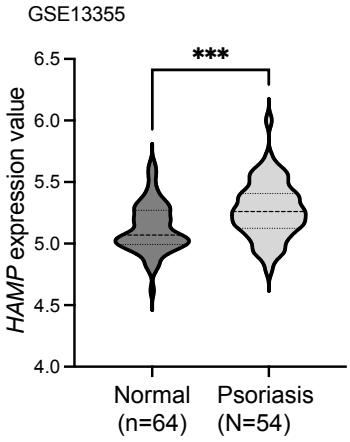
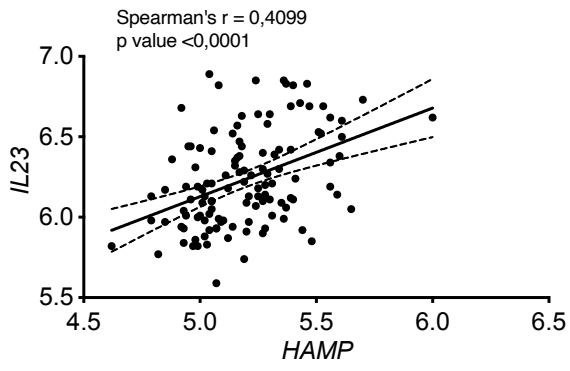
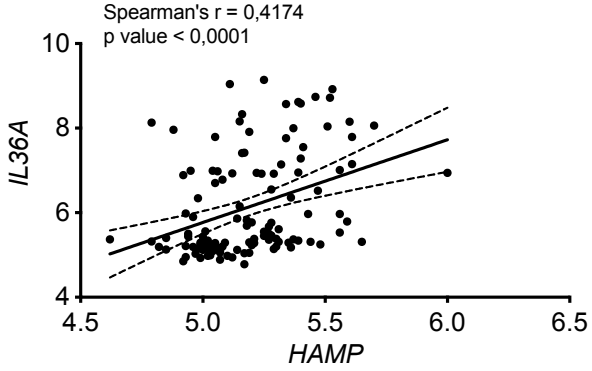
a



