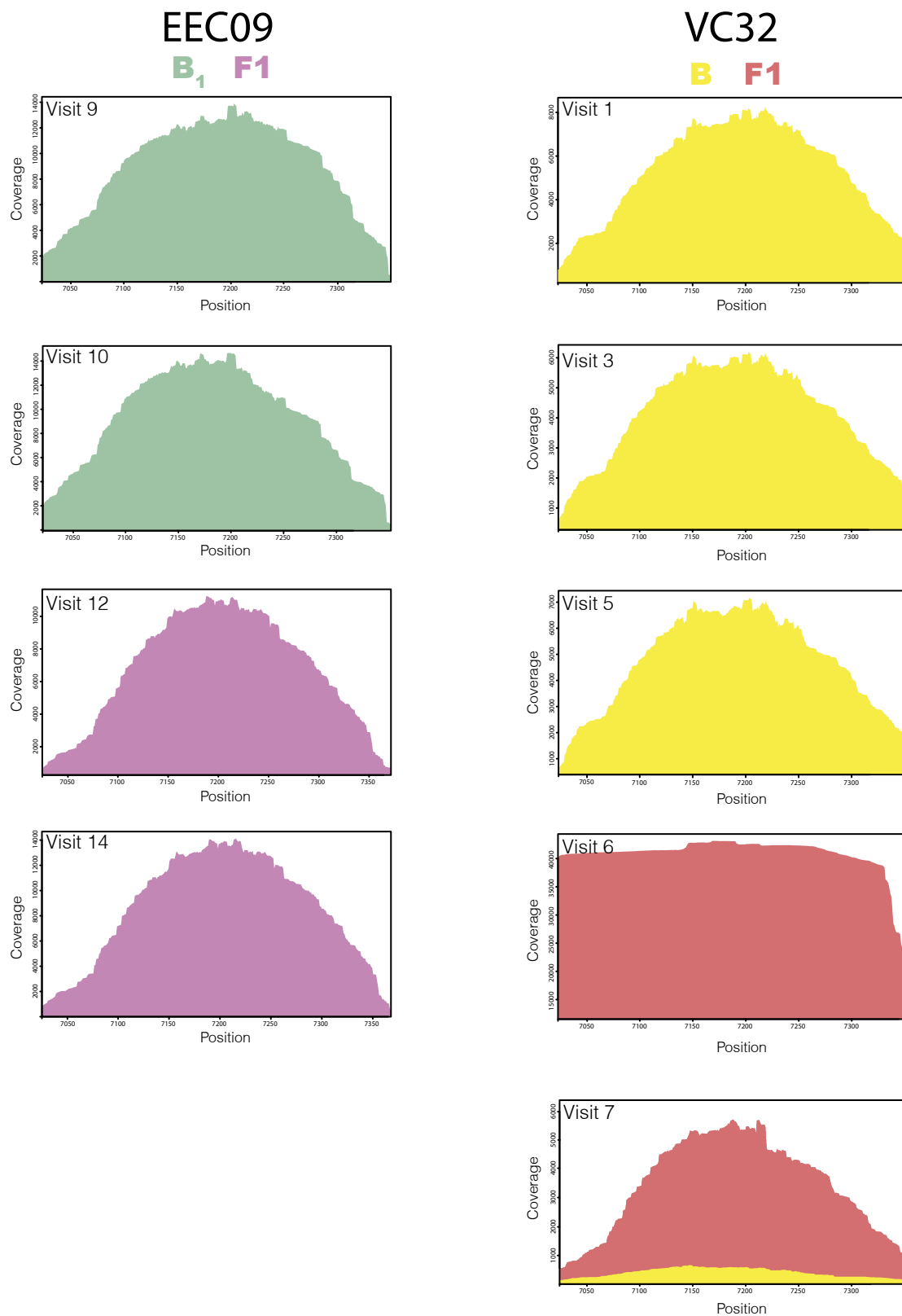
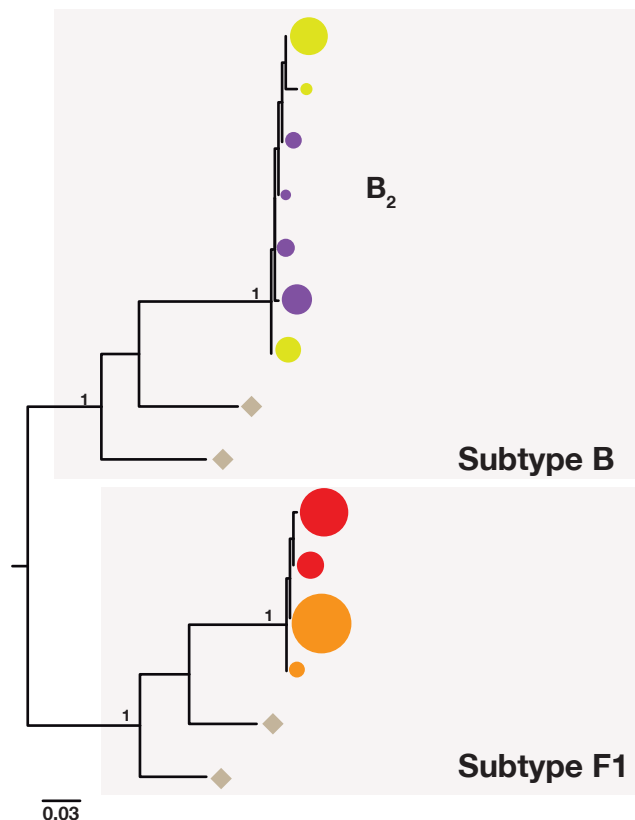




