Author’s response to reviews

Title: Benznidazole-treatment of late chronic Chagas' disease leads to an overall cytokine down-regulation that upon Trypanosoma cruzi antigen stimulation can be shifted towards a Type-1 modulated profile by monocytes, NK and CD8+ T-cells

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Author’s response to reviews:

To
Diana Marshall, BioMed Central
Editorial Office

Belo Horizonte, February 13th, 2012

Dear Editor,

Please find enclose the manuscript entitled “Benznidazole-treatment of late chronic Chagas' disease leads to an overall cytokine down-regulation that upon Trypanosoma cruzi antigen stimulation can be shifted towards a Type-1 modulated profile by monocytes, NK and CD8+ T-cells” by Sathler-Avelar and colleagues. We hope this manuscript will be found suitable for publication as full-length paper in the BMC infection Disease. We would like to inform that all data presented in this manuscript are original, unpublished and has not been simultaneously submitted elsewhere.

In this study, we have used short-term whole blood cultures to describe the cytokine profile of Bz-treated indeterminate Chagas disease patients-(INDt) as compared to untreated patients-(IND). Our findings demonstrated that IND presented increased levels of IL-10+neutrophils, IL-12+ and IL-10+monocytes and IFN-gamma+NK-cells. Moreover, IND showed slight increase of IL-4+CD4+T-cells and enhanced levels of IL-10+CD8+T-cells and B-cells. Additional analysis of cytokine Low and High producers also highlighted the presence of High cytokine producers within IND, including IL-10 from CD4+ T-cells and IFN-gamma from CD8+ T-cells, as compared to NI. The Bz-treatment lead to an overall cytokine down-regulation in the innate and adaptive
compartments, including low levels of IL-12+ and IL-10+ neutrophils and monocytes, IFN-gamma+NK-cells, IL-12+, TNF-alpha+, IFN-gamma+ and IL-5+CD4+T-cells and IL-10+B-cells, along with basal levels of cytokine-expressing CD8+ T-cells in INDt as compared to IND. The in vitro antigen stimulation shifted the cytokine profile toward a type 1-modulated profile, with increased levels of IL-12+ and IL-10+ monocytes, IFN-gamma+ and IL-4+NK-cells along with TNF-gamma+ and IFN-gamma+CD8+T-cells. Analysis of Low and High cytokine producers, upon in vitro antigen stimulation, further confirm these data. Together, our finding demonstrate the contribution of monocytes, NK and CD8+ T-cells as the major sources of cytokines to shift the down-regulated immune response of Bz-treated patients towards a type-1 modulated profile, to the beneficial effect of Bz-treatment during late chronic Chagas disease.

All subjects in this study signed an informed consent, approved by Ethical Committees of the Minas Gerais Federal University, Brazil. We all have seen and agreed to submit the present version of the paper.

Yours faithfully,