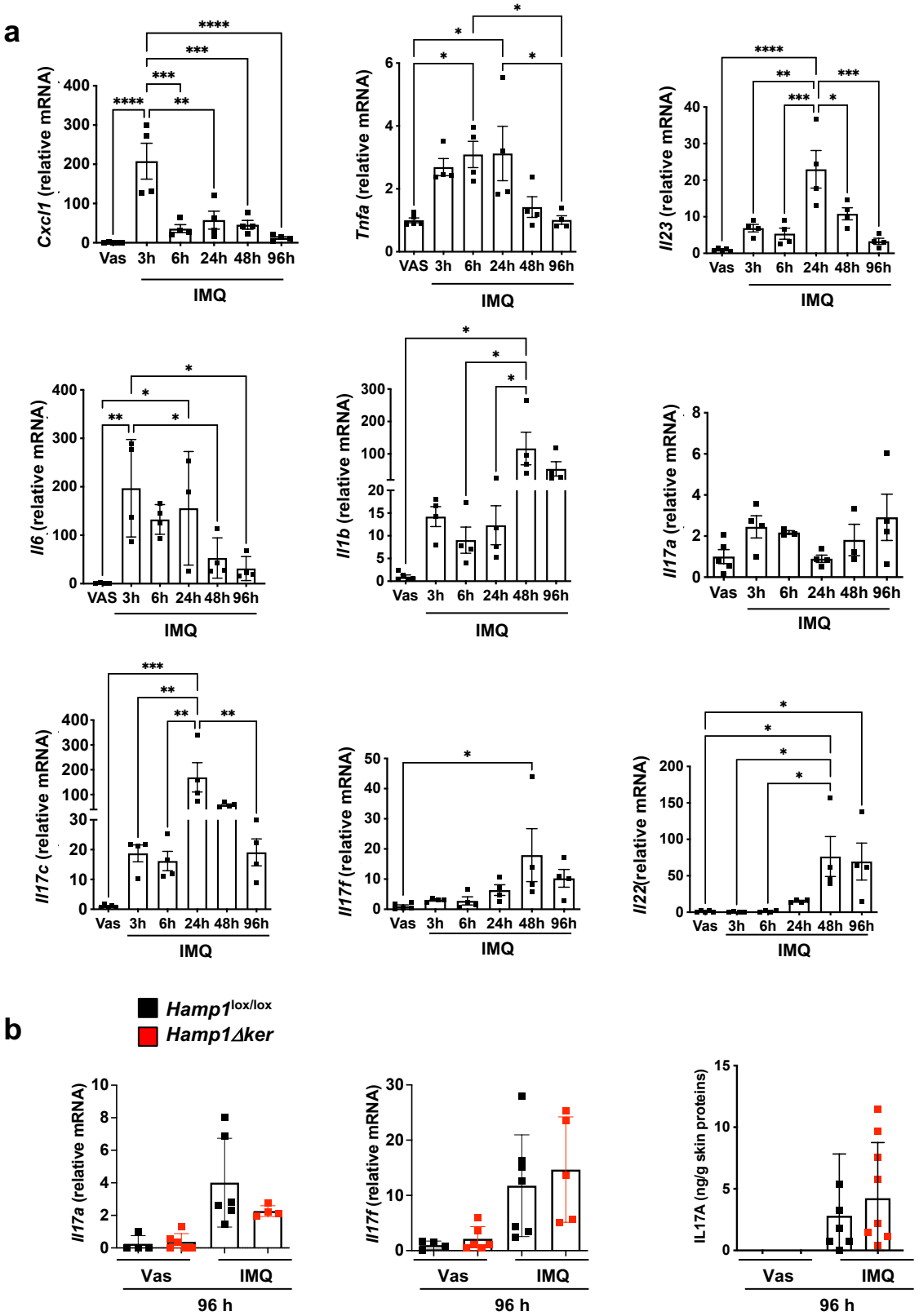
b



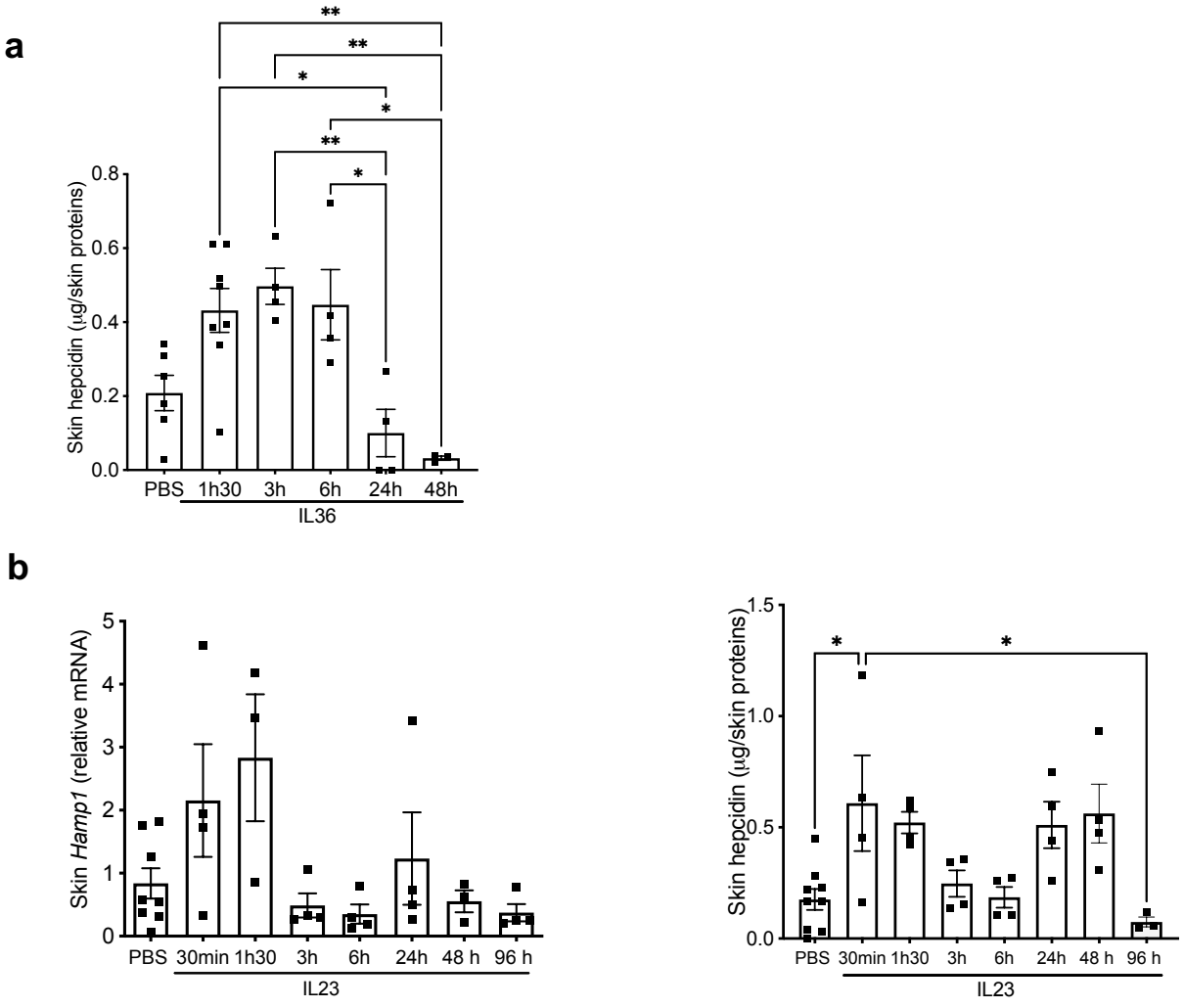


Supplementary fig. 1: Analysis of a cohort of psoriasis patients available in a public database (GSE A3355).

(**a**) *HAMP* expression value in the skin of psoriasis patients and healthy controls. Data analyzed by unpaired two-tailed Student t test. (n= 64 healthy controls; n=54 psoriasis patients; ***p=0.0002). (**b**) Correlation between *HAMP* and *IL23* or *IL36A* expression. N= 118 individuals. Spearman's r test with 95% confidence intervals. Source data are provided as a Source Data file.



