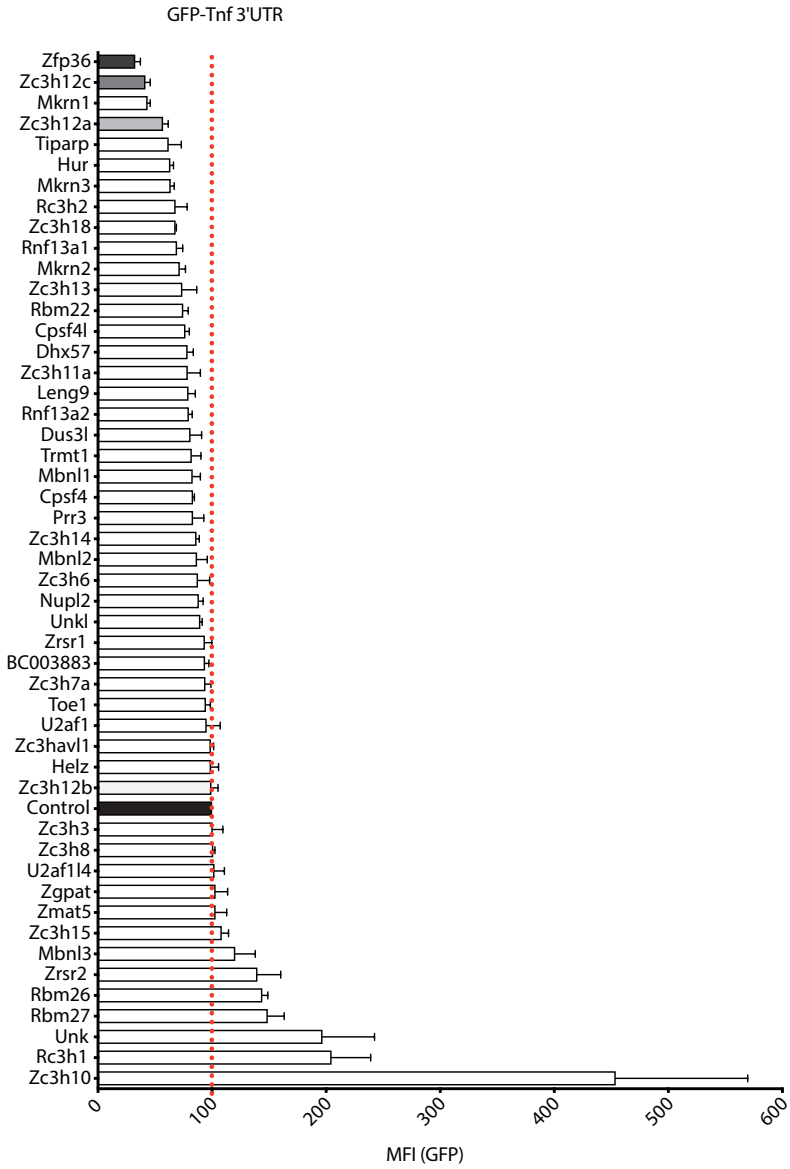
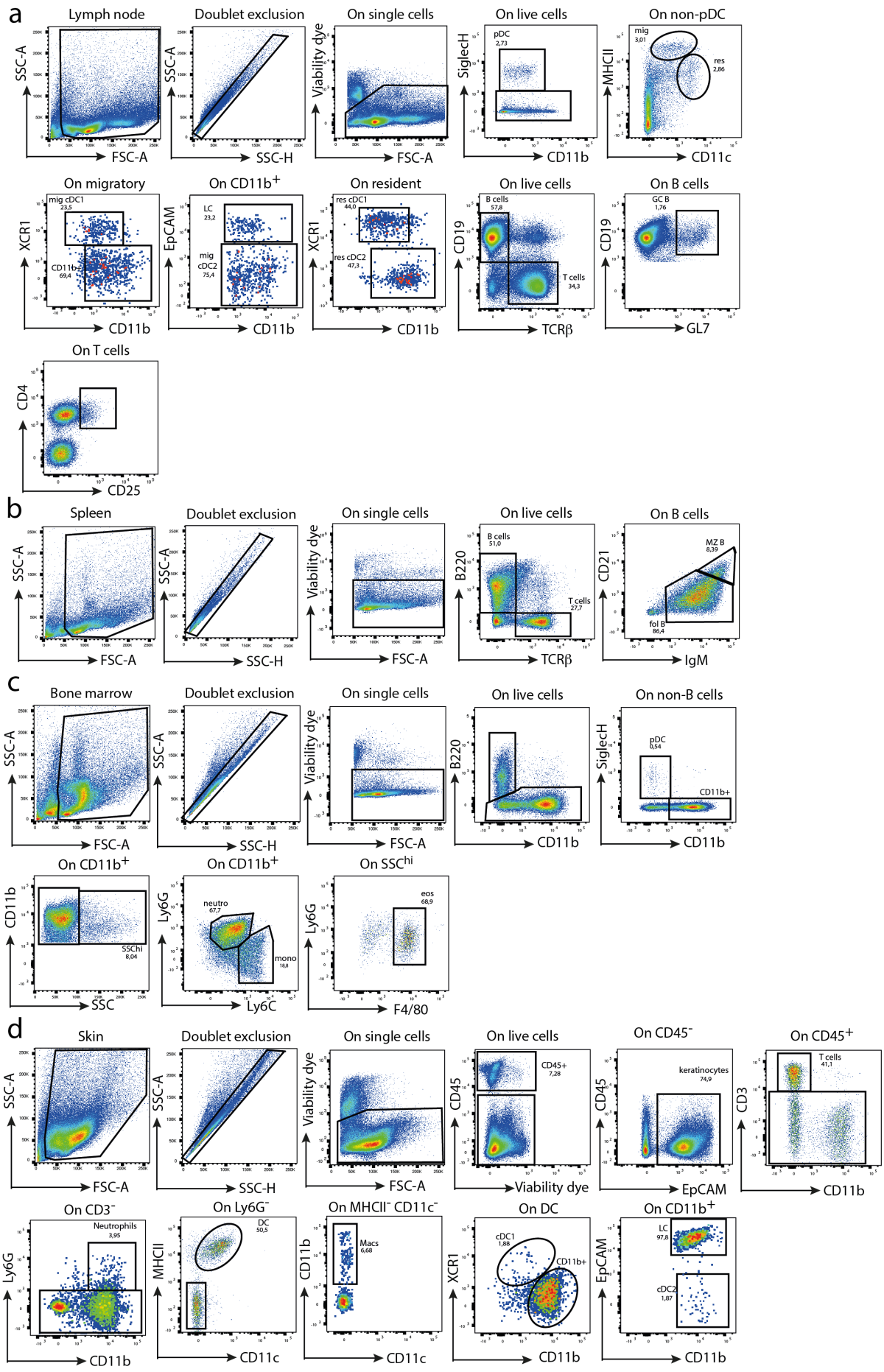
