A signed statement from the applicant to the effect that the research work under reference has not been given an award in the past. The applicant should also indicate the extent of the contribution of others associated with the research and he/she should clearly identify his/her achievements (not to exceed 500 words).

The age-related decline in immune tolerance contributes to a range of autoimmune and inflammatory diseases. Dendritic cells (DCs) play a vital role in maintaining immune balance by generating regulatory T-cells and cytokines. Aging disrupts the gut's microbial balance, resulting in immune system dysregulation. However, the reciprocal impact of gut dysbiosis on DC tolerance remains largely unknown. Consequently, we investigated how aging influences gut dysbiosis and its effect on DC tolerance loss.

We observed that DCs generated from aged individuals (DC^{Old}) or young individuals with gut dysbiosis ($DC^{Dysbiotic}$), but not from young individuals (DC^{Young}), exhibited diminished tolerance. This was evident from their inability to effectively induce regulatory T-cell generation and control CD4 T cell overactivity. The primary mechanism underlying tolerance loss in DC^{Old} and $DC^{Dysbiotic}$ was the hyperactivation of NF-κB, decreased regulatory T-cell frequency, heightened levels of pro-inflammatory molecules (IL-6, IL-1β, TNF-α, IL-12, IFN-γ), and reduced anti-inflammatory factors (IL-10, TGF-β, IL-4, IDO, arginase, NO, IRF-4, IRF-8, PDL1, BTLA4, ALDH2). Notably, there was a substantial reduction in the abundance of the Lactobacillus genus in the gut.

Restoring the *Lactobacillus plantarum* population in the gut of aged mice revitalized the tolerogenic function of DCs by reshaping inflammatory and metabolic pathways. This study highlights, for the first time, the impact of age-related gut dysbiosis on the breakdown of DC tolerance. This discovery could potentially pave the way for therapeutic strategies targeting age-related disorders using *Lactobacillus plantarum* interventions (**Aging Cell 2023, Impact factor: 11**).

Contributions: **I conceived the idea of the study, wrote and received grants, planned, designed, executed and troubleshooted the experimental problems, data analysis and interpretation, and manuscript writing.** H Bashir is my PhD student and did all the experiments. S Singh is my PhD student and worked with Hilal when big experiments

involving>50 mice were performed. RP Singh a PhD student of R Kumar, helped us with gut microbiota data analysis. R Kumar helped with gut microbiota data analysis and interpretation.

Mycobacterium tuberculosis (Mtb) is a smart and successful pathogen since it can persist in the intimidating environment of the host by taming and tuning the immune system. *Mtb* releases MPT64 (Rv1980c) protein in high amounts in patients with active tuberculosis (TB). Consequently, we were curious to decipher the role of MPT64 on the differentiating dendritic cells (DCs) and its relation to evading the immune system. We observed that pre-exposure of differentiating DCs to MPT64 (DC^{MPT64}) transformed them into a phenotype of myeloid-derived suppressor cells (MDSCs). DC^{MPT64} expressed a high level of immunosuppressive molecules PD-L1, TIM-3, nitric oxide (NO), arginase 1, IDO-1, IL-10 and TGF-β, but inhibited the production of pro-inflammatory cytokines TNF-α, IL-6 and IL-12. DC^{MPT64} chemotaxis function was diminished due to the reduced expression of CCR7. DC^{MPT64} promoted the generation of regulatory T cells (Tregs) but inhibited the differentiation of Th1 cells and Th17 cells. Further, high lipid and methylglyoxal content, and reduced glucose consumption by DC^{MPT64}, rendered them metabolically quiescent and consequently, reduced DC^{MPT64} ability to phagocytose *Mtb* and provided a safer shelter for the intracellular survival of the mycobacterium. The mechanism identified in impairing the function of DC^{MPT64} was through the increased production and accumulation of methylglyoxal. Hence, for the first time, we demonstrate the novel role of MPT64 in promoting the generation of MDSCs to favour *Mtb* survival and escape its destruction by the immune system (**Cell Mol Life Sci. 2022, Impact factor: 9.2**).

Contributions: **I conceived the idea of the study, wrote and received grants, planned, designed, executed and troubled shooting of the experiments, data analysis and interpretation, and manuscript writing.** S Singh is my PhD student and did all the experiments. SK Maurya, M Aqdas, and H Bashir are my PhD students and worked with S Singh when big experiments involving>50 mice were performed. A Arora provided control *Mtb* proteins ESAT-6 and CFP10. V Bhalla helped with electron microscope pictures and analysis.

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