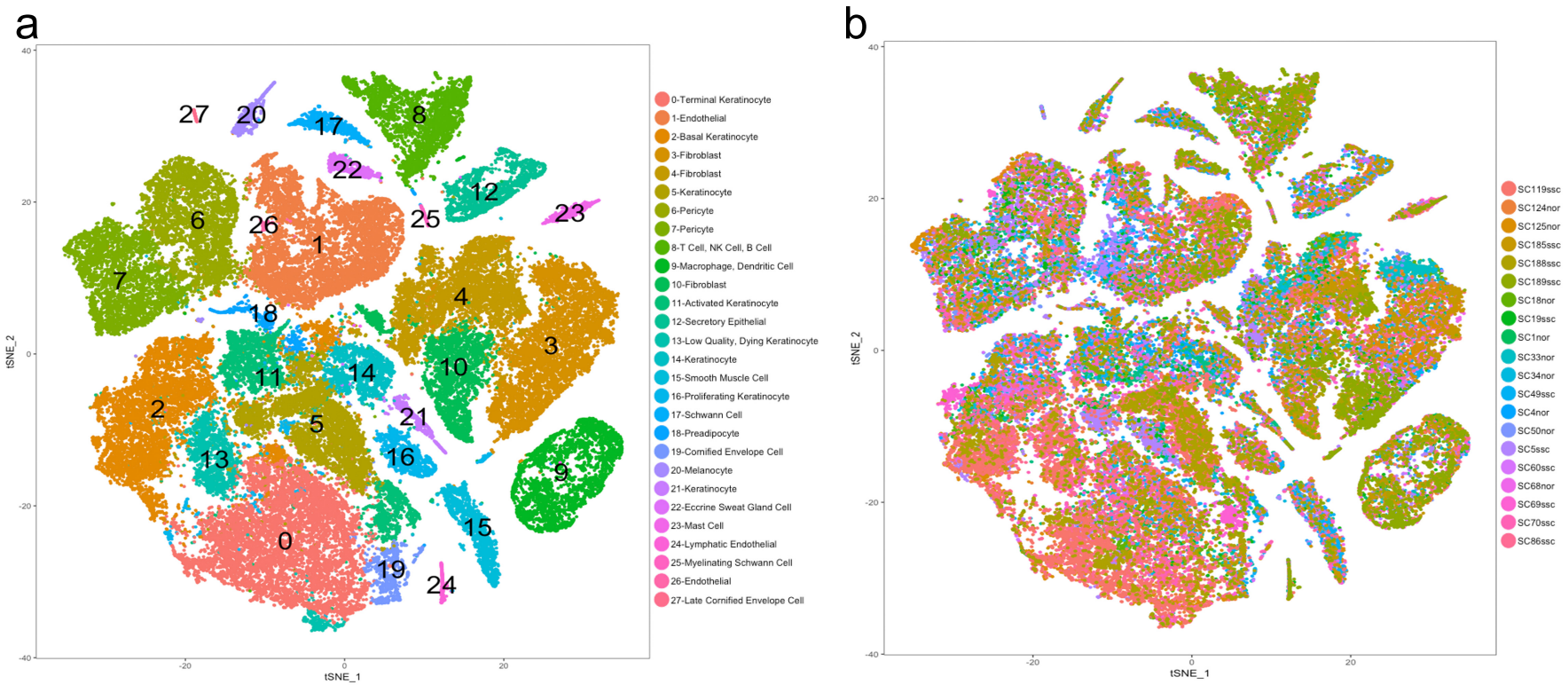


Figure S1. Cell transcriptomes identified in human skin. (**a**) Two-dimensional t-SNE shows dimensional reduction of cell transcriptomes. Each point represents a cell. (**b**) Cells were grouped by t-SNE as in Fig. S1**a**, but colored according to the subject original identity.

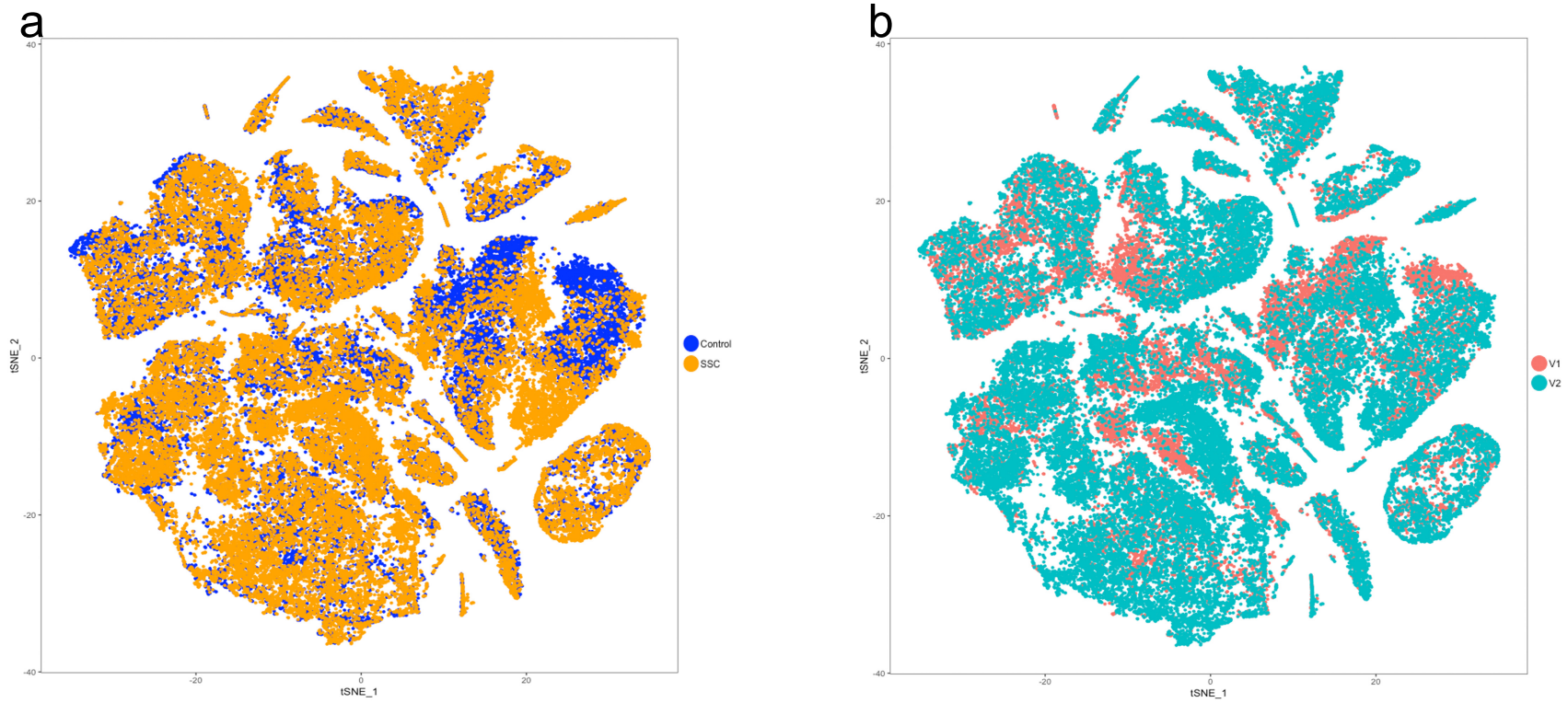


Figure S2. T-SNE showing clustering colored by health status and 10X Genomics chemistries (V1 or V2). Cells were grouped by t-SNE as in Fig S1**a**, but were colored according to the health status (panel a). Cells were grouped by t-SNE as in Fig S1**a**, but were colored according to 10X Genomics chemistries (V1 or V2, panel b).

