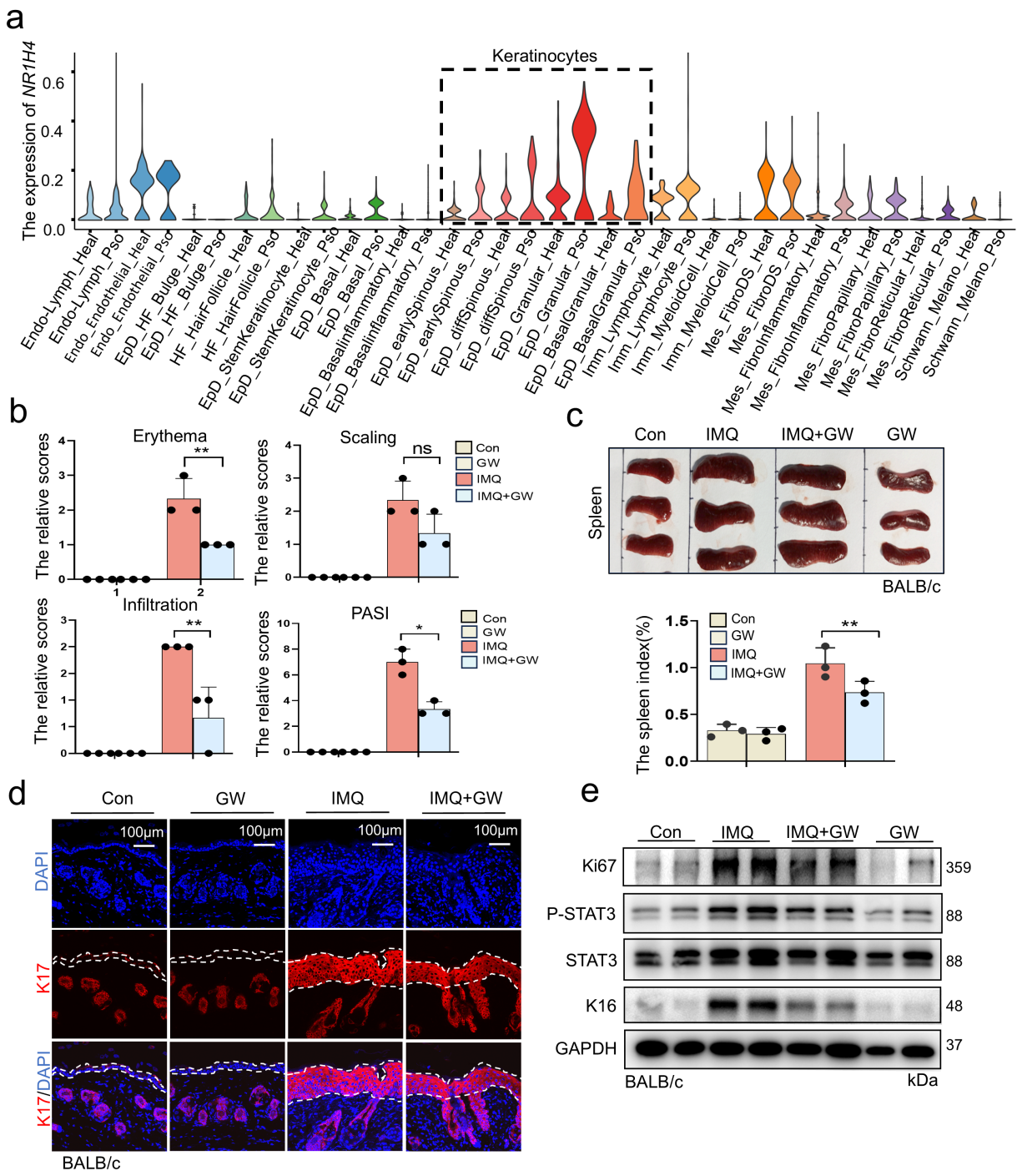
SUPPLEMENTARY INFORMATION

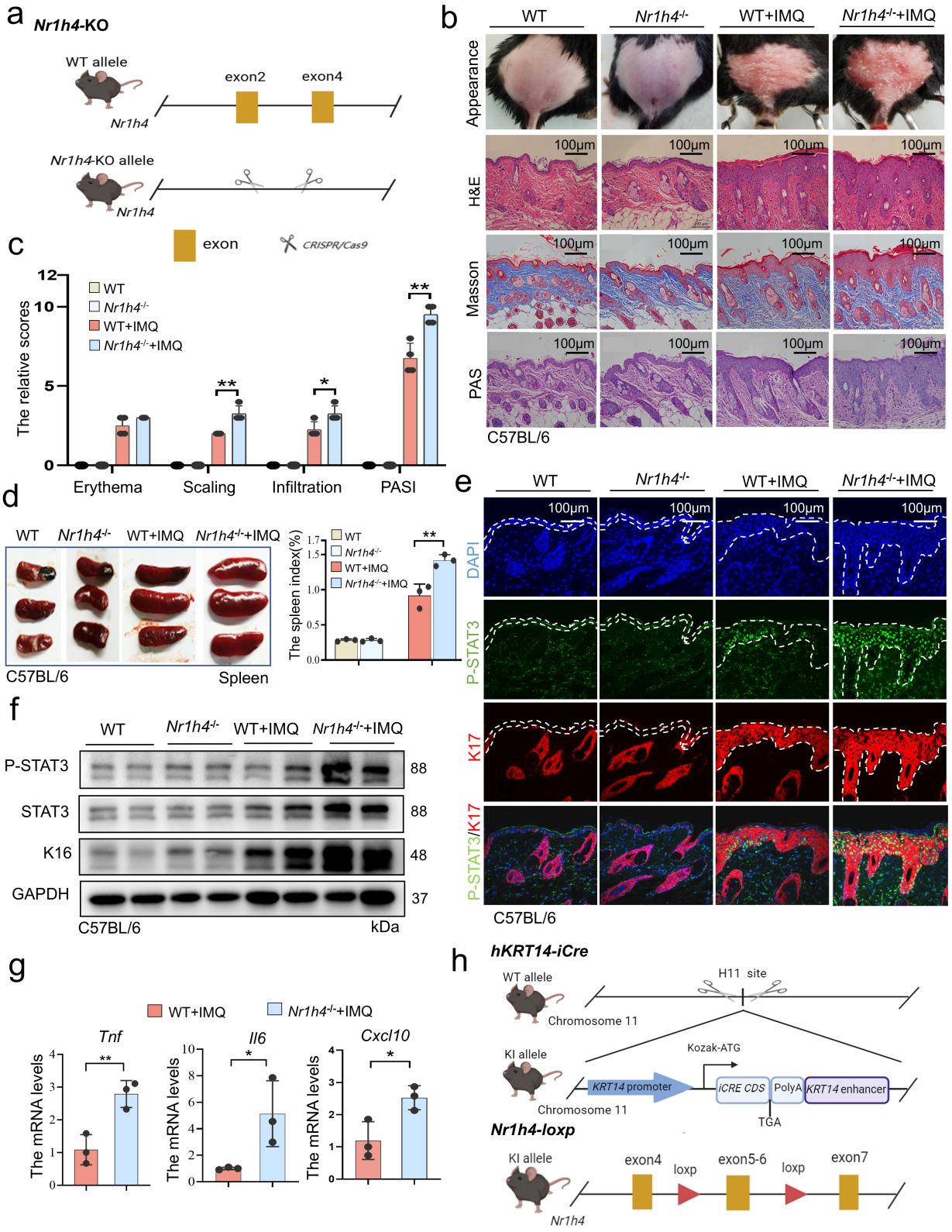
Lian et al. 2025

Fig S1


a
Keratinocytes
The expression of NR1H4
0.0
0.2
0.4
0.6
Endo-Lymph_Heal
Endo-Lymph_Pso
Endo_Endothelial_Heal
Endo_Endothelial_Pso
EpD_HF_Bulge_Heal
EpD_HF_Bulge_Pso
HF_HairFollicle_Heal
HF_HairFollicle_Pso
EpD_StemKeratinocyte_Heal
EpD_StemKeratinocyte_Pso
EpD_Basal_Heal
EpD_Basal_Pso
EpD_BasalInflammatory_Heal
EpD_BasalInflammatory_Pso
EpD_earlySpinous_Heal
EpD_earlySpinous_Pso
EpD_diffSpinous_Heal
EpD_diffSpinous_Pso
EpD_Granular_Heal
EpD_Granular_Pso
EpD_BasalGranular_Heal
EpD_BasalGranular_Pso
Imm_Lymphocyte_Heal
Imm_Lymphocyte_Pso
Imm_MyeloidCell_Heal
Imm_MyeloidCell_Pso
Mes_FibroDS_Heal
Mes_FibroDS_Pso
Mes_FibroInflammatory_Heal
Mes_FibroInflammatory_Pso
Mes_FibroPapillary_Heal
Mes_FibroPapillary_Pso
Mes_FibroReticular_Heal
Mes_FibroReticular_Pso
Schwann_Melano_Heal
Schwann_Melano_Pso
b
Erythema
Scaling
Infiltration
PASI
The relative scores
ns
**
*
Con
GW
IMQ
IMQ+GW
c
Con
IMQ
IMQ+GW
GW
Spleen
BALB/c
The spleen index(%)
d
Con
GW
IMQ
IMQ+GW
100μm
DAPI
K17
K17/DAPI
BALB/c
e
Con
IMQ
IMQ+GW
GW
Ki67
P-STAT3
STAT3
K16
GAPDH
359
88
88
48
37
BALB/c
kDa

