

CCR7⁺ Dendritic Cells Expressing Both IL-23A and IL-12B Potentially Contribute to Psoriasis Relapse

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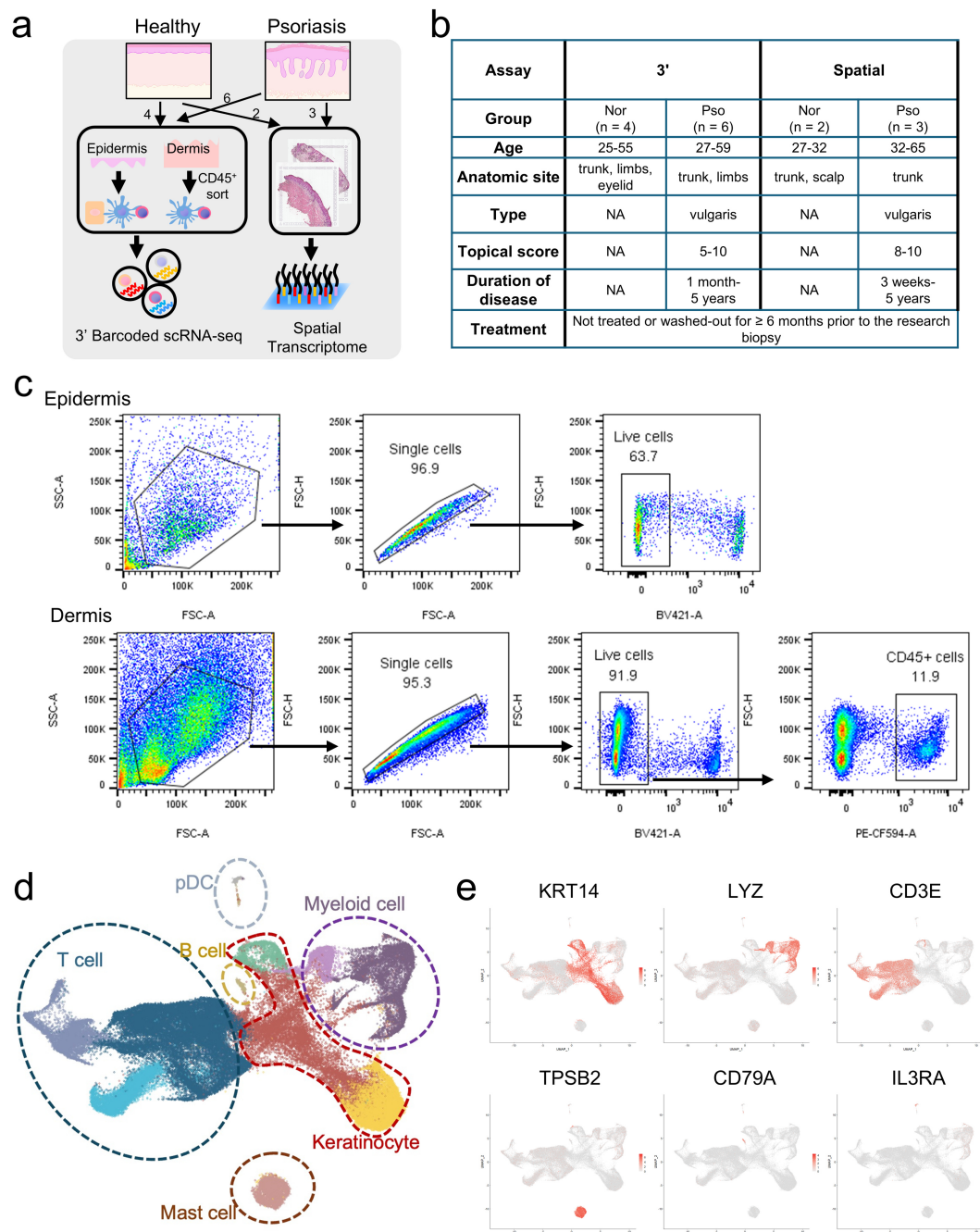
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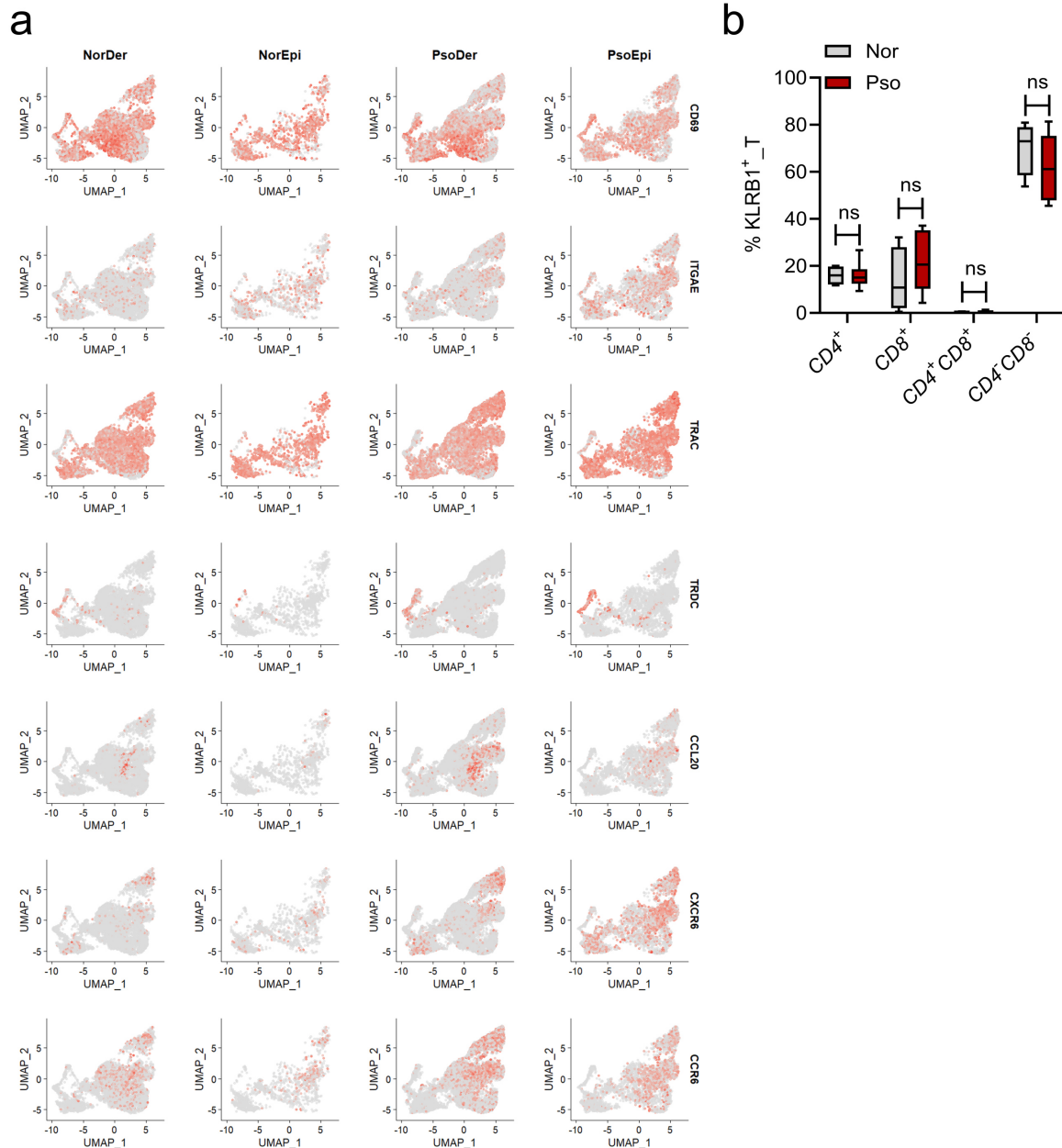
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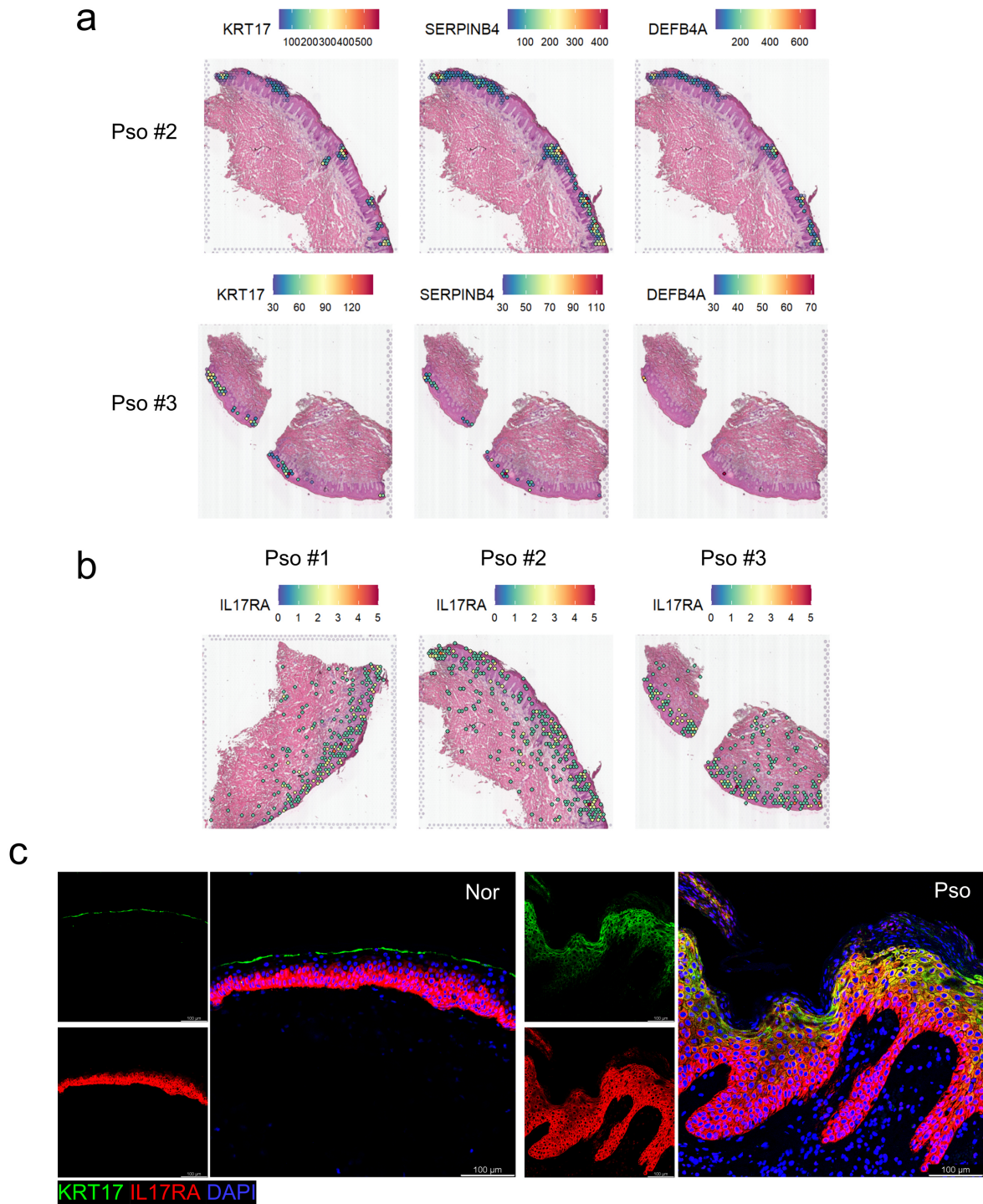
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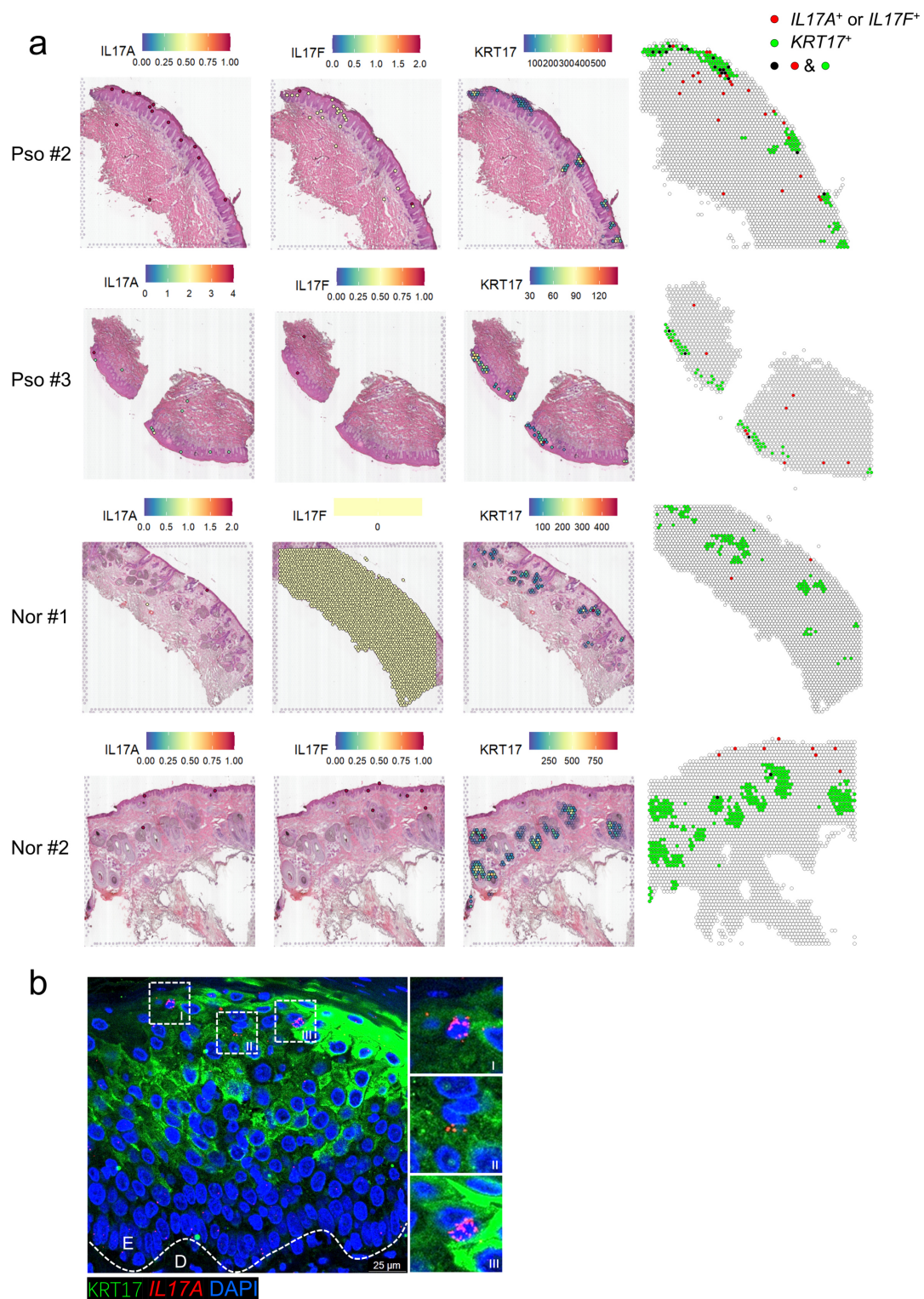
Supplementary Figure 1. A single-cell transcriptomic landscape in the skin of patients with psoriasis