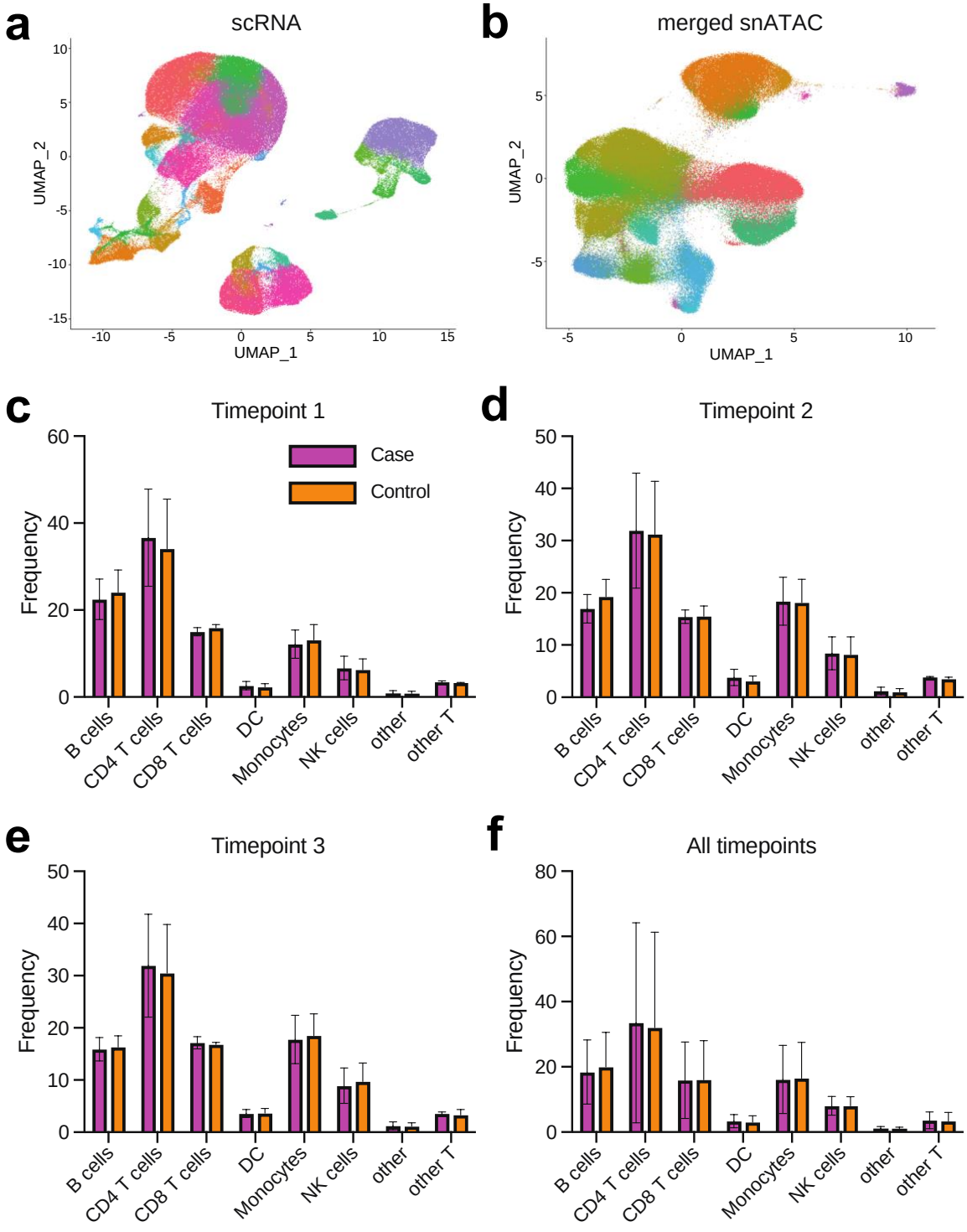
SUPPLEMENTARY MATERIAL

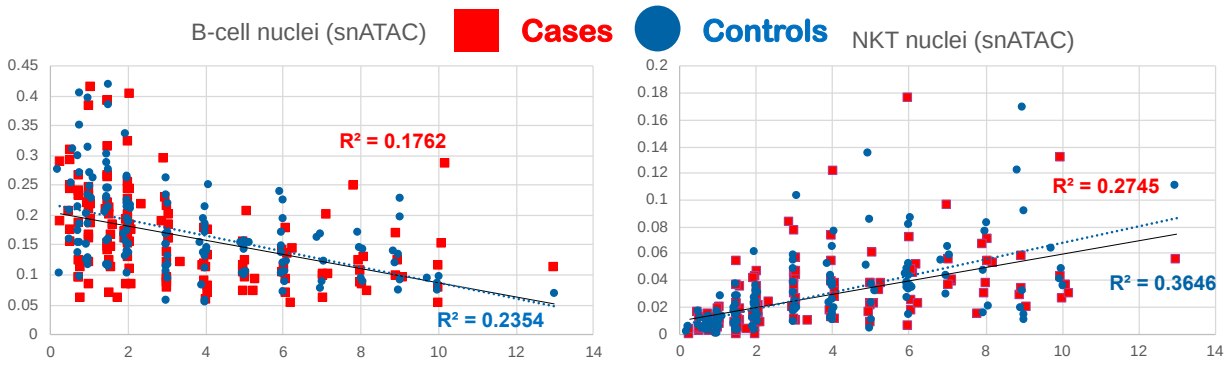
Evolving epigenomics of immune cells in type 1 diabetes at single nuclei resolution

Tomi Pastinen, Elin Grundberg, Todd Bradley, Jarno Honkanen, Warren Cheung, Arja Vuorela, Jeff J. Johnston, Byunggil Yoo, Santosh Khanal, Rebecca McLennan, Jorma Ilonen, Outi Vaarala, Jeffrey P. Krischer, and Mikael Knip

