

1 **Supplemental Figure 1: Specificity of tetramers with HCV-derived epitopes.**  
2 Representative dot plots of **(A)** PBMCs of healthy donors stained with HCV-tetramer and **(B)**  
3 HCV-infected patients stained with either HCV-Tetramer (upper panel) or with control (CLIP)  
4 - tetramer (lower panel).

5

6 **Supplemental Figure 2: Comprehensive presentation of HCV-specific CD4 T cell**  
7 **responses.** Pseudocolor plots of all 29 patients with detectable responses at baseline.  
8 Responses from baseline and W2 are displayed. \* = No Week 2 time point available, End of  
9 treatment depicted. The data of P3 are also presented in Figure 2 and 3, of P15 in Figure 2,  
10 of P16 and P17 in Figure 4, of P19 in Figure 3.

11

12 **Supplemental Figure 3: Genotypes, HLA-types and tetramer responses at baseline.** Pie  
13 Charts of all analyzed patients. Each Pie represents a group of patients, either having HLA  
14 DRB1\*01:01 or DRB1\*15:01, or Genotype 1 or Genotype 2/3, respectively. The blue color  
15 depicts the percentage of patients with detectable HCV-specific CD4 T cells at baseline.

16

17 **Supplemental Figure 4: Viral load and amino transferase levels of patients undergoing**  
18 **DAA therapy. (A)** Viral load and **(B)** alanine transaminase (ALT)-levels were determined  
19 from each patient at each time point. Each symbol represents 1 patient, bars represent  
20 medians; \*\*  $p < 0.01$ , \*\*\*\*  $p < 0.0001$ ; non-parametric distribution with Wilcoxon matched-  
21 pairs signed rank test between indicated groups. Due to multiple comparisons ( $n=3$ ),  
22 significance level was adjusted using Bonferroni correction and  $p$  values of  $< 0.01$  were  
23 considered statistically significant. Thus,  $p$  values  $> 0.01$  are not indicated.

24

25 **Supplemental Figure 5: Cytokine production of HCV-specific CD4 T cells.** PBMCs were  
26 stained with tetramer, enriched, stimulated for 3.5 h with PMA/ionomycin and stained with  
27 antibodies and analyzed for cytokine expression. **(A)** Representative dot plots are shown for  
28 two representative patients and each analyzed cytokine and **(B)** for all patients in the  
29 corresponding bar charts. **(C)** Multicytokine expression of IL-21, IFN, TNF and IL-2 was  
30 analyzed by SPICE. The analyzed cytokines are depicted as arcs in red hues and the  
31 multicytokine expression as blue pies. Each symbol represents 1 patient, bars represent  
32 medians; non-parametric distribution with Wilcoxon matched-pairs signed rank test with  
33 statistical significance level of 0.05 was adjusted using Bonferroni correction between  
34 indicated groups.

35

36 **Supplemental Figure 6: CD127 and Tcf1 expression on HCV-specific CD4 T cells and**  
37 **bulk non-naïve CD4 T cells.** Expression of CD127 **(A)** and Tcf1 **(B)** on HCV-specific CD4 T  
38 cells (corresponding to data shown in Figure 3) and non-naïve CD4 T cells was assessed at  
39 the indicated time points before and during antiviral therapy. The median fluorescence  
40 intensity (MFI) of the individual samples and the median MFI are displayed as white  
41 scattered dots and green bars, respectively (n = 20 for CD127; n = 8 for Tcf1). Non-  
42 parametric distribution with Wilcoxon matched-pairs signed rank test with statistical  
43 significance level of 0.05 was adjusted using Bonferroni correction between indicated groups.  
44 # each bulk time point is significantly different from each HCV-specific time point ( $p < 0,0005$ )

45

46 **Supplemental Figure 7: Phenotypic shift of HCV-specific CD4 T cells after initiation of**  
47 **antiviral therapy.** t-Distributed Stochastic Neighbor Embedding (tSNE) analysis of CD4 T  
48 cells based on polychromatic flow cytometry data including CCR6, CCR7, CXCR3, CXCR5,  
49 CD25, CD45RA, CD127, ICOS, OX40 and PD-1 was performed in longitudinal samples from  
50 three patients analyzed in a individual batches. Localization of bulk Tfh cells (CXCR5+PD-  
51 1+, dark blue) and bulk Th1 cells (CXCR5-CXCR3+CCR6-, powder blue) were assessed on

52 the tSNE map. HCV-specific CD4 T cells (red) were visualized on the tSNE map per time  
53 point analyzed, indicating phenotypic changes in high dimensional space of the virus-specific  
54 CD4 T cell response after initiation of treatment.

55

56 **Supplemental Figure 8: HCV-specific CD4 T cells shift from a Th1 to a cTfh phenotype.**

57 Differentially expressed genes between Th1 cells and bulk cTfh cells from all time points  
58 (Baseline, W2, FU) were used to generate a gene set of 297 genes. The heat maps were  
59 generated using this gene set in longitudinal samples (Baseline, W2, FU) to analyze changes  
60 of HCV-specific CD4 T cells. Cutoff for generation of the heat maps was FDR < 0.05.

61 **Supplemental Table 1: Patient characteristics.** w = weeks; nT = no Tetramer positive cells; (x) = Tetramer response, but not used for  
62 phenotyping; DCV = Daclastavir; SOF = Sofosbuvir; LPV = Ledipasvir; VEL= Velpatasvir; OBV = Ombitasvir; PTV = Paritaprevir; r = Ritonavir;  
63 DSV = Dasabuvir; RBV = Ribavirin; GRZ = Grazoprevir; ELB = Elbasvir; GLE = Glecaprevir; PIB = Pibrentasvir; VOX = Voxilaprevir. All patients  
64 achieved SVR12.

Patient	Age	Genotype	relevant HLA	Therapy	SVR12	Tetramer Staining	nABs	CXCL13 ELISA
P1	52y	1a	DRB1*01:01	LPV/SOF (8w)	yes	x	x	
P2	67y	1b	DRB1*01:01	SOF/DCV (16W)	yes	x	x	x
P3	67y	1b	DRB1*15:01	LPV/SOF + RBV (12W)	yes	x	x	
P4	55y	1b	DRB1*15:01	LPV/SOF + RBV (12W)	yes	x	x	x
P5	48y	3a	DRB1*15:01	SOF/VEL (12W)	yes	x		x
P6	41y	1b	DRB1*15:01	OBV/PTV/r + DSV (12W)	yes	x	x	
P7	59y	1	DRB1*15:01	LPV/SOF + RBV (12W)	yes	x		
P8	43y	1a	DRB1*15:01	LPV/SOF (12W)	yes	x		
P9	46y	1a	DRB1*15:01	LPV/SOF (12W)	yes	x		
P10	59y	1a	DRB1 *15	LPV/SOF + RBV (12W)	yes	x	x	x
P11	64y	1a	DRB1*15:01	LPV/SOF + RBV (12W)	yes	x	x	x
P12	58y	1b	DRB1*15:01	GRZ/ELB (12W)	yes	x		x
P13	42y	3a	DRB1*15:01	SOF/DCV (12W)	yes	x		x
P14	48y	1b	DRB1*15:01	LPV/SOF (8W)	yes	x		x
P15	47y	3a	DRB1*01:01	SOF/VEL + RBV (12W)	yes	x		
P16	44y	1b	DRB1*15:01	GLE/PIB (8w)	yes	x		
P17	55y	3a	DRB1*01:01	SOF/DCV + RBV (24W)	yes	x	x	
P18	36y	3a	DRB1*01:01	SOF/VEL (12W)	yes	x		
P19	73y	1b	DRB1*15:01	GRZ/ELB (12W)	yes	x		
P20	36y	2b	DRB1*01:01	SOF + RBV (12W)	yes	x	x	
P21	42y	1a	DRB1*15:01	OBV/PTV/r + DSV + RBV (24W)	yes	nT	x	
P22	55y	1b	DBR1*15:01	LPV/SOF (8w)	yes	nT		
P23	44y	1	DRB1*01:01	LPV/SOF + RBV (12W)	yes	nT	x	x

