Cell, Volume *176*

Supplemental Information

Chronic Inflammation Permanently Reshapes Tissue-Resident Immunity in Celiac Disease

Toufic Mayassi, Kristin Ladell, Herman Gudjonson, James E. McLaren, Dustin G. Shaw, Mai T. Tran, Jagoda J. Rokicka, Ian Lawrence, Jean-Christophe Grenier, Vincent van Unen, Cezary Ciszewski, Matthew Dimaano, Hoda E. Sayegh, Vinod Kumar, Cisca Wijmenga, Peter H.R. Green, Ranjana Gokhale, Hilary Jericho, Carol E. Semrad, Stefano Guandalini, Aaron R. Dinner, Sonia S. Kupfer, Hugh H. Reid, Luis B. Barreiro, Jamie Rossjohn, David A. Price, and Bana Jabri

Table S1. Summary of key cohorts, Related to Figures 1-7

	Control	Active	GFD
Figure 1A	n = 102 Average age = 28 Age range = 2 – 61 Male = 29 Female = 73	n = 66 Average age = 24.2 Age range = 6 – 66 Male = 26 Female = 40	n = 59 Average age = 34.8 Age range = 7 – 69 Male = 16 Female = 43
NCR cohort Figure 2, S1	n = 31 Average age = 25.3 Age range = 9 – 61 Male = 8 Female = 23	n = 25 Average age = 19.2 Age range = 6 – 66 Male = 9 Female = 16	n = 24 Average age = 35.7 Age range = 8 – 69 Male = 7 Female = 17
Cytokine cohort Figure 3	n = 8 Average age = 39.6 Age range = 16 – 54 Male = 5 Female = 3	n = 8 Average age = 29.9 Age range = 10 – 56 Male = 3 Female = 5	n = 16 Average age = 44.3 Age range = 19 – 69 Male = 5 Female = 11
RNA-seq cohort Figure 4, S2	n = 8 Average age = 18.5 Age range = 11 – 35 Male = 2 Female = 6	n = 9 Average age = 14 Age range = 6 – 36 Male = 3 Female = 6	n = 5 Average age = 35 Age range = 20 – 61 Male = 0 Female = 5
Gluten challenge cohort Figure 3			n = 4 Average age = 51.8 Age range = 26 – 66 Male = 1 Female = 3
TCR sequencing cohort Figure 5, 6, S3, S4	n = 8 Average age = 24.1 Age range = 10 – 54 Male = 2 Female = 6	n = 8 Average age = 27.9 Age range = 11 – 51 Male = 3 Female = 5	n = 7 Average age = 37 Age range = 17 – 55 Male = 2 Female = 5
BTNL expression cohort Figure 7, S5	n = 16 Average age = 23.9 Age range = 10 – 54 Male = 5 Female = 11	n = 16 Average age = 26 Age range = 10 – 66 Male = 6 Female = 10	n =15 Average age = 33.1 Age range = 10 – 55 Male = 6 Female = 9

