



June 1, 2017

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 33734-Revised Manuscript.doc).

**Title:** Mesenchymal stem cells for cartilage regeneration in osteoarthritis

**Author:** Baldur Kristjánsson, Sittisak Honsawek

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

**ESPS Manuscript NO:** 33734

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated.

2 Reviewer comments

2.1 Reviewer#1

How the effect on early, middle and late osteoarthritis by mesenchymal stem cells?

Whether there were reports on the effect of degeneration in the late posterior neonatal cartilage?

Whether there were test reports of newborn cartilage biomechanical?

Response: We address those points in the page 7, line 8-22:

"Murphy and co-workers revealed that MSCs isolated from end-stage OA patients showed impaired differentiation capacity as well as reduced proliferation activity *in vitro*<sup>[16]</sup>. They compared bone marrow-derived MSCs (BMSCs) from patients who underwent total knee arthroplasty (TKA) with cells isolated from healthy individuals. They reported that a significantly lower amount of MSCs could be isolated from osteoarthritis patients and that they had reduced proliferation activity. Interestingly, they also observed the MSCs having altered differentiation profiles, favouring osteogenic differentiation, whilst having reduced adipogenic and chondrogenic potentials. Another study found that patients' age and stage of osteoarthritis also affected the differentiation capability and expression of stemness genes of localized adipose-derived MSCs<sup>[17]</sup>. More shockingly, recent study reported that synovial fluid from osteoarthritis patients inhibited the *in vitro* chondrogenic differentiation in MSC cultures of healthy donors<sup>[18]</sup>. Albeit, these functional deficiencies can be ameliorated by culture media supplementation with growth factors<sup>[19]</sup>."

-and page 12, line 4-6 and reference#31:

"Recent evidences have highlighted the importance of MSCs from development to postnatal joint homeostasis and osteoarthritis<sup>[31]</sup>."

"31 De Bari C, Kurth TB, Augello A. Mesenchymal stem cells from development to postnatal joint homeostasis, aging, and disease. *Birth Defects Res C Embryo Today* 2010; **90**: 257-271 [PMID: 21181887 DOI: 10.1002/bdrc.20189]"

## 2.2 Reviewer#2

This is an interesting article. However, the manuscript contains some grammatical errors and conceptual questions, which require attention. Suggestions: 1. Grammar This manuscript contains certain level of scientific merit and it is clearly written. However, the manuscript has quite a number of misused and redundant sentences as well as grammatical errors. I would suggest that the authors find some help in English edition.

Response: -Thank you for your suggestion. We check on grammar and spelling errors throughout our manuscript and correct the entire paper carefully.

## 2.3 Reviewer#3

I have conducted detailed review of the manuscript. The review focuses on the therapeutic potentials of mesenchymal stem cells for therapeutic strategy of knee OA using either autogenous or allogenic cells. This review would be much better if you elaborate the specific mechanism of MSCs' effect in the treatment of OA.

Response: We address those points in the page 12 line 6-10 and reference#32:

"Possible mechanisms of MSCs in the treatment of osteoarthritis may be attributed to the ability of MSCs to initiate the repair process by promoting cartilage regeneration<sup>[32]</sup>. Further researches efforts will be needed to better understand the exact role of MSCs in the treatment of osteoarthritis."

"32 Gupta PK, Das AK, Chullikana A, Majumdar AS. Mesenchymal stem cells for cartilage repair in osteoarthritis. *Stem Cell Res Ther* 2012; 3: 25 [PMID: 22776206 DOI: 10.1186/scrt116]"

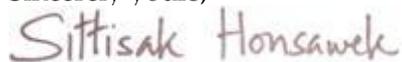
3 Would you please provide the decomposable figure, whose parts are movable and words can be edited.

Response: We provide the decomposable figures as requested.

4 References and typesetting were corrected. We also provide audio core tip and the required documents.

Thank you again for publishing our manuscript in the *World Journal of Orthopedics*.

Sincerely yours,



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