and healthy donors. **a**, Schematic overview of skin samples processed for 3'-barcoded scRNA-seq and spatial transcriptome. **b**, General information of patients with psoriasis and healthy donors. **c**, Representative flow cytometry plots showing the gating strategy of all live cells in the epidermis and CD45⁺ live leukocytes in the dermis. **d**, UMAP dimensional reduction and cell type clustering of 3'-barcoded scRNA-seq data containing epidermal cells and dermal CD45⁺ leukocytes from patients with psoriasis and healthy donors. **e**, Feature-plots of marker genes for cell clustering in (d).



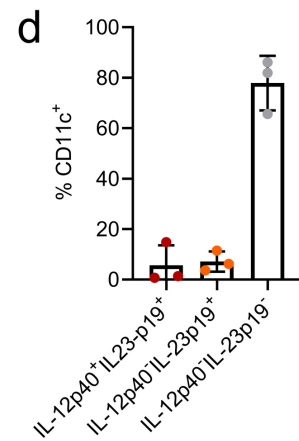
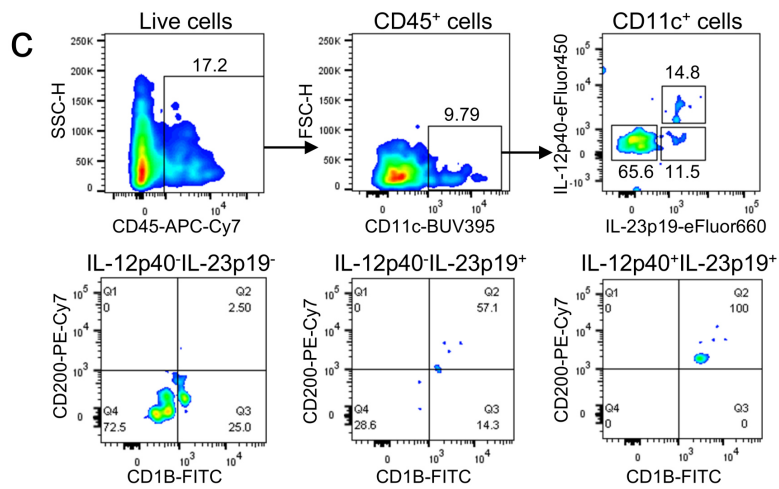
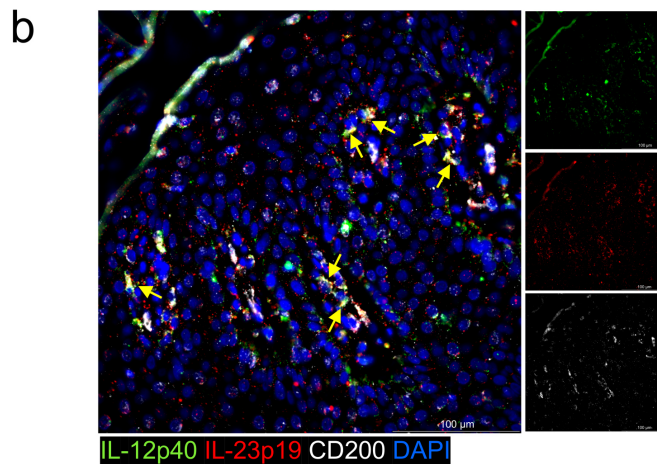
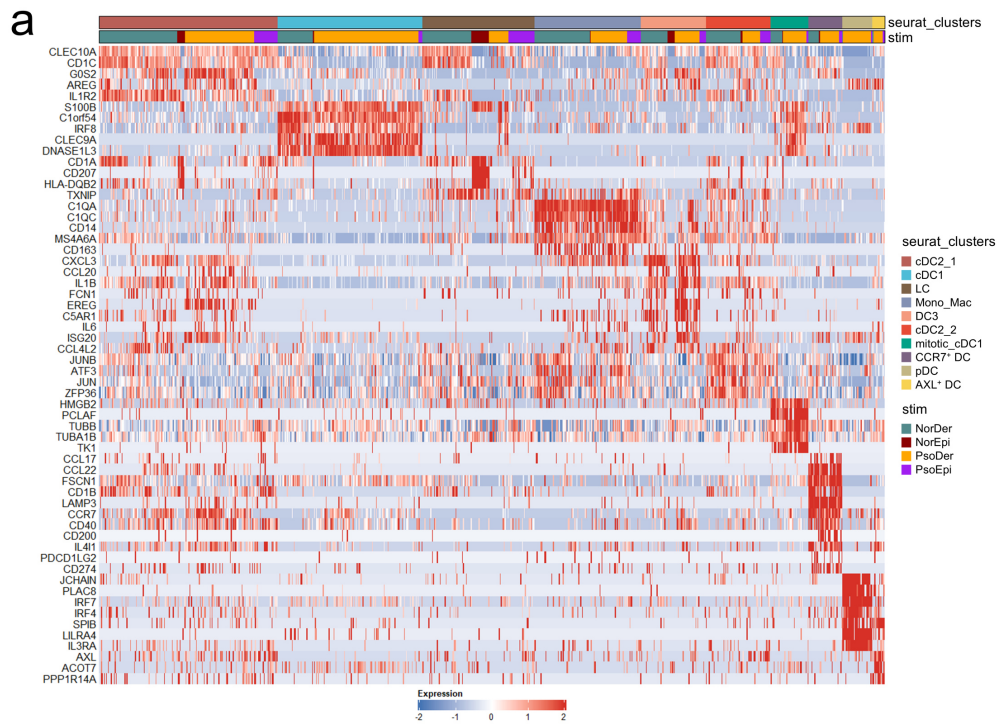
Supplementary Figure 3. Characterization of *KLRB1*⁺ T cells. **a**, Feature-plots of indicated genes in T cells. **b**, Percentages of *CD4*⁺, *CD8*⁺, *CD4*⁺*CD8*⁺ and *CD4*⁻*CD8*⁻ T cells in *KLRB1*⁺ T cells from psoriatic samples and healthy controls. Data represent the 25th to 75th percentiles (whiskers showing min to max and centre showing the mean value). ns, not significant. Source data are provided as a Source Data file.



