PHENOTYPIC CHANGES IN CD4$^+$T CELLS ASSOCIATED WITH ANTI-RETROVIRAL THERAPY INITIATION IN HIV ASSOCIATED CRYPTOCOCCAL MENINGITIS.

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Introduction

Since the introduction of antiretroviral therapy (ART), the prognosis for HIV-1 patients has improved remarkably. Initiation of ART has been associated with immune recovery, however without a clear understanding of its immunological effects on the CD4$^+$T cell repertoire in HIV associated cryptococcal meningitis (CM). Cell-mediated immunity is critical for the host defense to *Cryptococcus neoformans*, and a vital tool to predict treatment outcomes. We aimed at determining phenotypic changes in the CD4$^+$T cell subsets following ART initiation in HIV associated CM. We hypothesized that ART alters the clonotypic phenotype and structural composition of CD4$^+$T cells in HIV-associated CM.

Methods

Peripheral blood mononuclear cells (PBMCs) were isolated from HIV positive patients with Cryptococcal Meningitis at four time points following ART initiation through the parent study (ClinicalTrials.gov number, NCT01075152). Phenotypic characterization of CD4$^+$T cells isolated from a pool of PBMC samples was done by flow cytometry after in vitro stimulation using appropriate antigenic preparations.

Results

There was a variation in the expression of immunophenotypic markers over the time points. We noted an equipoise in the increase in the central memory (CD27$^+$CD45R0$^+$), reduction in immune activation (CD38$^+$,HLA-DR$^+$), effector memory markers (CD45R0$^+$,CD27$^-$) and exhaustion (PD-1). In comparison to the CD8$^+$T cells, markers of central memory declined gradually with trivial increases in the effector memory markers. Immune exhaustion and activation markers remained elevated throughout the time points.

Conclusion and future direction

The relative surge and decline in the expression of T cell surface markers outlines that the differentiation state of CD4$^+$T cells varies during ART administration. We noted that ART maintains the central memory pool in HIV associated CM despite persistent immune exhaustion. However, complete CD4$^+$T cell recovery after ART is a process that typically requires many years. Meanwhile, the CD8$^+$T cell pool does not seem to be influenced by the homeostatic forces associated with CD4$^+$T cell depletion. Our future plan is to investigate the immune mechanisms and effect of *C. neoformans* strain variation on the CD4$^+$T cell repertoire genetics after ART initiation in HIV associated CM.