Supplemental digital content TABLE 1: DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF DONORS IN DIFFERENT COHORTS

Sample	Age	Sex	Viral load	CD4 (cells/ul)
CONTROL				
ND023	24	F	--	--
ND030	62	M	--	--
LR33	31	F	--	--
ND037	25	M	--	--
EG41	52	F	--	--
YL43	47	F	--	--
ND045	30	M	--	--
MP068	51	F	--	--
ART				
NVS155	48	M	<50	830
NVS159	54	M	<50	541
NVS160	31	M	<50	380
NVS162	47	F	<50	382
NVS165	55	M	<50	570
NVS166	33	M	<50	614
NVS167	63	M	<50	486
NVS168	40	M	<50	673
NVS				
NVS 5	47	M	<25	589
NVS 9	50	M	<25	600
NVS 12	38	M	<25	1245
NVS 13	51	M	<25	1020
NVS 16	41	F	<25	581
NVS 19	56	M	<25	990
NVS 20	56	F	<25	485
NVS 22	59	M	<25	630
NVS 42	57	M	<25	647
VIR				
LVL 15	59	M	551	284
LVL 17	36	F	2100	1160
LVL 19	48	F	8339	483
LVL 20	50	M	1398	632
LVL 22	43	F	10144	700
LVL 23	47	M	7953	487
LVL 25	53	F	11554	829

The effect of HIV infection on TCR-Vγ2 repertoire was evaluated in 4 donor groups: Control group included uninfected individuals; Patient group ART was selected from a cohort of HIV+ individuals receiving antiretroviral therapy and having CD4+T cell counts $\geq$350/mm^3, these patients initiated ART near to the time of diagnosis and have durable ART suppression of viremia; Patient group Natural Viral Suppressors (NVS) were selected from a cohort of individuals who maintained stable undetectable viremia without ART; Patient group with persistent viremia (VIR) were selected from a cohort of individuals who do not receive ART yet maintain stable viral loads between 50-20,000 copies of vRNA/ml of plasma without overt disease progression.

Supplemental digital content TABLE 2: PUBLIC Vγ2 CLONOTYPES IN HEALTHY AND HIV+ DONORS

PUBLIC CLONOTYPES	CONTROL n=8	ART n=8	NVS n=9	VIR n=7
CALWEV--------QELGKKIKVFGPGTKLIIT	**8**	**8**	**5**	**5**
CALWEV--R------ELGKKIKVFGPGTKLIIT	6	7	4	2
CALWE---A-----QELGKKIKVFGPGTKLIIT	5	3	2	0
CALWE---G-----QELGKKIKVFGPGTKLIIT	6	2	1	0
CALWEV--G------ELGKKIKVFGPGTKLIIT	5	2	4	1
CALWEV--L------ELGKKIKVFGPGTKLIIT	5	1	3	1
CALWEV--P------ELGKKIKVFGPGTKLIIT	4	1	1	1
CALWE---P-----QELGKKIKVFGPGTKLIIT	4	1	3	0
CALWE---E------ELGKKIKVFGPGTKLIIT	3	4	3	1
CALWE---D-----QELGKKIKVFGPGTKLIIT	2	1	0	0
CALWE---T-----QELGKKIKVFGPGTKLIIT	3	2	3	0
CALWE---------QELGKKIKVFGPGTKLIIT	2	0	1	0
CALWE---S-----QELGKKIKVFGPGTKLIIT	2	2	1	0
CALWEV--H------ELGKKIKVFGPGTKLIIT	3	3	2	0
CALWEV--LE-----ELGKKIKVFGPGTKLIIT	3	1	0	0
CALWE---AK-----ELGKKIKVFGPGTKLIIT	2	0	0	0
CALWE---AP----QELGKKIKVFGPGTKLIIT	2	1	0	1
CALWE---AQ------LGKKIKVFGPGTKLIIT	2	0	0	0
CALWE---AS----QELGKKIKVFGPGTKLIIT	2	0	0	0
CALWEV--Q-----QELGKKIKVFGPGTKLIIT	2	1	1	0
CALWEV--RG-----ELGKKIKVFGPGTKLIIT	2	0	0	0

The most common public clonotypes were identified from 8 healthy African American subjects and were scored for their presence in HIV+ groups. The number beside each sequence represents the number of subjects carrying that sequence in the particular group. The most frequent public clonotype is the canonical sequence (in bold), representing the Vγ2 chain encoded by germline elements without N region additions.

