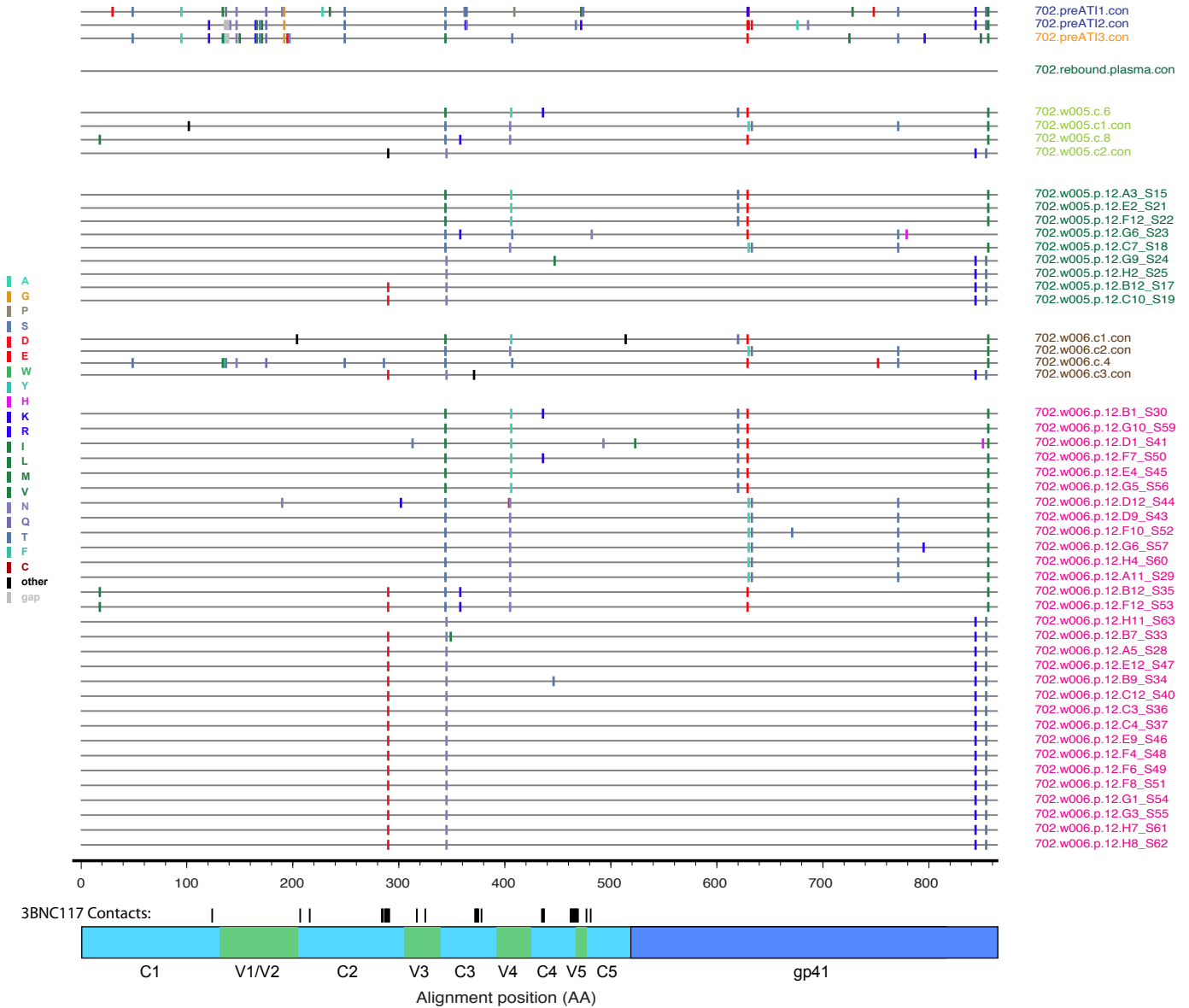
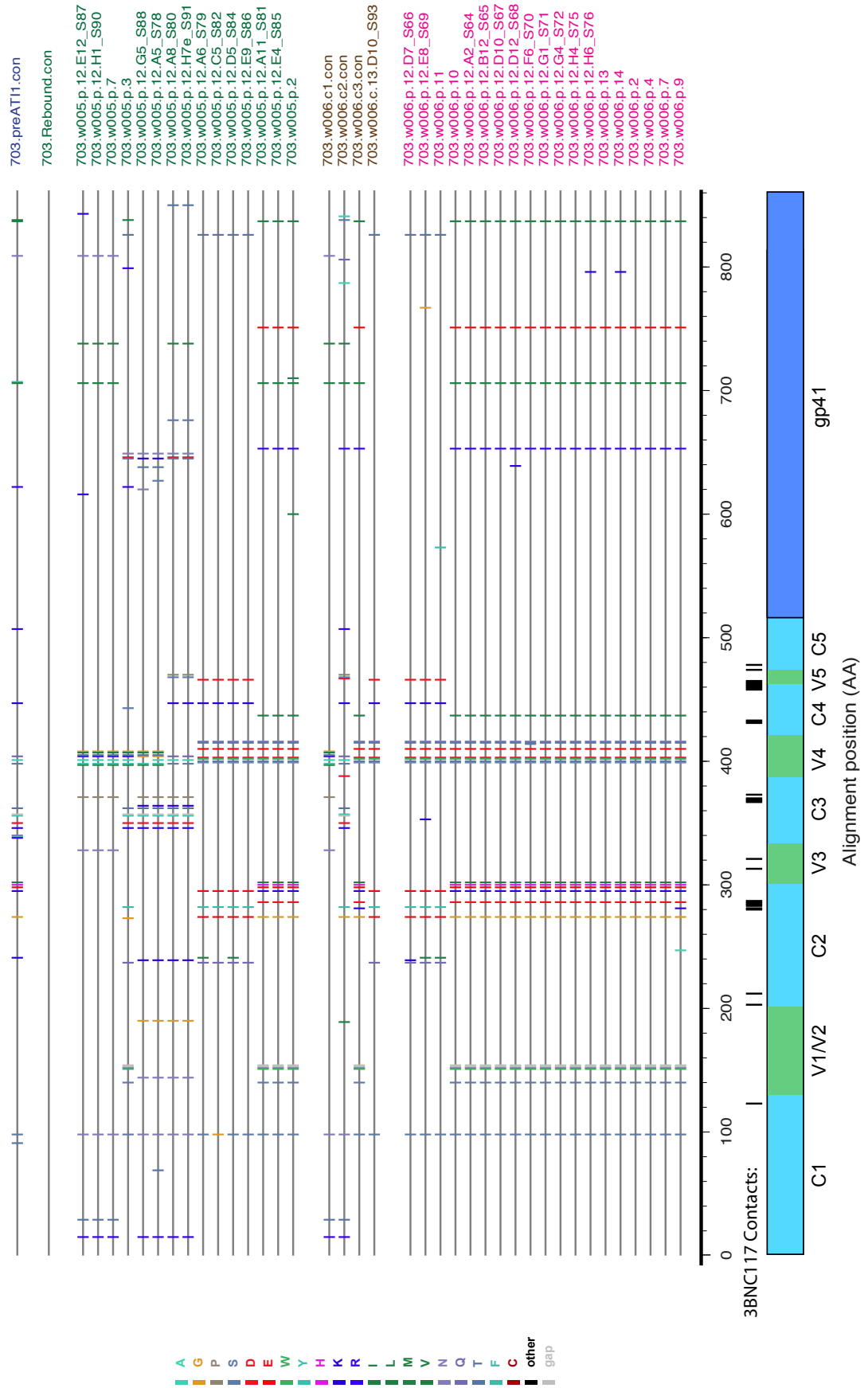




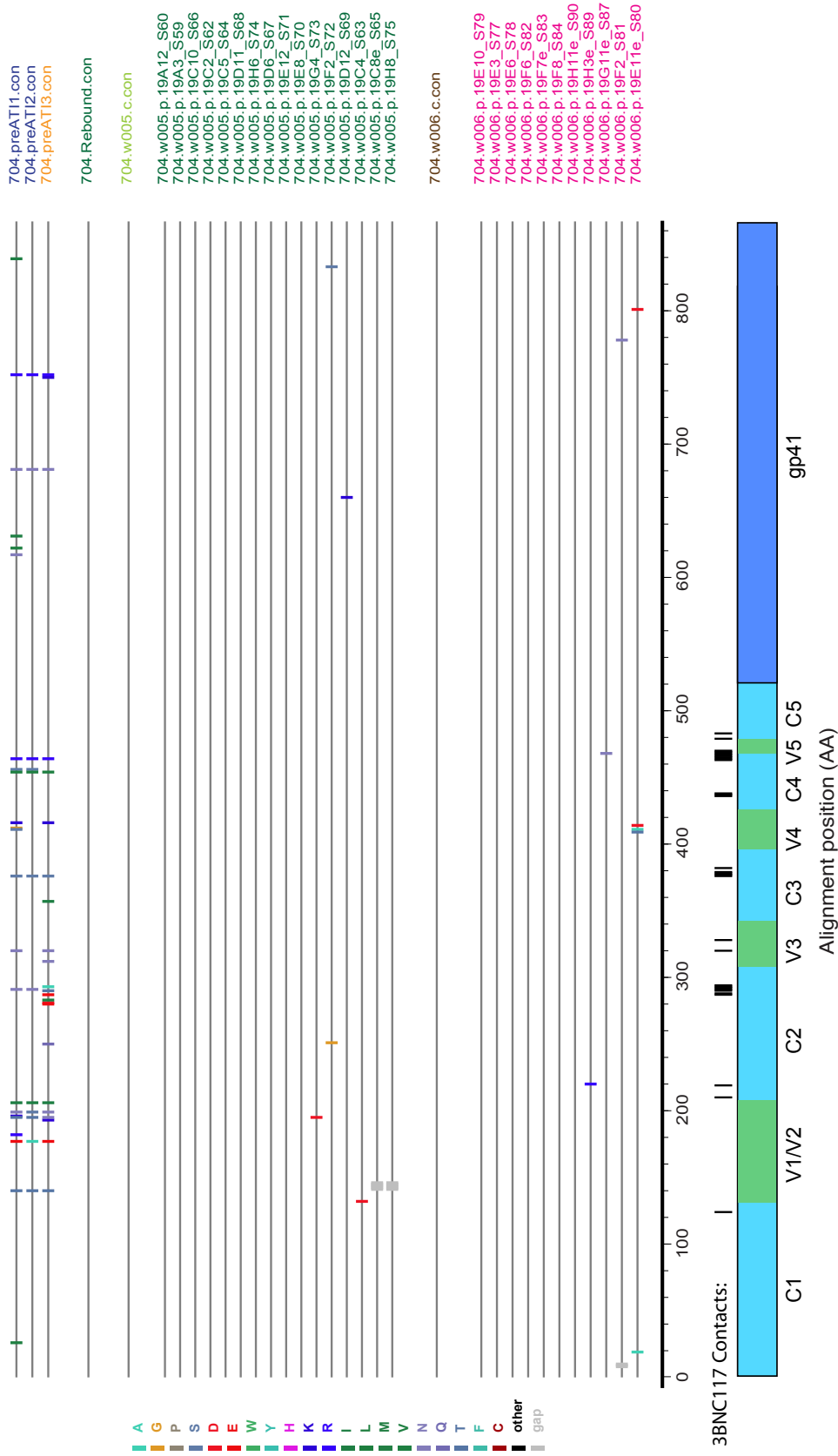
Supplementary Figure 1b. Amino Acid Highlighter Plot of 702