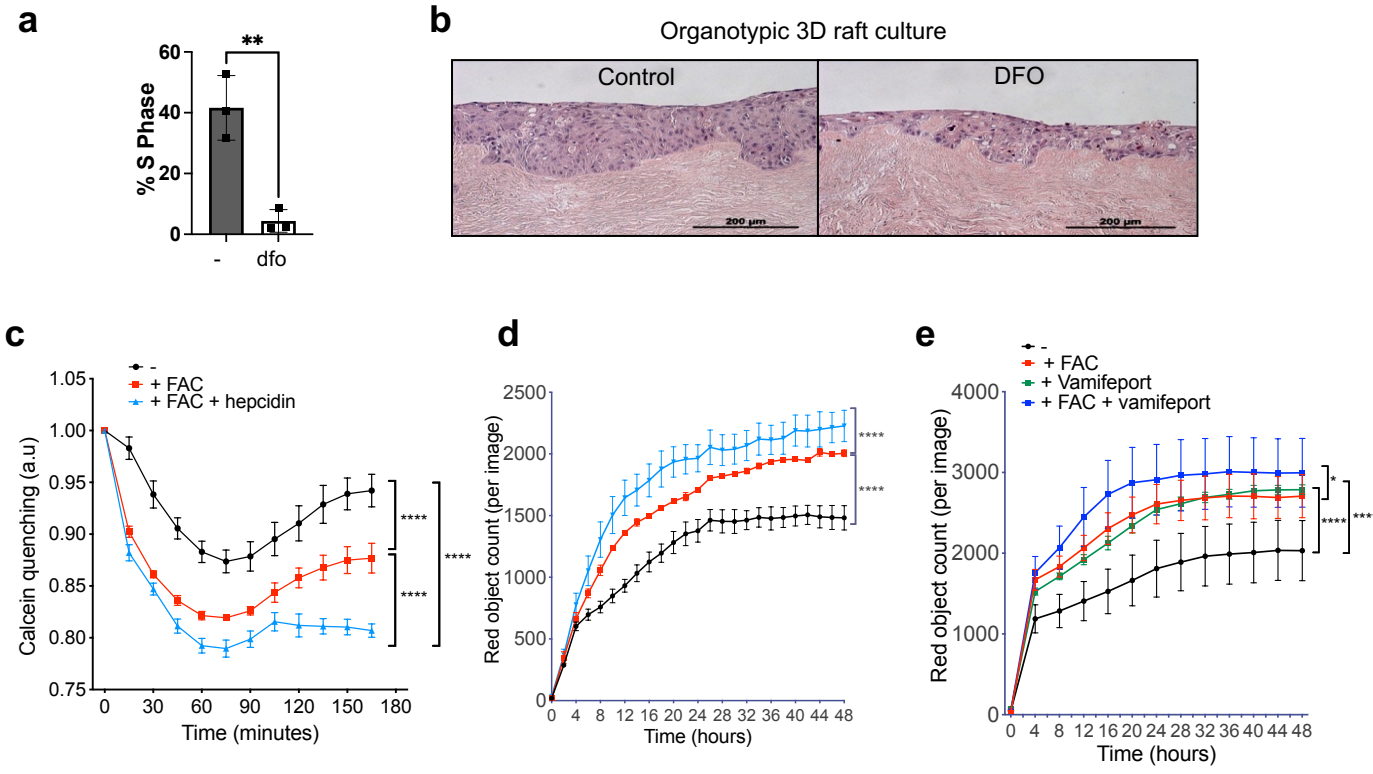
Supplementary fig. 2: Expression of key inflammatory cytokines in the skin of (a) Hamp1lox/lox or/and (b) Hamp1Δker mice treated with IMQ or Vas for 5 days. Cytokine expression measured by qPCR. Each point represents a mouse. Data are means ± SEM. N ≥ 3 mice per group (*p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0.0001). Data were analyzed by a one-way Analysis of Variance followed by a Tukey analysis. Source data are provided as a Source Data file.



Supplementary fig. 3: Hepcidin expression in the skin upon intradermal injection of IL-36α (A) or IL-23 (B)

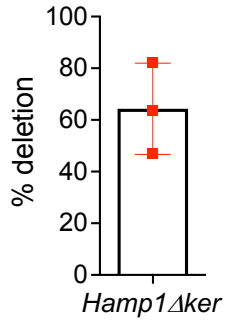
Skin hepcidin expression was measured by ELISA (**a, b**) or qPCR (b, right).

Each point represents a mouse. Data are means ± SEM. N ≥ 3 mice per group (*p < 0.05, **p < 0.01). Data were analyzed by a one-way Analysis of Variance followed by a Tukey analysis. Source data are provided as a Source Data file.



