

**Fig. S1 siRNA-mediated knock-down of STAT1, STAT3, STAT4 in human effector memory CD4<sup>+</sup> T cells.** FACS-isolated effector memory CD4<sup>+</sup> T cells were co-stimulated with DLL4/Cyt (Cyt = IFN- $\alpha$ /IL-6/IL-21) and treated with siRNA against STAT1 (siSTAT1), STAT3 (siSTAT3), STAT4 (siSTAT4) and control siRNA (siCtrl). Relative expression of *STAT1*, *STAT3*, *STAT4* after siRNA treatment, normalized to siCtrl treatment (set to 1).

**Fig. S2 FACS isolation of human blood-derived CD4<sup>+</sup> Th cell subsets.** **a)** Representative flow cytometric staining of various CD4<sup>+</sup> Th cell subsets (Th1, Th2, Th17, Th1/17) according to their chemokine receptor expression <sup>47</sup>. **b)** Expression of IFN- $\gamma$ , IL-4 and IL-17 by FACS-isolated CD4<sup>+</sup> Th cell subsets. Cells were either stimulated with PMA/Ionomycin *ex vivo* and stained intracellularly for indicated effector cytokines (upper panel) or cultivated for 120h to measure cytokines in cell culture supernatants by ELISA. Each dot represents on healthy donor (n=5-14). Data are cumulative from up to four independent experiments.

**Fig. S3 Monocyte suppression assay.** MACS separated CD14<sup>+</sup> blood monocytes were activated with LPS in the presence or absence of cell culture supernatants (dilution 1:50) from memory CD4<sup>+</sup> T cells activated for 48h with CD3/CD28 alone (sup w/o) or plus DLL4/STAT3 (sup DLL4/Cyt). To the latter culture also anti-IL-10 receptor antibody was added. Relative *CD40* and *HLA-DR* expression after 6 hours of activation was analyzed via RT-PCR. Experiments with supernatants from three independent CD4<sup>+</sup> T cell cultures are shown.

**Fig. S4 siRNA-mediated knock-down of Blimp-1 and c-Maf in human effector memory CD4<sup>+</sup> Th cell subsets.** **a)** FACS-isolated Th1, Th2, Th17 and Th1/17 cells were co-stimulated with DLL4/Cyt (Cyt = IFN- $\alpha$ /IL-6/IL-21) and treated with siRNA against c-Maf (siMAF) or Blimp-1 (siPRDM1) and control siRNA (siCtrl). Relative expression of *MAF* and *PRDM1* after siMAF or siPRDM1 treatment, respectively, normalized to siCtrl treatment (set to 1). **b)** Expression of IFN- $\gamma$ , IL-4 and IL-17 by CD4<sup>+</sup> Th cell subsets as measured by ELISA in cell culture supernatants after treatment with siMAF or siPRDM1. **c)** Relative expression of *PRDM1* and *MAF* after siMAF or siPRDM1 treatment, respectively, normalized to siCtrl treatment (set to 1).

**Fig. S5 Expression of Notch and cytokine receptors by T cells from IBD patient and healthy controls.** Naïve and memory CD4 T cells from CD, UC and healthy controls (each n= 7-10) were FACS-sorted and activated for 48 hours with CD3/CD28. Relative expression of Notch-1-4, and cytokine receptors for type I IFN, IL-6 and IL-21 were analyzed via RT-PCR.

**Tab. S1 Patient characteristics**

Patient	Underlying disease	Age	Sex	Harvey-Bradshaw-Index	Mayo Score	C-Reactive protein (mg/L)	Medication	Disease duration (year)
1	Ulcerative colitis	40	m		3	<1	Infliximab	20
2	Ulcerative colitis	27	m		1	<1	Prednisolon, Budesonid	7
3	Crohn's disease	40	w	5			Budesonid	10
4	Ulcerative colitis	22	m		1	<1	Thiopurine	5
5	Ulcerative colitis	24	m		0	<1	Vedolizumab	3
6	Crohn's disease	45	m	3		14,6	Thiopurine, Infliximab	21
7	Ulcerative colitis	44	m		5	1,2	Vedolizumab	6
8	Crohn's disease	64	w	0		<1,0	Thiopurine, Infliximab	16
9	Crohn's disease	56	w	1		1,2	Infliximab	n.a.
10	Crohn's disease	30	w	10		<1,0	Thiopurine, Infliximab	12
11	Ulcerative colitis	35	w		0	4,3	Infliximab	8
12	Crohn's disease	32	w	0		<1,0	Infliximab	13
13	Crohn's disease	50	w	3		3,9	Infliximab	1
14	Crohn's disease	53	w	3		19,3	Infliximab	13
15	Crohn's disease	55	w	15		2,6	Infliximab	16
16	Ulcerative colitis	35	w		0	1,1	Infliximab	1
17	Crohn's disease	49	m	1		6,5	none	1
18	Ulcerative colitis	41	w		2	<1	Infliximab	11
19	Crohn's disease	66	w	2		<1	Adalimumab	30
20	Ulcerative colitis	42	m		0	<1	5-aminosalicylic acid, E.coli Nissle	n.a.

