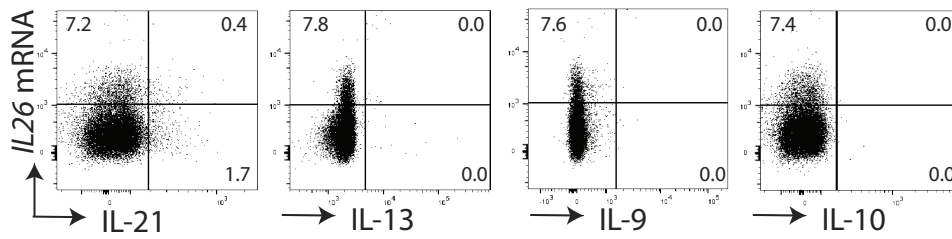
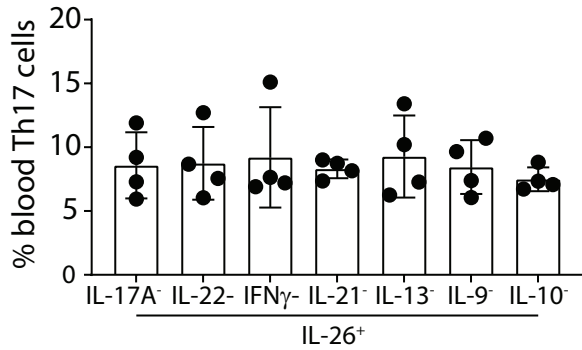


