

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Transplantation

ESPS manuscript NO: 21206

Title: B cells with regulatory properties in transplantation tolerance

Reviewer's code: 00498408

Reviewer's country: United States

Science editor: Fang-Fang Ji

Date sent for review: 2015-07-05 23:47

Date reviewed: 2015-07-06 20:33

| CLASSIFICATION | LANGUAGE EVALUATION | SCIENTIFIC MISCONDUCT | CONCLUSION |
|--|--|--|--|
| <input checked="" 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 |
| <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 checked="" type="checkbox"/> No | <input checked="" 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 checked="" type="checkbox"/> No | |

COMMENTS TO AUTHORS

In this excellent review authors reported an overview on how regulatory B cells may interfere and facilitate allograft acceptance. The review is well written although a little bit too long and on the other side lacking of a crucial paragraph (The clinical side). I thus suggest the following before publication: 1. Reduce by 30% the length of the review, particularly for the section on complement which appear to long and the section on IL10 / IL35 which is way too long 2. Chapter on B cells and transplant rejection: again please cut the section on C3/C4d too much. Please include some relevant reference when discussing how to depleting or targeting B cells, the use of anti-CD22 should be mentioned [(i) Carvello M et al. Diabetes. 2012 Jan;61(1):155-65, (ii) Fiorina P, Sayegh MH. F1000 Biol Rep. 2009 May 28;1:39], furthermore the use of anti Blyss strategy should be mentioned as well (Zekavat G et al. J Immunol. 2008 Dec 1;181(11):8133-44). 3. In the section on Emerging role of regulatory B cells authors should mention and reinforce the appearance and reshape of B cell pool after the use of B cell depleting strategy. It is interesting to note that more immature B cells appear to be more regulatory (Fiorina P et al. Diabetes. 2008 Nov;57(11):3013-24) and how the targeting of B cells may be a double edge sword (also discussed in Kim JJ1, Rothstein DM, Markmann JF. Curr Opin



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Organ Transplant. 2015). Where is really ending the benefit and starting the harm in B cells depletion therapy? This is an open point. 4. Again the chapter on IL10/IL35 appeared to extensive , clearly well developed should clarify how sïstudy on extreme phenotype may help (Kleffel S et al Diabetes. 2015 Jan;64(1):158-71). Is it possible to see if patients with operative tolerance have different levels of Bregs? can be some of the study simply doomed by the study of Breg peripheral instead of more properly at Breg generation ability? Finally I really would like to see a chapter on clinical relevance or take home message for the clinician.