ESTABLISHING A PHENOTYPE OF THE EFFECTS OF TNFRp75 ON ALVEOLAR MACROPHAGE AND NEUTROPHIL FUNCTION POST BCG INFECTION IN MICE

Avril Walters[1], Roanne Keeton[1], Nai-Jen Hsu[1], Muazzam Jacobs[1,2]

[1] Division of Immunology, Department of Pathology and Institute of Infectious Diseases and Molecular Medicine, Faculty of Health Science, University of Cape Town, Cape Town, South Africa
[2] National Health Laboratory Service

Mycobacterium tuberculosis (M.tb) is the cause of Tuberculosis (TB), one of the world's most devastating diseases, which results in approximately two million deaths and nine million new cases per year. During 2014 8.8% of all deaths in South Africa were reported to be caused by TB.

The innate immune system presents the first mode of protection against M.tb infection. Initial infection results in the recruitment of neutrophils and macrophages, which are phagocytic cells that engulf and destroy the pathogens. These phagocytes also produce tumour necrosis factor ligands and receptors (TNFRp55 and TNFRp75). Previous studies have shown that mice deficient of TNFRp75 have improved early protection against M.tb infection, which also translated into better long term protection. This study investigated the effects of TNFRp75 on the functionality of alveolar macrophages and neutrophils during early *M. bovis* BCG infection.

In this study we have both *in vitro* and *in vivo* components. For the *in vitro* component we cultured neutrophils and alveolar macrophages obtained from naïve mice and infected them with BCG. We analysed uptake and killing of the pathogen by the phagocytes and also the cell viability and activity of these phagocytes after infection. In the *in vivo* component we quantified the number of alveolar macrophages as well as the recruitment of neutrophils to the lungs after BCG infection and studied the activation status of these cells. We also investigated BCG uptake, bacilli burdens and, chemokine and cytokine production.

We were able to show that there were no significant differences in either alveolar macrophage or neutrophil recruitment or activation between WT and TNFRp75 deficient mouse strains after infection with BCG. We speculate that this result was due to the much less virulent nature of BCG compared to H37Rv M.tb data on which the study was based. Therefore, for future studies we will be using H37Rv M.tb and we also want to investigate if there are any similarities between mouse and human cells for possible translational studies.