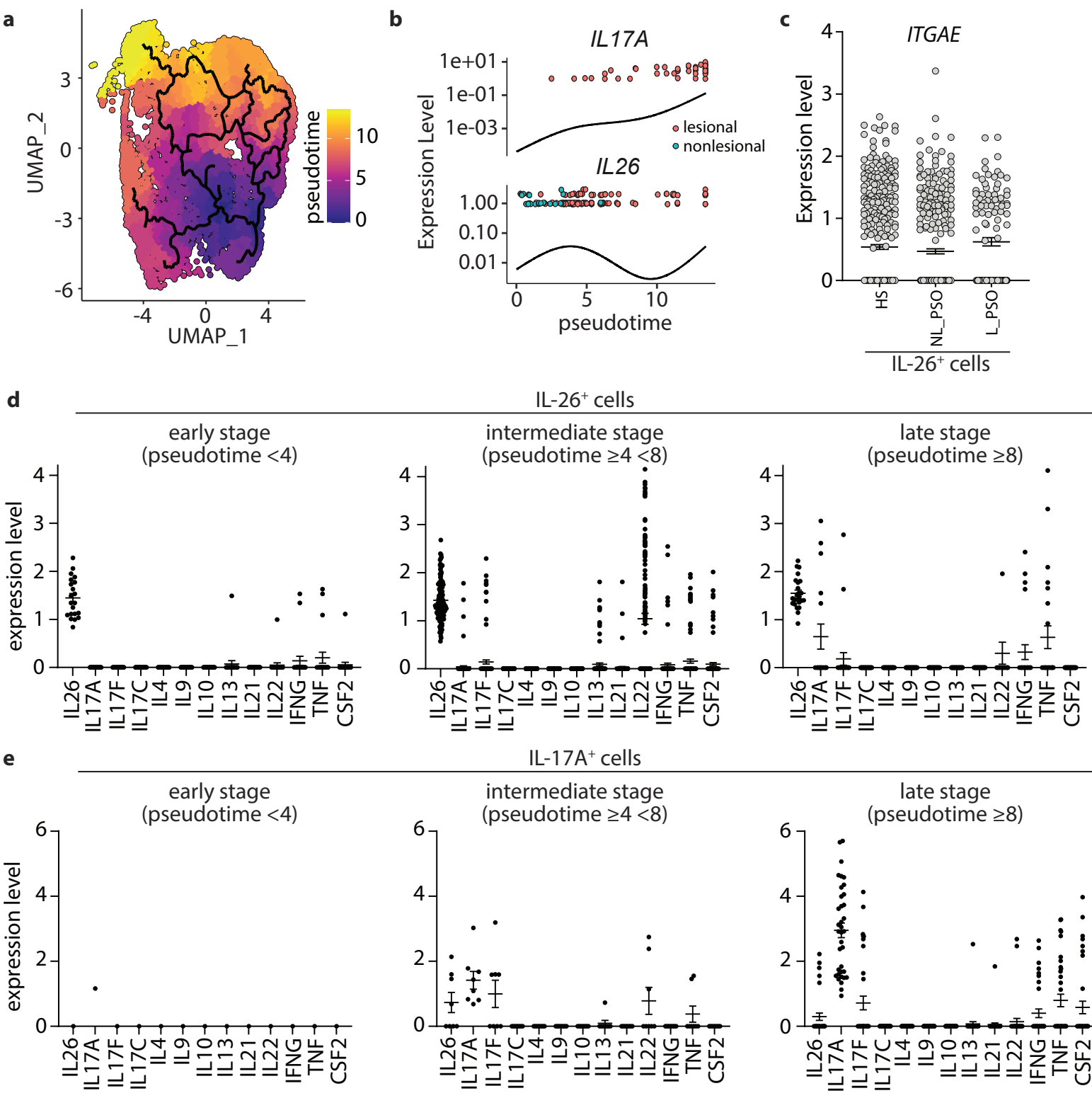
**a****b**

### Supplementary Figure 1. IL-26<sup>+</sup> IL17A<sup>-</sup> Th17 cells do not produce other Th17-derived cytokines

**a**, Flow-FISH analysis of the expression of IL-26 mRNA, and IL-21, IL-13, IL-9, and IL-10 protein in blood-isolated memory TH17 cells. Data from one representative donor is shown.

**b**, Frequencies of IL-26 positive cells and negative for other cytokines among blood memory TH17 cells. Data are mean $\pm$ SD, (n=4 donors).

Source data are provided as a Source Data file.



**Suppl Figure 2. IL-26 production in psoriatic skin occurs early, whereas other Th17-derived cytokines such as IL-17A, IL-22, IL-21 and GM-CSF are induced at later timepoints.**