Supplemental Fig. 1. Sequencing coverage of the env amplicon from RNA from plasma samples. The depth of each base's coverage is indicated on the y-axis while the corresponding position in the HIV-1 genome is indicated on the x-axis (according to the HXB2 coordinates). Plots were colored according to the viral variant/s detect at each visit.

A)

EEC09



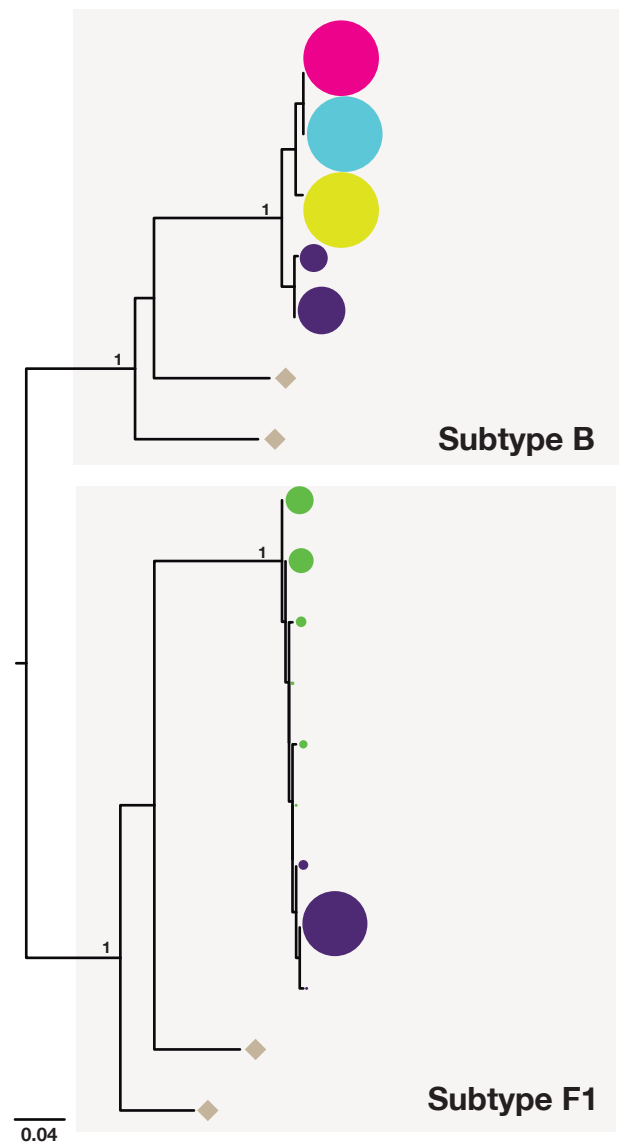
EEC09 | Visit 9 (12/2012)
 Visit 10 (09/2013)
 Visit 12 (11/2014)
 Visit 14 (07/2015)
 Reference

