

Supplemental material

Cohen et al., <https://10.1084/jem.20180936>

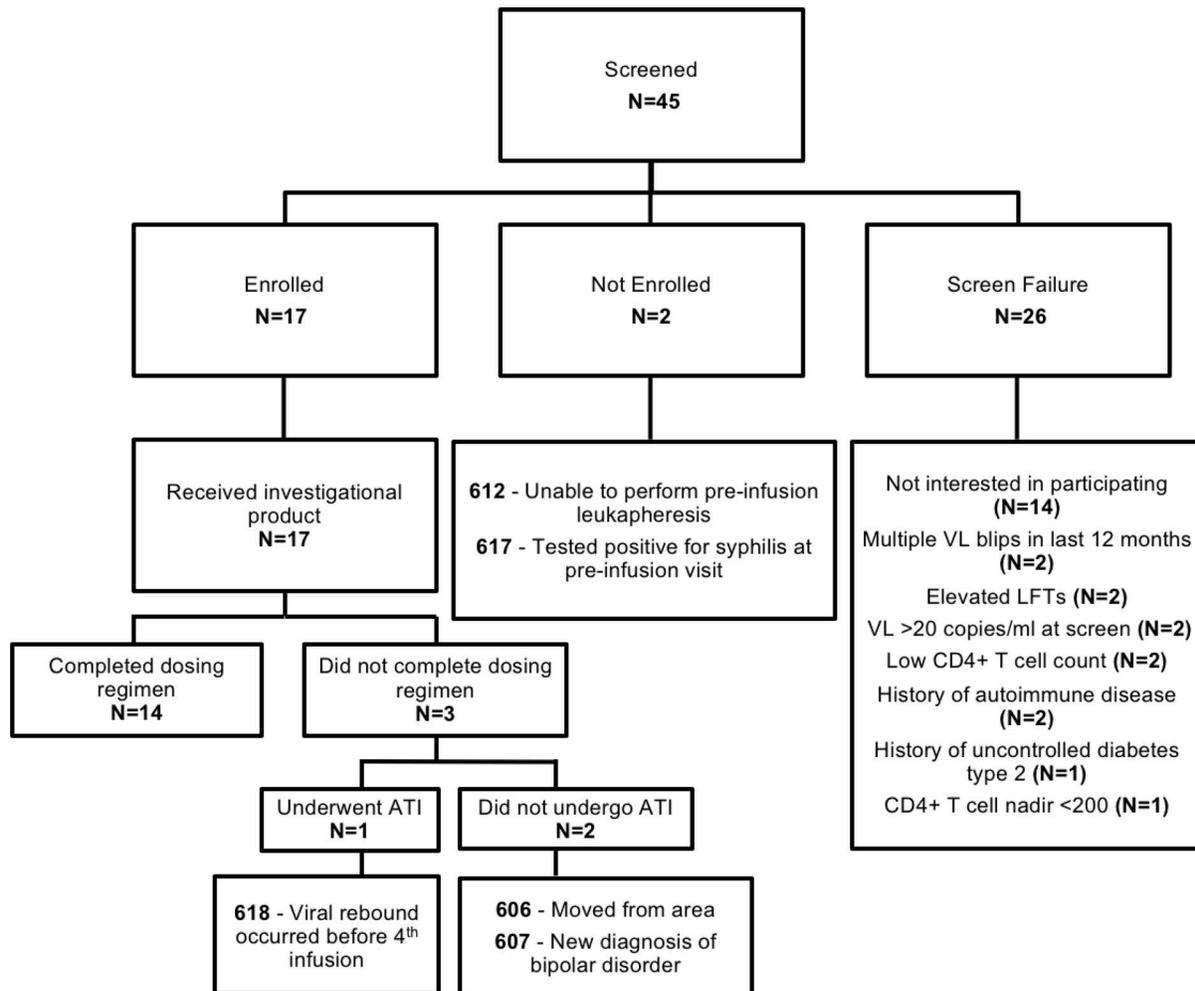


Figure S1. **Participant flow diagram.**

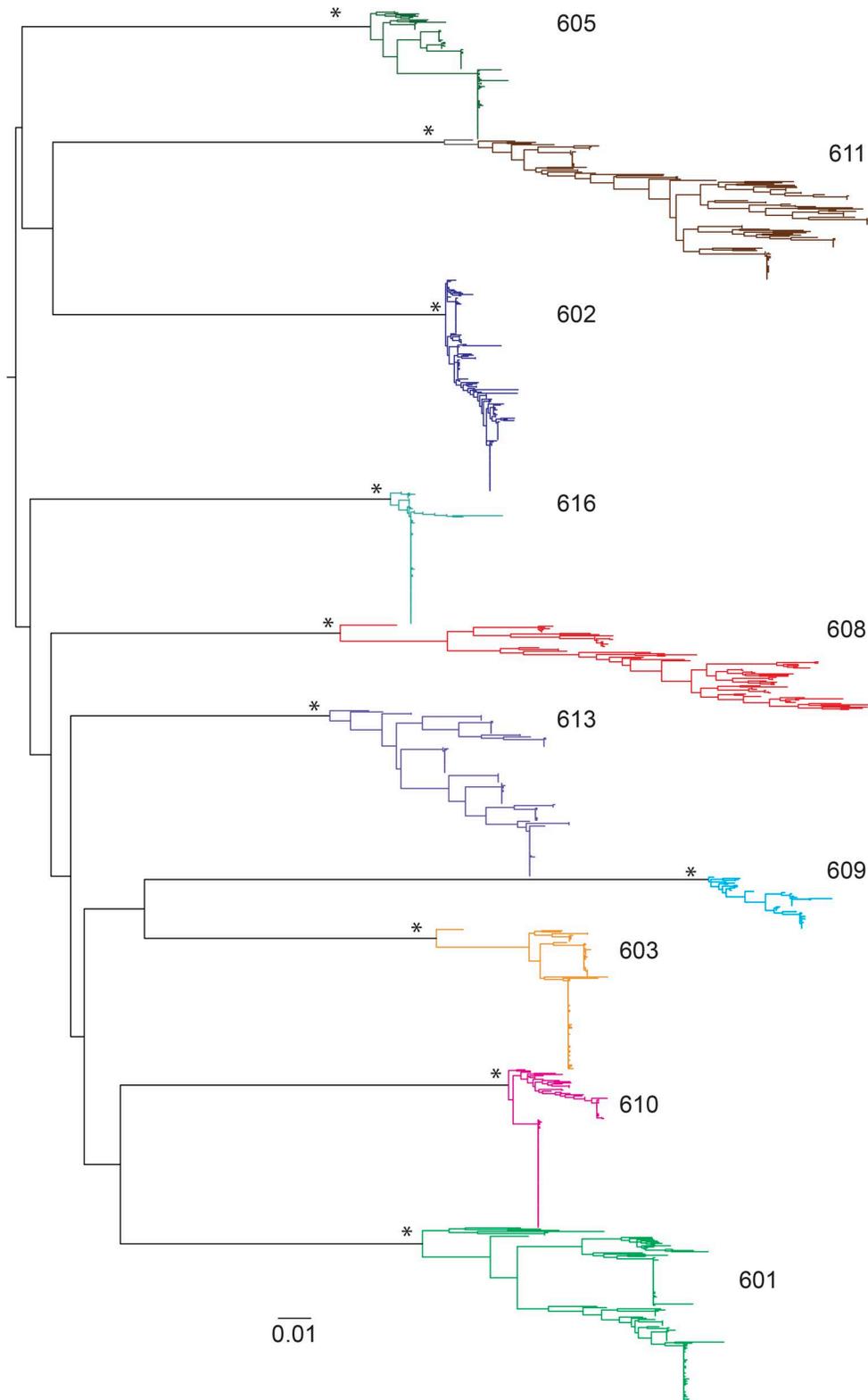


Figure S2. **Env sequences from all patients.** A maximum likelihood phylogenetic tree was constructed from all viral *env* sequences (Q²VOA, rebound SGA, and near full-length genome) from all participants. The tree was constructed using RAxML v.8.0.22 with a GTR GAMMA substitution model, with 1000 bootstrap replicates and midpoint rooted. Asterisks