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The *in vitro* T-cell profile induced by Moreau BCG monocyte infection in healthy volunteers

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Tuberculosis (TB) remains the world's leading cause of mortality. For its control, studies of TB vaccines are needed. Since BCG is the only vaccine against TB currently in use, studies addressing the protective role of BCG are urgent necessary.

OBJECTIVES: Emerging evidences suggest that early antigenic presentation is a pivotal mechanism leading to a better
immune response in TB vaccine models. Here, we aim to study the in vitro cellular immune response against Moreau BCG in Brazilian healthy voluntaries.

METHODS: In this study, voluntary cohorts of HIV-negative adult control donors (HD; n=18) and neonates umbilical vein (UV; n=10) have been enrolled, and BCG Moreau strain has primarily been used for *in vitro* PBMC infections. After 48 hours, CD4+ and CD8+ T lymphocytes were harvested and stained for PD-1 and CD25/FoxP3. In addition, supernates were assayed for broad cytokines detection by an array system.

RESULTS: The *in vitro* specific T cell-immune responses against PPD and *Mycobacterium bovis* BCG and hsp65 antigen were accessed using an in-house IFN-g ELISPOT assay, which showed to be positive exclusively for HD individuals. For PD-1 and Treg cells (CD4+/CD25high+/FoxP3+), higher levels were observed in HD-derived CD4 lymphocytes only ($p<0.05$). On the other hand, expression of CD25dim+ as an activation marker was dependent on BCG infection only in the UV group ($p<0.05$). The Th1 (IL-2, TNF-a and IFN-g) and regulatory (IL-10) cytokine profiles were promptly induced merely in the HD group.

CONCLUSIONS: The majority of the world's population has been vaccinated with BCG, with the potential condition for a booster immunization in adulthood for TB protection. In theory, a booster immunization may protect the BCG-immunized individuals and further studies are needed to evaluate these findings.