

TITLE: THE ROLE OF TREG CELLS IN THE ERYTHEMA NODOSUM LEPROSUM IN LEPROMATOUS LEPROSY

AUTHORS: CASTRO, K. K. G.; LEAL, J. M. P.; PEREIRA, M. M. P.; NERY, J. A. C.; SARNO, E. N.; ESQUENAZI, D.

INSTITUTION: LEPROSY LABORATORY, OSWALDO CRUZ FOUNDATION – RIO DE JANEIRO (AVENIDA BRAZIL, 4365, MANGUINHOS, CEP 21045-900 – RIO DE JANEIRO – RJ, BRAZIL).

ABSTRACT:

Leprosy is a chronic infectious disease that primarily affects peripheral nerves and skin. The *Mycobacterium leprae* (ML), its etiologic agent, preferably infects macrophages, Schwann cells and vascular endothelium. The presentation of the disease varies according to the balance between host's immune response and the dissemination of the pathogen, that leads to a spectrum of clinical forms, namely lepromatous and tuberculoid, and intermediate forms as well. Due to neurological damages resulting from skin lesions with reduced sensibility, leprosy can originate disabilities that are often irreversible. About half of lepromatous leprosy patients present acute inflammatory episodes known as reactions, in which cases patients undergo difficulties in the therapeutic management, in addition to the risk of hospitalization and death. The Erythema Nodosum Leprosum (ENL) is one of these episodes, that can occur at any step of multidrug therapy, including before treatment. At the onset of this clinical presentation, the cellular immune response evolves to a reactive scenario that still requires clarification. The purpose of this work was the phenotypic and functional characterization of peripheral Treg CD4⁺ and CD8⁺ lymphocytes, both *ex vivo* and in response to ML. For such, 10 LL patients were studied at the onset of ENL, whose data were compared to 10 non-reactional LL and to 10 healthy volunteers (HV) of endemic area to the disease, all of them living in Rio de Janeiro. The frequency of these cells was assessed *ex vivo* and the functionality thereof *in vitro*, through IL-10⁺ and TGF-β⁺ producing cells, by multiparametric flow cytometry. A significant reduction of Treg CD4⁺ cells was observed *ex vivo* and *in vitro* in ENL ($p < 0,001/p < 0,0001$), when compared to non-reactional LL. ML provoked a slight increase of this subset in both groups. As disclosed by the assessment of this functional activity *in vitro*, TGF-β producing Treg CD4⁺ cells were significantly reduced in ENL when compared to non-reactional LL ($p < 0.05$), while IL-10 producing Treg CD4⁺ cells did not vary among the groups. As indicated by our results, Treg CD8⁺ cells are not involved with the onset of ENL. Our data suggest a transient change in the regulation of the immune response shown by Treg CD4⁺ lymphocytes in ENL, thus transforming the microenvironment in a favorable scenario to the development of such reactional process.

KEYWORDS: leprosy, ENL, Treg, TGF-β, IL-10.

FINANCIAL SUPPORT: CNPq, PAPES-FIOCRUZ, PAEF-FIOCRUZ.