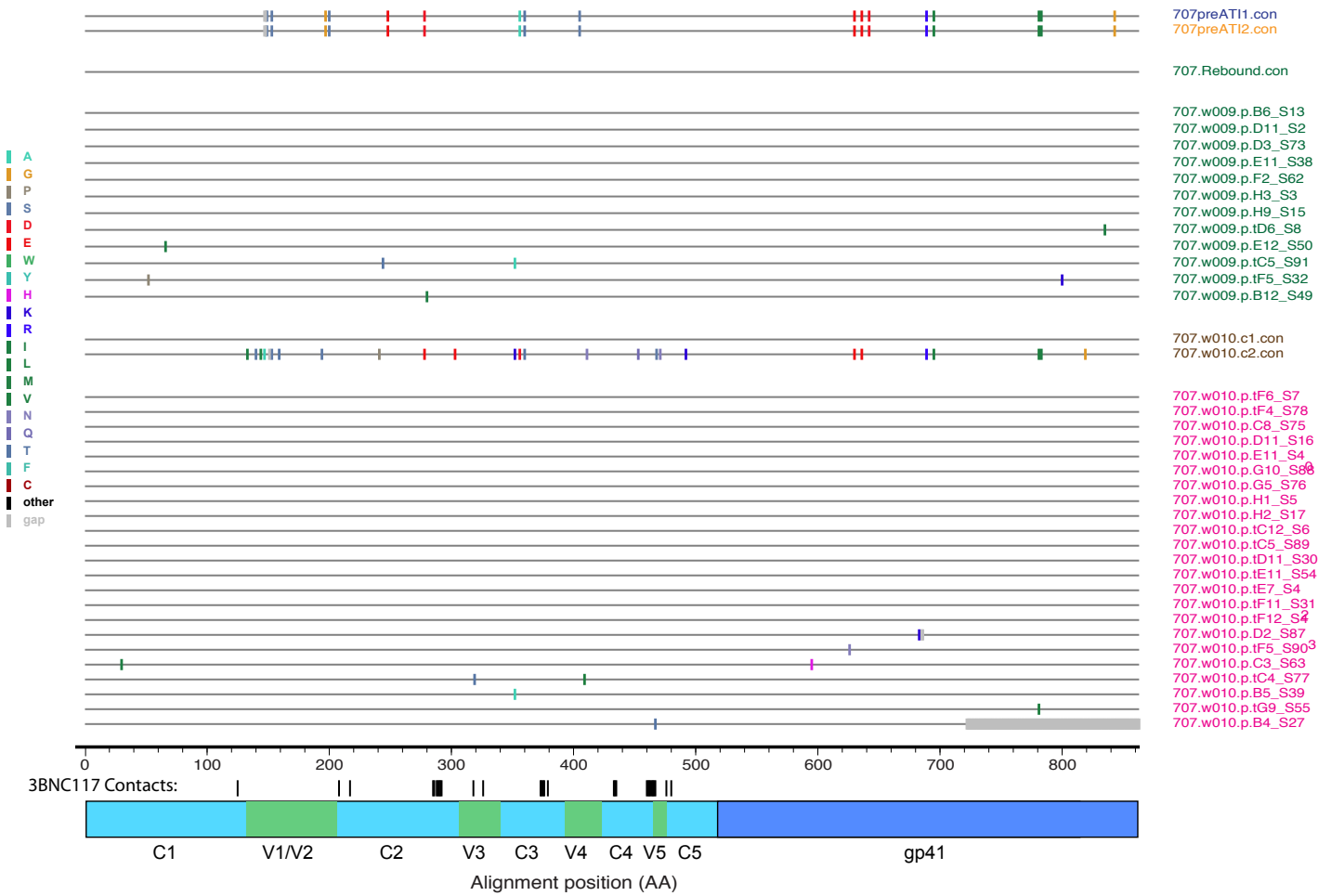
Supplementary Figure 1c. Amino Acid Highlighter Plot of 703



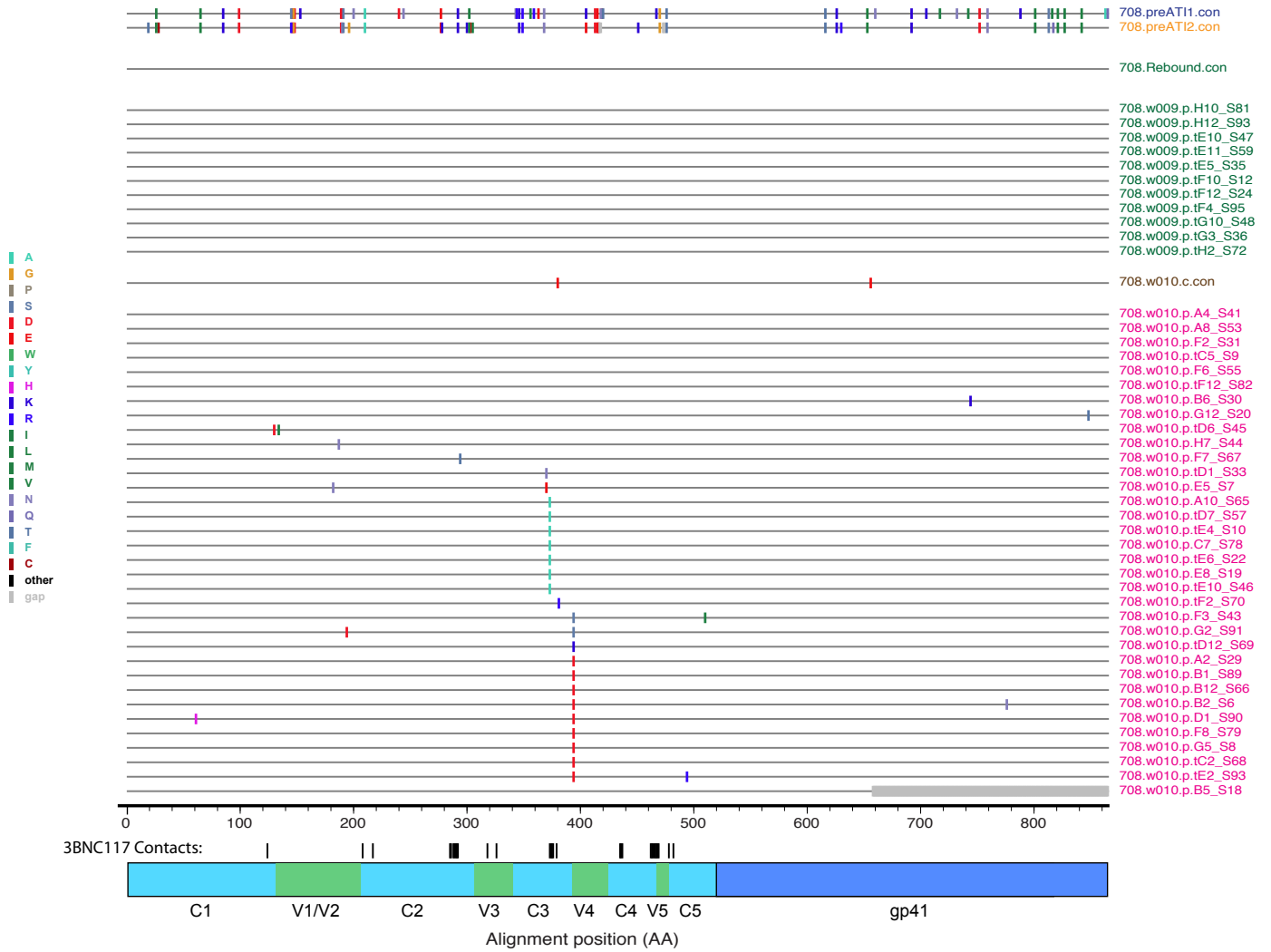
Supplementary Figure 1d. Amino Acid Highlighter Plot of 704



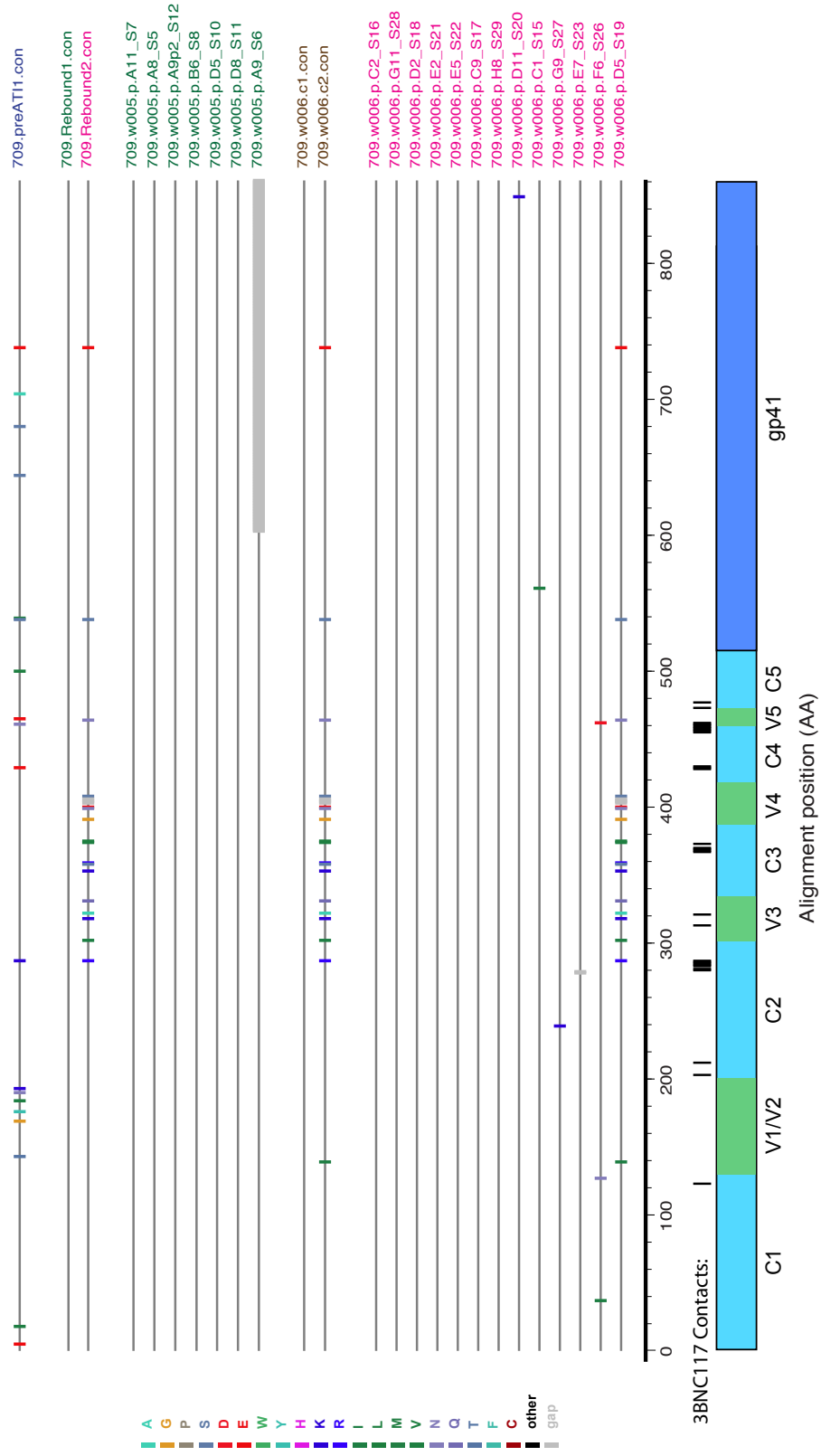
Supplementary Figure 1e. Amino Acid Highliter Plot of 707



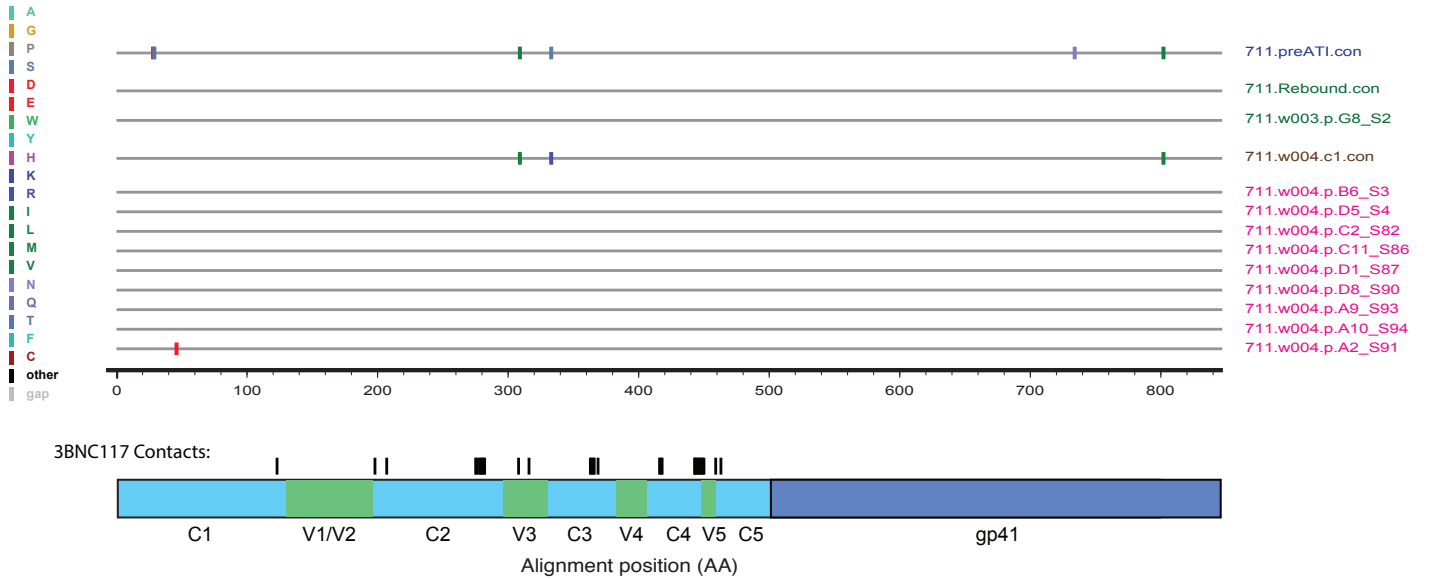
Supplementary Figure 1f. Amino Acid Highliter Plot of 708