Table S2: Gene modules, Related to Figure 4 and Figure 6

NK Module	Cytokine Module	Tissue-Repair Module	Transcription Factor Module	TCR Activation Module
NCR1	*EGF*	*HGF*	*TBX21*	*BCL10*
NCR2	*FGF2*	*EGF*	*GATA3*	*CARD11*
NCR3	*FLT3L*	*HB-EGF*	*FOXP3*	*CD247*
KLRC1	*GCSF*	*AREG*	*RORC*	*CD3D*
KLRC2	*GMCSF*	*FGF-2*	*EOMES*	*CD3E*
KLRC3	*IFNG*	*KGF*	*STAT1*	*CD3G*
TYROBP	*IL17A*	*FGF-10*	*STAT2*	*CHUK*
KIR2DL4	*IL4*	*IGF-1*	*STAT3*	*CSK*
KIR2DL1	*IL5*	*VEGF*	*STAT4*	*ENAH*
KIR2DL3	*IL3*	*TGFA*	*STAT5*	*EVL*
KIR3DL3	*IL6*	*TGFB*	*RUNX1*	*FYB*
KIR3DL2	*IL7*	*IGF1*	*RUNX2*	*GRAP2*
KIR3DL1	*CXCL8*	*CSF2*	*RUNX3*	*HLA-DPA1*
KIR3DL3	*IL9*	*MMP10*	*PLZF*	*HLA-DPB1*
FCGR3A	*MCP3*	*MMP25*	*THPOK*	*HLA-DQA1*
GNLY	*CCL4*	*FGF16*	*TCF7*	*HLA-DQA2*
CTSW	*CCL3*	*FGF18*	*FOXP1*	*HLA-DRB1*
PRF1	*TGFA*	*PDGFB*	*FOXO1*	*HLA-DRB5*
CD70	*TNFA*	*HMGB1*	*ELF1*	*IKBKB*
SIT1	*LTA*	*FURIN*	*IKAROS*	*IKBKG*
ICAM2	*VEGF*	*WNT11*	*ETS1*	*ITK*
SLAMF1	*SPP1*	*JAG1*	*SATB1*	*LAT*
GZMA	*IL10*	*WNT10A*	*IRF4*	*LCK*
GZMB	*AREG*	*HIF1A*	*IRF8*	*LCP2*
GZMK	*IL33*		*IRF2*	*LOC646626*
CD56	*IL22*		*IRF1*	*MALT1*
PRF1	*IL21*		*IRF3*	*MAP3K7*
FASL	*IL27*		*IRF5*	*NCK1*
	TGFB		*IRF7*	*NFKBIA*
	IL2		*BLIMP1*	*PAG1*
	RANTES		*HOBIT*	*PAK1*
	KGF		*LEF1*	*PAK2*
			KLF3	*PDPK1*
			ZEB2	*PIK3CA*
				PIK3CB
				PIK3R1
				PIK3R2
				PLCG1
				PRKCQ
				PTEN
				PTPRC
				RELA
				RIPK2
				TAB2
				TMEM189-UBE2V1

				TRAF6
				TRAT1
				UBE2N
				VASP
				WAS
				ZAP70
				NR4A1
				CD25
				CD69
				IL7R
				CCR7
				ZAP70
				NFKB1
				CTLA4
				MKI67
				PD1/PDCD1
				CD137
				CD38
				CD57
				CD5
				CD6
				CD28

Table S3: TCR sequencing cohort, Related to figure 5 and Figure 6

Group	Patient ID	Tissue	Age	Sex	HLA	Time on a GFD (years)	Cell number sorted for sequencing
Control	7	IEL	14	F	DQ2.5/DQ2.2		768
Control	7	PBL	14	F	DQ2.5/DQ2.2		4368
Control	13	IEL	18	F	DQ2/DQ8^{neg}		446
Control	13	PBL	18	F	DQ2/DQ8^{neg}		2188
Control	40	IEL	17	F	DQ2/DQ8^{neg}		273
Control	40	PBL	17	F	DQ2/DQ8^{neg}		4542
Control	53	IEL	10	F	DQ8/DQX		1456
Control	53	PBL	10	F	DQ8/DQX		10000
Control	110	IEL	32	M	DQ8/DQ2.5		257
Control	110	PBL	32	M	DQ8/DQ2.5		4361
Control	111	IEL	38	F	DQ8/DQX		257
Control	111	PBL	38	F	DQ8/DQX		1183
Control	144	IEL	10	M	DQ8/DQX		751
Control	144	PBL	10	M	DQ8/DQX		1266
Control	106	IEL	54	F	DQ2/DQ8^{neg}		946
Control	106	PBL	54	F	DQ2/DQ8^{neg}		NA
Active	22	IEL	44	M	DQ2.5/DQX		431
Active	22	PBL	44	M	DQ2.5/DQX		5000
Active	35	IEL	11	M	DQ8/DQ2.5		2238
Active	35	PBL	11	M	DQ8/DQ2.5		6591
Active	46	IEL	19	F	DQ2.5/DQX		5000
Active	46	PBL	19	F	DQ2.5/DQX		5000
Active	47	IEL	13	F	DQ2.5/DQX		10000
Active	47	PBL	13	F	DQ2.5/DQX		10000
Active	51	IEL	51	F	DQ8/DQX		10000
Active	51	PBL	51	F	DQ8/DQX		1394
Active	81	IEL	30	F	DQ2.5/DQ2.2		5000
Active	81	PBL	30	F	DQ2.5/DQ2.2		4012
Active	112	IEL	37	F	DQ2.5/DQX		3625
Active	112	PBL	37	F	DQ2.5/DQX		3625
Active	143	IEL	16	M	DQ2.5/DQX		2843
Active	143	PBL	16	M	DQ2.5/DQX		504
GFD	3	IEL	53	F	DQ2.5/DQX	4	5000
GFD	3	PBL	53	F	DQ2.5/DQX	4	5000
GFD	28	IEL	37	M	DQ2.5/DQX	3	1688
GFD	28	PBL	37	M	DQ2.5/DQX	3	1244
GFD	33	IEL	55	F	DQ2.5/DQX	6	1164
GFD	33	PBL	55	F	DQ2.5/DQX	6	3182
GFD	41	IEL	37	F	DQ2.5/DQ2.5	2	1945
GFD	41	PBL	37	F	DQ2.5/DQ2.5	2	2811
GFD	113	IEL	29	F	DQ8/DQ2.5	4	1356
GFD	113	PBL	29	F	DQ8/DQ2.5	4	1356
GFD	9	IEL	17	M	DQ8/DQ2.5	3	5640
GFD	9	PBL	17	M	DQ8/DQ2.5	3	NA
GFD	43	IEL	31	F	DQ2.5/DQ2.2	4	3001
GFD	43	PBL	31	F	DQ2.5/DQ2.2	4	NA