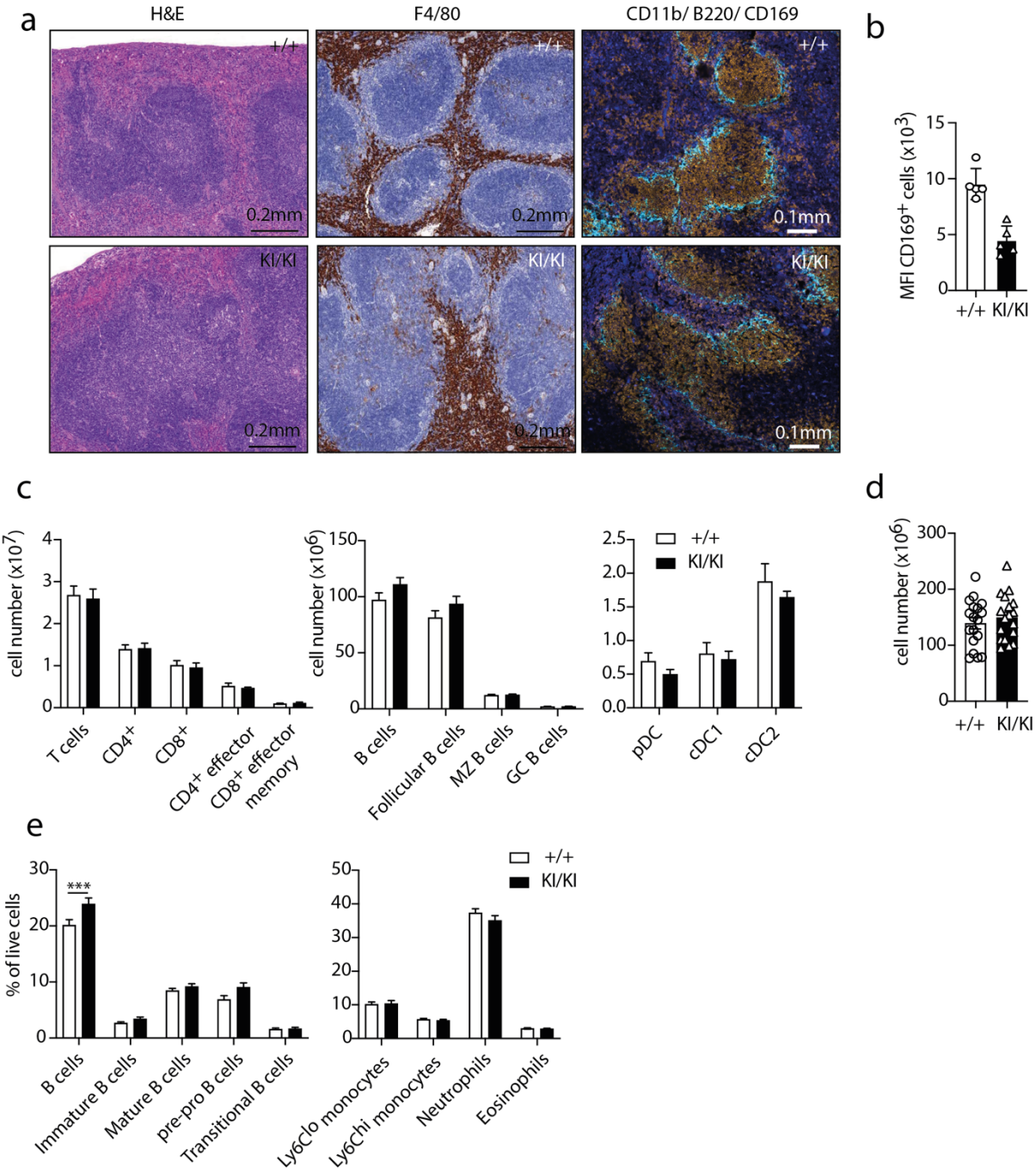

