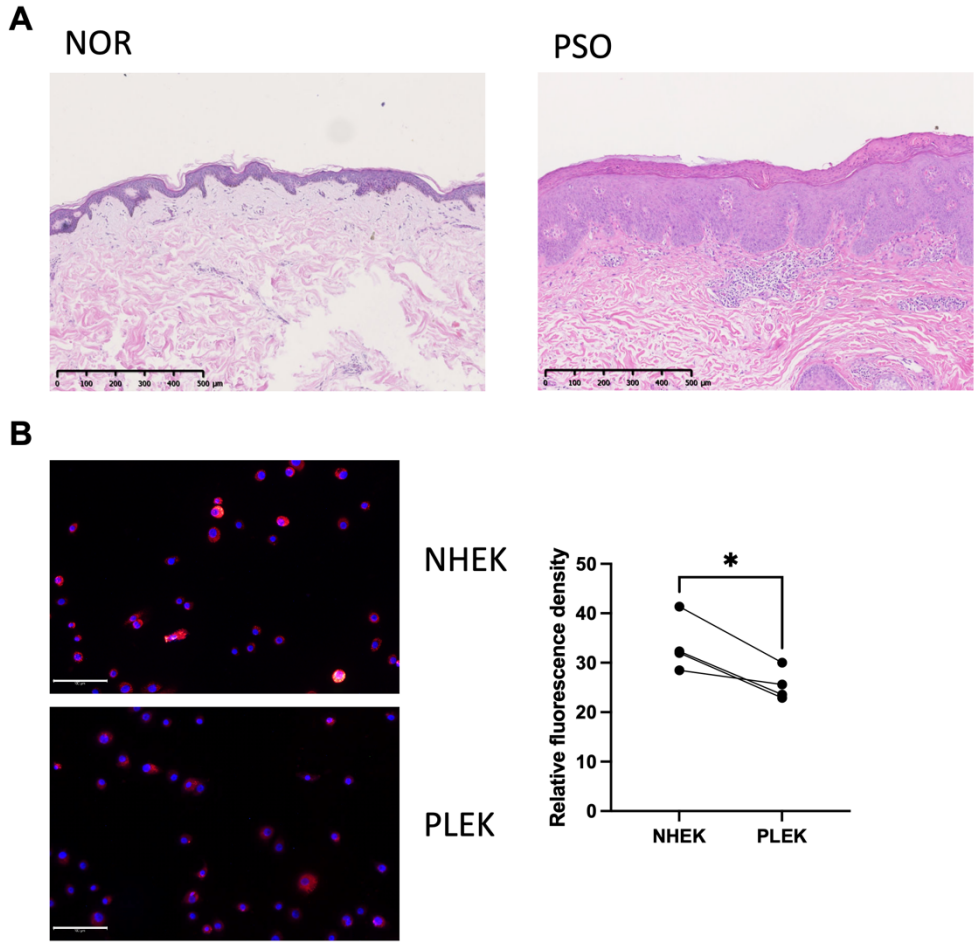
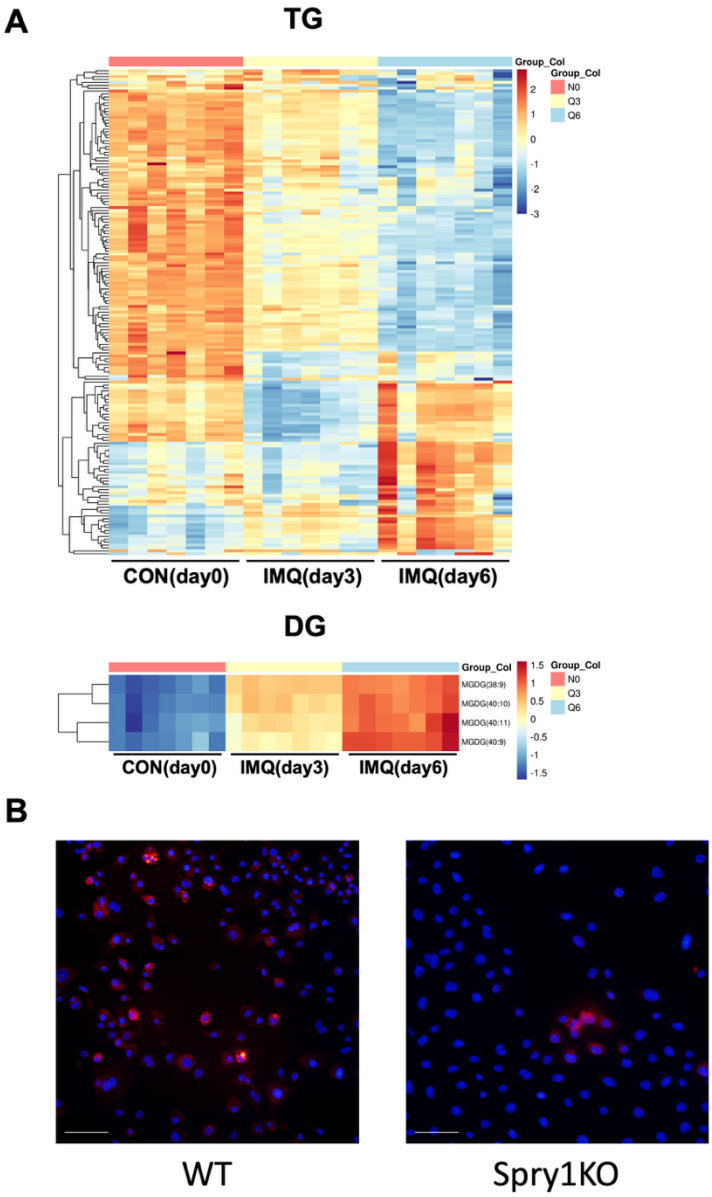
