

Characterising the transcriptome and TCR repertoire of CD8 T-cells during transient HIV virological control

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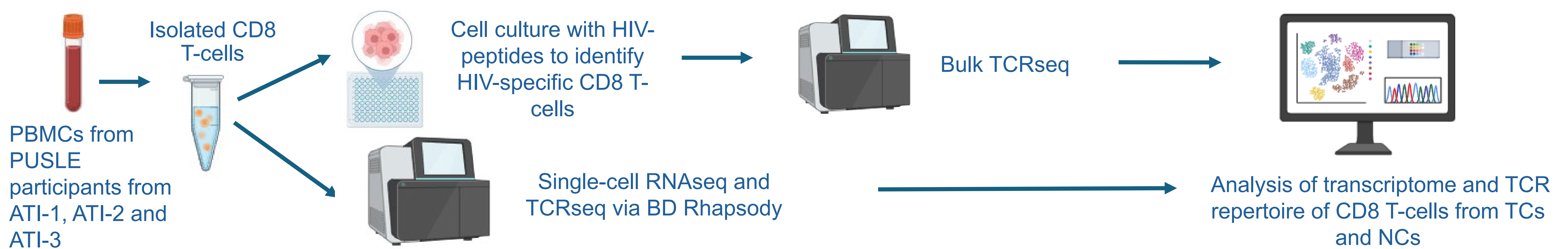
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Background

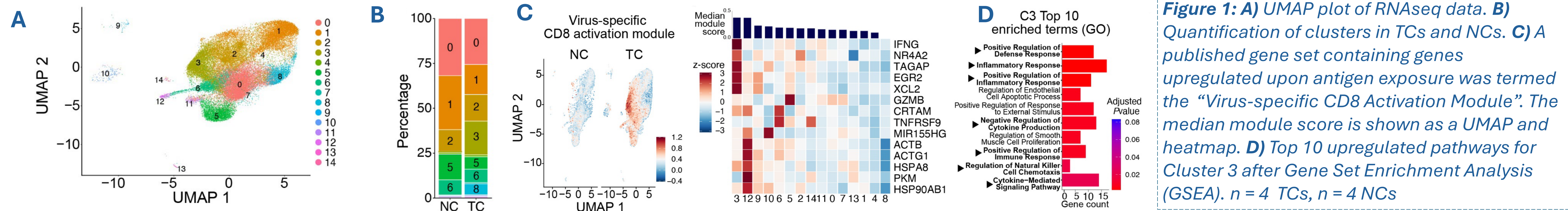
- The PULSE clinical trial recruited 68 Australian men living with HIV who underwent three consecutive analytical treatment interruptions (ATIs)¹.
- Seven PULSE participants exhibited transient HIV virological control during either the second and/or third ATI¹.
- CD8 T-cells are critical components of the anti-viral response during HIV infection², however the role of CD8 T-cells in transient HIV control after consecutive ATIs is unknown.
- **Here, we used samples from the PULSE study to investigate the transcriptome and T-cell receptor (TCR) repertoire of CD8 T-cells during three consecutive ATIs in transient HIV controllers (TCs) and non-controllers (NCs).**

Methods

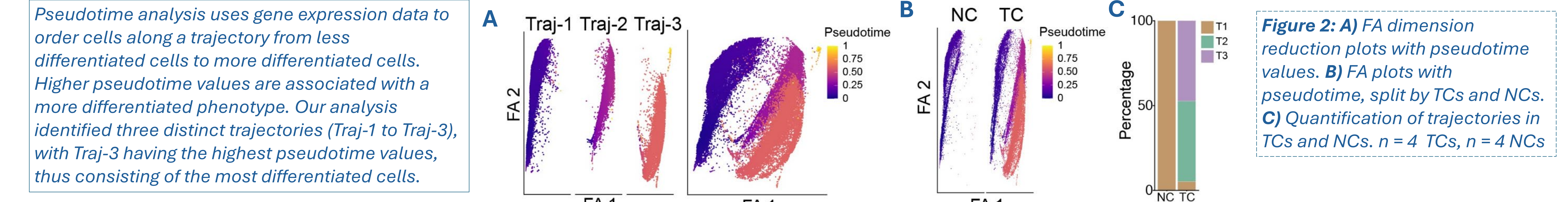


Results

• A highly inflammatory CD8 T-cell cluster (cluster #3) is more prominent in TCs compared to NCs