GFP-Tnf 3'UTR
Zfp36
Zc3h12c
Mkrn1
Zc3h12a
Tiparp
Hur
Mkrn3
Rc3h2
Zc3h18
Rnf13a1
Mkrn2
Zc3h13
Rbm22
Cpsf4l
Dhx57
Zc3h11a
Leng9
Rnf13a2
Dus3l
Trmt1
Mbnl1
Cpsf4
Prr3
Zc3h14
Mbnl2
Zc3h6
Nupl2
Unkl
Zrsr1
BC003883
Zc3h7a
Toe1
U2af1
Zc3havl1
Helz
Zc3h12b
Control
Zc3h3
Zc3h8
U2af1l4
Zgpat
Zmat5
Zc3h15
Mbnl3
Zrsr2
Rbm26
Rbm27
Unk
Rc3h1
Zc3h10
0
100
200
300
400
500
600
MFI (GFP)

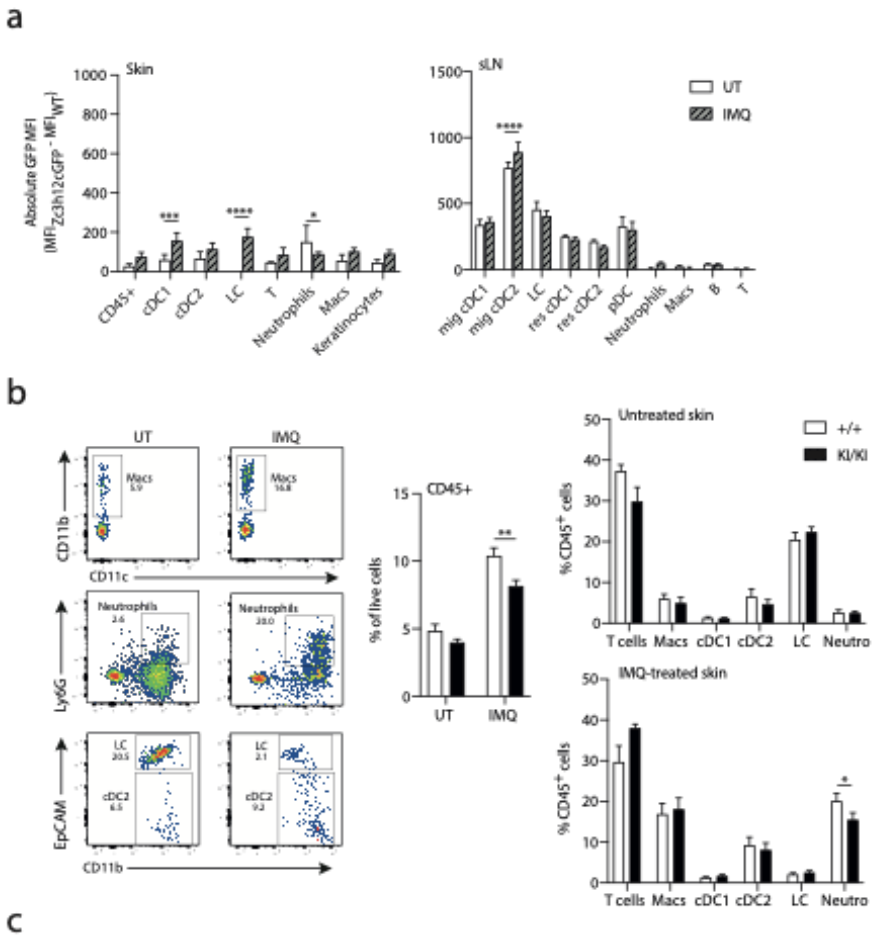
Supplementary figure 1: **Evaluation of the regulatory effect of CCCH-containing ZFPs on the expression of the GFP-*Tnf* 3' UTR reporter**. The regulatory effect of 50 CCCH-containing ZFPs on the expression of GFP-*Tnf* 3' UTR reporter was evaluated by cotransfection in HEK293T cells. The GFP mean fluorescence intensity (MFI) was measured in mCherry-positive cells by FACS and compared with GFP MFI obtained with the control vector (black bar). Results represent the mean ± SEM of at least three independent experiments.