P24	57y	1b	DRB1*15:01	OBV/PTV/r + DSV + RBV (12W)	yes	nT	x	x
P25	51y	1a	DRB1*01:01	GLE/PIB (8w)	yes	nT		
P26	63y	3a	DRB1 *01	SOF/VEL/VOX (12W)	yes	nT		
P27	57y	3a	DRB1*01:01	SOF/DCV (12W)	yes	nT		x
P28	19y	1a	DRB1*01:01	GLE/PIB (8w)	yes	nT		
P29	49y	1a	DRB1*15:01	LPV/SOF (12W)	yes	nT	x	
P30	55y	1a	DRB1*15:01	LPV/SOF (12W)	yes	(x)	x	x
P31	78y	1b	DRB1*15:01	GLE/PIB (8w)	yes	x		
P32	62y	2b	DRB1*01:01	SOF + RBV (12W)	yes	x		
P33	36y	1	DRB1*15:01	OBV/PTV/r + DSV (12W)	yes	x		
P34	61y	1a	DRB1*15:01	GRZ/ELB (12W)	yes	x		
P35	58y	1	DRB1*01:01	LPV/SOF + RBV (24W)	yes	x	x	
P36	24y	1b	DRB1*15:01	LPV/SOF (12W)	yes	x		
P37	55y	1a	DRB1*15:01	GLE/PIB (8w)	yes	x		
P38	45y	1a	DRB1*15:01	LPV/SOF (12W)	yes	x		
P39	50y	1b	DRB1*15:01	OBV/PTV/r + DSV + RBV (12W)	yes	x	x	
P40	68y	1a	DRB1*15:01	LPV/SOF (8w)	yes	nT		
P41	57y	1b	DRB1*01:01	LPV/SOF + RBV (12W)	yes	nT		
P42	62y	2c	DRB1*01:01	GLE/PIB (8w)	yes	nT		
P43	44y	3	DRB1*01:01	GLE/PIB (8w)	yes	nT		
P44	55y	1a	DRB1*01:01	LPV/SOF (12W)	yes	nT		
P45	41y	3a		SOF/DCV (12W)	yes		x	x
P46	71y	1		LPV/SOF + RBV (24W)	yes		x	
P47	42y	1b		LPV/SOF (8w)	yes		x	
P48	59y	1b		OBV/PTV/r + DSV + RBV (12W)	yes		x	
P49	35y	1b		LPV/SOF (8w)	yes		x	
P50	49y	1a		LPV/SOF (12W)	yes		x	x
P51	77y	1b		LPV/SOF (12W)	yes		x	x
P52	48y	1b		LPV/SOF (8w)	yes		x	
P53	31y	1b		LPV/SOF (8w)	yes		x	
P54	58y	3a		SOF + RBV (24W)	yes		x	x
P55	61y	3a		LPV/SOF + RBV (24W)	yes		x	
P56	40y	1b		GRZ/ELB (12W)	yes			x

P57	56y	1b		LPV/SOF (12W)	yes		x	
P58	60y	3a		SOF/VEL (12W)	yes			x
P59	51y	1a		LPV/SOF (12W)	yes		x	
P60	61y	1b		LPV/SOF (12W)	yes		x	
P61	20y	1b		LPV/SOF (8w)	yes		x	
P62	34y	1b		LPV/SOF (8w)	yes		x	
P63	64y	1a		LPV/SOF + RBV (12W)	yes		x	
P64	47y	1a		LPV/SOF (12W)	yes		x	
P65	59y	1b		LPV/SOF (8w)	yes		x	
P66	28y	1b		LPV/SOF (8w)	yes		x	
P67	56y	1b		LPV/SOF (8w)	yes		x	
P68	75y	1b		GRZ/ELB (12W)	yes			x
P69	59y	1a		SOF/VEL (12W)	yes			x
P70	32y	3a		GLE/PIB (8w)	yes			x
P71	32y	1a		LPV/SOF (8w)	yes			x
P72	67y	1b		OBV/PTV/r + DSV (8w)	yes			x
P73	56y	3a		SOF/VEL (12W)	yes			x
P74	46y	1a		LPV/SOF (12W)	yes			x
P75	42y	3a		SOF/VEL (12W)	yes			x
P76	50y	3a		SOF/VEL (12W)	yes			x

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66

67 **Supplemental Table 2: Used Tetramers.** Tetramers were purchased from MBL, Woburn,  
 68 United States.

HLA molecule	Protein	Position	Sequence
DRB1*01:01	HCV-NS4B	aa 1806–1818	TLLFNILGGWVAA
DRB1*15:01	HCV-NS3	aa 1411–1425	GINAVAYYRGLDVSV
DRB1*15:01	HCV-NS3	aa 1582–1597	NFPYLVAYQATVCARA
DRB1*15:01	CLIP		PVSKMRMATPLLMQA

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71 **Supplemental Table 3: Antibodies.**

Antigen	Fluorophore	Clone	Provider	Staining
CD4	FITC	RPA-T4	BD Bioscience	extracellular
CXCR5	BV421	RF8B2	BD Bioscience	extracellular
CD127	BV510	HIL-7R-M21	BD Bioscience	extracellular
CCR6	BV605	11A9	BD Bioscience	extracellular
PD-1	BV786	EH12.1	BD Bioscience	extracellular
OX40	PE-Cy7	ACT-35	BD Bioscience	extracellular
CCR7	BUV395	150503	BD Bioscience	extracellular
CD4	BV510	SK3	BD Bioscience	extracellular/ intracellular
CD45RA	BV711	HI100	BD Bioscience	extracellular
CTLA-4	BV421	BNI3	BD Bioscience	extracellular
CD39	BUV395	TU66	BD Bioscience	extracellular
CD38	BUV737	HB7	BD Bioscience	extracellular
CD45RA	PerCP-Cy5.5	HI100	eBioscience	extracellular
ICOS	APC	ISA-3	eBioscience	extracellular
CD14	APC-eFluor780	61D3	eBioscience	extracellular
CD19	APC-eFluor780	HIB19	eBioscience	extracellular
fixable viability dye	APC-eFluor780		eBioscience	extracellular
TIGIT	PE-Cy7	MBSA43	eBioscience	extracellular
CD25	BV650	BC96	Biolegend	extracellular
CXCR3	BV711	G025H7	Biolegend	extracellular
CCR7	AlexaFluor488	G043H7	Biolegend	extracellular
CD305	PerCP-Cy5.5	NKTA255	Biolegend	extracellular
BTLA	APC	MIH26	Biolegend	extracellular
IL-2	BV605	MQ1-17H12	BD Bioscience	intracellular
IL-21	AlexaFluor647	3A3-N2.1	BD Bioscience	intracellular
TNF	PE-Cy7	MAb11	BD Bioscience	intracellular
IFN $\gamma$	FITC	25723.11	BD Bioscience	intracellular
TCF-1	AlexaFluor647	7F11A10	Biolegend	Intranuclear
KI-67	PE-Cy7	KI-67	Biolegend	intranuclear

72

73 **Supplemental Table 4: Differentially expressed genes between bulk cTfh and bulk Th1**  
 74 **cells with FDR < 0.05.** RNAseq-based genes differentially expressed between bulk Th1 cells  
 75 (defined as CXCR3+CCR6-) and Tfh cells (defined as CXCR5+PD-1+CXCR3-) from all time  
 76 points of three individual patients. Cutoff was FDR < 0.05.

	padj	name	type
ENSG00000186810,7	2,10E-88	CXCR3	protein_coding
ENSG00000073861,2	1,80E-23	TBX21	protein_coding
ENSG00000007264,9	3,08E-18	MATK	protein_coding
ENSG00000145220,9	7,10E-18	LYAR	protein_coding
ENSG00000115607,5	1,07E-11	IL18RAP	protein_coding
ENSG00000115956,9	1,20E-11	PLEK	protein_coding
ENSG00000240535,4	1,20E-11	CTD-2313F11,1	processed_transcript
ENSG00000196549,6	1,22E-10	MME	protein_coding
ENSG00000115687,9	2,69E-10	PASK	protein_coding
ENSG00000163629,8	1,34E-09	PTPN13	protein_coding
ENSG00000137501,12	1,36E-09	SYTL2	protein_coding
ENSG00000020633,14	3,95E-09	RUNX3	protein_coding
ENSG00000078304,15	4,88E-09	PPP2R5C	protein_coding
ENSG00000026297,11	6,15E-09	RNASET2	protein_coding
ENSG00000151883,12	1,31E-08	PARP8	protein_coding
ENSG00000198915,7	1,31E-08	RASGEF1A	protein_coding
ENSG00000185046,14	2,18E-08	ANKS1B	protein_coding
ENSG00000077984,4	1,79E-07	CST7	protein_coding
ENSG00000169756,12	1,84E-07	LIMS1	protein_coding
ENSG00000169252,4	4,78E-07	ADRB2	protein_coding
ENSG00000240954,1	4,78E-07	RPL4P1	pseudogene
ENSG00000181847,7	5,92E-07	TIGIT	protein_coding
ENSG00000256069,3	6,16E-07	A2MP1	pseudogene
ENSG00000124564,13	6,83E-07	SLC17A3	protein_coding
ENSG00000118503,10	6,83E-07	TNFAIP3	protein_coding
ENSG00000116574,4	6,94E-07	RHOA	protein_coding
ENSG00000227036,2	7,41E-07	LINC00511	lincRNA
ENSG00000178573,6	7,51E-07	MAF	protein_coding
ENSG00000171435,9	8,39E-07	KSR2	protein_coding
ENSG00000176083,13	1,10E-06	ZNF683	protein_coding
ENSG00000026025,9	2,08E-06	VIM	protein_coding
ENSG00000111796,3	2,20E-06	KLRB1	protein_coding
ENSG00000167094,11	2,64E-06	TTC16	protein_coding
ENSG00000066468,16	2,91E-06	FGFR2	protein_coding
ENSG00000235532,1	3,46E-06	LINC00402	lincRNA



