

Format for ANSWERING REVIEWERS



December 9, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 6618-minireview revision.doc).

Title: Role of myeloid-derived suppressor cells in autoimmune disease

Author: Kristen R. Crook and Peng Liu

Name of Journal: *World Journal of Immunology*

ESPS Manuscript NO: 6618

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

Reviewer 1

This is a well-written review of Myeloid-Derived Suppressor cells (M-DSC) and covers the area well. Minor point, authors have to consider summarizing M-DSC phenotype, main mechanisms and regulatory functions in a figure and/or table.

Reply: We thank the reviewer's suggestion. We have added a table in the revised manuscript to summarize the phenotype, main mechanisms and regulatory functions of MDSCs in models of autoimmune diseases.

Reviewer 2

The review by Crook and Liu is well written and interesting; however some points need to be clarified:

1. I am not sure if the word "Regulation..." in the title is the right one.

Reply: Based on the reviewer's suggestion, we have changed the title to "Role of myeloid-derived suppressor cells in autoimmune disease"

2. The authors describe that MDSCs are involved in "autoimmune" conditions (although the pages are not numbered, it is mentioned in P3,p1,L2-3) describing MS and RA as autoimmune, I think it should say immune-mediated, rather than autoimmune.

Reply: We understand the reviewer's concern. Since MS and RA are autoimmune diseases, we changed autoimmune conditions to autoimmune disorders.

3. "Experiment autoimmune encephalomyelitis" should say "Experimental..." (P3,p1,L9).

Reply: It has been corrected.

4. It must be clearly defined which cytokines or chemical signals enhance and which inhibit the local accumulation and expansion of MDSCs; for instance in the same paragraph the authors mention that TNFalpha induce "accumulation" and others expansion", these terms should be clarified (P3,p2).

Reply: We thank the reviewer's suggestion. We have revised this paragraph and made these points clear.

5. Is the end result of G-MDSCs and M-MDSCs similar? if not this must be explained in the section of therapeutic possibilities.

Reply: We have inserted a sentence to state that there is not enough evidence to make a conclusion on whether the endpoint of G-MDSCs and M-MDSCs are similar in different autoimmune diseases. We made a table to show the study results and emphasized the challenge of MDSC plasticity in the potential MDSC-mediated

therapy.

6. “The cytokine environment of each disease influences MDSC differentiation and function” (P5,p2,L9-10) How does that? Please explain.

Reply: We have reworded our description to emphasize on the disease/inflammatory environment influencing MDSC differentiation and function rather than cytokines only.

7. “MDSCs are important in maintaining tolerance to self antigens” (P6,p1,L2-3) is a rather complex statement please explain how does it happen under normal conditions.

Reply: Sorry for the confusion. We have rewritten the sentence and inserted a comment on this point.

8. The line “MDSCs do not induce systemic immune suppression in cancer...” should be clarified (P7,p1,L4-5).

Reply: It has been clarified in the revised manuscript.

9. “Therapeutic treatments” is redundant (P7,p2,L1).

Reply: We have corrected it.

10. The fact that MDSCs are not differentiated but might do so as macrophages or dendritic cells (P8,p1) is a potential complication for therapeutic attempts, if so it should be clearly described.

Reply: Thanks for the suggestion. We have now clearly stated this potential complication.

3 References and typesetting were corrected

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

Sincerely yours,



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