a
Lymph node
SSC-A
FSC-A
Doublet exclusion
SSC-A
SSC-H
On single cells
Viability dye
FSC-A
On live cells
SiglecH
pDC
2,73
CD11b
On non-pDC
MHCII
mig
3,01
res
2,86
CD11c
On migratory
XCR1
mig cDC1
23,5
CD11b+
69,4
CD11b
On CD11b+
EpCAM
LC
23,2
mig
cDC2
75,4
CD11b
On resident
XCR1
res cDC1
44,0
res cDC2
47,3
CD11b
On live cells
CD19
B cells
57,8
T cells
34,3
TCRβ
On B cells
CD19
GC B
1,76
GL7
On T cells
CD4
CD25
b
Spleen
SSC-A
FSC-A
Doublet exclusion
SSC-A
SSC-H
On single cells
Viability dye
FSC-A
On live cells
B220
B cells
51,0
T cells
27,7
TCRβ
On B cells
CD21
MZ B
8,39
fol B
86,4
IgM
c
Bone marrow
SSC-A
FSC-A
Doublet exclusion
SSC-A
SSC-H
On single cells
Viability dye
FSC-A
On live cells
B220
CD11b
On non-B cells
SiglecH
pDC
0,54
CD11b+
CD11b
On CD11b+
CD11b
SSChi
8,04
SSC
On CD11b+
Ly6G
neutro
67,7
mono
16,8
Ly6C
On SSChi
Ly6G
eos
68,9
F4/80
d
Skin
SSC-A
FSC-A
Doublet exclusion
SSC-A
SSC-H
On single cells
Viability dye
FSC-A
On live cells
CD45
CD45+
7,28
Viability dye
On CD45-
CD45
keratinocytes
74,9
EpCAM
On CD45+
CD3
T cells
41,1
CD11b
On CD3-
Ly6G
Neutrophils
3,95
CD11b
On Ly6G-
MHCII
DC
50,5
CD11c
On MHCII- CD11c-
CD11b
Macs
6,68
CD11c
On DC
XCR1
cDC1
1,88
CD11b+
CD11b
On CD11b+
EpCAM
LC
97,8
cDC2
1,87
CD11b

