

Supplementary Table 1. Differential expression (DE) of 106 TR1/TFH/Treg-relevant genes in the various T-cell pools studied here (bulk RNAseq)

Gene type	Genes (protein)	Described in TR1 (ref)	Described in other Treg types (ref)	Described in TFH (ref)	DE in Tet+ (vs. Tet-)	Expressed in Tet+ (norm. counts)	DE in TFH+ (vs. Tconv)	DE in Tet+ (vs. Tconv)	DE in Tet+ (vs. TFH)	DE in Tet+ (vs. Tet- /CXCR5+/PD-1+) BASAL
Cell adhesion molecules	Cd226	+ (1)	ND	ND	+	65.23	--	++	+++	+
	Itga2 (CD49b)	+ (1)	ND	ND	--	1.38	---	NS	++	---
	Itgae (CD103)	+ (2)	+ (3)	ND	-	6.21	NS	+++	+++	NS
	Ocln	ND	ND	ND	+++	3.13	NS	+++	+++	+++
	S1pr2	ND	ND	+ (4)	+++	100.76	+++	+++	-	+
	Sell (CD62L)	- (5)	+ (6)	- (7)	---	101.52	---	---	+++	NS
	Selpig (Psg1)	ND	ND	- (8)	--	184.73	---	--	+++	NS
Chemokine receptors	Ccr5	+ (9)	+ (10)	+ (11)	+++	47.50	+++	+++	+++	++
	Ccr7	ND	+ (12)	- (13)	--	174.10	---	--	+++	NS
	Cxcr3	+ (14)	+ (12)	In some subsets (15)	++	153.84	+++	+++	+++	NS
	Cxcr4	ND	ND	+ (16)	NS	188.11	+++	++	NS	NS
	Cxcr5	ND	ND	+ (17)	+++	380.73	+++	+++	--	NS
Co-stimulatory molecules	Cd28	+ (18)	ND	+ (19)	++	627.72	++	++	+	NS
	Cd40lg	ND	ND	+ (20)	+	182.86	++	++	+	NS
	Icos	+ (21)	+ (22)	+ (23)	++	337.09	+++	+++	-	NS
	Klrk1 (NKG2D)	ND	+ (24)	ND	---	0.24	NS	NS	NS	NS
	Sh2d1a (SAP)	ND	ND	+ (25)	+	78.17	+++	++	--	-
	Tnfrsf4 (Ox40)	+ (26)	+ (27)	+ (28)	++	150.36	+++	+++	++	+
	Tnfrsf18 (GITR)	+ (18)	+ (29)	ND	+	128.13	+	++	+	NS
Tnfsf4 (Ox40L)	ND	ND	ND	++	1.93	+++	+++	+++	NS	
Co-inhibitory molecules	Ctla4	+ (30)	+ (31)	+ (32)	+++	663.75	+++	+++	++	++
	Fasl	ND	+ (33)	ND	--	4.58	--	NS	++	NS
	Havcr2 (TIM-3)	+ (34)	+ (35)	+ (36)	+++	7.95	NS	+++	+++	+++
	Lag3	+ (1)	+ (37)	ND	+++	347.33	+++	+++	+++	+++
	Pdcd1 (PD-1)	+ (9)	+ (38)	+ (17)	+++	383.95	+++	+++	--	NS
	Tigit	+ (39)	+ (40)	+ (41)	+++	190.61	+++	+++	NS	NS
Cytokines	Ebi3 (IL27b)	ND	+ (42)	ND	+++	7.41	+++	+++	+	NS
	Ifng	+ (43)	ND	ND	+++	71.48	+++	+++	+++	NS
	Il10	+ (44)	+ (45)	+ (46)	+++	94.78	+++	+++	+++	+++
	Il21	+ (47)	ND	+ (48)	+++	526.65	+++	+++	NS	++
	Il4	- (44)	ND	+ (49)	+++	13.22	+++	+++	-	NS
	Il5	+ (44)	ND	ND	NS	0.01	NS	NS	NS	NS
	Mucb (Areg)	+	+ (50)	ND	NS	0.15	NS	NS	NS	NS
Cytokine receptors	Tgfb1	+ (44)	+ (45)	ND	NS	114.49	NS	NS	NS	NS
	Il10ra	+ (51)	+ (52)	ND	++	128.32	NS	++	++	NS
	Il12rb2	ND	+ (53)	ND	-	1.44	+++	+++	--	NS
	Il21r	+ (47)	+ (54)	+ (48)	-	179.90	-	-	-	NS
	Il27ra	+ (55)	+ (56)	+ (57)	+	339.18	-	NS	+	NS
	IL7r (CD127)	- (21)	- (58)	- (59)	---	72.10	---	---	+++	NS
	IL17rc	ND	ND	ND	NS	0.03	NS	NS	NS	NS
	Il2ra (CD25)	- (18)	+ (60)	- (61)	--	29.27	--	NS	+++	NS
Tgfbbr1	- (51)	+ (62)	ND	NS	42.88	+	NS	-	NS	
Other	Tgfbbr2	- (51)	+ (63)	ND	-	384.31	-	-	NS	NS
	Tgfbbr3	- (51)	ND	ND	-	100.03	--	-	++	NS
	Atf6	- (51)	ND	ND	++	32.87	+++	+++	NS	+
	Ahr	+ (64)	ND	ND	+++	35.42	NS	+++	+++	+++
	Ajuba	ND	ND	ND	+++	1.89	NS	+++	+++	+++
	Ascl2	ND	ND	+ (65)	+++	35.56	+++	+++	-	NS
	Bach2	- (66)	+ (67)	- (68)	---	24.69	---	---	++	NS
	Batf	+ (69)	ND	+ (70)	+	61.67	+++	++	-	NS
	Bcl6	ND	ND	+ (71)	+++	238.34	+++	+++	--	NS
	Bhlhe40	+ (51)	ND	ND	++	202.27	+++	+++	++	+
Bmyc	- (51)	ND	ND	-	11.15	-	NS	NS	NS	
Cbfa2t3	ND	ND	ND	+++	25.96	+++	+++	-	NS	

Transcription factors	Cebpa	ND	ND	+(72)	+++	91.15	+++	+++	--	NS
	Dbp	-(51)	ND	ND	NS	16.29	NS	NS	NS	NS
	E2f1	+(51)	+(73)	ND	NS	3.92	NS	NS	NS	NS
	Egr2	+(74)	ND	ND	++	61.63	+++	+++	-	NS
	Elk4	-(51)	ND	ND	NS	172.79	NS	NS	-	NS
	Eomes	+(75)	+(76)	ND	NS	12.71	+	+++	++	--
	FoxP1	ND	ND	-(77)	-	174.93	--	-	+	NS
	FoxP3	ND	+(78)	ND	---	30.31	++	NS	--	--
	Grhl1	ND	ND	ND	+++	38.45	+++	+++	NS	NS
	Hmgb2	+(51)	ND	ND	+	38.12	++	++	NS	NS
	Id2	+(51)	+(79)	-(80)	+	180.43	-	++	++	+
	Id3	-(51)	+(79)	+(80)	+	37.87	+++	++	-	NS
	Irf1	+(69)	ND	ND	-	282.24	-	NS	+	NS
	Irf4	+(81)	+(3)	+(82)	+++	186.65	+++	+++	++	++
	Jdp2	ND	ND	ND	+++	11.36	+++	+++	--	NS
	Klf2	ND	ND	-(83)	--	116.99	---	--	+++	NS
	Lef1	ND	ND	+(84)	---	69.23	---	---	NS	--
	Lilrb4a	ND	+(85)	ND	#N/A	3.77	+++	+++	NS	NS
	Maf	+(47)	ND	+(86)	+++	642.44	+++	+++	-	NS
	Myb	-(51)	+(87)	ND	+	28.09	+++	++	NS	NS
	Mybl2	+(51)	ND	ND	NS	2.92	++	NS	--	NS
	Myc	-(51)	-(88)	ND	---	19.34	---	---	NS	NS
	Nfia	ND	ND	ND	+++	22.14	+++	+++	--	NS
	Nfil3	+(34)	ND	ND	+++	62.68	+++	+++	++	+
	Nr1h3 (LXRα)	+(51)	+(89)	ND	NS	1.16	++	NS	-	NS
	Pax5	ND	ND	ND	+++	8.94	+++	+++	--	NS
	Pax9	ND	ND	ND	+++	3.38	+++	+++	++	+++
	Pou2af1 (OcaB)	ND	ND	ND	+++	145.84	+++	+++	-	NS
	Prdm1 (Blimp-1)	+(90)	ND	+(91)	+++	100.20	NS	+++	+++	++
	Rbpj	+(51)	+(92)	ND	+	73.40	+	++	+	+
	Runx2	+(51)	ND	ND	++	43.71	+++	+++	++	NS
	Rora	+(51)	ND	-(93)	-	26.65	+++	+++	--	--
S1pr1	ND	ND	-(83)	--	141.34	---	--	++	--	
Six5	ND	ND	ND	+++	14.88	+++	+++	NS	NS	
Sox4	-(51)	-(94)	ND	---	1.07	NS	--	NS	---	
Sox8	ND	ND	ND	+++	1.29	+++	+++	--	NS	
Stat1	+(95)	ND	+(96)	NS	617.27	NS	NS	NS	NS	
Stat3	+(97)	ND	+(23)	+	345.04	+	+	NS	NS	
Stat4	ND	-(98)	+(99)	+	142.56	++	++	-	NS	
Tbx21 (T-bet)	+(75)	ND	-(84)	++	24.69	+++	+++	++	++	
Tcf7	ND	ND	+(84)	NS	1519.30	NS	NS	NS	NS	
Tox2	ND	ND	+(80)	+++	206.07	+++	+++	--	NS	
Vdr	ND	+(100)	ND	+++	65.44	+++	+++	NS	+++	
Zbtb16 (PLZF)	+(51)	ND	ND	---	0.18	NS	NS	NS	NS	
Secretion proteins	Chgb	ND	ND	+(101)	NS	0.15	NS	NS	NS	NS
	Gzmb (Granzyme B)	+(102)	+(103)	ND	++	11.54	NS	+++	+++	+++
Enzymes	Cblb	ND	+(104)	ND	NS	169.82	-	+	+	NS
	Entpd1 (CD39)	+(105)	+(106)	ND	+++	47.39	+++	+++	+++	++
	Itk	+(107)	+(108)	ND	NS	481.13	+	-	-	NS
	Nt5e (CD73)	+(105)	+(106)	+(109)	+++	268.63	+++	+++	NS	NS
	Serpinc6b	+(51)	+(110)	ND	+	19.23	++	++	NS	NS
Serpinc9	+(51)	ND	ND	+	23.74	NS	+	NS	NS	

+++ **FC>4**
 ++ **4>FC>2**
 + **2>FC>1**
 NS **1>FC>1**
 - **-1>FC>2**
 -- **-2>FC>4**
 --- **FC<-4**

Same results vs both KLH-induced TFH and Tet-/CXCR5+/PD-1+ cells from pMHCII-NP-treated mice
 Different results vs both KLH-induced TFH and Tet-/CXCR5+/PD-1+ cells from pMHCII-NP-treated mice
Text in red Normalized counts below expression cut-off

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Supplementary Table 2. Differential expression (DE) of 106 TR1/TFH/Treg-relevant genes in BDC2.5mi/IAg7 and FlA462/IAb Tet+ vs. Tconv cells (bulk RNAseq)

Gene type	Genes (protein)	DE in BDC2.5mi/IAg7 Tet+ (vs. Tet-)	Expressed in BDC2.5mi/IAg7 Tet+ (normalized counts)	DE in FLA462/IAb Tet+ (vs. Tet-)	Expressed in FLA462/IAb Tet+ (normalized counts)
Cell adhesion molecules	Cd226	+	65.23	+	45.99
	Itgae2 (CD49b)	--	1.38	NS	0.54
	Itgae (CD103)	-	6.21	--	2.25
	Ocln	++	3.13	NS	1.79
	S1pr2	++	100.76	++	61.50
	Sell (CD62L)	--	101.52	--	81.91
	Selp1g (Psgl1)	--	184.73	--	139.53
Chemokine receptors	Ccr5	++	47.50	NS	16.18
	Ccr7	--	174.10	--	1096.60
	Cxcr3	++	153.84	NS	83.47
	Cxcr4	NS	188.11	++	264.57
	Cxcr5	++	380.73	++	225.33
Co-stimulatory molecules	Cd28	++	627.72	NS	1127.26
	Cd40lg	+	182.86	+	412.86
	Icos	++	337.09	NS	593.69
	Klrk1 (NKG2D)	--	0.24	NS	0.22
	Sh2d1a (SAP)	+	78.17	++	131.28
	Tnfrsf4 (Ox40)	++	150.36	NS	329.34
	Tnfrsf18 (GITR)	+	128.13	NS	135.06
Tnfrsf4 (Ox40L)	++	1.93	++	6.89	
Co-inhibitory molecules	Ctla4	++	663.75	++	418.96
	Fasl	--	4.58	NS	37.41
	Havcr2 (TIM-3)	++	7.95	NS	1.05
	Lag3	++	347.33	++	56.39
	Pdcd1 (PD-1)	++	383.95	++	508.50
	Tigit	++	190.61	++	104.86
Cytokines	Ebi3 (IL27b)	++	7.41	++	13.92
	Ifng	++	71.48	++	68.87
	Il10	++	94.78	++	45.89
	Il21	++	526.65	++	238.83
	Il4	++	13.22	++	27.38
	Il5	NS	0.01	#N/A	#N/A
	Mcub (Areg)	NS	0.15	NS	15.43
Tgfb1	NS	114.49	NS	172.54	
Cytokine receptors	Il10ra	++	128.32	NS	31.50
	Il12rb2	-	1.44	--	1.38
	Il21r	-	179.90	--	297.94
	Il27ra	+	339.18	NS	342.57
	IL7r (CD127)	--	72.10	--	49.43
	IL17rc	NS	0.03	NS	0.22
	Il2ra (CD25)	--	29.27	--	6.04
	Tgfb1	NS	42.88	NS	26.98
Tgfb2	-	384.31	NS	444.77	
Tgfb3	-	100.03	-	45.09	
	Atf6	++	32.87	NS	29.05
	Ahr	++	35.42	NS	31.11
	Ajuba	++	1.89	NS	0.70
	Ascl2	++	35.56	++	41.10
	Batf	+	61.67	+	117.71
	Bcl6	++	238.34	NS	191.12
	Bhlhe40	++	202.27	++	1297.01
	Bmyc	-	11.15	NS	30.32
	Cbfa2t3	++	25.96	++	14.53
	Cebpa	++	91.15	++	50.92