ENSG00000154451,10	5,25E-06	GBP5	protein_coding
ENSG00000139187,5	5,70E-06	KLRG1	protein_coding
ENSG00000175899,10	8,06E-06	A2M	protein_coding
ENSG00000228509,1	8,18E-06	AC006460,2	antisense
ENSG00000125657,3	8,21E-06	TNFSF9	protein_coding
ENSG00000260807,2	9,49E-06	RP11-161M6,2	lincRNA
ENSG00000029534,15	1,09E-05	ANK1	protein_coding
ENSG00000263466,1	1,16E-05	RP1-56K13,2	antisense
ENSG00000261573,1	1,19E-05	RP11-553K8,5	antisense
ENSG00000110651,7	2,11E-05	CD81	protein_coding
ENSG00000176845,8	2,67E-05	METRNL	protein_coding
ENSG00000237945,3	2,76E-05	LINC00649	antisense
ENSG00000138386,12	2,79E-05	NAB1	protein_coding
ENSG00000012048,15	2,79E-05	BRCA1	protein_coding
ENSG00000169508,6	3,31E-05	GPR183	protein_coding
ENSG00000160310,12	3,93E-05	PRMT2	protein_coding
ENSG00000213071,6	4,79E-05	LPAL2	pseudogene
ENSG00000227963,1	5,00E-05	RP5-1074L1,1	antisense
ENSG00000235162,4	6,16E-05	C12orf75	protein_coding
ENSG00000142669,9	9,59E-05	SH3BGRL3	protein_coding
ENSG00000100298,11	0,000106075	APOBEC3H	protein_coding
ENSG00000230266,1	0,000111029	XXYL1-AS2	antisense
ENSG00000173585,11	0,000125997	CCR9	protein_coding
ENSG00000109743,6	0,000125997	BST1	protein_coding
ENSG00000145649,7	0,000129521	GZMA	protein_coding
ENSG00000189067,8	0,000137871	LITAF	protein_coding
ENSG00000102265,7	0,000140684	TIMP1	protein_coding
ENSG00000143153,8	0,000141401	ATP1B1	protein_coding
ENSG00000136111,8	0,000180723	TBC1D4	protein_coding
ENSG00000213735,2	0,000184679	ANAPC10P1	pseudogene
ENSG00000071539,9	0,000184679	TRIP13	protein_coding
ENSG00000105963,9	0,000186149	ADAP1	protein_coding
ENSG00000090104,7	0,000189643	RGS1	protein_coding
ENSG00000026751,12	0,0002115	SLAMF7	protein_coding
ENSG00000140859,11	0,000216659	KIFC3	protein_coding
ENSG00000138378,13	0,000218289	STAT4	protein_coding
ENSG00000107485,11	0,000238781	GATA3	protein_coding
ENSG00000198650,6	0,000239754	TAT	protein_coding
ENSG00000261390,1	0,00025532	RP11-345M22,2	lincRNA
ENSG00000239713,3	0,000283393	APOBEC3G	protein_coding
ENSG00000145819,11	0,000296581	ARHGAP26	protein_coding
ENSG00000134107,4	0,000302882	BHLHE40	protein_coding
ENSG00000249859,3	0,000315648	PVT1	processed_transcript
ENSG00000260905,1	0,000329126	RP11-105C19,1	lincRNA
ENSG00000240065,3	0,000341061	PSMB9	protein_coding
ENSG00000147533,12	0,000341061	GOLGA7	protein_coding

ENSG00000141401,7	0,00034904	IMPA2	protein_coding
ENSG00000255733,1	0,000433768	IFNG-AS1	antisense
ENSG00000205726,9	0,000447097	ITSN1	protein_coding
ENSG00000218357,3	0,000493234	LL22NC03-75H12,2	protein_coding
ENSG00000163508,8	0,000499351	EOMES	protein_coding
ENSG00000135318,7	0,000499351	NT5E	protein_coding
ENSG00000126264,5	0,000521324	HCST	protein_coding
ENSG00000166681,9	0,000521324	NGFRAP1	protein_coding
ENSG00000160932,6	0,000528143	LY6E	protein_coding
ENSG00000239272,1	0,000528143	RPL21P10	pseudogene
ENSG00000238164,2	0,000528589	RP3-395M20,8	processed_transcript
ENSG00000182383,8	0,000569235	RPL27AP5	pseudogene
ENSG00000188522,10	0,000697487	FAM83G	protein_coding
ENSG00000144290,12	0,000745593	SLC4A10	protein_coding
ENSG00000002586,13	0,000799399	CD99	protein_coding
ENSG00000197448,9	0,000818538	GSTK1	protein_coding
ENSG00000213394,3	0,000957042	RP4-747G18,5	pseudogene
ENSG00000182768,7	0,001015017	NGRN	protein_coding
ENSG00000128791,7	0,001059431	TWSG1	protein_coding
ENSG00000211898,3	0,001074202	IGHD	IG_C_gene
ENSG00000226499,1	0,001122598	RP5-882O7,1	pseudogene
ENSG00000231858,1	0,001236759	AC067945,4	processed_transcript
ENSG00000185920,11	0,001288745	PTCH1	protein_coding
ENSG00000165949,8	0,001553137	IFI27	protein_coding
ENSG00000138385,11	0,001589897	SSB	protein_coding
ENSG00000228915,3	0,001726439	OR7E128P	pseudogene
ENSG00000169398,15	0,001847027	PTK2	protein_coding
ENSG00000153250,13	0,001968546	RBMS1	protein_coding
ENSG00000168229,3	0,002150923	PTGDR	protein_coding
ENSG00000184588,13	0,002433011	PDE4B	protein_coding
ENSG00000143184,4	0,002433011	XCL1	protein_coding
ENSG00000211697,2	0,002433011	TRGV5	TR_V_gene
ENSG00000141232,4	0,002433011	TOB1	protein_coding
ENSG00000185864,12	0,002618627	NPIPBA	protein_coding
ENSG00000267986,1	0,002779713	AC130469,2	antisense
ENSG00000185710,5	0,002931321	RP11-645C24,2	pseudogene
ENSG00000167083,2	0,002931321	GNGT2	protein_coding
ENSG00000232564,1	0,003298392	RP4-591N18,2	antisense
ENSG00000260027,3	0,00334681	HOXB7	protein_coding
ENSG00000182253,10	0,003581818	SYNM	protein_coding
ENSG00000198846,5	0,003646208	TOX	protein_coding
ENSG00000240463,1	0,003646208	RPS19P3	pseudogene
ENSG00000213386,3	0,00373498	RP11-779O18,2	pseudogene
ENSG00000268204,1	0,003880625	CTD-3214H19,6	antisense
ENSG00000240219,1	0,003930347	RP11-430C7,5	lincRNA
ENSG00000241490,1	0,004015289	RP11-553L6,2	antisense