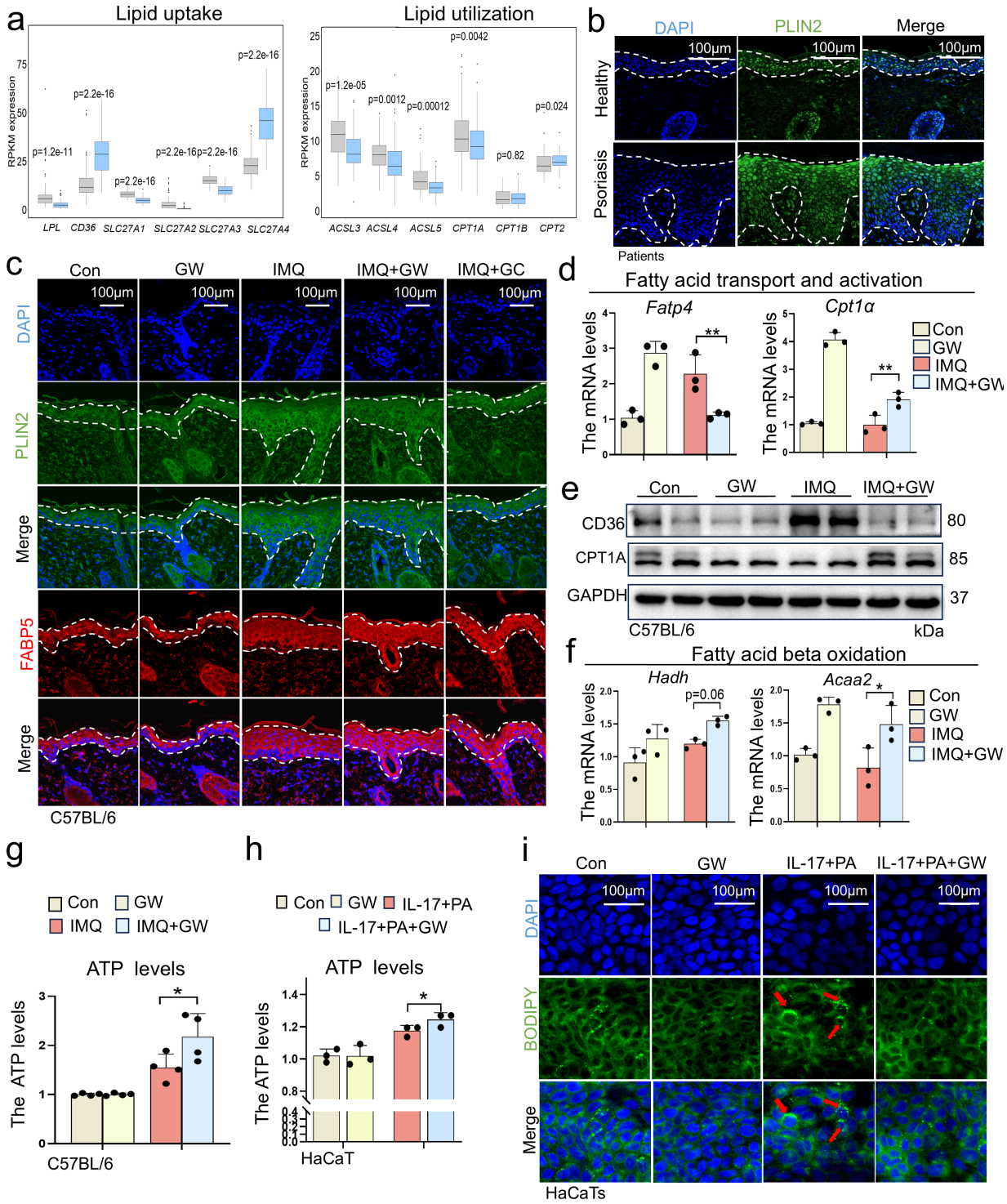
Supplementary Figure 1. Disrupted serum bile acid profile in psoriasis patients and IMQ-induced mice. a. scRNA-seq analysis showing *NR1H4* expression in various skin cells in psoriasis patients. **b.** PASI scores accessing the erythema, scaling, and infiltration on dorsal skin from control and IMQ-induced mice with or without GW treatment ($n = 3$). **c.** Macroscopic appearance of spleen and the spleen index in from control and IMQ-induced mice with or without GW treatment ($n = 3$). **d**. IF staining of K17 in dorsal lesions of control and IMQ-induced mice with or without GW treatment. **e**. Western blot of Ki67, K16, P-STAT3, and STAT3 in dorsal lesions from control and IMQ-induced mice with or without GW treatment. The data are presented as the mean ± SD. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, ****$p < 0.0001$.

Fig S2


a
Nr1h4-KO
WT allele
exon2
exon4
Nr1h4
Nr1h4-KO allele
Nr1h4
exon
CRISPR/Cas9
b
WT
Nr1h4-/-
WT+IMQ
Nr1h4-/-+IMQ
Appearance
H&E
Masson
PAS
100μm
C57BL/6
c
The relative scores
WT
Nr1h4-/-
WT+IMQ
Nr1h4-/-+IMQ
Erythema
Scaling
Infiltration
PASI
d
C57BL/6
Spleen
The spleen index(%)
e
DAPI
P-STAT3
K17
P-STAT3/K17
C57BL/6
f
P-STAT3
STAT3
K16
GAPDH
88
88
48
37
C57BL/6
kDa
g
WT+IMQ
Nr1h4-/-+IMQ
Tnf
Il6
Cxcl10
The mRNA levels
h
hKRT14-iCre
WT allele
H11 site
Chromosome 11
KI allele
Kozak-ATG
KRT14 promoter
iCRE CDS
PolyA
KRT14 enhancer
TGA
Chromosome 11
Nr1h4-loxp
KI allele
exon4
loxp
exon5-6
loxp
exon7
Nr1h4

