

Evaluation of the *Mycobacterium tuberculosis* cell wall lipid-induced response in individuals with pulmonary tuberculosis

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A large part of the genome of *Mycobacterium tuberculosis* (Mtb), the etiologic agent of tuberculosis (TB), is dedicated to lipids biosynthesis and degradation. Previous studies have shown that the Mtb cell wall lipids play important role in inducing the host immune response. One of the regulatory mechanisms involved in the Mtb cell wall reorganization involves the operon *mce1*. Disruption of this operon promotes an important remodelling of cell wall lipid composition in the bacillus, mechanism that seems to allow the Mtb to establish a long-term infection in the host. The Mtb cell wall lipids interact with human lipid sense nuclear receptors (LSNR) which modulate the expression of genes involved in immune responses, during the infectious process. Therefore, the aim of this study was to evaluate the Mtb cell wall lipid-induced responses in patients with active and latent TB infection (LTBI). Thus, peripheral blood mononuclear cells (PBMC) from eight, two and three volunteers with, respectively, active TB, LTBI and healthy controls were stimulated *in vitro* by apolar lipids extracted from the Mtb strains, *mce1* operon mutant ($\Delta 1$) and its parental wild-type (WT), for 72h. The quantification of LSRNs genes and their targets were obtained by reverse transcription quantitative PCR (RT-qPCR). Apolar lipid extract from WT strain induced a higher level of *TR4* and lower of *IFN- γ* genes in the cells from patients with active TB compared to individuals with LTBI. Lipid extract of both strains, WT and $\Delta 1$, induced a lower expression of *LXR- α* in cells of individuals with LTBI, as compared to healthy controls. Although the number of patients precluded us to obtain any statistically significant results, the data herein presented suggested that cell wall lipid extract from both WT and $\Delta 1$ strains seem to induce distinct responses in individuals with active TB and LTBI.

Keyword: active TB, latent TB infection, lipid-sensing nuclear receptors.

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