Transcription factors	Dbp	NS	16.29	NS	8.41
	E2f1	NS	3.92	NS	5.82
	Egr2	++	61.63	NS	96.53
	Elk4	NS	172.79	NS	92.34
	Eomes	NS	12.71	--	5.19
	FoxP1	-	174.93	NS	282.05
	FoxP3	--	30.31	--	16.33
	Grhl1	++	38.45	++	12.01
	Hmgb2	+	38.12	NS	121.17
	Id2	+	180.43	NS	188.96
	Id3	+	37.87	++	35.49
	Irf1	-	282.24	--	99.68
	Irf4	++	186.65	NS	22.46
	Jdp2	++	11.36	++	10.75
	Klf2	--	116.99	--	549.06
	Lef1	--	69.23	--	211.71
	Lilrb4a	#N/A	0.00	#N/A	#N/A
	Maf	++	642.44	++	346.78
	Myb	+	28.09	-	51.48
	Mybl2	NS	2.92	NS	1.57
	Myc	--	19.34	NS	53.86
	Nfia	++	22.14	++	13.47
	Nfil3	++	62.68	++	320.66
	Nr1h3 (LXRα)	NS	1.16	NS	2.13
	Pax5	++	8.94	++	3.31
	Pax9	++	3.38	NS	0.45
	Prdm1 (Blimp-1)	++	100.20	NS	10.05
	Rbpj	+	73.40	NS	76.01
	Runx2	++	43.71	NS	15.38
	Rora	-	26.65	NS	161.75
	S1pr1	--	141.34	--	363.10
	Six5	++	14.88	++	1.14
	Sox4	--	1.07	--	9.85
	Sox8	++	1.29	NS	0.93
	Stat1	NS	617.27	NS	569.13
	Stat3	+	345.04	NS	479.20
	Stat4	+	142.56	+	175.61
Tbx21 (T-bet)	++	24.69	NS	47.35	
Tcf7	NS	1519.30	+	2987.52	
Tox2	++	206.07	++	649.25	
Vdr	++	65.44	++	69.11	
Zbtb16 (PLZF)	--	0.18	--	0.41	
Secretion proteins	Chgb	NS	0.15	#N/A	#N/A
	Gzmb (Granzyme B)	++	11.54	--	0.50
Enzymes	Cblb	NS	169.82	NS	238.13
	Entpd1 (CD39)	++	47.39	NS	13.66
	Itk	NS	481.13	NS	633.92
	Nt5e (CD73)	++	268.63	++	235.00
	Serpib6b	+	19.23	NS	14.20
	Serpib9	+	23.74	-	20.43

+++ *FC>4* Expression consistent between *Tet+* cells
 ++ *4>FC>2* Text in red Normalized counts below expression cut-off
 + *2>FC>1* NA Not detected
 NS *1>FC>-1* NS Non-significant
 - *-1>FC>-2*
 -- *-2>FC>-4*
 --- *FC<-4*

Supplementary Table 3. Differential expression of the 106 TR1/TFH/Treg gene selection in the various SMARTseq2 and 10x scRNAseq cell clusters

Gene type	Genes	SMARTseq2 of pooled Tet+ vs Tconv	10X scRNAseq of pooled Tet+ vs Tconv	10X scRNAseq BDC Tet+ vs INS Tet+	10x scRNAseq TR1 cluster vs Tconv cluster	10x scRNAseq TFH cluster vs Tconv cluster	10x scRNAseq TR1 cluster vs TFH cluster	Bulk RNAseq TFH vs Tconv
Cell adhesion molecules	Cd226	+++	NS	NS	++	NS	++	--
	Itga2 (CD49b)	NS	NS	--	++	NS	+++	---
	Itgae (CD103)	NS	NS	--	+++	NS	+++	NS
	Ocn	NS	+++	NS	+++	+++	NS	NS
	S1pr2	NS	+++	NS	+++	+++	---	+++
	Sell (CD62L)	---	--	NS	---	---	++	---
	Selpg (Psg1)	--	NS	NS	NS	---	++	---
Chemokine receptors	Ccr5	NS	+++	NS	+++	+++	+++	+++
	Ccr7	--	--	NS	--	---	++	---
	Cxcr3	+++	++	NS	+++	+++	++	+++
	Cxcr4	+++	++	NS	NS	+++	---	+++
	Cxcr5	+++	+++	++	+++	+++	---	+++
Co-stimulatory molecules	Cd28	+++	NS	NS	+	++	NS	++
	Cd40lg	+	NS	NS	NS	++	-	++
	Icos	+++	+++	NS	+++	+++	NS	+++
	Klrk1 (NKG2D)	NS	NS	NS	+++	NS	+++	NS
	Sh2d1a (SAP)	+	NS	NS	++	++	NS	+++
	Tnfrsf4 (Ox40)	+++	++	NS	+++	+++	++	+++
	Tnfrsf18 (GITR)	+++	NS	NS	++	NS	NS	+
	Tnfrsf4 (Ox40L)	NS	++	NS	+++	NS	NS	+++
Co-inhibitory molecules	Ctla4	+++	+++	NS	+++	+++	++	+++
	Fasl	+++	NS	NS	++	--	+++	--
	Havcr2 (TIM-3)	NS	+++	--	+++	+++	+++	NS
	Lag3	+++	+++	NS	+++	+++	NS	+++
	Pdcd1 (PD-1)	+++	+++	NS	+++	+++	---	+++
	Tigit	+++	+++	NS	+++	+++	NS	+++
Cytokines	Ebi3 (IL27b)	NS	+++	NS	+++	+++	++	+++
	Ifng	+++	++	NS	+++	+++	++	+++
	Il10	+++	+++	NS	+++	+++	+++	+++
	Il21	+++	+++	NS	+++	+++	NS	+++
	Il4	+++	+++	NS	+++	+++	---	+++
	Il5	NS	#N/A	#N/A	#N/A	#N/A	#N/A	NS
	Mucb (Areg)	NS	NS	NS	NS	NS	NS	NS
	Tgfb1	NS	NS	NS	NS	NS	NS	NS
	Il10ra	+++	+	NS	+++	++	NS	NS
	Il12rb2	NS	NS	NS	+++	NS	++	+++
Cytokine receptors	Il21r	+++	NS	NS	NS	NS	NS	-
	Il27ra	+	NS	NS	NS	NS	NS	-
	IL7r (CD127)	---	--	NS	--	---	++	---
	IL17rc	NS	NS	NS	NS	NS	NS	NS
	Il2ra (CD25)	---	NS	NS	++	NS	+++	--
	Tgfb1	NS	NS	NS	NS	NS	NS	+
	Tgfb2	++	NS	NS	NS	NS	NS	-
	Tgfb3	NS	NS	NS	NS	NS	NS	--
	Atf6	NS	++	NS	+++	+++	NS	+++
	Ahr	NS	+++	NS	+++	+++	+++	NS
Ajuba	NS	+++	NS	+++	NS	NS	NS	
Ascl2	+++	+++	NS	+++	+++	---	+++	
Bach2	---	--	NS	--	---	+	---	
Batf	+++	NS	NS	++	++	NS	+++	
Bcl6	+++	+++	NS	++	+++	---	+++	
Bhlhe40	+++	++	NS	+++	+++	NS	+++	
Bmyc	---	NS	NS	NS	NS	NS	-	
Cbfa2t3	NS	+++	NS	+++	+++	---	+++	
Cebpa	NS	+++	NS	+++	+++	---	+++	
Dbp	NS	NS	NS	NS	NS	NS	NS	
E2f1	NS	++	--	+++	NS	++	NS	
Egr2	NS	++	NS	++	+++	--	+++	
Elk4	++	NS	NS	NS	++	NS	NS	
Eomes	NS	NS	NS	++	+++	NS	+	
FoxP1	--	NS	NS	NS	NS	NS	--	
FoxP3	---	NS	--	+++	--	+++	++	
Grhl1	NS	+++	++	+++	+++	NS	+++	
Hmgb2	++	+	NS	++	NS	+	++	
Id2	+++	NS	NS	++	NS	+	-	
Id3	-	++	++	NS	+++	---	+++	
Irf1	+++	NS	NS	NS	NS	NS	-	
Irf4	NS	++	++	+++	++	++	+++	
Jdp2	NS	+++	NS	+++	+++	---	+++	

Transcription factors	Klf2	---	NS	--	-	---	+++	---	
	Lef1	---	--	-	---	---	NS	---	
	Lilrb4a	NS	++	---	+++	NS	+++	#N/A	
	Maf	+++	+++	NS	+++	+++	NS	+++	
	Myb	NS	++	NS	++	+++	NS	+++	
	Mybl2	NS	NS	NS	+++	NS	+++	++	
	Myc	---	--	NS	--	---	+++	---	
	Nfia	+++	+++	NS	+++	+++	---	+++	
	Nfil3	+++	+++	NS	+++	+++	NS	+++	
	Nr1h3 (LXRα)	NS	++	NS	NS	NS	NS	++	
	Pax5	NS	+++	NS	++	+++	---	#N/A	
	Pax9	NS	+++	NS	NS	+++	---	+++	
	Pou2af1 (OcaB)	NS	+++	++	+++	+++	NS	+++	
	Prdm1 (Blimp-1)	+++	+++	NS	+++	NS	+++	NS	
	Rbpj	+++	+	NS	++	+	NS	+	
	Runx2	NS	+++	NS	+++	+++	++	+++	
	Rora	+	NS	NS	+++	++	NS	+++	
	S1pr1	---	NS	NS	-	---	++	---	
	Six5	NS	+++	++	+++	+++	NS	+++	
	Sox4	NS	NS	NS	---	---	NS	NS	
	Sox8	NS	+++	NS	+++	+++	---	+++	
	Stat1	-	NS	NS	NS	NS	NS	NS	
	Stat3	+++	NS	NS	NS	+	NS	+	
	Stat4	++	+	NS	++	++	NS	++	
	Tbx21 (T-bet)	NS	++	NS	+++	+++	++	+++	
	Tcf7	+	NS	NS	NS	+	--	NS	
	Tox2	+++	+++	NS	+++	+++	---	+++	
	Vdr	NS	+++	NS	+++	+++	NS	+++	
	Zbtb16 (PLZF)	NS	NS	NS	+++	NS	+++	NS	
	Secretion proteins	Chgb	NS	NS	NS	NS	NS	NS	
		Gzmb (Granzyme B)	NS	+++	---	+++	NS	+++	NS
	Enzymes	Cblb	NS	NS	NS	NS	NS	-	
		Entpd1 (CD39)	NS	+++	NS	+++	+++	++	+++
		Itk	NS	NS	NS	NS	NS	--	+
		Nt5e (CD73)	NS	+++	++	+++	+++	NS	+++
		Serpnb6b	NS	++	NS	+++	++	NS	++
	Serpnb9	NS	NS	NS	+	+	NS	NS	

+++

FC>4

++

4>FC>2

+

2>FC>1

NS

1>FC>-1

-

-1>FC>-2

--

-2>FC>-4

FC<-4

	Upregulated
	Downregulated
	scRNAseq concordant between BDC and Ins Tet+ cells
	scRNAseq non-concordant between BDC and Ins Tet+ cells
	Results concordant between TFH scRNAseq and TFH bulk RNAseq
	Differences between TFH scRNAseq and TFH bulk RNAseq
	NS Non-significant

Upregulated

Downregulated

scRNAseq concordant between BDC and Ins Tet+ cells

scRNAseq non-concordant between BDC and Ins Tet+ cells

Results concordant between TFH scRNAseq and TFH bulk RNAseq

Differences between TFH scRNAseq and TFH bulk RNAseq

NS
Non-significant

Supplementary Table 4. Metal-labeled antibodies for Mass Cytometry

Label	Target	Clone	Company	Conc.(µg/ml)
114Cd	CD4	RM4-5	BD Biosciences	2.5
169Tm	PE	PE001	BioLegend	5
172Yb	CXCR3	CXCR3-173	ThermoFisher	5
165Ho	Biotin	1D4C5	Fluidigm	5
151Eu	CD28	37.51	Fluidigm	5
176Yb	CD278 (ICOS)	7E.17G9	Fluidigm	5
161Dy	CD134 (OX-40)	OX-86	BD Biosciences	5
143Nd	CD357 (GITR)	DTA1	Fluidigm	5
173Yb	CD152 (CTLA-4)	UC10-4B9	ThermoFisher	5
174Yb	CD223 (LAG-3)	C9B7W	Fluidigm	5
159Tb	CD279 (PD-1)	J43	Fluidigm	5
152Sm	TIGIT	GIG7	ThermoFisher	5
158Gd	IL-10	JES5-16E3	Fluidigm	5
160Gd	IL-21	FFA21	ThermoFisher	5
166Er	IL-4	11B11	Fluidigm	5
168Er	AHR	RPT9	ThermoFisher	5
154Sm	BATF	D7C5	Fluidigm	5
163Dy	BCL-6	K11291	Fluidigm	5
170Er	CEBPalpha	Rb Poly	ThermoFisher	5
116Cd	EGR2	EPR4004	Abcam	5
145Nd	FoxP3	FJK-16s	ThermoFisher	5
147Sm	ID2	E991	Abbaxa	5
149Sm	IRF1	EPR18301	Abcam	5
155Gd	IRF4	3E4	Fluidigm	5
146Nd	LEF1	EPR2029Y	Abcam	5
141Pr	cMaf	sym0F1	ThermoFisher	5
162Dy	NFIL3	1218A	R&D systems	5
175Lu	PRDM1 (Blimp1)	6D3	BD Biosciences	5
150Nd	STAT3	232209	R&D systems	5
156Gd	STAT4	2H9L5	ThermoFisher	5
153Eu	TBX21 (Tbet)	4B10	BioLegend	5
171Yb	phospho-ITK	A16064A	BioLegend	5


*Labeling was done using Maxpar X8 or MCP9 Antibody Labeling Kits (Fluidigm) except Fluidigm antibodies

Supplementary Table 5. Differential expression of 106 TR1/TFH/Treg-relevant genes in the Blimp1-dependent (TR1) and independent (TR1-like) vs. the TFH subcluster from pMHCII-NP-treated mice (10x scRNAseq)

