

# IMMUNE RECONSTITUTION OF HIV INFECTED INDIVIDUALS ON ART: CENTRAL MEMORY T CELLS CORRELATE WITH DECREASED SUSCEPTIBILITY TO TUBERCULOSIS

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## Background

HIV infected persons are 20-30 times more likely to develop Tuberculosis (TB) than those uninfected who have a 5% chance of developing active TB in their lifetime. HIV is the best-recognised cause of susceptibility to TB and antiretroviral therapy (ART) is the most effective way to reduce the risk of TB in HIV-1 co-infected persons. We sought to define biomarkers that correlate with decreased susceptibility to tuberculosis by studying ART induced protective immune reconstitution in HIV infected persons sensitised by *Mycobacterium tuberculosis* (*Mtb*).

## Methods

HIV infected persons starting ART were recruited in Khayelitsha, South Africa, and followed up for 6 months. Peripheral blood mononuclear cells were separated from blood collected at day 0 and 1, 3 and 6 months of ART. A control group, consisting of HIV uninfected persons, was sampled once from the same site. A fourteen colour flow cytometry panel was used to phenotype cells stimulated with *Mtb* Whole Cell Lysate (WCL) for CD3, CD4, CD14, CD19, CD45RA, CD27, CXCR3, CCR4, CCR6, HLA-DR, KLRG-1, and intracellular cytokines IFN-gamma, TNF-alpha, IL-2 and IL-17A. Results (n=26) were analysed longitudinally. A cross-sectional comparison at 6 months of ART with the group of HIV uninfected persons (n=27) was also performed.

## Results

Central memory T cells (CD4<sup>+</sup>CD27<sup>+</sup>CD45RA<sup>+</sup>) expanded proportionally over time in response to ART (p<0.01), while effector memory T cells (CD4<sup>+</sup>CD27<sup>-</sup>CD45RA<sup>-</sup>) proportionally decreased over time in response to ART (p<0.01). T cell activation, measured as HLA-DR expression, decreased following six months of ART (p<0.0001) and T cell exhaustion as determined by KLRG-1 expression, also decreased during ART (p=0.04). The increase in central memory cells, decrease in effector memory cells, and overall activation and exhaustion of cells, tended to levels observed in the HIV uninfected individuals when compared to the healthy cohort.

## Conclusion

The expansion of central memory cells could thus play in role in reducing risk of opportunistic infections, including tuberculosis, correlates with reduced susceptibility to TB and is therefore a potential correlate of protection. This has implications for vaccine design and evaluation of efficacy in vaccine studies.

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