indicate nodes with significant bootstrap values (bootstrap support $\geq 90\%$).

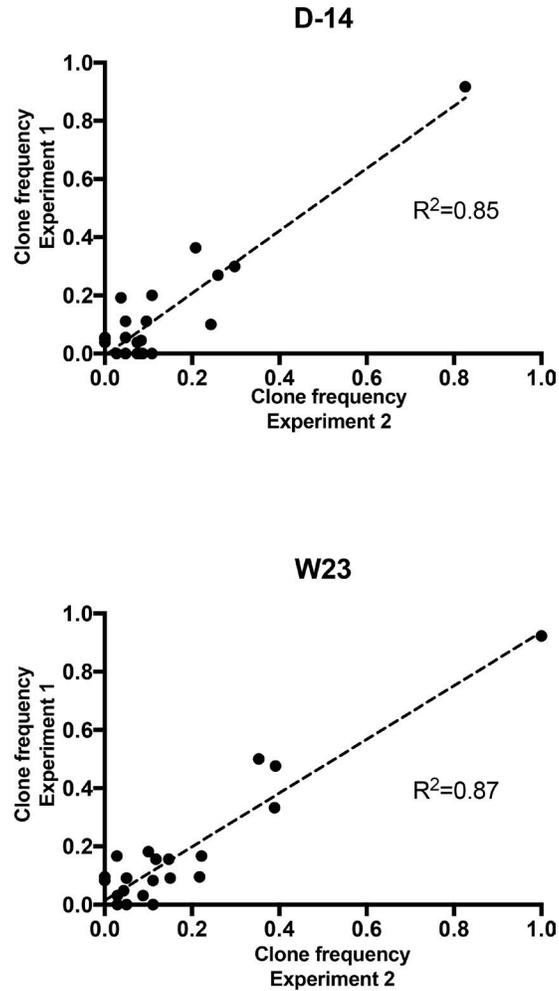


Figure S3. **Clone frequency in repeat Q²VOA experiments.** Q²VOA experiments were repeated for five participants (601, 602, 610, 611, and 613) to confirm reproducibility using samples from both time points. The total number of viruses isolated from the repeat experiments ranged from 25 to 60. Each dot represents a particular clone, and the x and y axes show the frequency of the clone in each experiment.