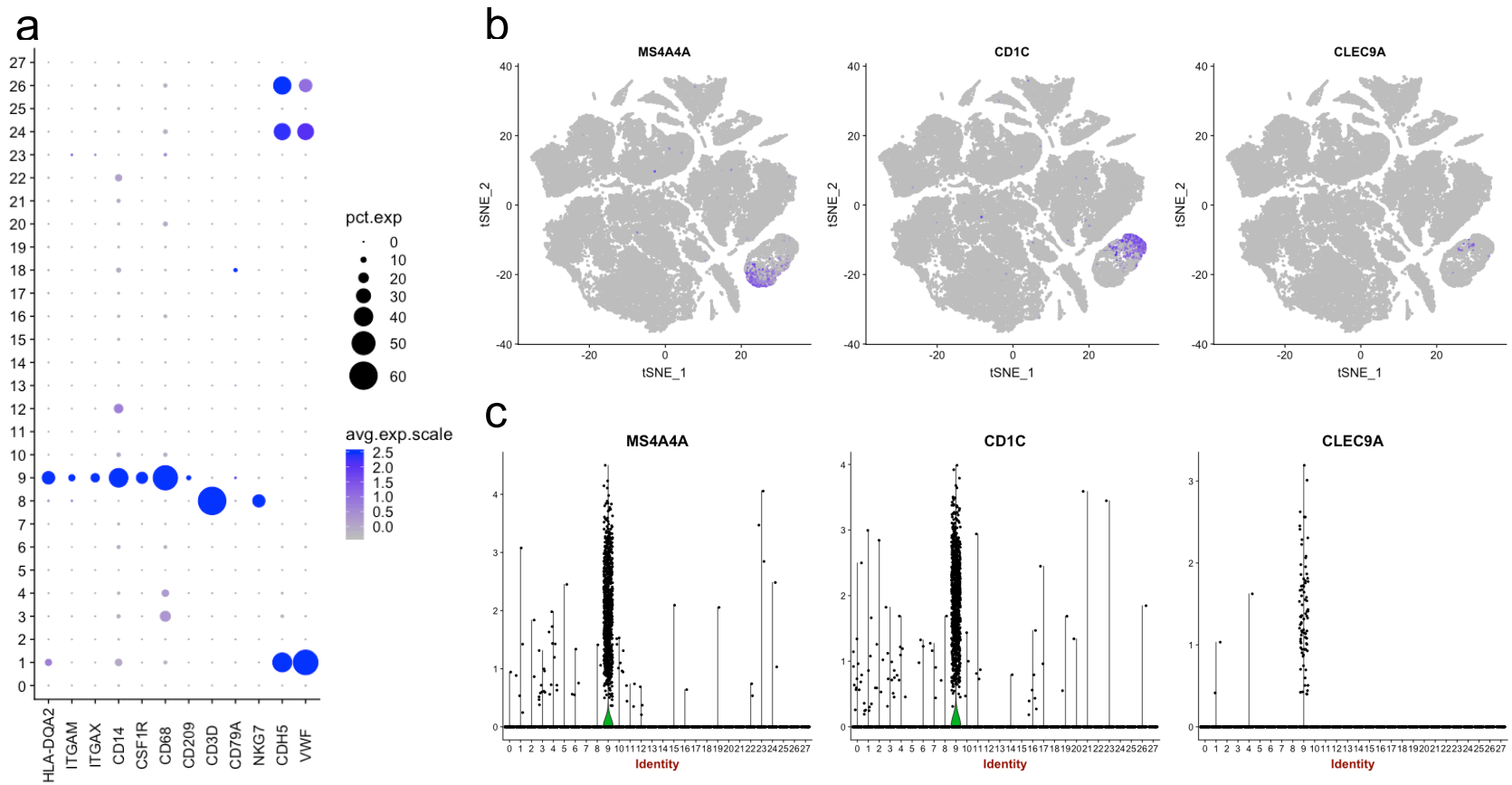


Figure S3A. One macrophage and dendritic cell (Mφ/DC) cluster was identified in human skin. Dot plot of genes defining Mφ/DC and distinguished from lymphocytes and endothelial cells (panel a). The intensity of the purple color indicates the level of average scaled gene expression. The size of the dot indicates the percentage of cells expressing this gene in each cluster (panels b and c). Feature plots and violin plots of genes defining one Mφ/DC cluster in human skin: MS4A4A to macrophages; CD1C to cDC2; CLEC9A to cDC1. Numbers in violin plots refer to cluster numbers as in Fig.S1a.

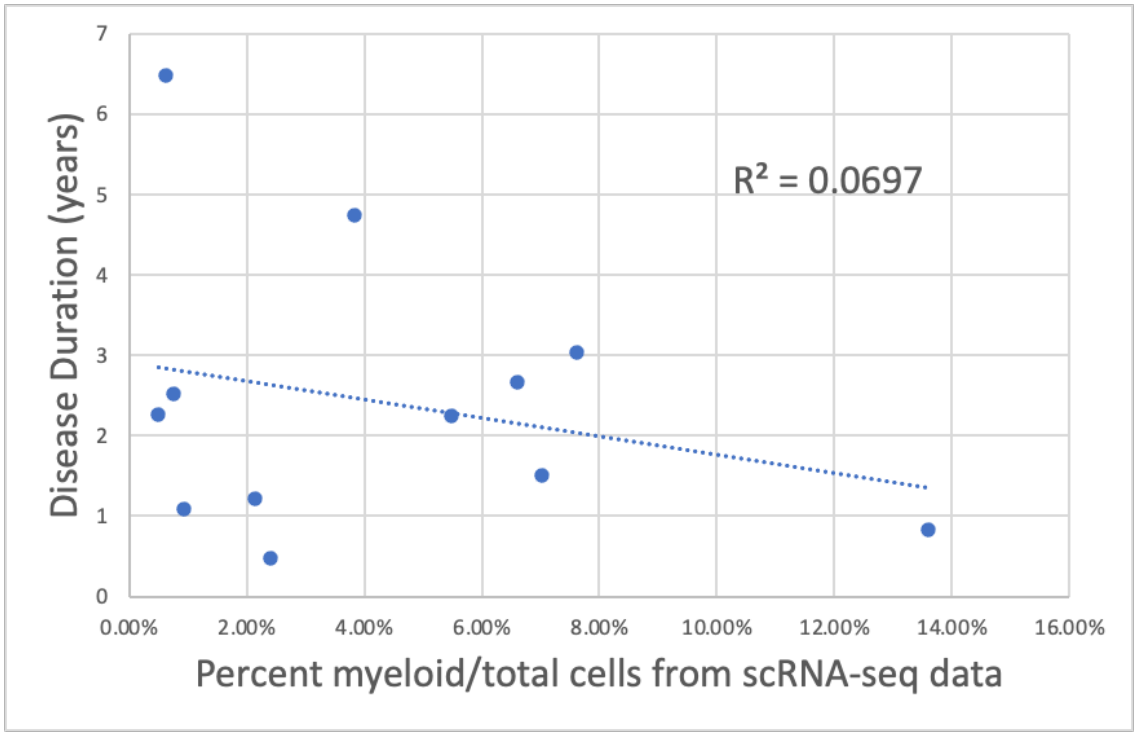


Figure S3B. Disease duration correlates weakly, negatively with percent myeloid cells in scRNA-seq samples in dcSSc skin biopsies.

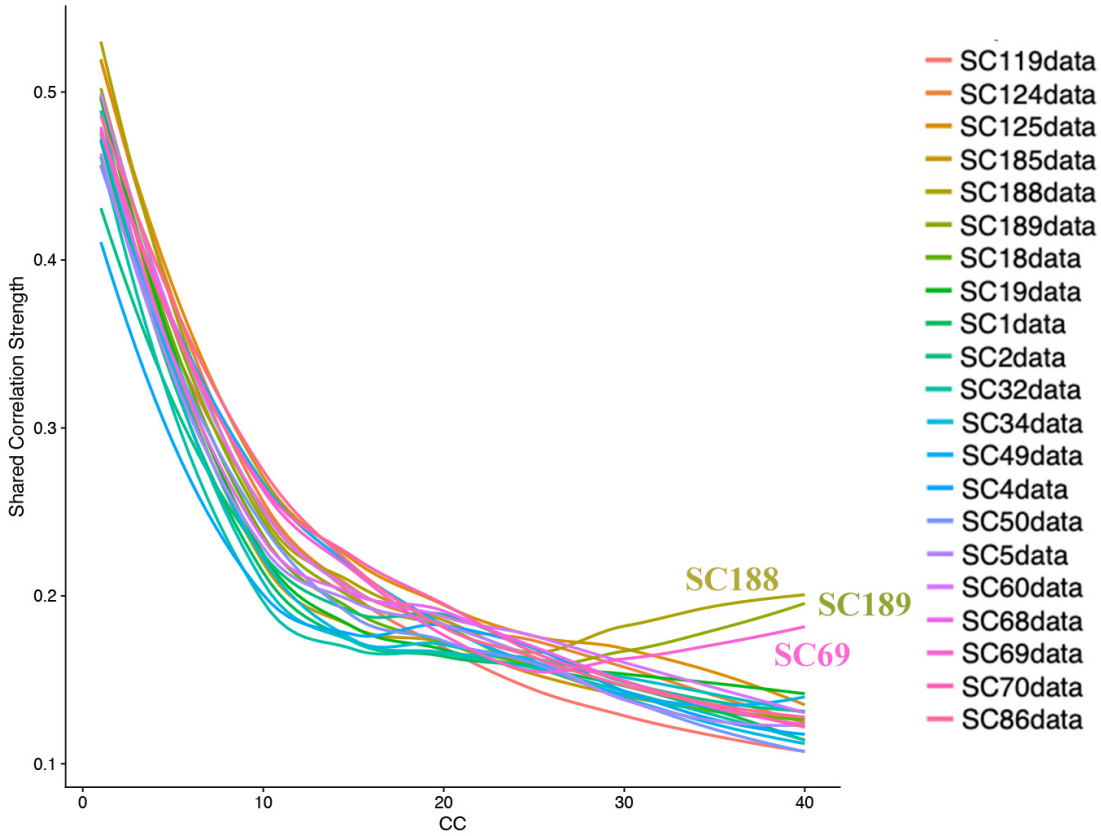


Figure S4. The shared correlation strength in Canonical Correlation Analysis (CCA) of each subject showing that SC188, SC189 and SC69 deviated from other samples.

