

# ESPS Peer-review Report

**Name of Journal:** World Journal of Immunology

**ESPS Manuscript NO:** 10362

**Title:** Costimulatory signals and activation of regulatory T cells

**Reviewer code:** 00698952

**Science editor:** Wen, Ling-Ling

**Date sent for review:** 2014-03-27 22:39

**Date reviewed:** 2014-04-04 17:29

| CLASSIFICATION  | LANGUAGE EVALUATION   | RECOMMENDATION                      | CONCLUSION  |
|---|---|-------------------------------------|---|
| <input checked="" 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"/> Existed    | <input checked="" 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"/> No records | <input type="checkbox"/> Rejection                                |
| <input type="checkbox"/> Grade D (Fair)                 | <input type="checkbox"/> Grade D: rejected                            | <input type="checkbox"/> Existed    | <input type="checkbox"/> Minor revision                           |
| <input type="checkbox"/> Grade E (Poor)                 |   | <input type="checkbox"/> No records | <input type="checkbox"/> Major revision                           |

## COMMENTS TO AUTHORS

The manuscript provides an excellent review on the mechanisms of the suppressive activity of Treg cells, and the regulation of Treg/T effector balance via the co-stimulatory CD28/CTLA-4/B7 and CD40/CD40L interactions. In addition, the authors provide valuable insights on the differential effects of blocking CD28/CTLA-4/B7 in relation to strength of the inhibition and the stage of the immune process. This is a thoroughly readable, enjoyable, and stimulating manuscript and highly recommended to readers interested in Treg cells and immunological tolerance induction, both in the preclinical and clinical perspectives. Raised below are just minor points, mainly concerning some slip-ups in English: 1) Should "several data" in Core Tip and Line 12 of Introduction be changed into "several studies"? 2) Line 22 of the next page of 2.1.1 where "divalent" should be "divalently" or "bivalently", and "monovalent" "monovalently". 3) Line 9 of 2.2: "So called" should be "the so-called"? 4) Line 11 of 3.2 "aglycosilated" and Line 13 "thomboembolic" are misspellings. 5) Line 3 of 3.3: it is not clear what the "alternative mechanisms of activation" refers to. Is it referring to the mechanisms mentioned in Section 3.4?

**ESPS Peer-review Report**

**Name of Journal:** World Journal of Immunology

**ESPS Manuscript NO:** 10362

**Title:** Costimulatory signals and activation of regulatory T cells

**Reviewer code:** 00503025

**Science editor:** Wen, Ling-Ling

**Date sent for review:** 2014-03-27 22:39

**Date reviewed:** 2014-04-10 23:46

| CLASSIFICATION  | LANGUAGE EVALUATION   | RECOMMENDATION                      | CONCLUSION   |
|---|---|-------------------------------------|--|
| <input type="checkbox"/> Grade A (Excellent)            | <input type="checkbox"/> Grade A: Priority Publishing                 | Google Search:                      | <input type="checkbox"/> Accept                        |
| <input checked="" type="checkbox"/> Grade B (Very good) | <input checked="" type="checkbox"/> Grade B: minor language polishing | <input type="checkbox"/> Existed    | <input type="checkbox"/> High priority for publication |
| <input type="checkbox"/> Grade C (Good)                 | <input type="checkbox"/> Grade C: a great deal of                     | <input type="checkbox"/> No records | <input type="checkbox"/> Rejection                     |
| <input type="checkbox"/> Grade D (Fair)                 | language polishing  | BPG Search:                         | <input type="checkbox"/> Rejection                     |
| <input type="checkbox"/> Grade E (Poor)                 | <input type="checkbox"/> Grade D: rejected                            | <input type="checkbox"/> Existed    | <input checked="" type="checkbox"/> Minor revision     |
|   |   | <input type="checkbox"/> No records | <input type="checkbox"/> Major revision                |

**COMMENTS TO AUTHORS**

The paper reviews an important issue concerning the regulation of effector and regulatory cells through costimulatory signals. The authors give us a precise review of current understandings on this subject. I will suggest some minor points to improve the quality of the paper: - the title could be more precise and restrict to B7 and CD40 molecules - a brief summary of B7 family could be included - since both molecules belong to TNF and TNFR families, other member could be included partially to summary difference and similarity between them in terms of regulation and effector of immune response - new function for IDO following crosslink with CTLA-4 could be added - difference in thymus and periphery and in induced and natural Tregs could be more detailed and received and special attention for readers - finally, many typing errors appear throughout the text.

**ESPS Peer-review Report**

**Name of Journal:** World Journal of Immunology

**ESPS Manuscript NO:** 10362

**Title:** Costimulatory signals and activation of regulatory T cells

**Reviewer code:** 00503107

**Science editor:** Wen, Ling-Ling

**Date sent for review:** 2014-03-27 22:39

**Date reviewed:** 2014-04-23 22:02

| CLASSIFICATION  | LANGUAGE EVALUATION  | RECOMMENDATION                      | CONCLUSION   |
|---|--|-------------------------------------|--|
| <input type="checkbox"/> Grade A (Excellent)            | <input checked="" type="checkbox"/> Grade A: Priority Publishing     | Google Search:                      | <input checked="" type="checkbox"/> Accept             |
| <input checked="" type="checkbox"/> Grade B (Very good) | <input type="checkbox"/> Grade B: minor language polishing           | <input type="checkbox"/> Existed    | <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"/> No records | <input type="checkbox"/> Rejection                     |
| <input type="checkbox"/> Grade D (Fair)                 | <input type="checkbox"/> Grade D: rejected                           | <input type="checkbox"/> Existed    | <input type="checkbox"/> Minor revision                |
| <input type="checkbox"/> Grade E (Poor)                 |  | <input type="checkbox"/> No records | <input type="checkbox"/> Major revision                |

**COMMENTS TO AUTHORS**

This is a nice review that talks about the specific role of costimulatory signals and their differential effects on blocking effector T vs. regulatory T (Treg) cells. The authors suggest that blocking CD40/CD40L pathway may provide a target to manipulate effector vs. regulatory T cell balance which may ultimately favor Treg activity. They also talk about other relevant factors that may affect these T cell subpopulations in the host. The information provided should help further understanding of the role of costimulatory signals in differential regulation of regulatory T cells in disease situations.