Supplementary Figure 4. Spatial distribution of IL-17A-downstream signatures.
a, b, Spatial feature-plots of indicated genes in psoriatic skin sections. **c,** Representative immunofluorescence images of KRT17 and IL17RA expression in normal ($n = 3$) and psoriatic skin sections ($n = 5$). Scale bar, 100 μm . Data are representative of two independent experiments.

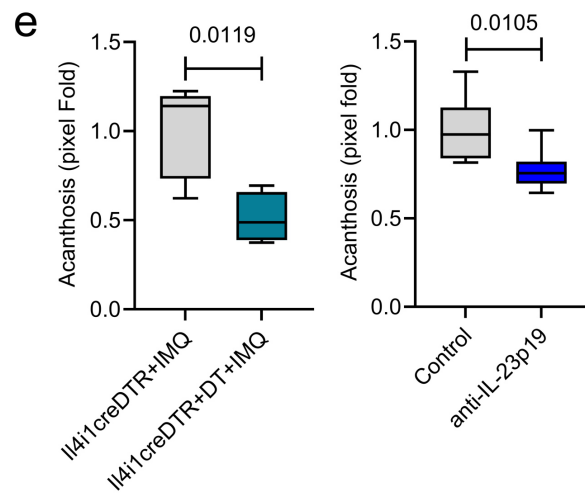
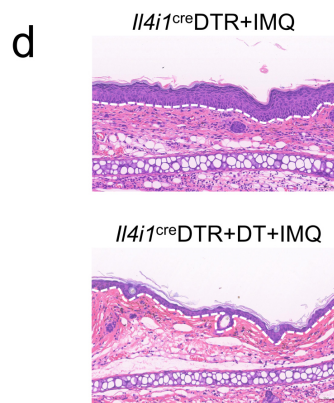
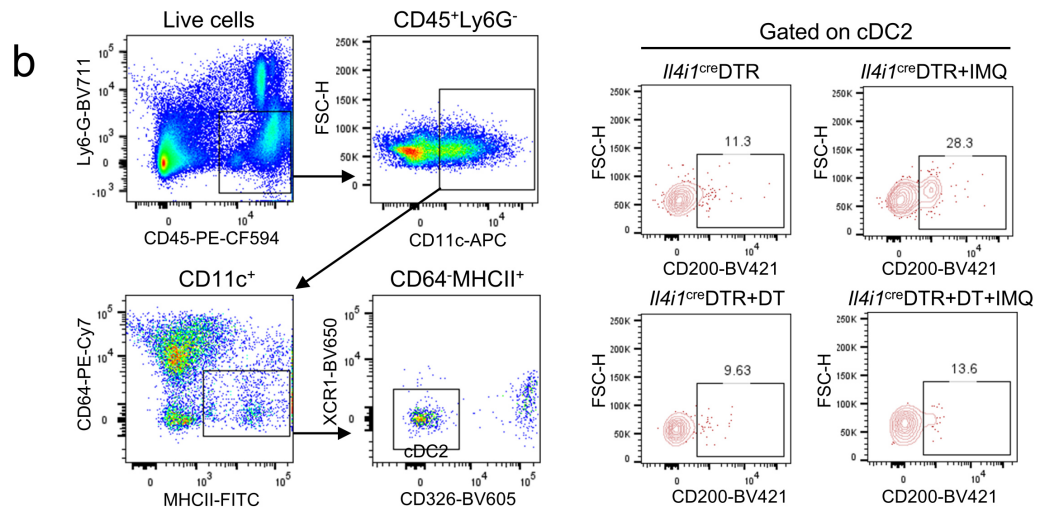
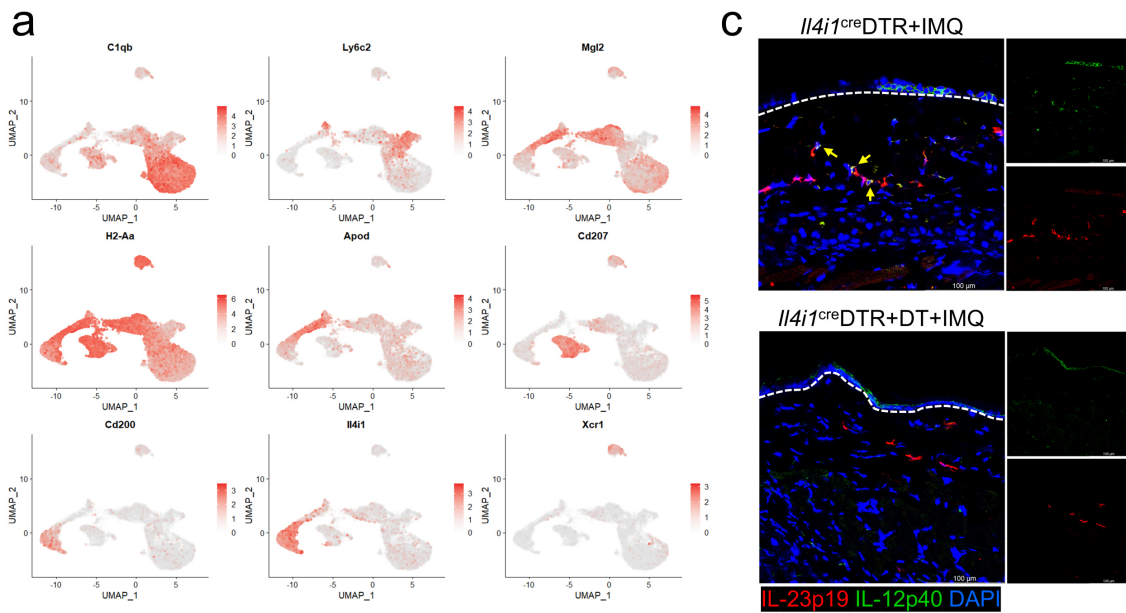