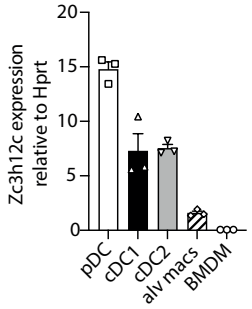
Supplementary figure 2 (related to Figure 3). **Gating strategies used to determine the different immune cell subsets in *Zc3h12c-GFP$^{KI/KI}$* mice**. (a) in the skin-draining lymph nodes, (b) in the spleen, (c) in the bone marrow and (d) in the skin. Cells were gated as indicated. Mig cDC1 ($CD45^+/CD19^-/CD3^-MHCII^{hi}/CD11c^{lo}/CD11b^-/XCR1^+$), mig cDC2 ($CD45^+/CD19^-/CD3^-MHCII^{hi}/CD11c^{lo}/CD11b^+/XCR1^-$), LC ($CD45^+/CD19^-/CD3^-MHCII^{hi}/CD11c^{lo}/CD11b^+/XCR1^-/EpCAM^+$), pDCs ($CD19^-/CD3^-/CD11b^-/SiglecH^+$), res cDC1 ($CD45^+/CD19^-/CD3^-MHCII^{lo}/CD11c^{hi}/CD11b^-/XCR1^+$), res cDC2 ($CD45^+/CD19^-/CD3^-MHCII^{lo}/CD11c^{hi}/CD11b^+/XCR1^-$), MC ($CD45^+/CD11b^-/Fc\varepsilon R1\alpha^+/c\text{-}kit^+$), T cells ($CD45^+/NK1.1^-/CD3^+$), Tregs ($CD45^+/NK1.1^-/CD3^+/CD4^+/CD25^+$), B cells ($B220^+$), macrophages ($CD19^-/CD3^-/MHCII^-/CD11c^-/CD11b^+$), neutrophils ($CD19^-/CD3^-/MHCII^-/CD11c^-/CD11b^+/Ly6G^+$), eosinophils ($B220^-/Ly6C^+/SSC^{hi}/F4\text{-}80^+$).


a
H&E
F4/80
CD11b/ B220/ CD169
+/+
KI/KI
0.2mm
0.1mm
b
MFI CD169+ cells (x10^3)
c
cell number (x10^7)
T cells
CD4+
CD8+
CD4+ effector
CD8+ effector
memory
cell number (x10^6)
B cells
Follicular B cells
MZ B cells
GC B cells
pDC
cDC1
cDC2
d
e
% of live cells
***
Immature B cells
Mature B cells
pre-pro B cells
Transitional B cells
Ly6Clo monocytes
Ly6Chi monocytes
Neutrophils
Eosinophils

Supplementary figure 3 (related to Figure 4): **Analysis of the spleen and bone marrow from *Zc3h12c-GFP$^{KI/KI}$* mice.** (a) Spleen sections from 200-day old *Zc3h12c-GFP$^{+/+}$* and *Zc3h12c-GFP$^{KI/KI}$* mice were subjected to routine H&E staining (left panel), and immunostaining with antibodies against F4/80 (middle panel). Frozen spleen sections were subjected to immunofluorescence staining for B cells (B220^{+}, in yellow), metallophilic macrophages (CD169^{+}, in cyan) and red-pulp macrophages (CD11b^{+}, in dark blue) (right panel). Representative results are shown. (b) The mean fluorescence intensity (MFI) of the CD169^{+} cells was measured using ImageJ. The image corresponding to the CD169 channel was used to determine the ring-like area of CD169^{+} cells for which the MFI was measured. The same process was performed on 5 distinct follicles in spleen of *Zc3h12c-GFP$^{+/+}$* and *Zc3h12c-GFP$^{KI/KI}$* mice. (c) Numbers of T cells, B cells and DCs in the spleen. (d) Total cell number in the spleen. (e) Numbers of B cells, monocytes, granulocytes and eosinophils. Results represent the mean ± SEM of 18 animals per genotype. Statistical analysis performed by *Two-way ANOVA*. ***: $P < 0.001$.


a
Skin
sLN
UT
IMQ
Absolute GFP MFI
(MFI Zc3h12cGFP+ - MFI WT)
CD45+
cDC1
cDC2
LC
T
Neutrophils
Macs
Keratinocytes
mig cDC1
mig cDC2
res cDC1
res cDC2
pDC
B
b
UT
IMQ
CD11b
CD11c
Macs
Neutrophils
Ly6G
EpCAM
LC
cDC2
% of live cells
Untreated skin
IMQ-treated skin
+/+
KI/KI
% CD45+ cells
T cells
Macs
cDC1
cDC2
LC
Neutro
c
sLN - untreated skin
sLN - IMQ treated skin
Neutro