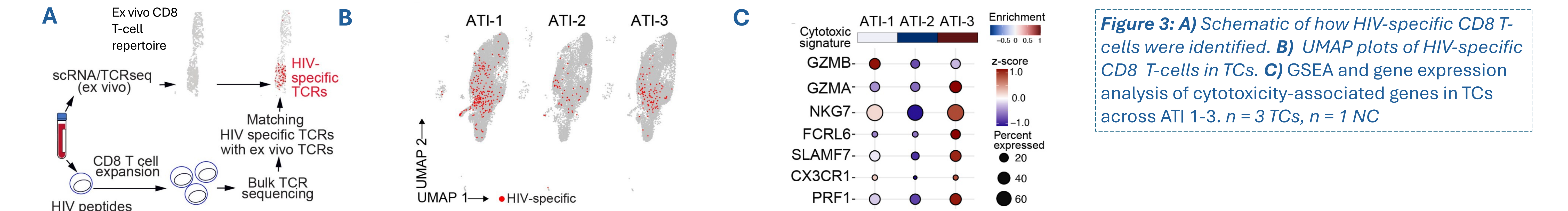


• CD8 T-cells are more differentiated in TCs compared to NCs, shown by pseudotime analysis

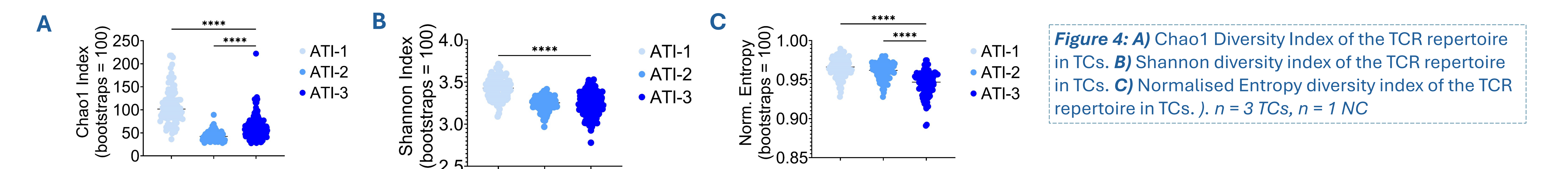


More differentiated CD8 T-cells are more activated in TCs compared to NCs across three consecutive ATIs.

• HIV-specific CD8 T-cells are more cytotoxic in ATI-3 compared to other ATIs in TCs



• The TCR repertoire of HIV-specific CD8 T-cells is less diverse after ATI-3 compared to ATI-1 in TCs



The TCR repertoire of HIV-specific CD8 T-cells is less diverse and more targeted in ATI-3 in TCs compared to ATI-1.

Conclusions

- Transient virological control is associated with a more activated and differentiated phenotype, and a more targeted TCR repertoire. This CD8 T-cell phenotype in TCs can inform future studies into novel CD8 T-cell immunotherapies

References and Acknowledgments

1. Bloch MT, et al. J Acquir Immune Defic Syndr. 2006 Jun;42(2):192-202. doi: 10.1097/01.qai.0000219779.50668.e6. PMID: 16688094.
2. Collins DR, Gaiha GD, Walker BD. CD8+ T cells in HIV control, cure and prevention. Nat Rev Immunol. 2020 Aug;20(8):471-482. doi: 10.1038/s41577-020-0274-9. Epub 2020 Feb 12. PMID: 32051540; PMCID: PMC7222980.

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

WITH GRATITUDE TO THE PARTICIPANTS OF THIS STUDY