Supplementary Figure 5. Co-localization of IL-17 and KRT17⁺ keratinocytes in psoriatic epidermis. a, Spatial feature-plots of *IL17A* and *IL17F* in skin sections from psoriatic patients and healthy donors and merged with KRT17⁺ (*KRT17* expression > 30) spots. **b**, Representative image of RNAscope detection of *IL17A* combined with immunofluorescence of KRT17 in psoriatic skin (n = 3). Scale bar, 25 μ m. Data are representative of two independent experiments.

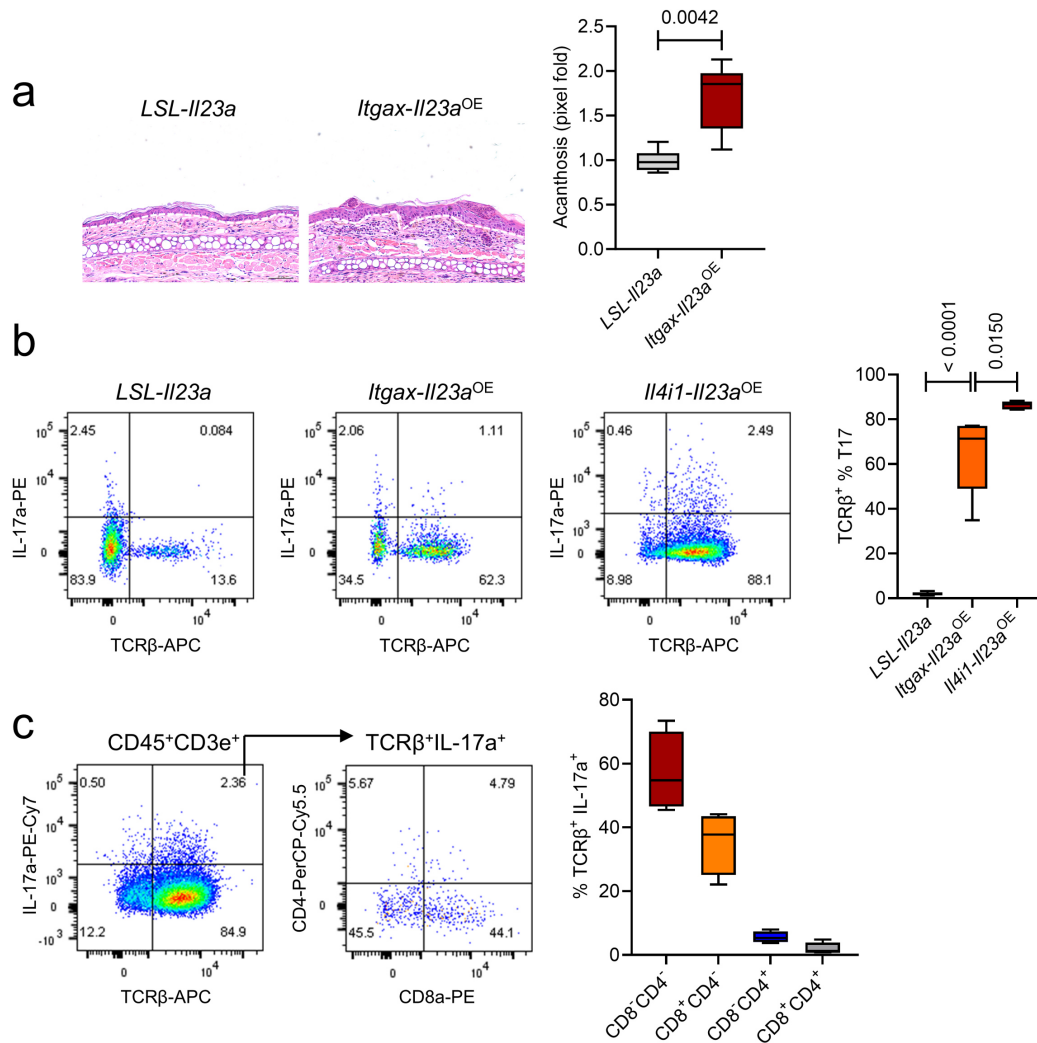


Supplementary Figure 6. DC and monocyte subtypes in psoriatic and normal skin.