**Tab. S2 TaqMan® Gene Expression Assays**

<b>Gen</b>	<b>Assay#</b>
<i>AHR</i>	Hs00907314_m1
<i>BACH2</i>	Hs00222364_m1
<i>BATF</i>	Hs00232390_m1
<i>EGR2</i>	Hs00166165_m1
<i>GAPDH</i>	Hs99999905_m1
<i>GATA3</i>	Hs00231122_m1
<i>IKFZ3</i>	Hs04329617_m1
<i>IL10</i>	Hs00961622_m1
<i>IRF4</i>	Hs00180031_m1
<i>MAF</i>	Hs04185012_s1
<i>NFIL3</i>	Hs00705412_s1
<i>PRDM1</i>	Hs00153357_m1

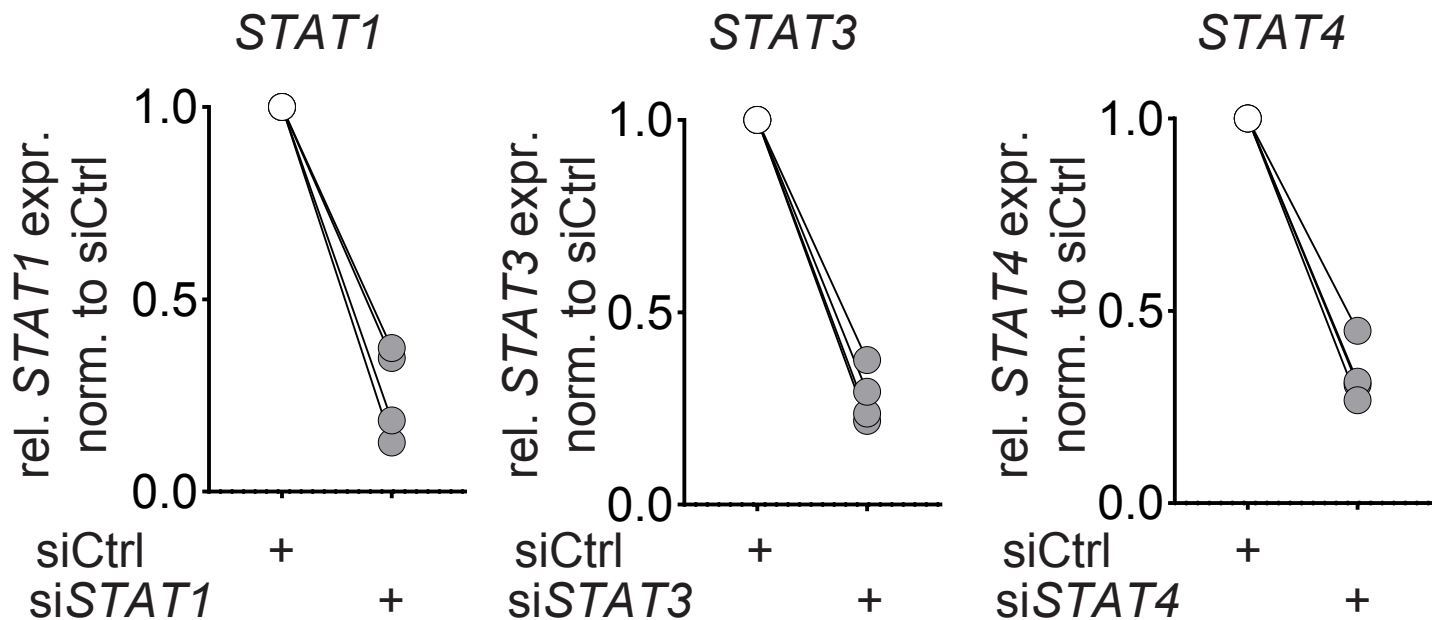
**Tab. S3 siRNA sequences**

<b>siRNA</b>	<b>sequence</b>	
siCtrl	sense	5' A AUU CUC CGA ACG UGU CAC GTT T 3'
	antisense	3' T TAA GAG GCU UGC ACA GUG CA 5'
siMAF	sense	5' A AAC GGC UCG AGC AGC GAC AAC C 3'
	antisense	3' T TUG CCG AGC UCG UCG CUG UT 5'
siPRDM1	sense	5' G ACG GCU UUA AUG AAG AGA AAA G 3'
	antisense	3' C TGC CGA AAU UAC UUC UCU UT 5'
siSTAT1	sense	5' ACA GAA AGA GCU UGA CAG TAA AG 3'
	antisense	3' UAU CUU UCU CGA ACU GUC AUT 5'
siSTAT3	sense	5' GCG GAG AAG CAU CGU GAG TGA GC 3'
	antisense	3' CGC CUC UUC GUA GCA CUC ACT 5'
siSTAT4	sense	5' AAA GAC AAA GCC UUC GGT AAA CA 3'
	antisense	3' TTU CUG UUU CGG AAG CCA UUT 5'