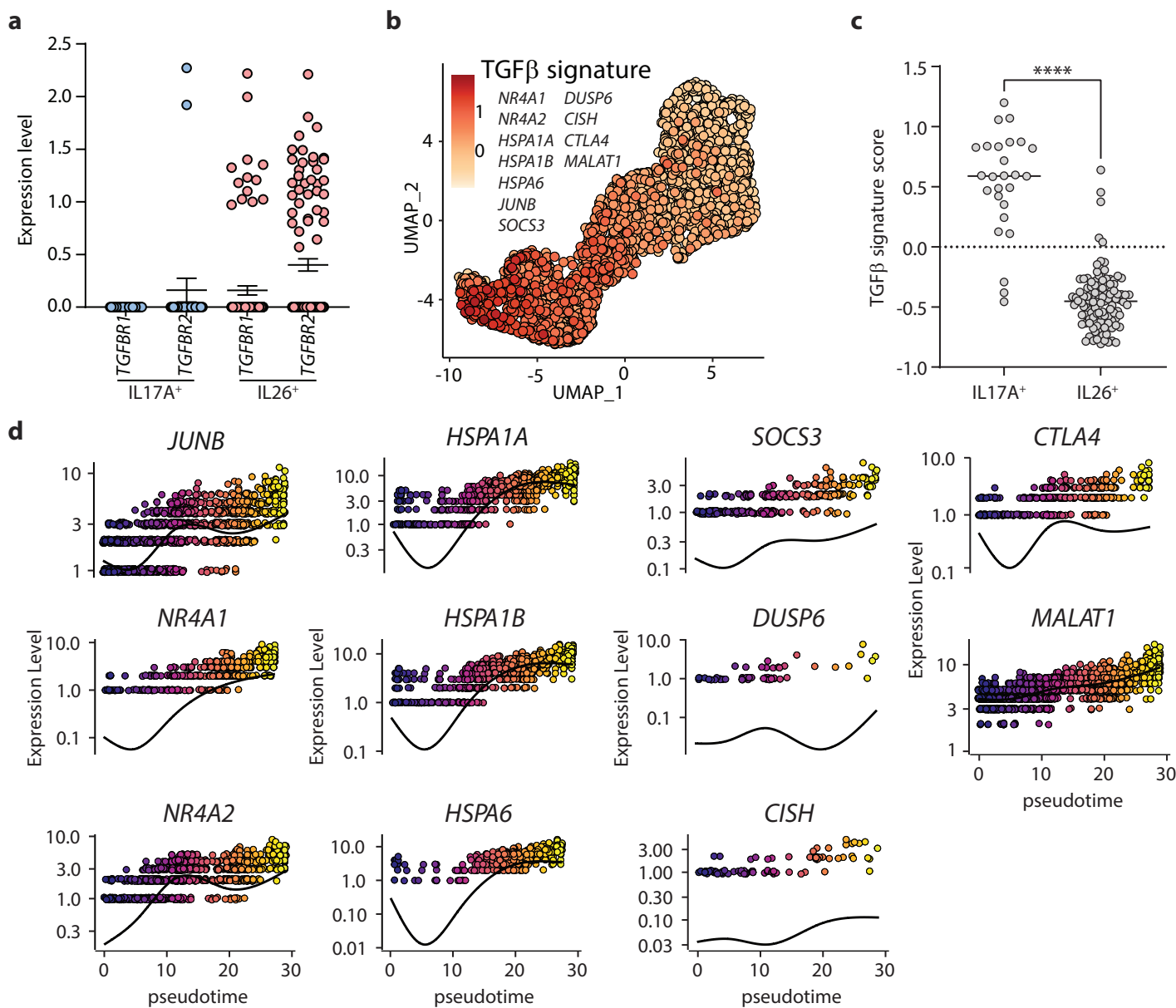
**a**, UMAP projection of the single cell transcriptomes of dermal CD4 T cells from nonlesional (left) and lesional (right) skin of 3 psoriasis patients colored according to the inferred pseudotime. Solid lines are trajectories of gene expression changes learned by Monocle3.

**b**, Dynamics of IL-17A and IL-26 gene expression in nonlesional and lesional dermal CD4 T cells over pseudotime. Solid lines show the expression average.

**c**, Expression of ITGAE (CD103) by IL26+ T cells from healthy (n=379), non lesional (n=304 cells), and lesional (n=116 cells) psoriatic skin. Data represent mean±SEM.

**d-e**, Expression level of different cytokines by IL-26 positive (d) and IL-17A positive (e) dermal CD4 T cells from the skin of 3 psoriasis patients at early (left, n=21 IL26+ cells and 1 IL17A+ cells), intermediate (middle, n=121 IL26+ cells and 8 IL17A+ cells), and late (right, n=24 IL26+ cells and 36 IL17A+ cells) stage of differentiation according to the inferred pseudotime. Data represent mean±SEM.

Source data are provided as a Source Data file.