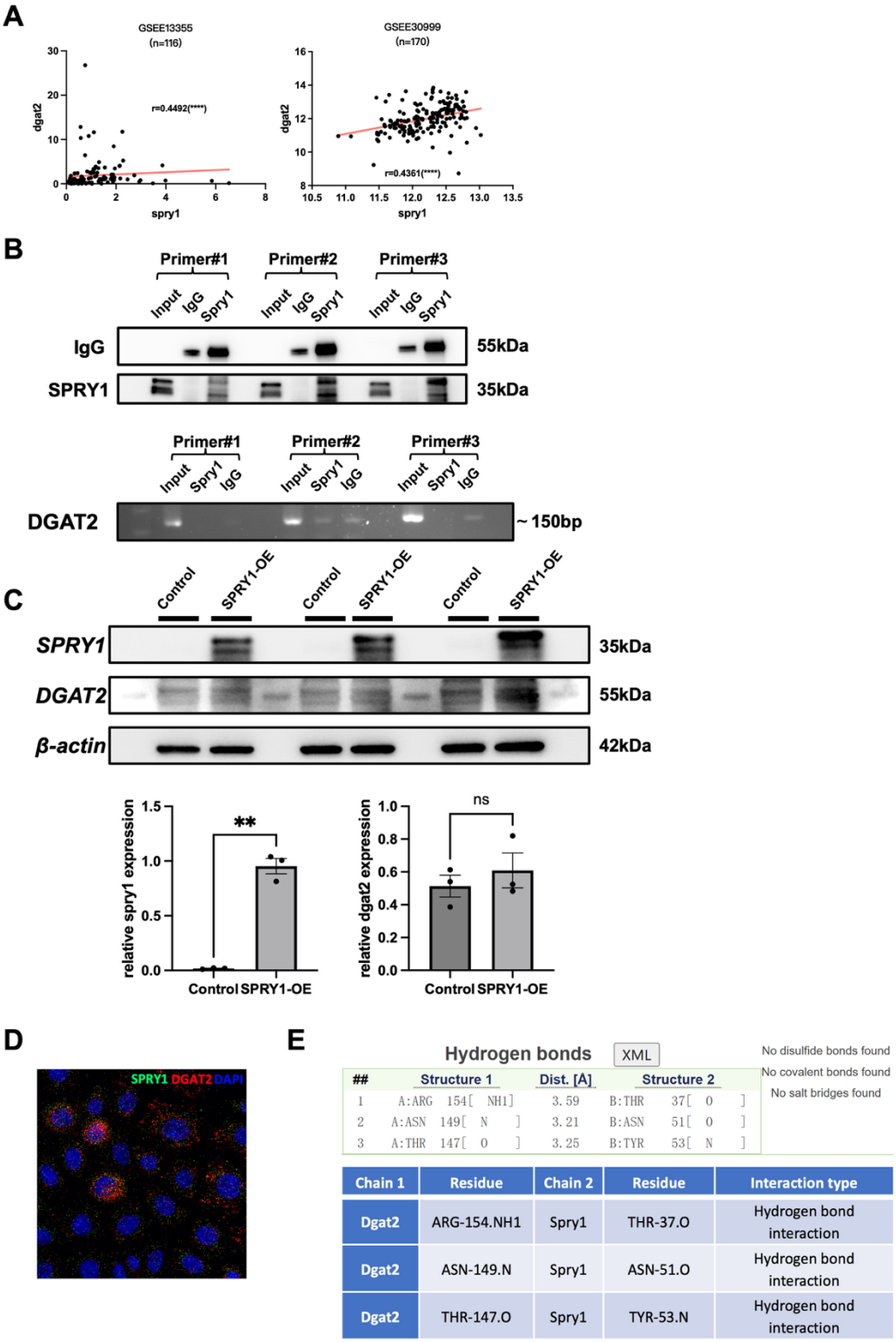
**SUPPLEMENTARY FIGURE**




