

Supplementary Information Guide

- Supplementary Table 1: Clinical profiles of study participants
- Supplementary Table 2: Adverse events
- Supplementary Table 3: List of top 25 HIV-specific clonotypes with respect to their time dependence across Weeks 0, 16, and 24
- Supplementary Table 4: List of TRBV-TRBJ gene pairs in the HIV-specific clonotypes with time dependence across Weeks 0, 16, and 24
- Supplementary Table 5: Antibodies used for T cell phenotyping and intracellular cytokine staining
- Supplementary Figure 1: Gating strategy for flow cytometry analysis

Supplementary Table 1: Clinical profiles of Study Participants

Group	Participant ID	Age	Gender	Race	HIV Risk	Reported Seroconversion Illness?	ART regimen at study entry	HLA Alleles	CD4 Count (cells/mm ³)			Plasma viremia (copies/ml)	
									Reported Nadir	Pre-ART	At study entry	Pre-ART	At study entry
Group 1: bNAb	01	45	Male	White	MSM	Yes	EVG/Cobi/TAF/FTC	A 03,24; B 07; DRB1 04,15; CW 07; DQB1AS 02, 04	520	520	1177	23,805	<40
	02	40	Male	Black	MSM	No	ABC/3TC/DTG	A 01,30; B 08,57; DQ 02,06; DRB1 03,13; CW 07,18; DQB1AS 02, 06	648	673	911	20663	<40
	05	27	Male	Asian	MSM	Yes	EVG/Cobi/TAF/FTC/ DRV/ RPV	A 24,31; B 35,51; DRB1 09,14; CW 03,14; DQB1AS 03, 04	460	630	543	469,000	<40
	06	40	Male	White	MSM	Yes	ABC/3TC/DTG	A 24,31; B 08,35; DRB1 01,03; CW 04,07; DQB1AS 02, 05	483	483	799	3,600,000	<40
	08	57	Male	White	MSM	Yes	EVG/Cobi/TAF/FTC	A 11,24; B 35,38; DRB1 07,13; CW04,12; DQB1AS 02, 06	500	-	598	140000	<40
	13	38	Male	White/Hispanic	MSM	Yes	DTG/ABC/3TC	A 30,68; B42,48; DRB1 04,11; CW 08,17; DQB1AS 03, 03	619	619	919	99,596	<40
	14	39	Male	White	MSM	No	EVG/Cobi/TAF/FTC	A 26,32; B 07,57; DRB1 07,08; CW 06,07; DQB1AS 03, 04	430	-	661	322	<40
Group 1: Placebo	03	32	Male	White	MSM	Yes	TAF/FTC/DTG	A1; B37,57; DRB1 07,15; CW06; DQB1AS 03, 06	280	360	596	131,215	<40
	04	33	Male	White	MSM	No	DTG/ABC/3TC	A 24,33; B 14,37; DRB1 01,08; CW 06,08; DQB1AS 04, 05	330	560	809	30,186	<40
	07	56	Male	White	MSM	No	EVG/Cobi/TAF/FTC	A 02,24; B 40,44; DRB1 08,15; CW 03,05; DQB1AS 04, 06	475	475	612	82,132	<40
	09	41	Male	White	MSM	No	DTG/ABC/3TC	A 02,26; B 35,50; DRB1 03,08; CW 04,06; DQB1AS 02, 04	296	296	832	100,400	<40
	10	52	Male	White	MSM	Yes	DTG/ABC/3TC	A 24; B 07,15; DRB1 04,15; CW 03,07; DQB1AS 03, 06	552	592	552	1,322,739	<40
	11	34	Male	White/Hispanic	MSM	Yes	DTG/ABC/3TC	A 02,26; B 35,40; DRB1 11,16; CW 03,15; DQB1AS 03	506	506	762	16,197	<40
	12	29	Male	Asian	MSM	Yes	EVG/Cobi/TAF/FTC	A 24,33; B 48,58; DRB1 11,13; CW 03,08; DQB1AS 03, 06	215	300	426	2,072	<40
Group 2	S1	35	Male	White	MSM	No	-	A 01,02; B 08,14; CW 07,08	371	-	527	-	2,984
	S2	44	Male	Multiple Race	MSM	No	-	A11,31; B7,52; CW07,12	575	-	610	-	493
	S3	40	Male	White	MSM	No	-	A3,26; B51,57; CW07,15	406	-	851	-	473
	S4	52	Male	White	MSM	No	-	A1,3; B8,57; DQ 02; DRB1 03; CW 06,07	590	-	1011	-	825
	S5	52	Male	Black	MSM	No	-	A3,26; B7,45; DQ 0202; DRB1 07,11; CW 06, 07	280	-	640	-	147