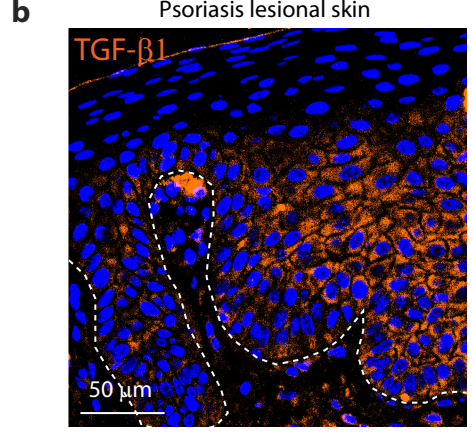
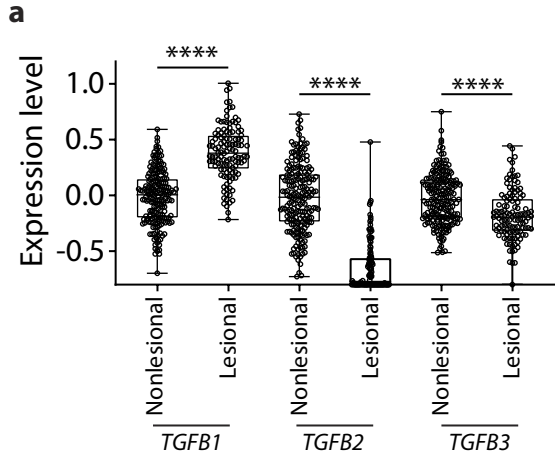
**Supplementary Figure 3. Transition from IL-26 to IL-17A producing T cells in psoriatic skin lesions display TGF-β imprinting**

**a**, Expression of TGFBR1 and TGFBR2 by IL17A<sup>+</sup> (n=26 cells) and IL26<sup>+</sup> T cells (n=107) from lesional psoriatic skin. Data represent mean±SEM.

**b**, UMAP projection of the single cell transcriptomes of dermal CD4 T cells as in Figure 4 colored according to the expression level of the TGF-β signature genes.

**c**, Quantification of TGF-β signature score in IL-17A<sup>+</sup> (n=26 cells) and IL-26<sup>+</sup> single positive cells (n=107). Bars represent mean values. Data were statistically analyzed using two-tailed unpaired Student's t-test. \*\*\*\*p<0.0001.

**d**, Dynamics of the TGF-β signature genes expression in dermal CD4 T cells over pseudotime. Solid lines show the expression average. Source data are provided as a Source Data file.



**Supplementary Figure 4. Increased expression of TGFB1, but not TGFB2 nor TGFB3 in keratinocytes of the basal layers in psoriatic skin**

**a**, Expression level of TGFB1, TGFB2, and TGFB3 in nonlesional (n=199) and lesional (n=120) skin from psoriasis patients using the SSF Bioinformatics hub.

Data are represented as a box plot which bounds extends from the 25th to 75th percentiles, a middle line is plotted at the median, and whiskers go from the minimal to maximal value.