Supplementary Figure 1g. Amino Acid Highlighter Plot of 709



Supplementary Figure 1h. Amino Acid Highlighter Plot of 711



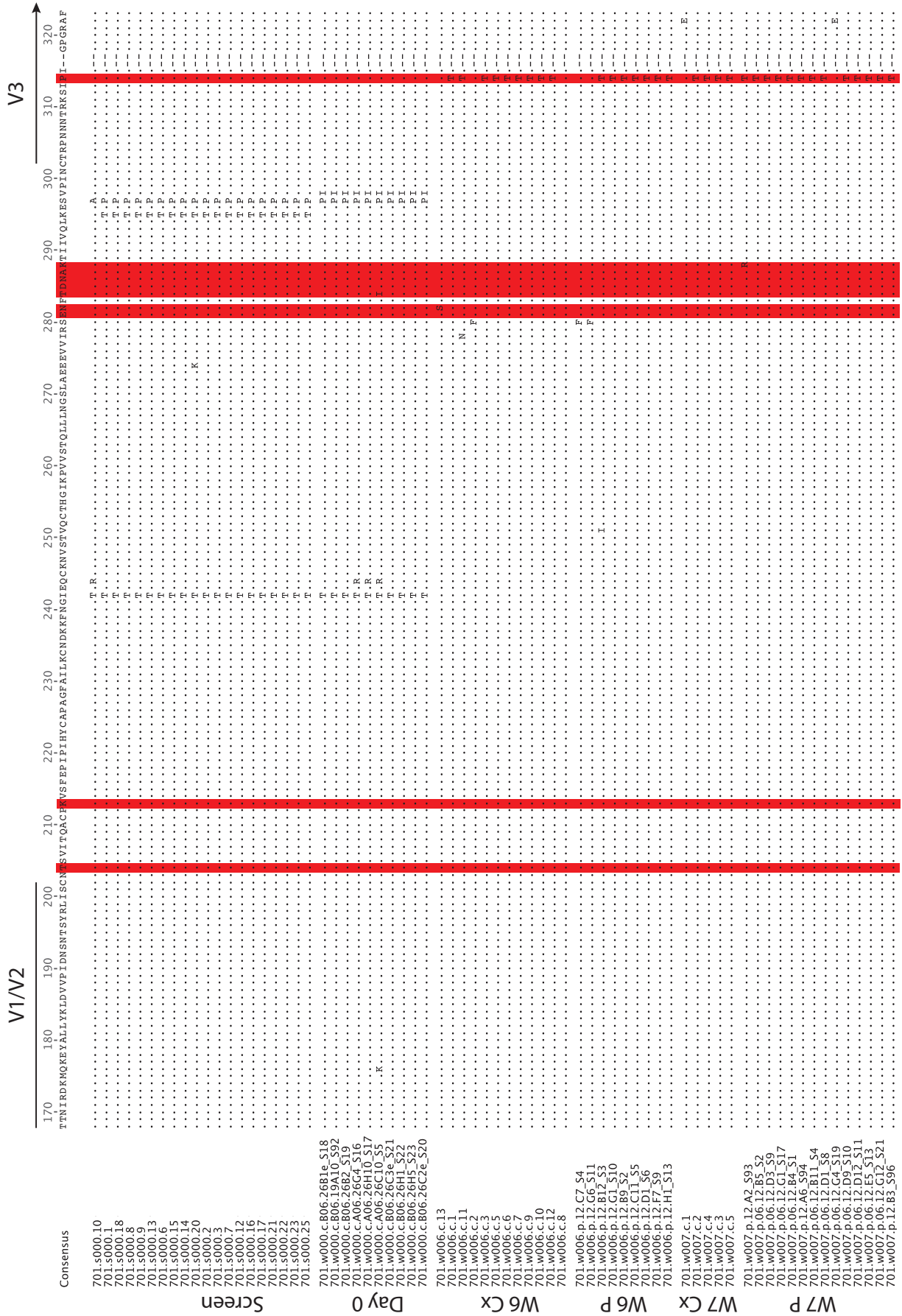
**Supplementary Figure 1. Amino acid highlighter plots.** Amino acid highlighter plots

([http://www.hiv.lanl.gov/content/sequence/HIGHLIGHT/highlighter\\_top.html](http://www.hiv.lanl.gov/content/sequence/HIGHLIGHT/highlighter_top.html)) are shown for all env genes analyzed in Fig. 3. Sequences are represented as horizontal lines with tick marks indicating amino acid changes (color coded) relative to the first rebound plasma derived Env protein consensus sequence. Gp160 landmarks are shown at the bottom, with 3BNC117 contacts depicted above in black tick marks. Numbering at the bottom corresponds to the alignment position. Pre-ATI sequences are shown above the rebound master sequence. Plasma and culture derived consensus sequences from rebound time points are shown below. In participants 702 and 703, an aspartate at HXB2 position 281 (alignment positions 290 and 286, respectively) was selected in the plasma rebound sequences. In other participants, sporadic mutations within 3BNC117 contacts are observed during rebound. In 708, selection in the C3-V4 region (outside of 3BNC117 contacts) is observed at the second rebound time point.





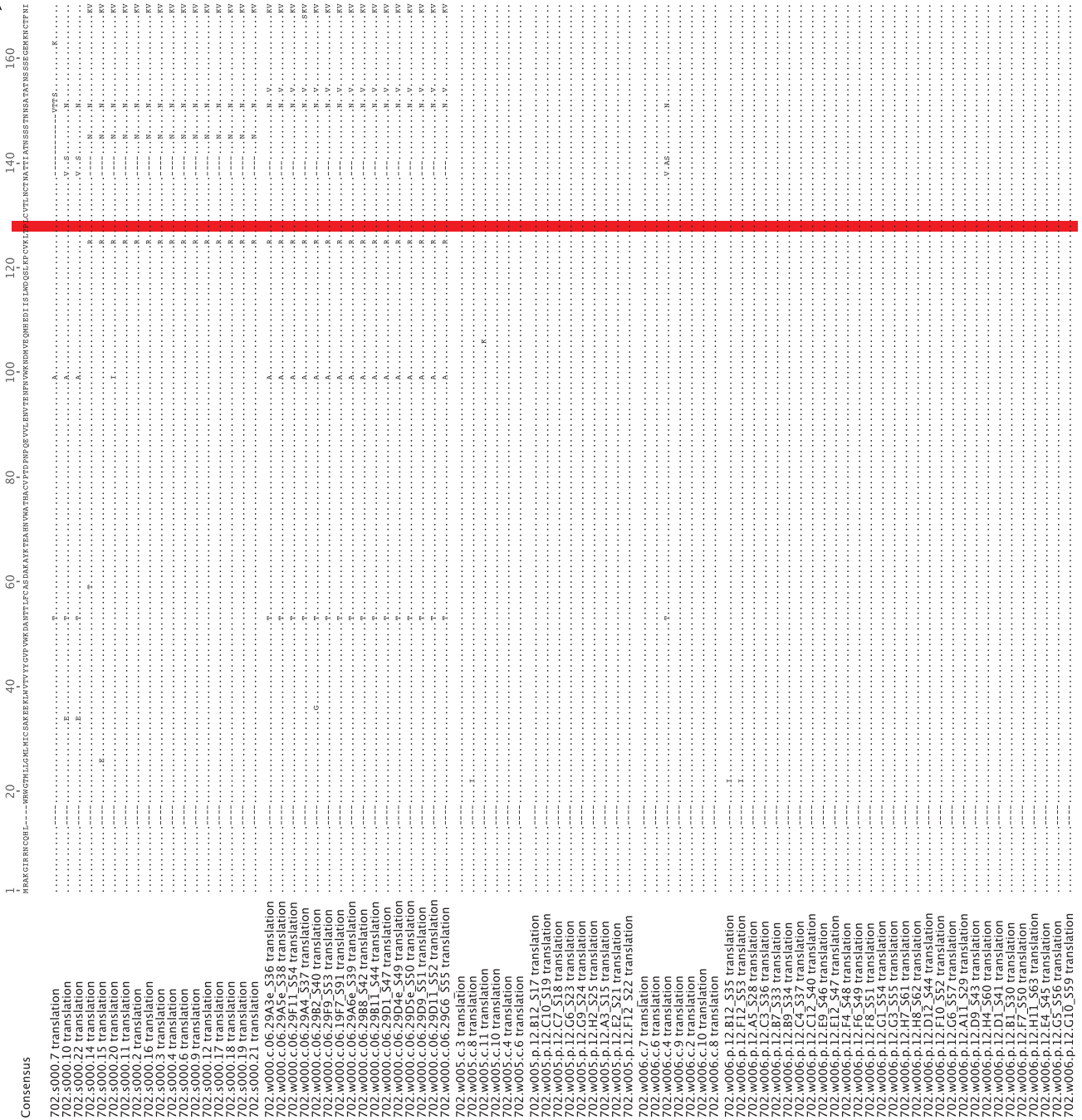
Supplementary Figure 2a continued. 701, All GP120 Single Genome Sequences