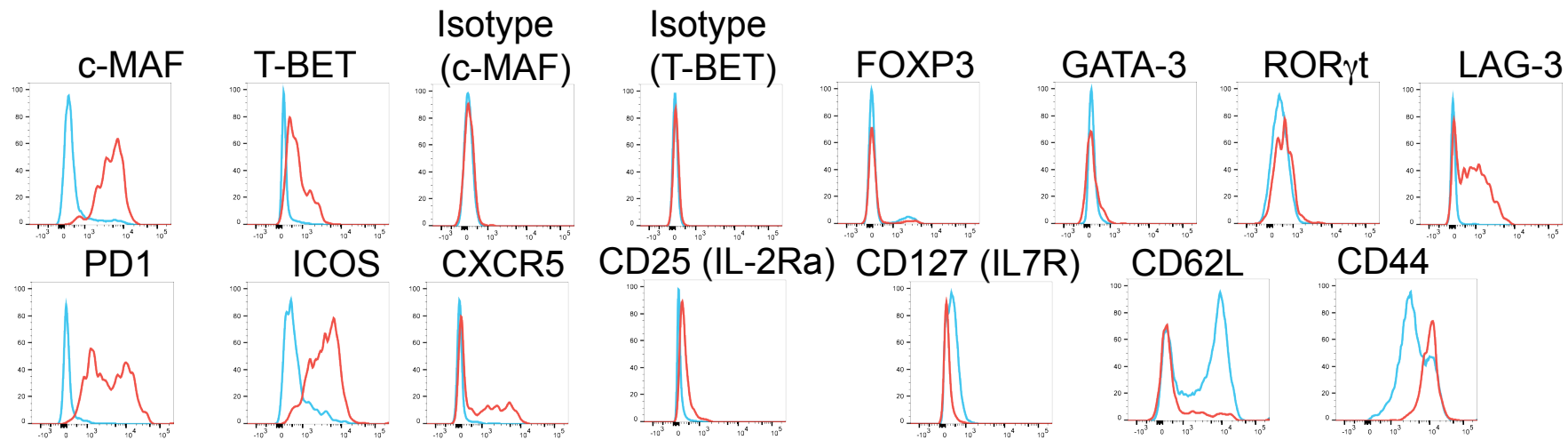
Gene type	Gene name	TR1 vs TR1-like	TR1-like vs TFH	TR1 vs TFH
Cell adhesion molecules	Cd226	-	++	NS
	Itga2 (CD49b)	NS	NS	NS
	Itgae (CD103)	NS	NS	NS
	Ocln	NS	NS	NS
	S1pr2	NS	-	-
	Sell (CD62L)	+	NS	+
	Selplg (Psgl1)	+	+	+
Chemokine receptors	Ccr5	+	NS	+
	Ccr7	-	+	+
	Cxcr3	NS	+	+
	Cxcr4	NS	-	-
	Cxcr5	-	-	--
Co-stimulatory molecules	Cd28	NS	NS	NS
	Cd40lg	-	NS	-
	Icos	+	+	+
	Klrk1 (NKG2D)	NS	NS	NS
	Sh2d1a (SAP)	NS	-	-
	Tnfrsf4 (Ox40)	NS	++	++
	Tnfrsf18 (GITR)	+	+	+
Tnfsf4 (Ox40L)	NS	NS	NS	
Co-inhibitory molecules	Ctla4	++	NS	++
	Fasl	NS	NS	NS
	Havcr2 (TIM-3)	+	NS	+
	Lag3	+	+	++
	Pdcd1 (PD-1)	-	--	--
	Tigit	NS	NS	NS
Cytokines	Ebi3 (IL27b)	NS	NS	NS
	Ifng	NS	+	+
	Il10	++	NS	++
	Il21	NS	+	+
	Il4	NS	-	-
	Il5	NS	NS	NS
	Mcub (Areg)	NS	NS	NS
	Tgfb1	NS	+	NS
Cytokine receptors	Il10ra	NS	NS	NS
	Il12rb2	NS	NS	NS
	Il21r	NS	NS	NS
	Il27ra	NS	NS	NS
	IL7r (CD127)	NS	NS	NS
	IL17rc	NS	NS	NS
	Il2ra (CD25)	NS	NS	+
	Tgfbr1	NS	NS	NS
	Tgfbr2	NS	-	-
	Tgfbr3	NS	NS	NS
	Atf6	NS	NS	NS
	Ahr	+	+	+
	Ajuba	NS	NS	NS
	Ascl2	NS	-	-
	Bach2	NS	NS	NS
	Batf	NS	+	NS
	Bcl6	-	-	--
	Bhlhe40	-	+	NS
	Bmyc	-	NS	NS
	Cbfa2t3	NS	-	-

Transcription factors	Cebpa	NS	-	-
	Dbp	NS	NS	NS
	E2f1	NS	NS	NS
	Egr2	NS	NS	NS
	Elk4	-	NS	-
	Eomes	NS	NS	NS
	FoxP1	NS	+	+
	FoxP3	NS	NS	NS
	Grhl1	NS	NS	NS
	Hmgb2	NS	NS	NS
	Id2	NS	+	+
	Id3	-	-	--
	Irf1	NS	+	+
	Irf4	NS	+	+
	Jdp2	NS	NS	NS
	Klf2	-	++	+
	Lef1	NS	-	-
	Lilrb4a	NS	NS	NS
	Maf	+	-	+
	Myb	NS	NS	NS
	Mybl2	NS	NS	NS
	Myc	NS	NS	NS
	Nfia	NS	-	-
	Nfil3	NS	NS	NS
	Nr1h3 (LXR α)	NS	NS	NS
	Pax5	NS	NS	NS
	Pax9	NS	NS	NS
	Pou2af1 (OcaB)	NS	-	-
	Prdm1 (Blimp-1)	++	NS	++
	Rbpj	NS	+	NS
	Runx2	NS	+	+
	Rora	NS	NS	NS
	S1pr1	NS	+	NS
	Six5	NS	NS	NS
	Sox4	NS	NS	NS
	Sox8	NS	NS	NS
	Stat1	-	+	NS
	Stat3	NS	NS	NS
	Stat4	-	NS	-
	Tbx21 (T-bet)	NS	NS	NS
Tcf7	--	-	--	
Tox2	-	-	--	
Vdr	NS	NS	NS	
Zbtb16 (PLZF)	NS	NS	NS	
Secretion proteins	Chgb	NS	NS	NS
	Gzmb (Granzyme B)	NS	NS	NS
Enzymes	Cblb	NS	NS	NS
	Entpd1 (CD39)	NS	NS	+
	Itk	NS	-	-
	Nt5e (CD73)	NS	NS	NS
	Serpinb6b	NS	NS	NS
Serpinb9	NS	NS	NS	

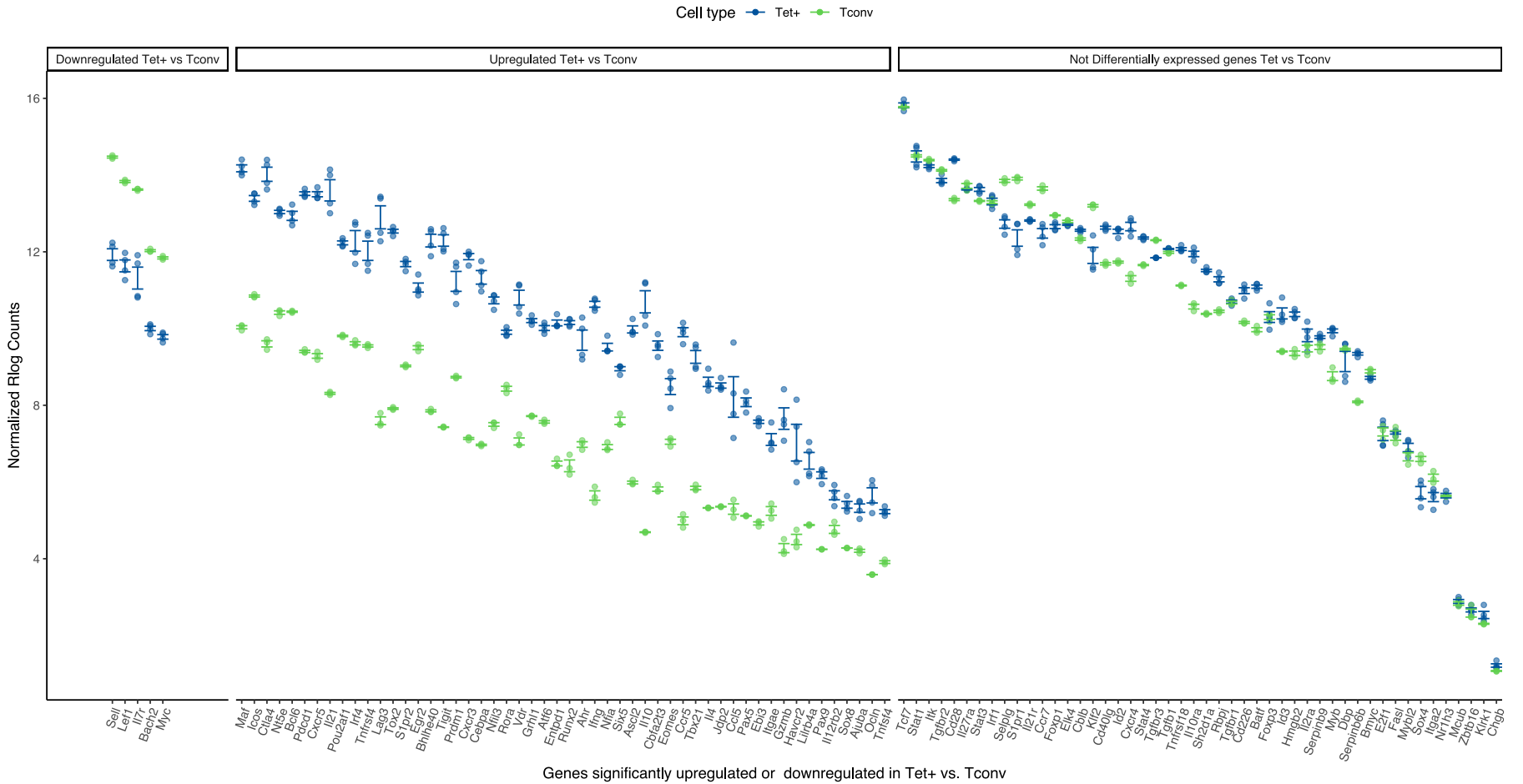
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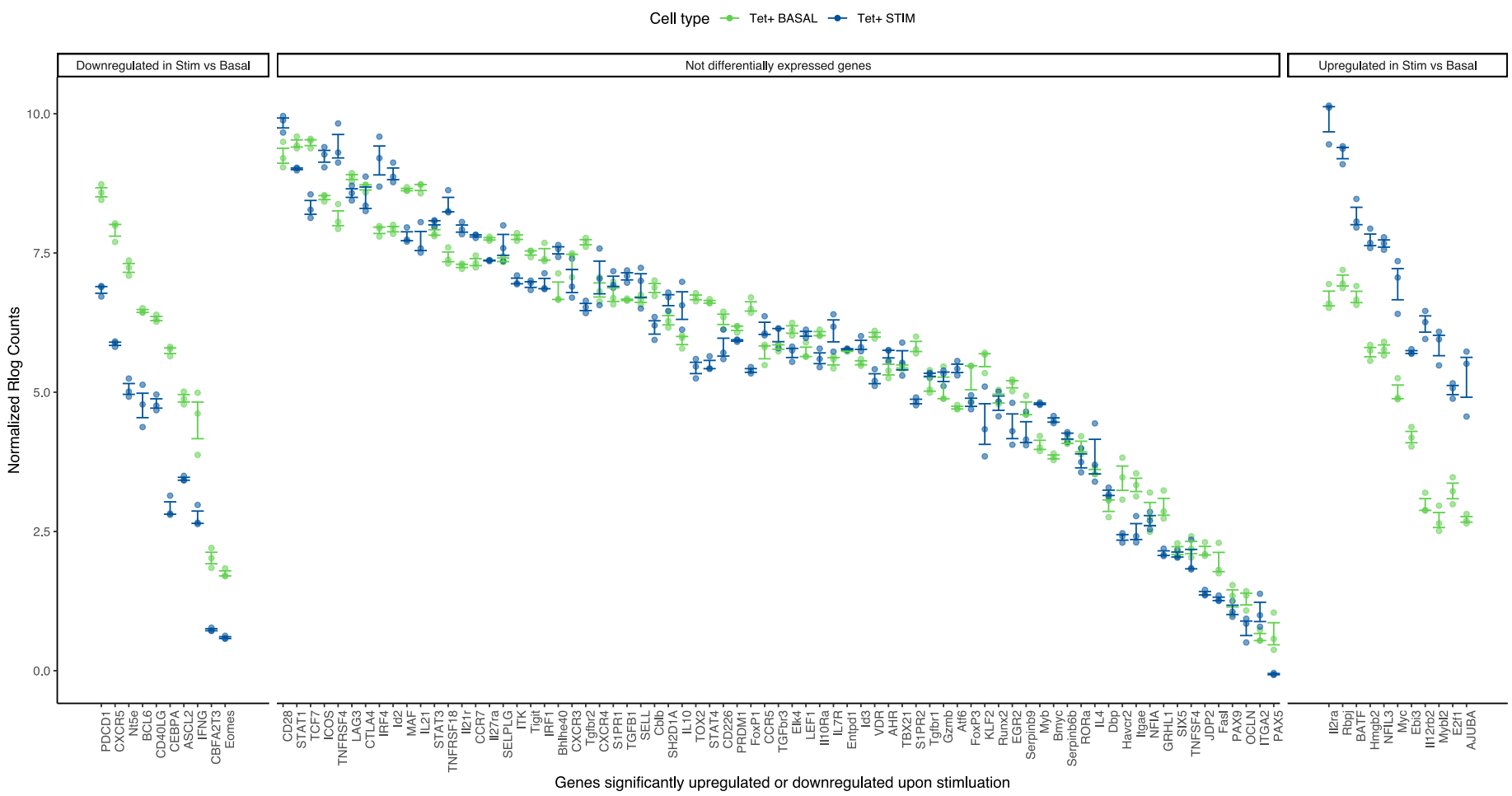
 Upregulated
 Downregulated
 NS Non-significant