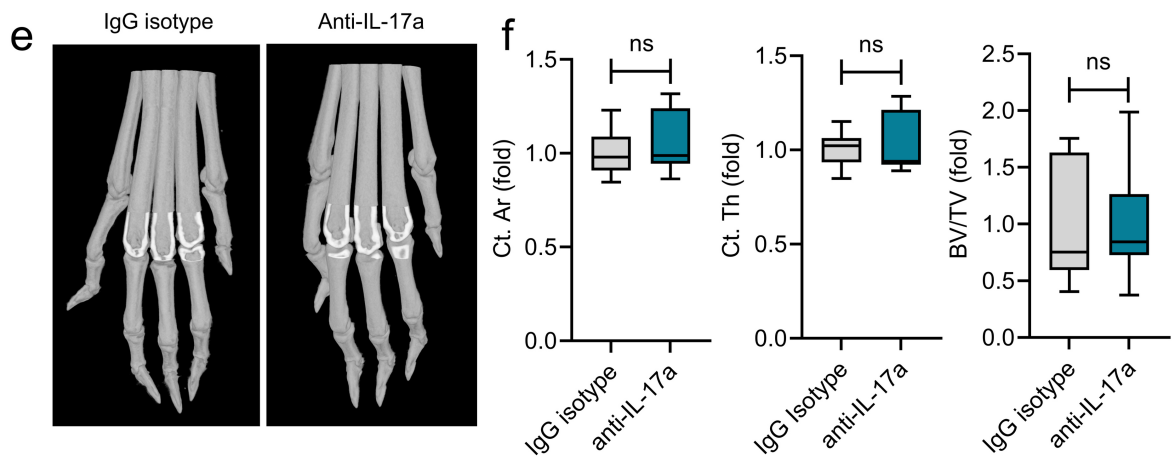
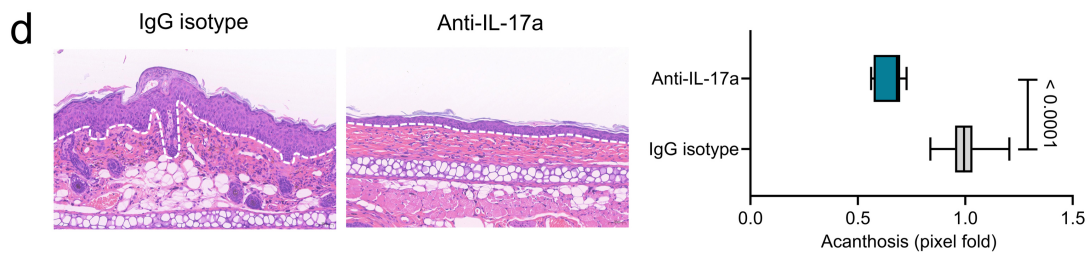
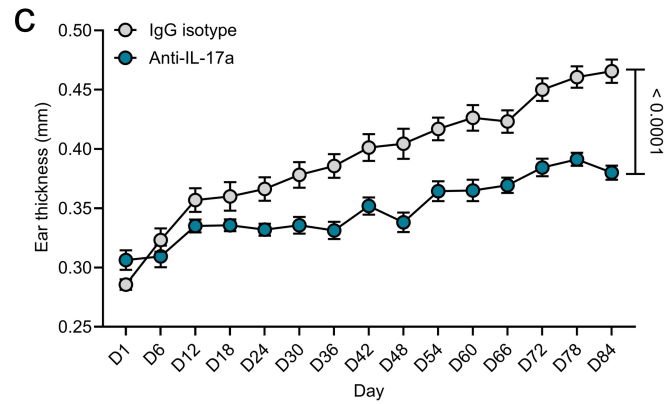
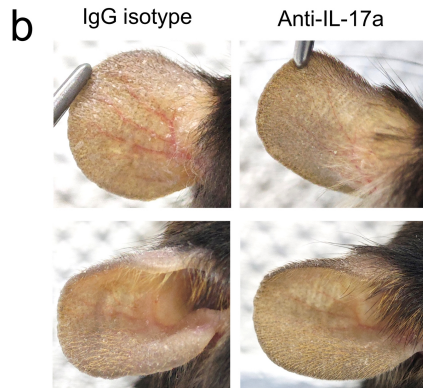
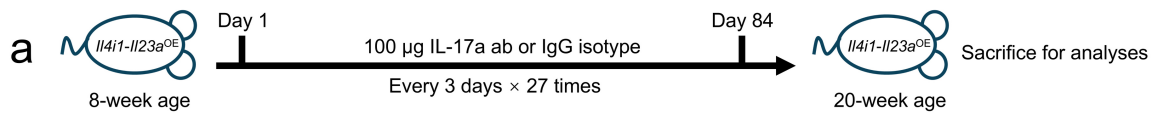
a, Heatmap of signature genes in DC and monocyte subtypes in **Figure 3a**. **b**, Representative immunofluorescent labeling of CD200, IL12B and IL23A in psoriatic skin (n = 3). Scale bar, 100 μ m. **c**, Representative flow cytometry plots of IL-12p40⁺IL-23p19⁺, IL-12p40⁻IL-23p19⁺ and IL-12p40⁻IL-23p19⁻ cells in CD45⁺CD11c⁺ cells from psoriatic skin samples (n = 3). **d**, Percentages of IL-12p40⁺IL-23p19⁺, IL-12p40⁻IL-23p19⁺ and IL-12p40⁻IL-23p19⁻ cells in CD45⁺CD11c⁺ cells from psoriatic skin samples (n = 3). Data represent the mean $\pm$ SEM. Data (**b-d**) are representative of three independent experiments. Source data are provided as a Source Data file.



