

## **Evaluation of the therapeutic potential of mesenchymal stem cells overexpressing lif in a model of chronic chagas cardiomyopathy**

**Maria Gabriela Sarah Santos<sup>1</sup>, Breno Cardim Barreto<sup>2</sup>, Milena Botelho Pereira Soares<sup>3</sup>**

<sup>1</sup> Gonçalo Moniz Institute, Oswaldo Cruz Foundation (IGM-FIOCRUZ/BA), Salvador, Brazil.

<sup>2</sup> SENAI Institute of Innovation in Health Advanced Systems (CIMATEC ISI SAS), University Center SENAI/CIMATEC, Salvador, Bahia, Brazil.

<sup>3</sup> Health Sciences Institute of UFBA (Federal University of Bahia), Salvador – BA, Brasil.

Chagas disease, caused by the protozoan parasite *Trypanosoma cruzi*, poses a significant global health challenge, particularly in endemic countries. Chronic cardiomyopathy, a severe manifestation of the disease, is characterized by inflammation, fibrosis, and subsequent heart failure. Current treatments, such as benznidazole, have limited efficacy during the chronic phase, underscoring the need for innovative therapeutic strategies. We hypothesize that the administration of MSC-LIF promotes cardiac repair through anti-inflammatory and regenerative mechanisms. The expected outcomes may provide insights into novel therapies for Chagas disease and contribute significantly to the field of regenerative medicine. Therefore, the aim of this work was evaluate the therapeutic potential of mesenchymal stem cells (MSCs) that overexpress leukemia inhibitory factor (LIF) in a model of chronic Chagas cardiomyopathy. This study utilizes an experimental model where black C-57mice were infected with *T.cruzi* Colombian strain, and after 4 months of infection they were treated with the cells, which was performed by weekly intravenous injections of cell suspensions containing  $1 \times 10^6$  MSCs or MSC\_LIF. Post-treatment, Mice underwent ergometric tests to evaluate cardiac function, and after euthanasia the organs were collected for analysis. Although there was no improvement in the exercise capacity of mice infected with *T. cruzi*, the administration of LIF-overexpressing MSCs (MSC-LIF) and wild-type MSCs (MSC-WT) resulted in a significant reduction in inflammation when compared to the vehicle group, with no significant difference between MSC-LIF and MSC-WT. However, in terms of fibrosis analysis, MSC-LIF demonstrated superior outcomes compared to all other groups.

Financial Viability: The project has financing from Pronex (PNX 0002/2014).

Keywords: Chronic Chagas cardiomyopathy (CCC); cell therapy; mesenchymal stem cells;