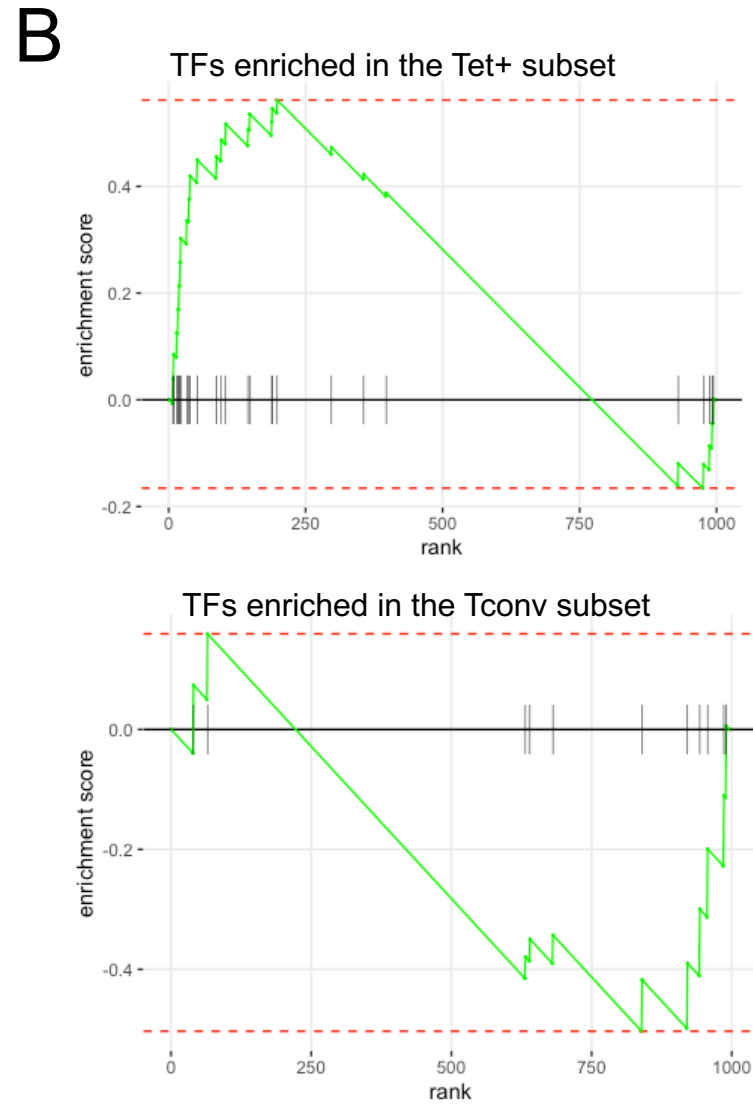
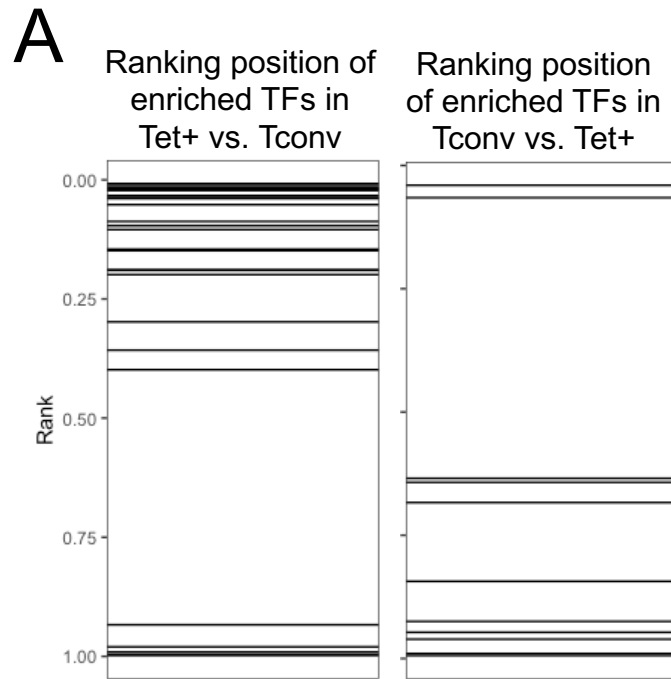
Supplementary Figure 1. Representative flow cytometry staining profiles of splenocytes from BDC2.5mi/IA^{g7}-NP-treated NOD mice (n=3 each from 3 experiments). The histogram overlays correspond to levels of expression of the different markers in the Tet⁺ (red) vs. Tet⁻ (blue) CD4⁺B220⁻ subsets.



Supplementary Figure 2. Normalized counts for 106 TR1/TFH/Treg-relevant genes in pMHCII-NP-induced TR1-like vs. Tconv CD4+ T-cells. Histogram of rlog normalized counts (normalization by counts per million (CPM)) of the 106 gene selection from **Supplementary Table 1** for BDC2.5mi/IA^{g7} Tet+ and Tconv subsets from the samples in **main Fig. 1A**. In blue, counts in Tet+ cells; in green, counts in Tconv cells. Genes are divided according to whether they are significantly upregulated or downregulated (or not differentially expressed) in Tet+ vs. Tconv cells ($FC \geq 4$ or $FC \leq -4$, respectively, and $FDR \leq 0.01$). Genes with < 10 total counts (for all three replicates) are not plotted. Data correspond to the average \pm SEM from 3 samples/cell type, from 1 experiment.

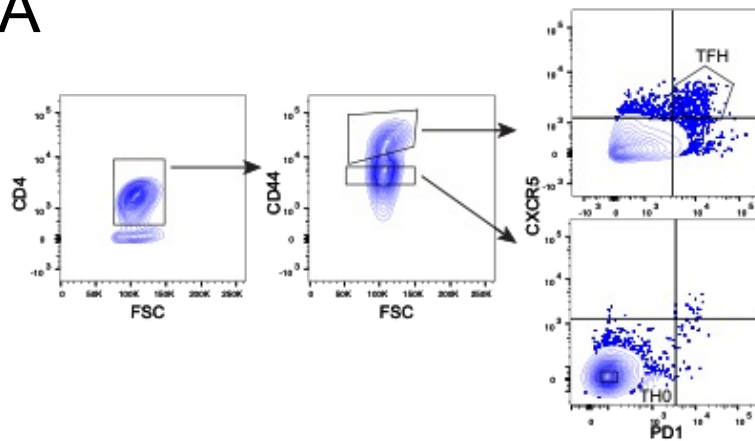


Supplementary Figure 3. Changes in gene expression in pMHCII-NP-induced Tet+ cells upon stimulation *ex vivo*. Histogram of rlog normalized counts (CPM) of the 106 gene selection from **Supplementary Table 1** in basal and stimulated conditions from the Tet+ samples from main **Fig. 1A** (n=3/condition). In green and blue, counts in BDC2.5mi/IA⁹⁷ Tet+ cells in basal and stimulated conditions, respectively. Genes are divided according to whether they are significantly upregulated or downregulated (or not differentially expressed) upon stimulation ($FC \geq 4$ or $FC \leq -4$, respectively, and $FDR \leq 0.01$). Genes with <10 total counts (for all three replicates) are not plotted. Data correspond to the average \pm SEM from 3 samples/condition, from 1 experiment.

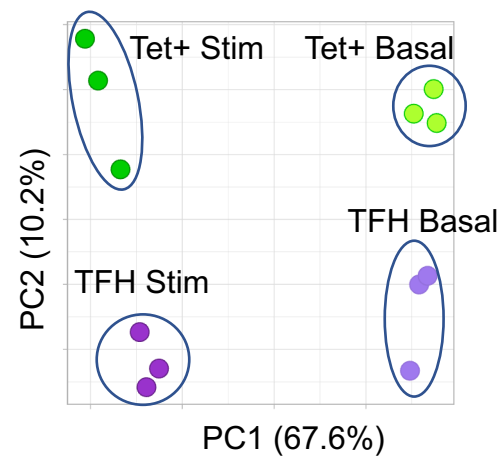


Supplementary Figure 4. Transcription factor upregulation vs. gene expression. **A**, Validation transcription factors from **Supplementary Table 1** represented over a relative rank (from 0 to 1) of activity obtained from VIPER based on ARACNe regulon. More active transcription factors in BDC2.5mi/IA^{g7} Tet⁺ cells appear at the top of the list, while less active appear at the bottom. Left shows transcription factors that are described to be active and right, those that are expected to be inactive/less active in the Tet⁺ subset. **B**, Pre-ranked GSEA of transcription factors expected to be active (left) or inactive (right) in the BDC2.5mi/IA^{g7} Tet⁺ subset.

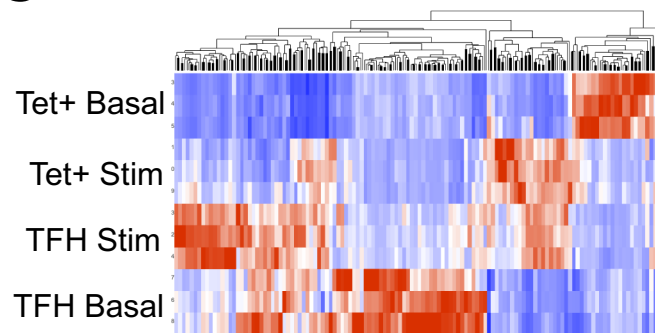
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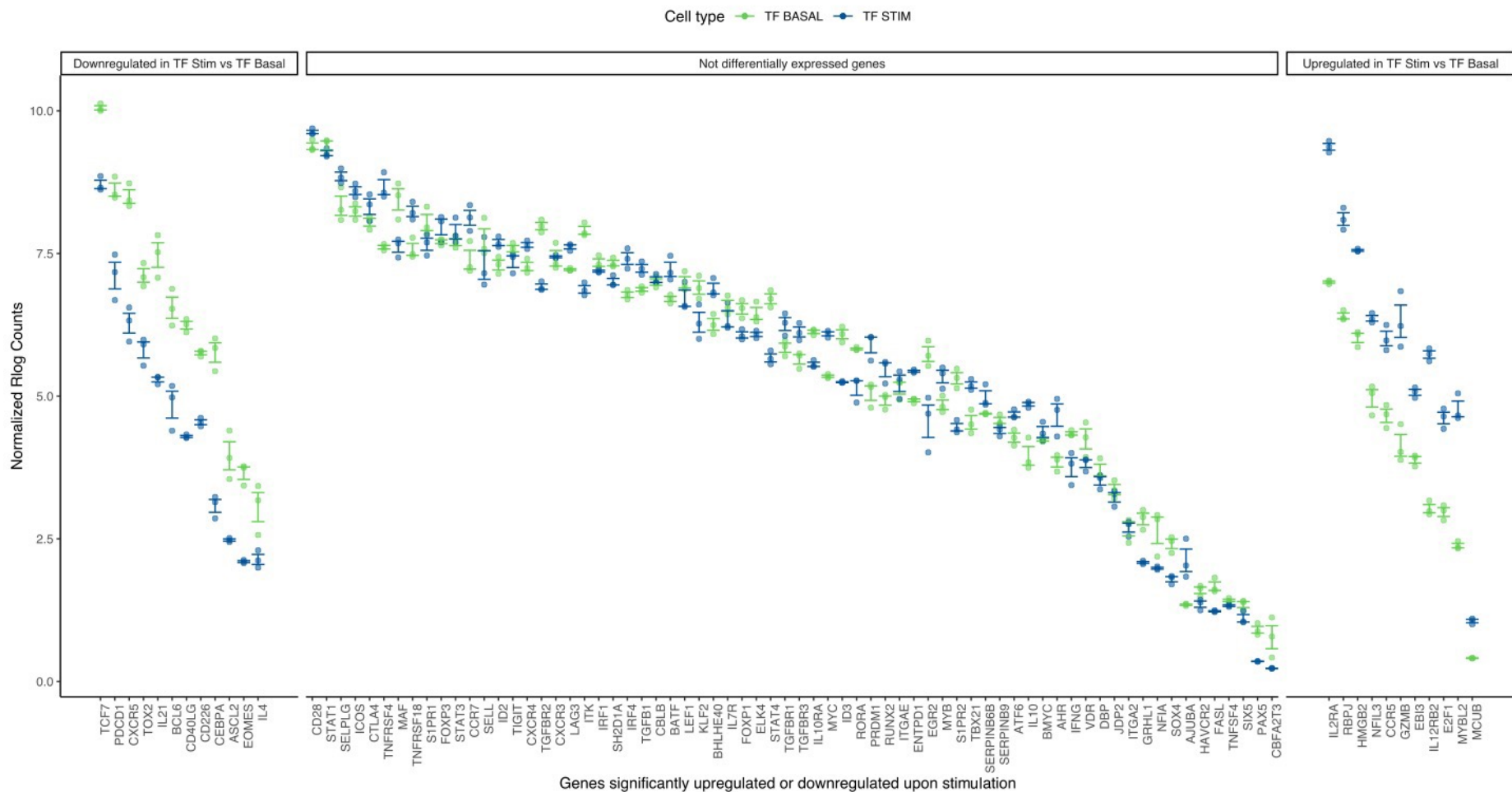
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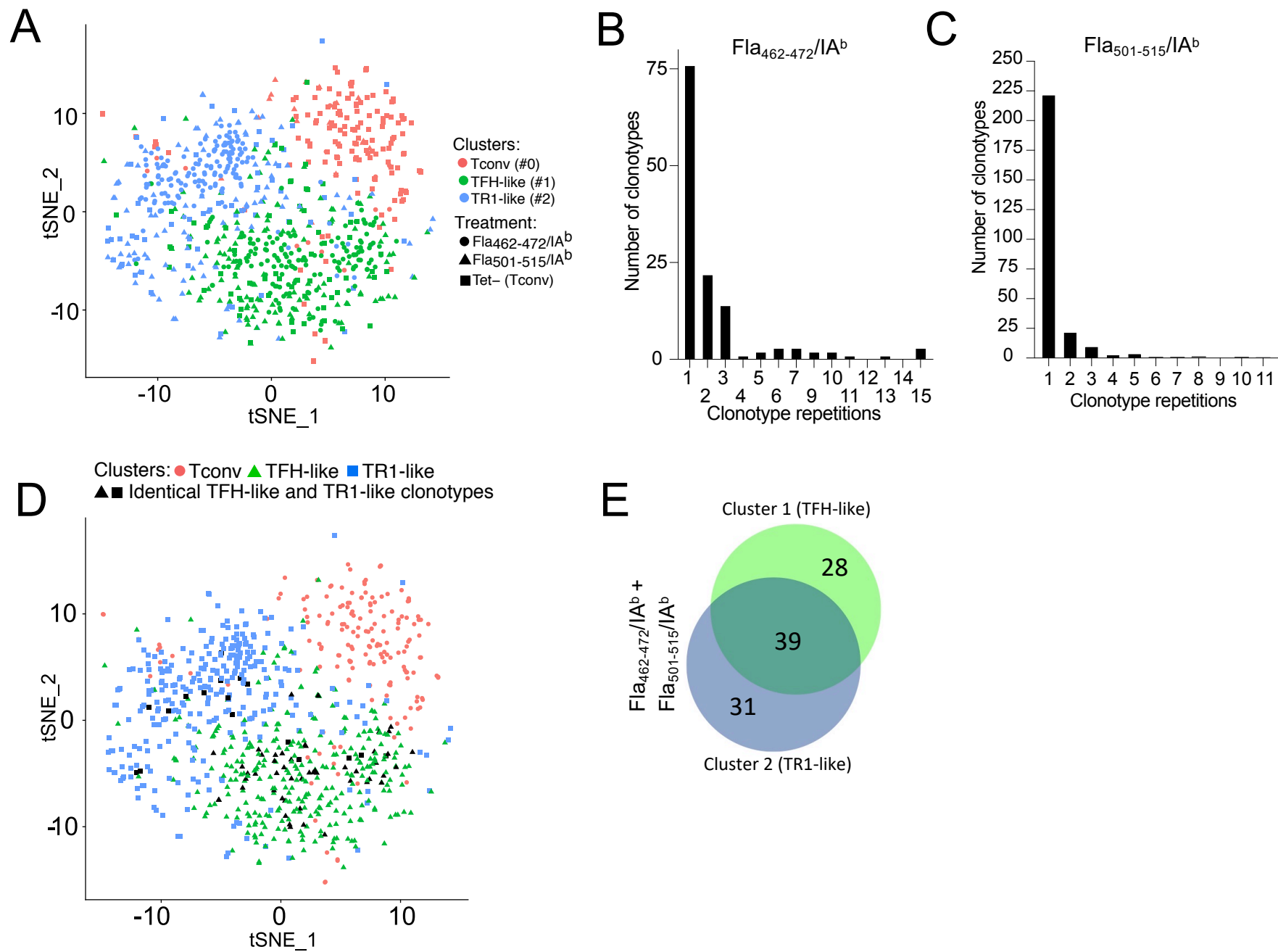
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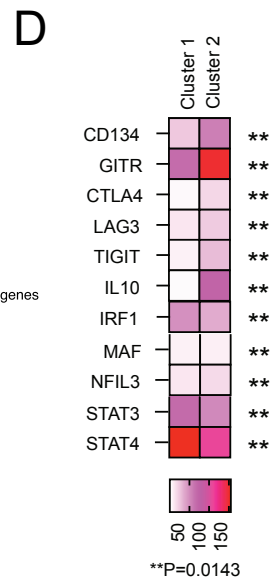
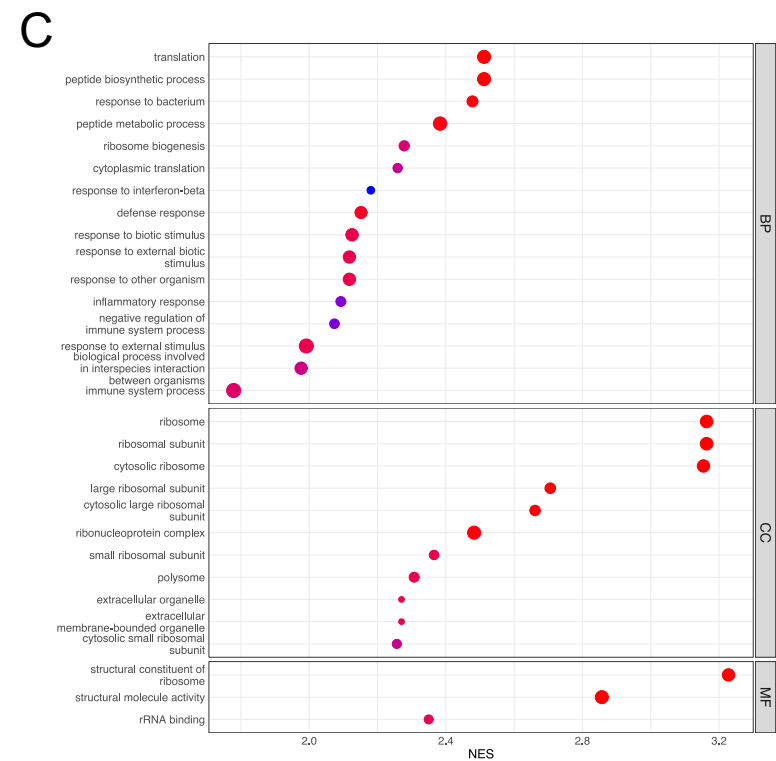
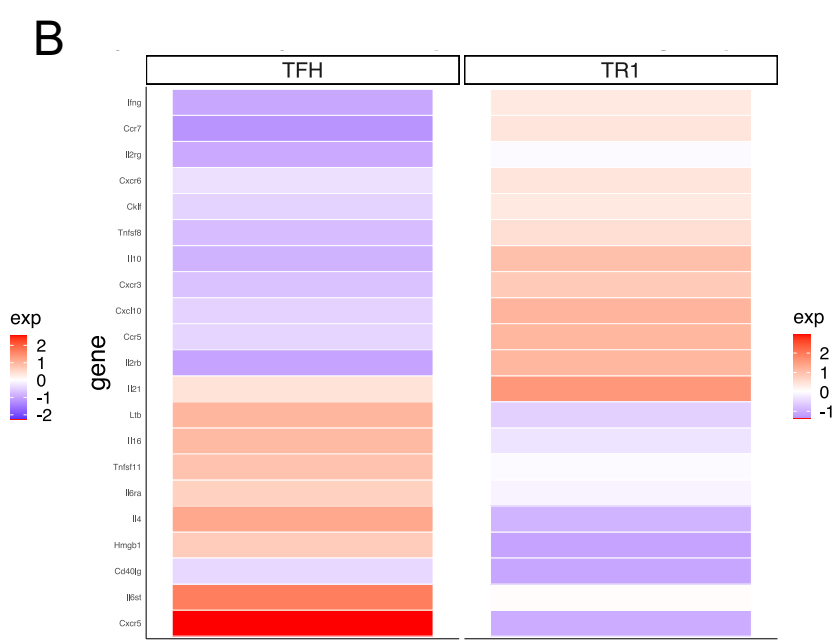
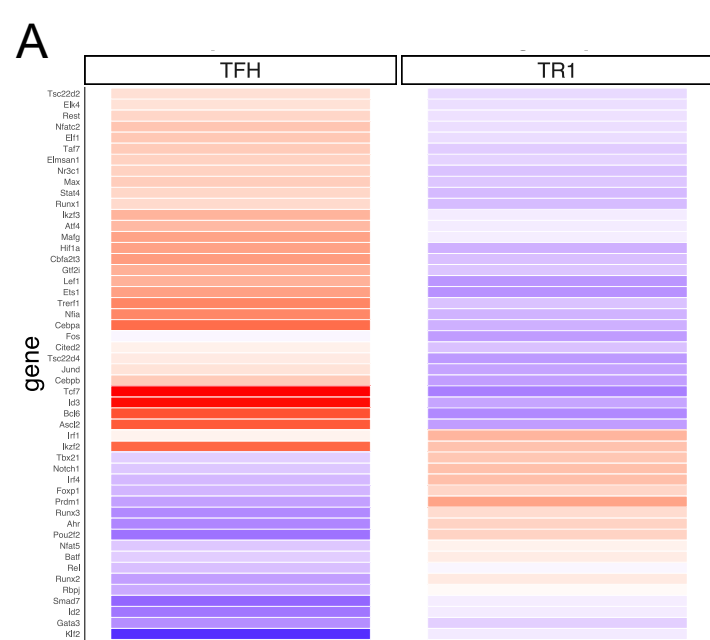
Supplementary Figure 5. pMHCII-NP-induced Tet⁺ cells vs. TFH cells. **A**, Gating strategy for TFH cell sorting for RNAseq. Three KLH-immunized NOD mice were processed in 2 batches (1 and 2 mice each, respectively) to obtain 3 samples of TFH cells (CD4⁺CD44^{hi}CXCR5^{hi}PD1^{hi}) and Tconv cells (CD4⁺CD44⁻CXCR5⁻PD1⁻). **B**, PCA plot comparing basal and stimulated BDC2.5mi/IA⁹⁷ Tet⁺ and TF cells (light green and light purple vs. dark green and dark purple, respectively) (n=3 samples per cell type, from 1 experiment). **C**, Heatmap comparing differentially-expressed genes ($|FC| \geq 4$ and $FDR \leq 0.01$) for all 4 populations from **B**. In red, upregulated genes for the corresponding population; in blue, downregulated genes.



