Immunomodulatory property of rifampicin during *Mycobacterium sp.* infection.

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Tuberculosis, a disease caused by mycobacteria of the *Mycobacterium tuberculosis* complex (MTC), is currently the leading cause of death by a single infectious agent according to the world health organization (WHO). Rifampicin is an antibiotic widely used against tuberculosis, inhibits the synthesis of DNA-dependent RNA polymerase from bacteria, forming a stable complex (Wehrli et al. 1968) but not of mammalian origin, even in high concentrations (Wehrli and Staehelin 1971). Even though this process is extremely specific, rifampicin presents immunomodulatory actions in the host (Rook 1973, Arioli et al. 1973, Nilsson 1971, Păunescu 1970) however; the host target is yet to be determined. Considering that, in the present work we demonstrated in the mice model of pleural infection by *M. bovis*- BCG, rifampicin treatment modulated the cell influx as well as the inflammation within the pleural cavity, in the same way as the steroidal anti-inflammatory, dexamethasone, which is excerpted of antibiotic properties. Both were able to inhibit the release of mediators and neutrophil influx to the site of infection. In agreement with our *in vivo* observations, rifampicin presented a predominant anti-inflammatory action in macrophages infected with the attenuated strain *M. bovis*- BCG and the virulent *M. tuberculosis* H37Rv. Nitric oxide (NO) was inhibited by rifampicin in the infected macrophages and TNF-α release by infected macrophages was impaired after rifampicin treatment. In addition, infected macrophages treated with rifampicin presented a well-balanced relationship between IL-12, IL-10 and PGE_2, where the second two were inhibited by the treatment. Furthermore, we observed a decreased in lipid bodies (LB) accumulation via PPAR-γ expression inhibition. Using computational models we also demonstrated that rifampicin was able to bind to PPAR-γ binding site.
Our results presented here evidence of an immunomodulatory property of rifampicin *in vivo* and *in vitro* and propose, *in silico*, a new mechanism of action by which rifampicin could be helpful to the host in order to restrict the mycobacteria infection and the inflammatory process harmful to the host.

Key words: Rifampicin, immunomodulation, tuberculosis

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