Supplementary figure 4: ***Zc3h12c* induction in dermal cells and skin-draining lymph nodes following 5 to 6 days of topical imiquimod treatment.** Leukocytes from the skin and neighboring skin-draining lymph nodes from *Zc3h12c-GFP*$^{+/+}$ (wild-type) and *Zc3h12c-GFP*$^{KI/KI}$ mice were analyzed by flow cytometry to monitor the changes in GFP expression between the untreated (UT) and the imiquimod-treated (IMQ) states. Results represent mean ± SD of the difference between the mean of the *Zc3h12c-GFP*$^{+/+}$ group and the mean of the *Zc3h12c-GFP*$^{KI/KI}$ group (SD = $\sqrt{}$ (SEM WT^2) + (SEM KI^2)). (b) Flow cytometry analysis on untreated and IMQ-treated skin from *Zc3h12c-GFP*$^{+/+}$ mouse, showing the efficacy of the treatment in inducing inflammation and recruitment of neutrophils and macrophages and migration of LC and the proportion of indicated immune populations in the untreated and IMQ-treated skin and (c) in the skin-draining lymph nodes of *Zc3h12c-GFP*$^{+/+}$ and *Zc3h12c-GFP*$^{KI/KI}$ mice, determined by flow cytometry. Results represent the mean of 14 animals per genotype and are a combination of 3 independent experiments. Statistical analysis performed by *Two-way ANOVA*. *: $P \leq 0.05$; ****: $P < 0.0001$.


Zc3h12c expression
relative to Hprt
20
15
10
5
0
pDC
cDC1
cDC2
alv macs
BMDM

Supplementary figure 5: ***Zc3h12c*** **is poorly expressed in macrophages.** (B) RT-qPCR analysis on RNA extracted from sorted primary cells (splenic pDC, cDC1 and cDC2 and alveolar macrophages) and cultured macrophages (BMDM) and dendritic cells (BMDC and moDC) from wild-type mice. Data represent mean ± SEM of three mice.

Supplementary table 1: **Antibodies**

Antigen	**Clone**	**Fluorophore**	**Manufacturer**	**Dilution**
CD45	30-F11	PE	BioLegend	1/500
CD19	1D3/CD19	APC	BioLegend	1/400
CD3	17A2	Biotin	BioLegend	1/500
MHCII (IA/IE)	M5/114.15.2	PerCPCy5.5	ThermoFisher Scientific	1/400
CD11c	N418	APCCy7; PeCy7	BioLegend	1/100; 1/800
CD11b	M1/70	PacificBlue	BioLegend	1/500
XCR1	ZET	BV650	BioLegend	1/500
EpCAM	G8.8	PeCy7	BioLegend	1/500
F4/80	BM8	FITC	WEHI WAF	1/50
SiglecH	551	PE	BioLegend	1/500
SiglecF	S17007L	PE	BioLegend	1/500
FcεR1α	MAR-1	Biotin	BioLegend	1/200
c-kit	2B8	AF700	BioLegend	1/100
NK1.1	PK136	Biotin	BioLegend	1/700
Ly6C	HK1.4	BV605	BioLegend	1/500
Ly6G	1A8-Ly6g	BV711	BioLegend	1/400
B220	RA3-6B2	Biotin	Invitrogen	1/400
CD206	MR6F3	AF700	Invitrogen	1/100
CD64	X54-5/7.1.1	PE	BD Pharmigen	1/100
IFNγ	XMG1.2	PE	BioLegend	1/200
TNF	D2D4	N/A	CST	1/500
GL7	GL-7	Alexa488	Invitrogen	1/500
CD4	GK1.5	PerCPCy5.5	BioLegend	1/800
TCRαβ	H57-597	PeCy7	BioLegend	1/400
TCRγδ	GL3	FITC	BioLegend	1/400
IgM	RMM-1	APC	WEHI WAF	1/200
Streptavidin	N/A	A594	BioLegend	1/1500
CD21	7E9	APCCy7	BioLegend	1/200
Anti-rabbit	Ab150077	Alexa488	Abcam	1/1000