**Tab. S4 Real-Time PCR Primers**

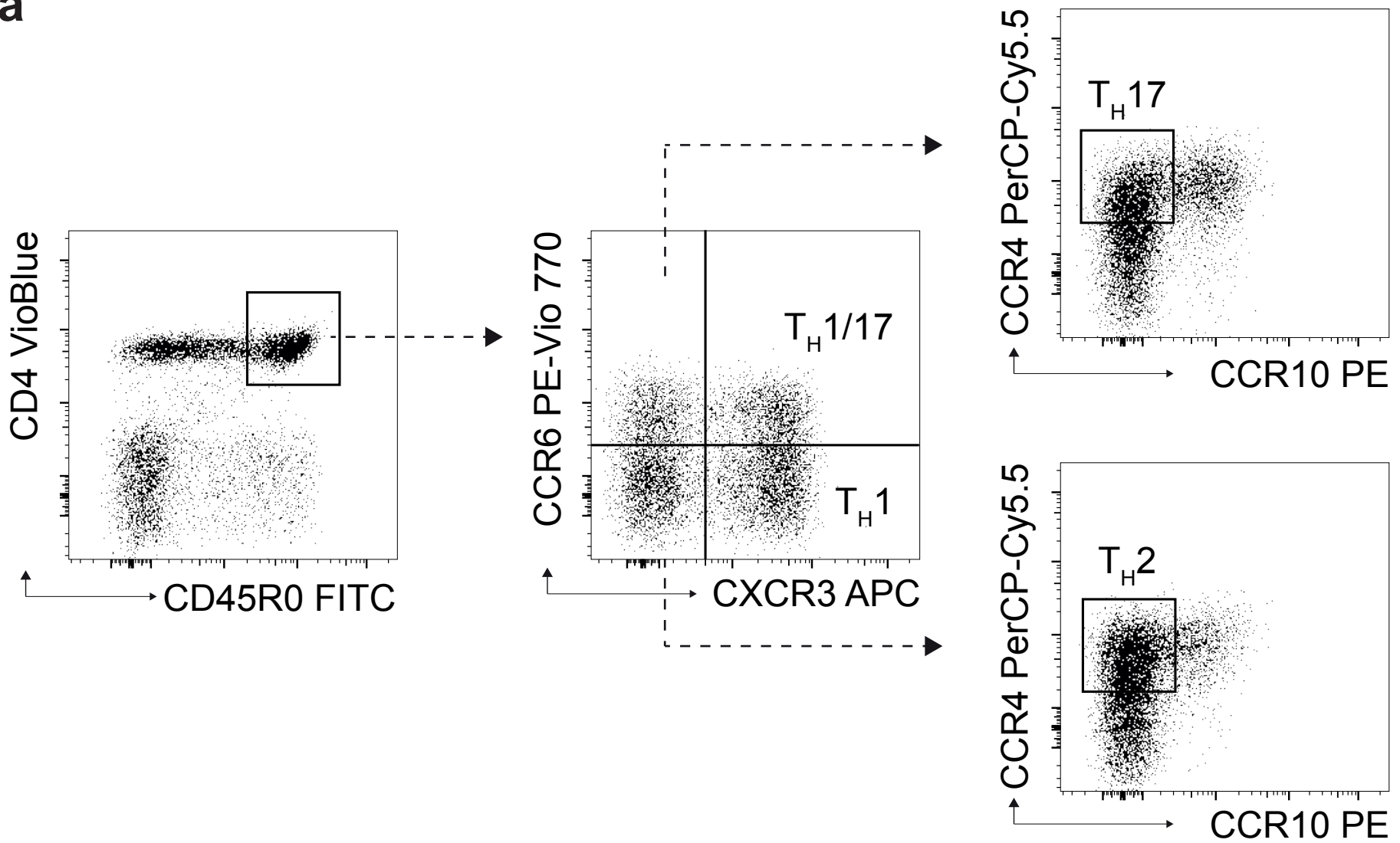
<b>target</b>	<b>sequence</b>	
<i>ACTB</i>	Forward 5'-3'	GAG CAC AGA GCC TCG CCT TT
	Reverse 5'-3'	TCA TCA TCC ATG GTG AGC TGG
<i>IFNAR</i>	Forward 5'-3'	AAA GCC AGA GCA CAC ACC AT
	Reverse 5'-3'	TGA CAA ACG GGA GAG CAA AT
<i>IL6R</i>	Forward 5'-3'	CTC AGT GTC ACC TGG CAA GAC
	Reverse 5'-3'	TCC TTG ACC ATC CAT GTT GTG
<i>IL21R</i>	Forward 5'-3'	GGG CTC TGT GAT GTA GGC AG
	Reverse 5'-3'	CCGT CTG GAG GTA ATC GGT G
<i>NOTCH1</i>	Forward 5'-3'	GGT GAA CTG CTC TGA GGA GAT C
	Reverse 5'-3'	GGA TTG CAG TCG TCC ACG TTG A
<i>NOTCH2</i>	Forward 5'-3'	GTG CCT ATG TCC ATC TGG ATG G
	Reverse 5'-3'	AGA CAC CTG AGT GCT GGC ACA A
<i>NOTCH3</i>	Forward 5'-3'	TAC TGG TAG CCA CTG TGA GCA G
	Reverse 5'-3'	CAG TTA TCA CCA TTG TAG CCA GG
<i>NOTCH4</i>	Forward 5'-3'	TTC CAC TGT CCT CCT GCC AGA A
	Reverse 5'-3'	TGG CAC AGG CTG CCT TGG AAT C
<i>PRDM1</i>	Forward 5'-3'	AGA GGT TAT TGG AGT GAT GAG
	Reverse 5'-3'	GTT CTT AGG AAC TGT GTC ATT G
<i>MAF</i>	Forward 5'-3'	AAG TCG ACC ACC TCA AGC AG
	Reverse 5'-3'	AAT GTG GCG TAT CCC ACT GA
<i>CD40</i>	Forward 5'-3'	GCA GGC ACA AAC AAG ACT GA
	Reverse 5'-3'	ATA AAG ACC AGC ACC AAG AGG
<i>HLA-DR</i>	Forward 5'-3'	CAA CAG AGC GCC CAA GAA GA
	Reverse 5'-3'	CTC GCC TGA TTG GTC AGG ATT