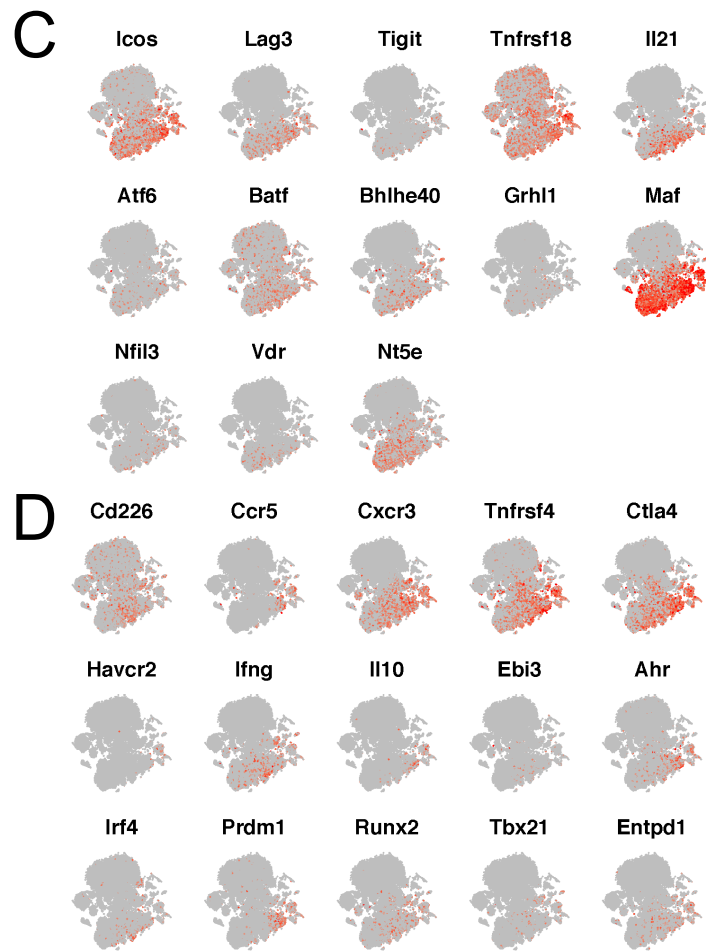
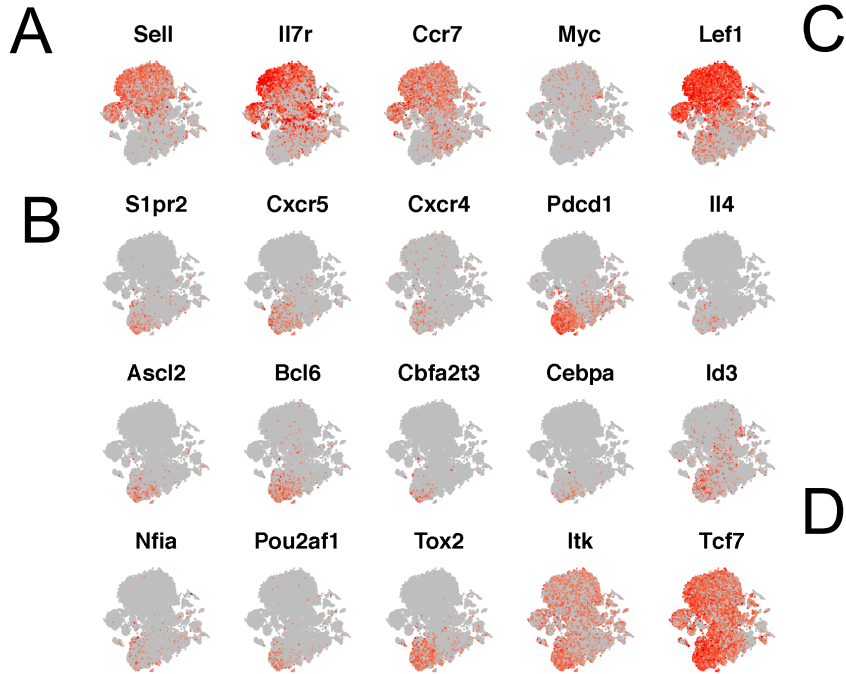
Supplementary Figure 6. Changes in gene expression in endogenous TFH cells upon stimulation *ex vivo*. Histogram of rlog normalized counts (CPM) of the 106 gene selection from **Supplementary Table 1** in TFH cells before and after stimulation *ex vivo* with anti-CD3/anti-CD28 mAb-coated beads (n=3/condition). In green and blue, counts in TFH cells in basal and stimulated conditions, respectively. Genes are divided according to whether they are significantly upregulated or downregulated (or not differentially expressed) upon stimulation ($FC \geq 4$ or $FC \leq -4$, respectively, and $FDR \leq 0.01$). Genes with <10 total counts (for all three replicates) are not plotted. Data correspond to the average \pm SEM from 3 samples/condition from 1 experiment.