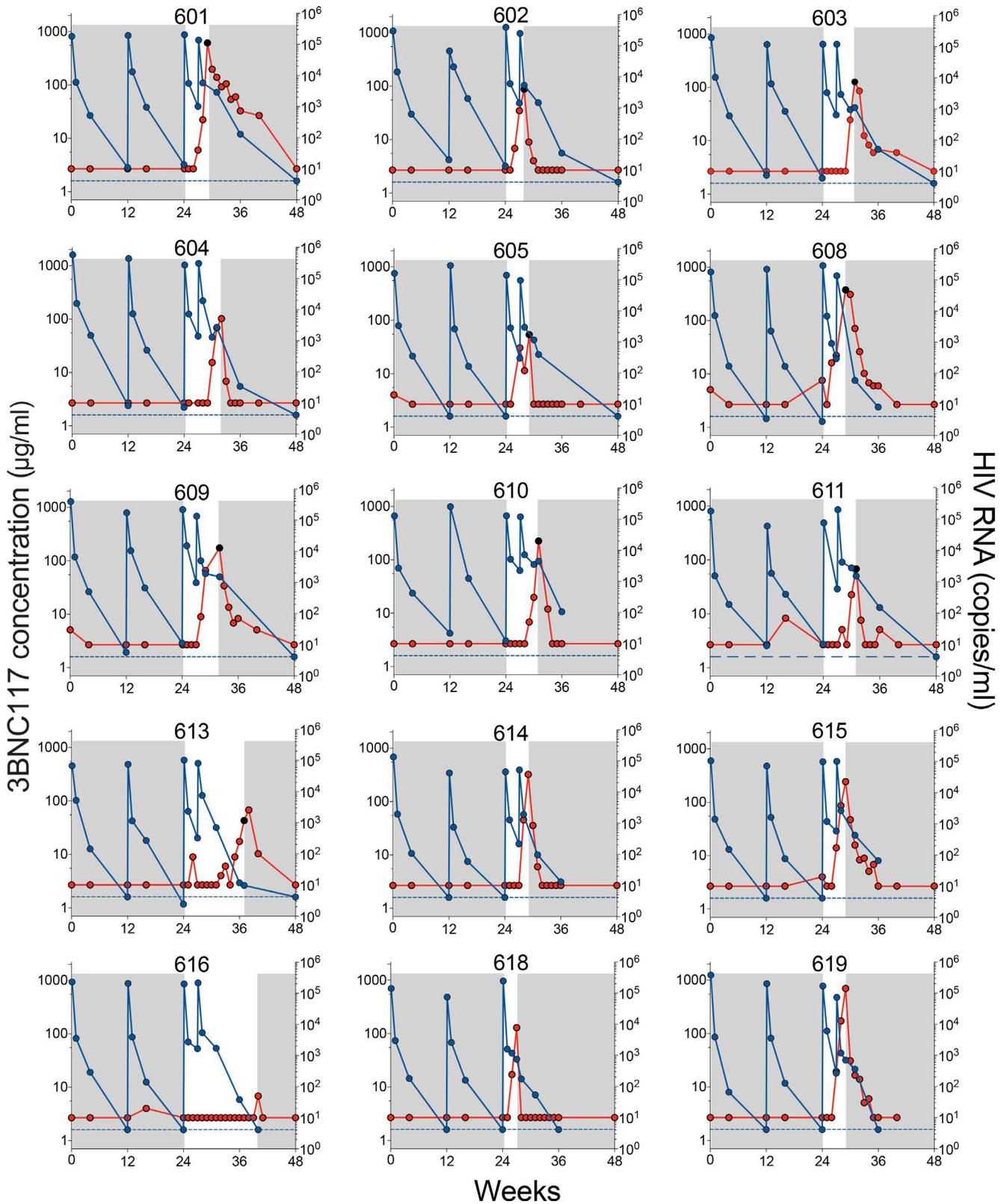


Figure S4. **Plasma viral loads and 3BNC117 levels.** The left y axis shows 3BNC117 levels (blue curves), the right y axis shows plasma viral loads in RNA copies/ml (red curves), and gray areas indicate ART use. Black circles represent time points from which plasma SGA was performed. Participant 616 did not demonstrate significant levels of viremia at rebound because the participant independently began ART when plasma viremia reached 100 copies/ml.

