European Respiratory Society
Annual Congress 2012

Abstract Number: 745

Publication Number: P2650

Abstract Group: 10.2. Tuberculosis

Keyword 1: Immunosuppression **Keyword 2:** Viruses **Keyword 3:** Infections

Title: Regulatory T-cells and high levels of FOXP3 mRNA lead to decreased immune responses during HIV-TB co-infection

Dr. Andre 6884 Loxton gl2@sun.ac.za [1], Dr. Teri 6885 Roberts teri.roberts@geneva.msf.org [1], Dr. Gillian 6886 Black gill.black@livelihoods.org.za [1] and Prof. Gerhard 6887 Walzl gwalzl@sun.ac.za [1]. [1] Biomedical Sciences, University of Stellenbosch, Cape Town, Western Cape, South Africa, 7505 .

Body: Tuberculosis causes 2 million deaths per year and is the most important opportunistic infection in patients infected with HIV. During the co-infection of HIV/TB, natural regulatory T cells down regulate Th1/Th2 responses. We performed direct ex vivo phenotyping of whole blood with antibodies to CD4, CD25, FOXP3, CD38 and PD-1. In a 7-day whole blood assay, diluted blood was incubated with M.tb proteins. The supernatant was removed and analysed for Interferon-gamma production by ELISA. The Multiplexed Ligation dependent Probe Amplification technique was used to amplify ex vivo RNA and compare gene expression of 45 genes. We found an increase in the ratio and frequency of regulatory T-cells in HIV/TB co-infected participants. PD-1 expression on highly activated T-cells was increased in participants infected with HIV or TB alone. The median Interferon-gamma responses to control and DOS-R M.tb antigens (ESAT-6/CFP10, TB10.4, Ag85A and TB10.3) were the highest in the control group. The response to p24 was higher in the HIV+ group than the HIV-TB participants. The FOXP3 gene was significantly upregulated in HIV/TB co-infected participants. Participants with HIV/TB co-infection have significantly more regulatory T-cells than those infected with either HIV or TB which leads to a dampened immune response to both HIV and TB. Differential gene expression and increased frequencies of regulatory T-cells in the HIV/TB co-infected participants may have important implications for future vaccine designs. A more precise characterization of the gene and cellular factors are needed in our attempt to unravel the mechanisms of immune failure which is present during HIV/TB co-infection.