UTILISING MULTI-OMICS ANALYSIS TO CHARACTERISE HIV PERSISTENCE AT THE SITE OF HIV AND TUBERCULOSIS COINFECTION

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Background:
HIV and *Mycobacterium tuberculosis* (Mtb) coinfection is a considerable burden on global mortality, with tuberculosis being the leading cause of death among people living with HIV (PLWH). Active Mtb infection is associated with pleural effusion (PE), and in PLWH, the PE exhibits higher HIV viral titres than the plasma, suggesting PE represents an important compartment for the antiviral response. To investigate HIV persistence during HIV/Mtb coinfection, we used single-cell multi-omics to characterise virus-specific CD8 T-cells and HIV-infected CD4 T-cells within the PE.

Methods:
PE mononuclear cells (PEMCs) were obtained from a participant living with HIV/Mtb coinfection. Single-cell RNA and T-cell receptor (TCR) sequencing of PEMCs was conducted using the BD Rhapsody pipeline. HIV-infected cells were identified by using a HIV consensus sequence previously obtained from this participant. TCR sequences for cells specific for HIV and other viruses were obtained from the IEDB database.

Results:
PEMCs exhibited a variety of cell subsets, with a dominance of T-cells. Analysis of antigen specificity identified CD8 T-cells specific for multiple viruses. HIV-specific CD8 T-cells showed a trend for elevated exhaustion markers *TIGIT* and *CTLA4* compared to cells with other viral specificities. HIV sequences were identified in RNA transcripts and examination of HIV-infected cells revealed enrichment of effector memory CD4 T-cells compared to central memory CD4 T-cells. Specifically, T-helper (Th)17 cells exhibited the highest number of HIV transcripts.

Conclusion:
Upregulation of genes related to HIV-specific CD8 T-cell exhaustion suggests these cells are less active within the PE during HIV/Mtb coinfection. Analysis of HIV transcripts revealed enrichment of Th17 cells; a cell type known to be expanded in the lung during Mtb infection. Together, these data suggest PE is a microenvironment that reduces CD8 T-cell functionality and possibly increases HIV target cells. Future analyses of the PE could provide strategies to ameliorate HIV/Mtb coinfection-associated morbidity.

Disclosure of Interest Statement:
We have an active collaboration with ViiV Healthcare, however, we received no funding for this specific project.