**Supplemental Results**

**Transcriptional profile of neutrophil cell subsets was described in murine psoriasis.**

A total of 1,261 neutrophil cells that were clustered into 5 clusters (Figure S11A). Neutrophils constituted 5.91% of total cells in Vsir$^{-/-}$ psoriatic mice. Most interestingly, this percentage was a little lower than that in WT psoriatic mice (6.56%) (Figure S4B). We noted that, while neutrophil cluster 0 (Ube2c$^{+}$ Rrm2$^{+}$ ) and 1 (Apoe$^{+}$ C4b$^{+}$ ) were the main neutrophil clusters involved in both groups, cluster 3 (Lcn2$^{+}$ Ngp$^{+}$ ) was present at high level in Vsir$^{-/-}$ psoriatic mice (Figure S11A-B). Flt3 and Clec9a were marker genes of cluster 4, which also expressed Klrd1, H2-Ob and Sept3. Cluster 2 expressed Chil3, Vcan and Plac8 (Figure S11C).

After defining the neutrophils in our dataset, we identified differentially expressed genes between WT and Vsir$^{-/-}$ psoriatic mice of the skin. We focused on the two-fold upregulated or two-fold downregulated genes in neutrophils of Vsir$^{-/-}$ psoriatic mice neutrophils compared to that of WT psoriatic mice. Heatmap for the expression of Hspb1, Cebpb, Gm8797 and Lyz1 demonstrated that these genes were upregulated, while Stab1 was downregulated in DCs from Vsir$^{-/-}$ psoriatic mice lesions compared to WT psoriatic mice lesions (Figure S11D). Compared to those isolated from WT psoriatic mice, neutrophils isolated from psoriatic Vsir$^{-/-}$ mice may have contributed to negative regulation of apoptotic process, negative regulation of programmed cell death and positive regulation of immune system process (Figure S12).

**T cell cluster was identified in Vsir$^{-/-}$ psoriatic mice.**

A total of 625 T cells were detected (Figure S13A). Cd3e and Cxcr6 were marker genes of T cells, which also expressed Trdv4, Cd3d and Cd3g (Figure S13B). T cells were generally present at low levels in WT psoriatic mice but proliferated in Vsir$^{-/-}$ psoriatic mice (Figure S4B). But approximately 5.82% of skin cells were T cells in Vsir$^{-/-}$ psoriatic mice, only 1.27% skin cells were T cells in WT psoriatic mice (Figure S4B). Based on these results, We suspected that T cells may not play major role such as macrophages in psoriatic mice.

After defining the T cells, we identified differentially expressed genes between the skin lesions of WT and Vsir$^{-/-}$ psoriatic mice. We focused on the two-fold upregulated or two-fold downregulated genes in T cells of Vsir$^{-/-}$ psoriatic mice T cells compared to that of WT psoriatic mice. Heatmap for the expression of Crem, Cebpb, Gzma and Tnfrsf9 demonstrated that these genes were upregulated, while Plaur was downregulated in T cells from Vsir$^{-/-}$ psoriatic mouse skin compared to WT psoriatic mouse skin lesions (Figure S14A). Furthermore, T cells isolated on Vsir$^{-/-}$ psoriatic mice were shown to be involved in regulation of leukocyte differentiation, regulation of hemopoiesis and leukocyte cell-cell adhesion (Figure S15).

We defined clonotypes based on CDR3 sequences of both TCR α and β chains using the Cell Ranger analysis pipeline. To adequately define T cell clonality, we strictly defined T cells with at least one pair of identical paired α-β chains to be one clone from the same ancestry, and the expanded clones were defined as those whose α and β TCR pairs were shared by at least three cells in a given cell population. We noted that, most cells contained unique TCRs in both two groups of mice. While only~10% T

cells harbored clonal TCRs in WT psoriatic mice, Vsir$^{-/-}$ psoriatic mice showed a much higher percentage at~20% (Figure S14B).

**Other small cell clusters were detected in murine psoriasis.**

In addition to the large populations of immune cells detected during murine psoriasis described above, other cell types were separated into 7 clusters, including natural killer (NK) cells, epithelial cells, endothelial cells, mast cells, B cells, myocytes and adipocytes (Figure S16). In addition, the different clusters were characterized by the expression of other relevant markers (Figure S17). We identified the NK cells characterized by Ncr1, Klra4, Klra8 and Gzma expression. Ifng also highly expressed in NK cells (Figure S17A). The proportion of NK cells increased in psoriatic Vsir$^{-/-}$ mice (Figure S4B). And NK cells played roles in the protein refolding in psoriatic Vsir$^{-/-}$ mice (Figure S19). Epithelial cells were identified by expression of Defb6, Krt15, Cst6 and Pla2g2f (Figure S17B). Gene expression patterns of established canonical markers of endothelial cells (Emcn, Sox17, Cldn5, Esam), mast cells (Fcer1a, Tpsg1, Slc6a4, Cyp11a1) and B cells (Iglv1, Jchain, Cd79a, Iglc2) allowed us to assign putative biological identities to these clusters (Figure S17). Furthermore, these three clusters increased in psoriatic Vsir$^{-/-}$ mice (Figure S4B). The increase of endothelial cells in Vsir$^{-/-}$ psoriatic mice may be relative to angiogenesis. B cells, epithelial cells and adipocytes contained the large numbers of UMIs. This finding might suggest that these clusters were more “active” (Figure 1C).

**Supplementary Figures**

**Figure S1.**

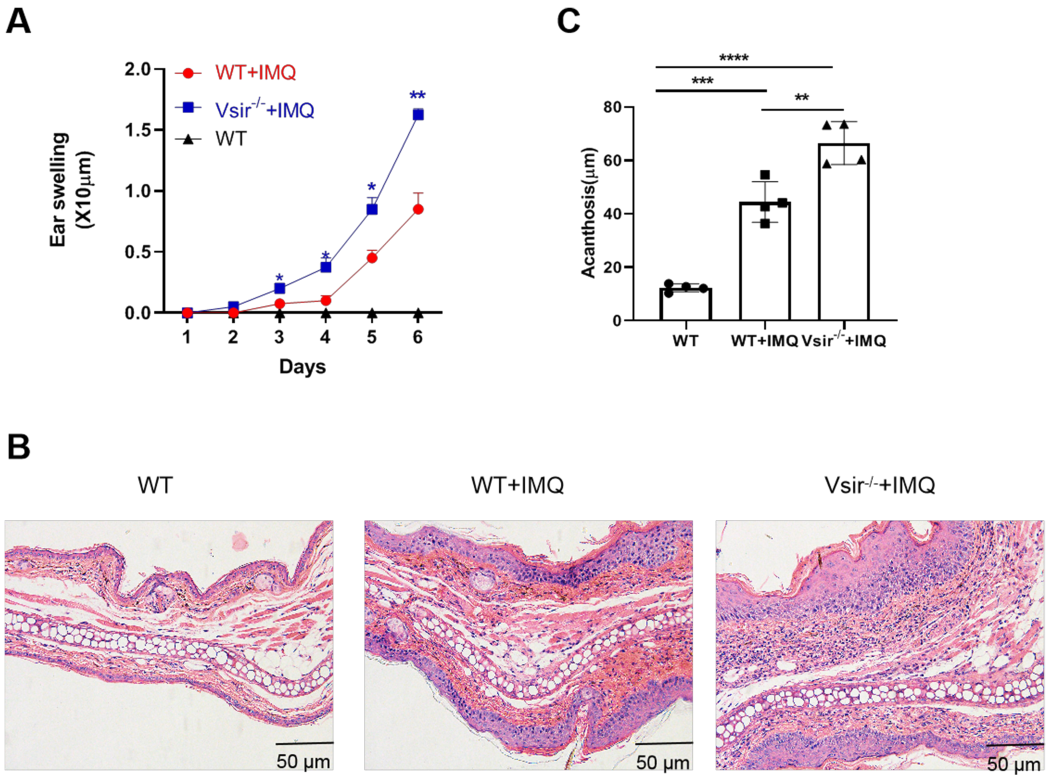



**Figure S1. VISTA deficiency exacerbated the IMQ-induced psoriasiform inflammation.**

**(A)** WT and Vsir$^{-/-}$ mice were topically treated daily on right ear and back skin with 5% IMQ cream for 5 days. Ear thickness was measured daily. Ear swelling is shown as the increase of ear thickness when compared to day 0, and expressed as mean ± SEM (n = 4). **(B)** H&E staining of the right ear skin of WT+IMQ and Vsir$^{-/-}$+IMQ mice; Scale bar 50 μm. (×200). **(C)** Ear skins were collected for H&E staining and analyzed for average acanthosis of ear. n=4. H&E, hematoxylin-eosin. IMQ, imiquimod. Vsir$^{-/-}$, Vsir knockout mice. WT, wild type.