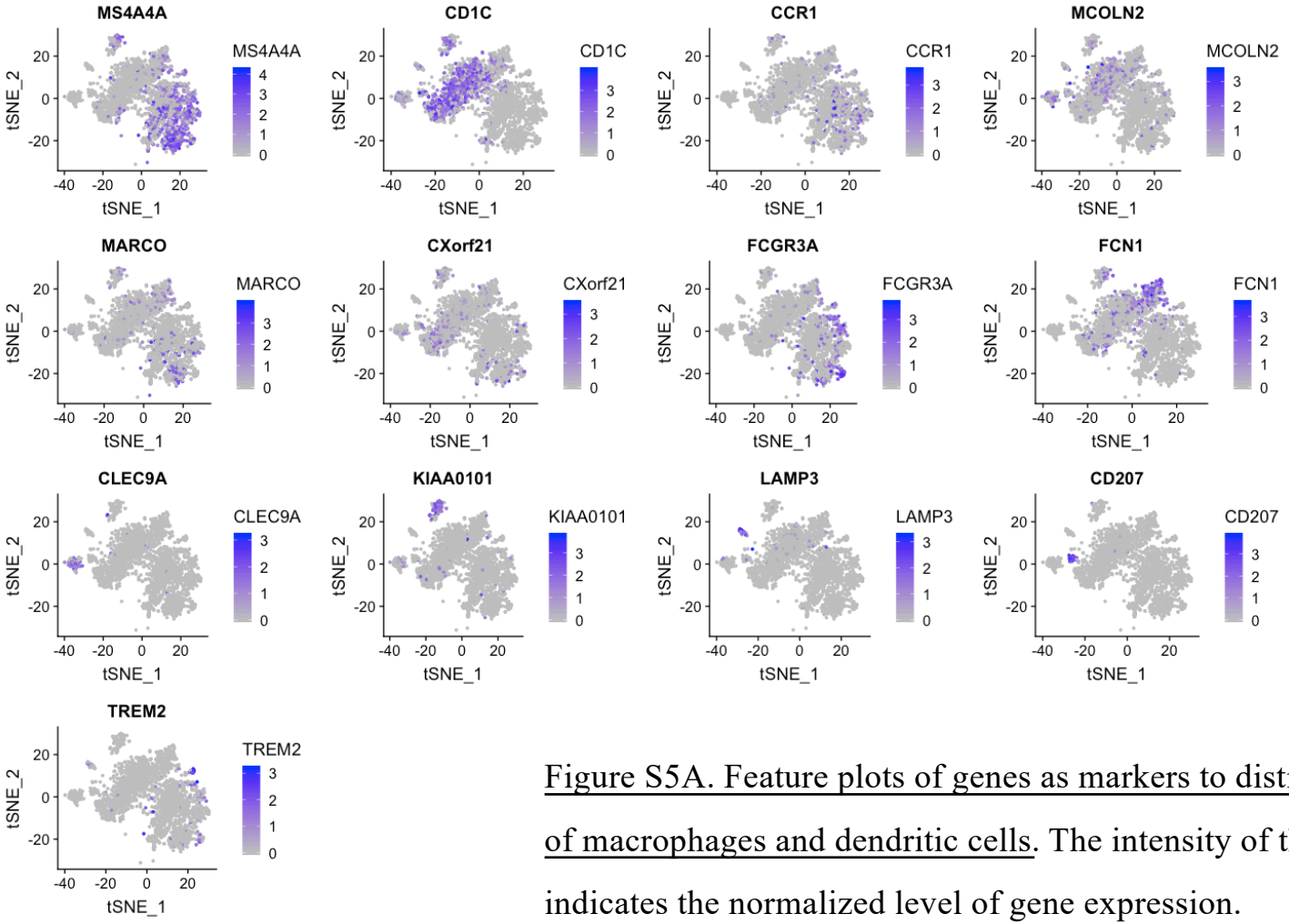


Figure S5A. Feature plots of genes as markers to distinguish each cluster of macrophages and dendritic cells. The intensity of the purple color indicates the normalized level of gene expression.

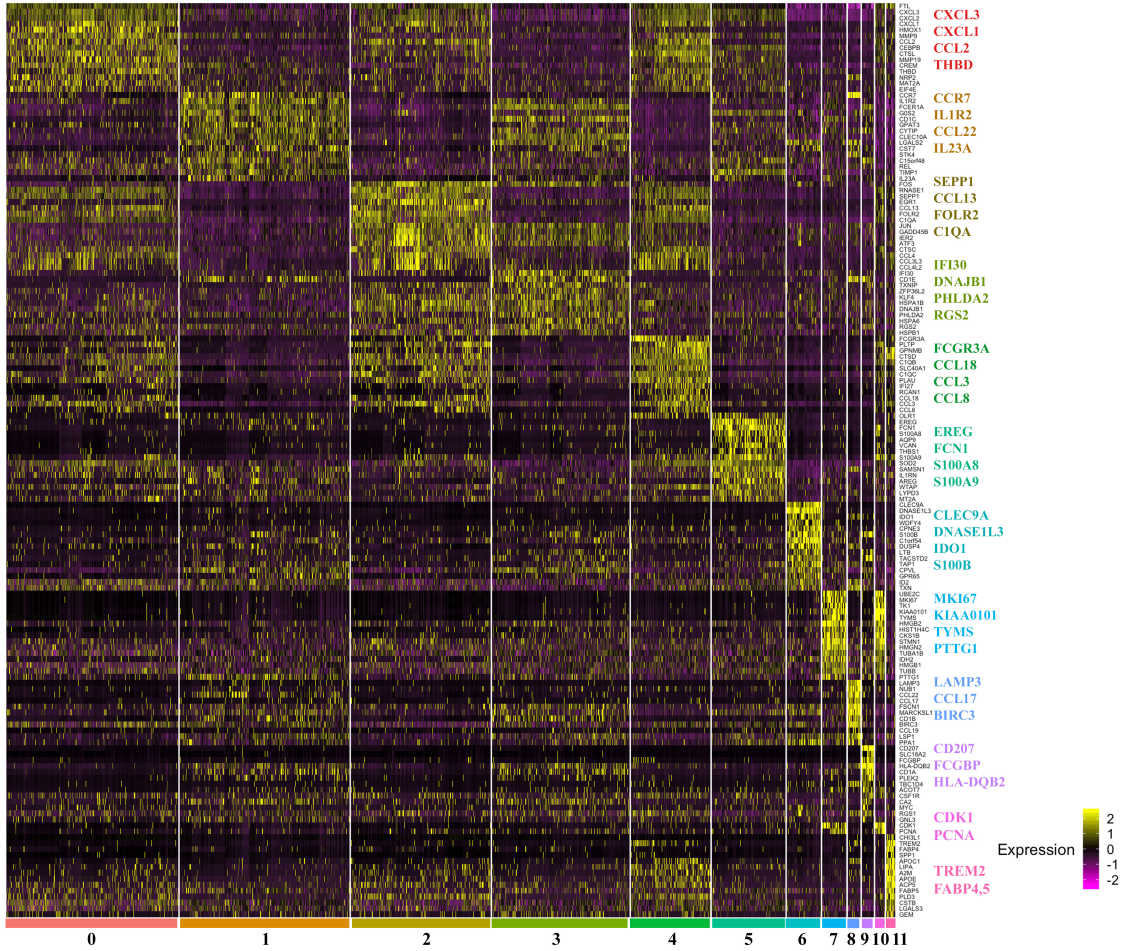
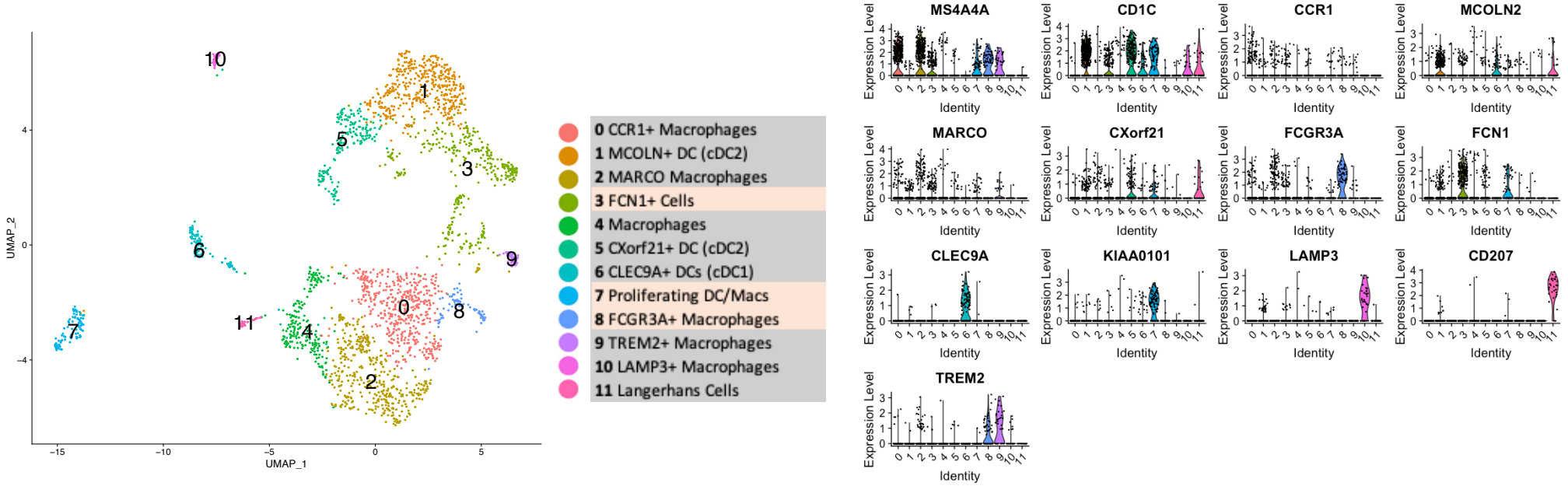
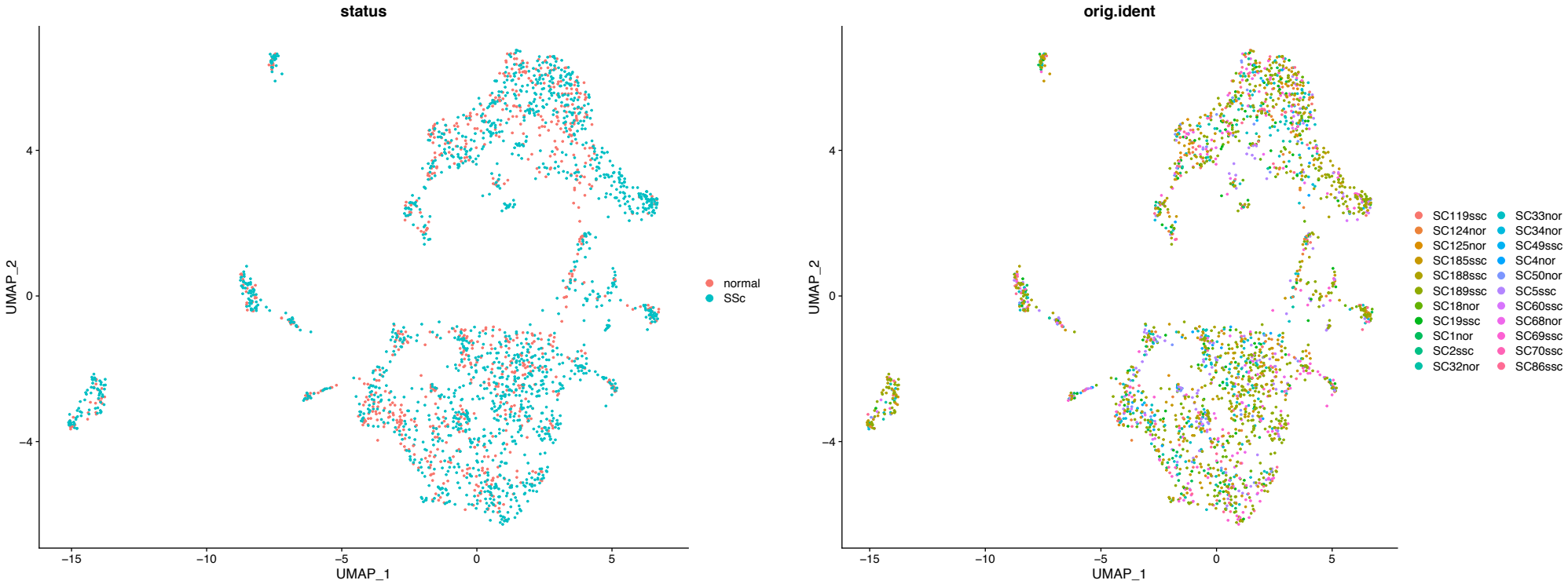