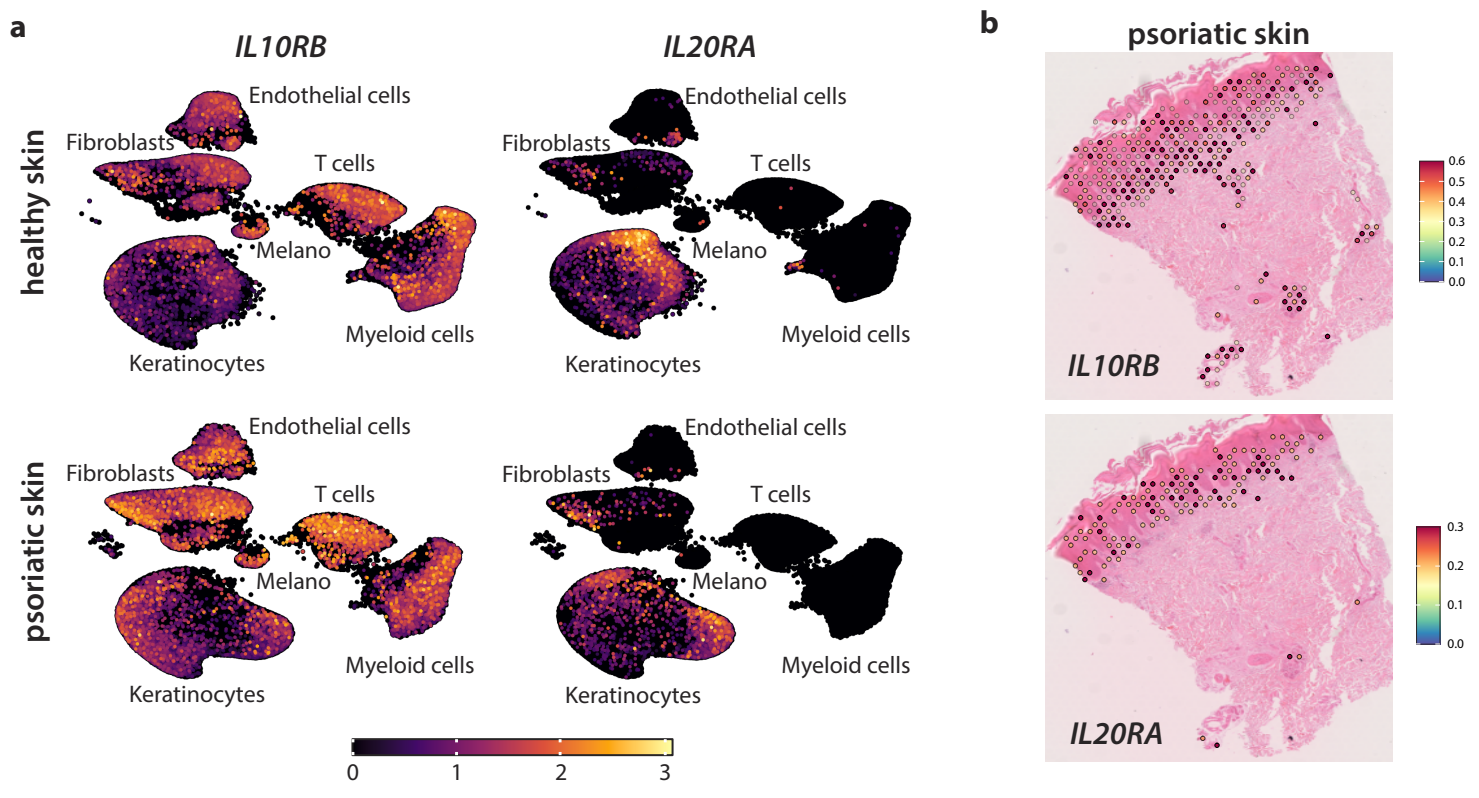
Data were statistically analyzed using one-way ANOVA followed by Tukey's multiple comparisons test. \*\*\*\*p<0.0001.

**b**, Confocal microscopy images of lesional psoriatic skin representative of 3 patients stained for TGF-β1 (orange).

Dashed line delineates the dermo-epidermal junction.

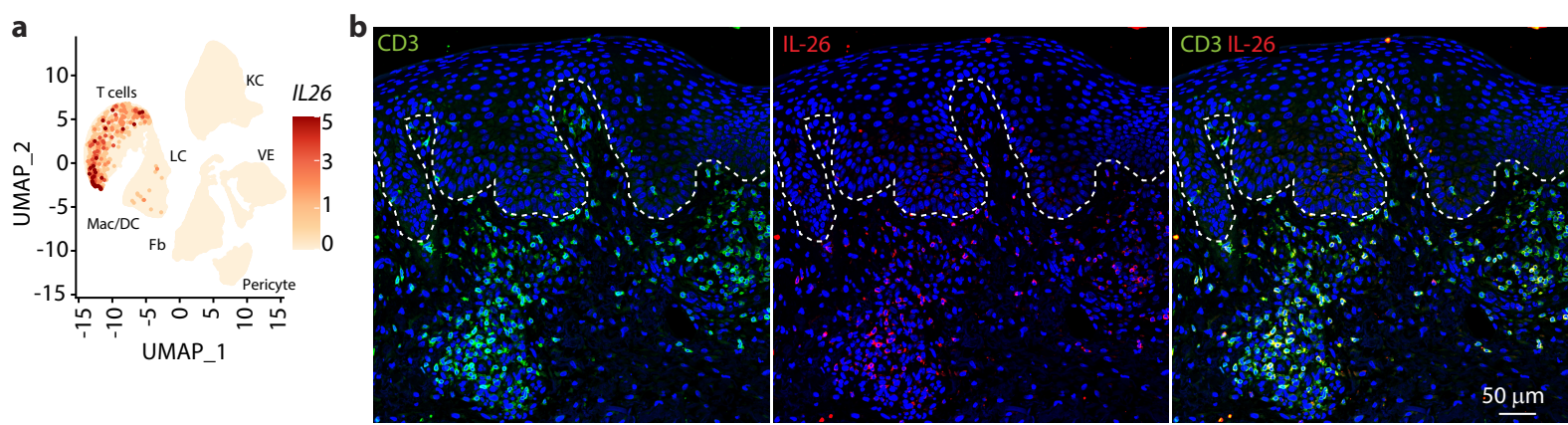
Source data are provided as a Source Data file.