**Figure S2.**

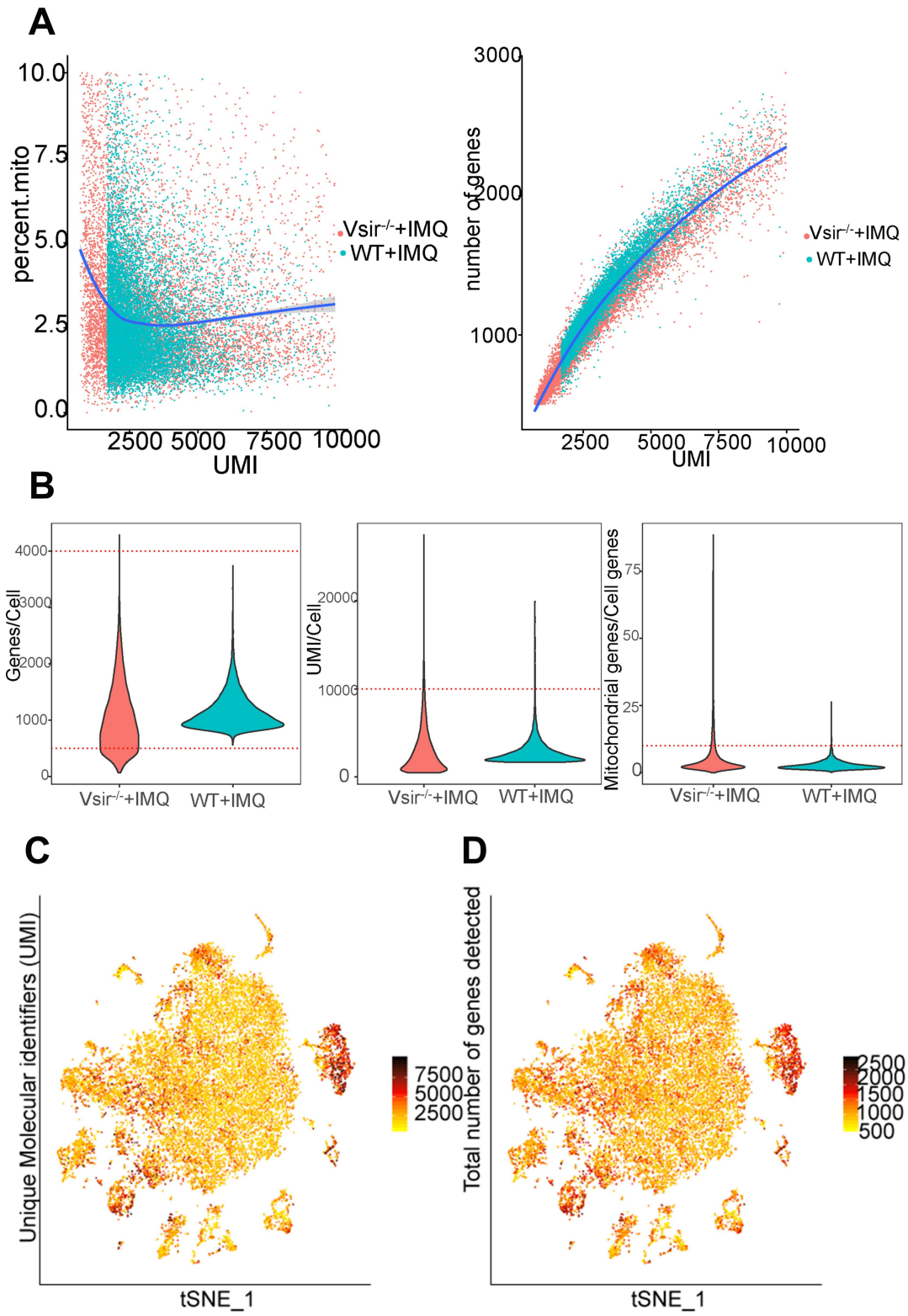



**Figure S2. Quality control metrics of scRNA-seq data from Vsir$^{-/-}$ psoriatic mice**

**were analyzed.**

**(A)** The percent of mitochondrial genes were shown. **(B)** Genes/Cell, Unique Molecular Identifiers (UMI)/Cell, and percent of mitochondrial genes/cell genes were shown. **(C)** tSNE plot with color-coded UMIs per cell is shown. Cells with the highest UMI are colored black. **(D)** tSNE plot with color-coded number of expressed genes per cell was shown. Cells with the highest number of expressed genes are colored black. tSNE, t-distributed stochastic neighbour embedding. UMIs, unique molecular identifiers.

**Figure S3.**

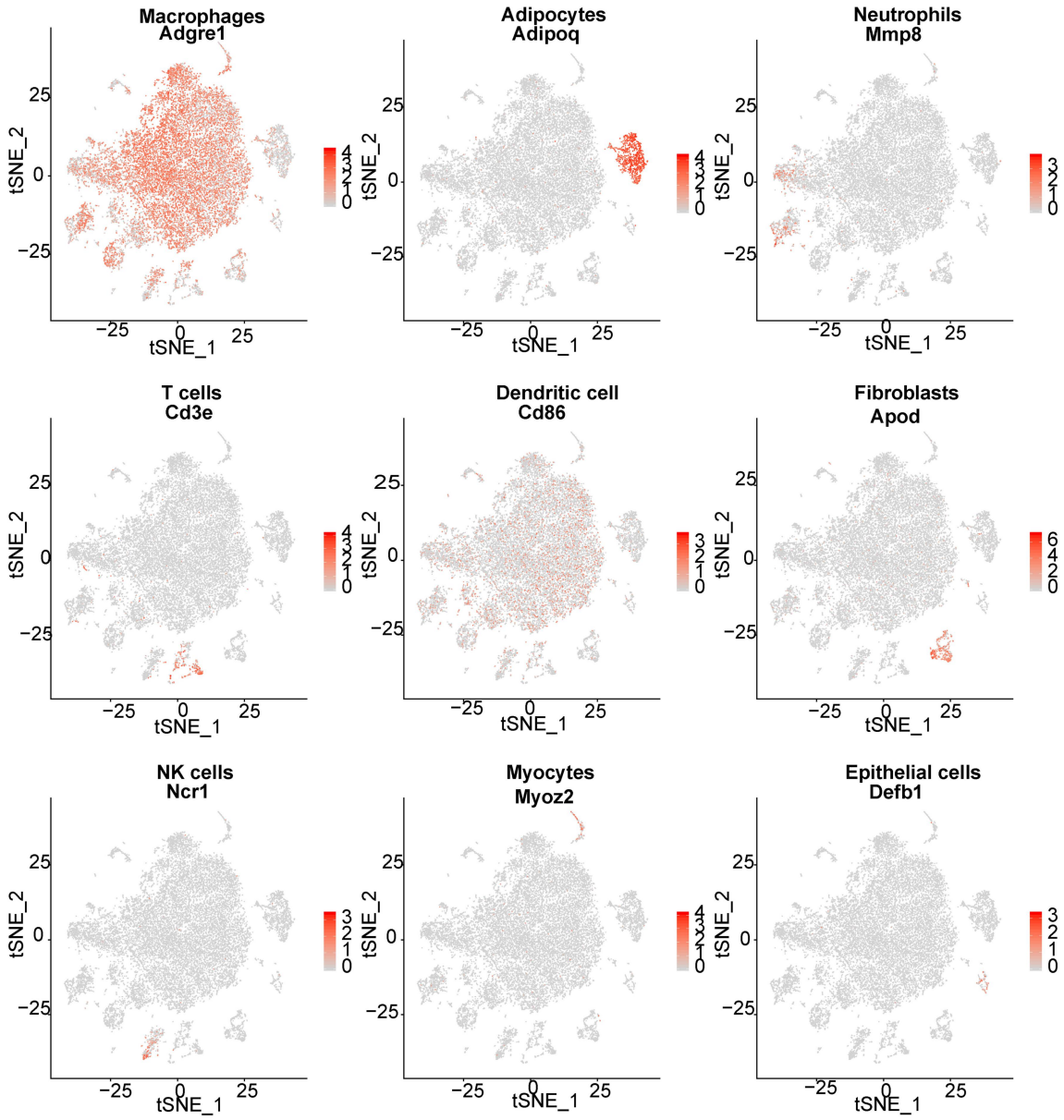



**Figure S3. Cell types were identified.**

Expression of the classical marker genes used to define different cell types. NK cells, natural killer cells.

**Figure S4.**

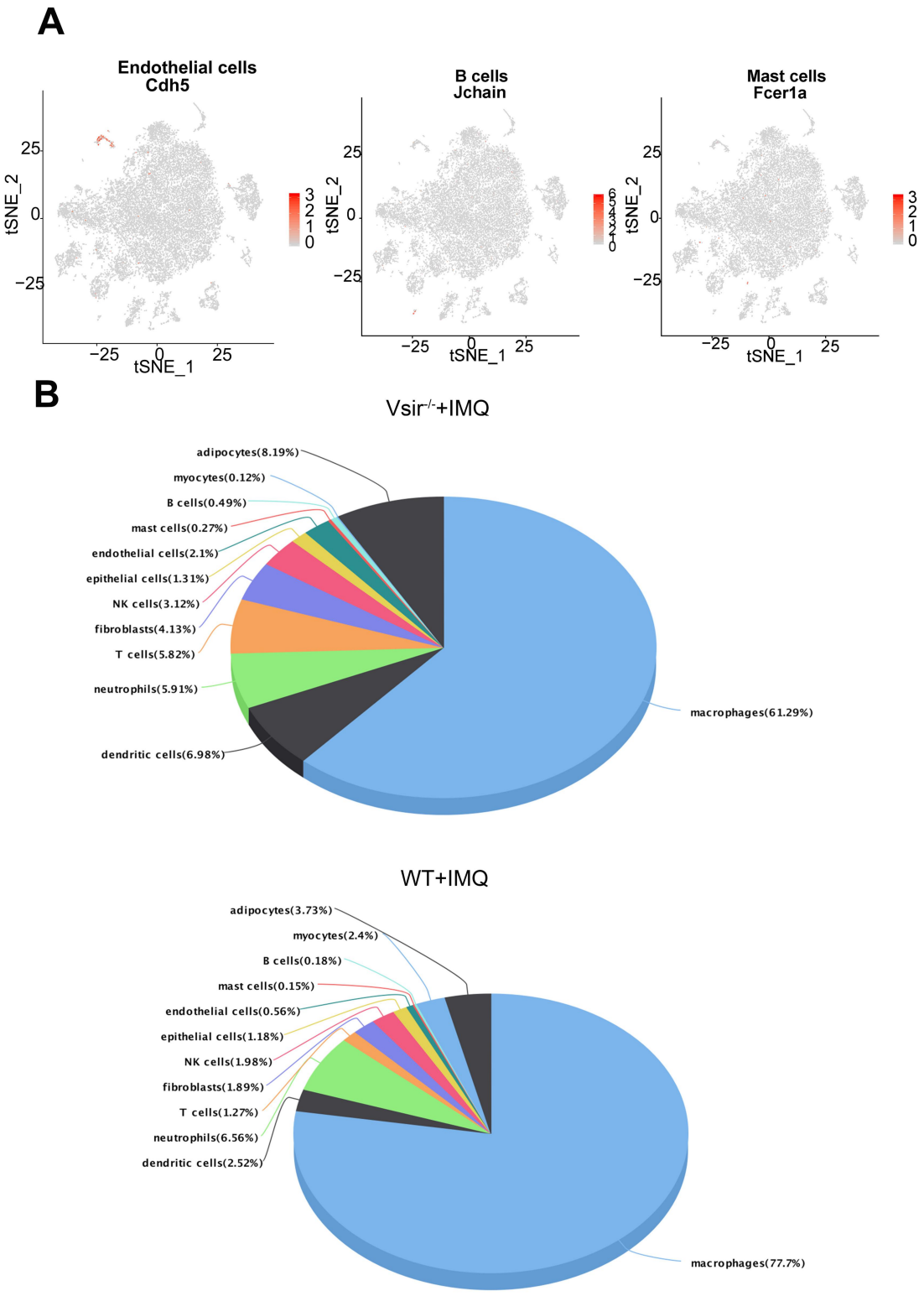



**Figure S4. Proportions of all cell populations in WT and Vsir$^{-/-}$ psoriatic mice**

**were shown.**

**(A)** Expression of the classical marker genes used to define different cell types. **(B)** Proportions of all cell populations within total skin cells in WT and Vsir$^{-/-}$ psoriatic mice.