Table 3. The proportions of individuals in each group that express individual public clonotypes (%) and the average number of nucleotypes per person for each of the public clonotypes (calculated from data in Fig. 3).

Clonotype	Control	ART	NVS	VIR
CALWEV--------QELGKKIKVFGPGTKLIIT	100%, 2.4	100%, 1.9	56%, 1.0	71%, 1.0
CALWEV---R-----ELGKKIKVFGPGTKLIIT	75%, 1.1	88%, 1.4	44%, 1.1	29%, 0.7
CALWEV---A----QELGKKIKVFGPGTKLIIT	63%, 0.9	38%, 0.6	22%, 0.3	0%, 0
CALWE----G----QELGKKIKVFGPGTKLIIT	75%, 0.75	25%, 0.4	11%, 0.1	0%, 0
CALWEV---G-----ELGKKIKVFGPGTKLIIT	63%, 1.0	25%, 0.4	44%, 0.6	14%, 0.1
CALWEV---L-----ELGKKIKVFGPGTKLIIT	63%, 0.9	13%, 0.1	33%, 0.4	14%, 0.1
CALWEV---P-----ELGKKIKVFGPGTKLIIT	50%, 0.63	13%, 0.1	11%, 0.1	14%, 0.1
CALWE---P-----QELGKKIKVFGPGTKLIIT	50%, 0.75	13%, 0.6	33%, 0.6	0%, 0
Avg.	67%, 1.1	39%, 0.7	32%, 0.5	18%, 0.3

ONLINE METHODS

Human subjects:

Four groups (Table 1) were designated control (HIV-negative), natural virus suppressors (NVS), long-term nonprogressors (VIR) and patients receiving antiretroviral therapy (ART). Patient group 1 includes HIV+ individuals receiving antiretroviral therapy and having CD4+T cell counts between 60 and 303 cells/mm^3 (average 188 CD4 cells/mm^3) at treatment initiation. These patients have ≥3 years of antiretroviral therapy with durable suppression of viremia and are described in Table 1 under the group heading ART. Patients in group 2, designated as Natural Virus Suppressors or NVS, were chosen randomly from a cohort of individuals characterized by confirmed HIV infection (an average of 9.7 years after a positive HIV test) and stable, viral RNA < 25 copies/ml plasma without ART[5]. This group was studied previously[6], and is similar to elite controllers[35] or elite suppressors[36]. Patient group 3 includes HIV individuals not receiving ART and having viral loads between 551 and 11,554 copies of vRNA/ml of plasma. These individuals were diagnosed with HIV infection between 4 and 20 years earlier (average 10.1 years) and have slow or inapparent disease. They are enrolled in a cohort for patients having stable disease with low viral loads, with ready access to ART[8], and are listed in Table 1 under VIR (viremic). Finally, an uninfected control group was assembled with HIV-negative African American volunteers. All subjects in the ART, NVS and VIR groups are self-reported African Americans. We use a race-matched control group because there are significant differences in baseline levels of circulating Vγ2Vδ2 T cells between HIV-negative white and African American donors[10]. Groups were matched for

age and gender (~65% male); the major risk factors for HIV were injection drug use and heterosexual sex. We obtained on average, 250 TCR-Vγ2 chain sequences from each blood sample. From 8 control, 8 ART, 9 NVS and 7 VIR subjects we compiled approximately 8,000 sequences and studied the pattern, abundance and distribution of Jγ1.2 segments within these sequences.