Figure S5B. Heatmap of myeloid cell gene expression in control and SSc skin samples. Each column represents a cell. The top 15 genes most differentially expressed between each cluster are shown, and some of these genes are enlarged to help identify each cluster. Cluster numbers, indicated at the bottom are as shown in Figure 1a.



A B

Figure S6A and 6B. Visualization clustering by UMAP plot of myeloid cells from all 22 combined healthy control subjects (HCs) and dcSSc skin samples after Harmony batch correction, Clusters are identified by cell type (panel a). Each point represents a cell. Two-dimensional UMAP shows the dimensional reduction of cell transcriptomes. Cells were colored by K-nearest neighbors graph based on Euclidean distance in principal component analysis space using a smart local moving (SLM) algorithm to iteratively group cells. Violin plots of marker genes to distinguish each cluster of myeloid cells (panel b). Numbers in violin plots refer to clusters numbers as in Figure 6A.



C D

Figure S6C and D. Cells were grouped by UMAP as in Figure S6A, but are colored according to original subject identity in (panel C), or according to health status (panel D; HC, healthy control; dcSSc, diffuse cutaneous systemic sclerosis).

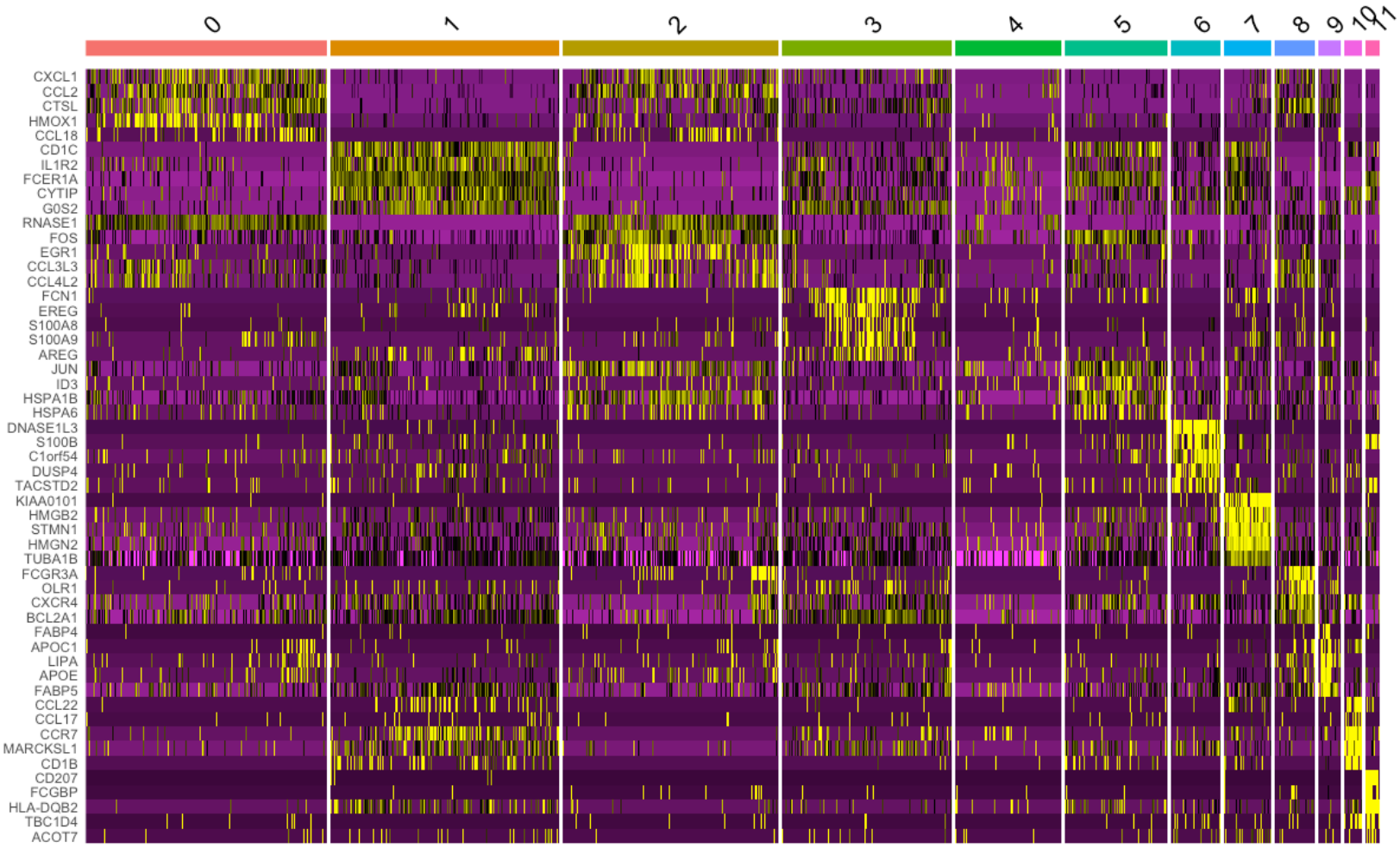


Figure S6E. Clustering of the top 5 differentially expressed genes in each cluster shown in Figure 6SA

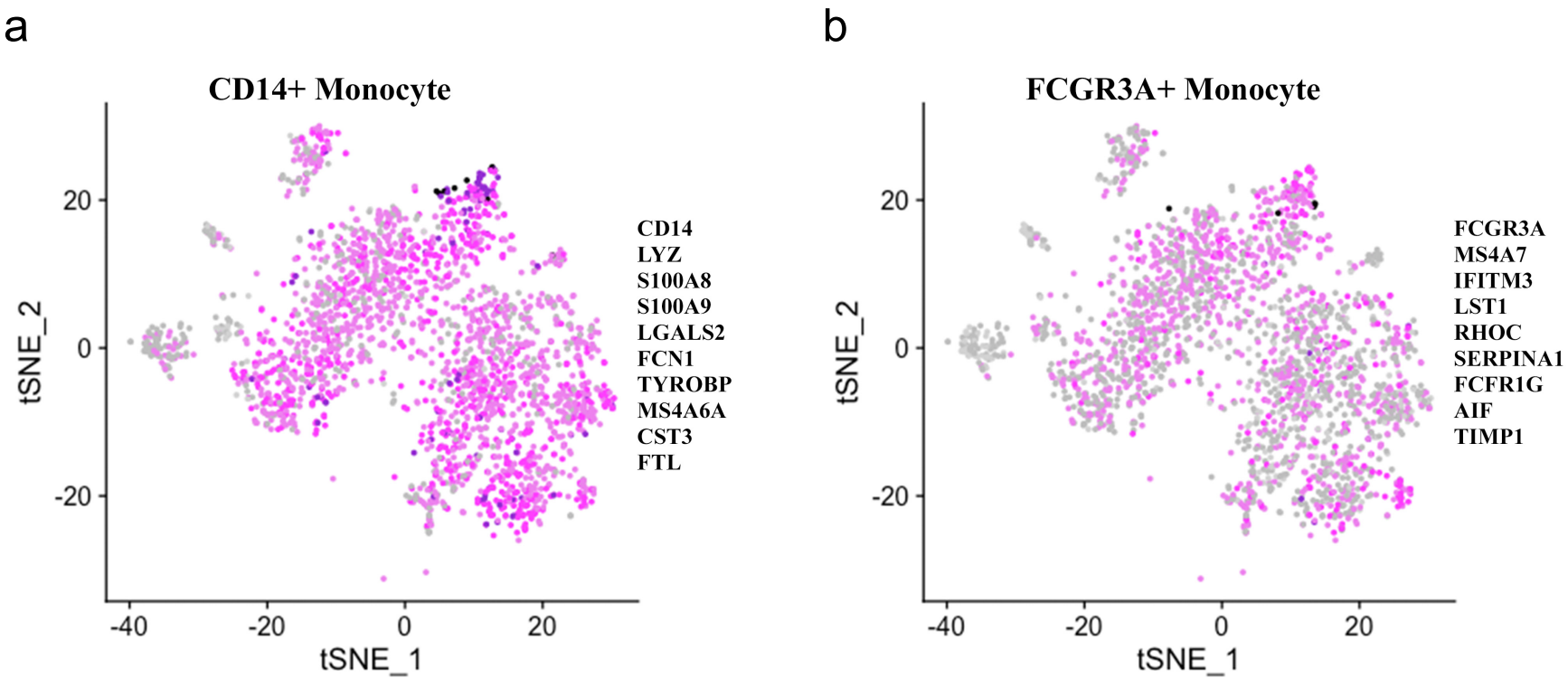


Figure S7. Relative signature scores of CD14^{+} monocyte, FCGR3A^{+} monocyte signatures. Feature plots of relative signature scores calculated on the expression levels of CD14 monocyte marker gene set (comprising CD14, LYZ, S100A8, S100A9, LGALS2, FCN1, TYROBP, MS4A6A, CST3 and FTL; panel a) and FCGR3A monocyte marker gene set (comprising FCGR3A, MS4A7, IFITM3, LST1, RHOC, SERPINA1, FCFR1G, AIF and TIMP1, panel b). The higher intensity of color indicates that more genes in the gene set are expressed more highly. FCN1^{+} mo-DC show higher CD14 monocyte marker gene signature expression.

