Microanatomy of the human atherosclerotic plaque by single-cell transcriptomics

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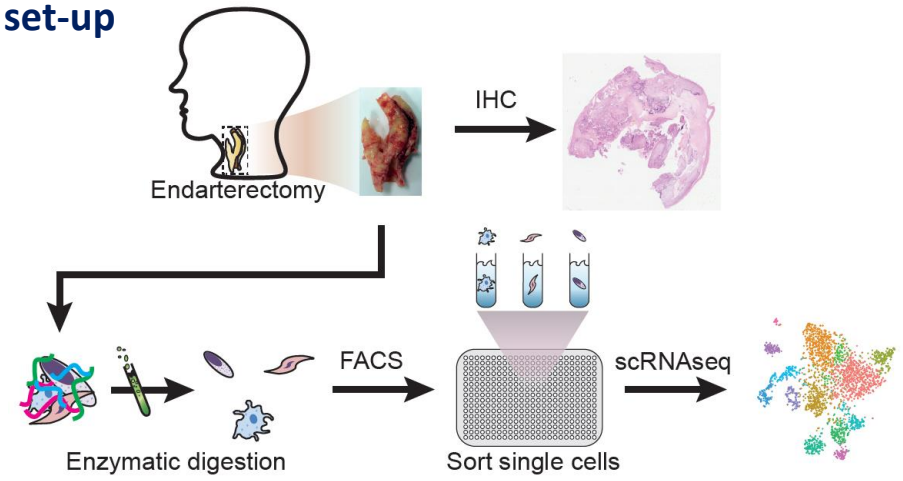
Background and aim

Atherosclerosis, the main underlying cause of cardiovascular disease and death worldwide, has been extensively investigated in numerous studies over the past decades. Both mouse and human studies have advanced our insights into the cellular composition and function of atherosclerotic plaques. Yet, especially in humans, detailed definition of cells at play in atherosclerosis is lacking and mainly based on a handful of selected markers. In the past year, four papers have shown the benefit of single-cell RNA sequencing in murine atherosclerosis. In our current study, we have applied single-cell RNA sequencing and single-cell ATAC sequencing to a cohort of human carotid atherosclerotic plaques and thereby provide an in-depth characterization of the highly diverse cellular communities in advanced human atherosclerosis.

Study set-up



Results

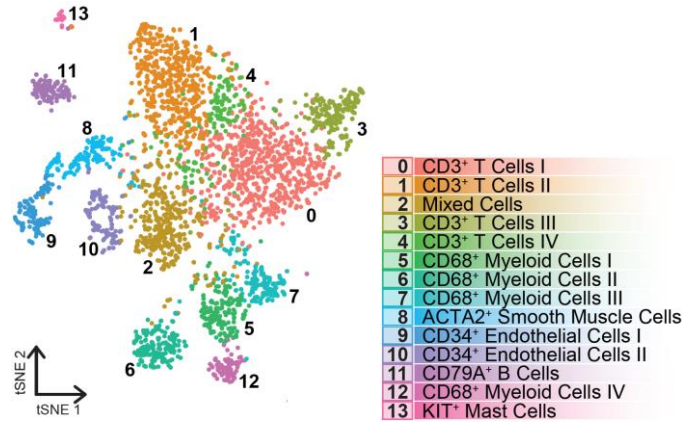


Figure 1. Single-cell RNA sequencing reveals 14 distinct cell clusters in human plaques

