

*Citation (summary) on the outstanding research work on which the award is claimed in about 250 words signed by the nominator.*

*Age-Related Immune Decline and Gut Dysbiosis.* This groundbreaking novel investigation of Prof Agrewala focuses on the age-related decline in immune tolerance, contributing to autoimmunity. Aging disrupts the gut's microbial balance, resulting in immune system dysregulation. The study explores the reciprocal impact of gut dysbiosis on DC tolerance, revealing significant insights. The main findings are: DCs from aged individuals (DC<sup>Old</sup>) and young individuals with gut dysbiosis (DC<sup>Dysbiotic</sup>) exhibited diminished tolerance.

Tolerance loss in DC<sup>Old</sup> and DC<sup>Dysbiotic</sup> involved NF- $\kappa$ B hyperactivation, reduced regulatory T-cell frequency, altered cytokine levels, and compromised anti-inflammatory factors. Understanding the mechanisms behind immune tolerance decline in aging and its association with gut dysbiosis opens avenues for novel interventions. The restoration of gut microbial balance, particularly through the reintroduction of Lactobacillus strains, holds promise for reversing age-related immune dysregulation and combating associated disorders.

*Mtb Pathogenesis and DC Transformation.* The research investigates *Mycobacterium tuberculosis* (*Mtb*) pathogenesis, focusing on the impact of the MPT64 protein. The main findings of the study are that pre-exposing differentiating DCs to MPT64 (DC<sup>MPT64</sup>) transforms them into myeloid-derived suppressor cells (MDSCs). The MDSCs display metabolic alterations that compromise *Mtb* phagocytosis, providing a safe shelter for the pathogen. The mechanism behind DC transformation involves increased production of methylglyoxal. Targeting the unique mechanisms revealed by this study could potentially pave the way for innovative interventions against tuberculosis.

These novel studies unveil age-related immune decline, gut dysbiosis effects, and *Mtb* interaction with DCs. They promise transformative therapies and immune understanding.



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