



SDI Review Form 1.6

Journal Name:	International Journal of TROPICAL DISEASE & Health
Manuscript Number:	2013_IJTDH_6481
Title of the Manuscript:	Thymic atrophy during infection as a host response to avoid tolerance to persistent pathogens
Type of the Article	Review

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound.

To know the complete guideline for Peer Review process, reviewers are requested to visit this link:

(<http://www.sciencedomain.org/page.php?id=sdi-general-editorial-policy#Peer-Review-Guideline>)



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PART 1: Review Comments

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
Compulsory REVISION comments	There are 2 points that need further clarification. In the second paragraph of page 7, it is not clear how OVA injection in <i>T. cruzi</i>-infected mice triggers immature thymocytes apoptosis. Was this experiment performed <i>in vitro</i>? If so, it is logic and is not infection-dependent. More details are required to explain that point and perhaps the mechanism behind this induction of DP thymocytes apoptosis. Second, How can re-circulating peripheral T cells undergo negative selection when they re-enter the thymus? Are there any studies clearly showing this process? Alternatively, T-cell death be mediated by other infectious agent-dependent mechanism(s)...	Point 1- In the revised manuscript, the appropriate changes were done in order to clarify the experiments in the CD4+ OVA-TCR specific transgenic mice (see page 7, line 163 and 165). Using this model, we have administered <i>in vivo</i> the OVA antigen into infected CD4+ OVA-TCR transgenic animals. As all the thymocytes undergoing differentiation from CD4+ OVA-TCR transgenic mice during intrathymic differentiation express T Cell Receptors OVA-specific, the majority of the CD4+ thymocytes recognizing OVA antigen in the thymus will undergo apoptosis in the negative selection phase. In this way, we show that the thymic negative selection, a crucial event of the thymopoiesis, was functional in <i>T. cruzi</i> infected animals. Point 2- The studies from Ref [33] show that infection of the thymus by mycobacteria targets T cell recirculation from the periphery to the thymus, which guarantees that the immune system can respond to thymic infection [lines 194-196, in the revised manuscript]. Since DCs are considered key players in the negative selection of specific-T cell [Ref. 49], presentation of mycobacterial antigens by thymic DCs would be able to induce clonal deletion of <i>M. avium</i>-specific T cells. This event is thought to be responsible for the observed host tolerance to <i>M. avium</i> [Ref. 48] – lines 186 to 190 in the revised manuscript.



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<u>Minor</u> REVISION comments	Some spaces between words are missing in the text; may be due to the processing of the document by the journal's system.	The new version of the manuscript has been reviewed accordingly to the indicated corrections.
<u>Optional/General</u> comments	Overall, this review provide a good general overview of some factors regulating/inducing thymic atrohy.	