ENSG00000005249,8	0,004015289	PRKAR2B	protein_coding
ENSG00000230747,1	0,004042364	AC021188,4	antisense
ENSG00000170571,7	0,004098637	EMB	protein_coding
ENSG00000160051,7	0,004402778	IQCC	protein_coding
ENSG00000042493,11	0,004846058	CAPG	protein_coding
ENSG00000129116,13	0,004888433	PALLD	protein_coding
ENSG00000003147,13	0,004888433	ICA1	protein_coding
ENSG00000168778,7	0,004936294	TCTN2	protein_coding
ENSG00000116985,6	0,005023049	BMP8B	protein_coding
ENSG00000140853,11	0,005023049	NLRC5	protein_coding
ENSG00000243829,1	0,005023049	CTB-33G10,1	pseudogene
ENSG00000131849,10	0,005023049	ZNF132	protein_coding
ENSG00000108861,4	0,005336277	DUSP3	protein_coding
ENSG00000170509,7	0,005653444	HSD17B13	protein_coding
ENSG00000121621,6	0,006227827	KIF18A	protein_coding
ENSG00000185442,8	0,006310393	FAM174B	protein_coding
ENSG00000250151,5	0,006458475	ARPC4-TTLL3	protein_coding
ENSG00000235781,1	0,006458475	XXbac-BPG249D20,9	antisense
ENSG00000271886,1	0,006597077	MIR98	miRNA
ENSG00000163612,10	0,007634216	FAM86KP	pseudogene
ENSG00000197830,2	0,007634216	AC011385,1	pseudogene
ENSG00000105472,8	0,007636275	CLEC11A	protein_coding
ENSG00000259641,1	0,007727843	RP11-279F6,3	lincRNA
ENSG00000183570,12	0,007810437	PCBP3	protein_coding
ENSG00000008256,11	0,007900887	CYTH3	protein_coding
ENSG00000152056,12	0,008267419	AP1S3	protein_coding
ENSG00000227507,2	0,008267419	LTB	protein_coding
ENSG00000254364,1	0,008267419	KB-1615E4,3	antisense
ENSG00000184613,6	0,008267419	NELL2	protein_coding
ENSG00000161791,9	0,008267419	FMNL3	protein_coding
ENSG00000265500,1	0,008267419	SEN3-EIF4A1	processed_transcript
ENSG00000264745,1	0,008267419	RP11-403A21,2	antisense
ENSG00000271554,1	0,008534246	RP4-665N4,8	antisense
ENSG00000125384,6	0,008601131	PTGER2	protein_coding
ENSG00000146540,10	0,008670895	C7orf50	protein_coding
ENSG00000157985,13	0,008988052	AGAP1	protein_coding
ENSG00000136738,10	0,008988052	STAM	protein_coding
ENSG00000135362,9	0,008988052	PRR5L	protein_coding
ENSG00000150457,7	0,009040023	LATS2	protein_coding
ENSG00000238294,1	0,009082758	snoU13	snoRNA
ENSG00000169896,12	0,009427611	ITGAM	protein_coding
ENSG00000228169,3	0,009558169	PPIAP19	pseudogene
ENSG00000183971,5	0,009558169	NPW	protein_coding
ENSG00000272690,1	0,009896756	RP11-803B1,8	lincRNA
ENSG00000106991,9	0,010267308	ENG	protein_coding
ENSG00000177030,12	0,010782958	DEAF1	protein_coding

ENSG00000188641,8	0,011111802	DPYD	protein_coding
ENSG00000162174,8	0,011111802	ASRGL1	protein_coding
ENSG00000235576,1	0,011244849	AC092580,4	lincRNA
ENSG00000207741,1	0,01143046	MIR590	miRNA
ENSG00000105953,10	0,011432382	OGDH	protein_coding
ENSG00000228653,2	0,011996969	HNRNPCP7	pseudogene
ENSG00000119632,3	0,012050423	IFI27L2	protein_coding
ENSG00000168685,10	0,01279692	IL7R	protein_coding
ENSG00000221714,2	0,01279692	AC130352,1	miRNA
ENSG00000204220,5	0,012833888	PFDN6	protein_coding
ENSG00000151651,11	0,012893964	ADAM8	protein_coding
ENSG00000165929,8	0,012925507	TC2N	protein_coding
ENSG00000233757,2	0,01329412	AC092835,2	lincRNA
ENSG00000152380,5	0,01329412	FAM151B	protein_coding
ENSG00000198208,7	0,013318993	RPS6KL1	protein_coding
ENSG00000273218,1	0,013318993	LLNLR-246C6,1	lincRNA
ENSG00000261008,2	0,013343645	AC004158,2	lincRNA
ENSG00000065548,13	0,013682057	ZC3H15	protein_coding
ENSG00000225986,1	0,014093423	RP3-340N1,5	antisense
ENSG00000149557,8	0,014609848	FEZ1	protein_coding
ENSG00000164086,8	0,015138301	DUSP7	protein_coding
ENSG00000164687,6	0,015138301	FABP5	protein_coding
ENSG00000172458,4	0,015138301	IL17D	protein_coding
ENSG00000155090,10	0,015328074	KLF10	protein_coding
ENSG00000115526,6	0,015644276	CHST10	protein_coding
ENSG00000106605,6	0,015752728	BLVRA	protein_coding
ENSG00000236790,1	0,01593652	LINC00299	lincRNA
ENSG00000235522,2	0,016335021	AC009505,2	antisense
ENSG00000260017,1	0,016335021	RP11-1035H13,2	antisense
ENSG00000136810,8	0,016367336	TXN	protein_coding
ENSG00000079277,15	0,017344558	MKNK1	protein_coding
ENSG00000170819,4	0,018116025	BFSP2	protein_coding
ENSG00000178075,15	0,019074308	GRAMD1C	protein_coding
ENSG00000204272,6	0,02066744	RP11-622K12,1	processed_transcript
ENSG00000099860,4	0,020930121	GADD45B	protein_coding
ENSG00000242100,2	0,020930121	RPL9P32	pseudogene
ENSG00000251891,1	0,021213214	RNU7-79P	snRNA
ENSG00000213963,2	0,021286413	AC074286,1	sense_overlapping
ENSG00000232439,1	0,021543672	RPL18AP7	pseudogene
ENSG00000211778,2	0,021604265	TRAV4	TR_V_gene
ENSG00000227492,1	0,022353943	RP11-316M21,6	antisense
ENSG00000115738,5	0,02269169	ID2	protein_coding
ENSG00000106829,14	0,022735006	TLE4	protein_coding
ENSG00000136104,14	0,022735006	RNASEH2B	protein_coding
ENSG00000103550,9	0,022735006	KNOP1	protein_coding
ENSG00000256222,1	0,022735006	MTRNR2L3	protein_coding

ENSG00000182247,5	0,022894274	UBE2E2	protein_coding
ENSG00000149260,10	0,023342468	CAPN5	protein_coding
ENSG00000237805,1	0,023659247	AC015849,2	antisense
ENSG00000196814,10	0,023823939	MVB12B	protein_coding
ENSG00000158545,11	0,023917945	ZC3H18	protein_coding
ENSG00000101294,12	0,024598496	HM13	protein_coding
ENSG00000135845,5	0,025034058	PIGC	protein_coding
ENSG00000135404,7	0,025036732	CD63	protein_coding
ENSG00000071205,7	0,025284343	ARHGAP10	protein_coding
ENSG00000104368,13	0,025644319	PLAT	protein_coding
ENSG00000267041,1	0,025644319	ZNF850	protein_coding
ENSG00000153283,8	0,025936837	CD96	protein_coding
ENSG00000254206,1	0,025936837	NPIP11	protein_coding
ENSG00000123146,15	0,025936837	CD97	protein_coding
ENSG00000270024,1	0,026161802	C8orf44-SGK3	protein_coding
ENSG00000169299,9	0,026439328	PGM2	protein_coding
ENSG00000257800,1	0,026785245	FNBP1P1	pseudogene
ENSG00000082074,11	0,027633712	FYB	protein_coding
ENSG00000115271,6	0,027699532	GCA	protein_coding
ENSG00000224856,2	0,02793534	RP4-796I17,5	pseudogene
ENSG00000266240,1	0,027939103	MIR5091	miRNA
ENSG00000080493,9	0,027954796	SLC4A4	protein_coding
ENSG00000159339,9	0,028473142	PADI4	protein_coding
ENSG00000159640,10	0,028614712	ACE	protein_coding
ENSG00000231503,3	0,029010103	PTMAP4	pseudogene
ENSG00000143198,8	0,029306297	MGST3	protein_coding
ENSG00000126838,5	0,029482418	PZP	protein_coding
ENSG00000269843,1	0,029497806	CTC-490E21,10	lincRNA
ENSG00000100097,7	0,029558465	LGALS1	protein_coding
ENSG00000175352,6	0,029823091	NRIP3	protein_coding
ENSG00000232006,4	0,029934835	AC005537,2	processed_transcript
ENSG00000259932,1	0,030092204	CTD-2651B20,7	sense_intronic
ENSG00000244733,4	0,030515139	RP11-506M13,3	lincRNA
ENSG00000159648,7	0,031138318	TEPP	protein_coding
ENSG00000224287,2	0,03239099	MSL3P1	pseudogene
ENSG00000126709,10	0,033280724	IFI6	protein_coding
ENSG00000143549,15	0,033281929	TPM3	protein_coding
ENSG00000136770,6	0,033345609	DNAJC1	protein_coding
ENSG00000234361,1	0,034983218	RP11-52J3,3	antisense
ENSG00000196355,2	0,035665782	AC021860,1	protein_coding
ENSG00000102908,16	0,03617965	NFAT5	protein_coding
ENSG00000257698,1	0,036246862	RP11-620J15,3	lincRNA
ENSG00000153885,10	0,036246862	KCTD15	protein_coding
ENSG00000171791,10	0,036504173	BCL2	protein_coding
ENSG00000168918,9	0,036571653	INPP5D	protein_coding
ENSG00000122694,11	0,036571653	GLIPR2	protein_coding

