CHARACTERISING THE TRANSCRIPTOME AND TCR REPERTOIRE OF CD8 T-CELLS DURING TRANSIENT HIV VIROLOGICAL CONTROL

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Background: The PULSE clinical trial featured 68 Australian men living with HIV who underwent three consecutive analytical treatment interruptions (ATIs). Seven PULSE participants exhibited transient HIV virological control at either the second or third ATI. The immune mechanisms underlying this transient control are still unclear. In this study, we conducted multi-omics analyses to investigate the transcriptome and T-cell receptor (TCR) repertoire of blood-derived CD8 T-cells pre-treatment and after ATIs in transient HIV controllers (TCs) and non-controllers (NCs).

Methods: CD8 T-cells were isolated from peripheral blood mononuclear cells (PBMCs) across the three ATIs from two TCs and two NCs. Whole PBMCs were used for the pre-treatment timepoint. Single-cell RNA and TCR sequencing of cells was conducted using the BD Rhapsody system. Transcriptomics data and TCR data were analysed using R packages Seurat and ScRepertoire respectively.

Results: Comparisons between TCs and NCs at the pre-treatment timepoint revealed a more activated CD8 T-cell phenotype in TCs compared to NCs, specifically, a significant enrichment of T-cell activation pathways and significant upregulation of activation-associated genes *CD38* and *GZMA.* During the third ATI (ATI-3), where virological control was observed, there was a trend for a more diverse CD8 T-cell TCR repertoire in TCs when compared with NCs. Furthermore, intra-participant analysis revealed a trend for increased TCR repertoire diversity at ATI-3 compared to previous timepoints in cells from TCs.

Conclusion: These data indicate an enhanced CD8 T-cell activation response prior to treatment correlates with, and may possibly predict, transient HIV control post multiple ATIs. At the timepoint when virological control was observed, a more diverse TCR repertoire suggests a more broad and comprehensive anti-viral response, possibly preventing viral immune escape. This study provides insight into specific immunological features associated with HIV control and suggests that boosting CD8 T-cell responses is a promising immunotherapeutic treatment for HIV infection.

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