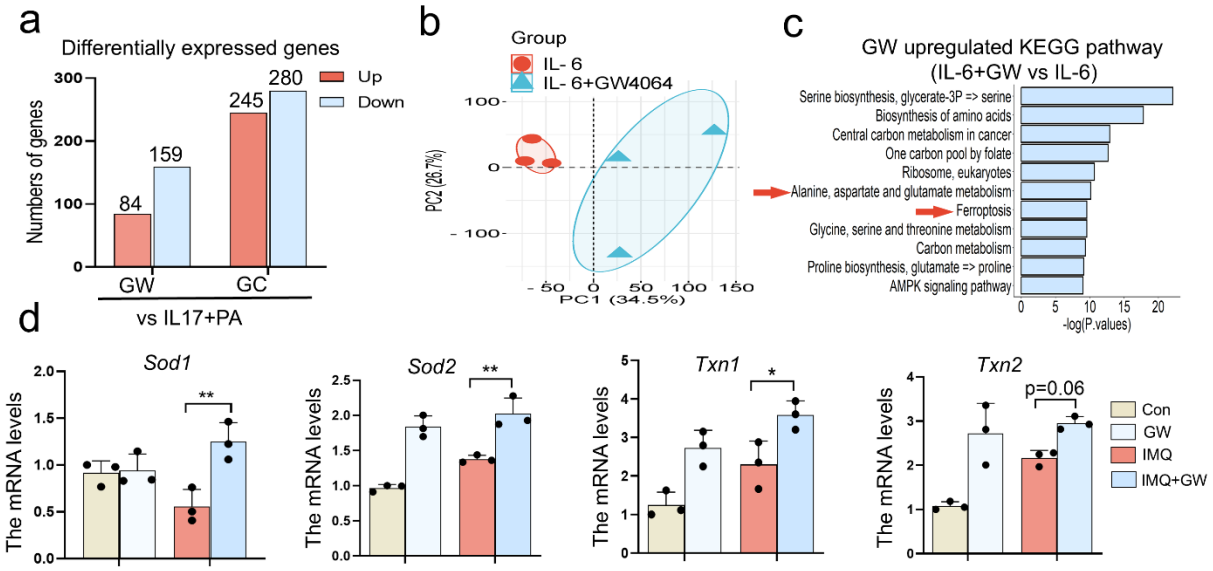
Supplementary Figure 2. Systemic *Nr1h4* knockout aggravates the IMQ-induced psoriatic lesions in Mice. a. Schematic illustration showing the strategy of constructing systemic *Nr1h4* knockout mice **b**. Representative images and histological staining (H&E staining, Masson's trichrome, and PAS) of dorsal skin from WT and *Nr1h4*-KO mice with or without IMQ treatment. **c**. PASI scores accessing the erythema, scaling, and infiltration in IMQ-induced mice (n = 3). **d**. Macroscopic appearance of spleen and the spleen index in WT and *Nr1h4*-KO mice with or without IMQ treatment (n = 3). **e**. IF staining of K17 and P-STAT3 in dorsal lesions from WT and *Nr1h4*-KO mice with or without IMQ treatment. **f.** Western blot of K16, P-STAT3, and STAT3 in dorsal lesions of WT and *Nr1h4*-KO mice with or without IMQ treatment. **g.** qRT-PCR analyzing key psoriasis-associated inflammatory mediators (*Tnf*, *Il6*, and *Cxcl10*) in dorsal skin of IMQ-induced WT and *Nr1h4*-KO mice (n = 3). **h**. Schematic illustration showing the strategy of constructing *KRT14-Cre* mice and *Nr1h4* $^{loxp/loxp}$ mice. The data are presented as the mean ± SD. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, ****$p < 0.0001$.