**Figure S5.**

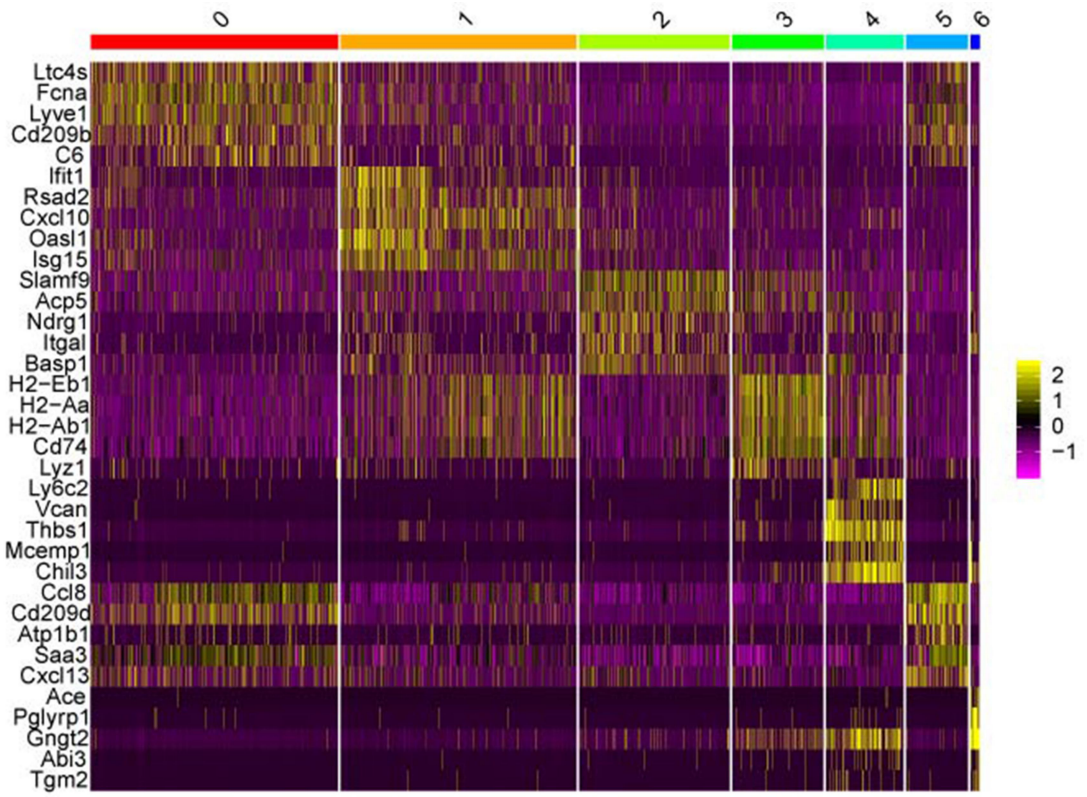



**Figure S5. Specific marker genes in each macrophage cluster were show in heatmap.**

**Figure S6.**

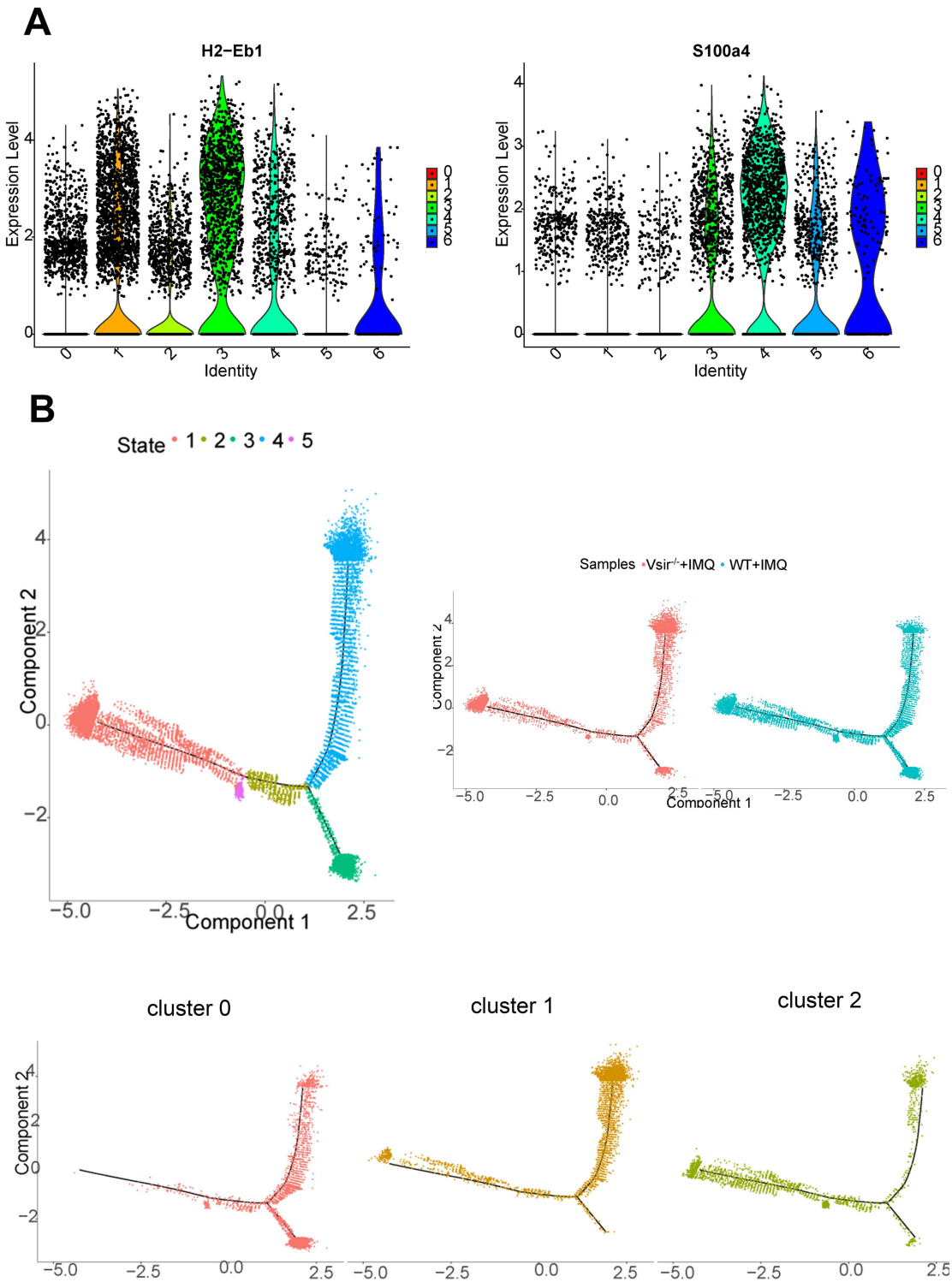



**Figure S6. Signature genes and distinct cell trajectory states for macrophage cell clusters were described.**

**(A)**Violin plots of specific marker genes in each macrophage cluster. **(B)** Distinct cell trajectory states defined by single cell transcriptomes and pseudotime trajectory of macrophages shown separately for WT and Vsir$^{-/-}$ psoriatic mice (top panel). Trajectory of macrophages from clusters 0, 1 and 2 using the Monocle 2 algorithm (bottom panel).