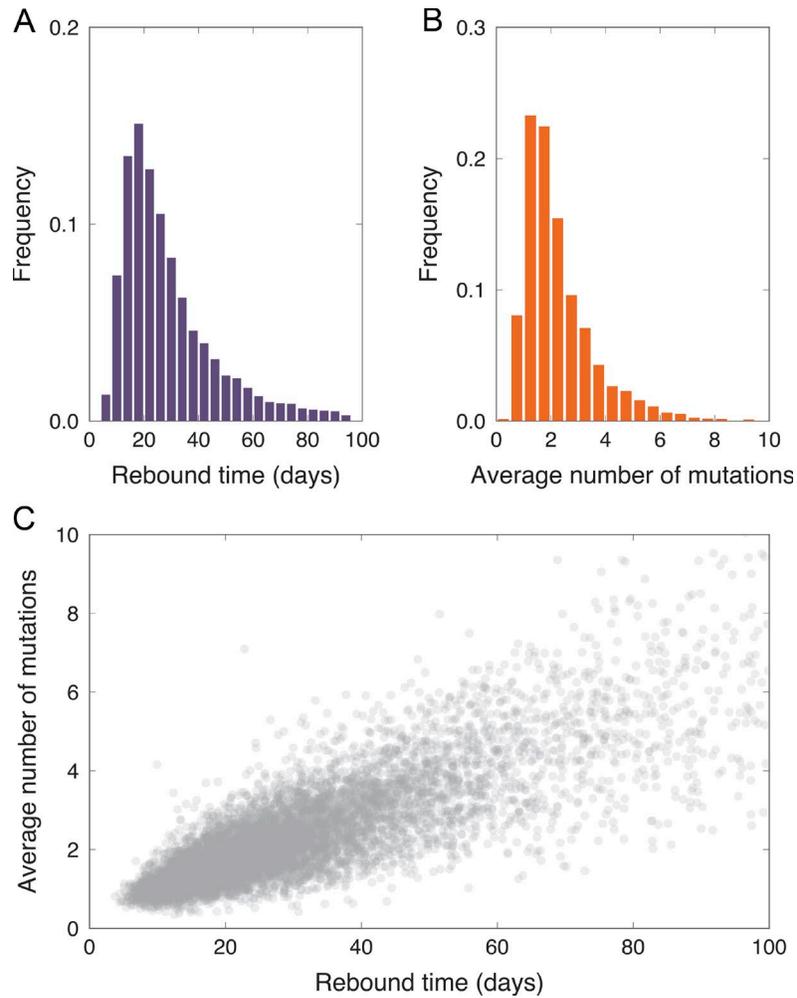


Figure S5. **Typical time to rebound and accumulated mutations in simulations.** **(A)** Histogram of the time to rebound across 10^4 simulations with randomly selected parameters. The typical time to rebound in simulation is around 3 wk, which is congruent with typical results in ATI. **(B)** Histogram of the mean number of mutations accumulated during rebound for each of the 10^4 simulations. **(C)** Scatter plot of rebound time versus the mean number of accumulated mutations for all simulations. There is considerable variation, but longer rebound times are strongly associated with a larger number of accumulated mutations.

Table S1. **Clinical characteristics of individual participants**

Study ID	Age (yr)	Sex	Race/ethnicity	Year of HIV diagnosis	Year ART started	Year since uninterrupted ART	Reported nadir	ART regimen	Baseline bulk culture 3BNC117 IC ₅₀
601	56	M	White	1994	1997	2007	350	Lopinavir/ritonavir/abacavir/lamivudine	3.03
602	49	M	White	2009	2011	2011	500	Raltegravir/emtricitabine/TDF	3.21
603	43	M	White/Hispanic	2003	2005	2005	300	Efavirenz/emtricitabine/TDF	0.513
604	29	M	Black	2008	2009	2009	300	Emtricitabine/rilpivirine/TDF	2.347
605	36	M	White/Hispanic	2001	2002	2014	372	Emtricitabine/rilpivirine/TDF	0.486
608	50	M	Black	1992	2013	2014	250	Dolutegravir/ emtricitabine/TDF	>20
609	39	M	White	2014	2014	2014	400	Dolutegravir/ emtricitabine/TDF	0.136
610	29	M	White	2011	2012	2012	380	Emtricitabine/rilpivirine/TDF	0.324
611	57	M	White	2002	2003	2003	282	Emtricitabine/rilpivirine/TDF	1.018
613	50	M	Multiple/Hispanic	1997	1998	2006	300	Atazanavir/ritonavir/emtricitabine/TDF	0.996
614	58	M	Black	2000	2000	2000	350	Efavirenz/emtricitabine/TDF	>20
615	34	M	Multiple	2011	2011	2011	411	Emtricitabine/rilpivirine/TDF	1.142
616	30	M	Black	2004	2005	2005	400	Emtricitabine/rilpivirine/TDF	0.371
618	26	M	Black	2014	2015	2015	450	Abacavir/dolutegravir/ lamivudine	1.96
619	53	F	Black	1992	1995	2013	280	Elvitegravir/cobicistat/emtricitabine/TAF	0.59

Table S2. Adverse events

Adverse events	No. AEs	No. mild	No. moderate	No. severe	No. of participants (n = 17)
Related to 3BNC117					
Malaise/fatigue	5	5			3
Nausea	5	5			4
Dizziness	4	4			3
Chills	2		2		1
Diarrhea	2	2			2
Headache	2	2			2
Abdominal pain	1	1			1
Bloating	1	1			1
Diplopia	1	1			1
Ecchymosis at infusion site	1	1			1
Elevated bilirubin	1			1 ^a	1
Eye twitching	1	1			1
Flushing	1	1			1
Myalgia	1		1		1
Pharyngitis	1	1			1
Total related AEs	29	25	3	1	10
Not related to 3BNC117					
Headache	10	2	6	2	5
Upper respiratory tract infection	9	5	4		6
Rash	5	3			4
Diarrhea	4	3	1		3
Musculoskeletal pain	3	2	1		2
Dizziness	3	3			2
Depressed mood or anxiety	2	1	1		2
Malaise/fatigue	2	2			2
Abdominal pain	1	1	0		1
Acute psychotic episode	1			1	1
Anemia	1	1			1
Blurry vision	1	1			1
Cold sore	1	1			1
Dry mouth	1	1			1
Dysuria	1	1			1
Erectile dysfunction	1	1			1
Gonorrhea	1	1			1
Gunshot wound	1	1			1
Hematuria	1	1			1
Hives	1	1			1
Lightheadedness	1	1			1
Nausea	1	1			1
Otic pruritus	1	1			1
Pleuritic pain	1		1		1
Priapism	1		1		1
Sore throat	1	1			1

Table S2. Adverse events (Continued)

Adverse events	No. AEs	No. mild	No. moderate	No. severe	No. of participants
Toe fracture	1	1			1
Urinary tract infection	1		1		1
Total not related AEs	58	35	22	2	12
Total AEs	87	60	25	3	16

^aA direct bilirubin of 0.7 mg/dL was recorded, which is considered a severe adverse event as per the DAIDS Toxicity Table Version 2.0.