**Supplementary Figure S1 Histological and TG Staining Analysis in Healthy and Lesional Psoriatic Skin.** (A) Histological analysis using H&E staining of healthy (NOR) and psoriatic (PSO) skin samples. Lesional psoriatic skin shows marked epidermal hyperplasia and inflammation. Scale bars in histological images = 500 µm. (B) TG staining in keratinocytes isolated from healthy individuals (NHEK) and psoriasis patients (PLEK). Scale bars = 50 µm. n = 4 samples per group.

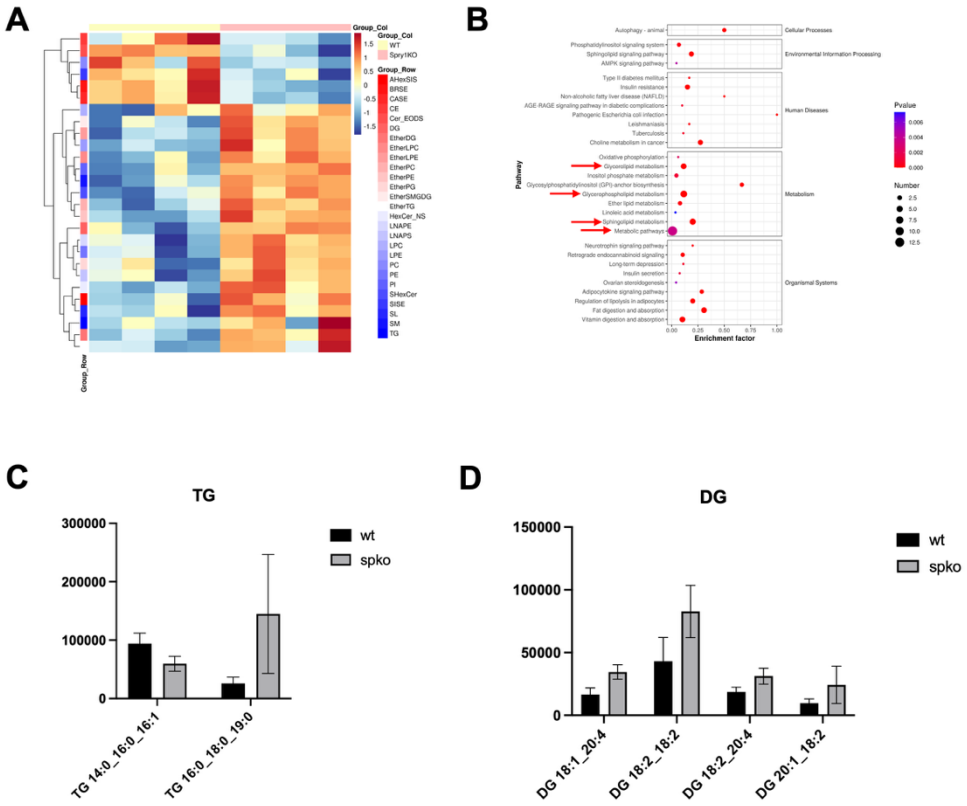



**Supplementary Figure S2 Altered Glyceride Levels in Psoriasis-like Skin and SPRY1-deficient Keratinocytes.** (A) Heatmaps showing TG and DG in wild-type mice and the IMQ-induced psoriasis-like mouse model across different IMQ induction times (CON(day0), IMQ(day3), and IMQ(day6)). (B) TG staining in keratinocytes isolated from wild-type (WT) controls and Spry1$^{\Delta Epi}$ (Spry1KO) mice.