ABC: Abacavir, AZT: Zidovudine, APV: Amprenavir, Cobi: Cobistat, DRV: Darunavir, DTG: Douletegravir, ETV: Etravirine, EVG: Elvitegravir, FTC: Emtricitabine, LPV/r: Loprinavir/ritonavir, MVC: Maraviroc, RAL: Raltegravir, RTV: Rilonavir, TAF: Tenofovir Alafenamide, TDF: Tenofovir, T20: Entuvirtide, 3TC: Lamivudine
MSM: Men who have sex with men, ART: Antiretroviral Therapy

Supplementary Table 2: Adverse events

Adverse Events^a	3BNC117/10-1074^b	Placebo
Infusion-related		
Rigors	1	0
Chills	1	0
Fever	1	0
Headache	0	1

^aAll adverse events were grade 1-2.

^bIncludes both Group 1 and 2 study participants.

Supplementary Table 3: List of top 25 HIV-specific clonotypes with respect to their time dependence across Weeks 0, 16, and 24

Group	CDR3	Time 1	Time 2	P value	Week 0	Week 16	Week 24
1 bNAbs	CASSPGTSSYEQYF	Wk0	Wk16	0.0625	1.14877E-05	1.5358E-06	5.70861E-06
1 bNAbs	CASSWDSNYGYTF	Wk0	Wk24	0.0625	0	3.9E-06	7.894E-06
1 bNAbs	CASSEGGYGYTF	Wk0	Wk16	0.100348246	6.05556E-06	1.5358E-06	5.28858E-07
1 bNAbs	CASSEGGYGYTF	Wk0	Wk24	0.100348246	6.05556E-06	1.5358E-06	5.28858E-07
1 bNAbs	CASSLAGGYTF	Wk0	Wk24	0.100348246	1.7457E-06	1.95E-06	5.5844E-06
1 bNAbs	CASSLGTGGNQPHF	Wk0	Wk16	0.100348246	9.27845E-06	5.72361E-06	1.64822E-05
1 bNAbs	CASSLGTGGNQPHF	Wk0	Wk24	0.100348246	9.27845E-06	5.72361E-06	1.64822E-05
1 bNAbs	CASSLGTGGNQPHF	Wk16	Wk24	0.100348246	9.27845E-06	5.72361E-06	1.64822E-05
1 bNAbs	CASSLRGTGELFF	Wk0	Wk24	0.100348246	5.30116E-06	8.46043E-06	1.35042E-05
1 bNAbs	CASSQGTGSTDQYF	Wk0	Wk16	0.100348246	1.87382E-06	5.2561E-06	8.06653E-07
1 bNAbs	CASSQGTGSTDQYF	Wk16	Wk24	0.100348246	1.87382E-06	5.2561E-06	8.06653E-07
1 bNAbs	CASSYTGELFF	Wk16	Wk24	0.100348246	6.65316E-06	0	5.5844E-06
1 bNAbs	CASSYTGELFF	Wk0	Wk16	0.100348246	6.65316E-06	0	5.5844E-06
1 bNAbs	CASSVGTGELFF	Wk0	Wk16	0.100348246	1.02826E-05	4.14083E-06	3.92846E-06
2	CASSGQGYGYTF	Wk16	Wk24	0.100348246	1.82715E-05	1.47503E-05	6.70228E-06
2	CASSGYGYTF	Wk0	Wk16	0.100348246	6.79655E-07	3.44938E-06	1.36023E-06