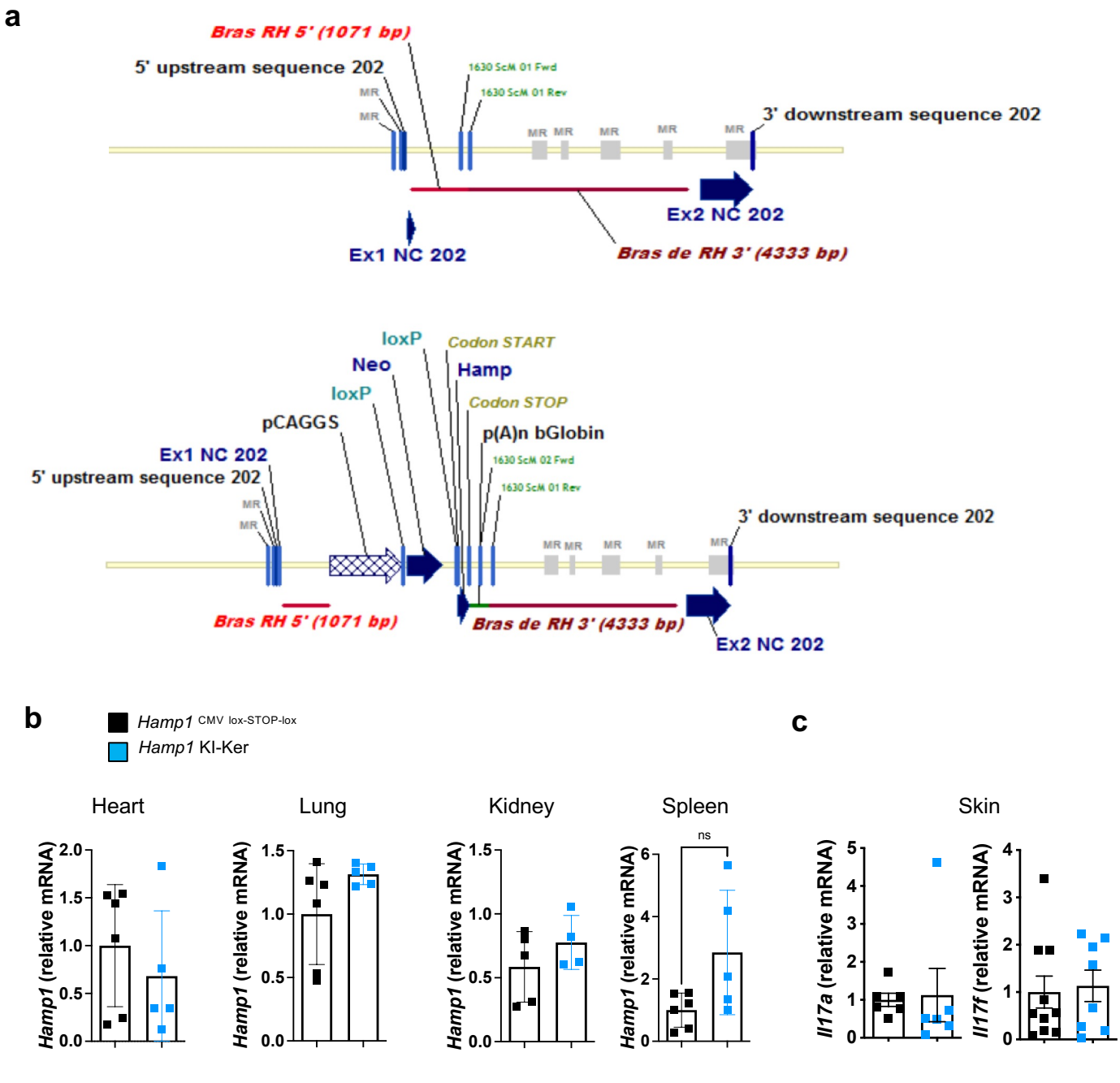
Supplementary fig. 4: Hepcidin controls intracellular iron levels and proliferation of keratinocytes

(a) Exponentially growing HaCaT cells were treated with 100 μM DFO for 72 h and then the percentage of cells in S phase were determined by BrdU-assay using flow cytometry. N=3 biological replicates. (**b**) Morphological study of DED-Raft HaCaT cultures treated with 100 μM DFO for 72 h following haematoxylin and Eosin staining Scale bar = 200 μM. (**c**) Calcein fluorescence quenching assay in HaCaT incubated or not with Ferric Ammonium Citrate (FAC) (500 μM) +/- synthetic hepcidin (3,6 μM), for measurement of the labile iron pool. N=6 biological replicates (**d**) Incucyte analysis for Red fluorescent objects over time in HaCaT cells labeled with Nuclight Rapid Red incubated or not with Ferric Ammonium Citrate (FAC) (500μM) +/- synthetic hepcidin (3,6 μM) or (**e**) Vamifeport (VIT-2763), a FPN inhibitor. N=3 biological replicates. Data are means ± SEM. (*p < 0.05, **p < 0.01, ****p < 0.0001). Data were analyzed by unpaired two-tailed Student t test (a), a two-way Analysis of Variance followed by a Tukey analysis [(c), (d), (e)]. Source data are provided as a Source Data file.



Supplementary fig. 5: Deletion level in primary keratinocytes of *Hamp1Δker* mice

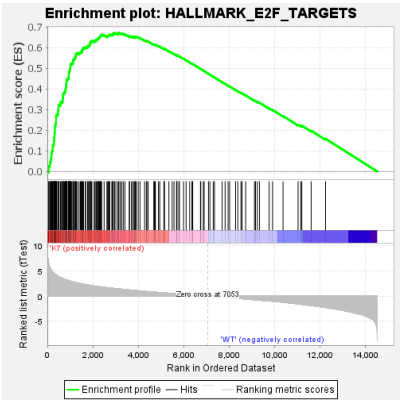
Deletion efficiency of the loxP-flanked allele in the primary keratinocytes was 65%. Data are means ± SEM. N= 3 mice. Source data are provided as a Source Data file.