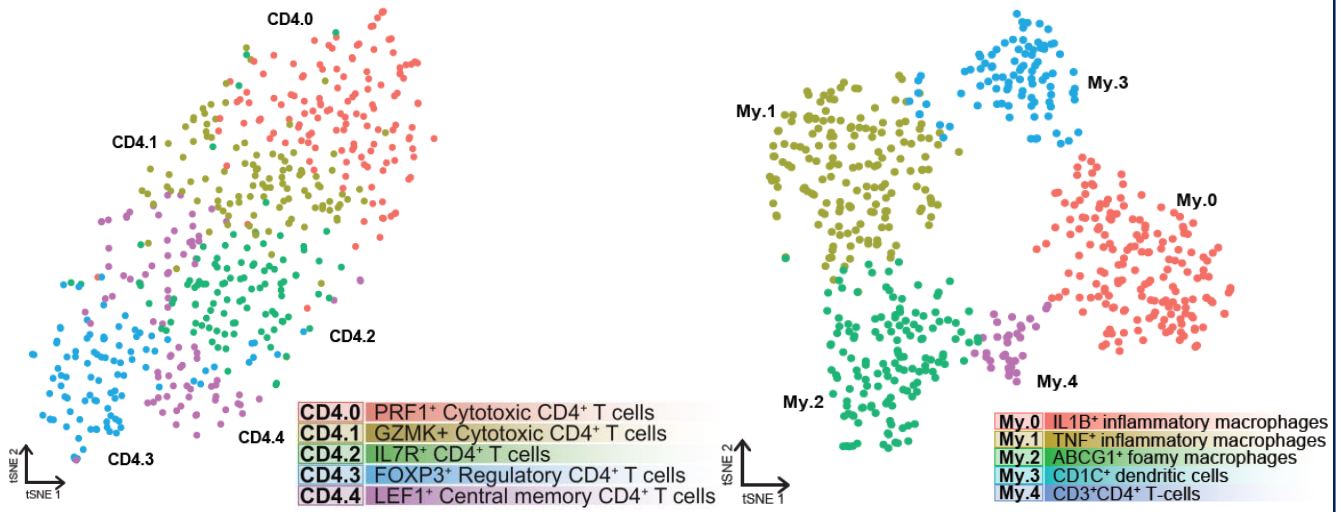
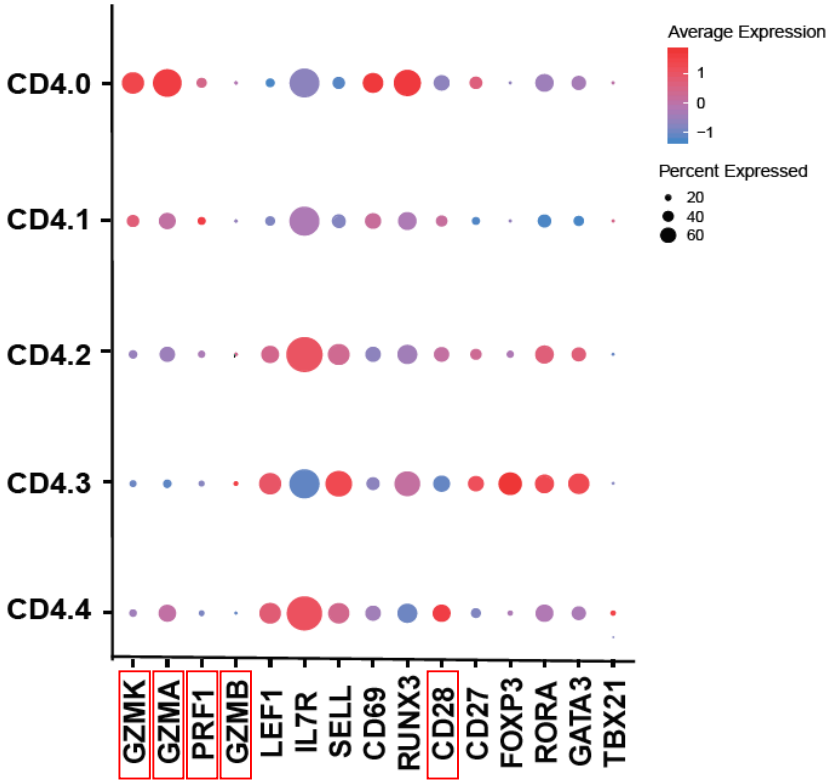


Figure 2. Subclustering of CD4⁺ T cells and myeloid cells revealing cluster division based on activation status.