2	CASSLAGGQETQYF	Wk0	Wk16	0.100348246	4.93018E-07	4.25397E-06	2.12393E-06
2	CASSLAGGQETQYF	Wk16	Wk24	0.100348246	4.93018E-07	4.25397E-06	2.12393E-06
2	CASSLGASYEQYF	Wk0	Wk16	0.100348246	1.28899E-05	1.96881E-05	1.3584E-05
2	CASSLGGDEQYF	Wk16	Wk24	0.100348246	6.68145E-06	1.15355E-05	3.56137E-06
2	CASSLGYTEAFF	Wk16	Wk24	0.100348246	7.7168E-06	4.39176E-06	1.18918E-05
2	CASSVGTGELFF	Wk0	Wk16	0.100348246	4.67035E-06	9.39099E-07	0
2	CASSVGTGELFF	Wk0	Wk24	0.100348246	4.67035E-06	9.39099E-07	0
1 bNAbs	CASRDSSYEQYF	Wk0	Wk24	0.125	2.76546E-06	9.74628E-06	4.47859E-06
1 bNAbs	CASSPGTSSYEQYF	Wk0	Wk24	0.125	1.14877E-05	1.5358E-06	5.70861E-06
1 bNAbs	CASSEGAYEQYF	Wk0	Wk16	0.181449208	3.28413E-06	0	0
1 bNAbs	CASSEGAYEQYF	Wk0	Wk24	0.181449208	3.28413E-06	0	0
1 bNAbs	CASSLDRNEQFF	Wk0	Wk16	0.181449208	5.1699E-06	2.41685E-06	1.1545E-06
1 bNAbs	CASSLDRNEQFF	Wk0	Wk24	0.181449208	5.1699E-06	2.41685E-06	1.1545E-06
1 bNAbs	CASSLEGGSNQPHF	Wk0	Wk24	0.181449208	0	8.33802E-07	3.4477E-06
1 bNAbs	CASSLGEQPQHF	Wk0	Wk16	0.181449208	4.44395E-06	1.1162E-06	0
1 bNAbs	CASSLGEQPQHF	Wk0	Wk24	0.181449208	4.44395E-06	1.1162E-06	0
1 bNAbs	CASSLGPTEAFF	Wk0	Wk16	0.181449208	3.7724E-06	1.95E-06	3.89558E-06
1 bNAbs	CASSLGRGQETQYF	Wk0	Wk16	0.181449208	0	3.92316E-06	3.01887E-06
2	CASSGTDYGYTF	Wk0	Wk24	0.181449208	4.13776E-06	3.7564E-06	5.93562E-07
2	CASSLAGTQETQYF	Wk0	Wk24	0.181449208	0	0	2.80404E-06
2	CASSLAGTQETQYF	Wk16	Wk24	0.181449208	0	0	2.80404E-06
2	CASSLASDTQYF	Wk16	Wk24	0.181449208	1.50342E-05	1.81239E-05	1.27748E-05
2	CASSLETANTEAFF	Wk0	Wk16	0.181449208	8.18635E-07	2.59652E-06	9.03546E-07
2	CASSLETANTEAFF	Wk16	Wk24	0.181449208	8.18635E-07	2.59652E-06	9.03546E-07
2	CASSLGADQPQHF	Wk0	Wk24	0.181449208	1.89882E-05	1.76452E-05	5.42128E-06
2	CASSLGASSYEQYF	Wk0	Wk24	0.181449208	4.16925E-06	4.33472E-06	1.18712E-06
2	CASSLGGGYTF	Wk0	Wk24	0.181449208	2.77258E-06	1.96057E-06	0
2	CASSLGPTEAFF	Wk0	Wk16	0.181449208	3.0982E-06	0	9.01766E-07
2	CASSLGTSSYEQYF	Wk0	Wk16	0.181449208	5.7421E-06	8.92435E-07	5.93562E-07