**Supplementary Figure 5. Healthy and psoriatic keratinocytes express the IL-26 receptor**

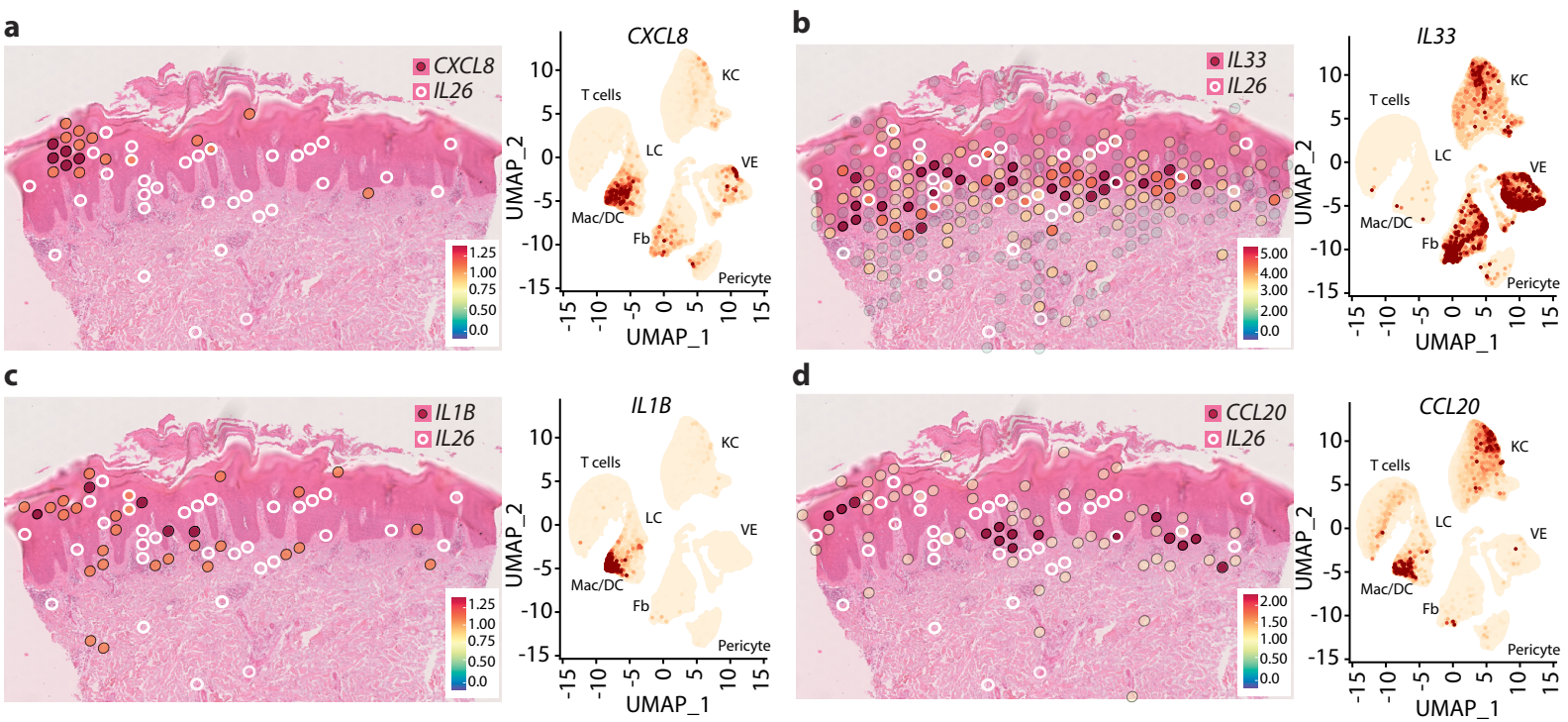
**a**, UMAP projection of the single cell transcriptomes of cells from the skin of 5 healthy donors (top) and 3 psoriasis patients (bottom) colored according to the expression level of *IL10RB* (left) and *IL20RA* (right). **b**, Spatial mapping of *IL10RB* (left) and *IL20RA* (right) expression in the lesional skin of a psoriasis patient.