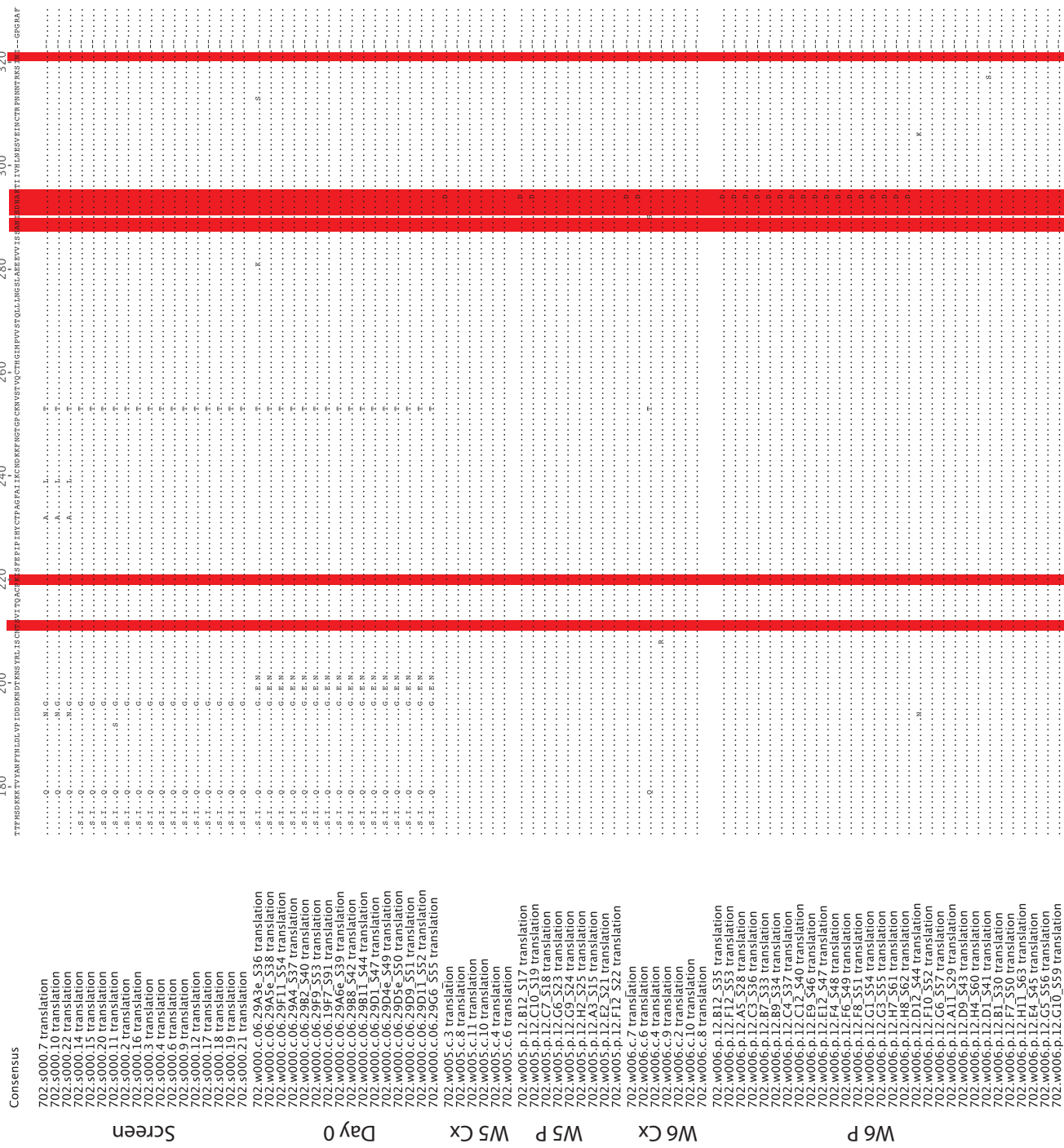
■ 3BNC117 Contacts



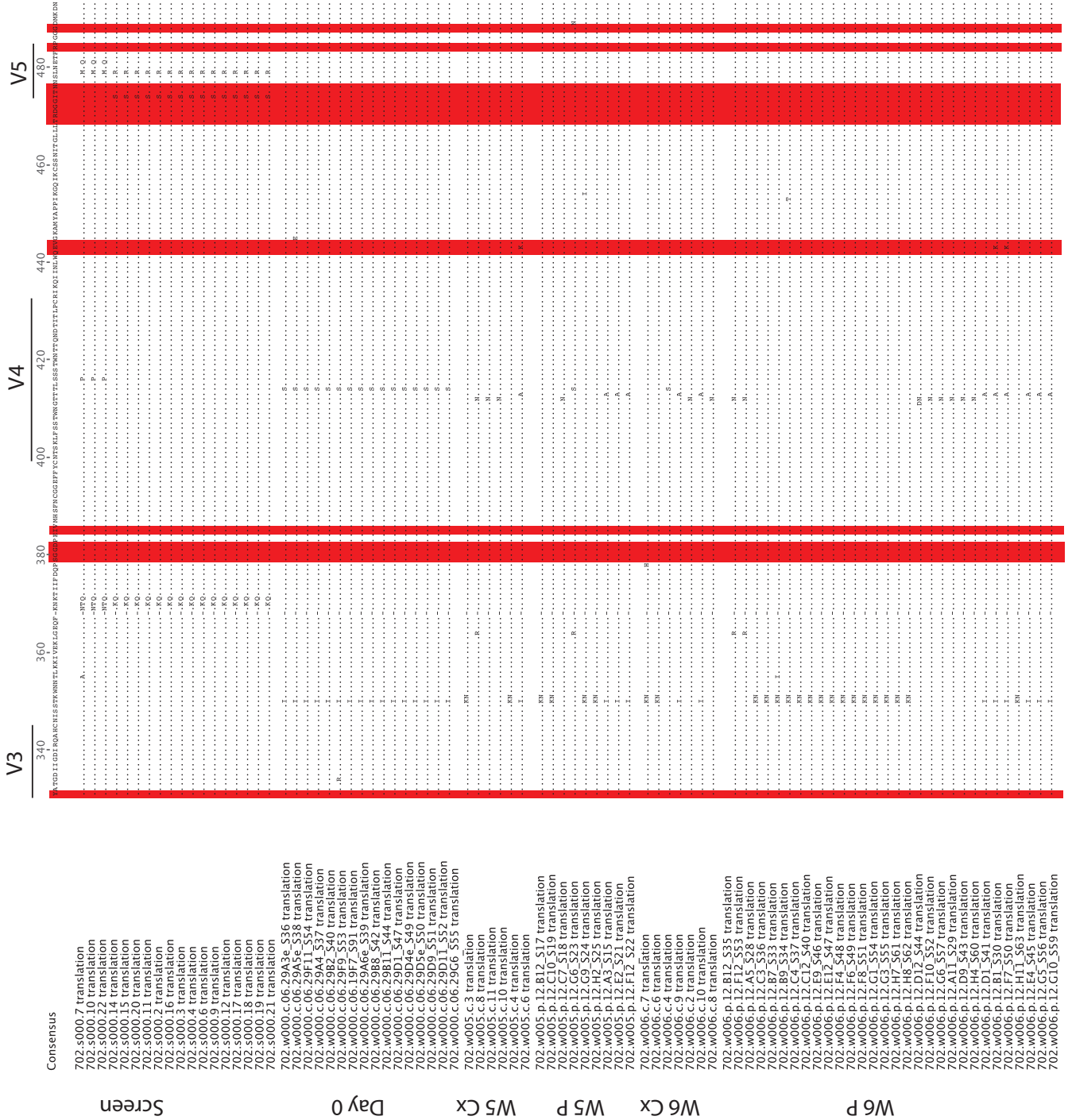
Supplementary Figure 2b. 702, All GP120 Single Genome Sequences



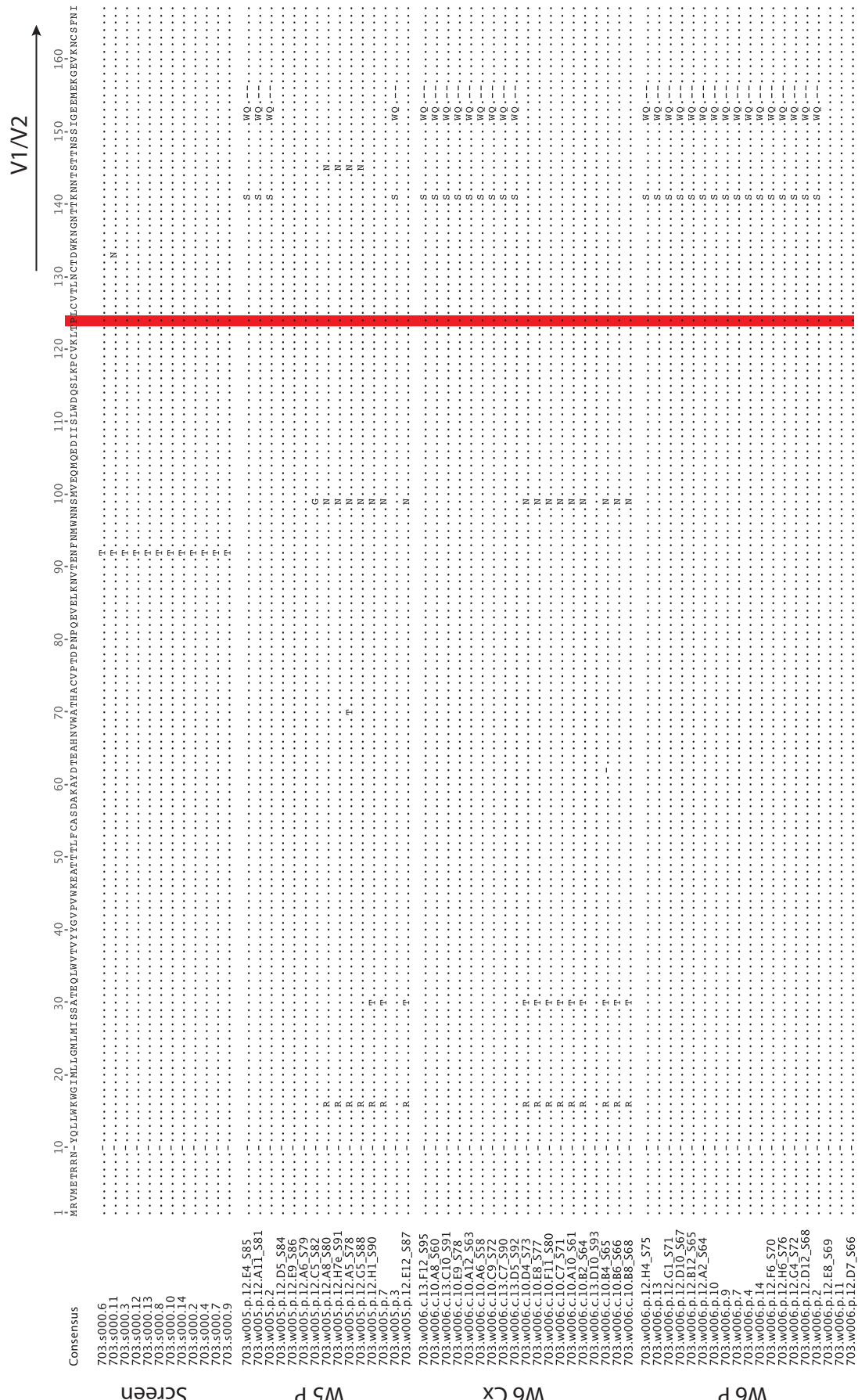
Supplementary Figure 2b continued. 702, All GP120 Single Genome Sequences