ENSG00000110324,5	0,036663944	IL10RA	protein_coding
ENSG00000198155,5	0,036712257	ZNF876P	pseudogene
ENSG00000133962,3	0,038510644	CATSPERB	protein_coding
ENSG00000271913,1	0,038919415	RP1-111C20,4	antisense
ENSG00000104154,5	0,03896442	SLC30A4	protein_coding
ENSG00000131899,6	0,03896442	LLGL1	protein_coding
ENSG00000272840,1	0,041082101	RP11-379B18,6	lincRNA
ENSG00000129968,11	0,041496516	ABHD17A	protein_coding
ENSG00000074657,9	0,043229305	ZNF532	protein_coding
ENSG00000118307,14	0,043261518	CASC1	protein_coding
ENSG00000179820,11	0,043261518	MYADM	protein_coding
ENSG00000162426,10	0,043347748	SLC45A1	protein_coding
ENSG00000109787,8	0,04378842	KLF3	protein_coding
ENSG00000188215,5	0,04378842	DCUN1D3	protein_coding
ENSG00000266222,1	0,04378842	RP11-433M22,1	sense_intronic
ENSG00000100030,10	0,04386809	MAPK1	protein_coding
ENSG00000144214,5	0,04493736	LYG1	protein_coding
ENSG00000230037,1	0,04493736	UBBP1	pseudogene
ENSG00000188451,7	0,04493736	SRP72P2	pseudogene
ENSG00000258640,3	0,04493736	RPL21P5	pseudogene
ENSG00000213967,6	0,04493736	ZNF726	protein_coding
ENSG00000131746,8	0,046644836	TNS4	protein_coding
ENSG00000211879,1	0,047649348	TRAJ10	TR_J_gene
ENSG00000252835,1	0,047649348	SCARNA21	snoRNA
ENSG00000223804,1	0,047661564	RP6-206I17,1	lincRNA
ENSG00000089012,10	0,048195155	SIRPG	protein_coding
ENSG00000138758,7	0,048939068	Sep 11	protein_coding
ENSG00000222501,1	0,048939068	RNU4-25P	snRNA
ENSG00000162843,13	0,049223976	WDR64	protein_coding
ENSG00000159618,11	0,049223976	GPR114	protein_coding
ENSG00000269680,1	0,049223976	CTD-3128G10,6	antisense
ENSG00000211667,2	0,049223976	IGLV3-12	IG_V_gene

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79 **Supplemental Table 5: Differentially expressed genes between bulk cTfh and HCV-**  
80 **specific CD4 T cells at baseline with FDR < 0.01.** RNAseq-based genes differentially  
81 expressed between HCV-specific CD4 T cells at baseline and Tfh cells (defined as  
82 CXCR5+PD-1+CXCR3-) from all time points of three individual patients. Cutoff was FDR <  
83 0.01.

	padj	name	type
ENSG00000188917.10	7,67E-26	TRMT2B	protein_coding
ENSG00000125657.3	8,59E-24	TNFSF9	protein_coding
ENSG00000211746.3	9,56E-18	TRBV19	TR_V_gene
ENSG00000186810.7	5,46E-12	CXCR3	protein_coding
ENSG00000075336.7	3,95E-10	TIMM21	protein_coding
ENSG00000184005.9	4,63E-10	ST6GALNAC3	protein_coding
ENSG00000168096.10	7,16E-10	ANKS3	protein_coding
ENSG00000099821.9	1,67E-09	POLRMT	protein_coding
ENSG00000211817.2	3,24E-09	TRAV38-2DV8	TR_V_gene
ENSG00000140688.12	4,15E-09	C16orf58	protein_coding
ENSG00000204789.3	9,38E-09	ZNF204P	pseudogene
ENSG00000177669.3	1,70E-08	MBOAT4	protein_coding
ENSG00000167083.2	3,16E-08	GNGT2	protein_coding
ENSG00000171657.5	3,38E-08	GPR82	protein_coding
ENSG00000246898.1	3,76E-08	LINC00920	lincRNA
ENSG00000267758.1	5,15E-08	RP11-358B23.5	antisense
ENSG00000236514.1	1,16E-07	RP11-162G10.5	antisense
ENSG00000134297.6	1,42E-07	PLEKHA8P1	pseudogene
ENSG00000184619.3	1,44E-07	KRBA2	protein_coding
ENSG00000107443.11	1,50E-07	CCNJ	protein_coding
ENSG00000252128.1	1,76E-07	SNORD27	snoRNA
ENSG00000137474.15	4,28E-07	MYO7A	protein_coding
ENSG00000183570.12	4,28E-07	PCBP3	protein_coding
ENSG00000234141.1	7,99E-07	AC009473.1	antisense
ENSG00000164291.12	1,56E-06	ARSK	protein_coding
ENSG00000211778.2	2,58E-06	TRAV4	TR_V_gene
ENSG00000149970.10	2,83E-06	CNKSR2	protein_coding
ENSG00000250889.2	3,00E-06	RP11-229C3.2	lincRNA
ENSG00000096717.7	3,10E-06	SIRT1	protein_coding
ENSG00000211706.2	3,20E-06	TRBV6-1	TR_V_gene
ENSG00000168243.6	3,28E-06	GNG4	protein_coding
ENSG00000175073.7	4,02E-06	VCPIP1	protein_coding
ENSG00000270164.1	5,35E-06	AC006129.4	lincRNA
ENSG00000079385.17	5,35E-06	CEACAM1	protein_coding
ENSG00000126787.8	6,60E-06	DLGAP5	protein_coding
ENSG00000154803.8	8,60E-06	FLCN	protein_coding
ENSG00000071073.8	1,32E-05	MGAT4A	protein_coding
ENSG00000169508.6	1,72E-05	GPR183	protein_coding
ENSG00000252835.1	1,72E-05	SCARNA21	snoRNA
ENSG00000241484.5	1,97E-05	ARHGAP8	protein_coding
ENSG00000260054.1	2,13E-05	RP11-611L7.1	lincRNA

ENSG00000154217.10	2,69E-05	PITPNC1	protein_coding
ENSG00000211797.2	2,78E-05	TRAV17	TR_V_gene
ENSG00000211886.1	3,59E-05	TRAJ3	TR_J_gene
ENSG00000178904.14	3,87E-05	DPY19L3	protein_coding
ENSG00000182118.5	5,11E-05	FAM89A	protein_coding
ENSG00000175449.9	5,32E-05	RFESD	protein_coding
ENSG00000102878.11	5,32E-05	HSF4	protein_coding
ENSG00000203497.2	5,32E-05	PDCD4-AS1	antisense
ENSG00000101842.9	5,32E-05	VSIG1	protein_coding
ENSG00000211796.1	5,43E-05	TRAV16	TR_V_gene
ENSG00000239272.1	5,60E-05	RPL21P10	pseudogene
ENSG00000185504.12	6,02E-05	C17orf70	protein_coding
ENSG00000133069.10	6,41E-05	TMCC2	protein_coding
ENSG00000164442.8	6,69E-05	CITED2	protein_coding
ENSG00000198856.8	7,26E-05	OSTC	protein_coding
ENSG00000211721.2	7,26E-05	TRBV6-5	TR_V_gene
ENSG00000144909.7	8,53E-05	OSBPL11	protein_coding
ENSG00000115137.7	0,000118722	DNAJC27	protein_coding
ENSG00000211779.3	0,000123508	TRAV5	TR_V_gene
ENSG00000211845.1	0,000137091	TRAJ44	TR_J_gene
ENSG00000239713.3	0,000140183	APOBEC3G	protein_coding
ENSG00000130684.9	0,000142311	ZNF337	protein_coding
ENSG00000100462.11	0,000146686	PRMT5	protein_coding
ENSG00000266913.1	0,000151864	CTC-548K16.2	lincRNA
ENSG00000019582.10	0,000159286	CD74	protein_coding
ENSG00000260588.1	0,000170805	RP11-930P14.2	lincRNA
ENSG00000088888.13	0,000170805	MAVS	protein_coding
ENSG00000205940.7	0,000176699	HSP90AB2P	pseudogene
ENSG00000152268.8	0,000176915	SPON1	processed_transcript
ENSG00000105135.11	0,000176915	ILVBL	protein_coding
ENSG00000160949.12	0,000216376	TONSL	protein_coding
ENSG00000100994.7	0,000217593	PYGB	protein_coding
ENSG00000224977.1	0,000291373	RP11-160H22.3	lincRNA
ENSG00000138600.5	0,000310902	SPPL2A	protein_coding
ENSG00000110987.4	0,000322217	BCL7A	protein_coding
ENSG00000261840.1	0,000346766	RP11-146F11.1	antisense
ENSG00000196151.6	0,000422885	WDSUB1	protein_coding
ENSG00000105011.4	0,000422885	ASF1B	protein_coding
ENSG00000249896.1	0,000440611	RP11-586D19.1	lincRNA
ENSG00000146677.6	0,000440611	AC004453.8	pseudogene
ENSG00000269305.1	0,000440611	AL158147.2	protein_coding
ENSG00000104866.6	0,00047304	PPP1R37	protein_coding