### Supplementary Figure 6. IL-26 is predominantly expressed by T cells in psoriatic plaques

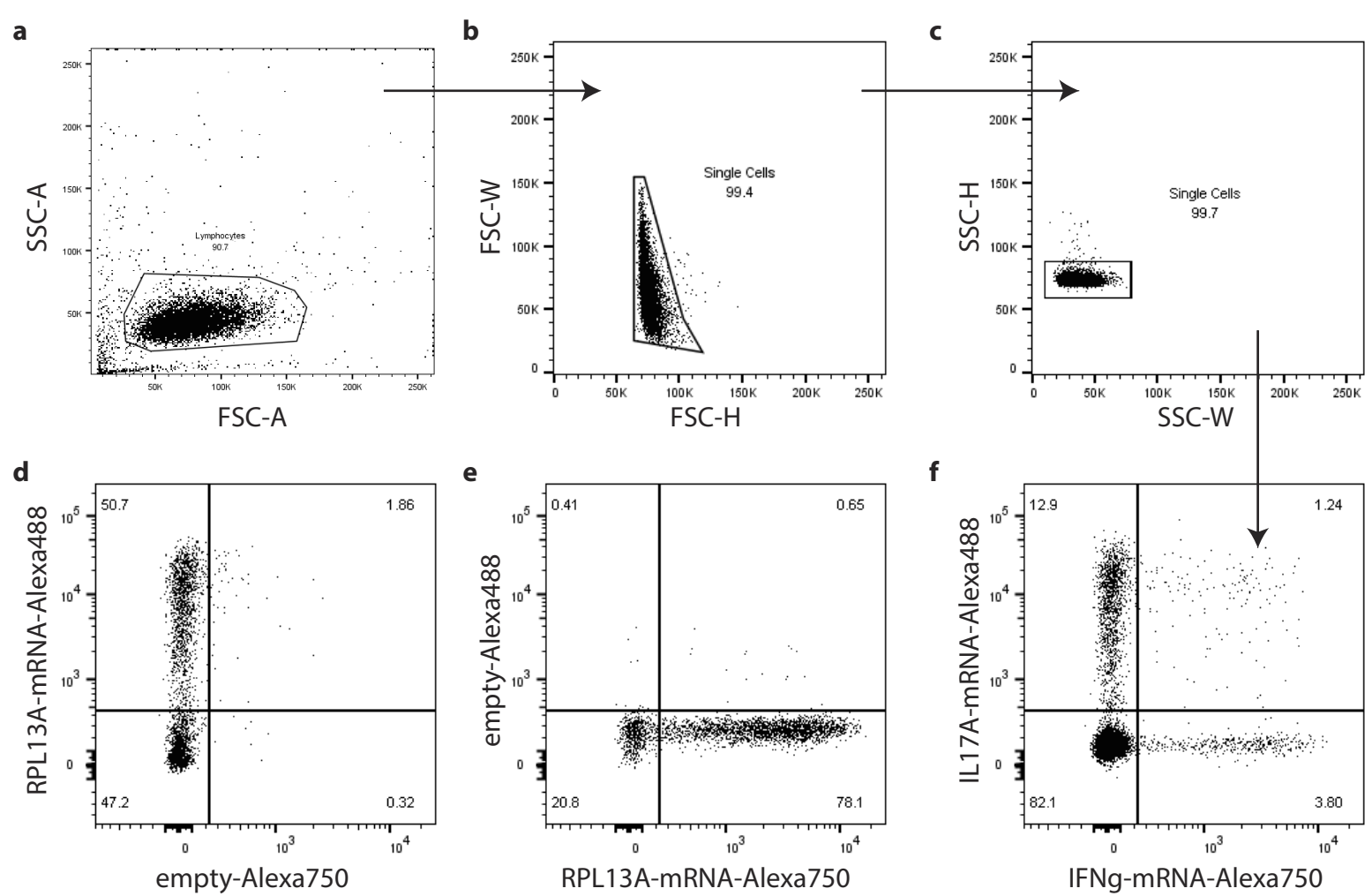
**a**, UMAP projection of the single cell transcriptomes of total cells from lesional skin of 3 psoriasis patients colored according to the expression level of IL26.