**Figure S7.**

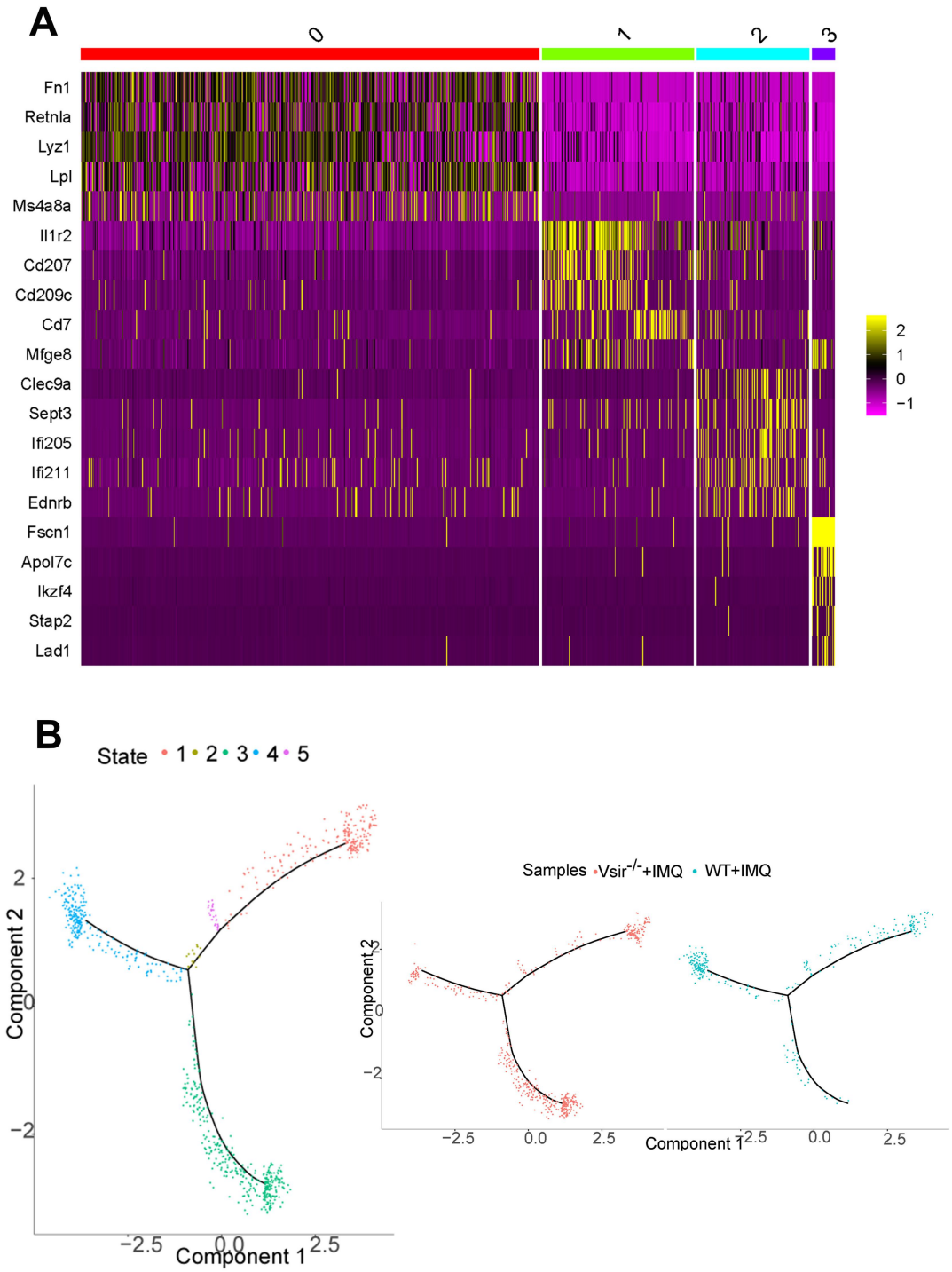
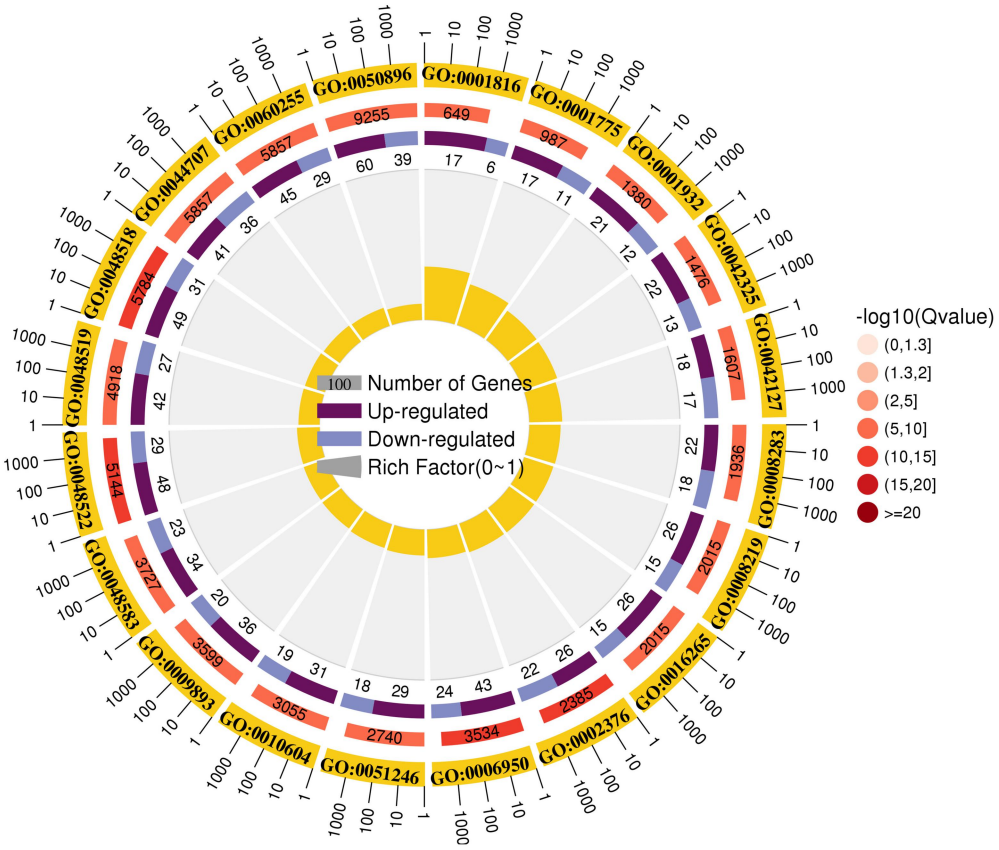



**Figure S7. Signature genes and distinct cell trajectory states for DC clusters were described.**

**(A)** Heatmap showing specific marker genes in each DC cluster. **(B)** Trajectory of DCs from clusters 0, 1, 2 and 3 using the Monocle 2 algorithm. DCs: dendritic cells.

**Figure S8.**




| GO ID | Description |
|---|---|
| GO:0006950 | response to stress |
| GO:0048522 | positive regulation of cellular process |
| GO:0048518 | positive regulation of biological process |
| GO:0002376 | immune system process |
| GO:0044707 | single-multicellular organism process |
| GO:0048519 | negative regulation of biological process |
| GO:0050896 | response to stimulus |
| GO:0042325 | regulation of phosphorylation |
| GO:0008219 | cell death |
| GO:0016265 | death |
| GO:0008283 | cell proliferation |
| GO:0009893 | positive regulation of metabolic process |
| GO:0048583 | regulation of response to stimulus |
| GO:0001775 | cell activation |
| GO:0001816 | cytokine production |
| GO:0001932 | regulation of protein phosphorylation |
| GO:0060255 | regulation of macromolecule metabolic process |
| GO:0051246 | regulation of protein metabolic process |
| GO:0010604 | positive regulation of macromolecule metabolic process |
| GO:0042127 | regulation of cell proliferation |

**Figure S8. GO term analysis of upregulated pathways in Vsir$^{-/-}$ versus WT DCs was performed.**

**Figure S9.**

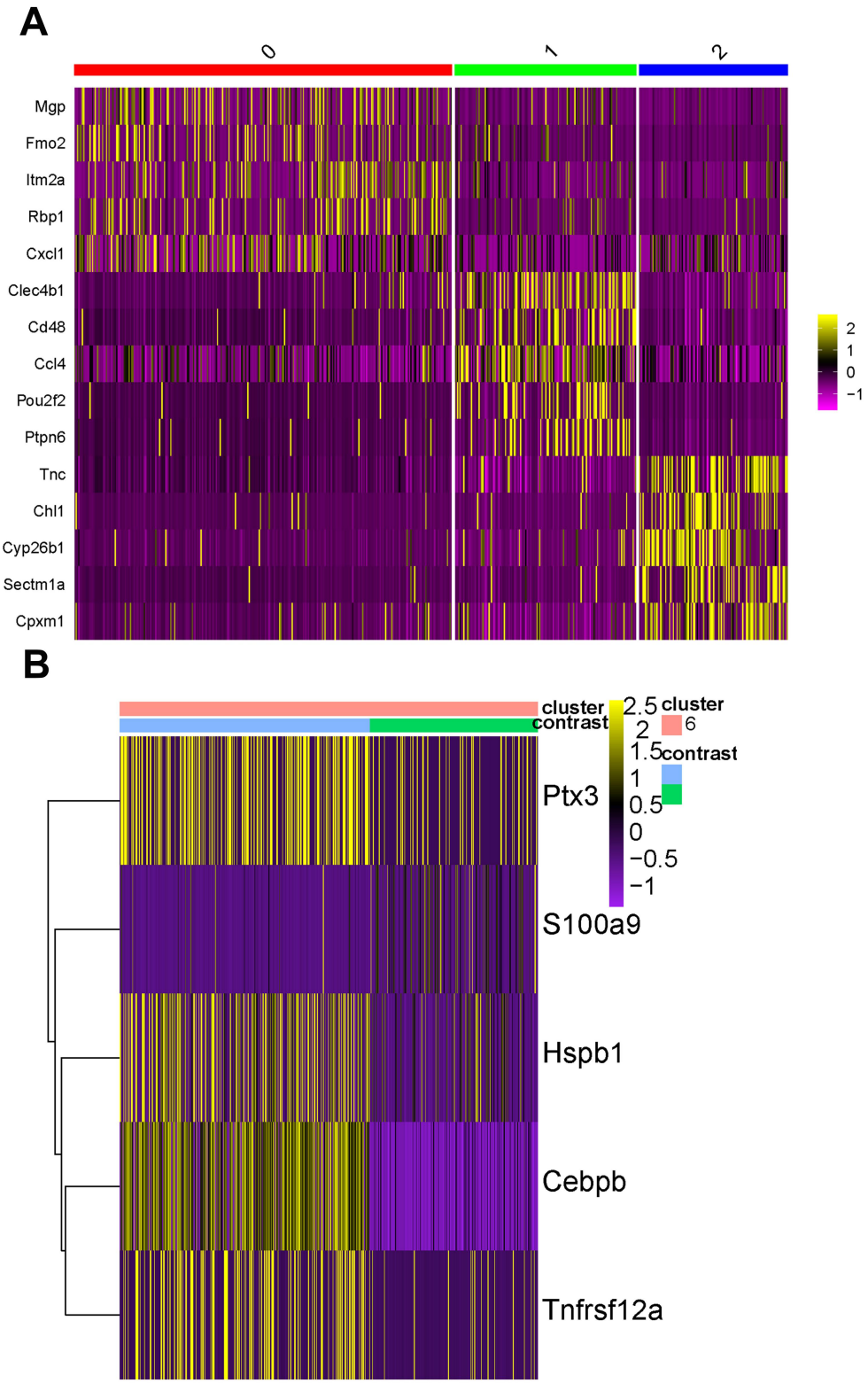
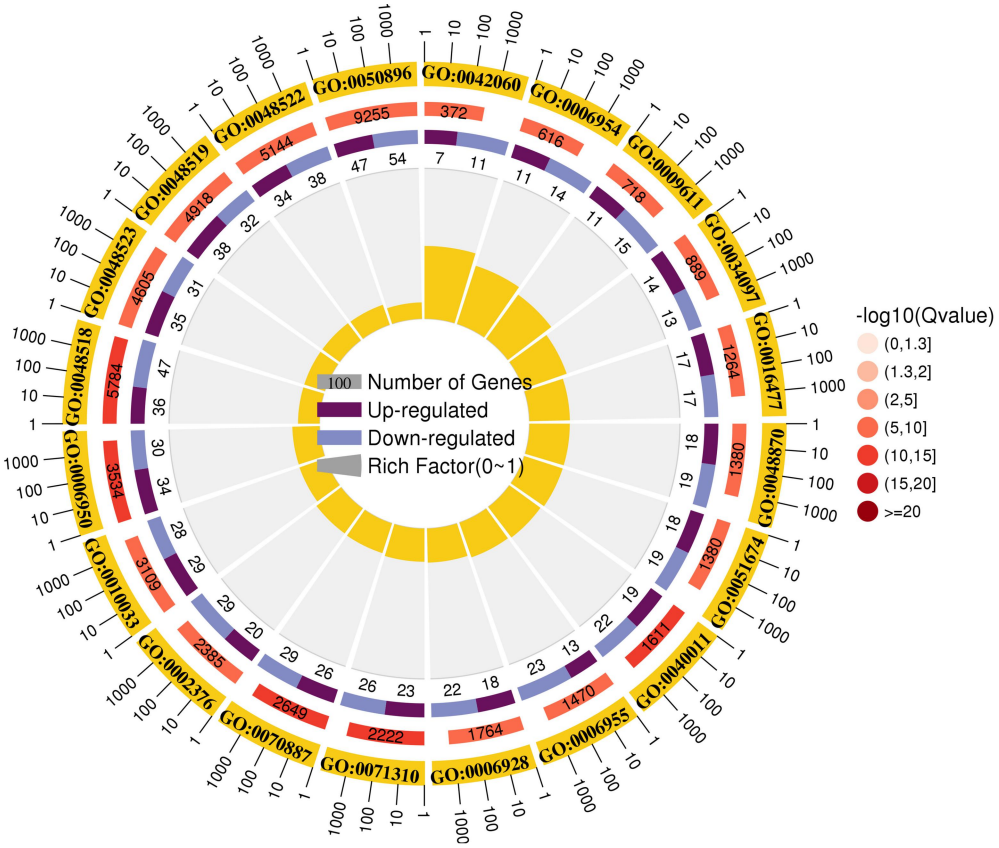