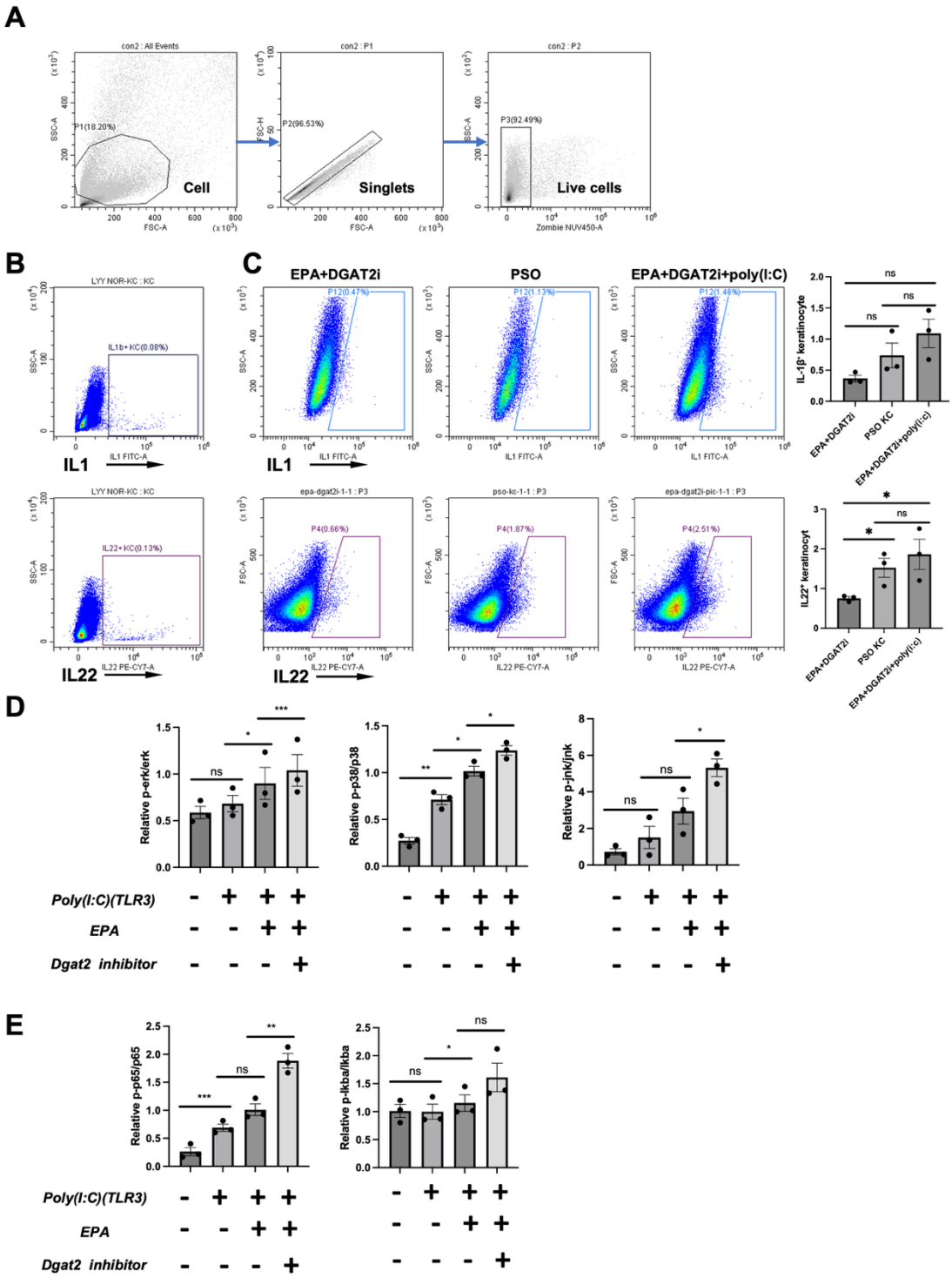



**Supplementary Figure S3 SPRY1 is associated with DGAT2 expression.** (A) Positive correlation between SPRY1 and DGAT2 expression in psoriatic skin (GSE13355, GSE30999). (B) Chromatin immunoprecipitation (ChIP) assay in mouse

keratinocytes showing that SPRY1 does not bind to the DGAT2 promoter region. (C) Western blot analysis showing that overexpression of SPRY1 in primary keratinocytes did not increase DGAT2 protein levels. n = 3 samples per group. (D) Immunofluorescence staining shows colocalization of SPRY1 and DGAT2 in keratinocytes. (E) Molecular modeling predicts hydrogen bonds between specific residues of SPRY1 and DGAT2, forming a stable interaction interface. Two-tailed Student's t test was performed. $^{**}P < 0.01$, $^{****}P < 0.0001$.