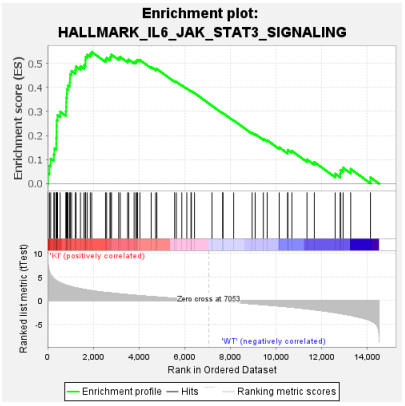


Supplementary fig. 6: (A) Scheme of the hepcidin knock-in strategy. (B) Hepcidin expression in different organs of *Hamp1* KI-Ker mice and control litermates.

(**a**) The sequence of the *Hamp1* gene has been inserted in the ROSA26 locus downstream a strong promoter (CMV Enhancer + pCAGGS promoter), which guaranteed the overexpression of the cDNA coding for hepcidin. The lox-STOP-lox (LSL) sequence was placed between the strong promoter and the *Hamp* gene sequence. After deletion of the LSL sequence by crossing with a "Cre" mouse, the *Hamp* gene can be transcribed and overexpressed in the tissue of interest. (**b**) *Hamp1*(N=5 mice per group) and (**c**) *Il17* expression (N ≥ 6 mice per group) measured by qPCR. Data were analyzed by unpaired two-tailed Student t test. Data are means ± SEM.

a


Enrichment plot: HALLMARK_E2F_TARGETS
Enrichment score (ES)
'KI' (positively correlated)
Ranked list metric (rTest)
Zero cross at 7053
'WT' (negatively correlated)
Rank in Ordered Dataset
Enrichment profile
Hits
Ranking metric scores


Enrichment plot:
HALLMARK_IL6_JAK_STAT3_SIGNALING
Enrichment score (ES)
'KI' (positively correlated)
Ranked list metric (rTest)
Zero cross at 7053
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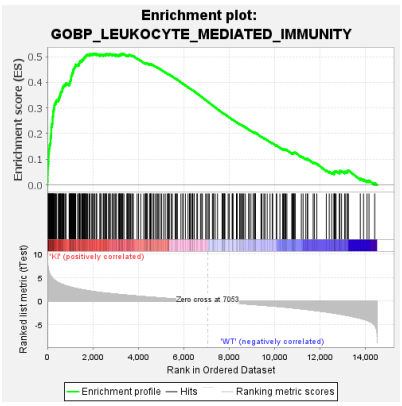
Rank in Ordered Dataset
Enrichment profile
Hits
Ranking metric scores

b


Enrichment plot:
GOBP_LEUKOCYTE_MEDIATED_IMMUNITY
Enrichment score (ES)
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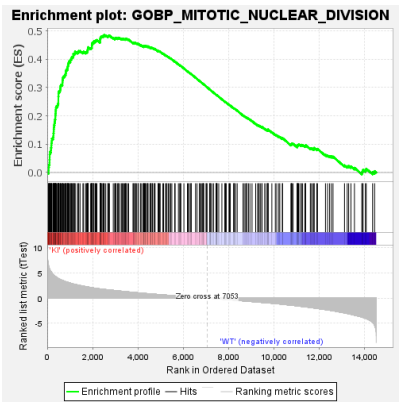
Ranked list metric (rTest)
Zero cross at 7053
'WT' (negatively correlated)
Rank in Ordered Dataset
Enrichment profile
Hits
Ranking metric scores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Enrichment score (ES)
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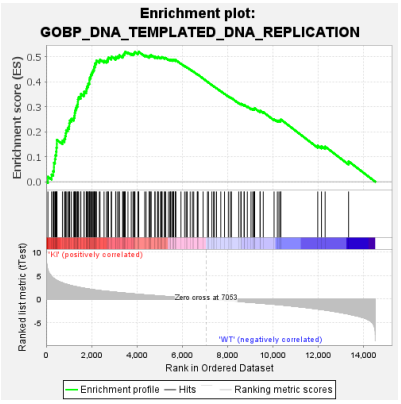
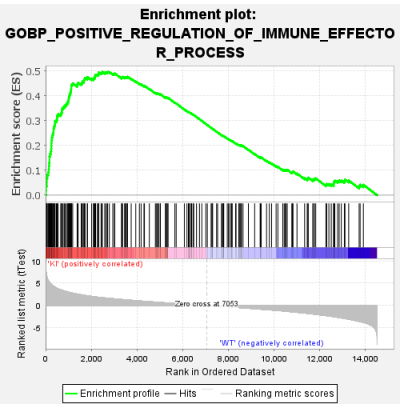
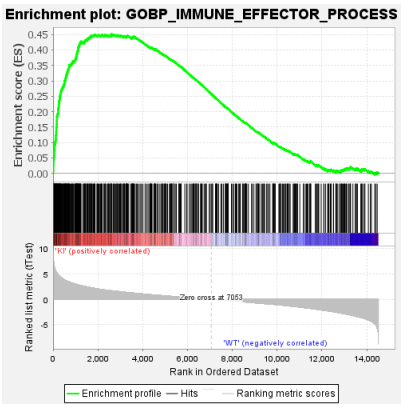
Ranked list metric (rTest)
Zero cross at 7053
'WT' (negatively correlated)
Rank in Ordered Dataset
Enrichment profile
Hits
Ranking metric scores