ENSG00000177542.6	0,000480918	SLC25A22	protein_coding
ENSG00000142669.9	0,000513721	SH3BGRL3	protein_coding
ENSG00000242659.1	0,000599389	RP11-271C24.2	lincRNA
ENSG00000140876.7	0,000624285	NUDT7	protein_coding
ENSG00000026025.9	0,000677219	VIM	protein_coding
ENSG00000078114.14	0,000702064	NEBL	protein_coding
ENSG00000179455.6	0,000702456	MKRN3	protein_coding
ENSG00000104783.7	0,000703425	KCNN4	protein_coding
ENSG00000161956.8	0,000717622	SENP3	protein_coding
ENSG00000116251.5	0,000718076	RPL22	protein_coding
ENSG00000060138.8	0,000784997	YBX3	protein_coding
ENSG00000170579.10	0,000829424	DLGAP1	protein_coding
ENSG00000171302.12	0,000836714	CANT1	protein_coding
ENSG00000179761.7	0,000837709	PIPOX	protein_coding
ENSG00000234737.1	0,0008558	KRT18P15	pseudogene
ENSG00000090104.7	0,000870023	RGS1	protein_coding
ENSG00000151229.8	0,000870023	SLC2A13	protein_coding
ENSG00000230433.1	0,000903607	RP1-20B11.2	antisense
ENSG00000259453.1	0,000903607	RP11-815J21.1	sense_intronic
ENSG00000106086.14	0,000942811	PLEKHA8	protein_coding
ENSG00000183087.10	0,001041989	GAS6	protein_coding
ENSG00000099284.9	0,001067938	H2AFY2	protein_coding
ENSG00000211801.3	0,00108732	TRAV21	TR_V_gene
ENSG00000048140.13	0,001112009	TSPAN17	protein_coding
ENSG00000259658.3	0,001112009	RP11-89K11.1	protein_coding
ENSG00000138385.11	0,001142215	SSB	protein_coding
ENSG00000176890.11	0,001142215	TYMS	protein_coding
ENSG00000130024.10	0,001260334	PHF10	protein_coding
ENSG00000081665.9	0,001260334	ZNF506	protein_coding
ENSG00000227124.4	0,001346977	ZNF717	protein_coding
ENSG00000196421.3	0,001346977	LINC00176	lincRNA
ENSG00000156234.7	0,001407139	CXCL13	protein_coding
ENSG00000263813.1	0,00146221	MIR3679	miRNA
ENSG00000159712.10	0,001503026	ANKRD18CP	pseudogene
ENSG00000196176.7	0,001533323	HIST1H4A	protein_coding
ENSG00000112486.10	0,001533323	CCR6	protein_coding
ENSG00000153363.8	0,001727437	LINC00467	processed_transcript
ENSG00000164056.6	0,001923455	SPRY1	protein_coding
ENSG00000227507.2	0,001962864	LTB	protein_coding
ENSG00000167447.8	0,00197187	SMG8	protein_coding
ENSG00000103269.9	0,002182382	RHBDL1	protein_coding
ENSG00000228399.1	0,002381987	RP4-575N6.2	pseudogene

ENSG00000185085.2	0,002527354	INTS5	protein_coding
ENSG00000133641.13	0,00266273	C12orf29	protein_coding
ENSG00000227705.1	0,00266273	RP11-15M15.2	antisense
ENSG00000260360.1	0,002775173	RP11-533E19.5	lincRNA
ENSG00000231062.1	0,002775173	AC103563.9	antisense
ENSG00000182541.13	0,003140982	LIMK2	protein_coding
ENSG00000258458.1	0,003243211	CTD-2555K7.2	processed_transcript
ENSG00000264462.1	0,003243211	MIR3648	miRNA
ENSG00000093009.5	0,003243211	CDC45	protein_coding
ENSG00000211874.1	0,003318314	TRAJ15	TR_J_pseudogene
ENSG00000173281.4	0,003377701	PPP1R3B	protein_coding
ENSG00000219928.2	0,00342406	RP11-40C6.2	pseudogene
ENSG00000149809.10	0,003495985	TM7SF2	protein_coding
ENSG00000144407.5	0,003507691	PTH2R	protein_coding
ENSG00000124205.11	0,003670829	EDN3	protein_coding
ENSG00000228509.1	0,003703159	AC006460.2	antisense
ENSG00000206560.6	0,003703159	ANKRD28	protein_coding
ENSG00000174327.6	0,003846575	SLC16A13	protein_coding
ENSG00000111796.3	0,004157413	KLRB1	protein_coding
ENSG00000235532.1	0,004157413	LINC00402	lincRNA
ENSG00000099139.9	0,004160848	PCSK5	protein_coding
ENSG00000154451.10	0,004364036	GBP5	protein_coding
ENSG00000113369.4	0,004391783	ARRDC3	protein_coding
ENSG00000002586.13	0,004421674	CD99	protein_coding
ENSG00000112029.5	0,004582599	FBXO5	protein_coding
ENSG00000230091.2	0,004582599	TMEM254-AS1	antisense
ENSG00000273199.1	0,004582599	AP000692.10	antisense
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84

85

86 **Supplemental Table 6: Number of RNAseq reads assigned to each gene (gencode v19)**  
87 **for each sample.**

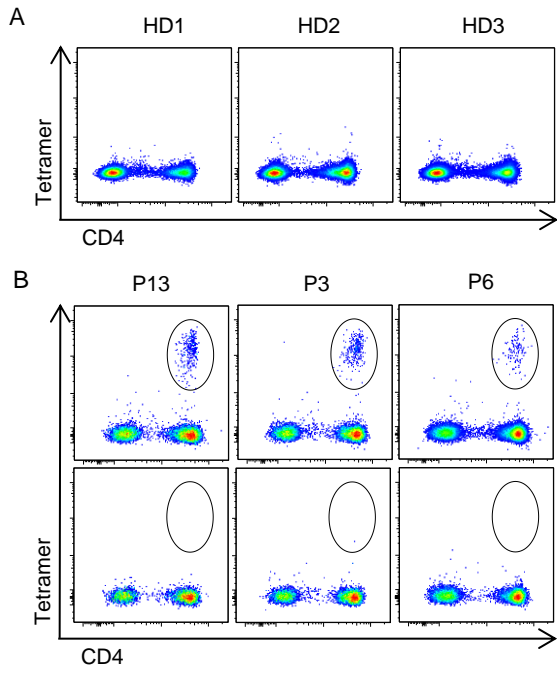
88 Individual Excel File attached.

