

Poster presentation

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PI6-01. Regulatory T-cells and high levels of FOXP3 mRNA leads to decreased immune responses in HIV-TB co-infection

A Loxton*, T Roberts, G Black and G Walzl

Address: Medical Biochemistry, University of Stellenbosch, Cape Town, South Africa

* Corresponding author

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Background

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 (CD4⁺ FOXP3⁺) down regulate Th1/Th2 responses. Our study analysed the regulatory T-cell phenotypes amongst participants dually infected with HIV/TB, HIV or TB alone and healthy HIV negative controls and used it as the basis for analysing anti-TB responses and gene expression in HIV infected participants.

Methods

We performed direct ex vivo phenotyping of whole blood with monoclonal antibodies to CD4, CD25, FOXP3, CD38 and PD-1. In a 7-day whole blood assay, diluted blood was incubated with 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.

Results

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 TB antigens (ESAT-6/CFP10, TB10.4, Ag85A, TB10.3) were the highest in the controls. 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.

Conclusion

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 is needed in our attempt to unravel the mechanisms of immune failure which is present during HIV/TB co-infection.