Fig S3


a
Lipid uptake
Lipid utilization
RPKM expression
p=1.2e-11
p=2.2e-16
p=2.2e-16
p=2.2e-16
p=2.2e-16
p=2.2e-16
LPL
CD36
SLC27A1
SLC27A2
SLC27A3
SLC27A4
p=1.2e-05
p=0.0012
p=0.00012
p=0.0042
p=0.82
p=0.024
ACSL3
ACSL4
ACSL5
CPT1A
CPT1B
CPT2
b
DAPI
PLIN2
Merge
Healthy
Psoriasis
Patients
100μm
c
Con
GW
IMQ
IMQ+GW
IMQ+GC
DAPI
PLIN2
Merge
FABP5
Merge
C57BL/6
d
Fatty acid transport and activation
Fatp4
Cpt1α
The mRNA levels
Con
GW
IMQ
IMQ+GW
e
Con
GW
IMQ
IMQ+GW
CD36
CPT1A
GAPDH
80
85
37
C57BL/6
kDa
f
Fatty acid beta oxidation
Hadh
Acaa2
p=0.06
The mRNA levels
Con
GW
IMQ
IMQ+GW
g
Con
GW
IMQ
IMQ+GW
ATP levels
The ATP levels
C57BL/6
h
Con
GW
IL-17+PA
IL-17+PA+GW
ATP levels
The ATP levels
HaCaT
i
Con
GW
IL-17+PA
IL-17+PA+GW
DAPI
BODIPY
Merge
HaCaTs

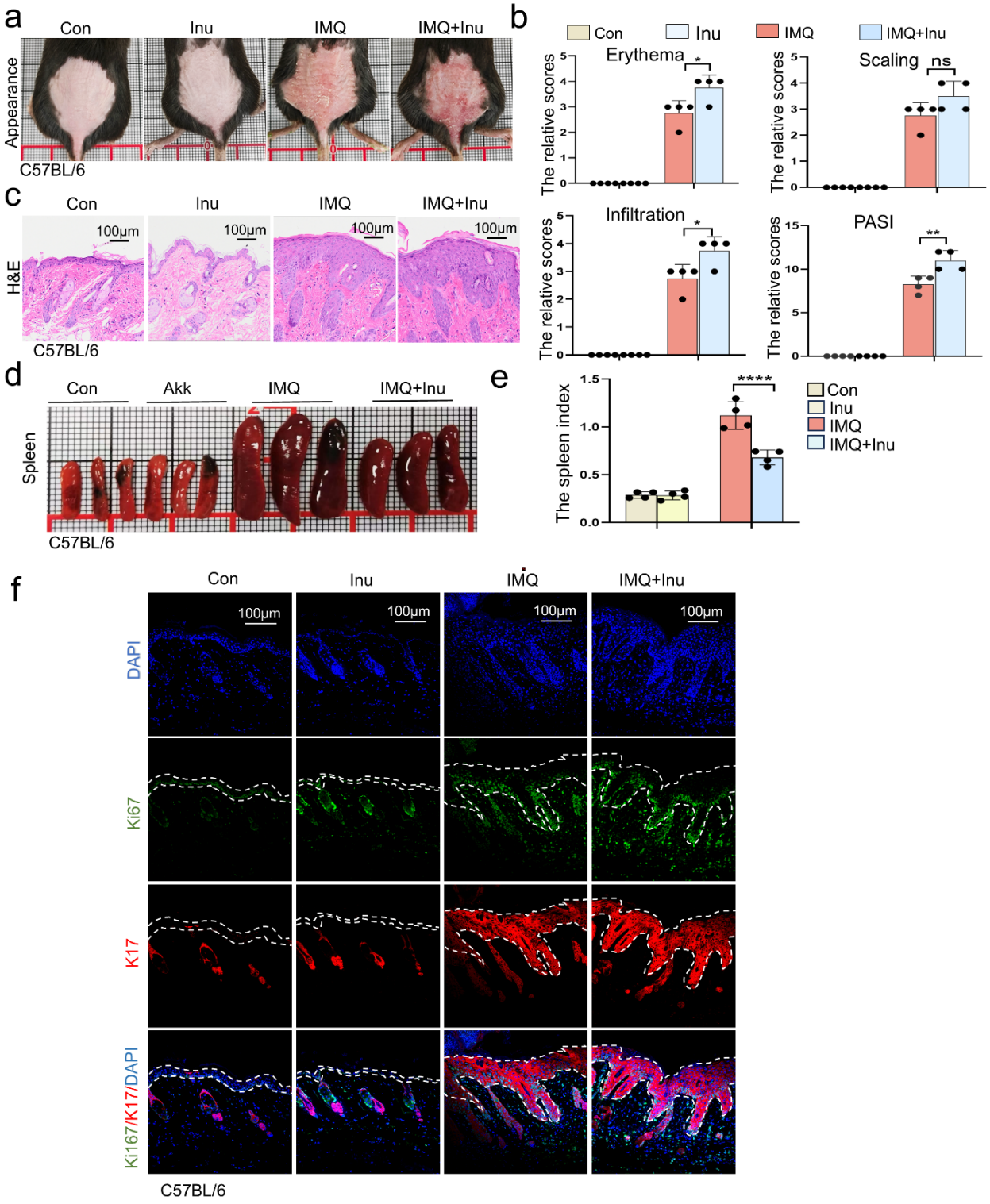
Supplementary Figure 3. FXR activation ameliorates psoriatic lesions through decreasing keratinocyte lipid accumulation. a. RPKM values of genes associated with lipid uptake and lipid utilization in psoriatic skin from GEO database (GSE54456). **b**. IF staining of PLIN2 in psoriatic lesions and healthy skin. **c.** IF staining of PLIN2 and FABP5 in the dorsal skin of control, IMQ-treated, and IMQ- treated mice with GC or GW treatment. **d**. qRT-PCR analyzing of key genes associated with fatty acid transport and activation (*Fatp4, Cpt1α*) in dorsal lesions of mice ($n = 3$). **e**. Western blot of CD36 and CPT1A in the dorsal lesions of control, IMQ-treated, and IMQ-treated mice with GC or GW. **f.** qRT-PCR analyzing of key genes associated with fatty acid beta oxidation (*Hadh*, *Ehhadh*, *Acaa2*) in dorsal lesions of mice ($n = 3$). **g.** ATP analysis of dorsal skin of control, IMQ-treated, and IMQ-treated mice with GW treatment ($n = 4$). **h**. ATP analysis of IL-17- and PA-induced HaCaTs with GW treatment ($n = 3$). **i.** BODIPY staining showing lipid droplets in IL-17- and PA-induced HaCaTs with GW treatment. The data are presented as the mean ± SD. $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$, $^{****}p < 0.0001$.