Supplementary Figure 2b continued. 702, All GP120 Single Genome Sequences

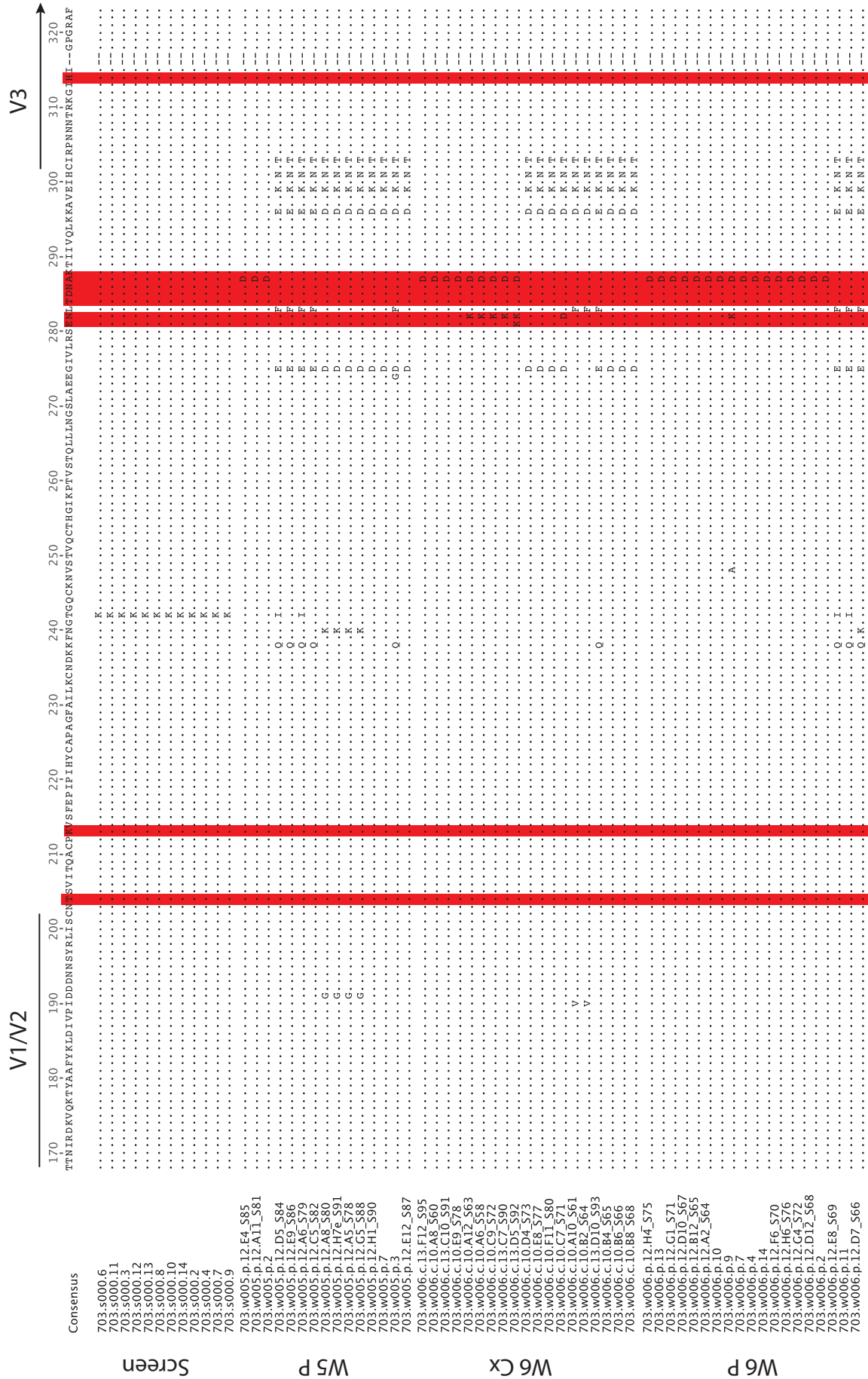


Supplementary Figure 2c. 703, All GP120 Single Genome Sequences



■ 3BNC117 Contacts

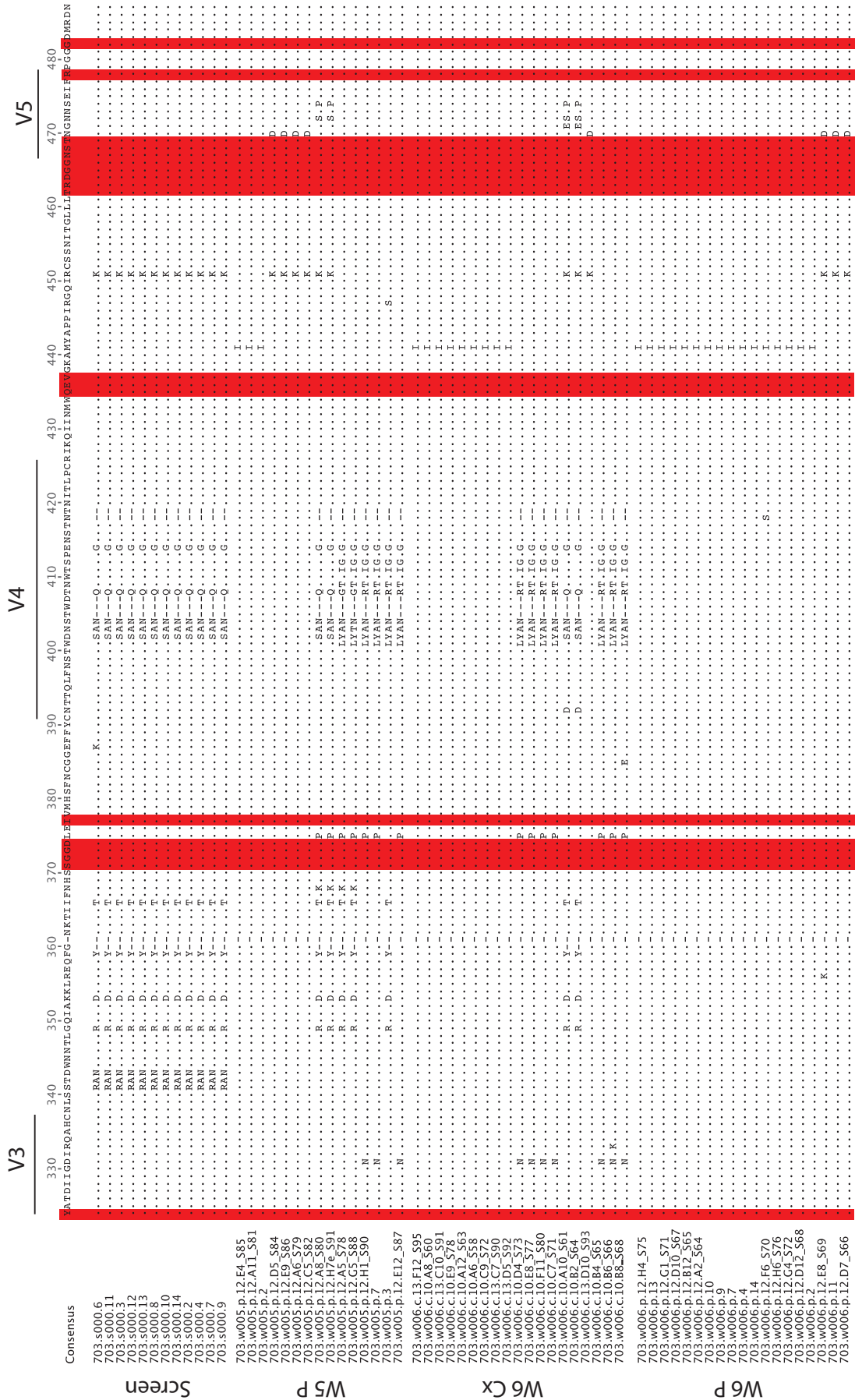
Supplementary Figure 2c continued. 703, All GP120 Single Genome Sequences