2	CASSLGTSSYEQYF	Wk0	Wk24	0.181449208	5.7421E-06	8.92435E-07	5.93562E-07
2	CASSLWGNTAEAFF	Wk0	Wk16	0.181449208	0	3.53014E-06	8.5025E-07
2	CASSLWGNTAEAFF	Wk16	Wk24	0.181449208	0	3.53014E-06	8.5025E-07
2	CASSLRGETQYF	Wk0	Wk16	0.181449208	4.93018E-07	2.42243E-06	0
2	CASSLRGETQYF	Wk16	Wk24	0.181449208	4.93018E-07	2.42243E-06	0
1 Placebo	CASSGTNYGYTF	Wk0	Wk16	0.220671362	0	8.69508E-06	4.29155E-06
1 Placebo	CASSLDGNTGELFF	Wk0	Wk16	0.220671362	0	3.57672E-06	0
1 Placebo	CASSLEGGSNQPHF	Wk0	Wk16	0.220671362	0	5.28284E-06	4.29155E-06
1 Placebo	CASSPGTSTYEQYF	Wk0	Wk16	0.220671362	7.08385E-06	0	0
1 Placebo	CASSTNNEOFF	Wk0	Wk16	0.220671362	0	3.57672E-06	0
1 Placebo	CASTGSYGYTF	Wk0	Wk16	0.220671362	4.89773E-06	0	0
1 Placebo	CATSDSYEQYF	Wk0	Wk16	0.220671362	7.60935E-06	0	0
1 Placebo	CASSDTGELFF	Wk0	Wk16	0.333333333	1.46932E-05	6.98896E-06	1.71662E-05
1 Placebo	CASSEGGYGYTF	Wk0	Wk16	0.333333333	4.89773E-06	1.87061E-06	0
1 Placebo	CASSISYEQYF	Wk0	Wk16	0.333333333	7.08385E-06	3.57672E-06	0
1 Placebo	CASSLGASYEQYF	Wk0	Wk16	0.333333333	1.79303E-05	3.57672E-06	4.29155E-06
1 Placebo	CASSLGTSAEQYF	Wk0	Wk16	0.333333333	4.89773E-06	3.57672E-06	0
1 Placebo	CASSLRGETQYF	Wk0	Wk16	0.333333333	7.08385E-06	1.87061E-06	0
1 Placebo	CASSLYGQYF	Wk0	Wk16	0.333333333	9.79546E-06	3.57672E-06	0
1 Placebo	CASSPGGGELFF	Wk0	Wk16	0.333333333	9.26996E-06	1.87061E-06	0
1 Placebo	CASSYRTGELFF	Wk0	Wk16	0.333333333	7.08385E-06	1.87061E-06	0
1 Placebo	CASSFDREAFF	Wk0	Wk24	0.479500122	0	0	4.29155E-06
1 Placebo	CASSFDREAFF	Wk16	Wk24	0.479500122	0	0	4.29155E-06
1 Placebo	CASSGMNTEAFF	Wk16	Wk24	0.479500122	5.42323E-06	0	4.29155E-06
1 Placebo	CASSGQSYGYTF	Wk0	Wk24	0.479500122	0	3.74121E-06	4.29155E-06
1 Placebo	CASSGTAYGYTF	Wk0	Wk24	0.479500122	0	0	4.29155E-06
1 Placebo	CASSGTAYGYTF	Wk16	Wk24	0.479500122	0	0	4.29155E-06
1 Placebo	CASSGTDYGYTF	Wk16	Wk24	0.479500122	2.71161E-06	0	4.29155E-06
1 Placebo	CASSGTNYGYTF	Wk0	Wk24	0.479500122	0	8.69508E-06	4.29155E-06
1 Placebo	CASSHGDIYEQYF	Wk16	Wk24	0.479500122	2.18612E-06	0	4.29155E-06