**Figure S9. Fibroblast cell clusters were described.**

**(A)** Heatmap showing specific marker genes in each fibroblast cluster. **(B)** Heatmap

of the genes that were at least two-fold upregulated in the fibroblasts from Vsir$^{-/-}$ psoriatic mice compared to that in the fibroblasts isolated from WT psoriatic mouse skin

**Figure S10.**




| GO ID | Description |
|---|---|
| GO:0070887 | cellular response to chemical stimulus |
| GO:0006950 | response to stress |
| GO:0048518 | positive regulation of biological process |
| GO:0071310 | cellular response to organic substance |
| GO:0040011 | locomotion |
| GO:0010033 | response to organic substance |
| GO:0048870 | cell motility |
| GO:0051674 | localization of cell |
| GO:0002376 | immune system process |
| GO:0006954 | inflammatory response |
| GO:0009611 | response to wounding |
| GO:0016477 | cell migration |
| GO:0006928 | movement of cell or subcellular component |
| GO:0006955 | immune response |
| GO:0048522 | positive regulation of cellular process |
| GO:0048519 | negative regulation of biological process |
| GO:0034097 | response to cytokine |
| GO:0042060 | wound healing |
| GO:0048523 | negative regulation of cellular process |
| GO:0050896 | response to stimulus |

**Figure S10. GO term analysis of upregulated pathways in Vsir$^{-/-}$ versus WT fibroblasts was performed.**

**Figure S11.**

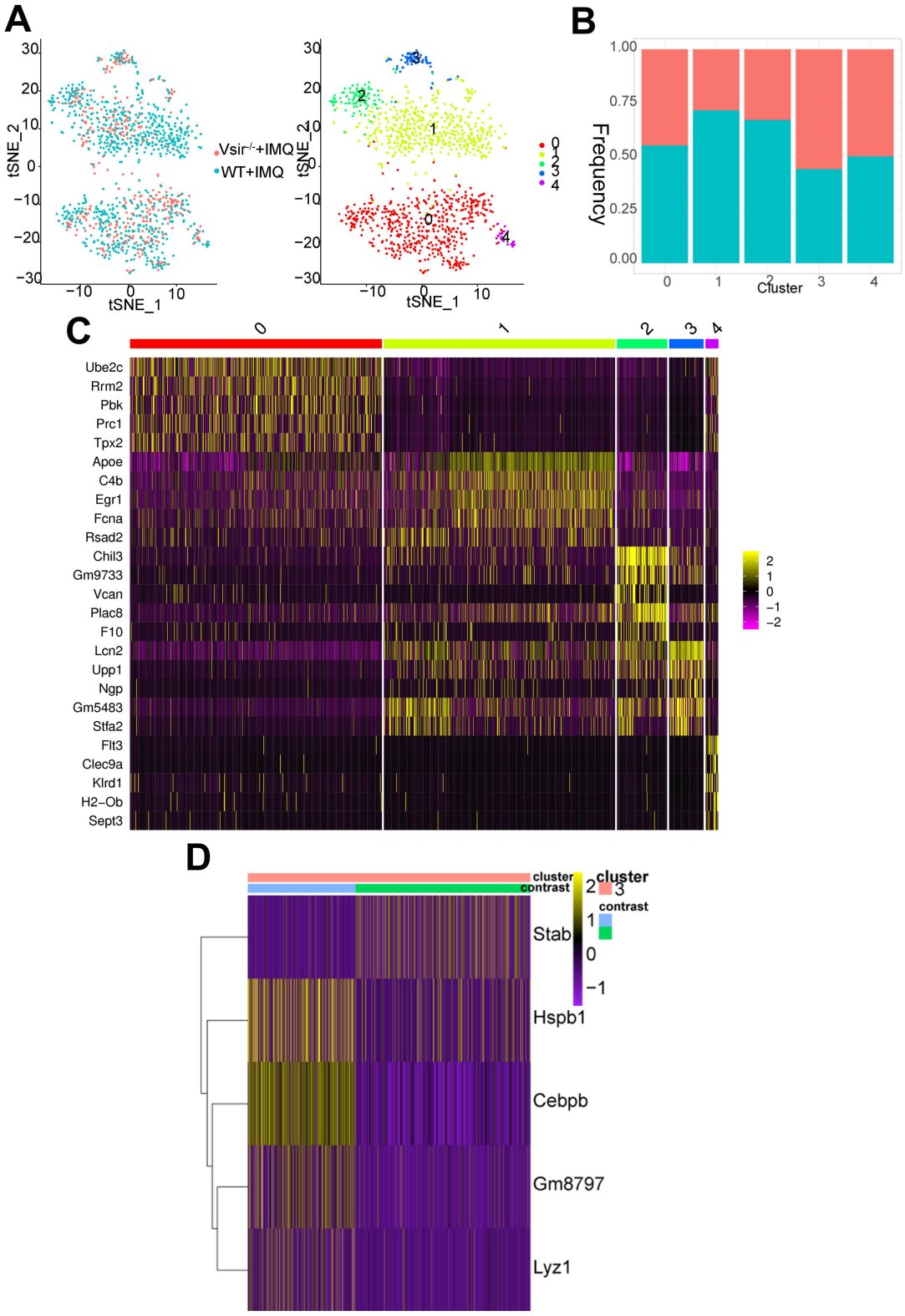
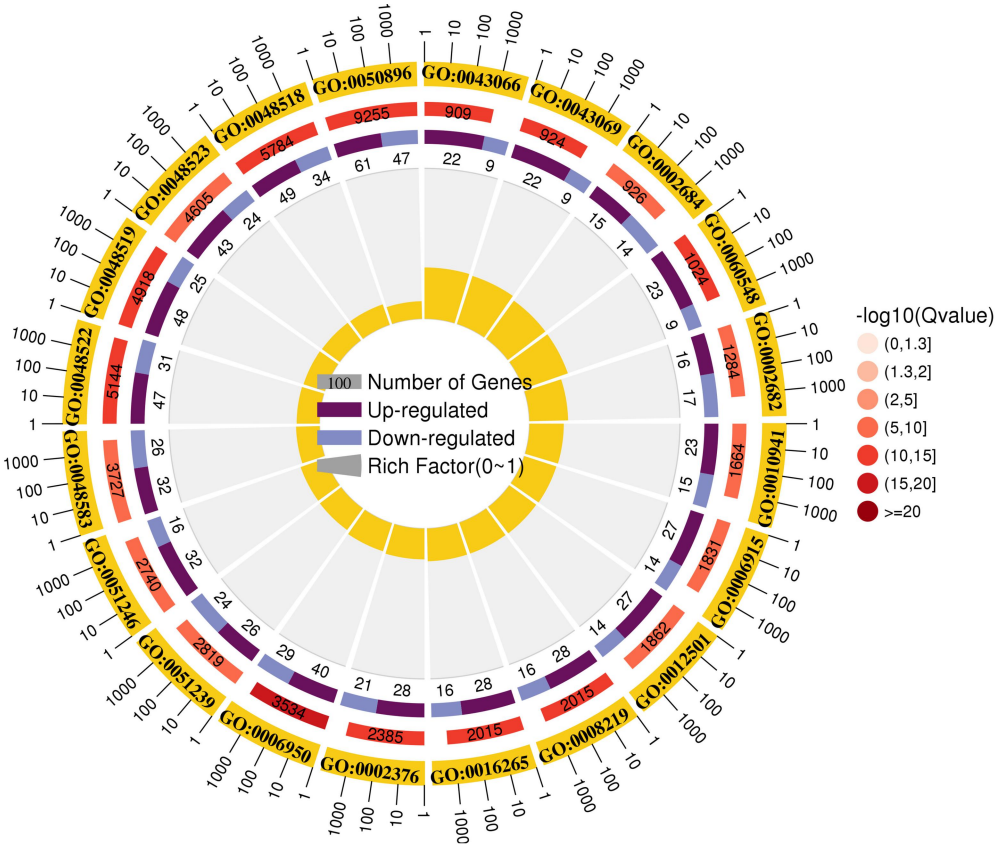