■ 3BNC117 Contacts

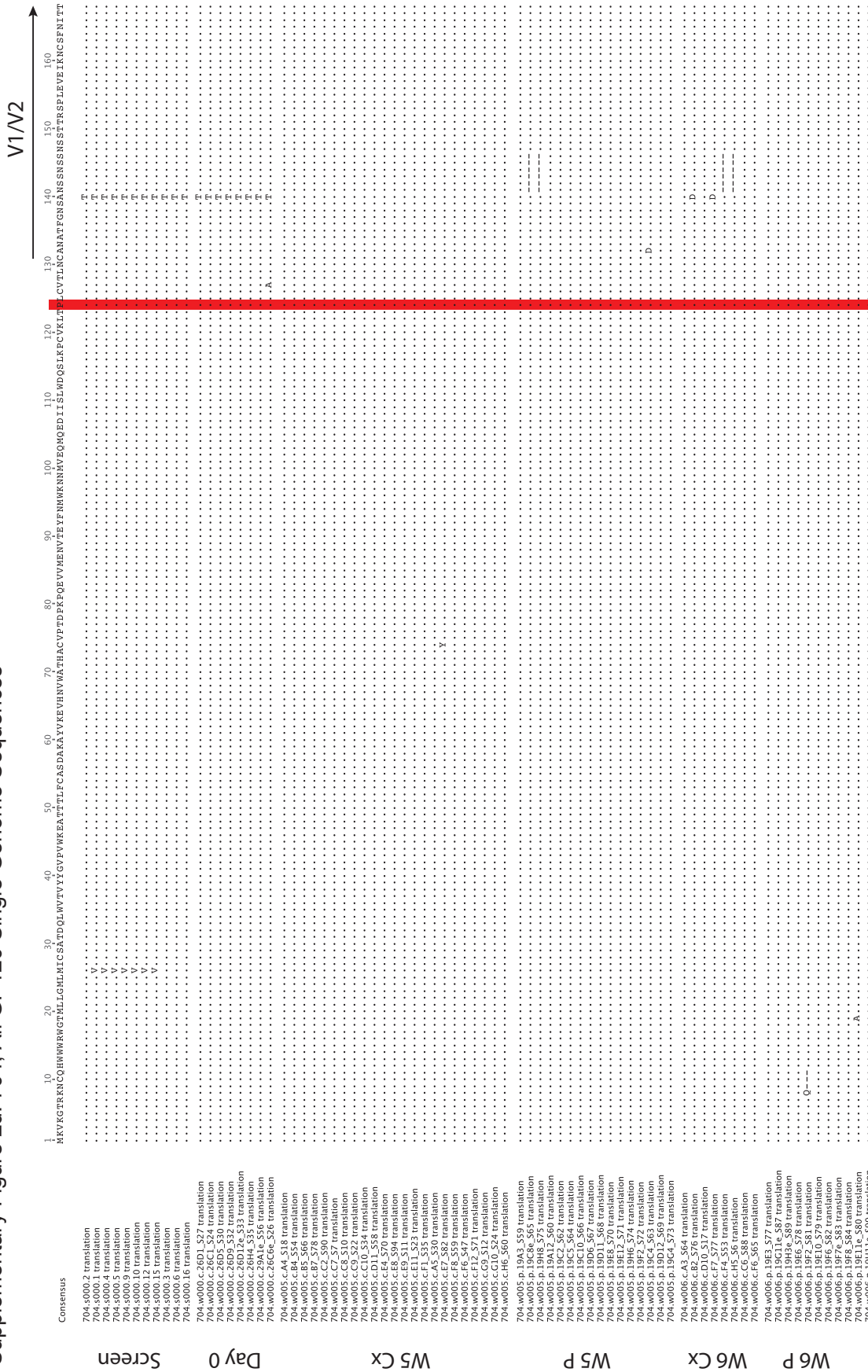


Supplementary Figure 2c continued. 703, All GP120 Single Genome Sequences



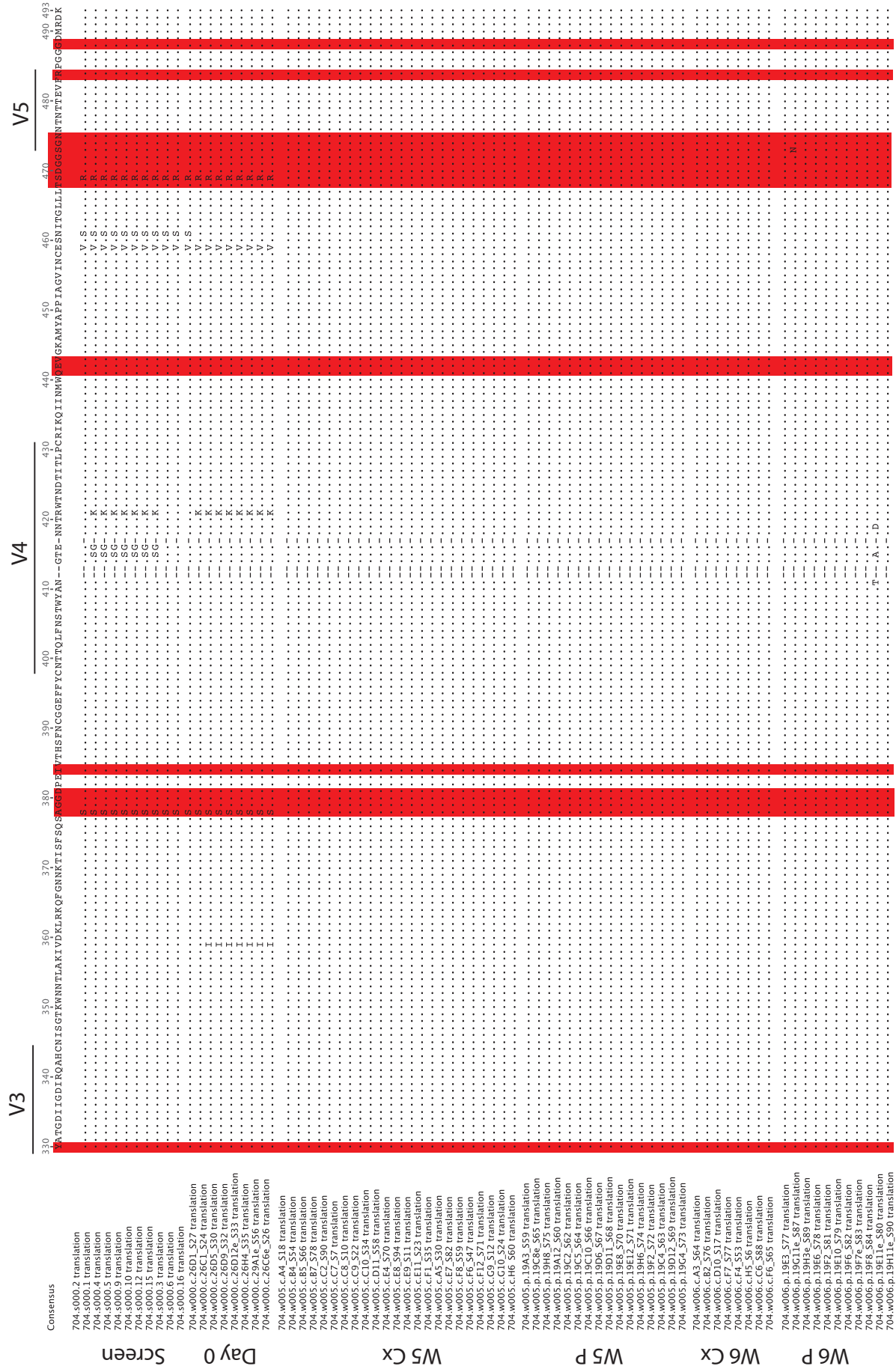
■ 3BNC117 Contacts

Supplementary Figure 2d. 704, All GP120 Single Genome Sequences



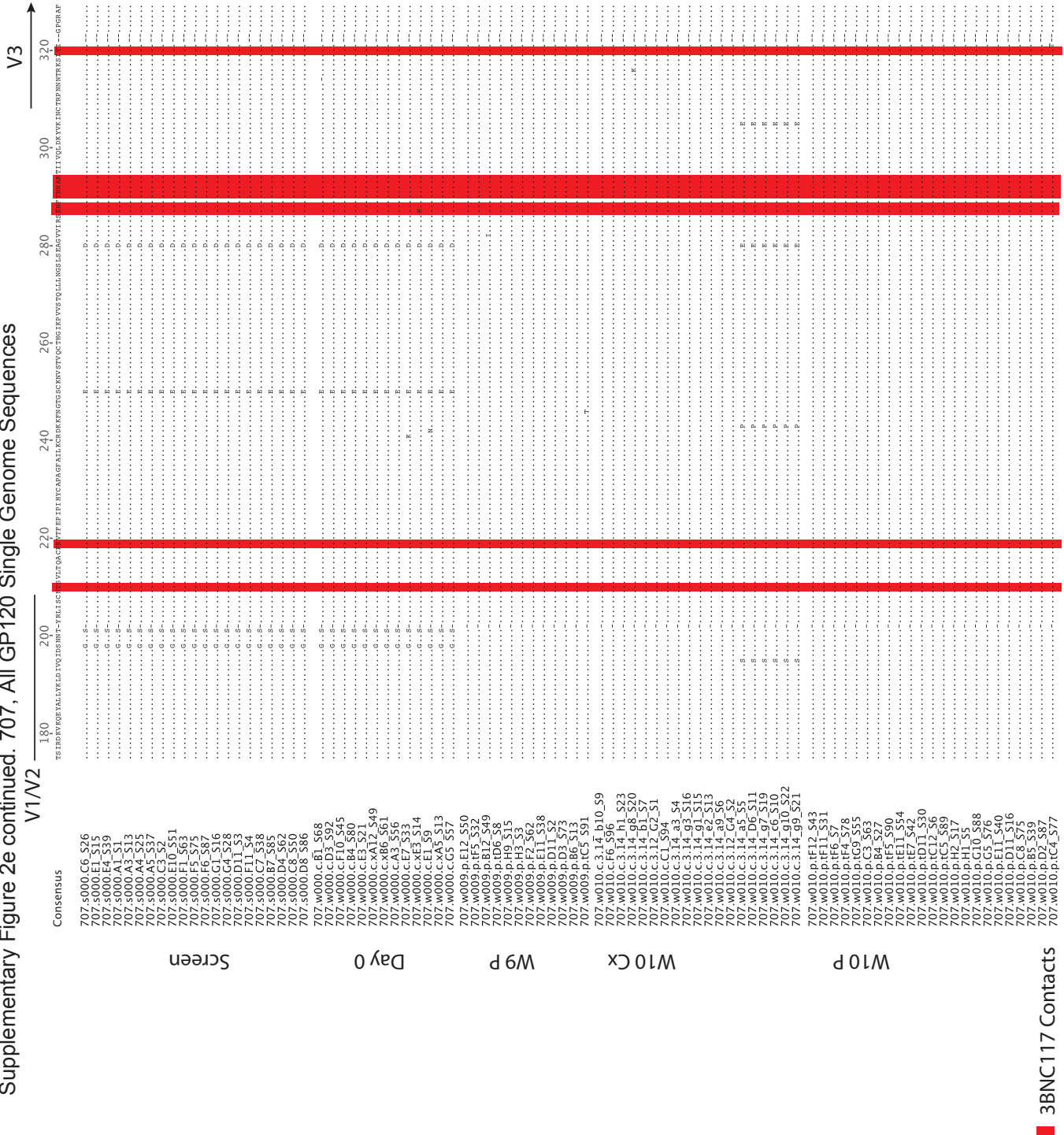


Supplementary Figure 2d continued. 704, All GP120 Single Genome Sequences