Fig S4



Supplementary Figure 4. FXR upregulates NQO1 expression to enhance antioxidative ability. **a.** Bar-chart showing differentially expressed genes (DEGs) in IL-17/PA-induced HaCaTs with GW or GC treatment. **b**. PCA plot of RNA sequencing in IL-6-induced HaCaTs with GW treatment (n = 3). **c**. KEGG enrichment analysis of upregulated genes in in IL-6-induced HaCaTs treated with GW. **d**. RT-PCR analyzing of the antioxidative genes (*Sod1*, *Sod2*, *Txn1*, *Txn2*) in dorsal skin of IMQ-induced mice with GW treatment. The data are presented as the mean ± SD. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, ****$p < 0.0001$.

Fig S5


a
Con
Inu
IMQ
IMQ+Inu
Appearance
C57BL/6
b
Con
Inu
IMQ
IMQ+Inu
Erythema
Scaling
ns
Infiltration
PASI
The relative scores
c
H&E
100μm
C57BL/6
d
Con
Akk
IMQ
IMQ+Inu
Spleen
C57BL/6
e
The spleen index
****
f
DAPI
Ki67
K17
Ki167/K17/DAPI
C57BL/6

Supplementary Figure 5. Inulin feeding exacerbates IMQ-induced psoriatic lesions in mice. **a.** Macroscopic images of dorsal skin from control and IMQ-induced mice with or without inulin (inu) treatment. **b**. PASI scores assessing the erythema, scaling, and infiltration on dorsal skin from control and IMQ-induced mice with or without inu treatment ($n = 4$). **c**. Histological H&E staining of dorsal skin from control and IMQ-induced mice with or without inu treatment. **d-e**. Macroscopic images of spleen and the spleen index in control and IMQ-induced mice with or without inu treatment ($n = 4$). **f**. IF staining of K17 and Ki67 in the dorsal lesions of control and IMQ-induced mice with or without GW treatment. The data are presented as the mean ± SD. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, ****$p < 0.0001$.

