Reviewer's report

Title: Cytokine profile, proliferation and phosphorylation pattern of ERK1/2 and Akt in circulating mononuclear cells from individuals with chronic intestinal phase of Schistosomiasis mansoni

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Reviewer: Fernanda de Araujo

Reviewer's report:

General Comments:
The authors evaluated the effects of Schistosoma mansoni antigens on cellular proliferation, cytokine production and ERK1/2 and Akt phosphorylation in PBMC from infected individuals from endemic area and control groups. The main result obtained indicates that CD4+ and CD8+ T cells from infected patients (XTO) have lower proliferation than BD group after SEA stimulation. SWAP antigens induced ERK1/2 phosphorylation but not SEA in XTO group and the culture supernatants showed a mix profile of cytokines production type 1 and type 2 after SEA and SWAP stimulation. The proposal is relevant in S. mansoni infection and the authors follow an important research line.

Major Compulsory Revisions

Abstract
Background: The sentence “To study the effects…” do not have a final conclusion. What is the objective? The sentence must start as: The aim of this project is to study…..
Conclusions: CD4+ PBMC? I assume that the authors meant: CD4+ T cells from PBMC ...

Results Section
First paragraph: The authors add in the results section figure 1 and do not discuss about that. They add the results in one sentence add the figure and do not justify the results during the discussion section. The discussion is necessary mainly because previous paper from the group showed differences in the Lymphocyte phenotyping. The previous work shows that “the HLA-DR+ expression on CD8+ was higher in PBMC from infected and non-infected individuals than from healthy donors”. The authors must explain better the difference between the studies and find some support in the literature about that.

Discussion Section
The authors should add the figures that they are referring next to the text.
Third paragraph: “fitting a typically Th0 profile.” The production of cytokine in the
present work was measured by CBA using supernatant of cultures. So, the authors should be careful when they said Th response. If the experiment have been done by intracitoplasmatic staining by flow cytometer (where do you separate the CD4 population) they could have said that, but the supernatant from culture includes all PBMC so it is hard to admit Th profile. It will be more reasonable said profile type 1 or 2.

The sentence “seems to fit a Th0 variation profile. What the authors meant by that? The sentence needs to be better explained.

All this part of the text must be more explored. The authors did not discuss about the meaning of having a mixture profile of cytokines during the chronic intestinal phase of S. mansoni infection. The authors must improve this section and find support in the literature to explain the importance of this pattern of cytokines for the evolution and pathology of the disease.

Fourth paragraph: I agree with the authors that IL-10 secretion was higher in SEA and SWAP from XTO cultures when compared with BD and that this cytokine can have a inhibitor role, but the text needs to be clarify, because the authors said that IL-10 appears to be blocking some cytokines such as IFN-#, IL-2 and TNF-a. However, when we go to the figure 3 the results showed that IFN-# is maintained after SWAP stimulation among the groups. IL-2 and TNF-a is increased after SWAP stimulation among the groups. So, I suggest that the authors should clarify better since this inhibition seams to be only after SEA stimulation when comparing XTO and BD.

Fifth paragraph: The authors suggest that CD8+T cells might be associated with increased synthesis of IL-4, IL-5 and IL-10, but again the experiment have been done in supernatant of cultures, not intracitoplasmatic staining. The authors should be careful when doing this association. How to explain the increase of TNF-a and IL-2 after SWAP stimulation?

Ninth paragraph: The authors during this section said that 120 hours time might have influenced the lack of results. Why the authors used this time must be better clarified in the text. Also the authors should be concern about the limitation of the results due to the number of patients per group in the phosphorylation assay.

Minor Essential Revisions

Background Section

Second paragraph: “….in infected patients (needs dot and also the references here). A typical PBMC…

Fifth paragraph: The authors discuss about MAPK and during the objective said ERK1/2. They must use the same name and also explain better what is ½.

Results Section

Second paragraph: Figure 2B should be 2B and F. Figure 2D and 2F should be Figure 2B,D and F.
Discussion Section
First Paragraph: The authors throughout the text said reactivity of CD8 or CD4. However they measured the proliferation and they did not show functional experiments to show the reactivity and also the activation markers are the same between the groups, so it is better instead said reactivity use proliferation.

Figure Legends: All the figure legends must contain the number of patients used in the experiment and the groups. Example: BD = blood donors volunteers; XTO = ..... 

Methods Section
First paragraph: The authors should standardize the text. Or the number should be written or add as numbers.

Eighth paragraph: the way that the authors describe the methodology is not well understood. For example the sentence: “Simultaneous quantification of six cytokines in a single sample using microparticle-based flow cytometry technology.”

The paper needs improvement in English writing and usage, to improve understanding.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.