Author’s response to reviews

Title: Human T lymphotropic virus type 1 (HTLV-1) proviral load induces activation of T-lymphocytes in asymptomatic carriers

Authors:

RAIMUNDO C COUTINHO JR (raimundocoutinhoj@globo.com)
MARIA FR GRASSI (grassi@bahia.fiocruz.br)
ANA B KORNGOLD (anabeatrizquima@gmail.com)
VIVIANA N OLAVARRIA (vini_olavarria@hotmail.com)
BERNARDO GALVAO-CASTRO (bgalvao@bahiana.edu.br)
RITA E MASCARENHAS (rbethm@terra.com.br)

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Author’s response to reviews: see over
Dear Editor,

We thank you for your valuable comments and the opportunity to revise our paper for resubmission to BMC Infectious Diseases. The comments certainly improved the quality of our manuscript. We have responded to the reviewers’ suggestions as follows:

**Reviewer:** Magnus Evander

**Query 1:** The authors should explain why they decided on PVL 1% as the cut-off for their study. What happens with the significance if they had, for instance, selected 1.5% (median value in their study)?

**Reply:** We have included the following sentence in the discussion (lines: 208-215): A cut-off value of 1% for PVL was chosen to distinguish between low and elevated levels in accordance with the literature review by Golçalves et al. [20], which considered <1% as low, between 1-5% as intermediate and >5% as high. Although the median PVL was determined to be 1.5%, a highly variable percentage of infected cells was observed in included individuals (interquartile range of 0.12-5.3%). When the cut-off of 1.5 was selected, no significant differences were detected in the results presented in the manuscript. As such, the 1% PVL cut-off value was chosen as a representative value.

**Query 2:** Line 234: change “clearance” to “clear”.

**Reply:** The manuscript has been modified accordingly.

**Query 3:** Line 238: “on T CD8+ T-subset” must be modified.
Reply: We agree with the reviewer and have modified the manuscript accordingly.

Reviewer: Sören Andersson

Query 1. Introduction, p 3, line 72. The immunodepression in HIV infection does is not only caused by destruction of CD4 T cells. Other factors, such as general immune activation and exhaustion, could be briefly mentioned.

Reply: We have included the following sentence in the introduction (lines: 82-84): “The general activation and exhaustion of the immune system caused by HIV also plays an important role in the immunodepression observed in AIDS patients.”

Query 2. Methods p5, line 109. The company address for Ficoll-Hypaque should be checked (could be correct, but Pharmacia Biotech has been merged with GE Healthcare and changed name).

Reply: We thank the reviewer for his correction and have modified the manuscript accordingly.

Query 3. Results, figures. The numbers of persons included in the different groups seem to vary between the text in the manuscript and the figures. Please check. Was there any selection of no. of samples analysed or were all included? Please clarify.

Reply: The reviewer is correct in his observation that discrepancies exist between the number of individuals represented in the figures with respect to specific markers. Due to limited resources, it was not possible to comprehensively evaluate all included individuals for each parameter, i.e. the number of individuals evaluated for spontaneous proliferation (29 HTLV-1+ individuals) was greater than the number that were tested for CD4 and CD8 levels (20 HTLV-1+ individuals and 10 uninfected controls), which were prioritized over CD4+FoxP3+ (15 HTLV-1+ individuals and 5 uninfected controls); as such, there are discrepancies in the number of patients in Figures 1 & 2 versus Figure 3, etc. We have included this information in the methods section (lines: 104-107)
**Query 4.** Discussion, p 9-10, lines 205, 208 and 234. Typos (e T, inflammatory, clearance).

**Reply:** We have corrected typos. In addition, we have excluded the reference “Romero IA, Prevost MC, Perret E, Adamson P, Greenwood J, Couraud PO, Ozden S. Interactions between brain endothelial cells and human T-cell leukemia virus type 1-infected lymphocytes: mechanisms of viral entry into the central nervous system. J Virol. 2000 Jul;74(13):6021-30” about CD18 because the study was performed using in animal model.