THE ROLE OF ADIPOCYTES IN MYCOBACTERIUM LEPRAE INFECTION, IMUNE MODULATION AND PERSISTANCE

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Leprosy, a chronic-systemic infectious disease that mainly affects the skin and peripheral nerves, is caused by *Mycobacterium leprae*. Currently, South Sudan and Brazil are the countries that lead the ranking of leprosy prevalence. Studies have shown the importance of host lipids for *M. leprae* survival. Despite the deep understanding of the mechanisms involved, there is no research about the interaction of mycobacteria within adipocytes, specialized cells in lipid homeostasis of the organism. Herein, we investigate the effects of *M. leprae* infection and its possible persistence in these cells. Murine 3T3-L1 fibroblasts were differentiated to adipocytes in DMEM high medium containing 10% fetal calf serum, 0.5 mM 3-isobutyl-methylxanthine, 1µM dexamethasone, 2µM rosiglitazone and 0.3 UI/ml of insulin. After day 3, medium was replaced by DMEM-10% FCS containing only 2µM rosiglitazone and 0.3 UI/ml insulin until day 10, then, cells were infected by *M. leprae*. Infection rate was measured as well as its viability within cells by detecting 16S RNA gene levels and the behavior of infected cells analyzed. We detected bacilli in multibacillary patients biopsies of subcutaneous adipose tissue, confirming the presence of intact mycobacteria associated to adipocytes in vivo. We also analyzed changes in lipid homeostasis and the production of adipokines in vitro. Our results showed that the bacilli remain viable in 3T3-L1 adipocytes for up to 25 days. We observed a 20-fold increase of IL-10 and TNF-α expression while IL-6 levels was not altered in infected cells, suggesting an immunosuppressive modulation profile during infection. Finally, we observed by fluorescence microscopy and flow cytometry changes in the lipid profile indicating lipolysis induction in cultures infected by *M. leprae*. Our investigations suggest that adipose tissue could act as a new niche for *M. leprae* persistence, opening new paradigms for description of immunopathological effects, chronicity and treatment of the disease.

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