Reviewer's report

Title: Phenotypic profiling of CD8+ T cells during Plasmodium vivax blood-stage infection

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Reviewer: Joseli Ferreira

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In this study, the authors report the phenotypic profiling of CD8+ T cells subsets from patient with uncomplicated symptomatic P. vivax malaria. The role of T-cell memory in the development of naturally acquired immunity to malaria is poorly understood. Therefore, data on this subject is important. However, the following are some of the concerns, which I raise about this manuscript. The authors must address these issues to achieve adequate level of clarity and quality of the information.

Major Compulsory revision

Introduction

It is not clear the author’s hypothesis for this study. What is the importance of CD8 T cells memory phenotypes during acute uncomplicated P. vivax infection?

Material and methods

The study is limited by the small sample size. The individuals should be described as patients and not as population (Study population and blood samples).

The manuscript would benefit with the inclusion of the information on parasitemia and previous exposure of patients.

Define what was considered uncomplicated malaria.

Describe the isolation of peripheral blood mononuclear cells in material and methods including if cells were used fresh or thawing cryopreserved cells. CD62L expression is lost following density gradient centrifugation, cryopreservation, TCR ligation or activation with PMA/ionomycin. Thus, CD62L is best utilized following overnight culturing subsequent to thawing cryopreserved cells.

The authors used PE-anti-human CCR7 and PE-anti-human CD62L; therefore, it is not possible to determine whether the CD62L- cells are CCR7+ or CCR7-.

Include a Figure (as supplementary figure) of representative dot plots showing the proportion CD8 T cells subsets defined by CD45RO, CD45RA, CCR7 and CD62L surface expression.

Results

It is very hard to evaluate central and effector circulating CD8 T memory cells in a small number of patients. It seems that the 20 P. vivax patients were tested for
plasma cytokine levels but only 16 patients had their cells phenotyped by flow cytometry. Is it true?

The reason why these CD8 T cells producing IL-10, IFN-# and TNF-# were specifically measured instead of others is not clear. It is also not clear the reason to do correlation analysis between these phenotypes.

Discussion

The authors highlight the high numbers of cells expressing IL-10 in the memory CD8 T cells subset, which correlates positively with the number of cells expressing TNF-# and the number of cells expressing IFN-# but does not give any hypothesis for their important findings

**Level of interest:** An article of limited interest

**Quality of written English:** Not suitable for publication unless extensively edited

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

**Declaration of competing interests:**

I do not have competing interests