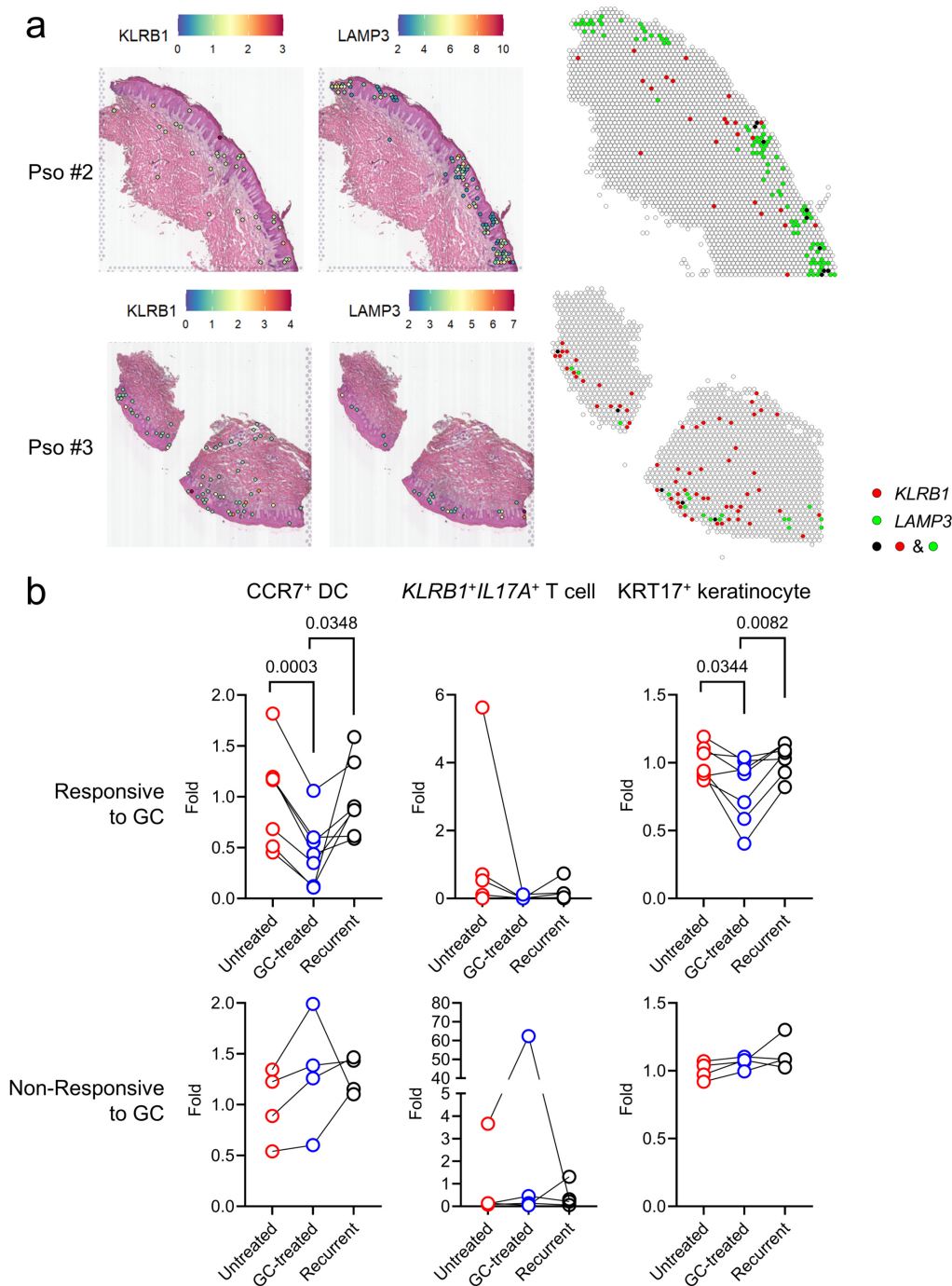
Supplementary Figure 7. Characterization of myeloid cells in IMQ-induced murine skin. **a**, Feature-plots of indicated genes in CD45⁺Ly6G⁺CD3⁺CD19⁺ myeloid cells from mouse ears treated or not with IMQ for 2 days or 5 days. **b**, Representative flow cytometry plots of CCR7⁺ DC subsets in cDC2 (CD45⁺Ly6G⁺CD11c⁺MHCII⁺CD64⁺CD326⁺XCR1⁺) of ears from *Il4l^{cre}*DTR mice treated under the indicated conditions (n = 3 for the IMQ-untreated conditions and n = 5 for the IMQ-treated conditions). **c**, Representative immunofluorescent labeling of Il12b and Il23a in ears of 3-day-IMQ-treated *Il4l^{cre}*DTR mice injected with DT or vehicle (n = 3). Scale bar, 100 μ m. **d**, Representative H&E images showing the ears of 5-day-IMQ-treated *Il4l^{cre}*DTR mice injected with DT (n = 4) or vehicle (n = 5). Scale bar, 50 μ m. **e**, Quantification of acanthosis in ears of IMQ-treated *Il4l^{cre}*DTR mice injected with DT (n = 4) or vehicle (n = 5), and of IMQ-treated C57BL/6 mice injected daily with 100 μ g IL-23p19 antibody (Clone: G23-8, n = 7) or control (n = 9). Data represent the 25th to 75th percentiles (whiskers showing min to max and centre showing the mean value). *P*-values were determined by two-tailed unpaired *t*-test. Data (**b-e**) are representative of two independent experiments. Source data are provided as a Source Data file.