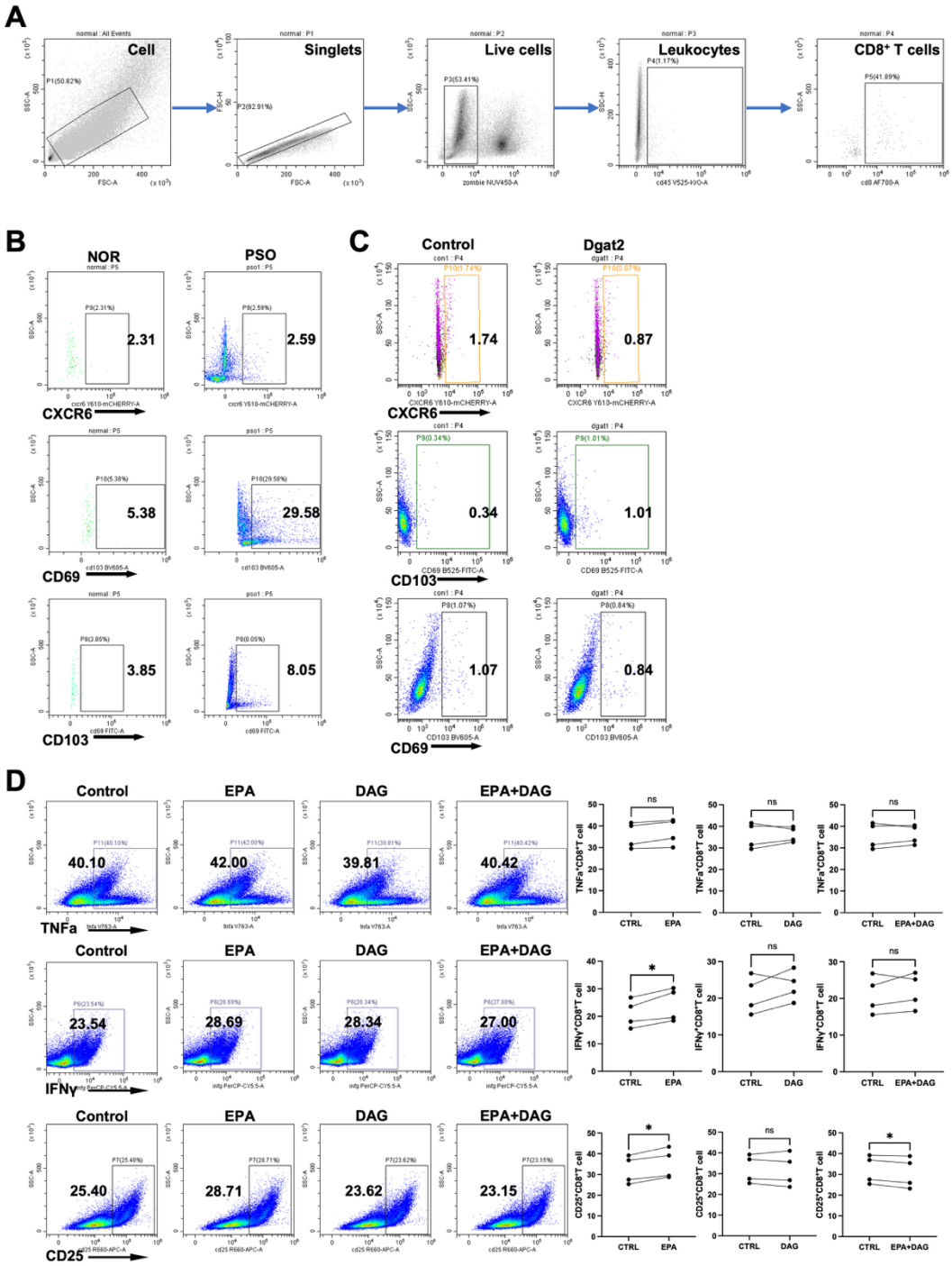

**Supplementary Figure S4 Systemic lipid alterations in plasma of Spry1$^{\Delta Epi}$ mice.** (A) Heatmap analysis of plasma lipids showing changes in lipid classes, including phospholipids and glycerides, in Spry1$^{\Delta Epi}$ mice compared to WT. (B) Pathway enrichment analysis showing disruptions in lipid metabolism, consistent with epidermal findings. (C–D) Quantitative analysis showing moderate changes in triglycerides and diacylglycerols in plasma, with less pronounced effects compared to epidermis. For lipid profiling, n = 4 mice per genotype.




**Supplementary Figure S5 Keratinocyte cytokine production and MAPK/NF-κB pathway activation are enhanced by lipid dysregulation under TLR3 stimulation.**

(A) Gating strategy for identifying cultured single live keratinocytes. (B) IL-1β$^{+}$ and IL-22$^{+}$ keratinocytes can be detected in human epidermis. (C) Flow cytometry analysis

showing differential expression of IL1B and IL22 between EPA+DGAT2i-treated keratinocytes and untreated primary lesional epidermal keratinocytes (PLEKs); upon poly(I:C) stimulation, the difference in IL22 expression was no longer significant. n = 3 samples per group. (D, E) Quantitative analysis of MAPK and NF-κB pathway activation from Western blot experiments confirming significant increases in phosphorylation of ERK, JNK, p38, p65, and IκBα with poly(I:C), EPA and DGAT2i treatment. For Western blotting, 20 μg of protein is loaded per well. n = 3 samples per group. Two-tailed Student's t test was performed. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.




