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CITATION OF THE RESEARCH WORK

Stimulating naïve T cells during initial infection or vaccination is crucial for the developing effector and memory T cells, which plays a pivotal role in offering immediate and long-term protection. However, the existing approaches like BCG vaccination and treatments haven't been successful in establishing long-lasting memory often leading to recurrent TB. Is this study, we have found that Berberine can bolster the body's natural defense mechanisms against *M.tb.* This compound also encourages the differentiation of Th1/Th17 specific effector memory (T_{EM}), central memory (T_{CM}), and tissue-resident memory (T_{RM}) responses ultimately enhancing the host protection against both drug-sensitive and drug-resistant TB. The study delved into the underlying mechanisms by analyzing the entire set of proteins in human PBMCs from PPD^+ individuals. We also discovered that BBR orchestrates the NOTCH3/PTEN/AKT/FOXO1 pathway in driving heightened T_{EM} and T_{RM} responses within $CD4^+$ T cells. Further, BBR-induced glycolysis led to stronger effector functions resulting in superior Th1/Th17 responses in both human and mice T cells. We observed that this regulation of T cell memory by BBR remarkably augmented the immune response triggered by BCG vaccination, effectively reducing the occurrence of TB recurrence due to relapse and reinfection. This finding highlights the potential of adjusting immunological memory as a viable strategy to enhance the host's ability to resist TB. This study identifies BBR as a promising supplementary approach for TB immunotherapy and immunoprophylaxis.

Place: New Delhi

Signature of the Nominator

Date: 29-08-2023