Table S4. Summary of obtained sequences

ID	CD4 ⁺ tested		Q ² VOA sequences		% in clones		No. of sequences		% identical between NFL and Q ² VOA
	W-2	W23	W-2	W23	W-2	W23	Rebound	NFL	
601	1.80 × 10 ⁸	1.98 × 10 ⁸	46	44	34.0	68.2	52	NT	NT
602	2.09 × 10 ⁸	2.66 × 10 ⁸	53	66	47.9	81.7	31	9	33.3
603	2.40 × 10 ⁷	1.44 × 10 ⁷	24	29	62.5	65.5	31	28	82.1
605	1.01 × 10 ⁸	1.73 × 10 ⁸	48	45	58.3	72.7	10	NT	NT
608	2.64 × 10 ⁷	5.52 × 10 ⁷	24	22	0.0	9.1	23	NT	NT
609	1.80 × 10 ⁸	NT	26	NT	19.2	NT	12	NT	NT
610	7.92 × 10 ⁷	9.84 × 10 ⁷	51	38	94.1	71.1	19	19	47.3
611	1.50 × 10 ⁸	4.32 × 10 ⁷	39	31	30.8	48.4	27	21	33.3
613	8.18 × 10 ⁷	2.88 × 10 ⁷	56	48	80.4	87.5	12	23	8.6
616	4.32 × 10 ⁷	9.60 × 10 ⁶	35	43	80.0	71.4	NT	33	87.8

NT, not tested; NFL, near full-length.

Table S5. **Virus neutralization by 3BNC117**

PPT and source	Method	Virus ID	3BNC117 IC₅₀	3BNC117 IC₈₀
601				
Reservoir	Bulk culture	601 Bulk	3.031	9.205
Reservoir	Q ² VOA	601 D-14 MB22	>50	>50
Reservoir	Q ² VOA	601 D-14 MG10	>50	>50
Reservoir	Q ² VOA	601 D-14 MB9	>50	>50
Reservoir	Q ² VOA	601 D-14 MD5	1.467	6.592
Reservoir	Q ² VOA	601 D-14 MG19	9.235	28.203
Reservoir	Q ² VOA	601 W23 MA17	1.605	4.005
Reservoir	Q ² VOA	601 W23 MO6	6.842	>50
Reservoir	Q ² VOA	601 W23 MQ17	>50	>50
Reservoir	Q ² VOA	601 W23 MQ19	>50	>50
Rebound virus	Bulk culture	601 W29 F Bulk	>50	>50
602				
Reservoir	Bulk culture	602 Bulk	3.206	8.671
Reservoir	Q ² VOA	602 W23 F5	2.686	10.026
Reservoir	Q ² VOA	602 W23 M6	3.959	24.951
Reservoir	Q ² VOA	602 W23 P2	0.948	2.532
Reservoir	Q ² VOA	602 W23 Y7	0.733	2.417
Rebound virus	Bulk culture	602 W28 F Bulk	6.036	23.885
603				
Reservoir	Bulk culture	603 Bulk	0.513	>20
Reservoir	Q ² VOA	603 D-14 N17	0.758	>50
Reservoir	Q ² VOA	603 W23 MB6	6.718	>50
Reservoir	Q ² VOA	603 W23 MC11	1.969	>50
Reservoir	Q ² VOA	603 W23 B9	3.381	>50
Rebound virus	Bulk culture	603 W31 F Bulk	4.337	12.110
605				
Reservoir	Bulk culture	605 Bulk	0.486	2.133
Reservoir	Q ² VOA	605 W23 ME7	2.507	8.203
Reservoir	Q ² VOA	605 W23 ME9	2.862	10.183
Reservoir	Q ² VOA	605 W23 MF12	1.870	6.541
Reservoir	Q ² VOA	605 W23 MG14	3.202	9.368
Reservoir	Q ² VOA	605 W23 MH10	2.442	9.03
Reservoir	Q ² VOA	605 W23 MK10	2.907	10.243
Reservoir	Q ² VOA	605 W23 MK15	0.974	3.43
Reservoir	Q ² VOA	605 W23 MK18	3.187	11.288
Rebound virus	Bulk culture	605 W29 F Bulk	3.066	11.188
608				
Reservoir	Bulk culture	608 Bulk	>20	>20
Reservoir	Q ² VOA	608 D-14 MF4	>50	>50
Reservoir	Q ² VOA	608 W23 MS9	>50	>50
Reservoir	Q ² VOA	608 W23 MJ5	>50	>50
Reservoir	Q ² VOA	608 W23 MK24	>50	>50
Reservoir	Q ² VOA	608 W23 MP12	>50	>50
Reservoir	Q ² VOA	608 D-14 MB4	>50	>50