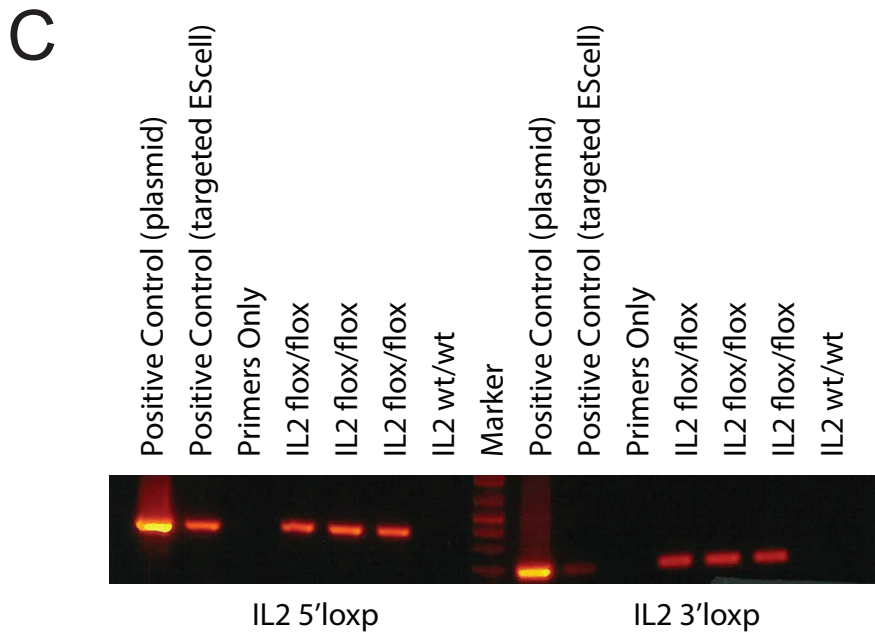
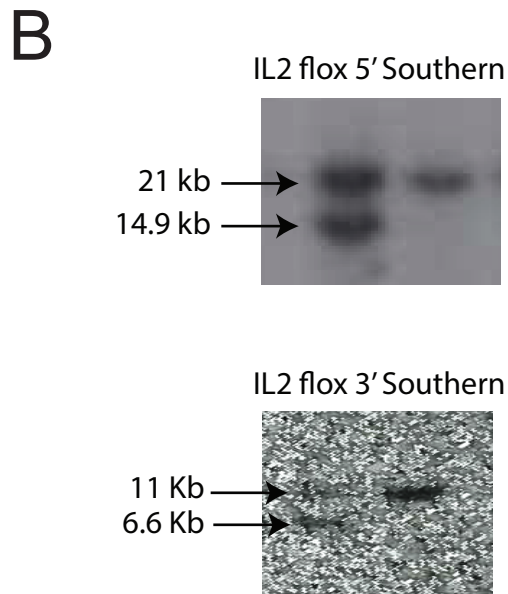
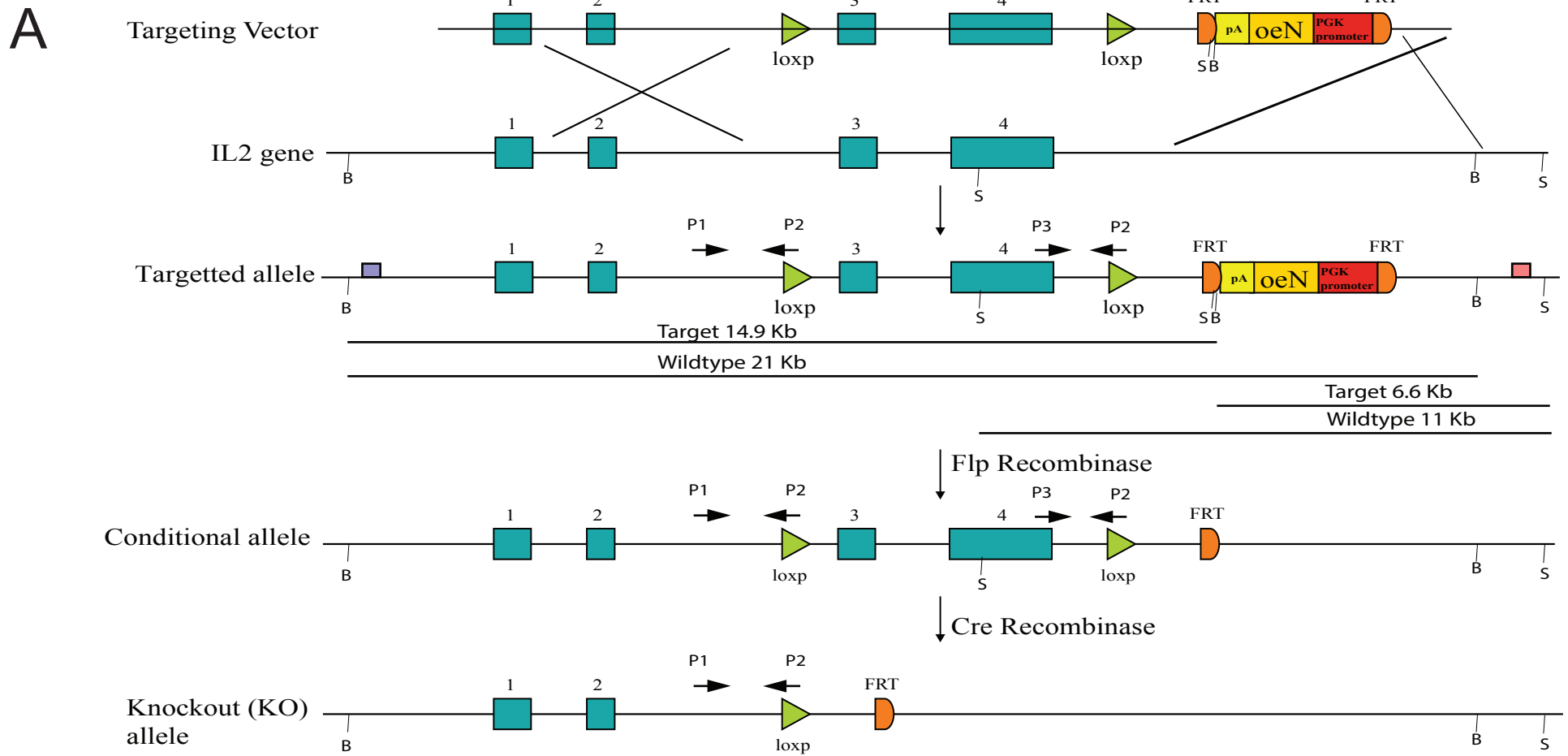
Supplementary Figure 7. pMHCII-NP-induced TR1-like cells are transcriptionally homogeneous but oligoclonal and co-exist with a Tet⁺ TFH-like subpopulation that contains identical clonotypes. **A**, Seurat clustering analysis of the Tet⁺ pools from Fla₄₆₂₋₄₇₂/IA^b- and Fla₅₀₁₋₅₁₅/IA^b-NP-treated C57BL/6 mice (n=6 and 5 mice, respectively, from 2 experiments). Data correspond to Smartseq2-based scRNAseq data for sorted Tet⁺ and Tet⁻ cells. **B-C**, Distribution of unique TCR sequences in the Tet⁺ pools arising in response to treatment with Fla₄₆₂₋₄₇₂/IA^b- or Fla₅₀₁₋₅₁₅/IA^b-NPs in C57BL/6 mice, respectively, from 1 experiment each. The histogram plot shows the distribution of the different TCRαβ clonotypes identified vs. the number of cells (clones) expressing each TCRαβ pair. **D**, tSNE plot from **A** showing the cluster location for TCRαβ pairs expressed by more than one cell. Data correspond to Fla₄₆₂₋₄₇₂/IA^b- or Fla₅₀₁₋₅₁₅/IA^b-NP-treated C57BL/6 mice. **E**, Venn diagram from **D** showing the distribution of repeated TCRαβ pairs in clusters 1 vs. 2. Most (39/67) of the clonotypes found in the TFH-like cluster (#1) were also found in the TR1-like cluster (#2) (39/70).



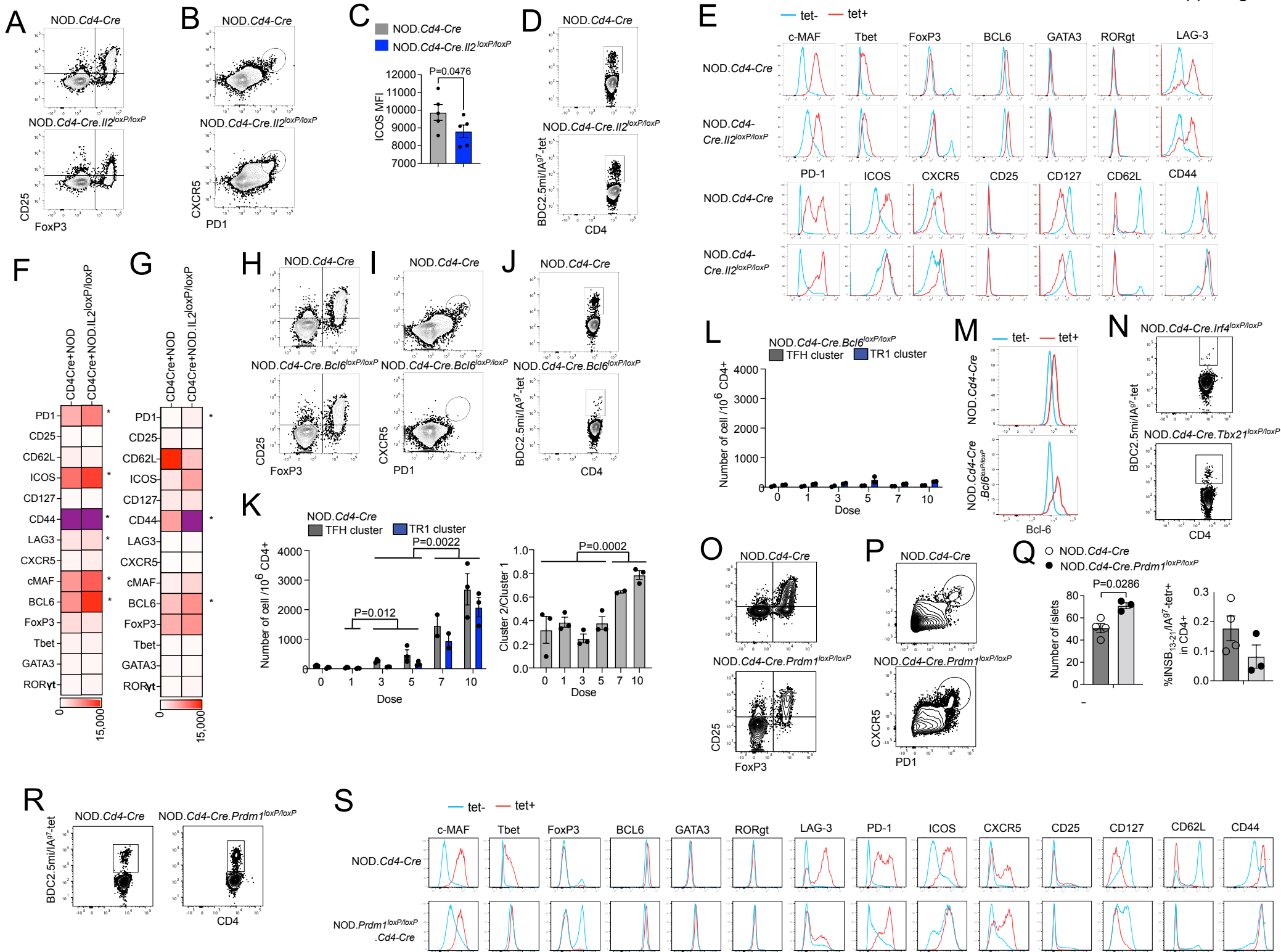
Supplementary Figure 8. Differential expression of transcription factor, cytokines/chemokine and cytokine/chemokine receptor genes, and gene ontology pathways between the Tet⁺ TFH-like and Tet⁺ TR1-like/TR1 clusters. **A-B**, Heatmaps showing scaled average gene expression for differentially expressed ($|FC| > 2$ and $FDR < 0.05$) transcription factor (GO:0003700) (**A**) and cytokine/chemokine and cytokine/chemokine receptor genes (GO:0005125, GO:0004896, GO:0019956) (**B**) in the TFH- and TR1-like/TR1 cell sub-clusters found within the BDC2.5/IAg7-NP-induced tetramer+ cell pool. Data were obtained from 10x genomics-based scRNAseq data for sorted Tet⁺ and Tet⁻ cells from NOD mice treated with BDC2.5mi/IA^{g7}-NP (from n=5 mice, from 1 experiment). **C**, Dot plot showing the differentially enriched gene ontology (GO) pathways (adjusted P value < 0.05) for differentially expressed genes ($|FC| > 2$ and $FDR < 0.05$) between the TFH- and TR1-like/TR1 sub-clusters from **A-B**. Pathways are ordered based on the normalized enrichment score. Color represents the value of the adjusted P value. Dot size represents the number of genes found for each pathway. Pathways are classified based on their ontology: BP: Biological process; CC: Cellular Components; and MF: Molecular function. **D**, Most differentially expressed markers ($P < 0.02$) between the TFH- and TR1-like/TR1 cell sub-clusters (#1 and #2, respectively), as determined via mass cytometry (n=4 mice, from 1 experiment).



Supplementary Figure 9. Differences in gene expression for representative genes in the cell clusters identified via 10x genomics scRNAseq. A, enriched in Tconv cells from main **Fig. 3. B**, enriched in the BDC2.5mi/IA^{g7}/InsB₉₋₂₃/IA^{g7} Tet+ TFH-like sub-cluster from **Fig. 3. C**, shared between the Tet+ TFH- and Tet+ TR1-like sub-clusters from **Fig. 3. D**, enriched in the Tet+ TR1-like sub-cluster from **Fig. 3**.



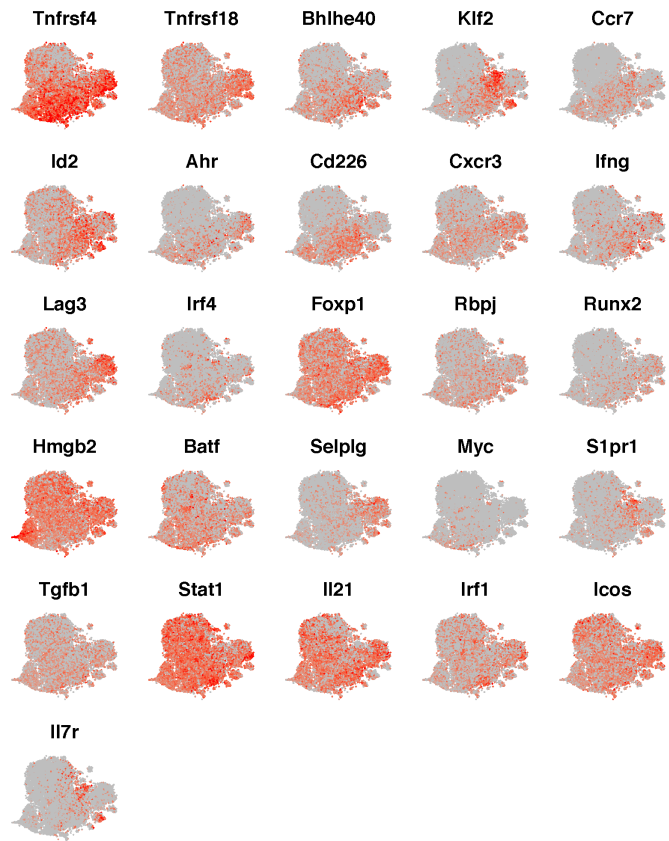
Supplementary Figure 10. Production of a conditional gene-targeted NOD.*Ii2*^{loxP} strain. A, Targeting strategy in embryonic stem cells and location of primers and probes for genotyping. **B-C,** Southern blotting (**B**) and PCR (**C**) documenting the presence of the loxP sites downstream of exon 3 and upstream of exon 4 of *Ii2*.