Enrichment plot:
GOBP_DNA_TEMPLATED_DNA_REPLICATION
Enrichment score (ES)
'KI' (positively correlated)
Ranked list metric (rTest)
Zero cross at 7053
'WT' (negatively correlated)
Rank in Ordered Dataset
Enrichment profile
Hits
Ranking metric scores


Enrichment plot:
GOBP_POSITIVE_REGULATION_OF_IMMUNE_EFFECTO
R_PROCESS
Enrichment score (ES)
'KI' (positively correlated)
Ranked list metric (rTest)
Zero cross at 7053
'WT' (negatively correlated)
Rank in Ordered Dataset
Enrichment profile
Hits
Ranking metric scores


Enrichment plot: GOBP_IMMUNE_EFFECTOR_PROCESS
Enrichment score (ES)
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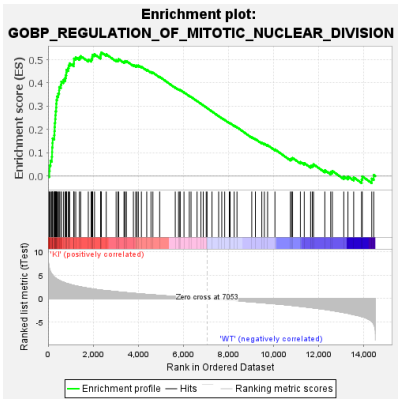
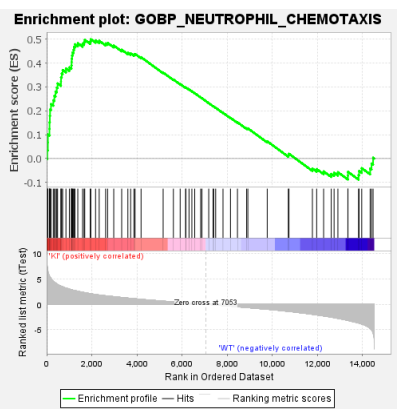
Ranked list metric (rTest)
Zero cross at 7053
'WT' (negatively correlated)
Rank in Ordered Dataset
Enrichment profile
Hits
Ranking metric scores


Enrichment plot:
GOBP_REGULATION_OF_MITOTIC_NUCLEAR_DIVISION
Enrichment score (ES)
'KI' (positively correlated)
Ranked list metric (rTest)
Zero cross at 7053
'WT' (negatively correlated)
Rank in Ordered Dataset
Enrichment profile
Hits
Ranking metric scores


Enrichment plot: GOBP_NEUTROPHIL_CHEMOTAXIS
Enrichment score (ES)
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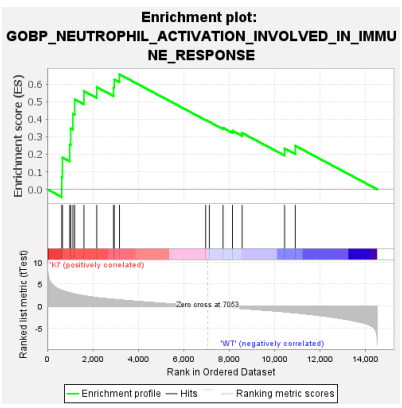
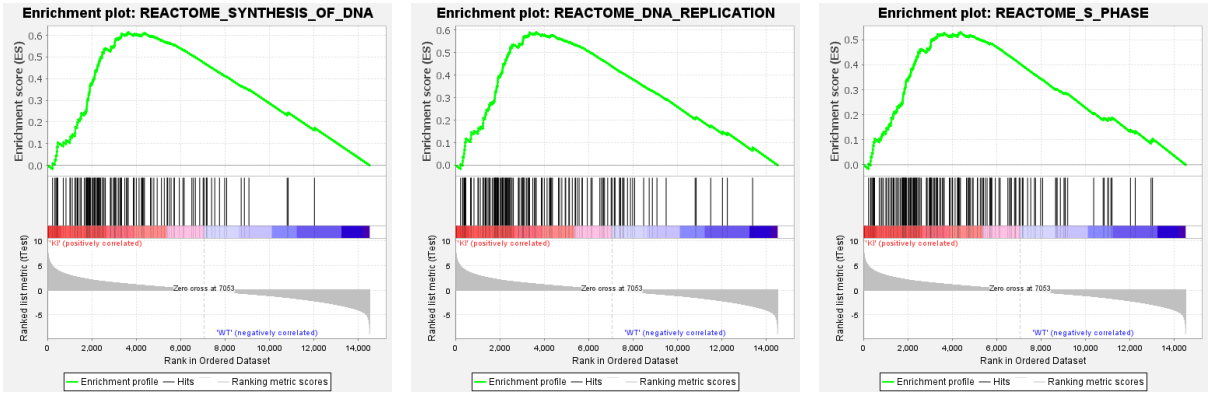
Ranked list metric (rTest)
Zero cross at 7053
'WT' (negatively correlated)
Rank in Ordered Dataset
Enrichment profile
Hits
Ranking metric scores