For the bNAbs arm of Group 1 and Group 2, P values were determined using the two-sided Wilcoxon signed rank test.

For the placebo arm of group 1, P values were determined using two-sided Wilcoxon rank sum (Mann-Whitney).

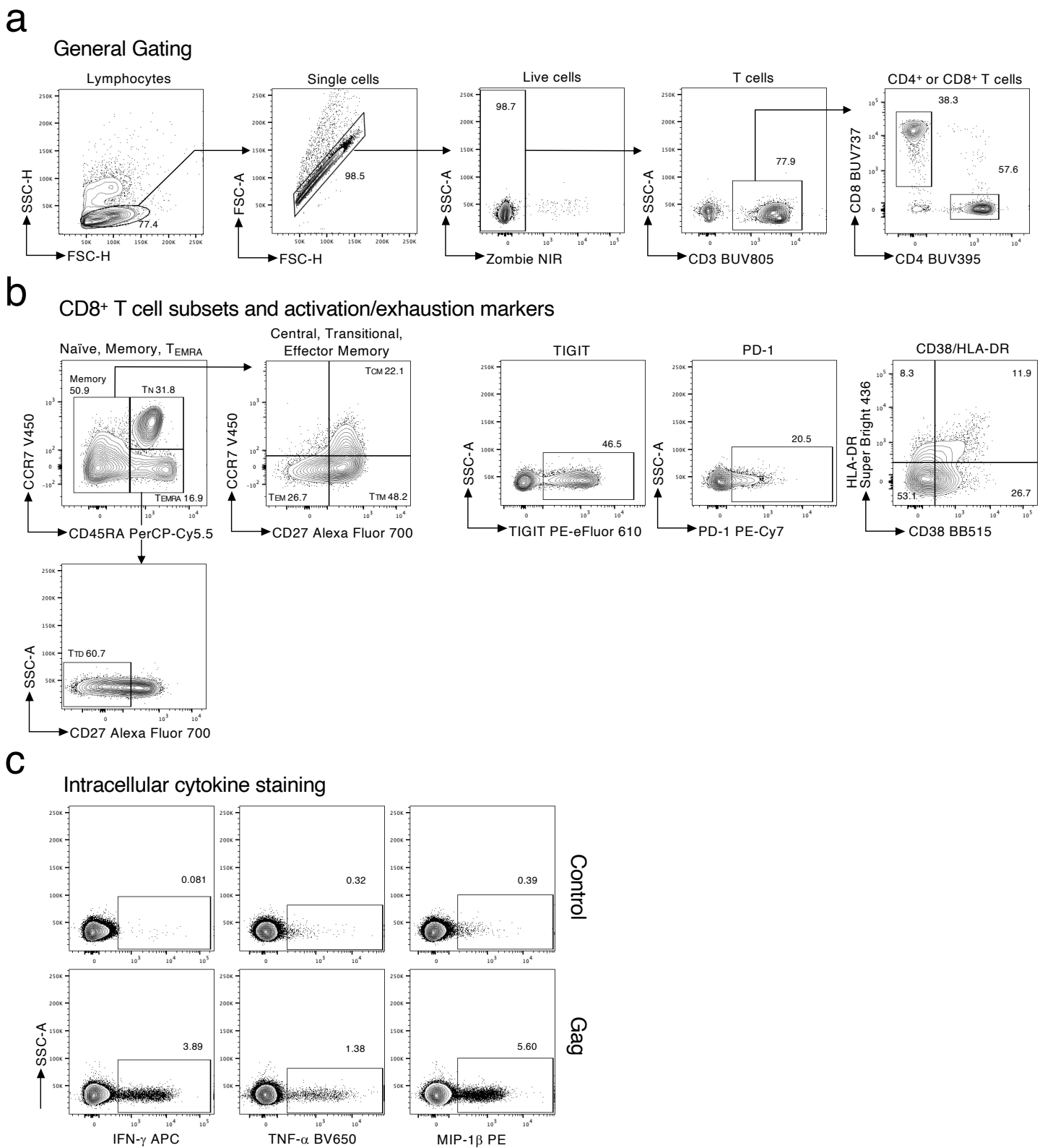
The reported P values have not been adjusted for multiple comparisons.

