THE IMPACT OF EXTRACELLULAR VESICLES DERIVED FROM *Trypanosoma cruzi* ON THE REGULATION OF PRIMARY MONOCYTES AND THEIR EFFECT ON THE DIFFERENTIATION OF M1/M2 MACROPHAGES

Juliana Fortes Di Iorio1,2; Anna Julia Pietrobon 3; Nadjania Saraiva de Lira Silva 2; Maria Notomi Sato 3; Ana Claudia Trocolli Torrecilhas1,2

[1] Universidade Federal de São Paulo (UNIFESP); Instituto de Ciências Ambientais, Químicas e Farmacêuticas; Departamento de Ciências Farmacêuticas; Laboratório de Imunologia Celular e Bioquímica de Fungos e Protozoários. Departamento de Ciências Farmacêuticas, UNIFESP, São Paulo, Brasil.
[2] Escola Paulista de Medicina, Universidade Federal de São Paulo, São Paulo, Brasil.
[3] Laboratory of Dermatology and Immunodeficiencies, LIM-56, Department of Dermatology, Tropical
Medicine Institute of São Paulo, University of São Paulo Medical School, São Paulo, Brazil
*Autor correspondente: juliana.fortes@unifesp.br

Chagas disease (CD) is defined as a neglected tropical disease. It is estimated that approximately 6 to 8 million individuals have been infected, with the majority of cases occurring in Latin American countries. The increase in immigration has also seen the amount increase up in the US, Europe, and Asia. Benznidazole and nifurtimox are used to treat the disease. It functions better in the acute phase, but they are not very effective and are quite risky in the chronic phase. The analysis of extracellular vesicles (EVs) derived by parasites, especially *Trypanosoma cruzi*, is important in the discovery of biomarkers, understanding of immunopathogenesis, and the development of novel therapeutic strategies for the treatment of Chagas disease (CD). Investigation of the modulation of the immunological response, specifically monocytes, promoted by extracellular vesicles from the trypomastigote form of the Y strain of *T. cruzi*. We obtained PBMCs using the Amnis flow cytometer. The flow cytometer Amnis, after incorporating *T. cruzi* EVs that were marked with PKH26. In the first 60 minutes of the contact, this method was carried out. We used actin markers, vinculin, and the nucleus to track how THP-1 cells changed shape with microscope scanning and confocal electron microscopy. Flow cytometry, using the kit BD™ CBA, was used to maintain track of the changes in cytokine production (IL-8, IL-1β, IL-6, IL-10, TNF, and IL-12P70). The results showed that the initial interaction between PBMCs and *T. cruzi* EVs resulted in an enhancement in the phagocytic activity of monocytes, in addition to an increased concentration of EVs in the peripheral region of the cells. Based on the decision, the studies that followed were performed using monocytes. The morphological analyses demonstrated that EVs change the cell surface, triggering communication tubules that emphasize a more dynamic cellular state and enhance interactions among cells that are adjacent. The rearranging of the actin cytoskeleton with vinculin. *T. cruzi*'s EVs can activate human monocytes and allow them to distinguish, which leads to an abundance of M1 macrophages. In conclusion, *T. cruzi* EVs interact with monocytes, changing their structure and helping them become M1 macrophages.

Palavras-chaves: Trypanosoma cruzi, Extracellular vesicles, Monocyte.

Apoio: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), Fundação de Amparo à Pesquisa do Estado de São Paulo - FAPESP (FAPESP)