# Supplement Fig. 1 Ahlers et al.

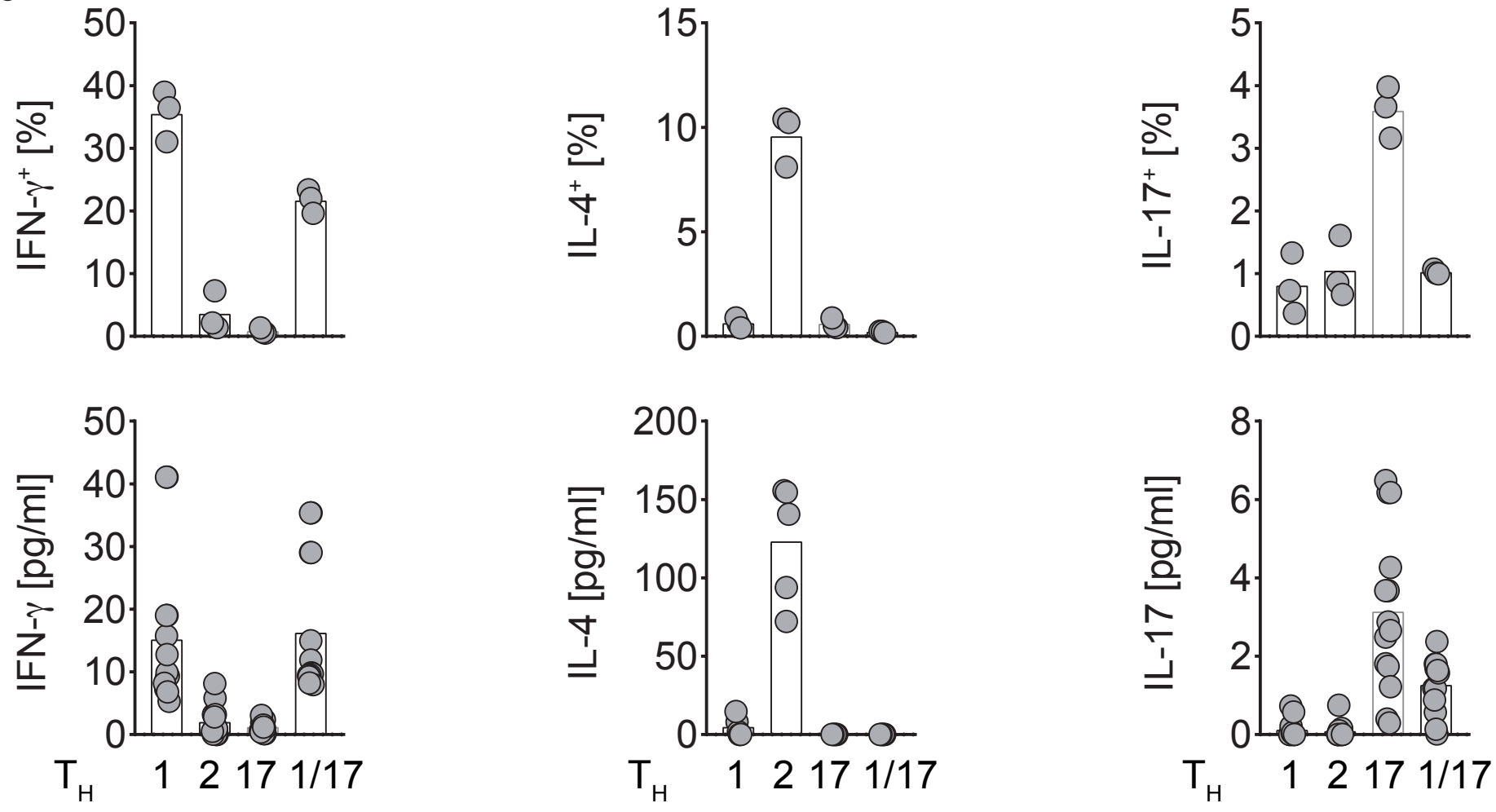


# Supplement Fig. 2 Ahlers et al.

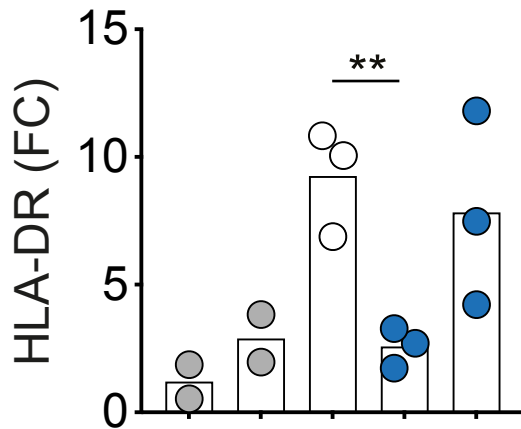
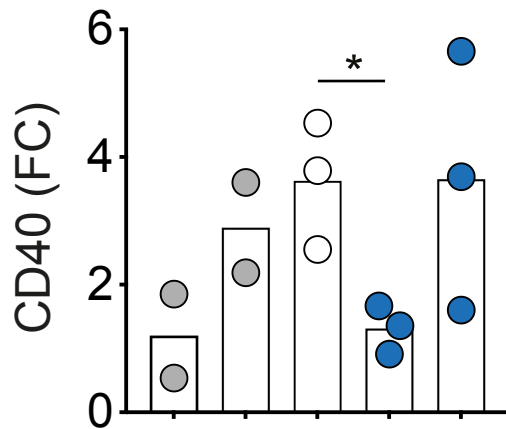
**a**



