

TITLE: COMPARATIVE STUDY OF THE BEHAVIOR OF *Mycobacterium bovis* BCG STRAINS MOREAU AND PASTEUR IN THE INTRACELLULAR ENVIRONMENT OF THP-1 MACROPHAGES

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ABSTRACT:

The BCG vaccine (Bacille Calmette-Guerin), only prophylactic measure against tuberculosis (TB), was obtained in the early twentieth century by Calmette and Guérin after 231 passages of a *M. bovis* clinical isolate in medium containing glycerin and bovine bile. Its protective efficacy against pulmonary TB in adults varies from 0-80% and the genetic differences among vaccine strains used worldwide contribute to this variation. The Brazilian vaccine strain, BCG Moreau, is considered to be a primitive strain and more immunogenic, closer to the original BCG when compared to more recent strains, such as BCG Pasteur. Data from our group identified differences between the genomes and the proteomic profiles of BCG Moreau and Pasteur. From this information, it became important to observe how these strains respond to the existing microenvironment in the macrophage. BCG phagocytized by the macrophage undergoes different types of stress, which can lead to different molecular responses. This pattern of response to stress varies between BCG strains and may impact on the protective efficacy of the vaccine. To evaluate the survival of the strains, their colocalization with acidified vesicles, the pattern of secret cytokines and biogenesis of the lipid droplets, THP-1 human monocytes were differentiated to macrophages with PMA and infected with BCG strains Moreau and Pasteur. Our results suggest different viability between these strains, with changes in colony morphology post-infection (p.i). At 6 hours p.i BCG Pasteur was found to be more colocalized with acidified vesicles when compared to BCG Moreau. This profile is altered at 24 hours p.i. The profile of cytokines secreted by THP-1 macrophages in response to infection also shows alteration according to the strain used, with increased secretion of IL-1 β and MCP-1 in the case of BCG Pasteur, and increased levels of TNF- α , MIP-1 β and IL-6 for BCG Moreau. The biogenesis of lipid droplets is also influenced by the strain used in the infection. This information can contribute to the characterization of the response profile of the two strains of BCG to the intracellular environment of the macrophage, identifying differences in BCG Moreau and a better understanding of the physiology of the Brazilian vaccine strain against tuberculosis.

Keywords: BCG Moreau, tuberculosis, THP-1 human monocyte, Stress

Financial Support : CNPq, IOC, Fiocruz

