1.25 Characterization of the role of human MIF in driving enhanced house dust mite-mediated trained immunity in vitro

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Background: Trained immunity (TI) describes a phenomenon by which innate immune cells acquire an immunological memory resulting in elevated levels of pro-inflammatory cytokines following exposure to secondary pathogenic stimuli. Trained responses can be harmful in the context of asthma as the surge in cytokine production can further drive exacerbations. Recent literature shows that increased expression of pro-inflammatory cytokine, macrophage migration inhibitory factor (MIF) enhances trained responses in macrophages from mice containing the high expressing human MIF polymorphism, in response to the allergen house dust mite (HDM). **Methods:** Bone marrow-derived macrophages (BMDMs) from humanized MIF mice with the low-expressing ($CATT_5$) or the high-expressing ($CATT_7$) promoter polymorphism or wild type (WT) controls, were HDM trained *in vitro*, prior to LPS exposure. Seahorse extracellular flux analysis and epigenetic inhibitors demonstrated altered cellular phenotypes.**Results:** HDM-trained $CATT_7$ BMDMs show significantly enhanced production of cytokines like IL-1b, IL-6, and TNFa in response to secondary insults with LPS in comparison to both $CATT_5$ and WT BMDMs. As well as having increased pro-inflammatory cytokine production, trained macrophages have altered metabolic and epigenetic phenotype post HDM-stimulation. **Conclusion:** High human MIF expression correlates to an enhanced HDM-induced trained response which may drive further more severe exacerbations in asthmatic patients. **Disclosures: Conflict of Interest:** The Authors declare that they have no conflict of interest.