**Figure S11. Neutrophil cell clusters were identified.**

**(A)**The sample origin (left panel) and the tSNE plots of 1,261 neutrophils (right panel). **(B)** Bar plots exhibiting the cellular sources for neutrophils subtypes. Blocks represent different subjects and are color-coded by their derived groups defined in figure A. **(C)** Heatmap showing specific marker genes in each neutrophil cluster. **(D)** Heatmap of differentially expressed genes that were at least two-fold upregulated in neutrophil cell clusters from $Vsir^{-/-}$ psoriatic mice compared to neutrophil cell clusters isolated from WT psoriatic mice skin. tSNE, t-distributed stochastic neighbour embedding

**Figure S12.**




| GO ID | Description |
|---|---|
| GO:0006950 | response to stress |
| GO:0050896 | response to stimulus |
| GO:0048522 | positive regulation of cellular process |
| GO:0048518 | positive regulation of biological process |
| GO:0048519 | negative regulation of biological process |
| GO:0043066 | negative regulation of apoptotic process |
| GO:0043069 | negative regulation of programmed cell death |
| GO:0002376 | immune system process |
| GO:0060548 | negative regulation of cell death |
| GO:0008219 | cell death |
| GO:0016265 | death |
| GO:0006915 | apoptotic process |
| GO:0012501 | programmed cell death |
| GO:0002684 | positive regulation of immune system process |
| GO:0048523 | negative regulation of cellular process |
| GO:0010941 | regulation of cell death |
| GO:0051239 | regulation of multicellular organismal process |
| GO:0002682 | regulation of immune system process |
| GO:0048583 | regulation of response to stimulus |
| GO:0051246 | regulation of protein metabolic process |

**Figure S12. GO term analysis of upregulated pathways of in Vsir$^{-/-}$ versus WT neutrophils was performed.**

**Figure S13.**

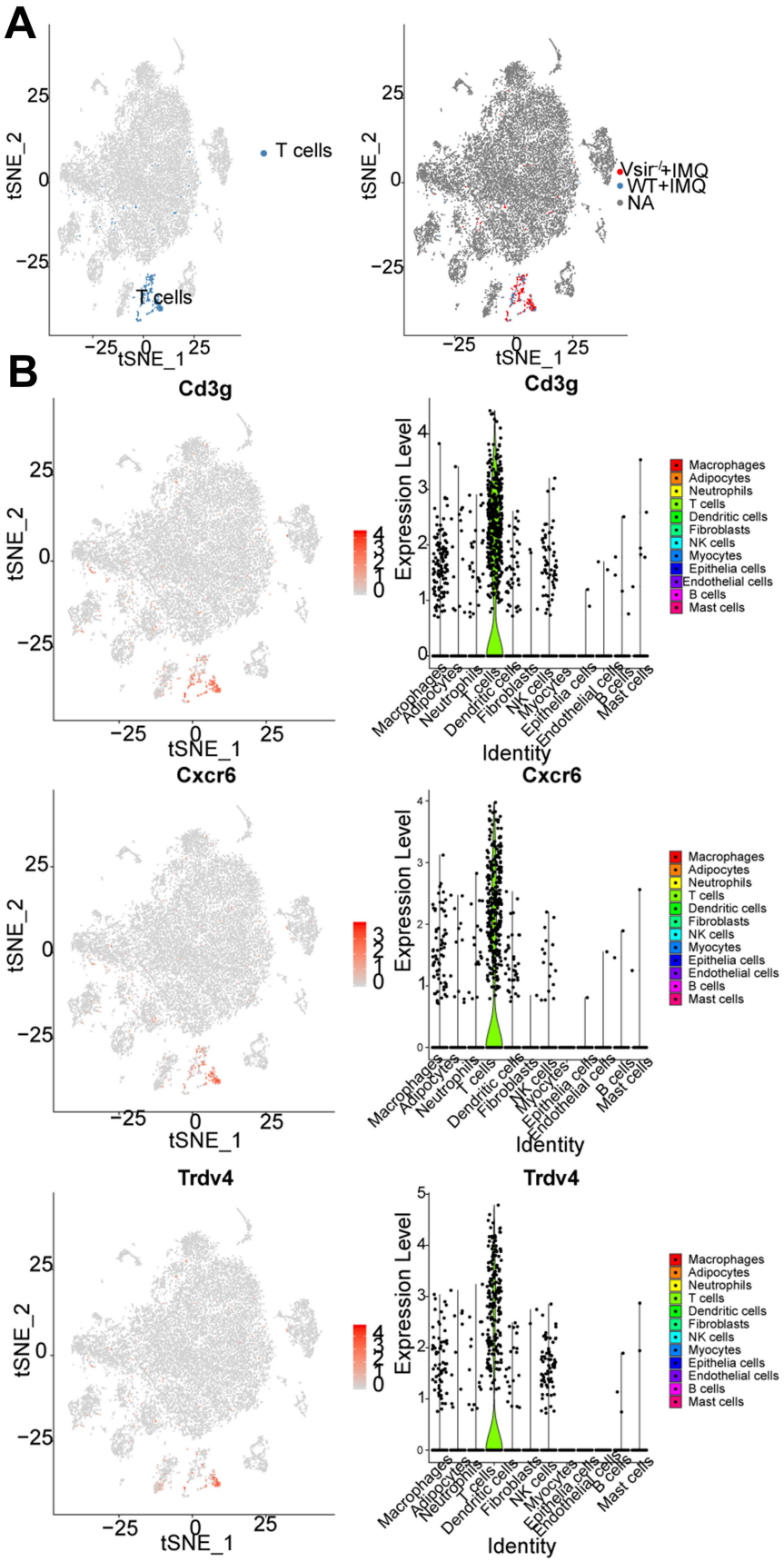

A
T cells
Vsir-/-+IMQ
WT+IMQ
NA
tSNE_1
tSNE_2
B
Cd3g
Cxcr6
Trdv4
Expression Level
Identity
Macrophages
Adipocytes
Neutrophils
T cells
Dendritic cells
Fibroblasts
NK cells
Myocytes
Epithelia cells
Endothelial cells
B cells
Mast cells

**Figure S13. T cells were identified.**

**(A)** The tSNE plots of 625 T cells (left panel) and the sample type of origin (right panel). **(B)** tSNE or expression (color bar, TP10K) of key T cell marker genes. tSNE, t-distributed stochastic neighbour embedding.

