A125 · Paired single-cell transcriptome and TCR-repertoire analysis reveals convergent CD4⁺ T cells in recurrent mucosal inflammation.

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Session: Day 1 · Thu Oct 1, 2026 · 2:15–4:15 PM

A challenge in T cell biology research is unraveling the connection between T cell phenotype and their antigen specificity in the context of health and disease. By means of paired single-cell transcriptomic and TCR sequencing technologies, it is now possible to analyze both T cell clonal diversity and functional dynamics at the single cell level. Here, we demonstrated that mucosal inflammation and recovery cycles have a long-lasting impact on the composition of the mucosal T-cell compartment. We isolated CD45+ cells from the gingiva of Foxp3DTR mice across four disease phases: 1) transient immune-regulatory breakdown and periodontal disease, 2) recovery, 3) disease recurrence, and 4) health. The cells were processed using the 10X Genomics Chromium 5′ gene expression and TCR platform. We used a pipeline including Seurat and SCrepertoire packages, performed iterative filtering, and annotated T cell subtypes. These were then paired with their respective clonal status. We identified an enrichment of highly expanded, antigen-experienced CD4+ T cells after recovery. Specifically, Tph-like cells were characterized by the expression of exhaustion and B-cell engagement genes. Within this cell type, the pipeline tracks a persistent expanded TCR sequence that displays pathogenic-related gene expression in recurrence. In conclusion, paired single-cell sequencing technologies allowed the identification of a specific T cell subtype and its TCR sequence that is involved in disease recurrence in our model.

Paired single-cell transcriptome and TCR-repertoire analysis reveals convergent CD4+ T cells in recurrent mucosal inflammation.

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