**Supplementary Figure S6 Flow cytometry reveals increased tissue-resident markers in psoriatic epidermal CD8⁺ T cells and minimal effects of lipid treatments on marker expression in vitro.** (A) Gating strategy for identifying cultured single live CD8⁺ T cells. (B) Flow cytometry analysis of epidermal CD8⁺ T cells from psoriasis patients and healthy controls showing increased expression of

CD103, CXCR6, and CD69 in psoriatic samples. (C) DGAT2-treated $CD8^+$ T cells showing no significant changes in tissue-resident markers CD103, CXCR6, or CD69. (D) Flow cytometry analysis of $CD8^+$ T cells following treatment with EPA, DAG, or a combination of both. n = 4 samples per group. Two-tailed Student's t test was performed. $*P < 0.05$.

## SUPPLEMENTARY TABLE

**Flow Cytometry Antibody Table (Table 1)**

| Reagent name | Company | Catalog number |
|---|---|---|
| IL-1 beta (Pro-form) Monoclonal Antibody | Invitrogen | #12-7114-82 |
| IL-17A Monoclonal Antibody | Invitrogen | #25-7177-82 |
| PerCP/Cyanine5.5 anti-mouse IL-22 Antibody | BioLegend | #516411 |
| APC anti-mouse IL-12/IL-23 p40 | BioLegend | #505206 |
| Brilliant Violet 650™ anti-mouse TNF-α Antibody | BioLegend | #506333 |
| Brilliant Violet 510™ anti-human CD45 Antibody | BioLegend | #368526 |
| Alexa Fluor® 700 anti-human CD8 Antibody | BioLegend | #344724 |
| APC anti-human CD25 | BioLegend | #985810 |
| Alexa Fluor® 488 anti-human CD69 Antibody | BioLegend | #310916 |

| | | |
|---|---|---|
| PE/Dazzle™ 594 anti-human CD186 (CXCR6) Antibody | BioLegend | #356016 |
| Brilliant Violet 605™ anti-human CD103 (Integrin αE) Antibody | BioLegend | #350218 |
| PerCP/Cyanine5.5 anti-human IFN-γ Antibody | BioLegend | #502526 |
| Brilliant Violet 785™ anti-human TNF-α Antibody | BioLegend | #502948 |
| PE/Cyanine7 anti-human 1L-22 Antibody | BioLegend | #366707 |
| FITC anti-human IL-1 beta Antibody | BioLegend | #511705 |
| PE anti-human IL-17A Antibody | BioLegend | #512306 |
| IL-23 p19 Monoclonal Antibody | Invitrogen | #50-7823-42 |