Supplementary table 1: Primers used in this study

RT-qPCR primers	Forward Primer (5'-3')	Reverse Primer (5'-3')
Mouse		
Il6	TAGTCCTTCCTACCCCAATTTCC	TTGGTCCTTAGCCACTCCTTC
Cxcl10	ATGAGTTTTTCCCTTATGGGGAC	GCTGGAAGTTGGACACCTCAA
Il17a	TGACCCCTAAGAAACCCCCA	TCATTGTGGAGGGCAGACAA
Il1b	GCAACTGTTCCTGAACTCAACT	ATCTTTTGGGGTCCGTCAACT
Tnf	CAGGCGGTGCCTATGTCTC	CGATCACCCCGAAGTTCAGTAG
S100a9	ACTCTTTAGCCTTGAAGAGCAAG	TTCTTGCTCAGGGTGTCAGG
Il23	CAAAGGATCCGCCAAGGTCT	GGAGGTGTGAAGTTGCTCCA
Fatp4	GATGAAGACCCGGATGAAACG	GATGAAGACCCGGATGAAACG
Cpt1α	CTCCGCCTGAGCCATGAAG	CACCAGTGATGATGCCATTCT
Hadh	TCAAGCATGTGACCGTCATCG	TGGATTTTGCCAGGATGTCTTC
Acaa2	CTGCTACGAGGTGTGTTCATC	AGCTCTGCATGACATTGCCC
Sod1	AACCAGTTGTGTTGTCAGGAC	CCACCATGTTTCTTAGAGTGAGG
Sod2	CAGACCTGCCTTACGACTATGG	CTCGGTGGCGTTGAGATTGTT
Txn1	CATGCCGACCTTCCAGTTTTA	TTTCCTTGTTAGCACCGGAGA
Txn2	TGGGCTTCCCTCACCTCTAAG	CCTGGACGTTAAAGGTCGTCA
Human		
SLC7A11	TGCAGTGGCAGTGACCTTTT	AAGCAGGAGAGGGCAACAAA
NQO1	CCTTGTGATATTCCAGAGTGGCA	CCAGGCGTTTCTTCCATCCT

Primers for *Nr1h4*-KO mice	Forward Primer (5'-3')	Reverse Primer (5'-3')
*K14_Cre*_KI	ATATCCCCTTGTTCCCTTTCTGC	ATATCCCCTTGTTCCCTTTCTGC
*K14_Cre*_WT	CAGCAAAACCTGGCTGTGGATC	ATGAGCCACCATGTGGGTGTC
Nr1h4_Floxp	TGTAGGCTTCTAGGTGTTGGC	ACCCTTCACATGGTGGGAGAT
*Nr1h4*_KO	GGCTATTAGAGTTTTAAGTGCTGGAGG	GCTGTTCCCTCACTCTGTCTTTAG
*Nr1h4*_WT	CTTCCGAAGAAGCATTACCAAG	CGTCCGACATAGCTCATTAAAGC

NQO1 siRNA	Forward Primer (5'-3')	Reverse Primer (5'-3')
NQO1	UAUAUGUCAGUUGAGGUUCUU	UAUAUGUCAGUUGAGGUUCUU
Scramble	UUCUCCGAACGUGUCACGU	ACGUGACACGUUCGGAGAA

ChIP-qPCR	Forward Primer (5'-3')	Reverse Primer (5'-3')
*NQO1*_site1	GAATAGCCAAAACGGGACCAG	GTACAGACGGGGCTTCACCA
*NQO1*_site2	TGGGTGACGAAGTGAGACTC	CTTTTGCACTGGAGGGACAA