10.02 IL-10 induces homeostatic plasticity in Th1 primed human alveolar macrophages.

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Background: Alveolar macrophages (AM) are the most prevalent immune cells in the lung and the first line of defence against pathogens. AM are of yolk-sac derived origin and self-renewing in the lung. Th1 mediated immunity is crucial to control infections in the lung, however, there is a paucity of data on the plasticity of AM after activation by Th1 cytokines such as Interferon-γ (IFN-γ).

Methods: To model homeostatic plasticity *in vitro*, human AM were treated with IFN-γ before subsequent treatment with IL-10. Activation marker expression was determined using flow cytometry. Metabolic profiles were assessed by Seahorse metabolic-flux analysis and PCR. To examine functional responses, AM were stimulated with Lipopolysaccharide (LPS) or *Mycobacterium tuberculosis* (Mtb) lysate and cytokine production was quantified by ELISA.

Results: IFN-γ increased expression of CD40 and HLA-DR in human AM, subsequent IL-10 stimulation only reduced HLA-DR. IFN-γ treated AM stimulated with LPS or Mtb lysate had increased TNF production which was attenuated by IL-10 treatment. IFN-γ primed IL-10 treated AM had increased glycolysis and oxidative phosphorylation compared to controls, suggesting metabolic control of homeostasis in human AM.

Conclusion: Th1 induced inflammatory AM can revert to a homeostatic state by IL-10 involving an increase in metabolism.

Keywords: Infection, Alveolar Macrophage, *Mycobacterium tuberculosis*, glycolysis, oxidative phosphorylation

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