89

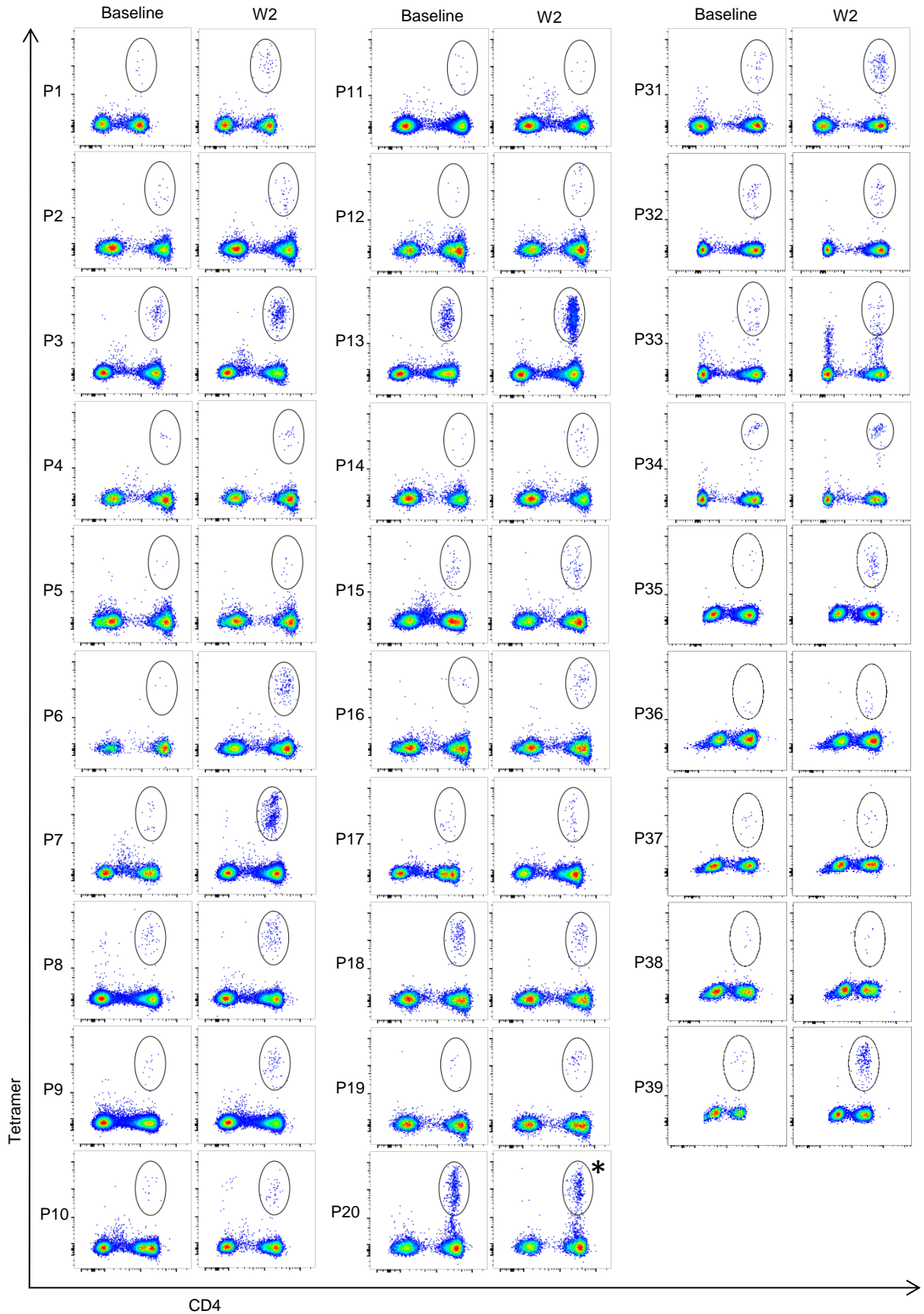
90

- 91 **Supplemental Table 7: RNAseq quality control metrics called by RNAseQC and**  
92 **samtools flagstat.**
- 93 Individual Excel File attached.