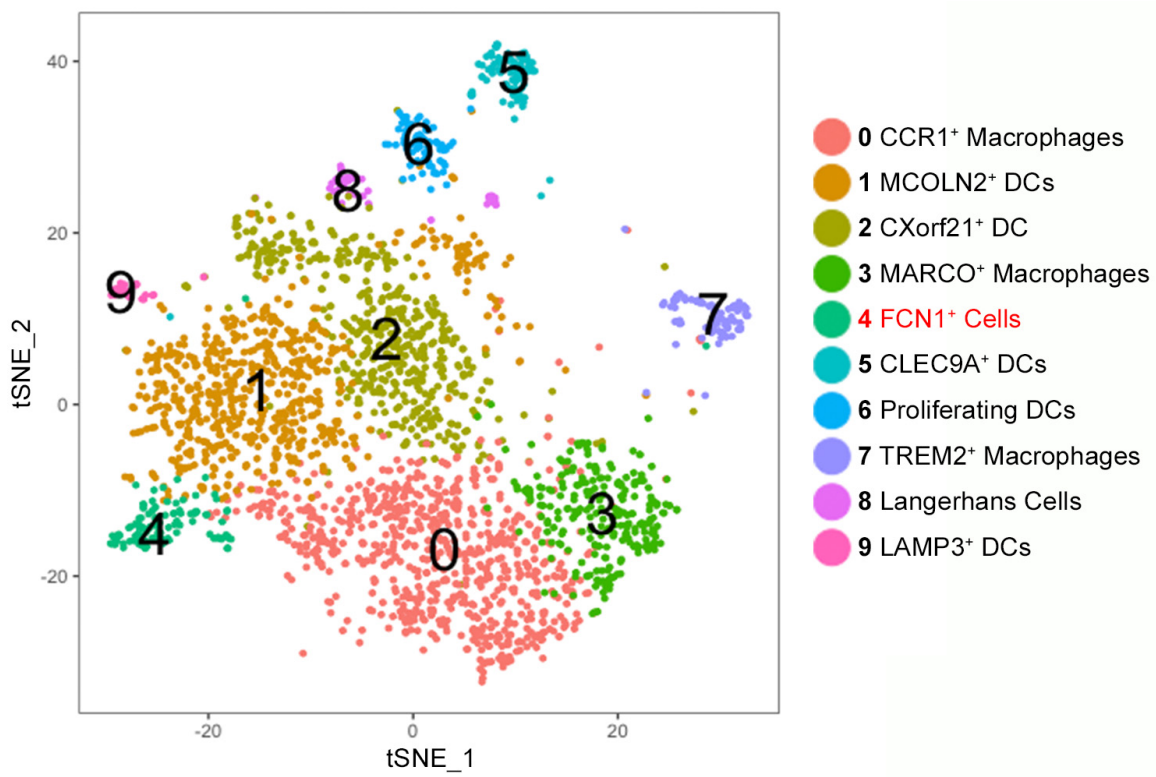


Figure S8. Second database combining 10 HC and 15 additional dcSSc samples also showing FCN1$^+$ cells. t-SNE shows clustering of myeloid cells. FCN1$^+$ mo-DC are seen in cluster #4.

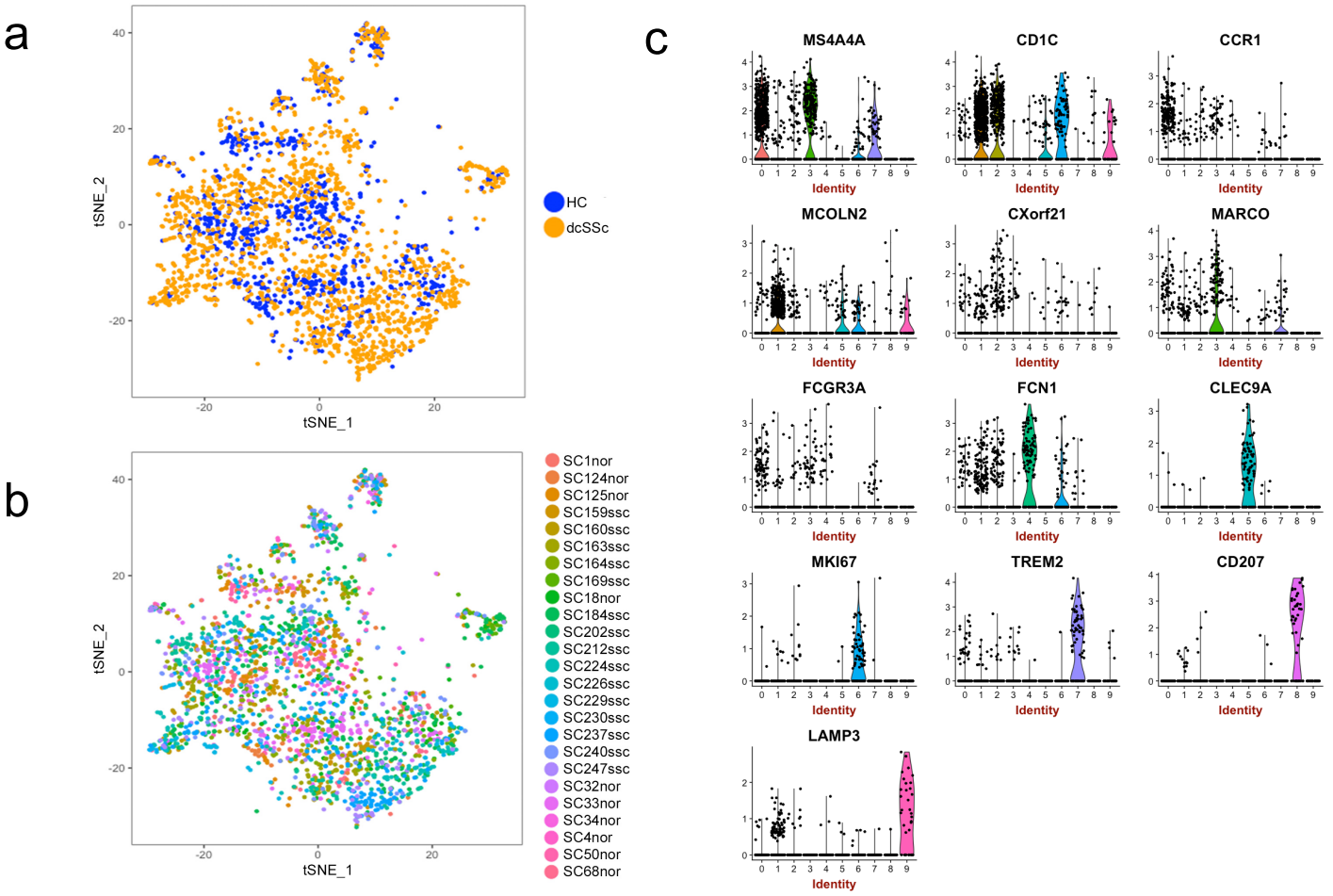


Figure S9. Second database combining 10 HC and 15 additional dcSScsamples. t-SNE shows clustering of myeloid cells colored according to health status (panel a) and original identity (panel b). Marker genes used to identify each cluster are shown as violin plots (panel c); $FCN1^{+}$ mo-DC are seen in cluster #4.