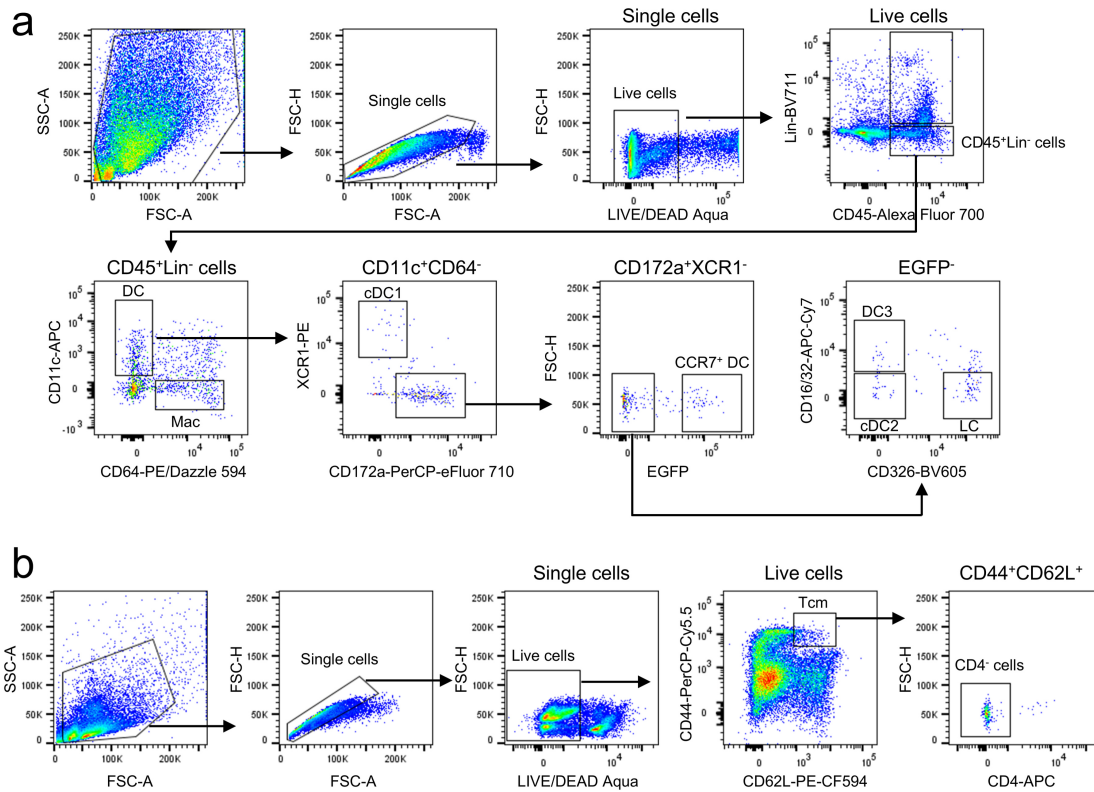
Supplementary Figure 8. Pathological features of ear skin in *Itgax-Il23a^{OE}* and *Il4i1-Il23a^{OE}* mice. **a**, Representative H&E images and quantification of acanthosis of 12-week-old *Itgax-Il23a^{OE}* mice ($n = 6$) and *LSL-Il23a* mice ($n = 7$). Scale bar, 50 μ m. Data represent the 25th to 75th percentiles (whiskers showing min to max and centre showing the mean value). P -value was determined by two-tailed unpaired t -test. **b**, Flow cytometry showing the expression of TCR β and IL-17a in CD3⁺ T cells of ears from 12-week-old *LSL-Il23a* mice ($n = 5$), *Itgax-Il23a^{OE}* mice ($n = 5$) and *Il4i1-Il23a^{OE}* mice ($n = 5$). Statistics showing the percentages of TCR β ⁺ cells in IL-17a⁺ T cells (T17). Data represent the 25th to 75th percentiles (whiskers showing min to max and centre showing the mean value). P -values were determined by one-way ANOVA. For $P < 0.0001$, the exact P -value is $1.4\text{e-}6$. **c**, Flow cytometry showing the percentages of CD4⁺, CD8⁺, CD4⁺CD8⁺ and CD4⁺CD8⁻ T cells in TCR β ⁺IL-17a⁺ T cells of ears from 12-week-old *Il4i1-Il23a^{OE}* mice ($n = 4$). Data represent the mean $\pm$ SEM. Data are representative of three independent experiments. Source data are provided as a Source Data file.



Supplementary Figure 9. Phenotypes of *Il4i1-Il23a*^{OE} mice after anti-IL-17a treatment. **a**, Schematic graph showing that *Il4i1-Il23a*^{OE} mice were injected with 100 µg IL-17a neutralizing antibody (Clone 17F3, n = 8) or isotype control (Clone MOPC-21, n = 8) every 3 days from 8- to 20-week age. **b**, Representative macroscopic views of skin lesions of *Il4i1-Il23a*^{OE} mice treated with isotype or anti-IL-17a. **c**, Ear thickness (n = 8 per group with 2 ears per mouse) was measured every 6 days throughout the treatment procedure. *P*-value was determined by two-way ANOVA. For *P* < 0.0001, the exact *P*-value is 4.4e-7. **d**, Representative H&E images and quantification of acanthosis in *Il4i1-Il23a*^{OE} mice treated with isotype or anti-IL-17a. Scale bar, 50 µm. Data represent the 25th to 75th percentiles (whiskers showing min to max and centre showing the mean value). *P*-value was determined by two-tailed unpaired *t*-test. For *P* < 0.0001, the exact *P*-value is 1.3e-6. **e**, Representative microCT images of the hind paws from *Il4i1-Il23a*^{OE} mice treated with isotype or anti-IL-17a. **f**, Quantification of bone structural parameters of *Il4i1-Il23a*^{OE} mice treated with isotype (n = 8 with 2 hind paws per mouse) or anti-IL-17a (n = 8 with 2 hind paws per mouse) shown in (e). Data represent the 25th to 75th percentiles (whiskers showing min to max and centre showing the mean value). *P*-values were determined by two-tailed unpaired *t*-test. Ct. Ar, cortical bone area; Ct. Th, cortical bone thickness; BV/TV, bone volume to total volume ratio; ns, not significant. Data are representative of two independent experiments. Source data are provided as a Source Data file.



Supplementary Figure 10. Alterations of type 17 module in the epidermis during psoriasis maintenance, remission and recurrence. **a**, Spatial feature-plots of *KLRB1* and *LAMP3* in skin sections from psoriatic patients and the merged plots. **b**, Deconvolution analysis of bulk RNA-seq data (GSE114729) showing the cellular constitution (presented as the folds relative to the average values in Untreated) of psoriatic epidermis samples from patients treated with GC and experienced recurrence. *P*-values were determined by one-way ANOVA. Source data are provided as a Source Data file.



Supplementary Figure 11. Gating strategies of FACS for myeloid cell subsets and T cells from *Il4i1-Il23a*^{OE} mice. **a, Representative flow cytometry plots showing the gating strategy of myeloid cell subsets isolated from the skin and lymph nodes of *Il4i1-Il23a*^{OE} mice. **b**, Representative flow cytometry plots showing the gating strategy of CD4⁺ Tcm cells isolated from the spleens of *Il4i1-Il23a*^{OE} mice.**