**Figure S14.**

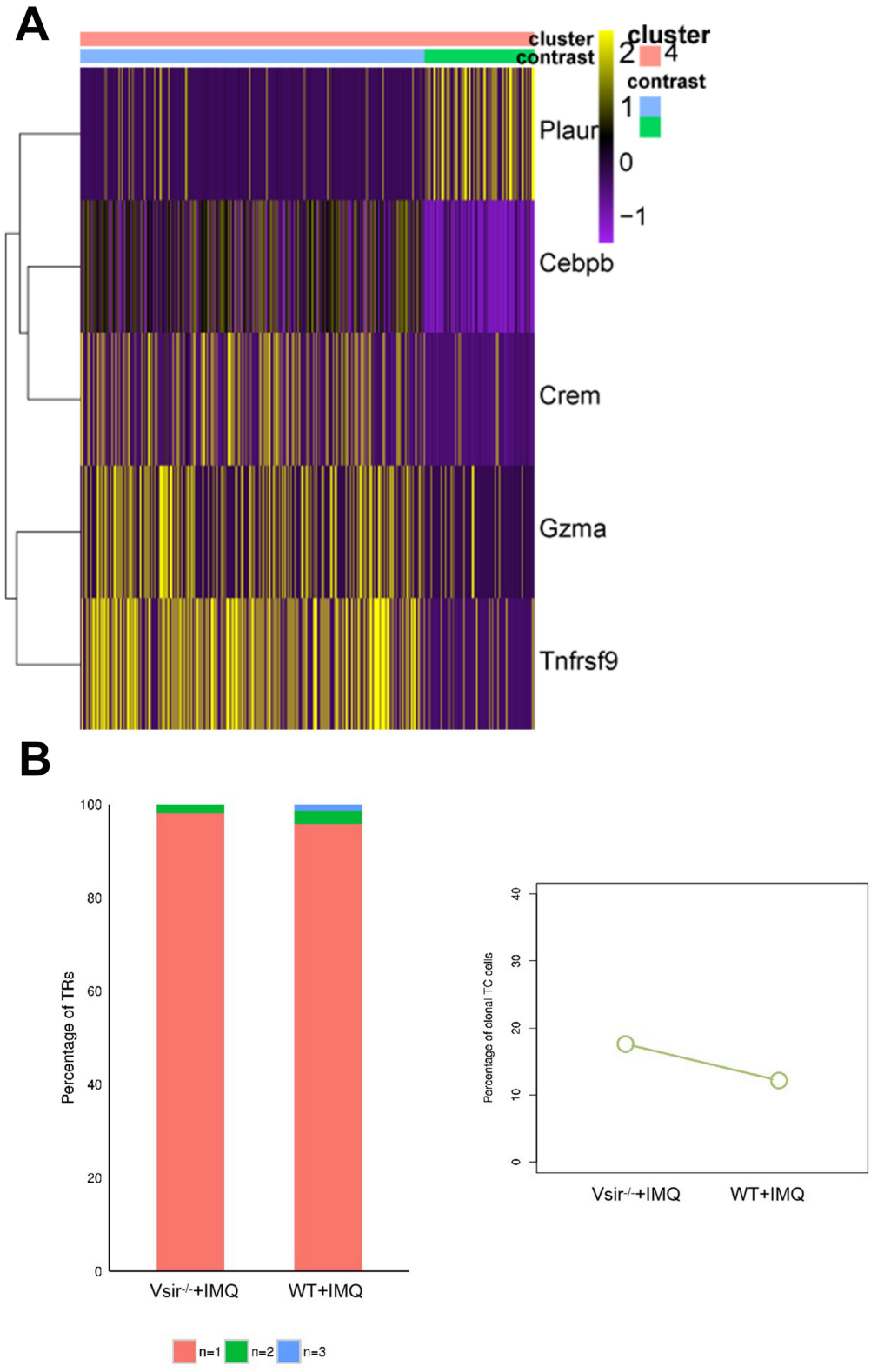
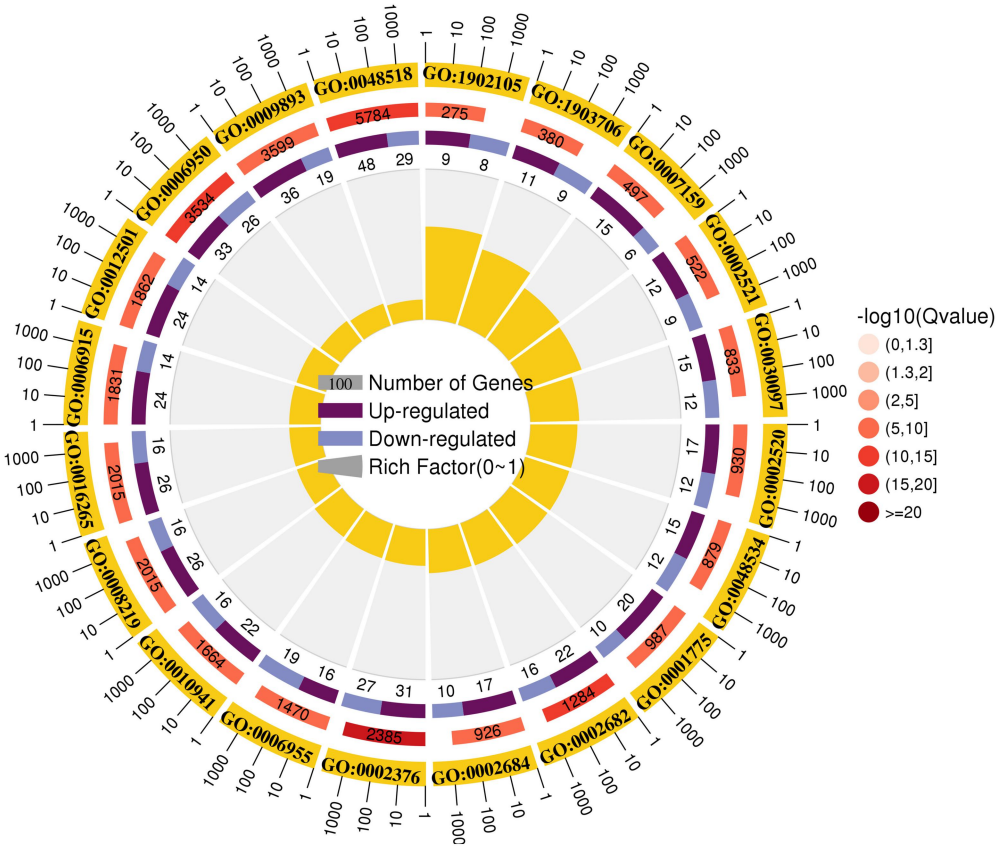



**Figure S14. The signature of T cells in Vsir$^{-/-}$ psoriatic mice has been described.**

**(A)** Heatmap of genes that were at least two-fold upregulated in T cells from Vsir$^{-/-}$

psoriatic mice compared to T cells isolated from WT psoriatic mice skin. **(B)** The TCR distribution of T cells across different groups. Unique (n = 1), duplicated (n = 2), and clonal (n ≥ 3) TCRs are labeled with different colors (left panel). The proportions of clonal T cells in two different groups (right panel).

**Figure S15.**




| GO ID | Description |
|---|---|
| GO:0002376 | immune system process |
| GO:0002682 | regulation of immune system process |
| GO:0006950 | response to stress |
| GO:0048518 | positive regulation of biological process |
| GO:1903706 | regulation of hemopoiesis |
| GO:0001775 | cell activation |
| GO:0002520 | immune system development |
| GO:0008219 | cell death |
| GO:0016265 | death |
| GO:0010941 | regulation of cell death |
| GO:0030097 | hemopoiesis |
| GO:1902105 | regulation of leukocyte differentiation |
| GO:0006955 | immune response |
| GO:0007159 | leukocyte cell-cell adhesion |
| GO:0048534 | hematopoietic or lymphoid organ development |
| GO:0002521 | leukocyte differentiation |
| GO:0002684 | positive regulation of immune system process |
| GO:0006915 | apoptotic process |
| GO:0009893 | positive regulation of metabolic process |
| GO:0012501 | programmed cell death |

**Figure S15. GO term analysis of upregulated pathways of in Vsir$^{-/-}$ versus WT T cells were performed.**

**Figure S16.**

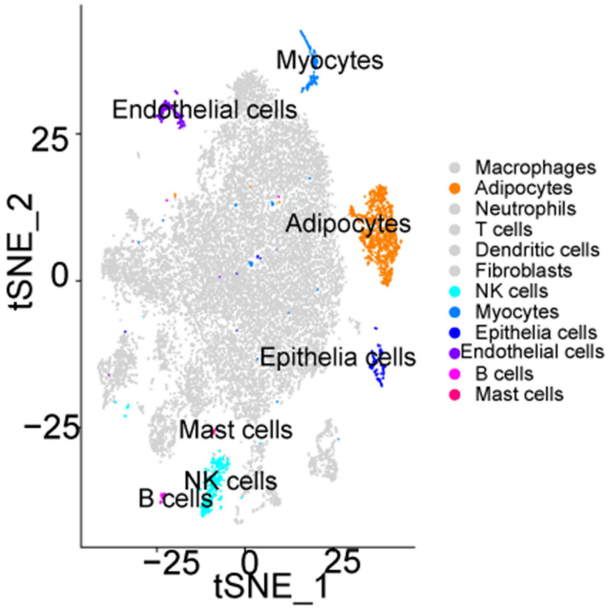



**Figure S16. Other clusters in murine psoriasis were defined.** The tSNE plot of NK cells, B cells, mast cells, endothelial cells, epithelia cells, myocytes and adipocytes was shown. NK cells, natural killer cells. tSNE, t-distributed stochastic neighbour embedding

**Figure S17.**

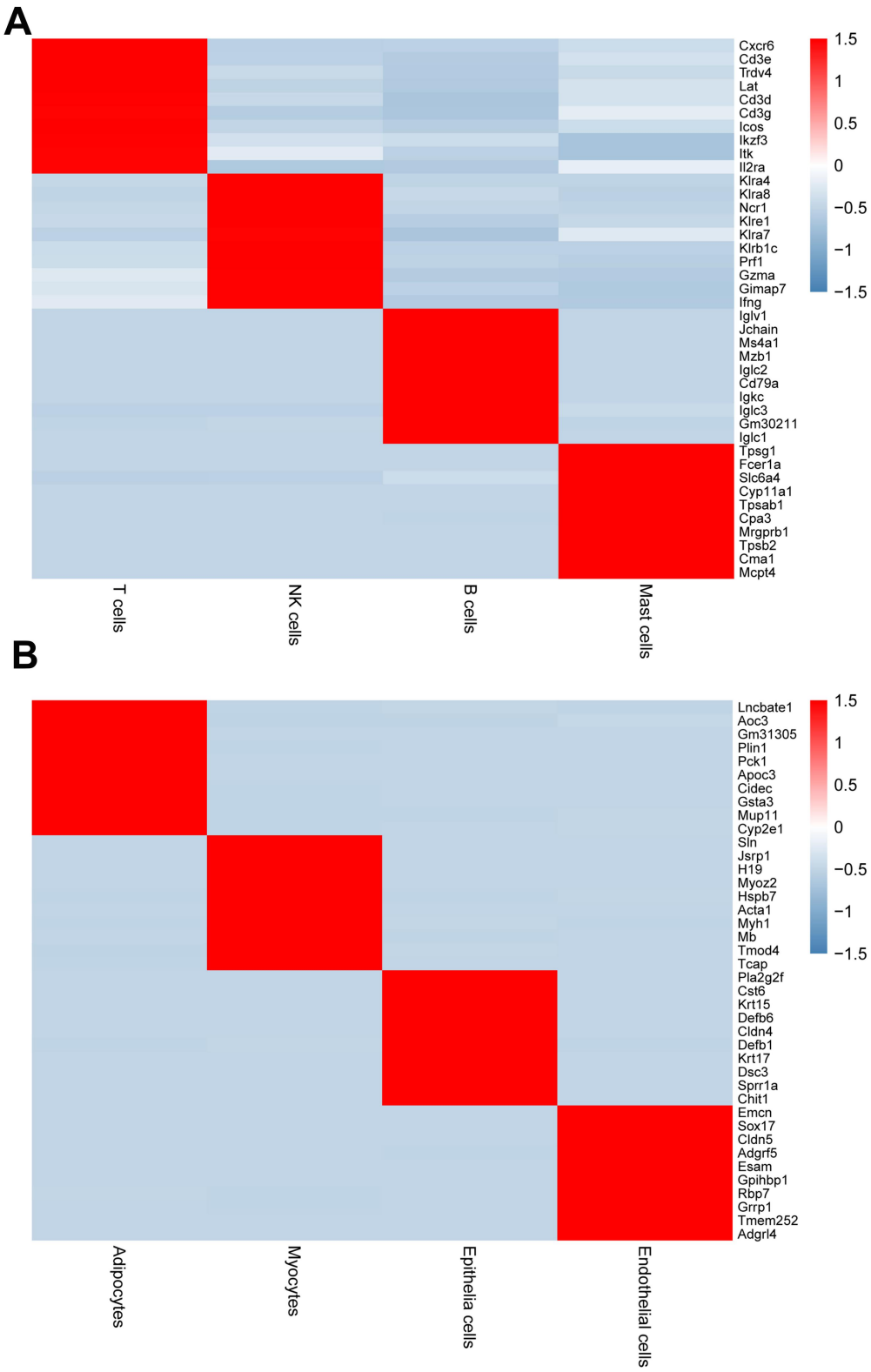



**Figure S17. (A)** Heatmap showing the 10 most upregulated genes (ordered by

decreasing p-value) in T cells, NK cells, B cells and mast cells defined in Figure S16, and selected enriched genes used for biological identification of clusters. **(B)** Heatmap showing the 10 most upregulated genes (ordered by decreasing p-value) in adipocytes, myocytes, epithelia cells and endothelial cells, and selected enriched genes used for biological identification of clusters. NK cells, natural killer cells.