Supplementary Table 5: Antibodies used for T cell phenotyping and intracellular cytokine staining

Antibody	Fluorophore	Clone	Vendor	Catalog #	Detection	Assay*	Volume per test (μ l)**
CCR7	V450	150503	BD	560864	Surface	P, ICS	5
CD160	Alexa Fluor 647	BY55	BD	562362	Surface	P, ICS	3
CD226	BV480	DX11	BD	746405	Surface	P, ICS	5
CD27	Alexa Fluor 700	M-T271	BD	560611	Surface	P, ICS	2
CD28	BUV496	CD28.2	BD	741168	Surface	P, ICS	5
CD3	BUV805	SK7	BD	612894	Surface	P, ICS	2
CD38	BB515	HIT2	BD	564498	Surface	P, ICS	3
CD4	BUV395	M-T477	BD	742738	Surface	P, ICS	0.5
CD45RA	PerCP-Cy5.5	HI100	BD	563429	Surface	P, ICS	0.5
CD8	BUV737	SK1	BD	612755	Surface	P, ICS	2
CD96	BV711	6F9	BD	563174	Surface	P, ICS	5
CTLA-4	PE-Cy5	BNI3	BD	561717	Surface	P, ICS	10
CXCR5	BV510	RF8B2	BD	563105	Surface	P, ICS	5
HLA-DR	Super Bright 436	LN3	eBioscience	62-9956	Surface	P, ICS	1.5
ICOS	BV421	DX29	BD	562901	Surface	P	3
OX40	BV786	ACT35	BD	743285	Surface	P, ICS	5
PD-1	PE-Cy7	EH12.1	BD	561272	Surface	P, ICS	1.5
TIGIT	PE-eFluor 610	MBSA43	eBioscience	61-9500	Surface	P, ICS	5
2B4	PE	C1.7	eBioscience	Dec-38	Surface	P	2
2B4	BV605	C1.7	BioLegend	329536	Surface	ICS	3
4-1BB	APC	4B4-1	BioLegend	309810	Surface	P	2
IFN-g	APC	B27	BD	554702	Intracellular	ICS	0.5
MIP-1b	PE	D21-1351	BD	550078	Intracellular	ICS	0.5
TNF-a	BV650	MAb11	BD	563418	Intracellular	ICS	1

*P: phenotyping, ICS: intracellular cytokine staining

**One test: 2×10^6 PBMCs in 100 μ l staining buffer



Supplementary Fig. 1: Gating strategy for flow cytometry analysis

a. General gating strategy to identify CD4⁺ and CD8⁺ T cells in PBMCs. **b.** Identification of subsets (T_N, naïve; T_{CM}, central memory; T_{TM}, transitional memory; T_{EM}, effector memory; T_{EMRA}, effector memory RA; and T_{TD}, terminally differentiated), TIGIT⁺, PD-1⁺ and HLA-DR⁺CD38⁺ CD8⁺ T cells. This gating strategy was used to generate Extended Data Fig. 3b. **c.** Representative plots showing intracellular cytokine staining in unstimulated (Control) or HIV Gag peptide-stimulated (Gag) CD8⁺ T cells. The unstimulated cells served as a control for background subtraction. This gating strategy was used to determine the frequency of HIV-specific CD8⁺ T cells in Extended Data Fig. 6b.