Table S5. **Virus neutralization by 3BNC117 (Continued)**

PPT and source	Method	Virus ID	3BNC117 IC₅₀	3BNC117 IC₈₀
Rebound virus	Bulk culture	608 W30 F Bulk	>50	>50
609				
Reservoir	Bulk culture	609 Bulk	0.136	0.301
Reservoir	Q ² VOA	609 MI21	0.193	0.514
Reservoir	Q ² VOA	609 D-14 12 11	0.154	0.59
Reservoir	Q ² VOA	609 D-14 MD14	0.230	0.898
Reservoir	Q ² VOA	609 D-14 MF13	0.118	0.337
Reservoir	Q ² VOA	609 D-14 MG11	0.788	2.629
Reservoir	Q ² VOA	609 D-14 MI15	0.320	0.901
Rebound virus	Bulk culture	609 W32 F Bulk	1.674	4.481
610				
Reservoir	Bulk culture	610 Bulk	0.324	1.091
Reservoir	Q ² VOA	610 D-14 MB17	0.813	2.199
Reservoir	Q ² VOA	610 D-14 MB8	0.853	3.109
Reservoir	Q ² VOA	610 D-14 ME17	0.436	1.267
Reservoir	Q ² VOA	610 W23 MI14	0.395	1.315
Reservoir	Q ² VOA	610 W23 MJ3	0.720	1.888
Rebound virus	Bulk culture	610 W31 F Bulk	0.490	1.678
611				
Reservoir	Bulk culture	611 Bulk	1.018	2.782
Reservoir	Q ² VOA	611 D-14 2G 18	1.175	3.371
Reservoir	Q ² VOA	611 D-14 2i 20	1.973	3.61
Reservoir	Q ² VOA	611 D-14 B23	0.604	2.427
Reservoir	Q ² VOA	611 D-14 MH8	1.256	4.444
Reservoir	Q ² VOA	611 D-14 MH12	0.482	1.682
Reservoir	Q ² VOA	611 D-14 MH7	0.447	1.574
Reservoir	Q ² VOA	611 D-14 MI10	0.795	2.153
Reservoir	Q ² VOA	611 D-14 MJ3	0.749	2.503
Reservoir	Q ² VOA	611 D-14 MK21	0.545	2.046
Reservoir	Q ² VOA	611 W23 MC1	0.572	2.437
Reservoir	Q ² VOA	611 W23 MC23	0.147	0.489
Reservoir	Q ² VOA	611 W23 MS1	0.163	0.439
Reservoir	Q ² VOA	611 W23 MS14	0.599	1.935
Reservoir	Q ² VOA	611 W23 MS13	0.514	1.83
Reservoir	Q ² VOA	611 W23 MP16	1.560	5.129
Reservoir	Q ² VOA	611 W23 MO22	0.548	1.725
613				
Reservoir	Bulk culture	613 Bulk	0.996	2.479
Reservoir	Q ² VOA	613 W23 MS18	0.148	0.484
Reservoir	Q ² VOA	613 D-14 C16	0.995	8.987
Reservoir	Q ² VOA	613 D-14 C6	0.612	1.337
Reservoir	Q ² VOA	613 D-14 D15	0.412	2.23
Reservoir	Q ² VOA	613 D-14 F12	0.341	0.88
Reservoir	Q ² VOA	613 D-14 MB10	0.590	1.846
Reservoir	Q ² VOA	613 D-14 MB23	0.265	0.872

Table S5. **Virus neutralization by 3BNC117 (Continued)**

PPT and source	Method	Virus ID	3BNC117 IC₅₀	3BNC117 IC₈₀
616				
Reservoir	Bulk culture	616 Bulk	0.371	1.102
Reservoir	Q ² VOA	616 D-14 300K B12	0.347	0.817
Reservoir	Q ² VOA	616 D-14 MF8	0.298	0.989
Reservoir	Q ² VOA	616 D-14 MF21	0.245	0.781
Reservoir	Q ² VOA	616 D-14 MA11	0.262	0.856
Reservoir	Q ² VOA	616 D-14 300K A19	0.281	0.956
Reservoir	Q ² VOA	616 W23 MU12	0.377	1.4
Reservoir	Q ² VOA	616 W23 MU18	0.323	0.93