Cell samples, cDNA preparation and DNA sequencing:

Purified PBMC were obtained for ART, NVS and VIR donors. Total RNA was extracted from 1-10 million cells using the RNeasy mini Kit (Qiagen, Valencia, CA), as described by the manufacturer. One μg of total RNA was then converted into cDNA using the reverse transcription system kit (Promega, Madison, WI), as described previously [37]. Polymerase chain reactions was performed as described [37] using the following primers: for the Vγ2 (Vg9 according to the IMGT nomenclature) chain, oligo Vγ2 (5' ATC AAC GCT GGC AGT CC 3') and oligo Cγ1 (5' GTT GCT CTT CTT TTC TTG CC 3'). PCR products were separated on 1% agarose/Tris-acetate-EDTA buffer (TAE) gels containing 0.5 μg/ml ethidium bromide. PCR products for the Vγ2 chain were purified by gel extraction, using QIAquick gel extraction kits (Qiagen, Valencia, CA) according to the manufacturer's instructions. Purified products were denatured (1 minute at 94°C), incubated for 30 minutes at 72°C with 2mM $MgCl_2$, 0.2mM dATP, and 2.5 units of Amplitaq gold (Promega, Madison, WI), then ligated into a pCR2.1 vector (Invitrogen, Carlsbad, CA). Ligated vector were transfected into TOP 10F' competent cells (TA cloning kit, Invitrogen, Carlsbad, CA), and bacterial colonies representing a library of Vγ2 chain sequences were grown overnight on agar plates containing 50 μg/ml ampicillin, 500 mM IPTG and 80 μg/ml X-Gal (Promega, Madison, WI). Colonies containing recombinant plasmids were cultured overnight in LB media and bacterial suspensions were used as template to amplify the Vγ2 chain inserted in the plasmid. M13 polymerase chain reactions were performed using: 2 μl of bacterial suspension as template, 100 nM each of M13 forward (5' GTA AAA CGA CGG CCA G 3') and M13 reverse primer (5' CAG GAA ACA GCT ATG AC 3'), 0.2 mM dNTPs, 2 mM $MgCl_2$, 10 mM Tris pH 8.8, 50 mM KCl, 0.1%Triton X-100 and 1 unit of AmpliTaq Gold (Promega, Madison, WI). PCR were run with the following profile: denaturation: 1 min at 94°C; 25 cycles (45 s at 94°C, 1 min at 60°C, 1 min at 72°C); extension: 10 min at 72°C. PCR products were purified by size exclusion, after running through a bed of Sephacryl S400 (200 μl) (GE Healthcare, Uppsala, Sweden) packed into 96 well MultiScreen HTS filtration plates (Millipore, Billerica, MA).

Sequencing reactions were performed with a Big Dye v3.1 fluorescent sequencing kit (Applied Biosystems, Foster City, CA), and M13F or M13R oligonucleotide primers for each sample. Sequencing reactions were run with the following profile: denaturation: 1 min at 94°C; 25 cycles (30 s at 96°C, 20 s at 50°C, 4 min at 60°C). Sequences were loaded on an automated sequencer ABI3700 and analyzed using Sequencher and MacClade softwares.

Repertoire analysis:

DNA sequences surrounding and including the TCR-Vγ2 chain CDR3 regions were aligned. We determined how many sequences were repeated in the library from each donor and generated the corresponding amino acid sequences. Data were expressed as the frequency of $V\gamma2_{990\text{-}996}$ and the proportion of Vγ2-Jγ1.2 rearranged sequences among all Vγ2 chains, with average values calculated for 8 control, 8 ART, 7 VIR and 9 NVS donors. We also identified public clonotypes within the ART, VIR and the NVS groups based on the previous results generated for the control group [10] and deduced the frequency of appearance for individual public clonotypes in each donor.

Statistical analysis:

The similarity between TCR-Vγ2 repertoires was assessed using the number of clonotypes (or nucleotypes) common between individual repertoires and the Morisita-Horn similarity index [13, 14]. The Morisita-Horn similarity index accounts for the clonal dominance hierarchy and is a relative measure of similarity that ranges in value from 0 (minimal similarity) to 1 (maximal similarity). To account for differences in the sizes of the TCR-Vγ2 repertoire samples, all the similarity measures were estimated for each pair of individuals as the median value of 25,000 random draws from subsamples of 98 sequences out of the total TCR-Vγ2 repertoire sample for each individual [13, 14]. The diversity and similarity analysis was performed using Matlab (The Mathworks, Natick, MA).