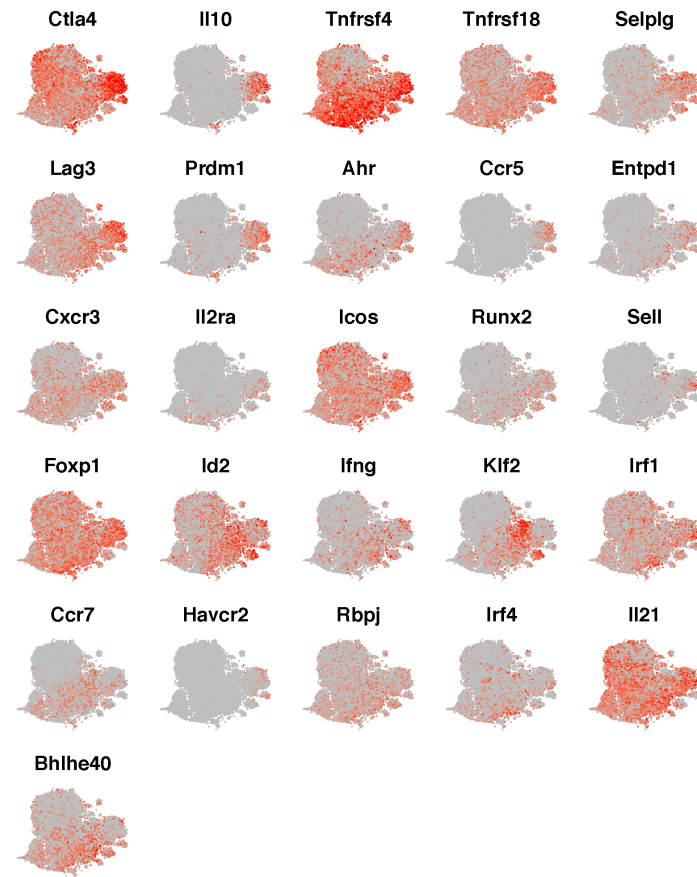
Supplementary Figure 11. Representative flow cytometry profiles for FoxP3+ Tregs and TFH cells in conditional knockout mice from Figures 4 and 5. **A**, Representative staining profiles for CD25⁺FoxP3⁺ CD4⁺ T-cells in NOD.*Cd4-Cre.II2^{loxP/loxP}* and NOD.*Cd4-Cre* mice. **B**, Representative staining profiles for endogenous PD-1^{high}/CXCR5^{high} cells in splenocytes from NOD.*Cd4-Cre.II2^{loxP/loxP}* and NOD.*Cd4-Cre* mice. **C**, Mean fluorescence intensity for splenic PD-1^{high}/CXCR5^{high} cells of NOD.*Cd4-Cre.II2^{loxP/loxP}* and NOD.*Cd4-Cre* mice. Data correspond to 5 mice per strain, from 2 experiments. **D**, Representative flow cytometry profiles for BDC2.5mi/IA^{g7} Tet⁺ CD4⁺ T-cells from the spleen of BDC2.5mi/IA^{g7}-NP-treated NOD.*Cd4-Cre.II2^{loxP/loxP}* and NOD.*Cd4-Cre* mice. **E**, Representative FACS staining profiles for TR1-associated and -non-associated cell markers in the BDC2.5mi/IA^{g7} Tet⁻ and Tet⁺ CD4⁺ T-cells of the mice from main Fig. 4 panel **E**. **F and G**, heatmaps comparing the mean fluorescence intensity for the markers from panel **E** in Tet⁻ and Tet⁺ cells, respectively. **H**, Representative staining profiles for CD25⁺FoxP3⁺ CD4⁺ T-cells in NOD.*Cd4-Cre.Bcl6^{loxP/loxP}* and NOD.*Cd4-Cre* mice. **I**, Representative staining profiles for PD-1^{high}/CXCR5^{high} (TFH) cells in the spleens of NOD.*Cd4-Cre.Bcl6^{loxP/loxP}* and NOD.*Cd4-Cre* mice. **J**, Representative flow cytometry profiles for BDC2.5mi/IA^{g7} Tet⁺ CD4⁺ T-cells from the spleen of BDC2.5mi/IA^{g7}-NP-treated NOD.*Cd4-Cre.Bcl6^{loxP/loxP}* and NOD.*Cd4-Cre* mice. **K**, Changes in the absolute numbers of BDC2.5mi/IA^{g7} Tet⁺ TFH- and TR1-like cells (left) or cluster 2 (TR1):cluster 1 (TFH) ratios (right) in NOD.*Cd4-Cre* mice as a function of BDC2.5mi/IA^{g7}-NP dose numbers, as measured by mass cytometry. Data correspond to 3 mice per dose number, except the 7-dose group (n=2), from 3 experiments. **L**, Changes in the absolute numbers of BDC2.5mi/IA^{g7} Tet⁺ TFH- and TR1-like cells in NOD.*Cd4-Cre.Bcl6^{loxP/loxP}* mice as a function of BDC2.5mi/IA^{g7}-NP dose numbers. Data correspond to 2 mice per dose number, from 3 experiments. **M**, Representative BCL-6 staining profile for Tet⁺ vs. Tet⁻ cells of BDC2.5mi/IA^{g7}-NP-treated NOD.*Cd4-Cre.Bcl6^{loxP/loxP}* and NOD.*Cd4-Cre* mice. **N**, Representative flow cytometry profiles for BDC2.5mi/IA^{g7} Tet⁺ CD4⁺ T-cells from the spleen of BDC2.5mi/IA^{g7}-NP-treated NOD.*Cd4-Cre.Irf4^{loxP/loxP}* and NOD.*Cd4-Cre.Tbx21^{loxP/loxP}* mice. **O**, Representative flow cytometry profiles for CD25⁺FoxP3⁺ CD4⁺ T-cells in NOD.*Cd4-Cre.Prdm1^{loxP/loxP}*

and NOD.*Cd4-Cre* mice. **P**, Representative flow cytometry profiles for PD-1^{high}/CXCR5^{high} (TFH) cells in the spleens of NOD.*Cd4-Cre.Prdm1^{loxP/loxP}* and NOD.*Cd4-Cre* mice. **Q**, Left, average number (\pm SEM) of isolated islets in pancreata from NOD.*Cd4-Cre.Prdm1^{loxP/loxP}* and NOD.*Cd4-Cre* mice. Right, average percentage (\pm SEM) of InsB₁₃₋₂₁/IA^{g7}-specific CD4⁺ T-cells in islets from NOD.*Cd4-Cre.Prdm1^{loxP/loxP}* and NOD.*Cd4-Cre* mice. Data correspond to n=3 and n=4 mice, respectively. P values were calculated via Mann-Whitney U. **R**, Representative flow cytometry profiles for BDC2.5mi/IA^{g7} Tet⁺ CD4⁺ T-cells from the spleen of BDC2.5mi/IA^{g7}-NP-treated NOD.*Cd4-Cre.Prdm1^{loxP/loxP}* and NOD.*Cd4-Cre* mice. **S**, Representative flow cytometry profiles for TR1-associated and -non-associated cell markers in the BDC2.5mi/IA^{g7} Tet⁻ and Tet⁺ CD4⁺ T-cells of the mice from main Fig. 5 panel **L**.

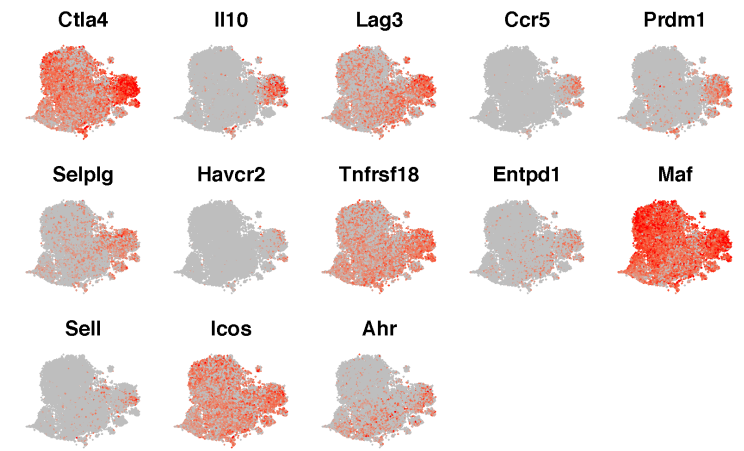
Up in TR1-like vs TFH



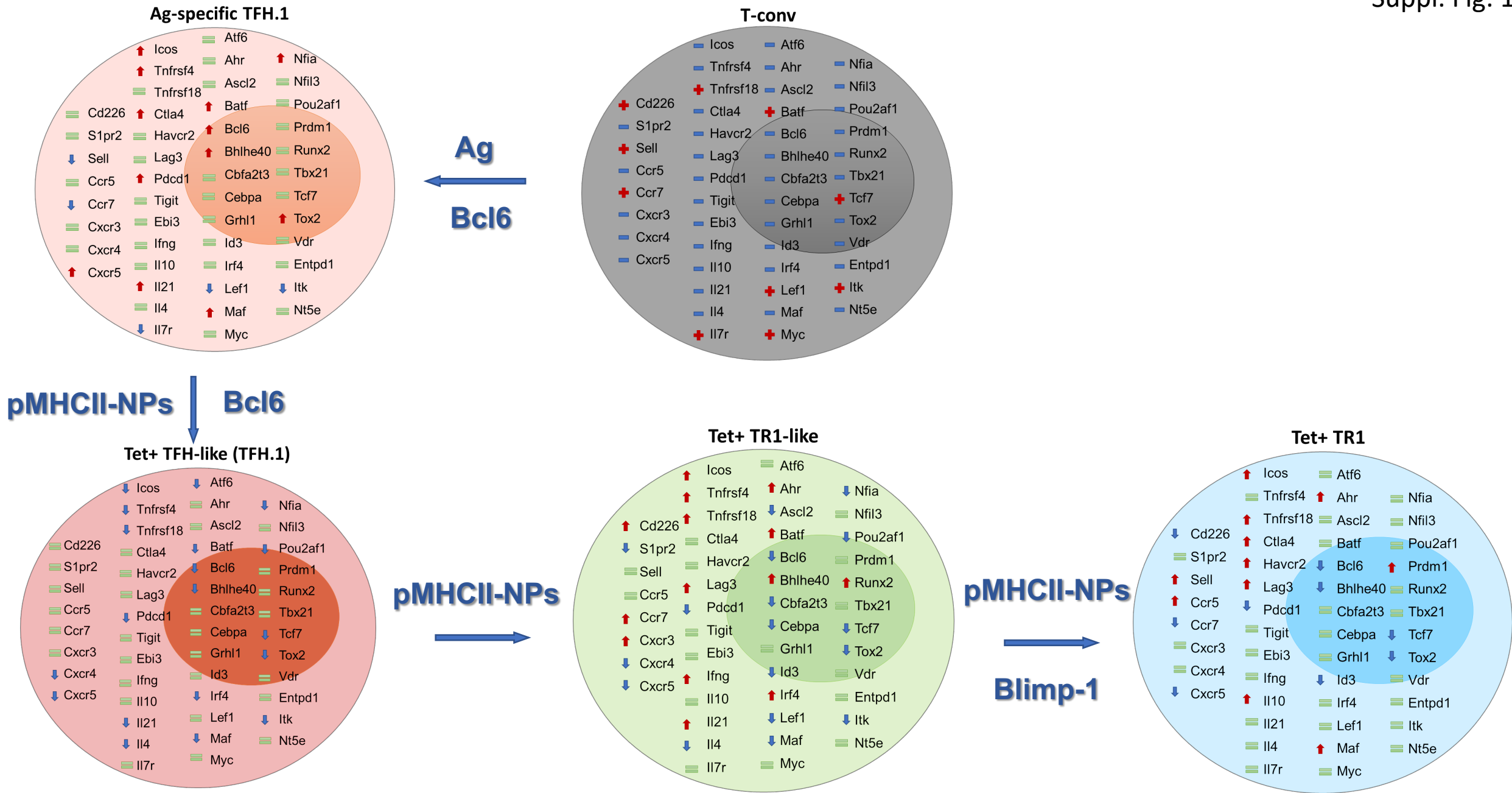
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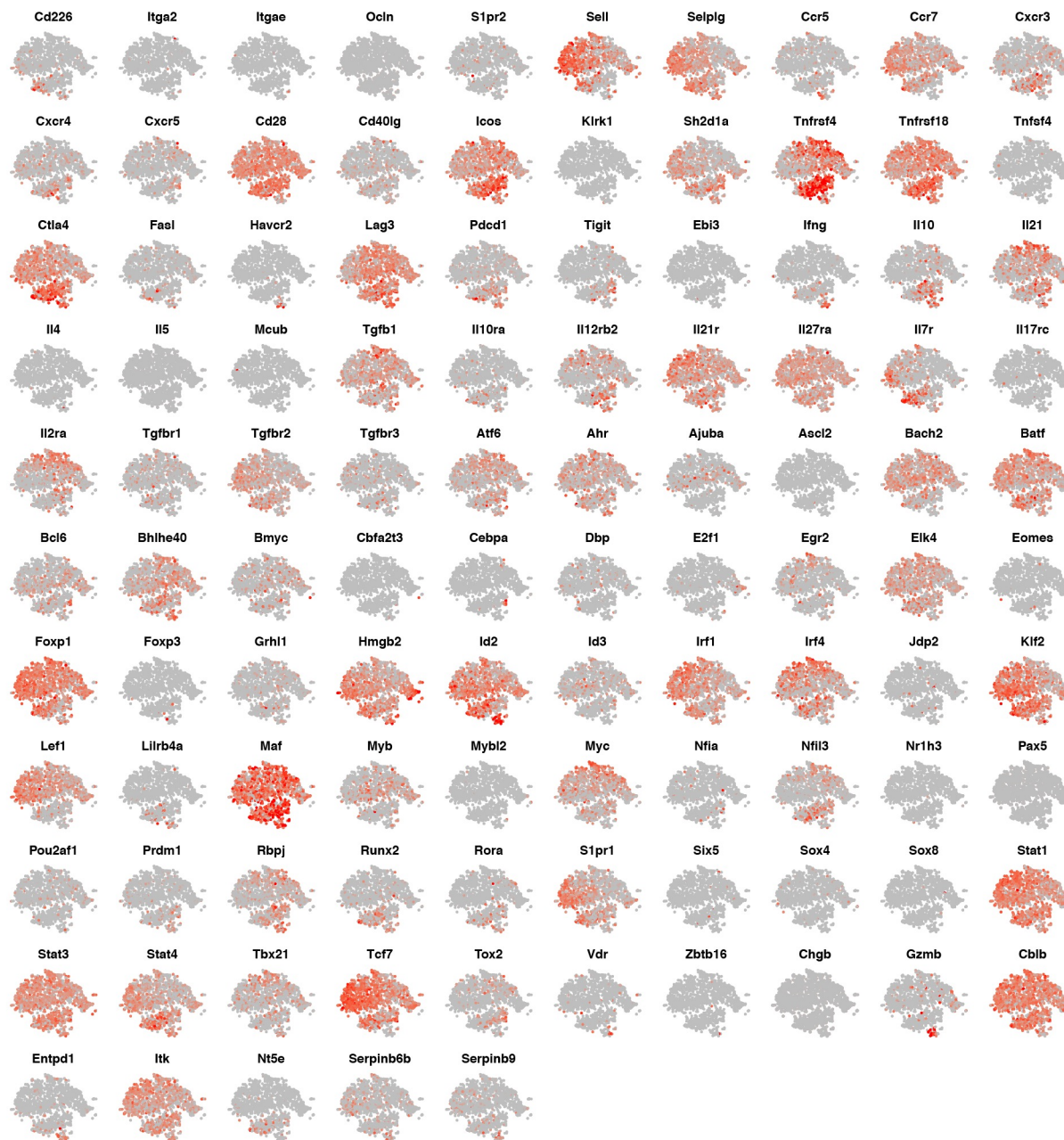
Up in TR1 vs TR1-like