Frequency scale (%)



B)

VC32



VC32 | Visit 1 (04/2012)
 Visit 3 (04/2013)
 Visit 5 (01/2014)
 Visit 6 (06/2015)
 Visit 7 (01/2016)
 Reference

Frequency scale (%)



Supplemental Fig. 2. Frequency of viral haplotypes at different points in time found in the plasma compartment of the HIV controllers. ML phylogenetic tree of env sequences from subjects EEC09 (A) and VC32 (B) (circles) and HIV-1 subtype reference sequences (diamonds). The circles in the tips are colored according to the time point analyzed and their sizes are proportional to the haplotype frequency according to the scale at the right corner. Horizontal branch lengths are proportional to the bar at the bottom indicating nucleotide substitutions per site. The subtype of each cluster is indicated in the footer of the shaded boxes.

Supplemental Table 1. Coreceptor tropism prediction in quasispecies from PBMC and plasma compartments.

Patient ID	Variants	Visits	Source	V3 loop	Frequency of clones ^a	Predicted coreceptor use	Geno2pheno ^b
EEC09	B ₁	V1-14	PBMC	CTRPSNNTRKGIHIGPGRAFYATGDIIGDIRQAHC	98	R5	51.8
		V6	PBMC	CTRPSNNTRKGIHIGPGRAFYATGDRIGDIRQAHC	1		21.4
		V10	PBMC	CTRPSNNTRKGIHIGPGRAFYATGDIIGDIR-A--	1		91.7
	B ₂	V1-9	PBMC	CTRPNNNTRKGIHMGWGKALYATEKIIIGDIRQAHC	100	X4	4
		V9,10	Plasma	CTRPNNNTRKGIHVGWGRALYATEKIIIGDIRQAHC	100		2.6
	F1	V10,12,14	PBMC	CTRPNNNTRKSIPIIGPGRAFYATGEIIGDIRKAHC	98	R5	59.2
		V12,14	Plasma	CTRPNNNTRKSIPIIGPGRAFYATGEIIGDIRKAHC	100		59.2
		V10	PBMC	CTRPNNNTRKSIPIIGLGRAFYATGEIIGDIRKAHC	2		38
VC32	B	V1-8	PBMC	CTRPNNNTRKSINIGPGRAFYATGEIIGDIRQAHC	32	R5	64
		V1-8	PBMC	CTRPNNNTRKSIHIGPGRAFYATGEIIGDIRQAHC	22		42.6
		V1-8	PBMC	CTRPNNNTRKSINIGPGRAFYATEEIIIGDIRQAHC	14		17
		V5	Plasma	CTRPNNNTRKSINIGPGRAFYATEEIIIGDIRQAHC	100		
		V1-8	PBMC	CTRPNNNTRKSINIGPGRAFYATEGIIIGDIRQAHC	13.5		13.5
		V1,3	Plasma	CTRPNNNTRKSINIGPGRAFYATEGIIIGDIRQAHC	100		
		V1-8	PBMC	CTRPNNNTRKSINIGPGRAFYATGKIIGDIRQAHC	11.5		11.5
		V7	Plasma	CTRPNNNTRKSINIGPGRAFYATGKIIGDIRQAHC	100		
		V1,7,8	PBMC	CTRPNNNTRKSIHIGPGKAFYATGEIIGDIRQAHC	3		49.9
		V1,3	PBMC	CTRPNNNTRKSINIGPGRAFYATKGIIGDIRQAHC	2		30.1
		V1,5	PBMC	CTRPNNNTRKSINIGPGRAFYATGEVIGDIRQAHC	1		50.5
		V5	PBMC	CTRPNNNTRKSINIAFGRAFYATGEIIGDIRQAHC	0.5		88
		V8	PBMC	CTRPNNNTRKSIHIGPGRAFYATGEIIGDIRQAYC	0.5		38
	F1	V6-8	PBMC	CTRPNNNTRKGIHLGPGRTFYATGDIIGDIRQAQC	100		75.6
		V6,7	Plasma	CTRPNNNTRKGIHLGPGRTFYATGDIIGDIRQAQC	100		