Enrichment plot:
GOBP_NEUTROPHIL_ACTIVATION_INVOLVED_IN_IMMU
NE_RESPONSE
Enrichment score (ES)
'KI' (positively correlated)
Ranked list metric (rTest)
Zero cross at 7053
'WT' (negatively correlated)
Rank in Ordered Dataset
Enrichment profile
Hits
Ranking metric scores

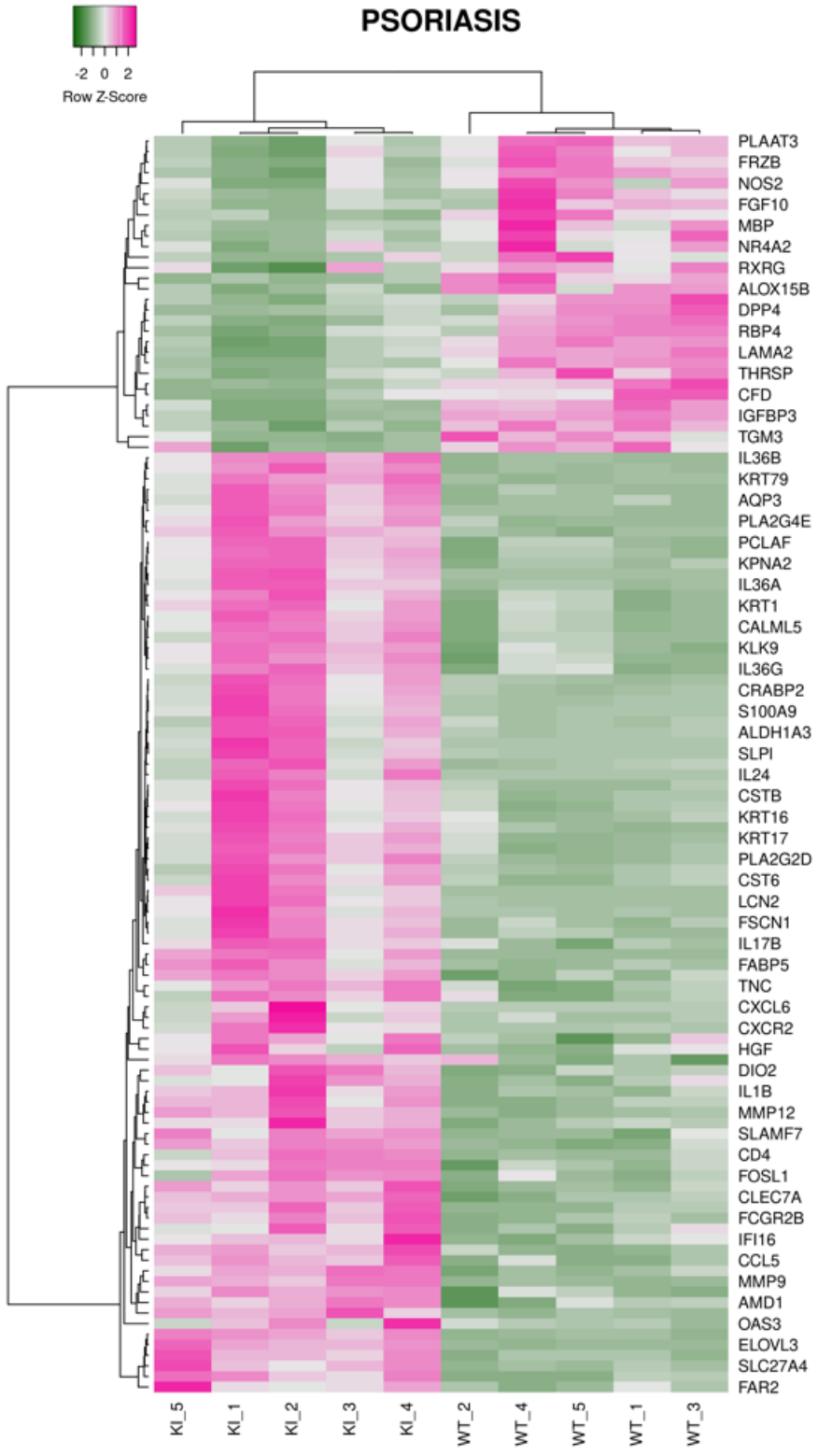
C



Supplementary fig. 7: GSEA plots related to (a) HALLMARKS, (b) Gene Ontology Biological Process (GOBP) and (c) to REACTOME

GSEA plots showing a significant enrichment (p.val = 0.00) of involved genes among upregulated transcripts in *Hamp1* KI-Ker samples compared to controls.

