

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Biological Chemistry

ESPS manuscript NO: 29780

Title: B-1 cells modulate the murine macrophage response to Leishmania major infection

Reviewer's code: 02618027

Reviewer's country: United States

Science editor: Jin-Xin Kong

Date sent for review: 2016-08-29 08:38

Date reviewed: 2016-10-22 20:27

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
		BPG Search:	<input checked="" type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

In the manuscript entitled "B-1 cells modulate the innate response of murine macrophages to Leishmania major infection" by Arcanjo AF and Nanes MP et al., the authors investigate the immunomodulatory effect of B-1 cells in L. major infected macrophages. Results suggest that PGE-2 and IL-10 released from infected B-1 cells increase intracellular parasite replication. The manuscript is generally well-written; however, the text should be carefully checked for spelling and other minor errors throughout. Although the findings are interesting, the following concerns should be addressed prior to publication: Major Comments: 1) What is it about B-1 cells that triggers IL-10 production? 2) What is it about B-1 cells that favors lipid production? 3) It is interesting that the B-1 CDP cells produce anti-inflammatory mediators yet they can be infected with L. major. Besides inflammation, there are other mechanisms involved in macrophage immune response, such as respiratory burst, etc., which should be addressed in the Discussion section. 4) Although the authors report that B-1 CDP cells produce anti-inflammatory mediators, they also suggest that phagocytic ability of these cells to ingest promastigotes are not compromised. This dichotomy in macrophage activation should be addressed in the Discussion section. 5) The authors show that B-1 cells induce



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parasite replication when co-cultured with L. major infected macrophages, but the study lacks any mechanistic studies to elucidate the role of B-1 cells themselves in parasite replication. Therefore, the results, with regard to B-1 cells, just become interesting observations. 6) The x-axis labels in Figure 3 are very difficult to read since the labels seem to be cut off. Changing the labels to be angled rather than horizontal would be clearer. 7) In all figure legends, it is stated that graphs are "representative result of three similar experiments". It is unclear what is meant by this statement. Did each experiment have n=3? It does not make sense that means are presented in the bar graphs and yet they are denoted as "representative" findings. 8) In experiments containing more than two experimental groups (Figure 3 in particular), Student's t-test is inappropriate. ANOVA followed by posthoc tests of statistical significance are more appropriate. 9) Representative images should be provided for each experimental condition shown in Figure 4. 10) In Figure 8, were the B-1 KO groups statistically significantly different compared to the B-1 wt groups in both C57BL/6 and KO IL-10 animals? Minor Comments: 1) BALB/c XID mice should be defined in the Methods section on page 2. 2) I think the word "Exposition" on page 2 should be "Exposure". 3) The word "confirm" on page 2 should be in past tense, i.e. "confirmed". 4) Please check the manuscript carefully for errors. For example, the title for the legend of Figure 2 contains the misspelled word "independent" and the end of the sentence is missing a period. 5) Figure 3 legend has the word "factor" misspelled. 6) "Student's t-test" is misspelled throughout as "Student". 7) In Figure 6, the "AAS" group should be defined in the figure legend.



ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Biological Chemistry

ESPS manuscript NO: 29780

Title: B-1 cells modulate the murine macrophage response to Leishmania major infection

Reviewer's code: 00055041

Reviewer's country: Italy

Science editor: Jin-Xin Kong

Date sent for review: 2016-08-29 08:38

Date reviewed: 2016-09-08 16:59

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> [Y] Accept
<input type="checkbox"/> [Y] Grade B: Very good	<input type="checkbox"/> [Y] Grade B: Minor language polishing	<input type="checkbox"/> [] The same title	<input type="checkbox"/> [] High priority for publication
<input type="checkbox"/> [] Grade C: Good	<input type="checkbox"/> [] Grade C: A great deal of language polishing	<input type="checkbox"/> [] Duplicate publication	<input type="checkbox"/> [] Rejection
<input type="checkbox"/> [] Grade D: Fair	<input type="checkbox"/> [] Grade D: Rejected	<input type="checkbox"/> [Y] No	<input type="checkbox"/> [] Minor revision
<input type="checkbox"/> [] Grade E: Poor		BPG Search:	<input type="checkbox"/> [] Major revision
		<input type="checkbox"/> [] The same title	
		<input type="checkbox"/> [] Duplicate publication	
		<input type="checkbox"/> [] Plagiarism	
		<input type="checkbox"/> [Y] No	

COMMENTS TO AUTHORS

The paper is interesting. My comments are: The manuscript would benefit from inclusion of introducing/bridging sentences between the individual parts of the "Results" that explain the logical order and rationale for the experiments. In the Discussion, the Authors should highlight the possible clinical significance of their findings.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Biological Chemistry

ESPS manuscript NO: 29780

Title: B-1 cells modulate the murine macrophage response to Leishmania major infection

Reviewer's code: 00736297

Reviewer's country: Poland

Science editor: Jin-Xin Kong

Date sent for review: 2016-08-29 08:38

Date reviewed: 2016-10-24 19:53

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
		BPG Search:	<input checked="" type="checkbox"/> Major revision
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		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

The paper is interesting. My comments are: - how many mice were used in experiment - clarify how many experiments n=3? or replicates =3 were done for each measurement - why authors used Student's t test? probably the number of replicates was not too high, so non-parametric test seems to be better. If the number of experiments was high enough to check the distribution of variables, it shall be done and after that decision on using parametric or non-parametric test shall be made - the function of B-1 cells directly linked with paper topic shall be described e.g. triggering IL-10 production and lipid mediators production - description on Figures' axis and Figure legends

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Biological Chemistry

ESPS manuscript NO: 29780

Title: B-1 cells modulate the murine macrophage response to Leishmania major infection

Reviewer's code: 02269286

Reviewer's country: United States

Science editor: Jin-Xin Kong

Date sent for review: 2016-08-29 08:38

Date reviewed: 2016-10-25 22:12

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
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		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

The manuscript by Arcanjo et al have shown that B-1 cells contribute to the Leishmania major infection of murine macrophages. Their studies have demonstrated that Leishmania major infection first increases PGE-2 levels in the infected cells, which subsequently induce IL-10 expression in B-1 cells and further facilitate the proliferation of Leishmania major inside infected cells. Here are some issues that are needed to be clarify or corrected.

1. It is not clear if B-1 cells are much prone to Leishmania major infection? The authors only used B-1 cells as co-cultured cells. The authors had no data regarding the direct infection of Leishmania major on B-1 cells. In the experiment, the authors use a very high B-1: macrophage ratio of 10:1. What is the usual frequency of B-1 cells in macrophages?
2. The authors tried to point out that B-1 cells contribute to Leishmania major infection by providing IL-10. Although the anti-IL-10 antibody was used to in the study to support this hypothesis, it would be better for the authors to examine if simply providing macrophage cells with IL-10 instead of B-1 cells will also increase the infection. If IL-10 can be confirmed as the most critical factor, it can explain why macrophages from Balb/c XID mice (B-1 cells null) were still infected by Leishmania major, although at a lower infection rate than macrophages



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from Balb/c. 3. Fig 8, the authors stated that B-1 cells from IL-10 deficient mice were more competent to control L.major infection. This statement is misleading, as “control” means that the infection should be reduced. As shown in the figure, with or without IL-10 deficient B1 cells, infection of macrophages by L.major was not changed. Maybe it is much more proper to say that the IL-10 deficient mice failed to promote L.major infection. 4. Some references were missing. For example, in the section of “B1 cells” of Materials and Methods , the reference by Almeida et al is missing.