

Format for ANSWERING REVIEWERS

August 25, 2014



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: Uth K WJSC 2014 R1.doc).

Title: Stem Cell Application for Osteoarthritis in the Knee Joint –A Minireview

Author: Kristin Uth, Dimitar Trifonov

Name of Journal: *World Journal of Stem Cells*

ESPS Manuscript NO: 12841

The manuscript has been improved according to the suggestions of reviewers (please find our answers on the following pages). Revised parts of the manuscript are highlighted in yellow. Manuscript format has been updated. References and typesetting were corrected.

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

Sincerely yours,

A handwritten signature in blue ink, appearing to be 'K. Uth'.

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Reviewer 1:

This paper needs a major review. First it is too long and contains some parts which are not suitable for the journal and in some parts contains false details. Second it should really focus on the current status of treating OA with stem cells - what are the current results of clinical trials and what should we expect in the short future.

We thank the reviewer for his helpful comments and suggestions for the revision of this manuscript. We have shortened the manuscript by briefly summarizing the sections **PATHOPHYSIOLOGICAL BASIS OF KNEE OSTEOARTHRITIS; CLINICAL BASIS OF KNEE OSTEOARTHRITIS; EPIDEMIOLOGY** in the introduction of the manuscript. The section **CHONDROCYTES PRODUCED BY DIFFERENTIATION OF PLURIPOTENT CELLS (ESC, iPSC) OR DE-DIFFERENTIATION/TRANSDIFFERENTIATION OF SOMATIC CELLS**, which covers basic research in the area of chondrogenesis in vitro and in vivo, has been removed from the manuscript. However, a brief future perspective about basic research in chondrogenesis (in vitro and in vivo) with relevance to future clinical trials has been included in the conclusion of this manuscript. All false details have been corrected. Furthermore, we revised the other parts of the manuscript. The list of references has been accordingly updated.

Reviewer 2:

The manuscript reviewed the current knowledge on stem cell application for knee OA. The below are some minor comments: 1. OA and osteoarthritis were used interchangeably throughout the manuscript. After short term "OA" was introduced, it should be used afterwards throughout the rest of the manuscript. 2. in the Risk Factors section, an updated summary should be provided on genetics of OA. up to date, there are at least 10 GWAS reported, and most of those reports were on knee OA. 3. Page 11 first paragraph, it is not clear to me for the statement "this treatment is pliable only if there is no degeneration of cartilage", does it mean the completed loss of cartilage or partial loss? this needs to be clarified.

We thank the reviewer for his helpful comments.

1. OA and osteoarthritis were used interchangeably throughout the manuscript. After short term "OA" was introduced, it should be used afterwards throughout the rest of the manuscript.

We have introduced the short term "OA" throughout the manuscript after it was first used in the introduction of the manuscript.

2. in the Risk Factors section, an updated summary should be provided on genetics of OA. up to date, there are at least 10 GWAS reported, and most of those reports were on knee OA.

We have provided an updated overview of knee OA genetics in the introduction of the manuscript.

3. Page 11 first paragraph, it is not clear to me for the statement "this treatment is applicable only if there is no degeneration of cartilage", does it mean the completed loss of cartilage or partial loss? this needs to be clarified.

We have revised the statements as follows: "this treatment is applicable only if the degeneration of the cartilage is not complete."

Reviewer 3:

In this article, Dr. Uth and his colleagues review the current stem-cell therapies on knee osteoarthritis, which becomes more and more common in the elderly and in obese people. The review was well written and well organized. Minor comment: It will be very helpful if some of conclusion or predication in each stem-cell treatment is mentioned in the text.

We thank the reviewer for his complaisant comment. We have added conclusions about each stem-cell treatment in the manuscript.

Reviewer 4:

This is an interesting review manuscript on the potential application of stem Cell to treat osteoarthritis in the knee joint. The content would have valuable information of the readers of the journal. The following points are suggested: 1. As it is a review on the treatment of osteoarthritis of knee joint, using stem cell, the authors are suggested to focus on this point. Hence, the content of the first three sections: PATHOPHYSIOLOGICAL BASIS OF KNEE OSTEOARTHRITIS; CLINICAL BASIS OF KNEE OSTEOARTHRITIS; EPIDEMIOLOGY would all be briefly summarized in the Introduction section. 2. The persistent use of the abbreviation of OA should be adhered after the first usage.

We thank the reviewer for his helpful comments.

1. As it is a review on the treatment of osteoarthritis of knee joint, using stem cell, the authors are suggested to focus on this point. Hence, the content of the first three sections: PATHOPHYSIOLOGICAL BASIS OF KNEE OSTEOARTHRITIS; CLINICAL BASIS OF KNEE OSTEOARTHRITIS; EPIDEMIOLOGY would all be briefly summarized in the Introduction section.

We have briefly summarized the sections PATHOPHYSIOLOGICAL BASIS OF KNEE OSTEOARTHRITIS; CLINICAL BASIS OF KNEE OSTEOARTHRITIS; EPIDEMIOLOGY in the introduction of the manuscript as suggested.

2. The persistent use of the abbreviation of OA should be adhered after the first usage.

We have introduced the short term "OA" throughout the manuscript after it was first used in the introduction of the manuscript.