**b**, Confocal microscopy images of lesional psoriatic skin representative of 5 patients stained for CD3 (green) and IL-26 (red). Dashed line delineates the dermo-epidermal junction.



**Supplementary Figure 7. IL-1 $\beta$ , IL-33, and CCL20 are expressed by dermal monocytes/macrophages and fibroblasts, and do not co-localize with IL-26-expressing T cells**

**a-d**, Spatial mapping of CXCL8 (a), IL33 (b), IL1B (c), and CCL20 (d) expression in the lesional skin of a psoriasis patient (left) and UMAP projection of the single cell transcriptomes of total cells from lesional skin of 3 psoriasis patients colored according to the expression level of each gene (right). White circles in the spatial image show IL26+ spots.



### Supplementary Figure 8. Gating strategy for Flow-FISH analysis

**a**, Live blood-isolated Th17 cells (or in vitro differentiated Th17 cells) were gated based on SSC and FSC area parameters as an homogenous population.

**b-c**, doublet cells were then excluded using the height and width of FSC and SSC respectively.

**d-e**, The Flow-FISH procedure was verified by assessing the housekeeping RPL13A mRNA expression using positive control probes labeled with Alexa488 or Alexa750.

**f**, The mRNA expression of cytokines of interest were measured (e.g. IL17A, INFg).

**Supplementary Table 1. Human samples and datasets used in this study**

<b>Number of patients</b>	<b>Age in years Median (Range)</b>	<b>Material</b>	<b>Ethics/Consent</b>	<b>Figures</b>	<b>Reference</b>
5 psoriasis skin samples	36 (32-55)	Biobanked FFPE material	CER-VD 2020-02204	Fig.6c; Fig.7; SuppFig.4b; SuppFig.5b, SuppFig.6b	NA
3 healthy skin samples	43 (30-52)	Fresh residual material from excisional surgery	CER-VD 2020-02204	Fig.6f	NA
15 healthy blood samples	unknown	Buffy coats	Interregional Blood Transfusion Center, project 85	Fig.1 to 3; SuppFig.1, SuppFig.8	NA
134 psoriasis skin samples	See publication	Re-analysis of published microarray datasets	See publication	Fig.6a; SuppFig.4a	(36)
3 psoriasis skin samples	See publication	Re-analysis of published single-cell RNAseq datasets	See publication	Fig.4; Fig.6b; SuppFig.2, SuppFig.3, SuppFig.5a, SuppFig.6a, SuppFig.7	(24)
10 psoriasis	See publication	Re-analysis of published single-cell RNAseq and TCRseq datasets	See publication	Fig.5	(25)