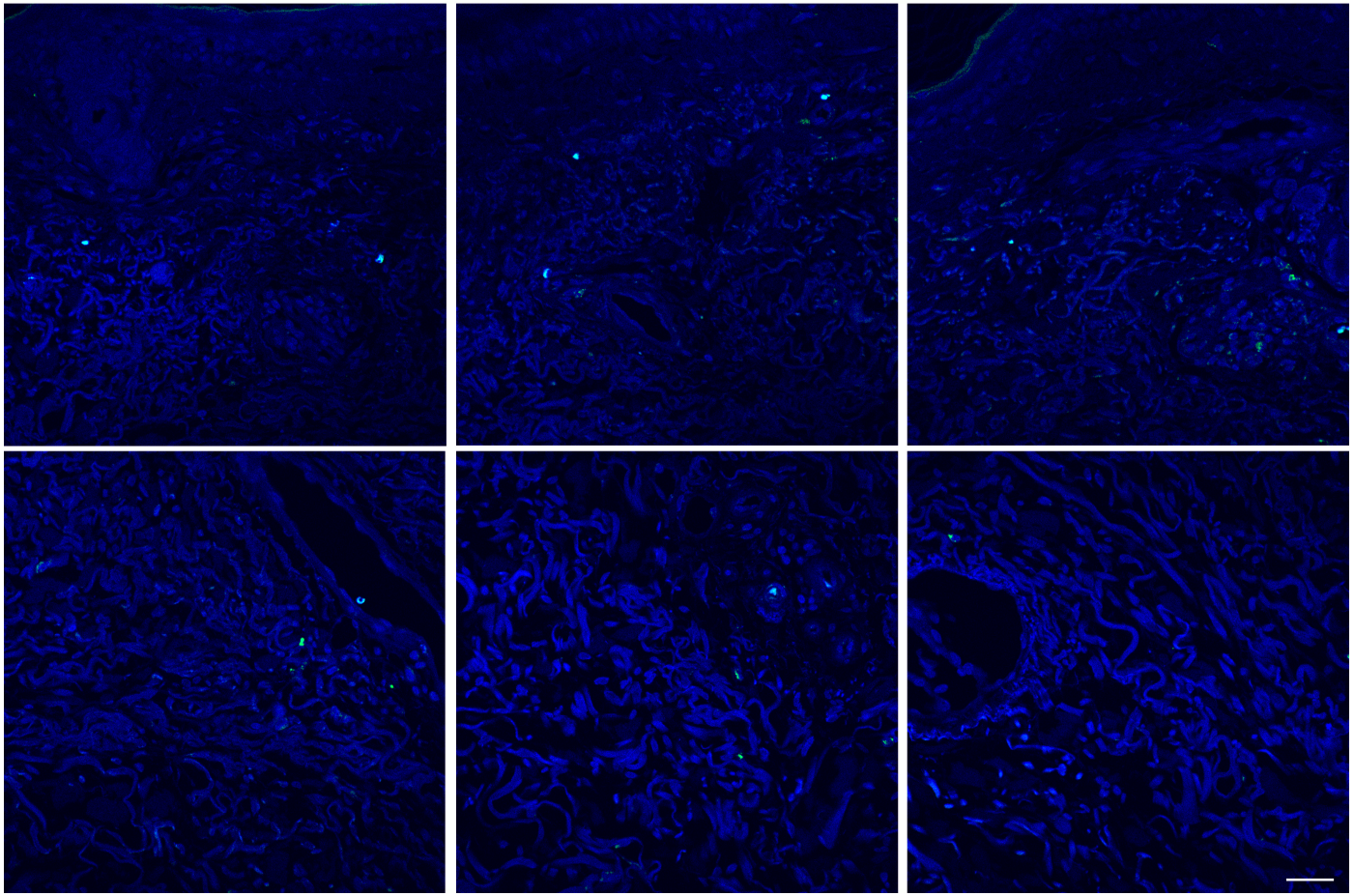


Figure S10A. Total number. of FCN1^{+} cells staining by IF a representative skin biopsy from one dcSSc patient (sd12-5) were counted from six images at 40Xmagnification. Scale bar =100 mm. The total number of FCN1^{+} cells for this patient is 20. The number of FCN1^{+} cells for each biopsy was counted in three 40X images of the low dermis (closed to the epidermis) and three 40X images of deep dermis.

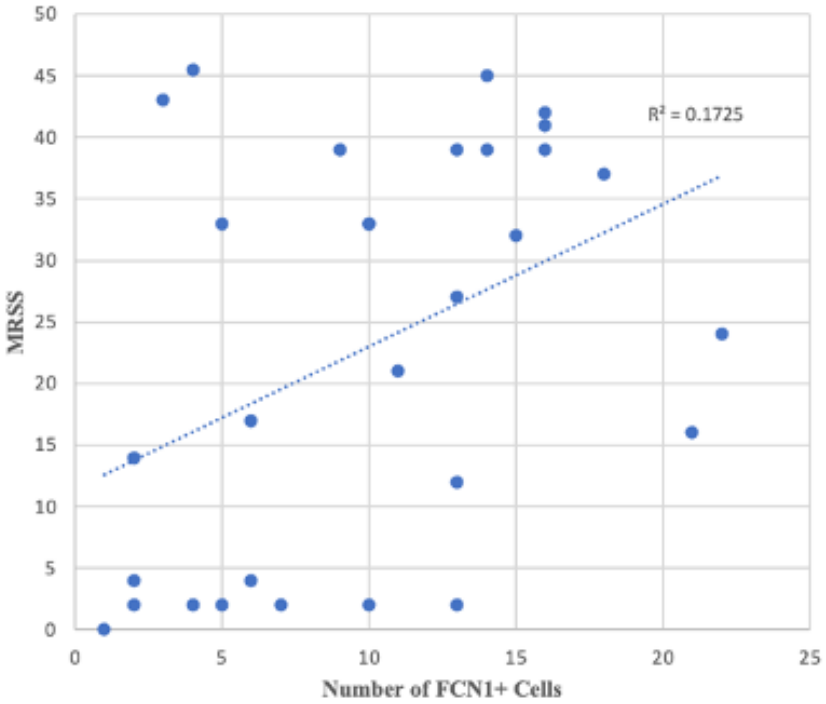


Figure S10B. The number of FCN+ staining cells correlates with the MRSS; R^2=0.1725, $p<0.05$

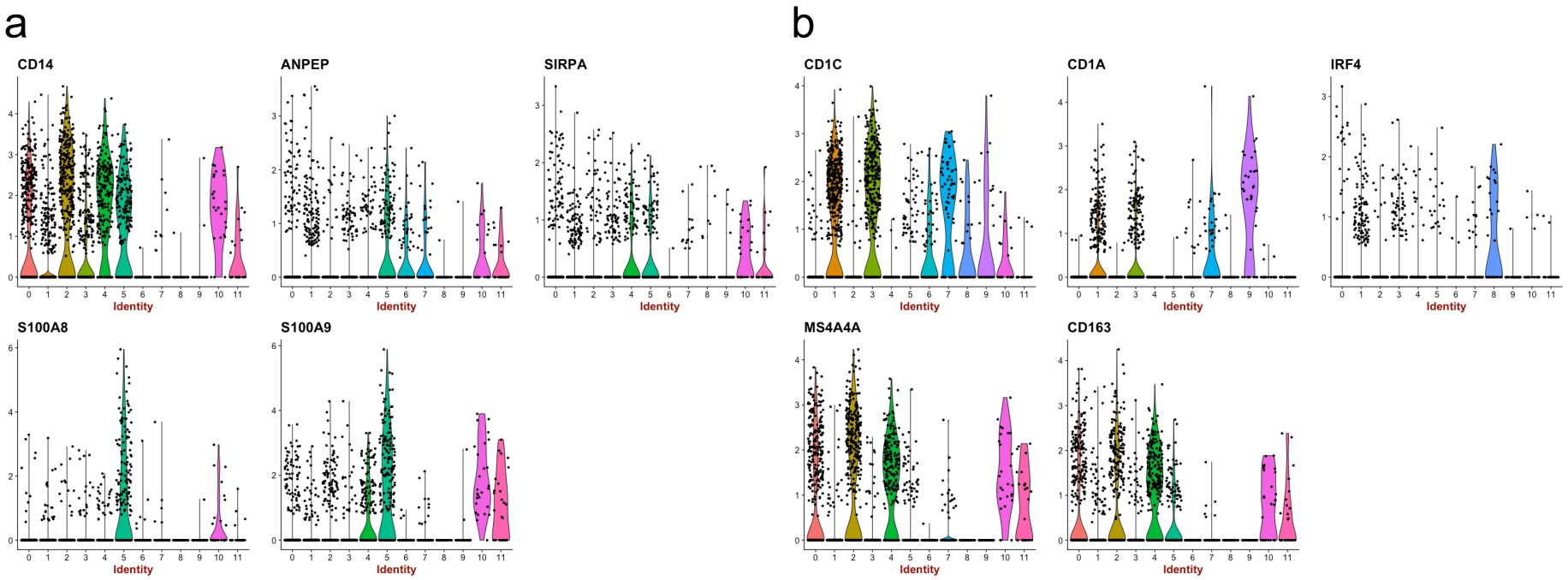


Figure S11. Gene expression demonstrated cluster #5: FCN1^{+} mo-DC markers. Expression of CD14, CD13/ANPEP, CD172a/SIRPA, S100A8 and S100A9 by FCN^{+} mo-DC (panel a). Low level expression of CD1c and absent expression of DC markers: CD1A and IRF4 and low-level expression of macrophage markers: MS4A4A and CD163 (panel b).