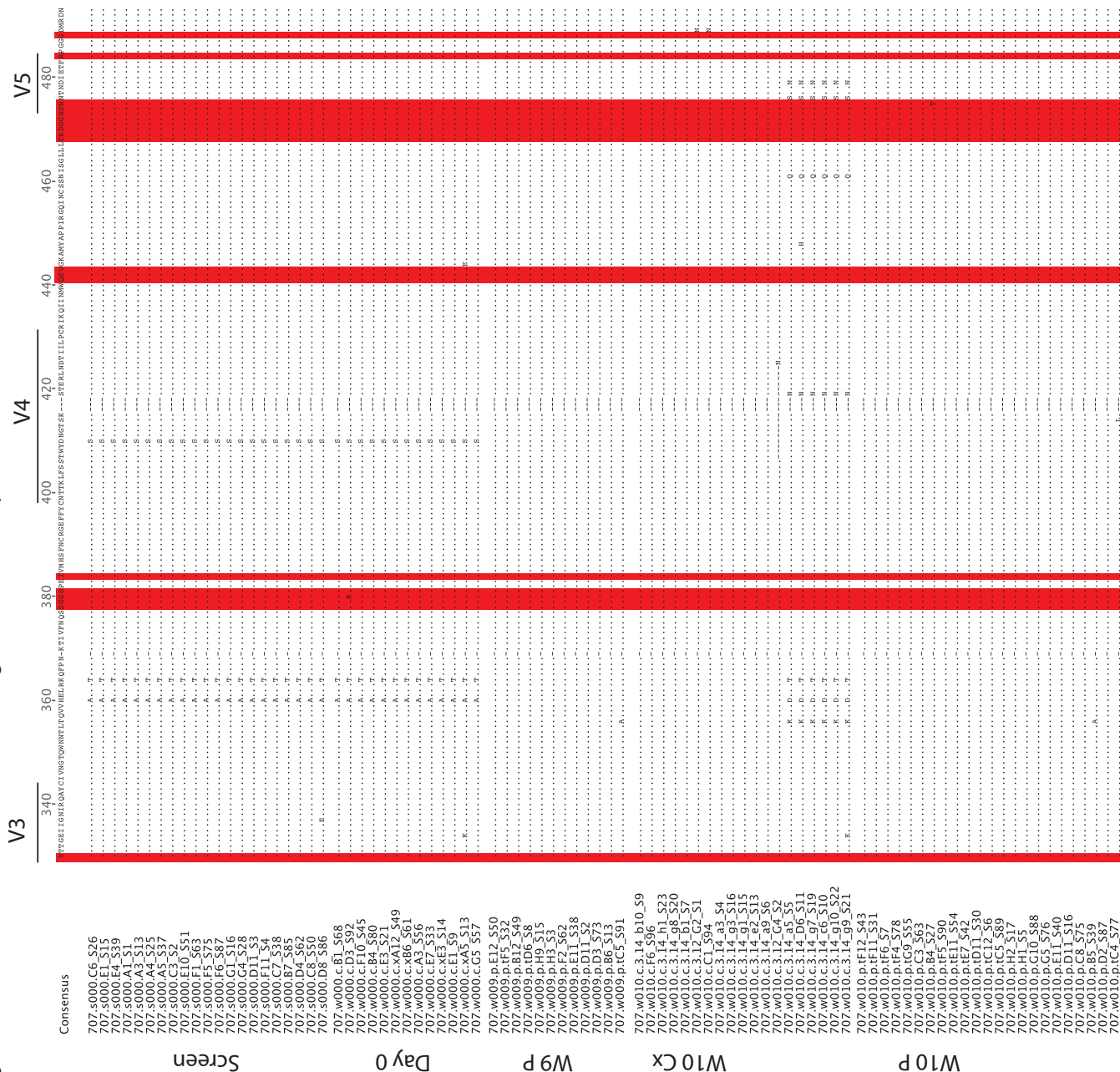




Supplementary Figure 2e continued. 707, All GP120 Single Genome Sequences

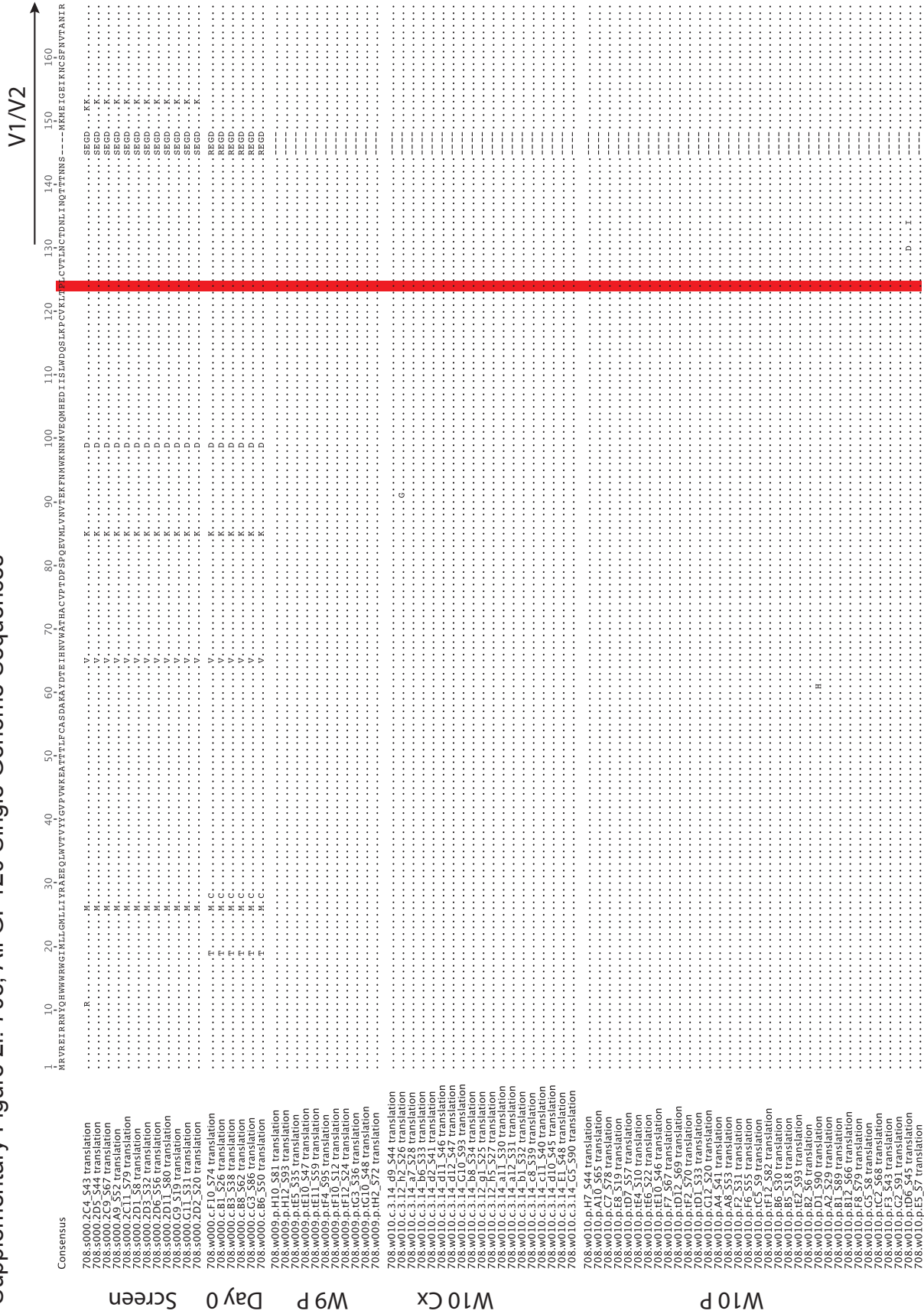


Supplementary Figure 2e continued. 707, All GP120 Single Genome Sequences



■ 3BNC117 Contacts

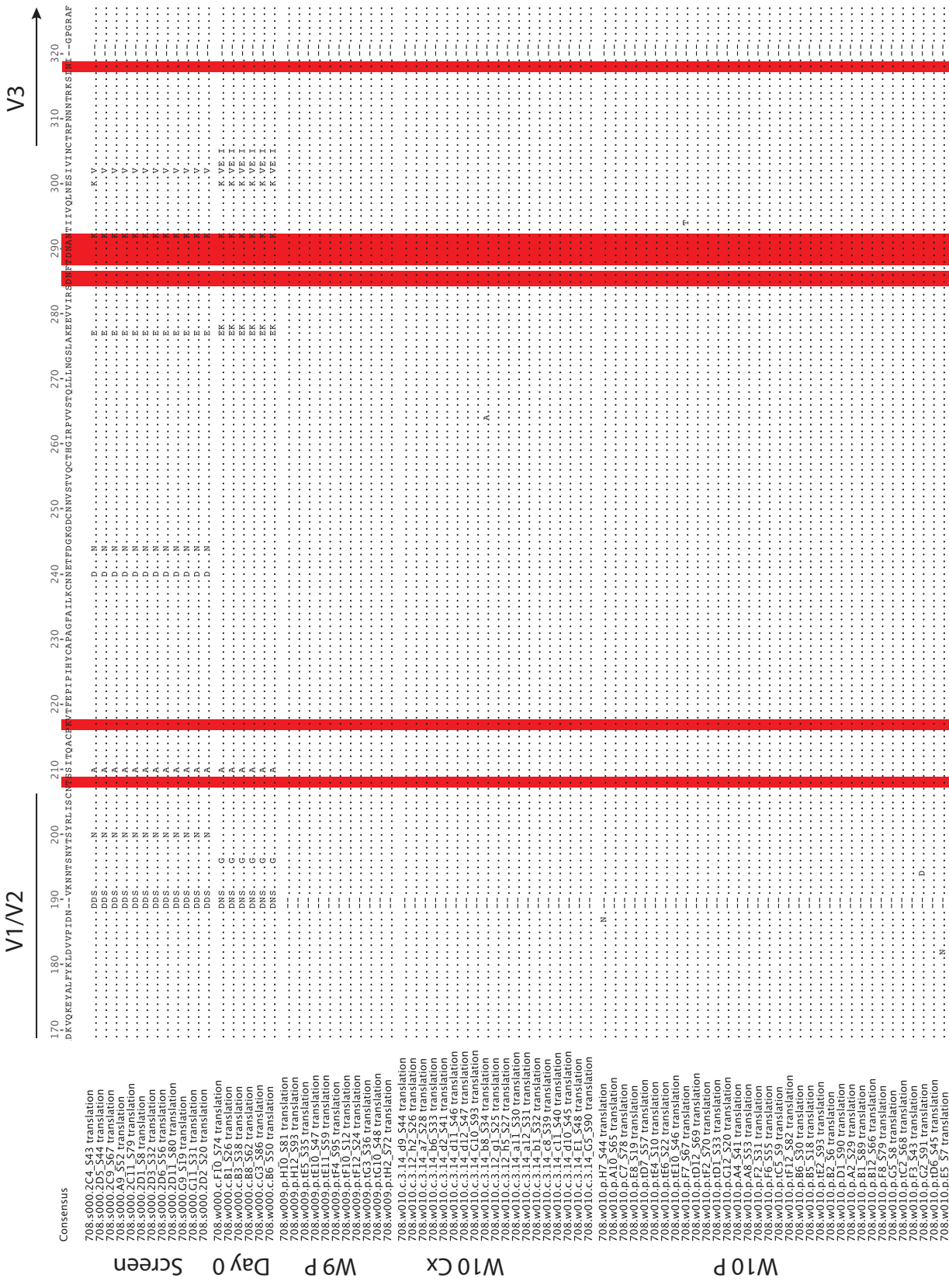
Supplementary Figure 2f. 708, All GP120 Single Genome Sequences