**b**



# Supplement Fig. 3 Ahlers et al.



LPS - + + + +

Sup w/o - - + - -

Sup DLL4/Cyt - - - + +

anti-IL-10R - - - - +

- + + + +

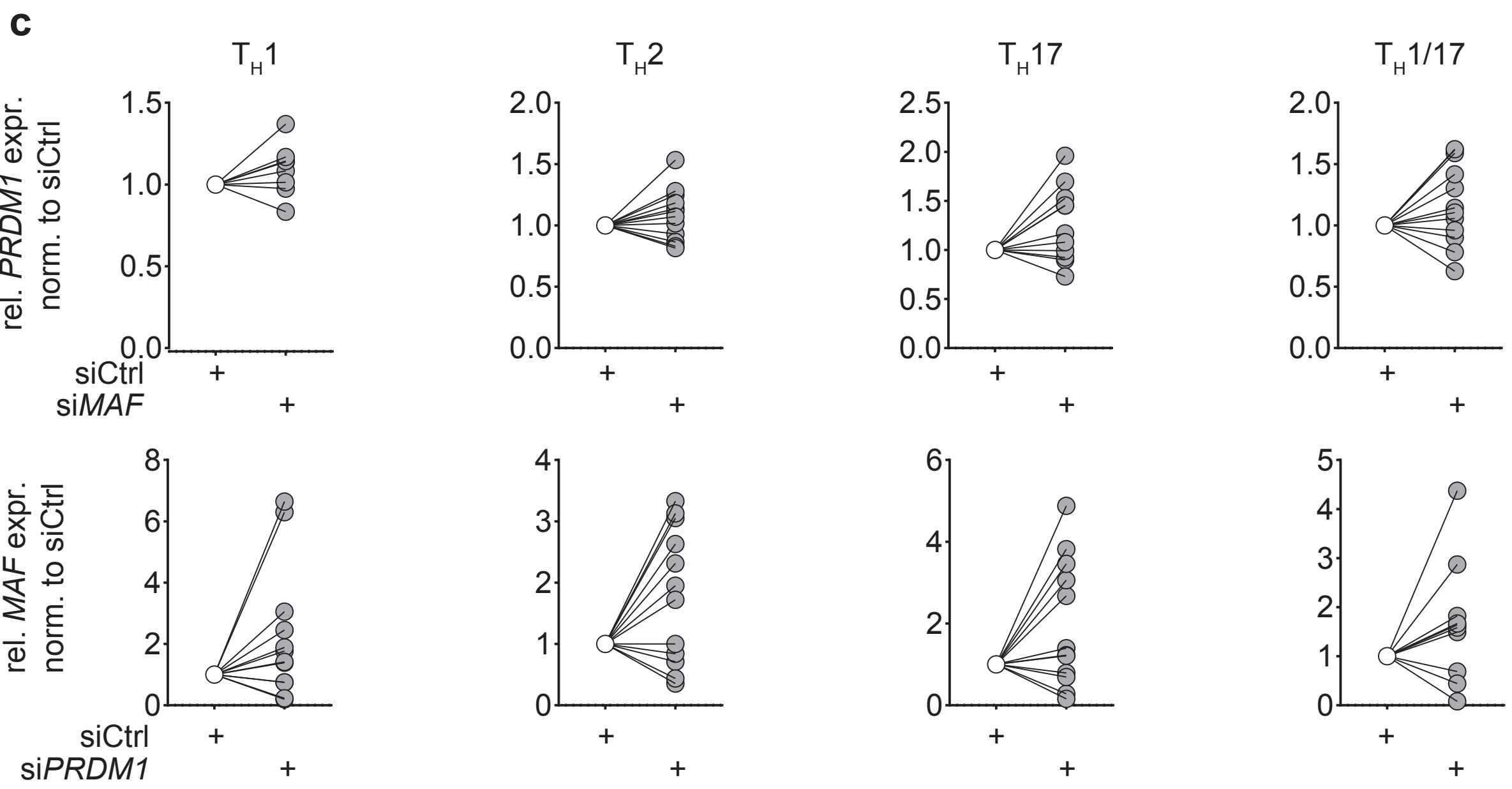
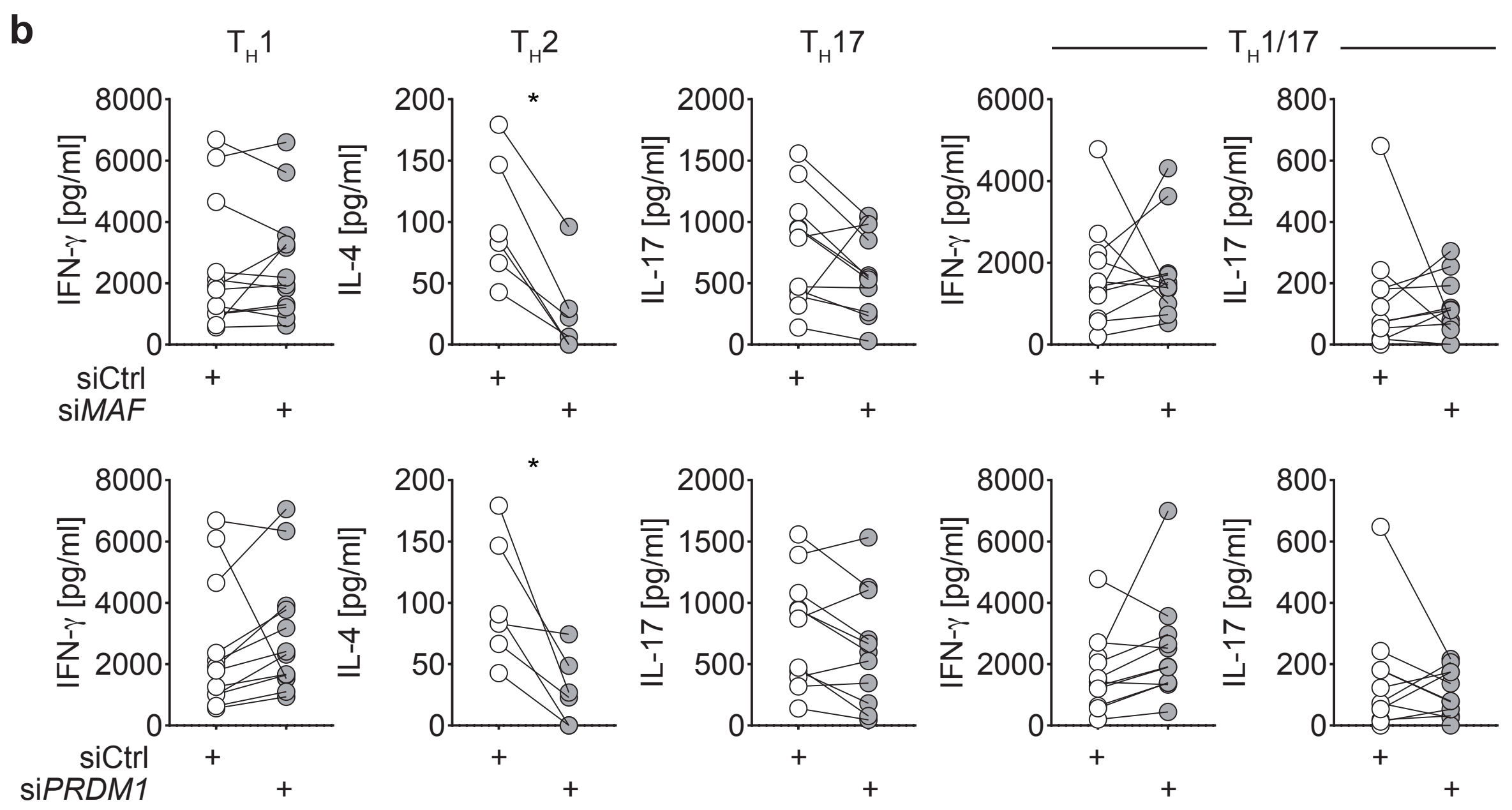
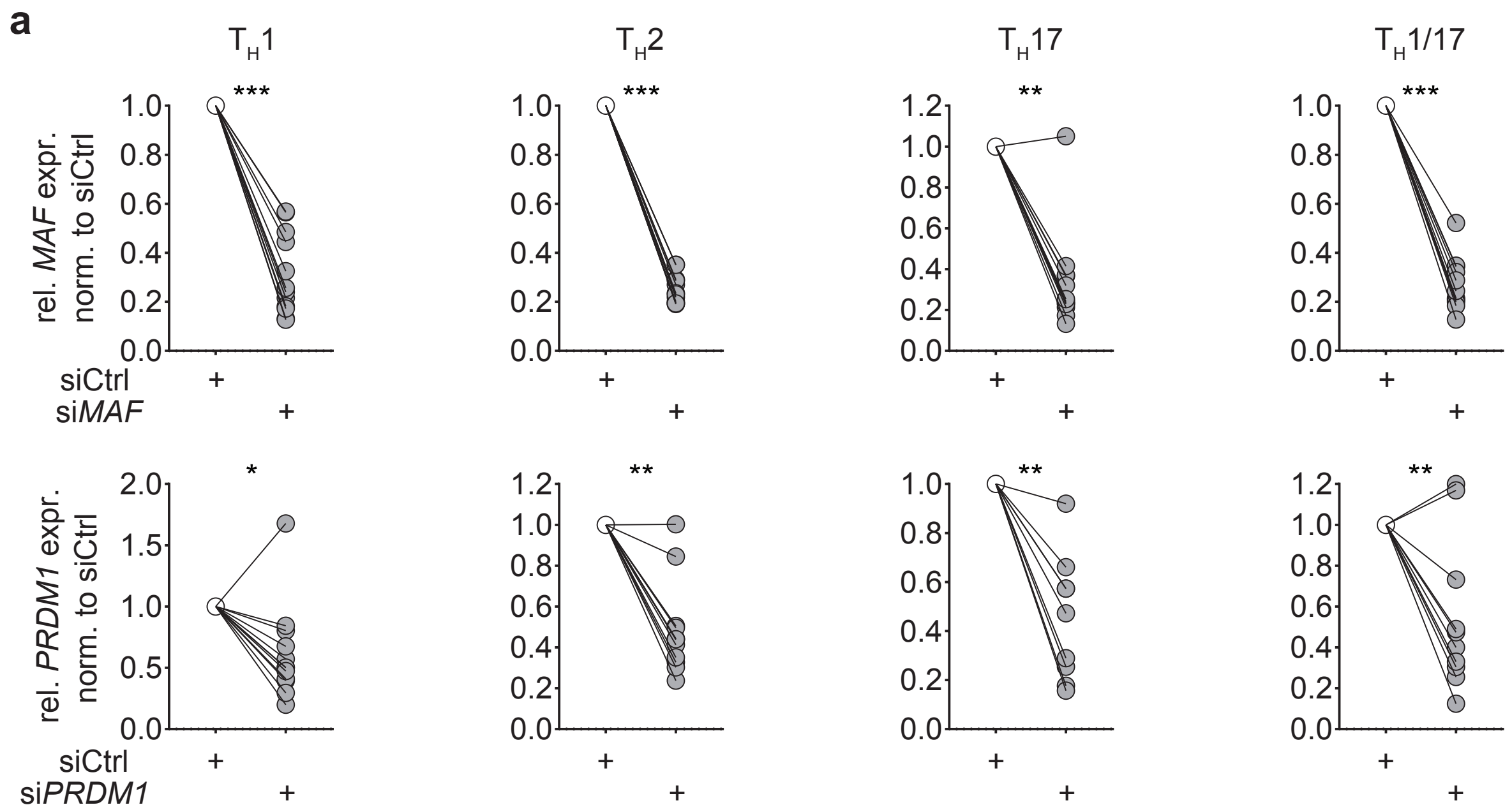
