TITLE: INFLUENCE OF *P. brasiliensis* INFECTION AND THE PEPTIDE (P10) ON THE DIFFERENTIATION OF DRENDRITIC CELLS FROM BONE MARROW OR MONOCYTE CELLS IN EXPERIMENTAL MODEL

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ABSTRACT:
Paracoccidioides spp. is a thermodymorphic fungus responsible for causing Paracoccidioidomycosis (PCM), which is a major Plublic Health problem, due to the existence of extensive endemic areas, extending from Mexico to Argentina, to the high disabling potential and causing large numbers of premature deaths. Therefore, studies for new treatment proposals for PCM have been performed, and clinical and experimental data indicate that a cell-mediated immunity plays significant role in host defense against *Paracoccidioides* infection. Experimental studies have shown that infection with *P. brasiliensis* (Pb18) can influence the differentiation of dendritic cells from bone marrow (BMDCs) or circulating monocytes (MoDCs). In the present study, circulating monocytes and bone morrow were obtained from non-infected or infected mice (BALB/c) with Pb18. BMDCs and MoDCs were differentiated in RPMI mediums in the presence of GM-CSF, IL-4 for 9 days, after incubation, both BMDCs and MoDCs were pulsed or not with P10 and labeled and analyzed in flow cytometry. BMDCs and MoDCs were divided into two subtypes and analyzed for the mean fluorescence intensity (MFI) of the surface molecules (CD80, CD86, MHC-II). BMDCs from infected mice showed no significant increase for both subtypes of BMDCs. However, when BMDCs obtained from infected or non-infected mice and pulsed with P10, they showed significant increase in MHC-II and CD86 molecules in $CD8a^-$ subtype, and a significant increase in MHC-II, CD80 and CD86 molecules in $CD8a^+$ subtype when compared to the BMDC from non-infected mice. MoDCs subtype $CD8a^+$ from infected mice showed higher expression of the CD80, whereas MoDCs from infected and non-infected mice, pulsed with P10, had higher expression of the MHC-II and CD86 for $CD8a^-$ and $CD8a^+$ subtypes when compared to MoDCs from non-infected mice. The infection with Pb18 does not seem to affect the generation of both BMDCs and MoDCs, since the percentages of $CD11c^+MHC\text{-}II^+$ cells after differentiation are similar. The fact that the mice were infected with pb18 positively modulated the MoDCs, where these cells present a phenotypic profile favorable to combat infection. Our results demonstrate that there is previous modulation in MoDCs when from infected mice. And the P10 peptide is able to positively modulate both the BMDCs and MoDCs.

Keywords: Paracoccidioidomycosis; *Paracoccidioides brasiliensis*, Dendritic Cells, Peptide P10

Development Agency: Fundação de Amparo à Pesquisa da Estado de São Paulo (FAPESP) (Processo: 2016/08730-6; 2018/25171-6)