Results



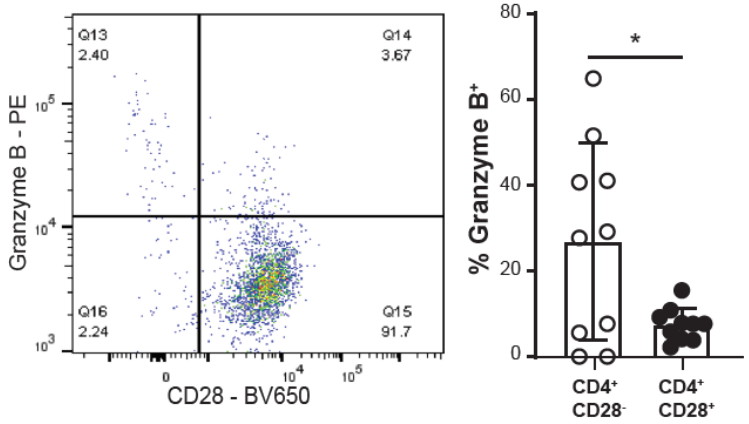
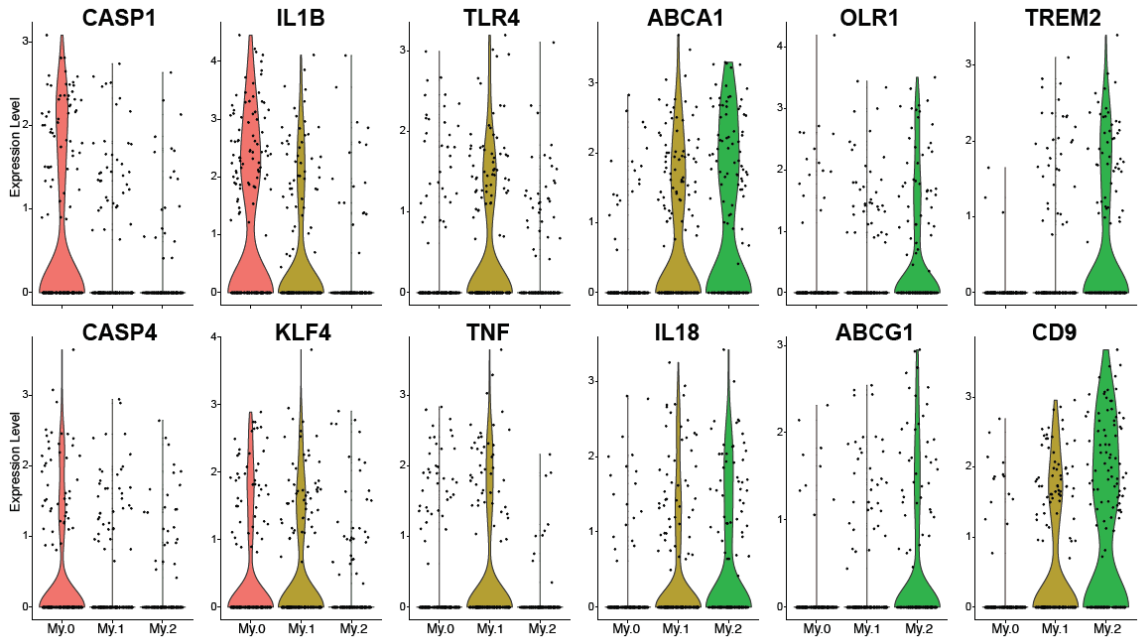


Figure 4. Cluster CD4.0 consists of $CD4^{+}CD28^{null}$ cells that have previously been associated with cardiovascular disease.



