10.01 Supporting alveolar macrophage function to enhance immune responses to *Mycobacterium tuberculosis* in the lung.

Sarah A. Connolly*[1], Donal J. Cox[1], Gráinne Jameson[1], Joseph Keane[1], Jean M. Fletcher[2] and Sharee A. Basdeo[1]

[1]Trinity Translational Medicine Institute, St James's Hospital, Trinity College Dublin, Dublin 8, Ireland. [2]Trinity Biomedical Sciences Institute, Trinity College Dublin, Dublin 2.

Background: Alveolar macrophages (AM) are the first line of defence to mediate protection against Mycobacterium tuberculosis (Mtb). However, Mtb can reduce AM defence mechanisms to facilitate its own growth and survival, therefore, AM function is critical in determining disease outcome. The interplay between structural and immune cells contribute to mounting effective immunity but also mediates tissue pathology, supporting disease progression, for example during Tuberculosis disease.

Methods: AM were treated with IFN-γ or IL-4 for 24 hours and subsequently stimulated with irradiated Mtb strain H37Rv or LPS for a further 24 hours. Expression of antigen presentation and co-stimulatory molecules, and cytokine production were quantified by flow cytometry and ELISA, respectively. A549 alveolar epithelial and MRC-5 lung fibroblast cells were stimulated with TNF and IL-1β to mimic in vivo alveolar conditions during inflammation and IL-6 and IL-8 from structural cells were determined by ELISA.

Results & Conclusion: When IFN-γ primed AM were challenged with Mtb, AM exhibited enhanced expression of antigen presentation and co-stimulatory molecules and had augmented cytokine production compared with controls, suggesting inhaled IFN-γ may have therapeutic potential as an immuno-supportive host directed therapy. Additionally, IL-1β and TNF synergise to induce enhanced IL-6 and IL-8 production, propagating inflammation through structural cells in the lung.

Conflict of Interest: The authors declare that they have no conflict of interest.