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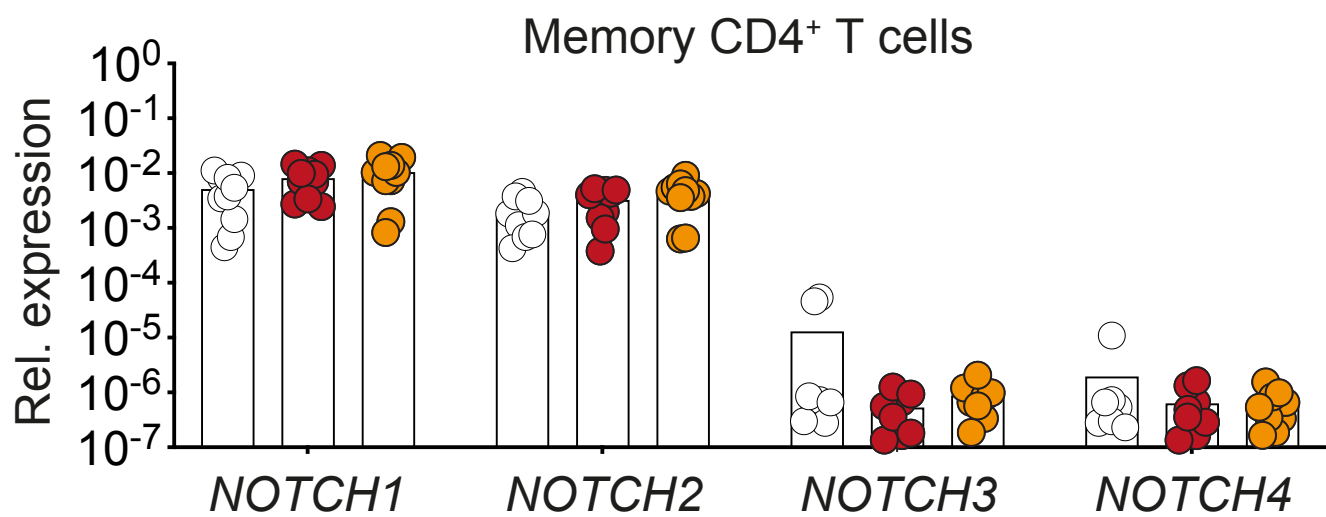