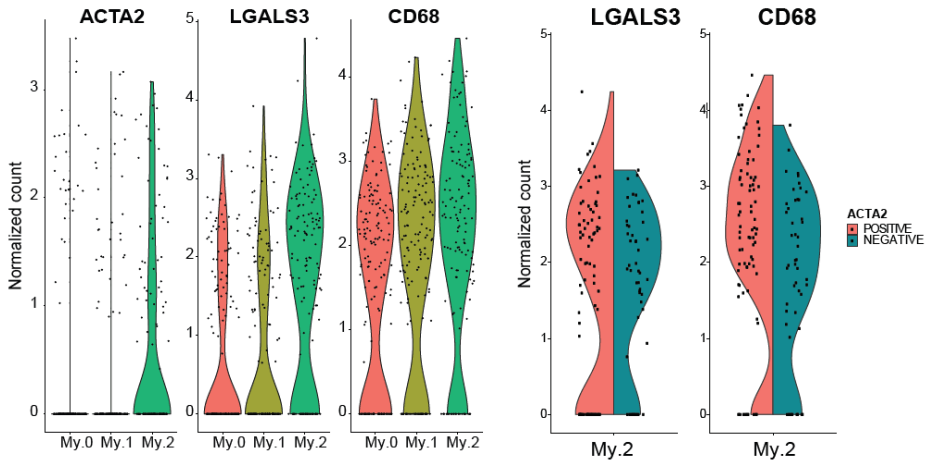


Figure 5. Macrophage cluster My.0 and My1 exhibit a clear pro-inflammatory phenotype, whereas cluster My2 shows a more foam-cell like phenotype, displaying a fibrosis-promoting phenotype.

Results

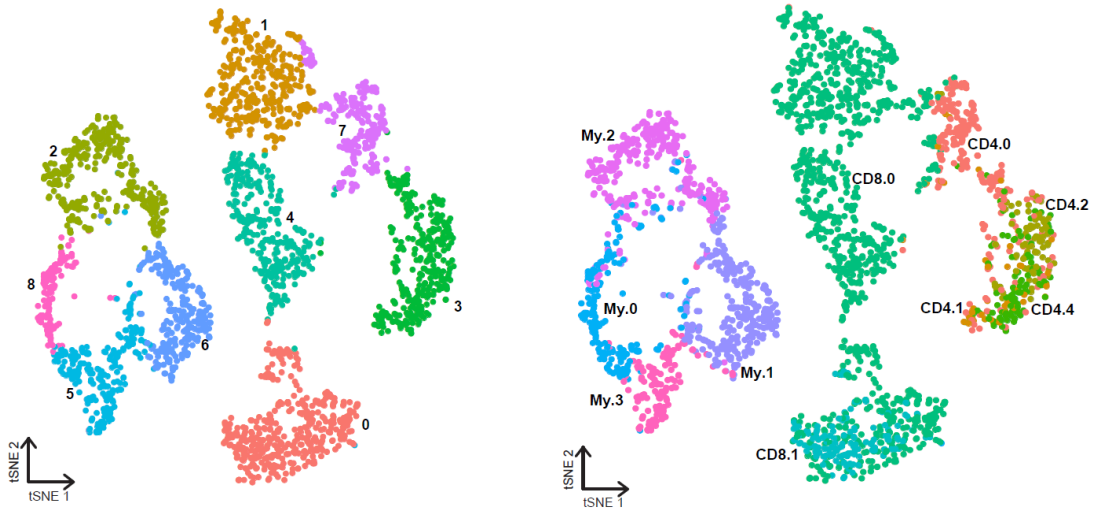


Figure 5. scATAC-seq reveals 4 myeloid clusters and 4 T cell clusters that show good agreement with the scRNA-seq clusters

