

August 31st, 2015

Dear Editor,

Please find attached the edited manuscript as a Word file (21656-Revised manuscript.docx).

Title: Dendritic cells and the extracellular matrix: a challenge for maintaining tolerance/ homeostasis

Author: Sucharita P Shankar, May Griffith, John V Forrester, Lucia Kuffová

Name of Journal: *World Journal of Immunology*

ESPS Manuscript No: 21656

The manuscript has been revised taking into account the Reviewer's suggestions.

Please see our point-by-point responses to the Reviewers' comments below.

Reviewer 1 (No. 02565578)

Overall comments: The authors review available data on ECM-dendritic cell interaction for immunological tolerance or response activation (for instance in skin, intestine, liver, cornea and spleen) and highlighting the need for consideration of the effects of tissue engineering biomaterials on DC behaviour and function. The review is comprehensive, exhaustive, and discusses a wide array of different perspectives and applications of the topic.

We thank Reviewer 1 for the highly positive feedback on the submitted manuscript.

No specific comments.

At this time, there are no revisions required by this Reviewer.

Reviewer 2 (No. 02505493)

Overall comments: The present m/s is reviewing the evidence describing the interactions between dendritic cells and extracellular matrix and the constantly changing role of the latter in directing dendritic cell responses in normal conditions versus in inflammation. The m/s is well organized. The authors describe the dendritic cells and their properties, as well as the various dendritic cell subsets, the functions of extracellular matrix, especially its active role in regulating normal or pathological states of inflammatory cells, the role of tissue matrices and dendritic cells in homeostasis, the modulation of matrices by dendritic cells, the major ECM components impinging on dendritic cells, the receptors of dendritic cells for ECM, the design of intelligent biomaterial to mimic ECM in tissue regeneration and they close their review with the concluding remarks. It is a very interesting review, especially because it focuses to the dual role of extracellular matrix in inflammation.

We thank Reviewer 2 for summarizing the main content of our submitted Review and for the positive and constructive feedback provided.

Specific comments:

1. **However, there are several points to be considered, in order to be suitable for publication. Major points Page 5, line 2 (and elsewhere, for cell type abbreviations): Use DCs and APCs, instead of DC and APC, respectively.**

The authors have revised the manuscript to consistently use the terms DCs or APCs throughout, as appropriate. Other cell type abbreviations including Langerhans cells (LCs), hepatic stellate cells (HSCs), Kupffer cells (KCs) etc. have also been revised accordingly throughout the text.

2. **Page 7, lines 16-19: the sentence needs rephrasing.**

The sentence has been modified for accuracy.

3. Page 13, lines 19-21: the sentence needs rephrasing.

The sentence has been rephrased and the redundant term 'spleen' at the end has been removed since it was already used at the start of the sentence.

4. Page 14, line 28 - page 15, line 4: the sentence needs rephrasing.

The sentence has been revised by breaking it down into smaller sentences to facilitate easier reading.

5. Page 23, line 14: the authors write "The ECM protein hyaluronan ...", although they have previously described the structure of hyaluronan (page 17, line 24).

The authors thank the Reviewer for pointing this out and have since modified the sentence such that it now begins with the word "Hyaluronan...", since redefining it here is redundant.

6. Minor points Page 8, line 11: "homeostasis" instead of "homestasis".

The typo has been noted and corrected.

7. Page 11, line 10: Remove the parenthesis.

The parenthesis has been removed and the words have been integrated with the text to allow the sentence to flow more smoothly.

8. Page 12, line 9: "activates" instead of "activated".

The change in tense has been made.

9. Page 13, line 24: "has" instead of "have".

The grammatical correction has been incorporated.

10. Page 13, line 25: Use one term for “hematopoiesis”/“haematopoiesis” (see also hematopoietic).

The term and associated forms of it have now been consistently spelt throughout the text.

11. Page 14, line 8: “was” instead of “were”.

The grammer has been amended as recommended.

12. Page 14, line 17: the plural of the word “stroma” is “stromata”, otherwise use the singular “stroma”.

The singular ‘stroma’ has been used here.

13. Page 14, line 29 (and elsewhere): “heparan” instead of “heparin”.

Thank you for pointing out the typo. The spelling has been corrected throughout the text.

14. Page 18, line 12: insert the word “and” between the words “arthritis myocarditis”.

The word ‘and’ has been added as suggested.

15. Page 18, line 23: “remodelling”.

The spelling has been corrected. Thank you for bringing it to our attention.

16. Page 20, lines 1-4: insert commas in the sentence at the suitable positions.

This sentence has been amended slightly for easier reading.

17. Table 1: Do not align columns at right end.

The suggestion has been taken. The table is now easier to read.

Thank you once again for accepting our review manuscript for publication in *World Journal of Immunology*.

Yours sincerely,

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