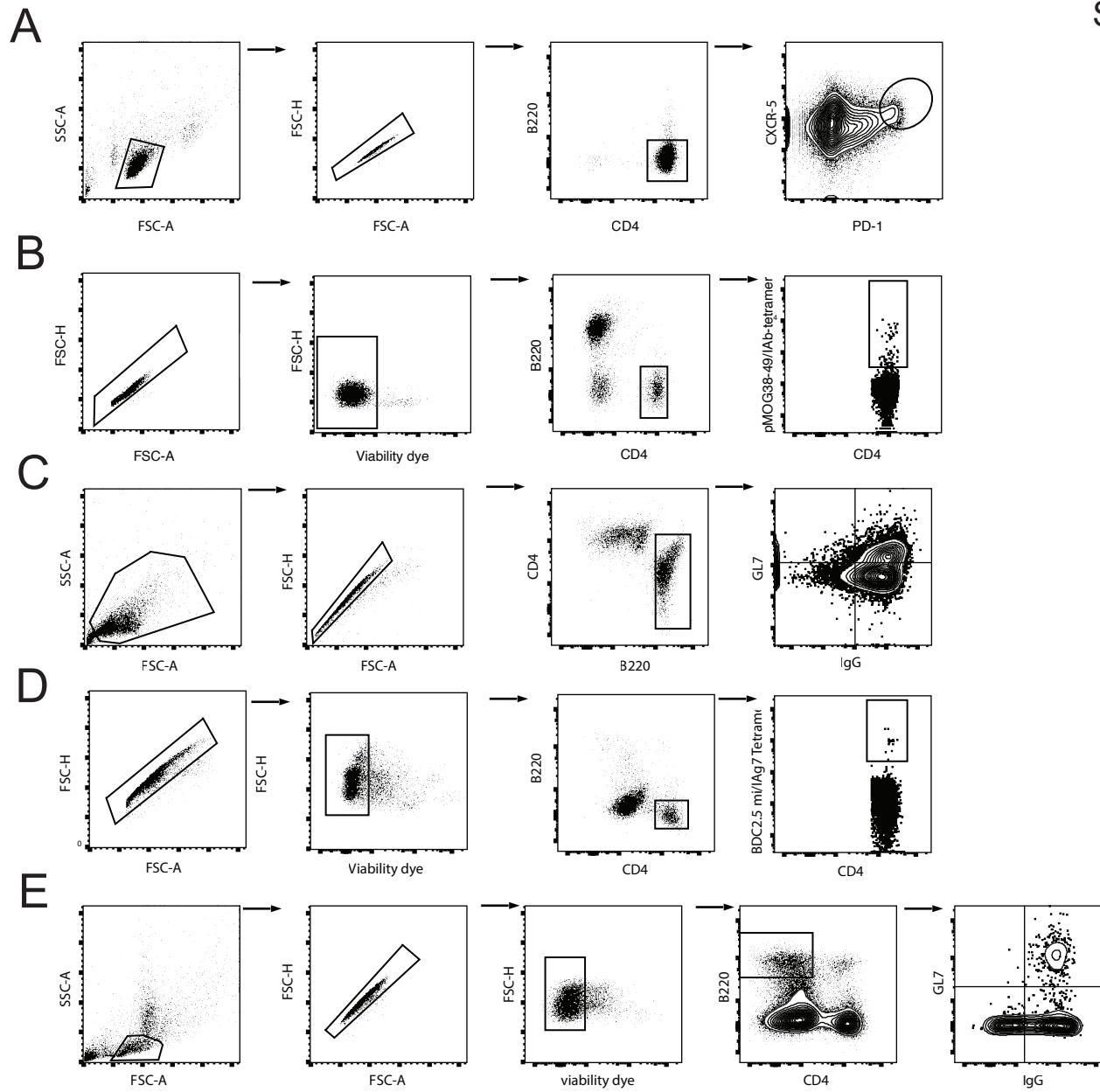
Supplementary Figure 12. Differences in gene expression for representative genes in Tet+ TFH, transitional TR1-like and terminally differentiated TR1 clusters identified via 10x genomics scRNAseq. Feature plots correspond to the Tet+ cells isolated from NOD.*Cd4-Cre* and NOD.*Prdm1^{loxP/loxP}* mice from main Fig. 6A. Only genes listed in Supplementary Table 1 are shown. **Left**, specifically enriched in Tet+ TR1-like vs. Tet+ TFH. **Middle**, specifically enriched in terminally differentiated Tet+ TR1 vs. Tet+ TFH. **Right**, specifically enriched in terminally differentiated Tet+ TR1 vs. transitional Tet+ TR1-like.



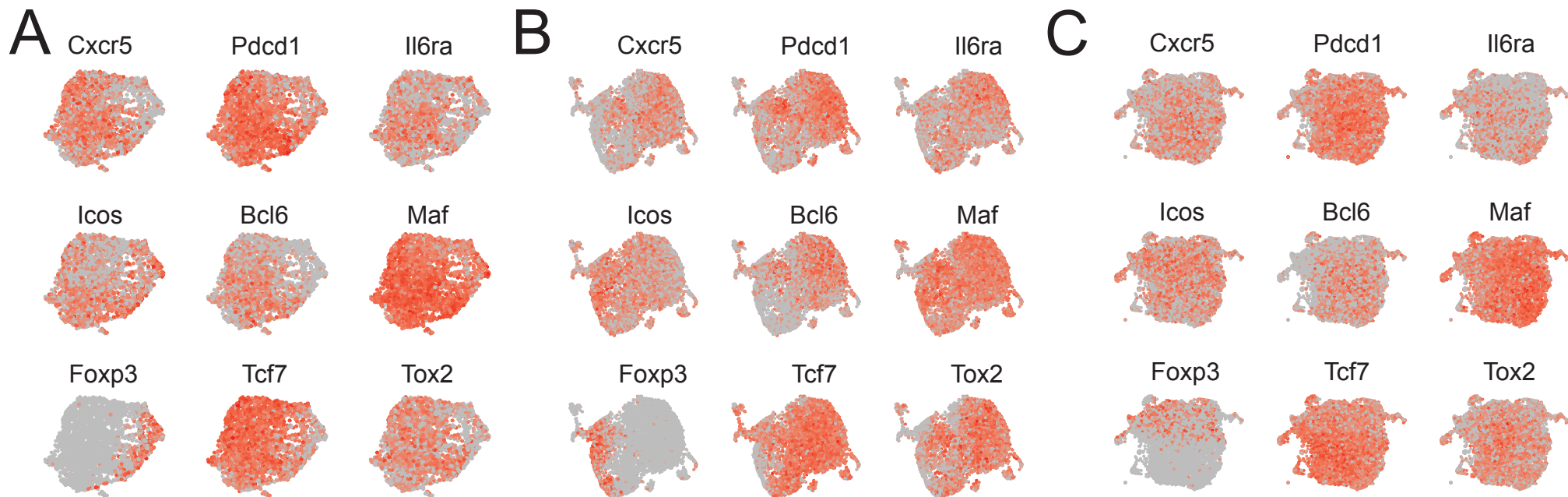
Supplementary Figure 13. Cartoon summarizing progressive changes in the expression of key Tconv, TFH and TR1 genes from Suppl. Table 1 in the different clusters from main Fig. 8A. Differential analysis compares each cell type to the hypothetical preceding cell state (Ag-induced TFH.1 vs Tconv, Tet+ TFH-like (TFH.1) vs Ag-induced TFH.1, Tet+ TR1-like vs Tet+ TFH-like (TFH.1), and Tet+ TR1 vs Tet+ TR1-like). T conventional markers were obtained by differential analysis relative to the other cell subsets. Data are consistent with pMHCII-NP-induced conversion of autoantigen-experienced TFH cells into transitional TR1-like and terminally differentiated TR1 cells *in vivo*.



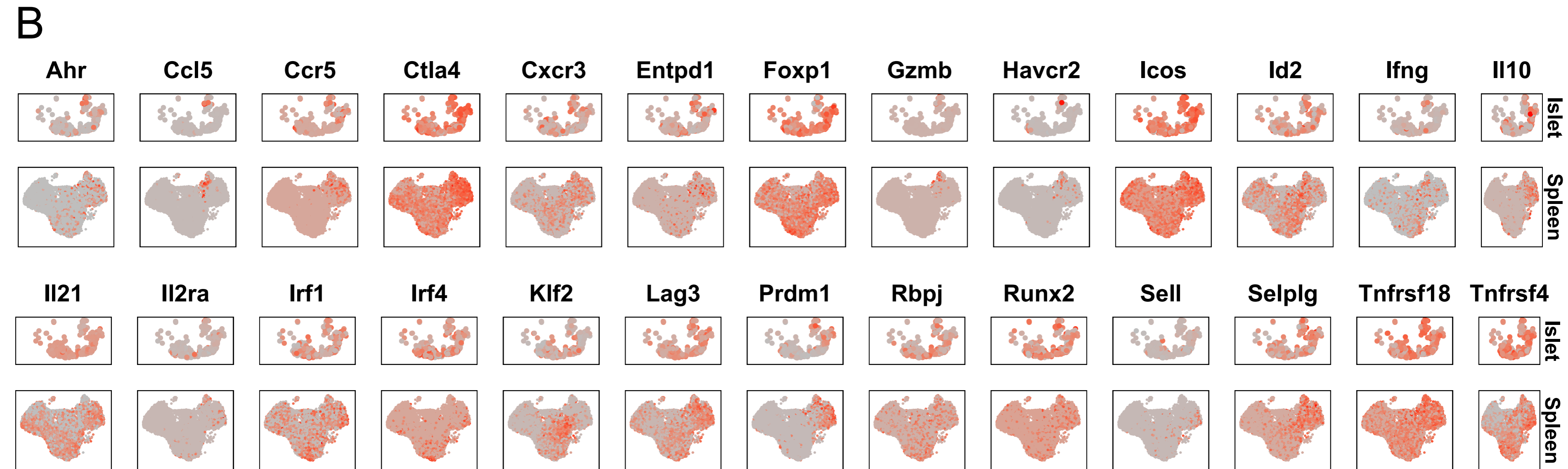
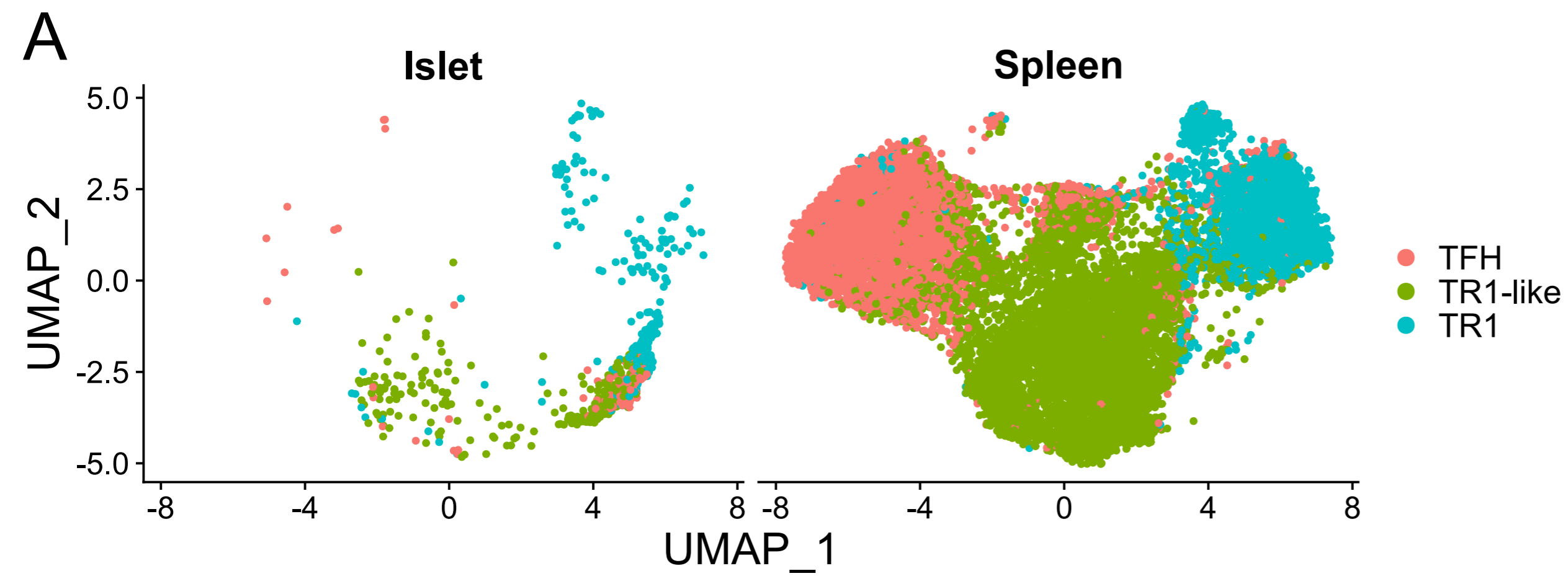
Supplementary Figure 14. Expression of 106 TR1/TFH/Treg-relevant genes in eGFP (IL-10)+ CD4+ T-cells from anti-CD3 mAb-treated NOD.*Il10-eGFP* and NOD.*Il10-eGFP.Cd4-Cre Bcl6^{loxP/loxP}* mice. Figure shows feature plots for the 106 TR1/TFH/Treg genes from **Supplementary Table 1**. Since gene expression in individual cells as detected by scRNAseq is less sensitive than eGFP reporter expression, a significant number of the eGFP+ cells used for scRNAseq express low levels of IL-10 mRNA and are therefore not coloured in red in the feature plots.



Supplementary Figure 15. Representative flow cytometry gating profiles for main Figures 9 and 10. **A**, Gating profile for CXCR5^{hi}PD-1^{high} CD4⁺ T-cells transfused into NOD.*Scid* hosts in **Fig. 9A**. **B**, Gating profile for pMOG₃₈₋₄₉/I-A^b Tet⁺ cells in mice treated with pMOG₃₈₋₄₉/I-A^b-NPs. **C**, Gating profile for B220⁺/GL7⁺/IgG⁺ B cells from **Fig. 10C**. **D**, Gating profile for the BDC2.5mi/I-A^{g7} Tet⁺ cells of the NOD.*Scid* hosts from **Fig. 10E**. **E**, Gating profiles for the GL7⁺sIgG⁺, GL7⁻sIgG⁺ and GL7⁻sIgG⁻ cells from **Fig. 10F**.



Supplementary Figure 16. UMAP-based feature plots for representative TFH-associated gene transcripts (and FoxP3) corresponding to the CXCR5^{hi}PD-1^{high} CD4⁺ T-cells from NOD (A), NOD.Cd4-Cre (B) and NOD.Cd4-Cre/Prdm1^{loxP/loxP} mice (C) used for the NOD.Scid transfer experiments from Fig. 9.



Supplementary Figure 17. UMAP plots and UMAP-based feature plots for TR1-associated gene transcripts for tetramer⁺ CD4⁺ cells isolated from islets vs spleen of pMHCII-NP-treated NOD mice. A, UMAP plots. B, Comparison of the expression of genes from Suppl. Table 1 that are differentially upregulated by terminally differentiated TR1 cells vs. TR1-like and/or TFH cells (from Fig. 6C), by the tetramer⁺ cells isolated from islets vs spleen of BDC2.5mi/IA^{g7}-NP-treated NOD mice.