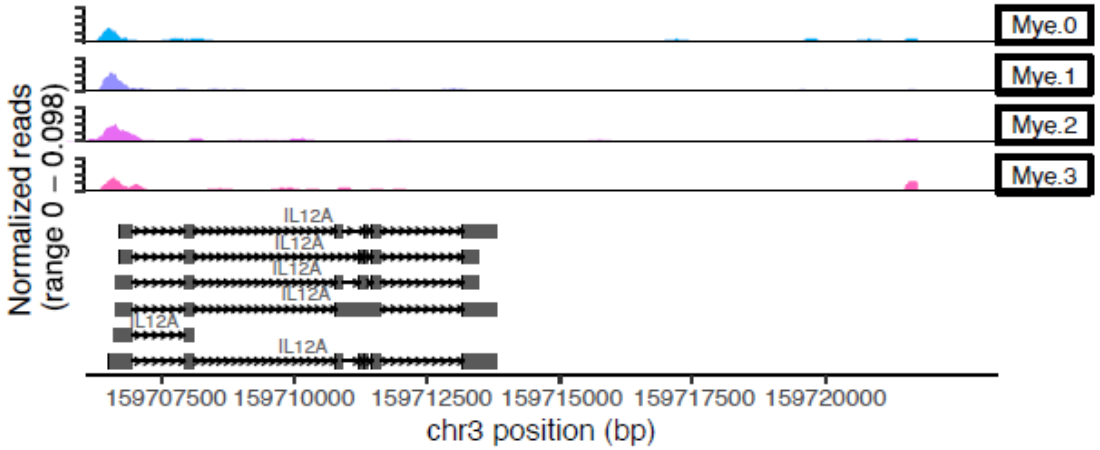
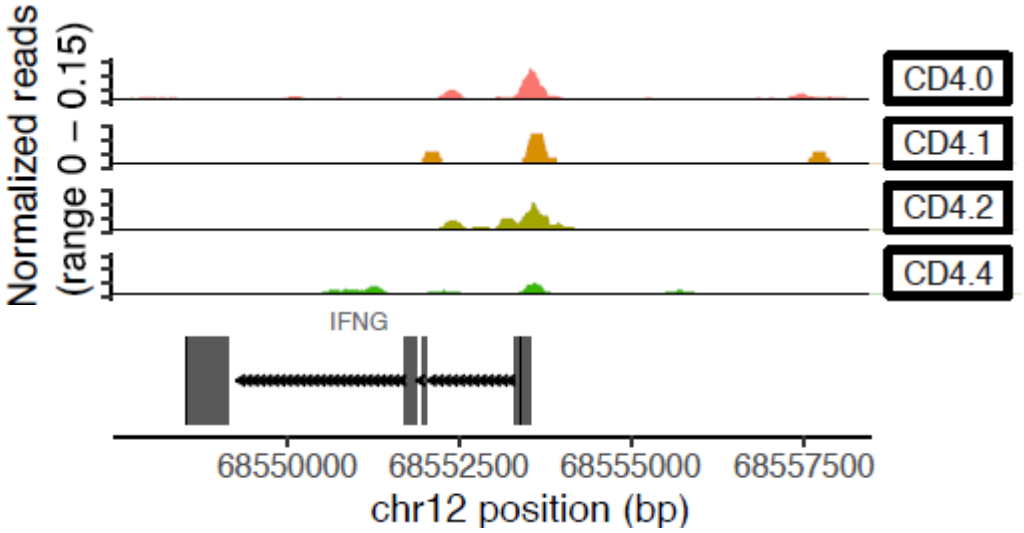


Figure 6. Pseudobulk genome browser visualization identifies open chromatin of IL-12 in CD1c^{+} dendritic cells.