Table S6. **Virus neutralization by other bNAbs**

Virus ID	10-1074		PGDM1400		10E8		8ANC195	
	IC ₅₀	IC ₈₀						
601 D-14 MB22	0.427	1.187	NT	NT	NT	NT	NT	NT
601 D-14 MG10	0.315	0.824	NT	NT	NT	NT	NT	NT
601 D-14 MB9	0.538	1.023	>50	>50	23.840	>50	>50	>50
601 D-14 MD5	NT							
601 D-14 MG19	1.142	2.411	24.813	>50	28.243	>50	>50	>50
601 W23 MA17	0.119	0.255	>50	>50	19.947	>50	0.716	2.496
601 W23 MO6	0.340	1.566	>50	>50	3.524	23.617	>50	>50
601 W23 MQ17	0.444	1.001	5.409	49.053	14.720	>50	>50	>50
601 W23 MQ19	0.311	0.840	7.256	>50	11.250	47.993	>50	>50
601 W29 F bulk (rebound)	0.521	1.151	8.667	>50	3.283	30.381	NT	NT
602 W23 F5	0.491	1.361	0.177	0.510	15.523	>50	1.435	5.269
602 W23 M6	0.718	3.919	0.627	4.072	12.745	>50	>50	>50
602 W23 P2	0.696	1.823	0.241	0.841	15.322	>50	1.333	5.178
602 W23 Y7	0.640	2.165	0.317	1.014	22.099	>50	2.326	6.309
602 W28 F bulk (rebound)	2.242	6.564	1.174	4.703	4.324	30.828	NT	NT
603 D-14 N17	1.019	3.184	NT	NT	NT	NT	NT	NT
603 W23 MB6	NT							
603 W23 MC11	NT							
603 W23 B9	1.653	5.452	>50	>50	13.844	>50	0.265	0.956
603 W31 F bulk (rebound)	3.617	9.211	>50	>50	2.925	17.296	NT	NT
605 W23 ME7	0.078	0.182	4.758	13.038	11.782	49.448	0.406	1.541
605 W23 ME9	NT							
605 W23 MF12	0.162	0.438	11.995	47.915	32.100	>50	0.555	1.974
605 W23 MG14	0.028	0.068	>50	>50	2.337	13.947	6.061	19.628
605 W23 MH10	0.021	0.051	>50	>50	1.999	19.042	4.756	18.891
605 W23 MK10	0.025	0.068	>50	>50	2.170	12.043	5.482	17.070
605 W23 MK15	0.230	0.631	0.741	2.760	33.225	>50	0.634	1.896
605 W23 MK18	0.030	0.101	>50	>50	1.439	14.120	7.483	23.698
605 W29 F bulk (rebound)	0.205	0.709	>50	>50	1.379	10.950	NT	NT
608 MF4	NT							
608 W23 MS9	4.663	16.759	>50	>50	0.770	7.130	1.034	3.706
608 W23 MJ5	NT							
608 W23 MK24	>50	>50	NT	NT	NT	NT	NT	NT
608 W23 MP12	10.538	37.781	>50	>50	1.726	11.193	1.278	7.611
608 W30 F bulk (rebound)	13.943	>50	>50	>50	3.586	21.783	NT	NT
609 MI21	1.159	3.041	0.552	1.932	19.581	>50	1.325	16.654
609 D-14 12 11	1.160	3.250	0.903	2.777	18.860	>50	1.371	20.221
609 D-14 MD14	0.726	2.083	NT	NT	NT	NT	NT	NT
609 D-14 MF13	0.948	2.597	NT	NT	NT	NT	NT	NT
609 D-14 MG11	0.252	1.272	NT	NT	NT	NT	NT	NT
609 D-14 MI15	1.172	4.000	NT	NT	NT	NT	NT	NT
609 W32 F bulk (rebound)	0.234	0.794	0.085	0.230	6.418	30.642	NT	NT
610 D-14 MB17	0.130	0.371	>50	>50	10.896	>50	0.954	2.735

Table S6. **Virus neutralization by other bNAbs (Continued)**

Virus ID	10-1074		PGDM1400		10E8		8ANC195	
	IC ₅₀	IC ₈₀						
610 D-14 MB8	NT							
610 D-14 ME17	0.020	0.061	NT	NT	NT	NT	NT	NT
610 W23 MI14	0.103	0.221	>50	>50	18.319	>50	1.039	5.307
610 W23 MJ3	0.143	0.486	>50	>50	2.625	14.121	0.720	5.262
610 W31 F bulk (rebound)	0.037	0.125	10.033	>50	10.333	42.481	NT	NT
611 D-14 2G 18	NT							
611 D-14 2I 20	4.149	7.511	>50	>50	>50	>50	NT	NT
611 D-14 B23	0.159	0.371	>50	>50	13.964	>50	>50	>50
611 D-14 MH8	1.607	7.542	>50	>50	18.267	>50	0.543	2.658
611 D-14 MH12	4.753	18.823	NT	NT	NT	NT	NT	NT
611 D-14 MH7	1.239	4.297	NT	NT	NT	NT	NT	NT
611 D-14 MI10	0.175	0.475	19.758	>50	14.932	>50	23.440	>50
611 D-14 MJ3	1.106	4.959	>50	>50	>50	>50	0.827	2.869
611 W23 MC1	2.836	10.552	>50	>50	19.035	>50	0.324	1.154
611 W23 MC23	0.599	1.607	>50	>50	16.326	>50	0.436	1.507
611 W23 MS1	0.157	0.343	4.852	>50	>50	>50	>50	>50
611 W23 MS14	12.072	45.504	>50	>50	20.659	>50	0.842	2.974
611 W23 MS13	3.264	9.715	NT	NT	NT	NT	NT	NT
611 W23 MP16	0.394	2.698	>50	>50	22.112	>50	>50	>50
611 W23 MO22	3.323	8.581	>50	>50	>50	>50	2.261	7.195
611 D-14 MK21	2.428	9.339	NT	NT	NT	NT	NT	NT
613 W23 MS18	0.035	0.115	0.032	0.084	6.237	46.470	0.191	0.671
613_D-14_C16	NT							
613_D-14_C6	0.189	0.494	0.114	0.545	16.077	>50	0.451	1.281
613_D-14_D15	NT							
613_D-14_F12	0.097	0.248	>50	>50	33.428	>50	0.450	1.011
613 D-14 MB10	0.147	0.309	>50	>50	22.020	>50	0.836	2.265
613 D-14 MB23	0.080	0.177	12.241	>50	5.493	30.324	0.364	1.311
616 D-14 300K B12	0.108	0.250	22.217	>50	15.198	47.695	14.942	>50
616 D-14 MF8	0.120	0.260	7.898	40.705	2.280	11.461	9.399	>50
616 D-14 MF21	0.111	0.371	22.388	>50	0.789	5.652	3.979	>50
616 D-14 MA11	0.130	0.347	6.705	30.075	0.837	3.900	8.139	>50
616 D-14 300K A19	0.114	0.253	7.052	42.667	4.090	18.338	1.406	>50
616 W23 MU12	0.117	0.269	10.063	>50	4.422	21.211	2.190	>50
616 W23 MU18	0.133	0.304	13.447	>50	4.382	36.312	2.440	>50

NT, not tested.