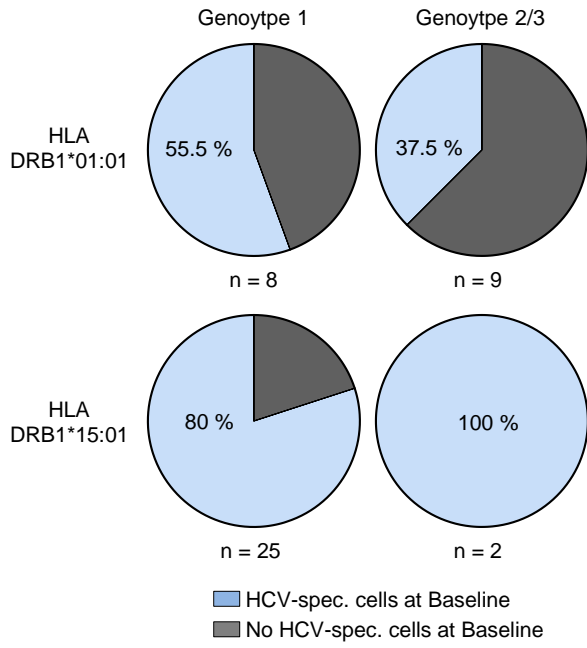
Supplemental Figure 1



Supplemental Figure 2

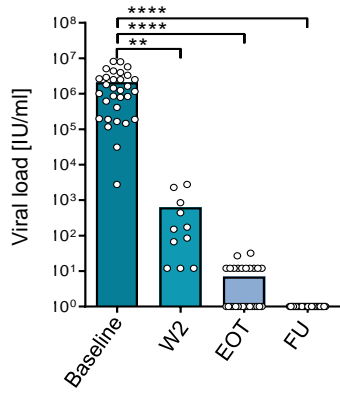


Supplemental Figure 3

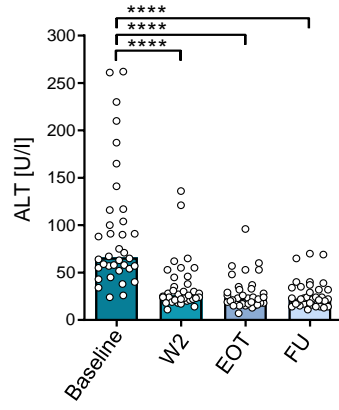


Supplemental Figure 4

A

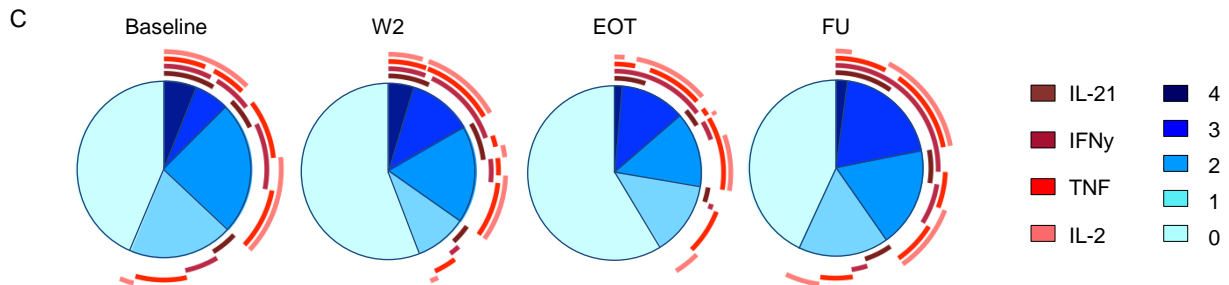
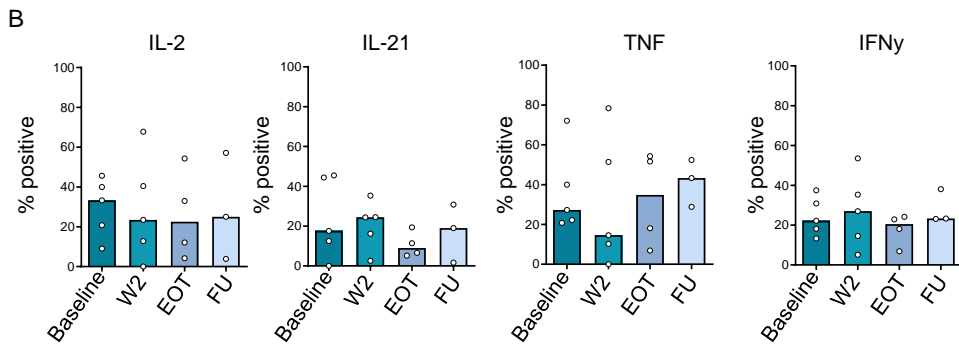
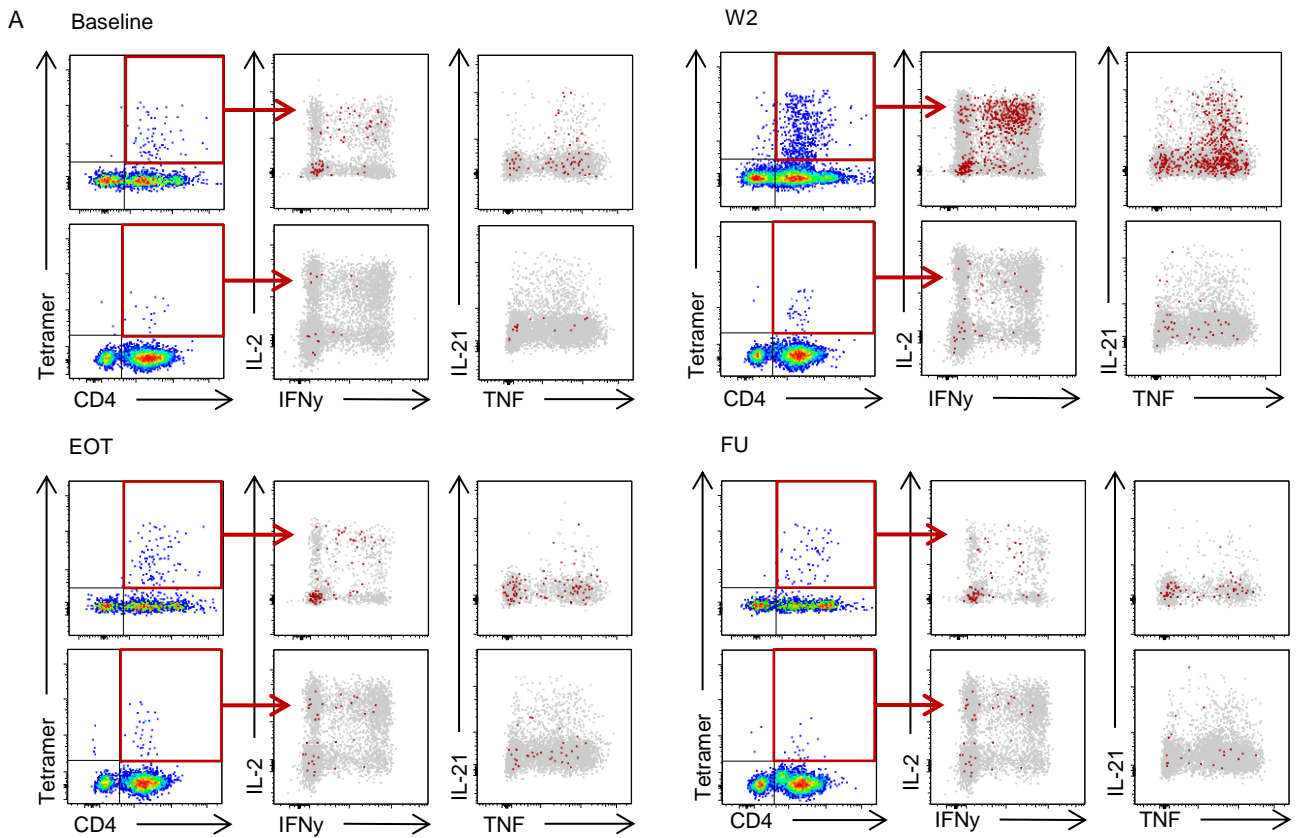


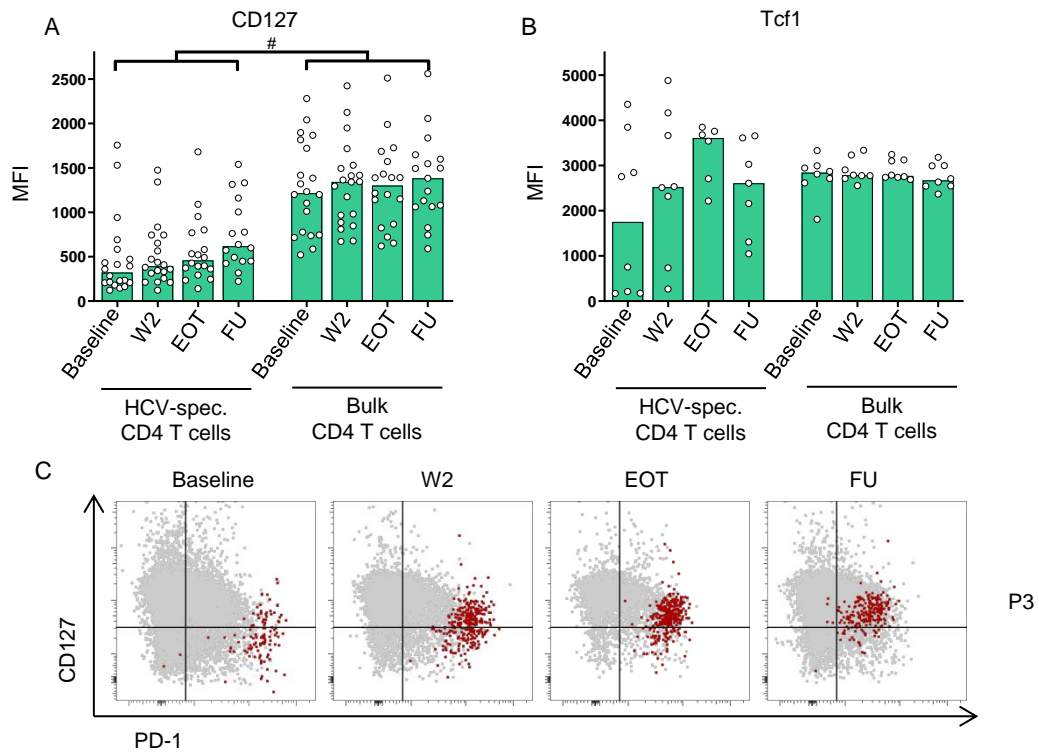
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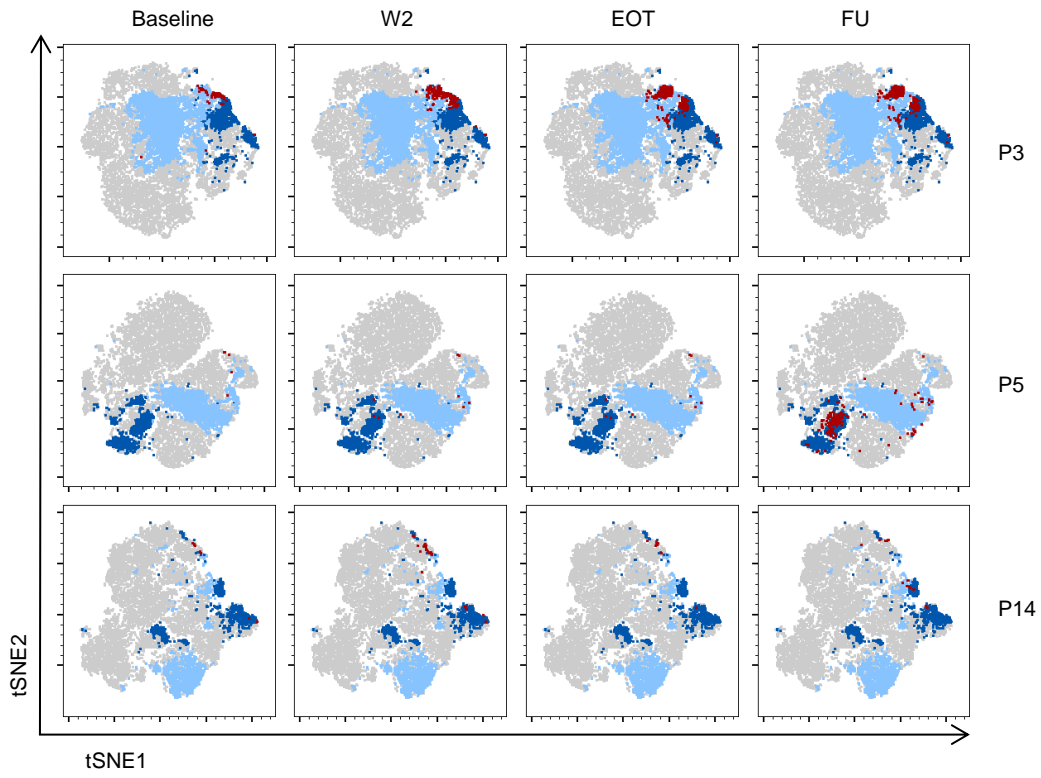


Supplemental Figure 5





Supplemental Figure 7



Supplemental Figure 8