a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FRZB
NOS2
FGF10
MBP
NR4A2
RXRG
ALOX15B
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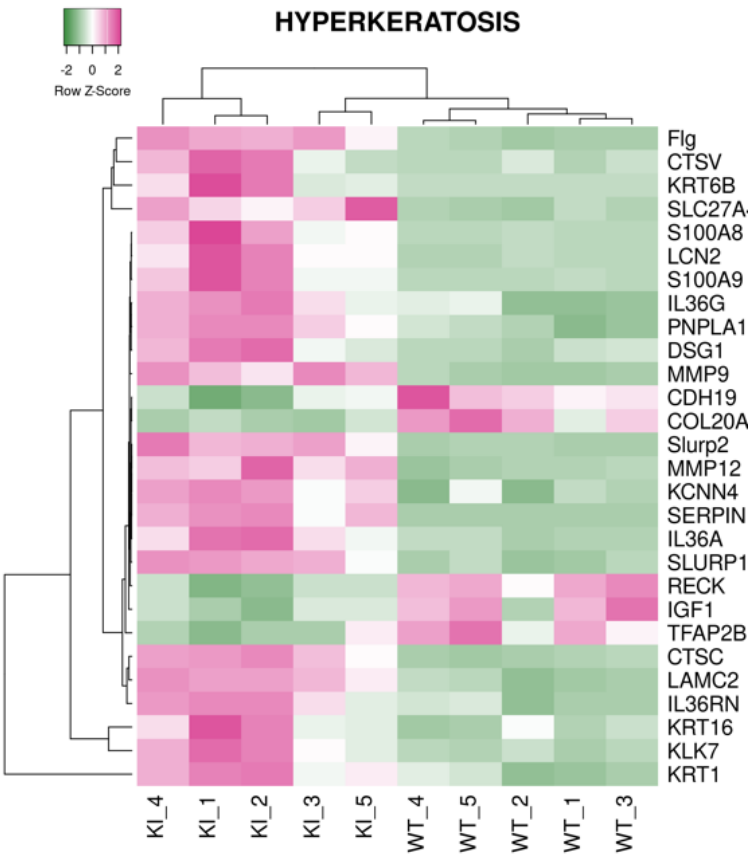
RBP4
LAMA2
THRSP
CFD
IGFBP3
TGM3
IL36B
KRT79
AQP3
PLA2G4E
PCLAF
KPNA2
IL36A
KRT1
CALML5
KLK9
IL36G
CRABP2
S100A9
ALDH1A3
SLPI
IL24
CSTB
KRT16
KRT17
PLA2G2D
CST6
LCN2
FSCN1
IL17B
FABP5
TNC
CXCL6
CXCR2
HGF
DIO2
IL1B
MMP12
SLAMF7
CD4
FOSL1
CLEC7A
FCGR2B
IFI16
CCL5
MMP9
AMD1
OAS3
ELOVL3
SLC27A4
FAR2
KI_5
KI_1
KI_2
KI_3
KI_4
WT_2
WT_4
WT_5
WT_1
WT_3

b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LCN2
S100A9
IL36G
PNPLA1
DSG1
MMP9
CDH19
COL20A
Slurp2
MMP12
KCNN4
SERPIN
IL36A
SLURP1
RECK
IGF1
TFAP2B
CTSC
LAMC2
IL36RN
KRT16
KLK7
KRT1
KI_4
KI_1
KI_2
KI_3
KI_5
WT_4
WT_5
WT_2
WT_1
WT_3

c

Supplementary fig. 8: Heat maps showing transcripts involved in (a) psoriasis, (b) migration, recruitment, influx and cell movement of neutrophils and (c) hyperkeratosis, according to IPA.
Hierarchical clustering of rows and columns was performed using Pearson-Average Linkage correlation on z-scored normalized counts (psoriasis and neutrophils) or Euclidean-Average Linkage correlation (hyperkeratosis).
Hierarchical clustering was performed using Heatmapper tool (http://www.heatmapper.ca).

Psoriasis patients	Number	Treatment
Vulgaris	PSO1	Topical steroid + calcipotriol
	PSO2	Topical steroid + retinoid
	PSO3	-
	PSO4	Topical steroid
	PSO5	-
	PSO6	-
	PSO7	-
	PSO8	Topical steroid
	PSO9	-
	PSO10	Topical steroid
	PSO11	-
	PSO12	-
	PSO13	Topical steroid + calcipotriol
	PSO14	-
	PSO15	Topical steroid
	PSO16	-
	PSO17	Topical steroid
	PSO18	-
	PSO19	Steroid
	PSO20	Topical steroid
	PSO21	Topical steroid
	PSO22	-
	PSO23	Topical steroid
	PSO24	Topical steroid
Pustular	PSOP1	-
	PSOP2	-
	PSOP3	Topical steroid
	PSOP4	Topical steroid + retinoid
	PSOP5	-
	PSOP6	-
	PSOP7	-
	PSOP8	-
	PSOP9	-
	PSOP10	-
	PSOP11	-
	PSOP12	-
	PSOP13	-
	PSOP14	anti-TNF

SupplementaryTable 1 : Characteristics of psoriasis patients.
In red: patients whose hepcidin IHC are shown in figure 1a.

Psoriasis patients	Number	Mutational status
Pustular	PSOP15	*IL36RN*
	PSOP16	*No mutation in IL36RN, CARD14, AP1S3, MPO, SERPINA*
	PSOP17	*CARD14*
	PSOP18	*No mutation in IL36RN, CARD14, AP1S3, MPO, SERPINA*
	PSOP19	*AP1S3*
	PSOP20	*AP1S3*
	PSOP21	*CARD14*
	PSOP22	*No mutation in IL36RN, CARD14, AP1S3, MPO, SERPINA*
	PSOP23	*IL36RN*
	PSOP24	*No mutation in IL36RN, CARD14, AP1S3, MPO, SERPINA*
	PSOP25	*No mutation in IL36RN, CARD14, AP1S3, MPO, SERPINA*
	PSOP26	*CARD14*

Supplementary Table 2 : Characteristics of pustular psoriasis patients analyzed in figure 1c