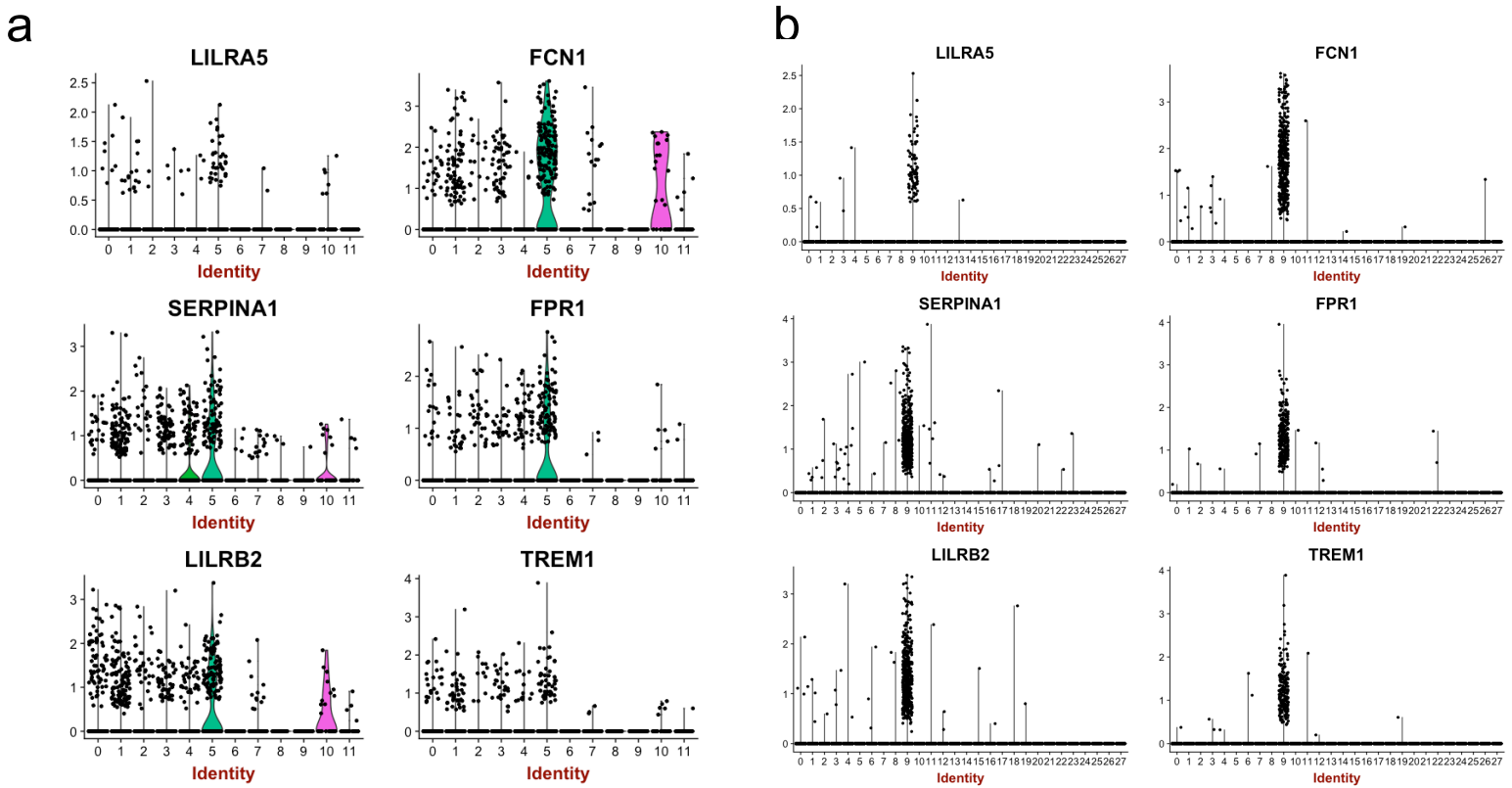


Figure S12. Markers of cluster #5: FCN1^{+} mo-DC are only highly expressed by these cells. Dot plot of specific markers for cluster #5: FCN1^{+} cells in all myeloid cell clusters identified in Fig.1**a.** (**b**) Violin plots of these markers for cluster #5: FCN1^{+} cells in all clusters of cells in human skin. Numbers in violin plots refer to clusters numbers as in Fig.S1**a.**

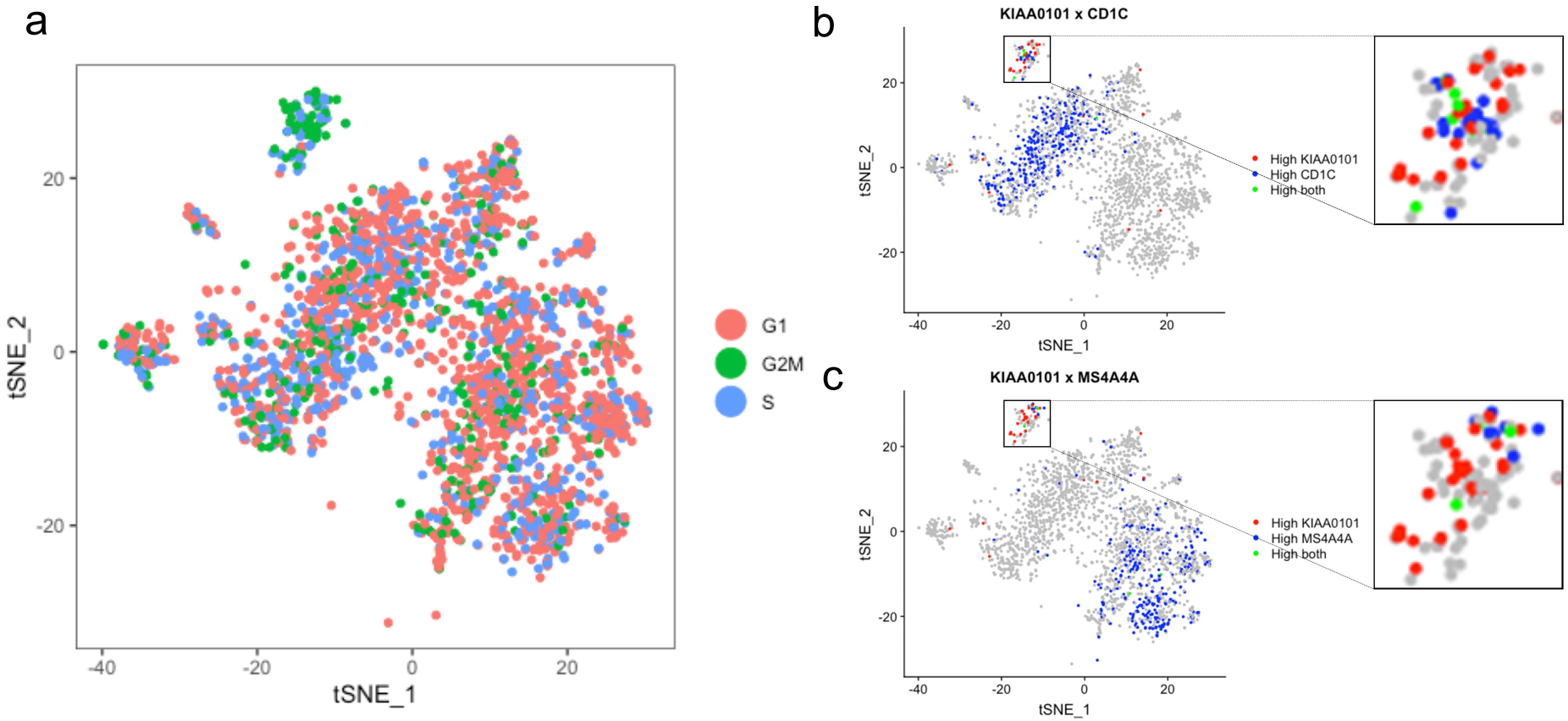


Figure S13. The proliferating macrophages detected along with proliferating DCs. T-SNE colored cells according to cell cycle phase based on canonical markers showing all cells in Mφ/DC cluster #7 and #10 in G2M (green, panel a). KIAA0101, as a proliferative marker, identified proliferating DCs co-expressing cDC2 marker, CD1C, magnified feature-plots of cluster #7 and #10 (panel b). KIAA0101, as a proliferative marker, identified proliferating macrophages co-expressing macrophage marker MS4A4A, magnified feature-plots of cluster #7 and #10 (panel c).