**Figure S18.**

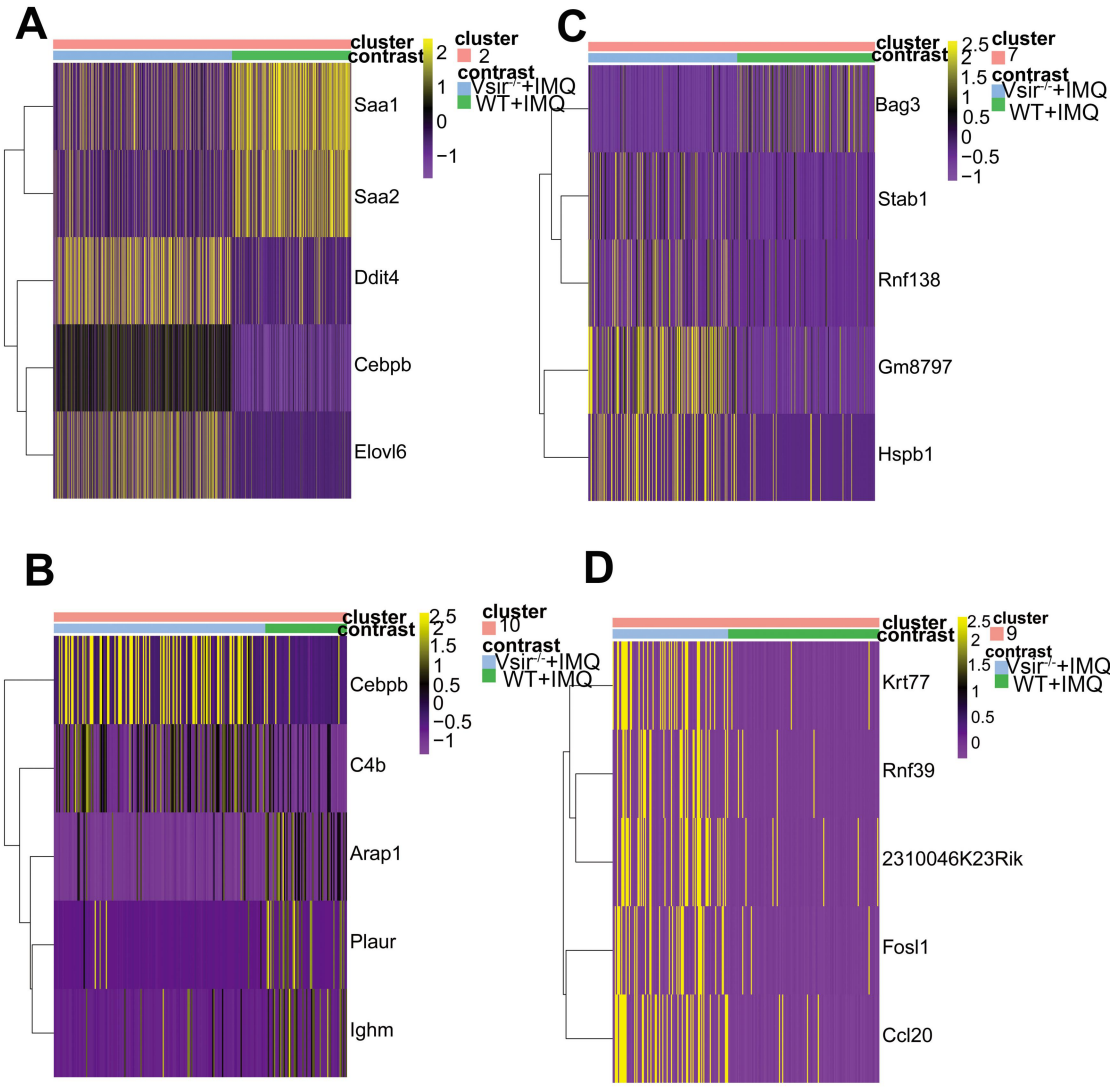
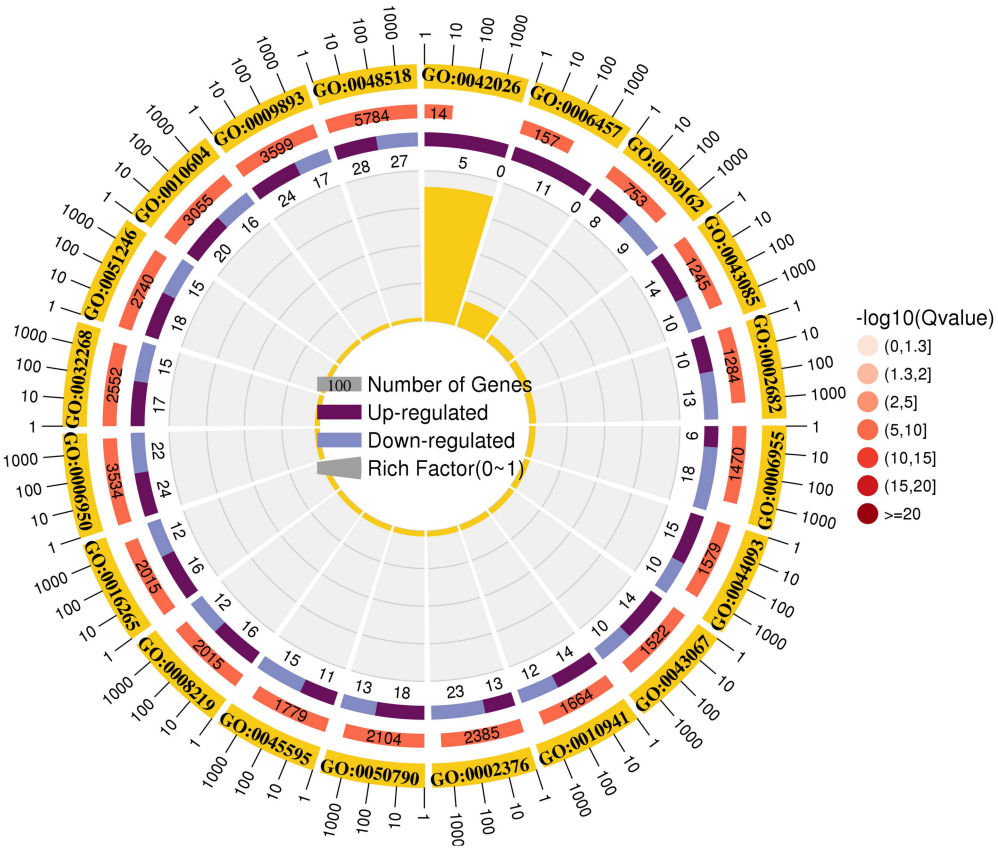



**Figure S18. Heatmap showed differentially expressed genes in other cell types.** **(A-D)** Heatmap of genes that were at least two-fold upregulated in adipocytes **(A)**, endothelial cells **(B)**, NK cells **(C)**, epithelia cells **(D)** from $Vsir^{-/-}$ psoriatic mice compared to WT psoriatic mice skin. NK cells, natural killer cells.

**Figure S19.**




| GO ID | Description |
|---|---|
| GO:0006950 | response to stress |
| GO:0002376 | immune system process |
| GO:0006457 | protein folding |
| GO:0048518 | positive regulation of biological process |
| GO:0043085 | positive regulation of catalytic activity |
| GO:0050790 | regulation of catalytic activity |
| GO:0009893 | positive regulation of metabolic process |
| GO:0042026 | protein refolding |
| GO:0002682 | regulation of immune system process |
| GO:0010941 | regulation of cell death |
| GO:0010604 | positive regulation of macromolecule metabolic process |
| GO:0044093 | positive regulation of molecular function |
| GO:0006955 | immune response |
| GO:0032268 | regulation of cellular protein metabolic process |
| GO:0008219 | cell death |
| GO:0016265 | death |
| GO:0030162 | regulation of proteolysis |
| GO:0051246 | regulation of protein metabolic process |
| GO:0043067 | regulation of programmed cell death |
| GO:0045595 | regulation of cell differentiation |

**Figure S19. GO term analysis of upregulated pathways of in Vsir$^{-/-}$ versus WT NK cells.**

**Table S1**

Table S1 Overview of sequencing data quality metrics for cells extracted from WT and Vsir$^{-/-}$ psoriatic mice.

| | WT+IMQ | Vsir$^{-/-}$+IMQ |
|---|---|---|
| Estimated number of cells | 12,040 | 11,218 |
| Number of Reads | 318,400,966 | 285,931,105 |
| Valid Barcodes | 93.7% | 93.2% |
| Reads Mapped Confidently to Transcriptome | 71.8% | 69.4% |
| Reads Mapped Confidently to Exonic Regions | 76.5% | 73.1% |
| Reads Mapped Confidently to Intronic Regions | 7.2% | 6.0% |
| Reads Mapped Confidently to Intergenic Regions | 5.0% | 6.4% |
| Reads Mapped Antisense to Gene | 3.9% | 2.7% |
| Sequencing Saturation | 73.4% | 77.5% |
| Q30 Bases in Barcode | 96.1% | 95.0% |
| Q30 Bases in RNA Read | 91.1% | 92.4% |
| Q30 Bases in UMI | 95.5% | 93.5% |