

## Format for ANSWERING REVIEWERS

August 19, 2014

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 12552-review.doc).

**Title:** SECRETION OF IMMUNOREGULATORY CYTOKINES BY MESENCHYMAL STEM CELLS

**Author:** Dobroslav Kyurkchiev, Ivan Bochev, Ekaterina Ivanova-Todorova, Milena Mourdjeva, Tsvetelina Oreshkova, Kalina Belemmezova, Stanimir Kyurkchiev

**Name of Journal:** *World Journal of Stem cells*

**ESPS Manuscript NO:** 12552

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

1. Format has been updated
2. Revision has been made according to the suggestions of the reviewer
  - (1) The suggestions of the highly esteemed reviewer 364986 are highly appreciated and adhered to.
    1. A paragraph is added which briefly informs about the currently run clinical trials and studies on animal models related the immunomodulating activities of MSCs. Results from the animal studies are also discussed in the review while presenting data about the precise effects of cytokines, chemokines and cell adhesion molecules: TGF $\beta$ , CCL2/MCP-1, RANTES/CCL-5, IDO, VEGF, sICAM, PGE2.
    2. A table is added presenting in a concise way the secreted cytokines and the cells which are targets of the cytokines.
    3. Spelling and typo mistakes and unclear sentences are corrected by a native English speaking person including some Cyrillic symbols (p.6) and the sentence in the abstract pointed by the reviewer.
    4. The conclusion is clearly separated from the PGE2 describing paragraph.
  - (2) We thank very much for the opinion of the highly esteemed reviewer 609371.
    1. We fully agree with the opinion that the perfect review would contain and discuss combined information about both immunomodulation by human MSCs and their role and significance for the regenerative medicine. It is true that the cytokines described are involved in both activities of MSCs and they are not strictly discriminated in vivo. However it is widely accepted in the scientific literature to use somewhat artificial classifications which aim to

systematize the enormous information in order to make it easier to apprehend. Being specialists in the field of autoimmunity we discuss strictly the immunoregulatory activities of cytokines secreted by human MSCs which is shown in the title of this review and the statement we make on p.6-7 as well. The question "where do we stand from here?" is waiting for an answer in numerous other papers. The present review is not aiming the answer of this question.

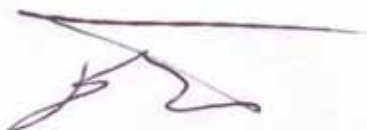
2. We fully agree with the remark that there are not categorical logical conclusions but please keep in mind that this is almost impossible when discussing cytokines and their multifaceted effects.

3. Spelling and typo mistakes and unclear sentences are corrected by a native English speaking person.

3 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 dark ink, appearing to be 'Dobroslav Kyurkchiev', written in a cursive style.

Dobroslav Kyurkchiev, MD, PhD

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