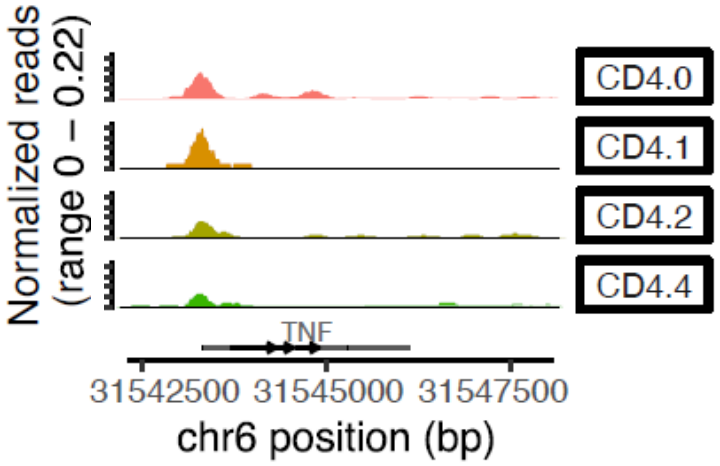
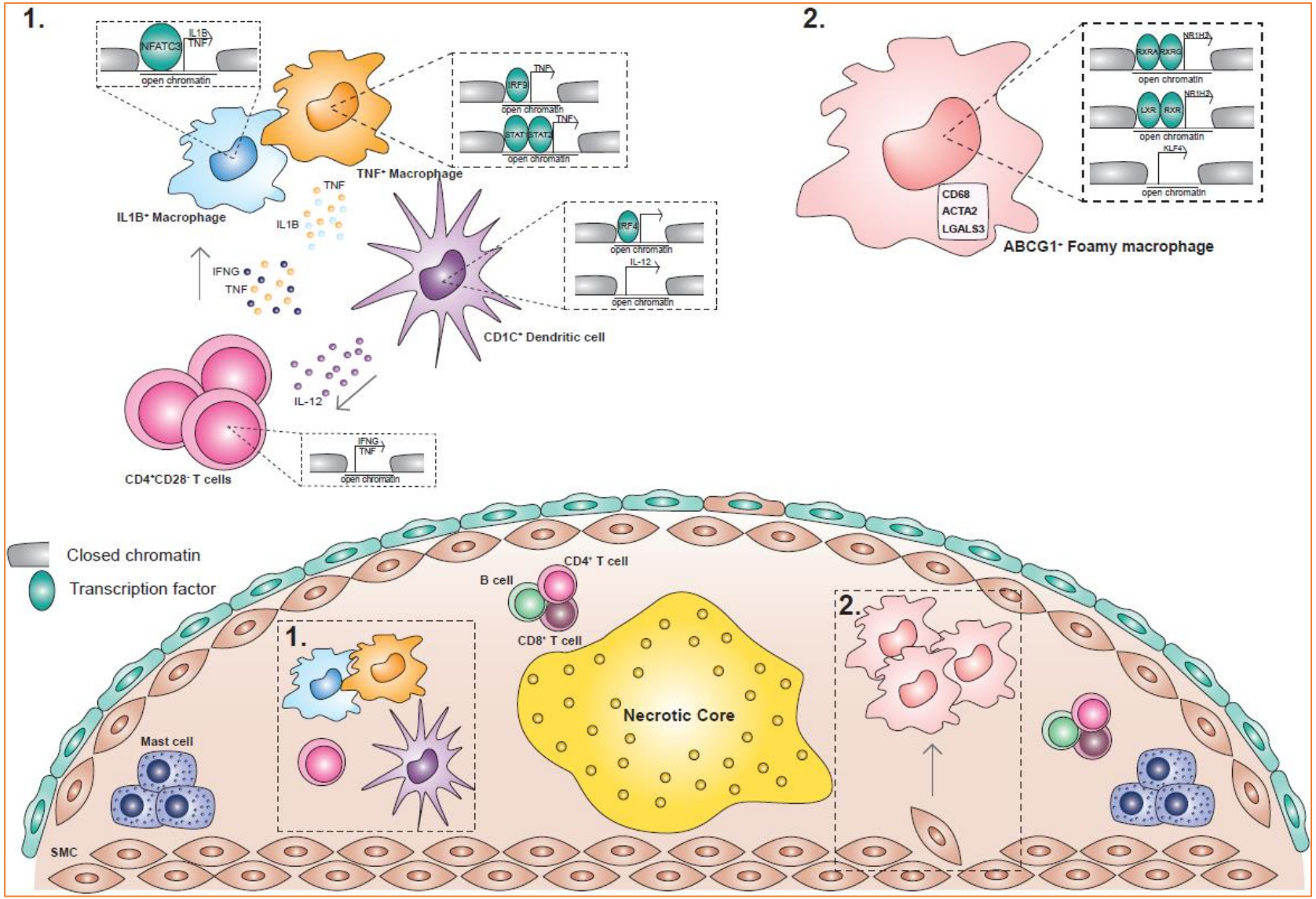


Figure 7. Pseudobulk genome browser visualization identifies open chromatin of IFNG and TNF in CD4^{+}CD28^{null} T cells.

Summary



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