Table S6: Overlapping CDR3 sequences, Related to Figure 6

Group	Patient ID	Tissue	Chain	TRV	CDR3	TRJ	Frequency
Active	35	IEL	TRD	1	CALGDQRVPIPWTGGYRHTDKLIF	1	86.1702
Active	46	PBL	TRD	1	CALGDQRVPIPWTGGYRHTDKLIF	1	1.2658
Active	51	IEL	TRD	1	CALGEGFQRLGDCKLIF	1	2.7778
Active	51	PBL	TRD	1	CALGEGFQRLGDCKLIF	1	23.0769
Active	143	IEL	TRD	1	CALGGAPLGDTRKDKLIF	1	1.3333
Active	143	PBL	TRD	1	CALGGAPLGDTRKDKLIF	1	53.2468
GFD	3	IEL	TRG	9	CALWEVDYKKLF	1	5.1282
GFD	3	PBL	TRG	9	CALWEVDYKKLF	1	61.2500
GFD	3	PBL	TRG	9	CALWEVHYYKKLF	2	1.2500
Active	22	PBL	TRG	9	CALWEVHYYKKLF	1	7.2464
GFD	33	IEL	TRG	9	CALWEVLYKKLF	1	3.4091
Active	46	IEL	TRG	9	CALWEVLYKKLF	1	1.0870
Active	51	IEL	TRG	9	CALWEVLYKKLF	1	1.5873
GFD	3	IEL	TRG	9	CALWEVRYKKLF	1	2.5641
GFD	4	PBL	TRG	9	CALWEVRYKKLF	1	97.7778
Active	51	IEL	TRG	9	CALWEVRYKKLF	1	1.5873
Active	81	IEL	TRG	9	CALWEVRYKKLF	1	6.7416
GFD	9	IEL	TRG	9	CALWEVRYYKKLF	1	7.9365
Active	22	PBL	TRG	9	CALWEVRYYKKLF	1	1.4493
GFD	28	IEL	TRG	3	CATWDGGEKLF	1	98.8889
GFD	41	PBL	TRG	2	CATWDGGEKLF	1	25.7143
Control	106	IEL	TRG	4	CATWDGGEKLF	1	86.9565
GFD	3	IEL	TRG	2	CATWDGLYYKKLF	1	2.5641
Active	112	IEL	TRG	4	CATWDGLYYKKLF	1	1.7544
Active	35	PBL	TRG	4	CATWDGPHYKKLF	1	43.9024
Active	143	IEL	TRG	2	CATWDGPHYKKLF	1	1.8868
Active	22	PBL	TRG	2	CATWDGPNYKKLF	1	4.3478
Active	51	IEL	TRG	2	CATWDGPNYKKLF	1	3.1746
GFD	3	IEL	TRG	2	CATWDGPNYYKKLF	2	5.1282
Active	46	PBL	TRG	2	CATWDGPNYYKKLF	2	1.5385
Active	47	PBL	TRG	2	CATWDGPRYYKKLF	1	56.7568
Active	143	PBL	TRG	4	CATWDGPRYYKKLF	1	6.5217
Control	13	PBL	TRG	4	CATWDGQGYKKLF	2	11.1111
Active	51	IEL	TRG	2	CATWDGQGYKKLF	1	1.5873
Active	143	IEL	TRG	4	CATWDGRGSDWIKTF	P2	1.8868
Control	144	IEL	TRG	4	CATWDGRGSDWIKTF	P2	2.8986
Control	53	IEL	TRG	4	CATWDGRTTGWFKIF	P1	5.2632
Control	144	PBL	TRG	8	CATWDGRTTGWFKIF	P1	2.4390
Active	51	PBL	TRG	2	CATWDGTNYYKKLF	1	12.5000

