Cell-type specific bioinformatics analysis of Ets1 activity and their relevance in systemic lupus erythematosus (SLE)

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Systemic lupus erythematosus (SLE) is an autoimmune disease in which immune cells are abnormally activated. The transcription factor Ets1 plays key roles in lymphocyte development, but its behavior in specific blood cell types from SLE patients is not well defined. We performed computational analysis of single-cell RNA sequencing data on peripheral blood mononuclear cells from two healthy donors and four SLE patients. After data integration using Seurat, cells were grouped into eight major immune types—$CD14^+$ monocytes, $FCGR3A^+$ monocytes, B cells, $CD8^+$ T cells, naïve $CD4^+$ T cells, NK cells, dendritic cells, and platelets—based on known marker genes. Within each cell type, we compared Ets1 expression levels between SLE and healthy samples. Ets1 expression was significantly higher in SLE-derived $CD14^+$ monocytes, NK cells, and $CD8^+$ T cells. Most other cell types also trended upward, while naïve $CD4^+$ T cells showed a slight decrease. Beyond Ets1 expression, we explored cell-type specific transcription factor motif accessibility based on computational analysis of scATAC-seq from healthy donors and SLE patients. Lastly, we investigated Ets1 binding sites, Ets1 target genes and co-factors using CUT&RUN analysis in mouse primary T cells. Through these methods, we would be able to gain insights into how the activity of the Ets1 regulatory network varies across different immune cell types in SLE.