Table S7. **Rejection of the null hypothesis of clonal evolution in latent and rebound sequences in the 3SEQ recombination algorithm**

ID	P value	Significant for multiple comparisons	Source of parent sequences for recombination	NFL available
601	3.79×10^{-21}	Yes	Q ² VOA, Rebound SGA	No
602	1.65×10^{-7}	Yes	Q ² VOA	Yes
603	4.23×10^{-2}	No	N/A	Yes
605	3.20×10^{-20}	Yes	Q ² VOA, Rebound SGA	No
608	1.32×10^{-40}	Yes	Q ² VOA, Rebound SGA	No
609	5.35×10^{-4}	Yes	Q ² VOA, Rebound SGA	No
610	1.15×10^{-1}	No	N/A	Yes
611	1.20×10^{-19}	Yes	Q ² VOA, NFL, Rebound SGA	Yes
613	3.23×10^{-6}	Yes	Q ² VOA, NFL	Yes

NFL, near full-length.

Table S9. **Rejection of the null hypothesis of clonal evolution in latent sequences in the 3SEQ recombination algorithm**

ID	P value	Significant for multiple comparisons
601	8.13×10^{-21}	Yes
602	1.20×10^{-14}	Yes
603	3.48×10^{-4}	Yes
605	3.09×10^{-9}	Yes
608	1.82×10^{-18}	Yes
609	1.51×10^{-4}	Yes
610	6.25×10^{-4}	Yes
611	4.36×10^{-18}	Yes
613	1.55×10^{-8}	Yes
616	8.66×10^{-14}	Yes

Table S10. Latent parent viruses among rebound recombinants

ID	Number of recombinant rebound sequences with both parents latent	Number of rebound SGA sequences isolated	Number of latent viruses that serve as parents	Parent viruses	Parent viruses are an expanded clone
601	48	52	5	601_D14_MB17	No
				601_D14_MC13	No
				601_D14_ME10	No
				601_D14_2E_19	No
				601_D14_2G_10	No
602	31	31	3	602_W23_2Q_2	No
				602_W23_2M_11	No
				602_W23_2T_15	No
605	0	10	2	605_W23_MK18	No
				605_W23_MC1	No
608	4	23	6	608_D14_MA7	No
				608_W23_MO19	No
				608_D14_MA9	No
				608_D14_MJ8	No
				608_W23_MR14	No
609	11	12	3	609_D14_MI23	No
				609_D14_MI8	No
				609_D14_MH15	No
611	25	27	5	611_W23_P8_A6_FL	No
				611_D14_2C_9	No
				611_W23_2C_9	No
				611_W23_P8_B1_FL	No
				611_W23_2G_5	No
613	12	12	3	613_W23_P7_H3_FL	No
				613_W23_MS3	No
				[613_W23_MS18/613_W23_MAB_11/613_W23_MAA_20/613_W23_2J_14/613_W23_MR_21]	Yes

Tables S3 and S8 are provided as Excel tables. Table S3 shows laboratory values and 3BNC117 concentrations. Table S8 presents the output from the 3SEQ recombination algorithm.

Dataset S1 is provided as a PDF and shows Env sequences from rebound outgrowth cultures and rebound SGA. Maximum-likelihood phylogenetic trees of full-length env sequences of viruses from rebound outgrowth cultures and rebound SGA from seven participants. Viruses from outgrowth culture are represented in red rectangles and from rebound SGA in black rectangles. For participants 611 and 613, culture-derived viruses were either identical to latent viruses or different from both latent and rebound SGA viruses. Rebound SGA viruses could not be isolated from participant 616.

Dataset S2 is provided as a PDF and shows Env sequences from Q²VOA cultures and rebound SGA. Maximum-likelihood phylogenetic trees of full-length env sequences of viruses from Q²VOA outgrowth cultures from the six participants not shown in Fig. 3. Viruses from week -2 are represented in empty black rectangles, week 23 in full black rectangles, and rebound SGA viruses in red rectangles. Asterisks indicate nodes with significant bootstrap values (bootstrap support $\geq 90\%$). The color on the rectangles near the group of sequences defines the clones as shown in Fig. 1 C. Numbers correspond to 3BNC117 IC₅₀

neutralization values. For rebound viruses, neutralization values shown were determined from culture-derived viruses that were identical or highly similar to the particular SGA viruses.

Dataset S3 is provided as a PDF and shows maximum likelihood phylogenetic trees of full-length env sequences from Q²VOA cultures, rebound SGA, and near full-length (NFL) genome. Viruses from week -2 are represented in green, from week 23 in blue, rebound SGA in red, and from NFL in purple. Asterisks indicate nodes with significant bootstrap values (bootstrap support $\geq 90\%$). Green stars represent the recombinant parents, and red stars represent the child recombinant for the examples shown in [Fig. 5 B](#).