Control	144	IEL	TRG	4	CATWDGTNYYKKLF	2	2.8986
Control	13	PBL	TRG	2	CATWDGYKKLF	1	4.7619
GFD	41	IEL	TRG	2	CATWDGYKKLF	1	8.6207
Active	81	PBL	TRG	2	CATWDGYKKLF	1	32.7586
GFD	3	IEL	TRG	2	CATWDGYYKKLF	1	1.2821
Control	13	PBL	TRG	2	CATWDGYYKKLF	1	7.9365
GFD	41	IEL	TRG	2	CATWDGYYKKLF	1	5.1724
Active	143	PBL	TRG	2	CATWDGYYKKLF	1	28.2609
Active	143	IEL	TRG	4	CATWDGYYKKLF	1	3.7736
Active	47	IEL	TRG	8	CATWDNYKKLF	1	14.0625
Active	112	PBL	TRG	8	CATWDNYKKLF	1	5.1282
GFD	33	IEL	TRG	4	CATWDPYYKKLF	1	1.1364
GFD	41	PBL	TRG	3	CATWDPYYKKLF	1	18.5714
Active	46	PBL	TRG	5	CATWDRHYKKLF	1	44.6154
Active	51	IEL	TRG	2	CATWDRHYKKLF	1	1.5873
GFD	3	IEL	TRG	3	CATWDRPEKLF	1	2.5641
GFD	33	IEL	TRG	3	CATWDRPEKLF	1	3.4091
Active	143	IEL	TRG	3	CATWDRPEKLF	1	1.8868
GFD	3	IEL	TRG	5	CATWDRPGYKKLF	1	1.2821
Control	111	PBL	TRG	5	CATWDRPGYKKLF	1	1.7241
Control	53	PBL	TRG	3	CATWDSPNYYKKLF	2	18.7500
Active	112	IEL	TRG	3	CATWDSPNYYKKLF	2	1.7544
GFD	113	IEL	TRG	4	CATWDTTGWFKIF	P1	10.7692
Active	143	PBL	TRG	8	CATWDTTGWFKIF	P1	4.3478
GFD	4	PBL	TRG	8	CATWDYYKKLF	1	1.1111
GFD	28	PBL	TRG	4	CATWDYYKKLF	1	43.5294
Active	51	PBL	TRG	8	CATWDYYKKLF	1	6.9444
Control	110	PBL	TRG	5	CATWDYYKKLF	1	13.7255
GFD	113	PBL	TRG	3	CATWGRLYYKKLF	1	1.9608
Control	144	PBL	TRG	8	CATWGRLYYKKLF	1	4.8780
Active	47	IEL	TRG	4	CATWSHYYKKLF	1	28.1250
Active	51	IEL	TRG	3	CATWSHYYKKLF	1	3.1746
GFD	3	IEL	TRG	8	CATWVYYKKLF	1	1.2821
GFD	4	IEL	TRG	5	CATWVYYKKLF	1	11.7647
GFD	41	IEL	TRG	4	CATWVYYKKLF	1	3.4483