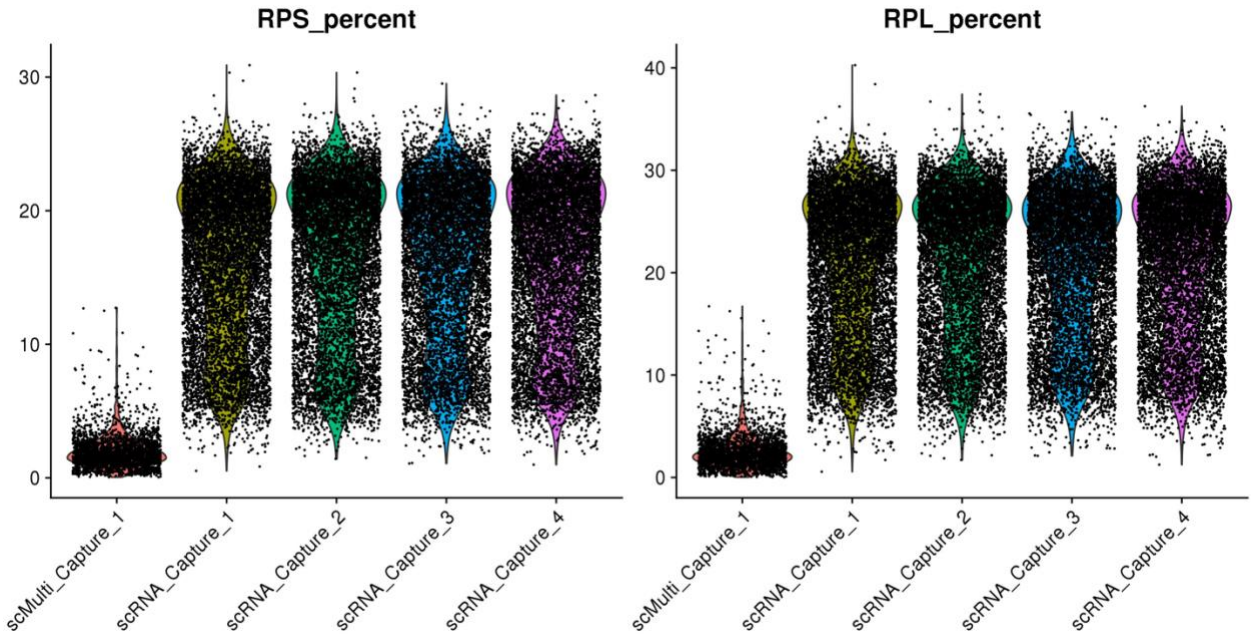
Table of contents



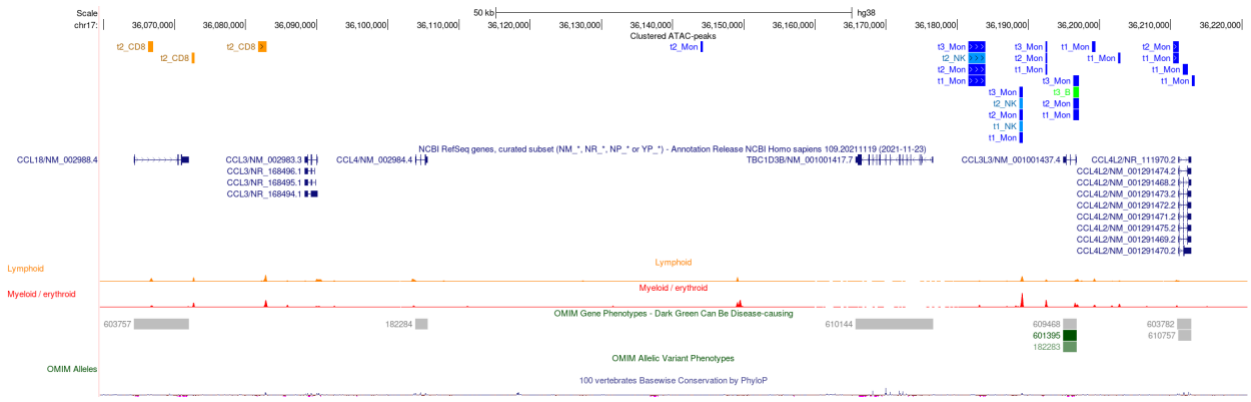
Supplementary Figure 1: a) Seurat analyses and clustering of independently analyzed PBMCs by scRNA sequencing. b) Signac analyses and clustering of merged snATAC object derived from 263,308 QC'd singleton nuclei included in separate 10X ATAC-seq. capture and 10X multiome capture. **c-d)** Proportions of jajor cell types inferred from cell and nuclei labeling by Seurat across all sc and sn captures in the study. No statistically significant differences in major cell type abundancies were observed between cases and controls.



Supplementary Figure 2: Many cell types demonstrate age-dependent abundancies. Examples (y-axis = cell-type fraction, x-axis = calendar age in years) shown for B-cell nuclei showing age dependent decline and NKT-nuclei showing age-dependent increase in abundancy. We note cases and controls are age-matched.



Supplementary Figure 3: Four scRNA captures (scRNA_Capture1-4, x-axis) each show stable fractions of ribosomal RNA transcripts of ~50% of reads (RPS + RPL %, y-axis), whereas only 5-10% RNA reads from single nuclei from 10X multiome experiment (scMultiome_Capture1) maps to ribosomal RNAs.



Supplementary Figure 4: We looked for regional clustering of case vs. control differential peaks in snATAC-seq. Specifically, a total of ~1,500,000 case-control chromatin association tests (99,799 peaks x 5 cell types x 3 timepoints) were tested with 5,487 associations at qv<0.1 Observing any two signals from same 100kb windows has an empirical probability of 0.00014. We observed over 1,700 “regional peak enrichments” representing greater than 8x enrichment from random distribution. An example region in UCSC Browser snapshot shows multiple peak associations also included in **Figure 2** illustrating chemokine cluster in chr17 with abundance of clustered differentially open monocyte (blue) peaks across timepoints (top track). Some regional clustering of CD8 differential chromatin (orange) is evident proximal to monocyte chromatin cluster. These differentially regulated chromatin regions overlap previously mapped DHS peaks in blood leukocytes (“Lymphoid”/Orange and “Myeloid/Erythroid”/Red tracks).