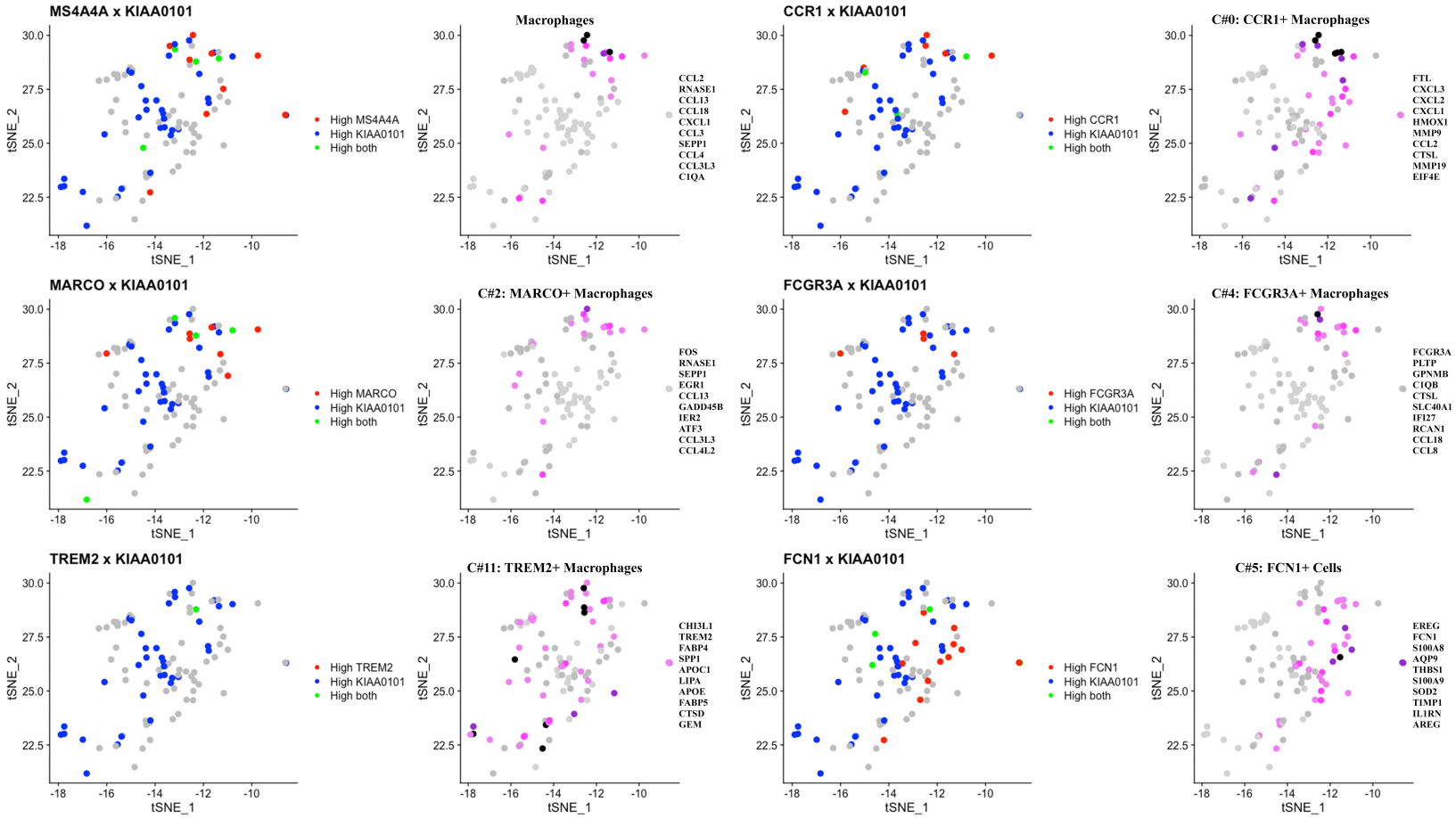


Figure S14. Tracking proliferating macrophage subsets. Feature plots of co-expression of KIAA0101 with module scores of macrophage subsets, shown magnified in feature-plots of clusters #7 and #10. Feature plots of module scores were calculated on the top 10 high expressed genes of each macrophage cluster.

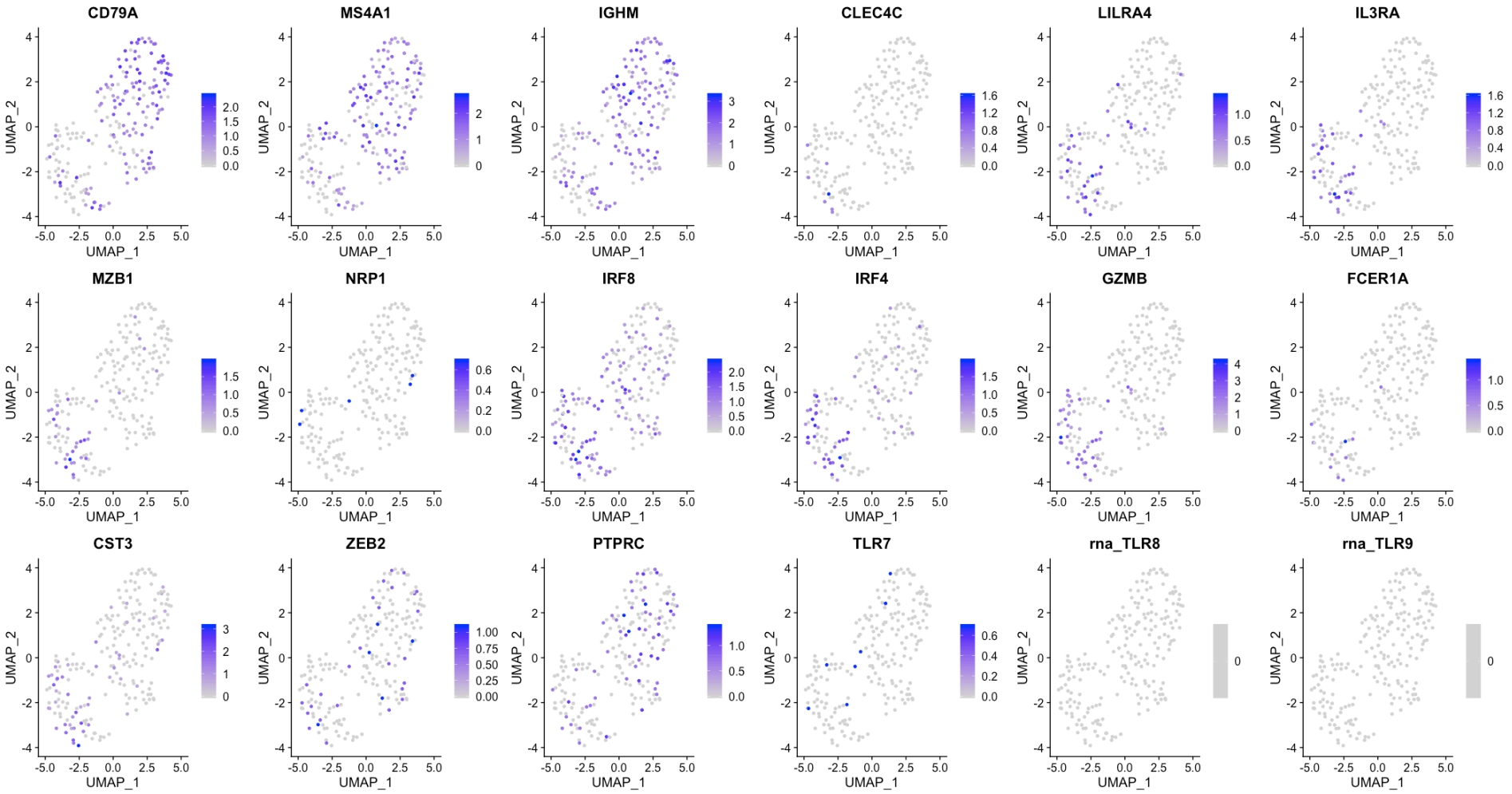


Figure S15. Expression of select genes expressed in B cells or plasmacytoid dendritic cells. Feature plots of gene expression clustered as in Figure 5b (purple indicates increased expression).

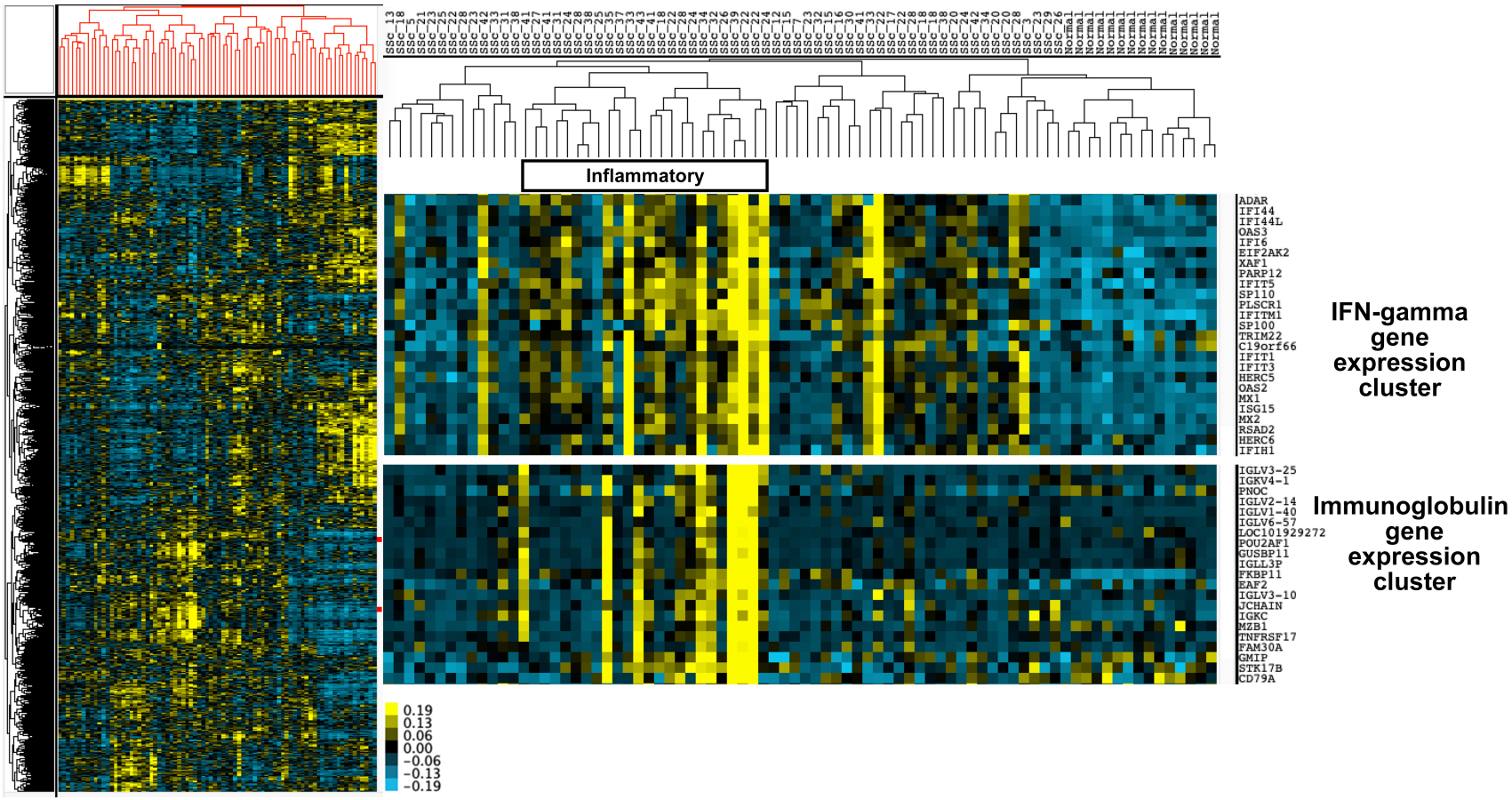


Figure S16. The patient subset with high expression in makers of FCN1^{+} cells was aligned to the previously described inflammatory SSc subset with the exclusive expression of the IFN-gamma genes (such as IFI44, IFI6, IFIT3, IFIH1) and immunoglobulin genes (such as IGLV3, IGKC, IGLL3P).