66 **DNA Primers Table (Table 2)**

| Gene Name | Primer Type | Sequence (5' → 3') |
|---|---|---|
| Dgat2 | Forward Primer1 | CCACTCATCATGCAAGTGTTTC |
| | Reverse Primer1 | CACCTTTGGGTTGCATACTGT |

| | | |
|---|---|---|
| | Forward Primer2 | AGCCTAGTCTACATAGTGCCAG |
| | Reverse Primer2 | CAGGGTGTCTTTTGTTTGGCT |
| | Forward Primer3 | GTCAGGTCCAGCTGTAACCT |
| | Reverse Primer3 | GCCTCTCTCTCAGACGTTAGT |

**Secondary Antibody Table (Table 3)**

| Reagent name | Company | Catalog number |
|---|---|---|
| HRP-conjugated Rabbit Anti-Goat IgG H&L | Abcam | #ab6741 |
| Anti-rabbit IgG, HRP-linked Antibody | Cell Signaling Technology | #7074 |
| HRP-conjugated Goat Anti-Mouse IgG(H+L) | Proteintech | #SA00001-1 |

**Primary Antibody Table (Table 4)**

| Reagent name | Company | Catalog number |
|---|---|---|
| DGAT2 Goat mAb | Abcam | #ab59493 |
| DGAT2 Mouse mAb | Santa Cruz Biotechnology | #sc-293211 |
| Spry1 Rabbit mAb | Cell Signaling Technology | #13013 |

| | | |
|---|---|---|
| β-Actin Rabbit mAb | Cell Signaling Technology | #4970 |
| Anti-FLAG | Sigma-Aldrich | #F3165 |
| HA-tag Rat mAb | Cell Signaling Technology | #7C9 |
| JNK Mouse mAb | Santa Cruz Biotechnology | #sc-7345 |
| Phospho-SAPK/JNK (Thr183/Tyr185) (81E11) Rabbit mAb | Cell Signaling Technology | #4668S |
| p44/42 MAPK (Erk1/2) (137F5) Rabbit mAb | Cell Signaling Technology | #4695S |
| Phospho-p44/42 MAPK (Erk1/2) (Thr202/Tyr204) Rabbit mAb | Cell Signaling Technology | #4370S |
| p38 MAPK Polyclonal antibody | Proteintech | #14064-1-AP |
| Phospho-p38 MAPK (Thr180/Tyr182) Rabbit mAb | Cell Signaling Technology | #4511S |
| NF-κB p65 Rabbit mAb | Cell Signaling Technology | #8242T |
| Phospho-NF-κB p65 (Ser536) Rabbit mAb | Cell Signaling Technology | #3033S |
| IκBα Mouse mAb (Amino-terminal Antigen) | Cell Signaling Technology | #4814T |

| | | |
|---|---|---|
| Phospho-IκBα (Ser32) Rabbit mAb | Cell Signaling Technology | #2859T |

**RNA Primers Table (Table 5)**

| Gene Name | Primer Type | Sequence (5' → 3') |
|---|---|---|
| Il1b | Forward Primer | GAAATGCCACCTTTGACAGTG |
| | Reverse Primer | TGGAATCCCTCACACTCAGGACAG |
| Il6 | Forward Primer | CTGCAAGAGACTTCCATCCAG |
| | Reverse Primer | AGTGTGATGAGAGCAGGGTCTGTGG |
| Il17a | Forward Primer | TCACGGTGTCCTCACACATCAG |
| | Reverse Primer | CGCCAAGGGAGTTAAAGACTT |
| Il22 | Forward Primer | ATGAGTTTTTCCCTTATGGGAC |
| | Reverse Primer | GCTCGAAGGAGCAAACCTCAA |
| Il23 | Forward Primer | AATAATGTGCCCGCATACCATG |
| | Reverse Primer | GCTCCCTTTGGAAGATGCTAG |
| Tnfα | Forward Primer | CTGAACTTCGGGGTGATCGG |
| | Reverse Primer | GGCTGTCCCTCTGATGGCATTTCAGA |
| Spry1 | Forward Primer | ACACCTGCATGGTGGTGTTCA |

| | | |
|---|---|---|
| | Reverse Primer | CTGCTATTCACATTGCTGGGTAT |
| | Forward Primer | GGCGTACTCAGCGACTATCTT |
| Dgat2 | | |
| | Reverse Primer | GGGCCTTATGCAGGAAACT |