grammatical mistakes and typos. Furthermore, The writing style in the manuscript was very carefully revised and long sentences rephrased to be opportunely shortened.

Reply to Reviewer 02446319

- 1: As suggested by the reviewer a Scheme depicting BMP signaling pathways has been added (Scheme 1A and B) and two tables summarizing the use of BMPs in osteoinduction and chondrogenesis in vitro (Table 1) and in vivo (Table 2) have been added for clarity
- 2: Repetitive sentences have all been checked in the abstract, core tip, introduction and conclusions and eliminated or rephrased as suggested by the reviewer
- 3: The writing style in the manuscript was very carefully revised, grammatical errors and typos attentively corrected throughout the manuscript as suggested by the reviewer.

Reply to Reviewer 02928802:

- 1: a paragraph (highlighted in red at page 9 lines 27-30 and page 10 lines 1-11) has been

added discussing the adverse effects of BMP use in clinics as suggested by the reviewer  
2: the manuscript has been divided in more detailed sections as suggested by the reviewer (namely: Introduction, Bone morphogenetic proteins, Bone morphogenetic proteins in bone formation, Mesenchymal stem cells, MSCs in chondrogenic and osteogenic differentiation, The use of BMPs and MSCs in cartilage repair, The use of BMPs and MSCs in bone tissue repair, Conclusions).

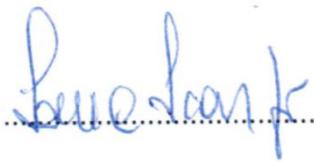
3: The writing style in the manuscript was very carefully revised, and long sentences have been shortened throughout the manuscript as suggested by the reviewer

4: the two sections mentioned by the reviewer were provided with the opportune references as suggested by the reviewer

5: As suggested by the reviewer a Scheme depicting BMP signaling pathways has been added (Scheme 1A and B) and two tables summarizing the use of BMPs in osteoinduction and chondrogenesis in vitro (Table 1) and in vivo (Table 2) have been added for clarity

Thank you again for publishing this manuscript in the *World Journal of Stem Cells*.

Sincerely yours,



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