CD8+ T-Cell Signature in Acute SARS-CoV-2 Infection Identifies Memory Precursors with dCODE Dextramer®

Adamo, S., Michler, J., Zurbuchen, Y. et al. Signature of long-lived memory CD8+ T cells in acute SARS-CoV-2 infection. Nature 602, 148–155 (2022). https://doi.org/10.1038/s41586-021-04280-x

BACKGROUND

In this study, Adamo *et al.* investigate the signature of SARS-CoV-2 specific long-lived memory CD8+ T cells using spectral flow cytometry combined with cellular indexing of transcriptomes and T-cell receptor (TCR) sequences in PCR confirmed COVID-19 patients.

STUDY DESCRIPTION

SARS-CoV-2-specific CD8+ T cells were profiled directly *ex vivo* by single-cell RNA (scRNA) and TCR sequencing in PBMCs from 33 patients during acute COVID-19 as well as at six and 12 months after primary infection. SARS-CoV-2-specific CD8+ T cells were detected by using HLA-A*01:01, HLA-A*11:01, and HLA-A*24:02 MHC-I dCODE Dextramer® reagents.

RESULTS

scRNAseq analysis of the temporal phenotypic changes separated the SARS-CoV-2 specific CD8+ T cells into 12 distinct clusters based on gene expression (**Fig. 1A**). Clusters 1, 2, and 12 dominated the acute phase, while cluster 11 dominated the recovery phase (**Fig. 1B**). Clusters 1, 2, and 12 corresponded to cytotoxic, activated, and proliferating cells, while cluster 11 was enriched in IFN, TNF, and LT-α genes.

TCR sequencing revealed that the number of persistent clones decreased over time (**Fig. 1C**) and that those were enriched in genes involved in IFN-γ response, IFN-α response, and TNF signaling. Non-persisting cells were enriched in mTOR signaling genes and genes related to mitosis (**Fig. 1D**).

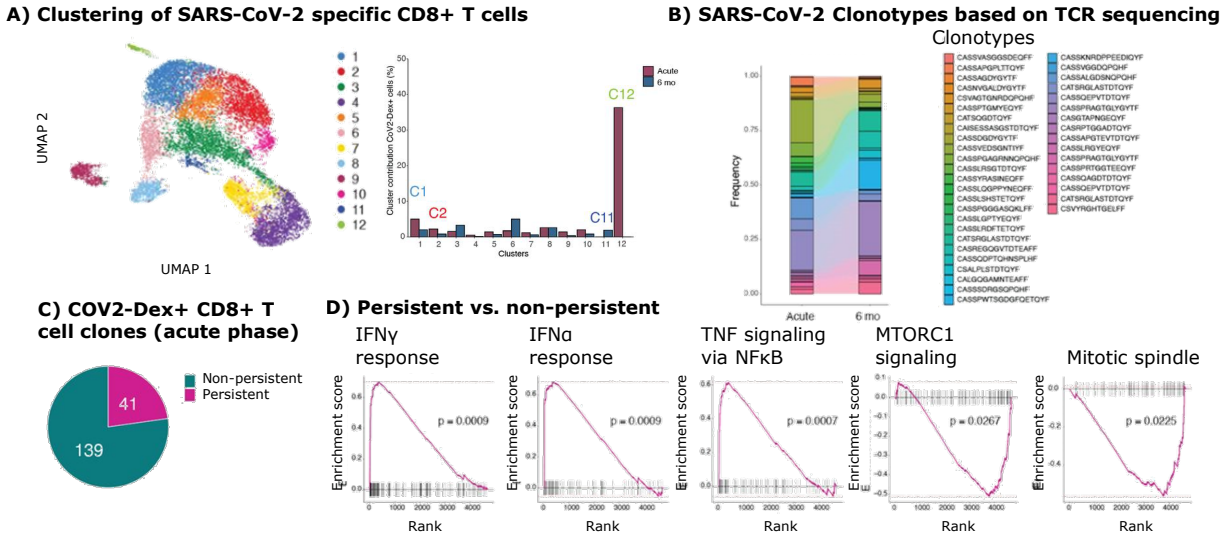

Fig. 1: Temporal phenotypic transcriptional changes in SARS-CoV-2 CD8+ T cells. A) scRNASeq analysis of SARS-CoV-2 specific CD8+ T cells revealed 12 clusters with certain clusters dominating either acute or recovery phase. B) Clonotypes of SARS-CoV-2 specific CD8+ T cells determined by TCR sequencing. C) Distribution of persistent and non-persistent clones in acute phase. D) Gene expression in persistent and non-persistent SARS-CoV-2 CD8+ T cells.

CONCLUSIONS

- SARS-CoV-2 specific CD8+ T cells detected using dCODE Dextramer® reagents exhibited a $T_{effector}$ phenotype during acute disease expressing genes related to cytotoxic, activated, and proliferating cells. During recovery, a progressive switch to a memory CD8+ T-cells phenotype with expression of genes related to IFN, TNF, and LT-α genes was observed in the SARS-CoV-2 specific CD8+ T cells
- Persisting SARS-CoV-2 CD8+ T-cell clones decreased over time but were enriched in genes involved in the IFN-γ response, IFN-α response, and TNF signaling

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