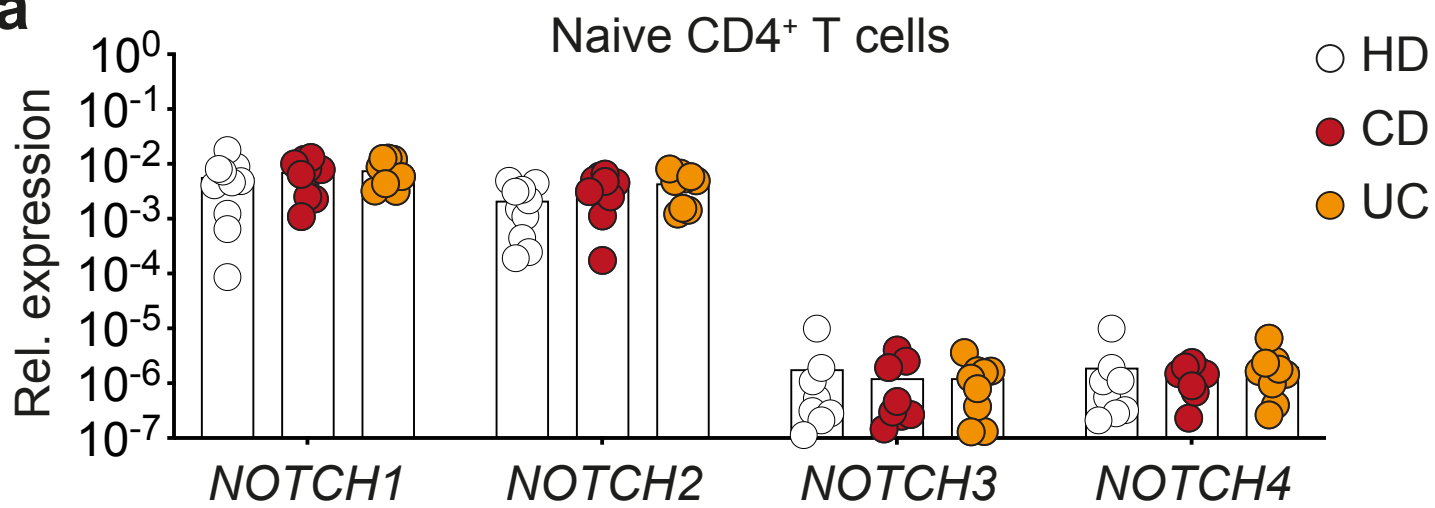


# Supplement Fig. 4 Ahlers et al.



# Supplement Fig. 5 Ahlers et al.

**a**



**b**