^a Frequency represented in percentages (%); ^b Predicted using geno2pheno with a false positive rate (FPR) cutoff of 5%. Red shades represent changes related to the major haplotype of each variant. Grey shades highlight the crown of the V3 loop region.

Supplemental Table 2. Virological characteristics of HIV controllers EEC09 and VC32.

Patient ID	Visit (month/year)	RNA load (cp/mL) ^a	DNA load (cp/10 ⁶ cells)	Viral variant DNA-PBMCs			Viral variant RNA-Plasma	
EEC09	V1 (Feb 2009)	< 50	61	B ₁ = 9 (47%) π^c = 0.9%	B ₂ =10 (53%) π = 0.2%	-	-	-
	V2 (Dec 2009)	< 50	< 40	B ₁ = 13 (87%) π = 0.2%	B ₂ = 2 (13%) π = 1.2%	-	-	-
	V6 (Aug 2011)	< 50	43	B ₁ = 27 (96%) π = 0.7%	B ₂ = 1 (4%) π = ND	-	-	-
	V9 (Dec 2012)	170	< 40	B ₁ = 13 (87%) π = 0.3%	B ₂ = 2 (13%) π = 0.2%	-	B ₂ = 100% π = 0.5%	-
	V10 (Sep 2013)	159	< 40	B ₁ = 11 (58%) π = 1.4%	B ₂ = 8 (42%) π = 0.2%	F1 = 8 (42%) π = 0.2%	B ₂ = 100% π = 0.3%	-
	V12 (Nov 2014)	388	87	B ₁ = 12 (36%) π = 0.5%		F1= 21 (64%) π = 0.2%	-	F1 = 100% π = 0.1%
	V14 (Jul 2015)	581	45	B ₁ = 1 (4%) π = ND		F1= 26 (96%) π = 0.3%	-	F1 = 100% π = 0.1%
VC32	V1 (Apr 2012)	82	ND ^b	B = 33 (100%) π = 3.2%		-	B = 100% π = ND	-
	V3 (Apr 2013)	136	136	B = 30 (100%) π = 3.6%		-	B = 100% π = ND	-
	V5 (Jan 2014)	403	106	B = 34 (100%) π = 3.0%		-	B = 100% π = ND	-
	V6 (Jun 2015)	722	74	B = 17 (89%) π = 3.5%		F1 = 2 (11%) π = 0.1%	-	F1 = 100% π = 0.3%
	V7 (Jan 2016)	472	< 40	B = 19 (90%) π = 2.7%		F1 = 2 (10%) π = 0%	B = 10% π = 0.1%	F1 = 90% π = 0.1%
	V8 (Apr 2016)	58	< 40	B = 27 (96%) π = 3.3%		F1 = 1 (4%) π = ND	-	-

^acp, copies/ml; ^bND, not determined; ^c π , mean nucleotide diversity.