

**Título: CHARACTERIZATION OF THE BCG MOREAU RESPONSE PROFILE TO THE INTRACELLULAR ENVIRONMENT OF MACROPHAGES.**

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**Resumo:**

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 vaccines strains used worldwide contribute to this variation. The Brazilian vaccine strain, BCG Moreau, is considered a primitive strain and more immunogenic, closer to the original BCG when compared to newer strains, such as BCG Pasteur (reference strain). Data of 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 are responding to the existing microenvironment in the macrophage. The BCG phagocytized by 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 effect of the vaccine. To evaluate the viability of the strains, their colocalization with acidified vesicles and the pattern of protein expression linked to response to stress, THP-1 human monocytes were differentiated to macrophages and infected with BCG strains Moreau, Pasteur and Tokyo. The results suggest different viability between strains, with similar profile between BCG Moreau and Tokyo, distinguished from the BCG Pasteur. At 6 hours post-infection (p.i.) no bacilli colocalized with acidified vesicles, whereas within 24 hours all strains studied were colocalized with acidified vesicles. Detection of the HspX protein in BCG Moreau, Pasteur and Tokyo indicates the opening of DevR regulon, responsible for hypoxia response. The HspX protein was detected in BCG Moreau and Tokyo only at 24 hours p.i., while in BCG Pasteur the expression of this protein is detected as early as 4 hours p.i., increasing throughout the studied times. This information aim to contribute to the characterization of the response profile of the three strains of BCG to the intracellular environment of the macrophage, identifying differences in BCG Moreau that will contribute to a better understanding of the physiology of the Brazilian vaccine strain against tuberculosis.

**Palavras-chaves:** BCG Moreau, tuberculosis, THP-1 human monocyte, Stress

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