■ 3BNC117 Contacts

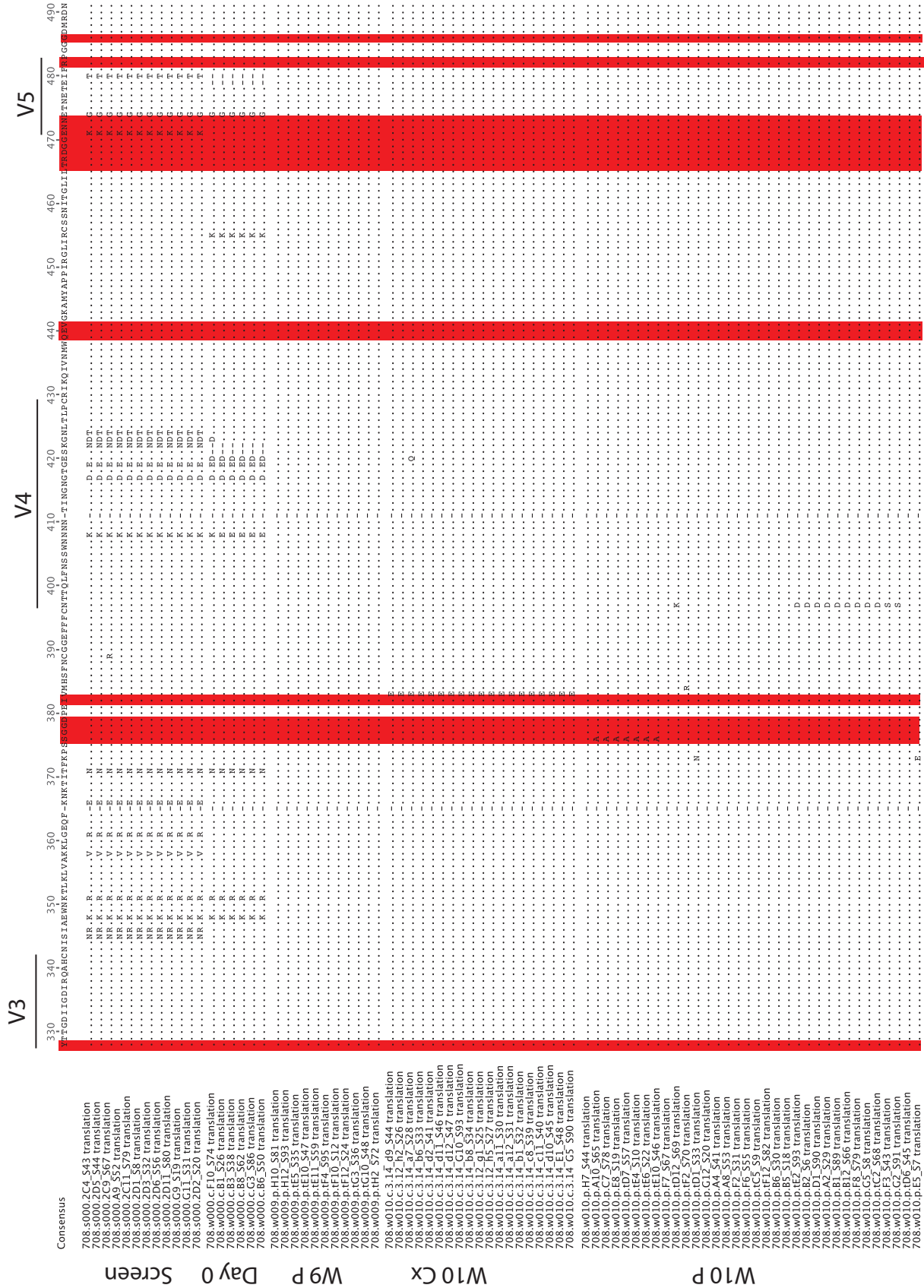


Supplementary Figure 2f continued. 708, All GP120 Single Genome Sequences



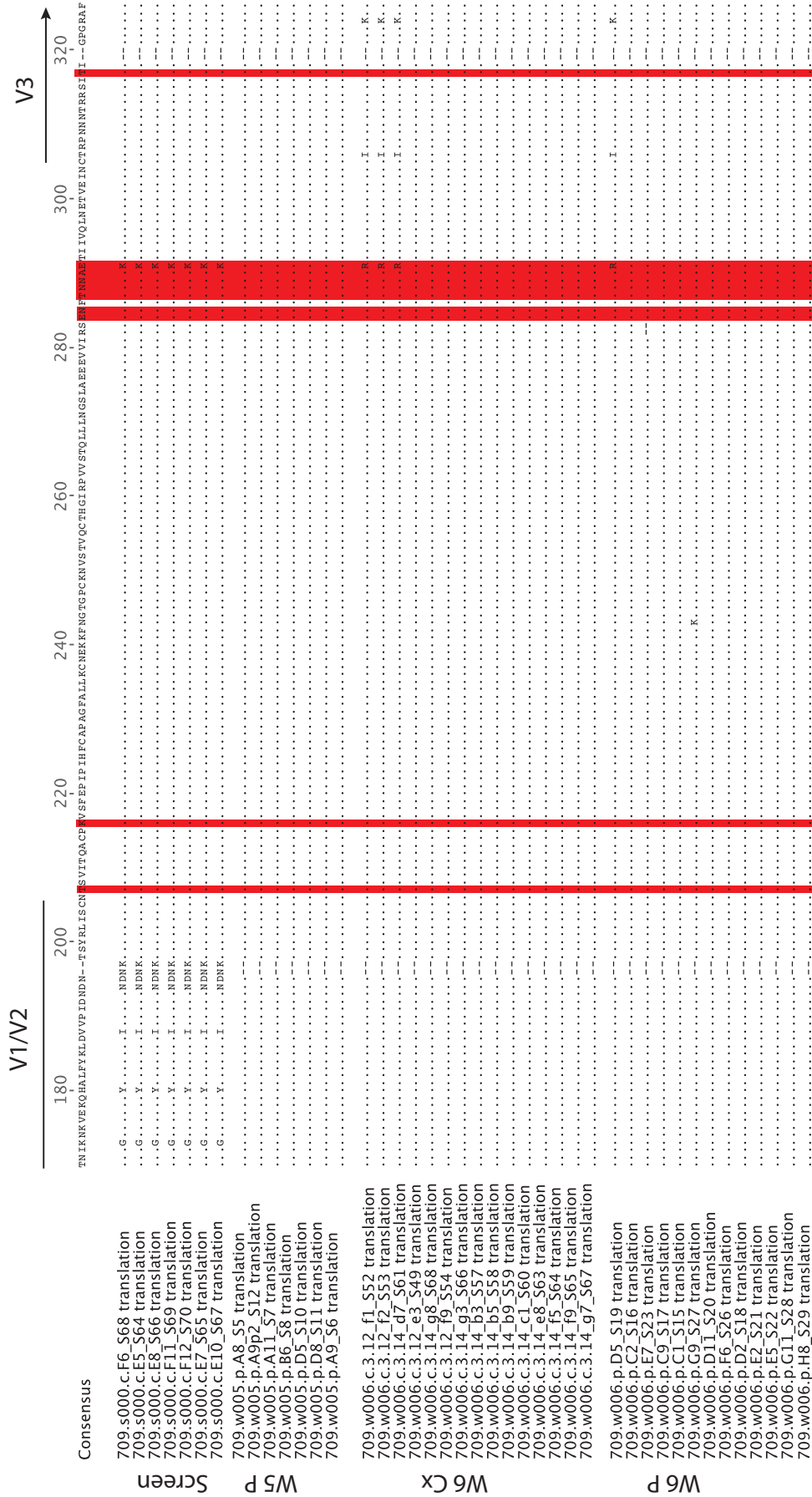
■ 3BNC117 Contacts

Supplementary Figure 2f continued. 708, All GP120 Single Genome Sequences

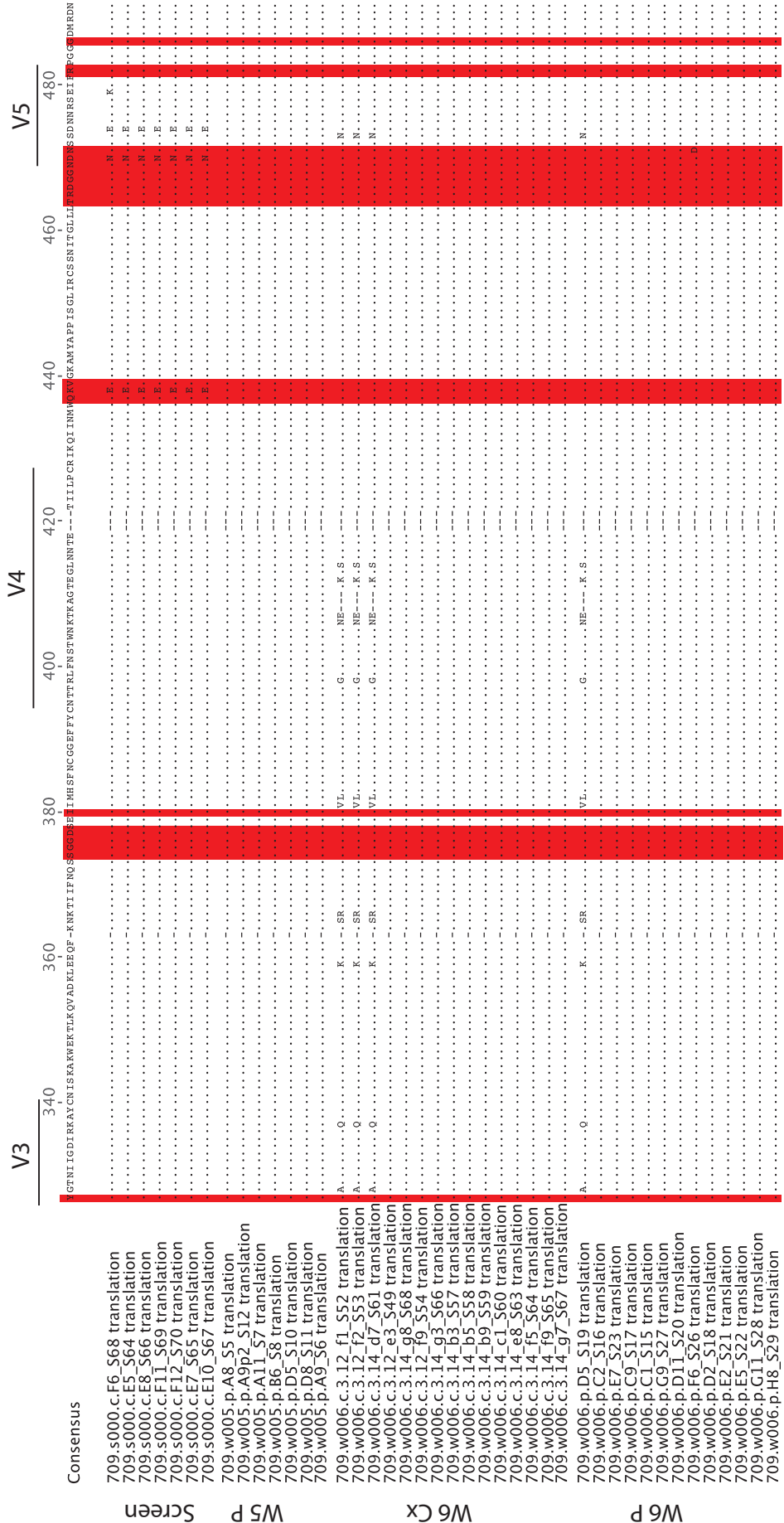




Supplementary Figure 2g continued. 709, All GP120 Single Genome Sequences



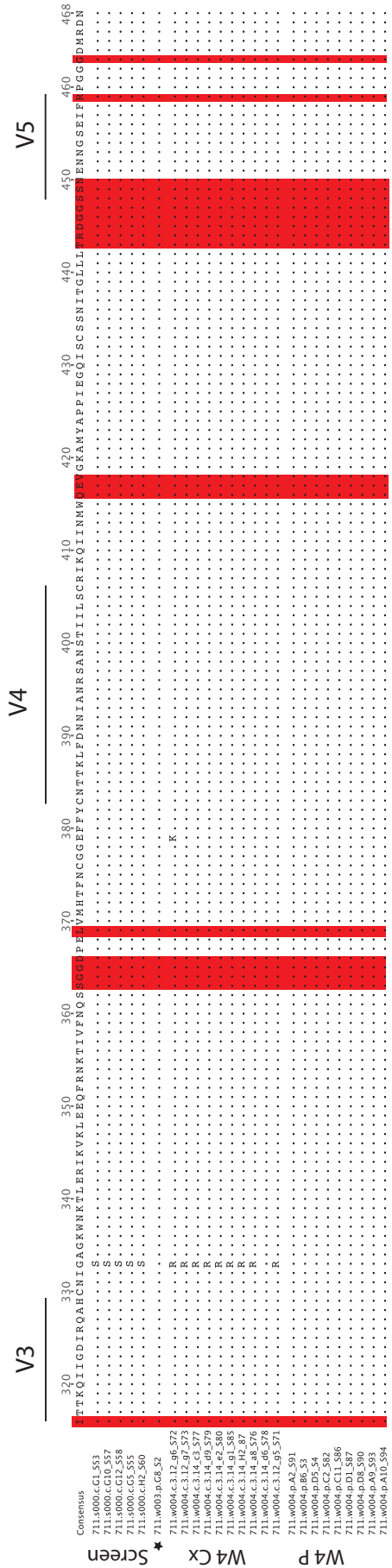
Supplementary Figure 2g continued. 709, All GP120 Single Genome Sequences



■ 3BNC117 Contacts



Supplementary Figure 2h continued. 711, All GP120 Single Genome Sequences



**Supplementary Figure 2. Alignment of gp120 Single Genome Sequences (SGSs) from Participants.** Sequences were aligned to individual participant consensus sequences for participants 701 (a), 702 (b), 703 (c), 704 (d), 707 (e), 708 (f), 709 (g) and 711 (h). Amino acids that differ from the consensus are indicated within individual sequences. All alignments were performed using the MUSCLE alignment tool in the Geneious software, version 8.1.3<sup>1</sup>. 3BNC117 contact sites are shaded in red<sup>2,3</sup>, and variable loops are indicated. Samples were obtained at screening, on Day 0 and at rebound time points as indicated (Fig. 2a and b).

Supplementary Table 1. Virus outgrowth culture neutralization screen.

Subject ID	TCID50/ml	Titer in TZM.bl cells (ug/ml)											
		3BNC117		10-1074		PG16		G52K5		VRC01			
		< 2.0	IC50	IC80	IC50	IC80	IC50	IC80	IC50	IC80	< 2.0	IC50	IC80
B69	267,184		1.281	4.647	0.974	5.741	>50	>50	0.173	0.528		2.539	11.176
B73	2,795		0.102	0.288	0.024	0.084	<0.023	0.077	2.122	7.431		0.716	2.325
B74	69,877		0.542	1.622	0.062	0.198	<0.023	<0.023	0.214	1.101		3.230	14.771
B76	3,655		2.331	8.516	>50	>50	>50	>50	>50	>50		13.855	41.714
B77	456,878		0.077	0.221	0.128	0.292	0.014	0.068	4.268	47.764		ND	ND
B80	6,679,594		0.248	0.908	0.126	0.366	>50	>50	0.372	2.098		1.204	4.354
B82	91,376		2.347	6.781	0.674	2.435	0.040	0.344	0.898	2.591		>50	>50
B88	6,679,594		0.904	3.111	3.551	23.522	4.533	>50	0.501	1.429		ND	ND
B89	39,493,845		3.189	11.365	0.825	2.223	9.810	>50	0.535	1.536		ND	ND
B92	13,471,913		6.625	27.427	0.658	1.768	0.012	0.106	0.294	1.085		12.663	>50
B93	1,335,919		>50	>50	15.646	>50	1.318	>50	0.224	0.816		>50	>50
B96	3,906,250		0.415	1.116	0.096	0.268	0.721	45.948	1.006	5.829		ND	ND
B98	2,284,389		5.787	17.308	0.758	2.031	0.006	0.034	0.444	1.250		16.555	41.063
B99	781,250		0.387	1.430	0.330	0.919	>50	>50	0.172	0.624		2.034	5.404
B100	69,877		4.384	16.923	0.051	0.124	0.124	>50	13.813	>50		ND	ND
B103	69,877		0.138	0.645	>50	>50	0.001	0.005	2.103	>50		1.199	9.020
B104	31,250		0.237	0.843	>50	>50	0.053	36.619	0.160	0.437		0.508	2.306
B105	349,386		13.994	>50	0.537	1.816	0.022	0.324	1.731	5.835		>50	>50
B106	349,386		0.346	1.605	0.246	0.843	0.002	0.008	1.799	6.078		3.793	14.243
B107	2,284,389		>50	>50	0.732	2.024	>50	>50	0.630	1.686		ND	ND
B109	349,386		0.486	2.133	0.040	0.109	>50	>50	1.184	5.538		11.681	37.067
B112	349,386		0.355	1.206	0.299	0.982	>50	>50	0.900	2.980		2.204	5.904
B114	349,386		0.134	0.362	>50	>50	0.176	1.014	0.441	1.175		ND	ND
B115	91,376		1.462	2.634	0.197	0.690	0.015	0.033	1.118	3.595		7.465	17.297
B116	1,746,928		3.652	12.244	26.072	>50	0.094	0.764	>50	>50		39.206	>50
B119	1,746,928		0.525	2.418	0.089	0.410	6.672	>50	2.400	11.247		ND	ND
B123	18,275		0.269	0.768	0.152	0.346	0.291	7.603	0.220	0.515		2.426	9.356
B124	349,386		0.772	2.572	0.198	0.675	<0.001	0.003	0.519	1.422		9.378	38.331
B125	85,449		0.348	1.123	0.088	0.187	0.016	0.039	0.813	2.531		ND	ND
B127	349,386		0.857	7.362	0.043	0.101	>50	>50	0.292	1.072		4.826	13.040
B129	1,746,928		0.572	2.833	1.395	14.138	0.016	0.051	>50	>50		ND	ND
B130	1,746,928		1.989	5.285	>50	>50	0.027	0.303	0.515	1.714		ND	ND
B133	1,579,754		0.875	2.369	15.587	>50	0.269	6.092	>50	>50		8.887	31.487
B136	53,437		0.181	0.502	0.010	0.039	>50	>50	0.229	0.771		ND	ND
B139	1,746,928		0.499	3.380	0.044	0.493	9.192	>50	1.817	14.253		ND	ND
B140	597,441		0.239	1.032	0.175	0.739	0.004	0.014	>50	>50		ND	ND
B142	2,795		>50	>50	0.020	0.155	ND	ND	ND	ND		ND	ND
B143	349,386		0.488	1.595	>50	>50	>50	>50	2.002	13.490		16.550	>50
B144	156,250		0.139	0.456	0.132	0.426	0.005	0.017	5.469	21.407		0.375	1.347
B148	456,878		1.142	3.043	0.521	1.373	0.014	0.087	>50	>50		3.905	10.735
B149	1,132,637		0.632	2.088	0.043	0.114	>50	>50	>50	>50		10.264	24.846
B151	18,275		0.075	0.368	0.025	0.086	0.004	0.010	0.141	0.474		0.066	0.317
B152	69,877		0.154	0.417	0.012	0.034	0.008	0.342	0.326	0.836		0.758	2.233
B153	267,184		1.170	4.099	>50	>50	1.572	>50	0.277	0.724		ND	ND
B155	5,663,186		2.725	7.564	>50	>50	14.735	>50	>50	>50		5.477	21.327
B156	31,250		>50	>50	ND	ND	ND	ND	ND	ND		5.835	17.435
B161	69,877		0.158	0.538	0.500	3.408	0.103	4.989	3.356	12.404		1.443	5.019
B164	69,877		0.486	1.620	0.459	1.461	0.240	11.974	0.186	0.462		6.793	27.406
B165	156,250		0.385	0.750	ND	ND	ND	ND	ND	ND		2.118	9.272
B166	69,877		0.185	0.404	ND	ND	ND	ND	ND	ND		0.897	3.350
B167	91,376		>50	>50	0.489	2.574	3.220	>50	0.214	0.576		ND	ND
B168	53,437		35.349	>50	0.280	0.745	0.007	0.019	0.299	1.000		>50	>50
B169	91,376		4.989	15.443	>50	>50	0.008	0.069	>50	>50		ND	ND
B175	349,386		0.291	0.810	ND	ND	ND	ND	ND	ND		3.525	13.023
B177	456,878		12.387	>50	ND	ND	ND	ND	ND	ND		6.912	20.223
B183	13,975		15.489	>50	0.021	0.056	>50	>50	>50	>50		ND	ND
B184	6,250		0.187	0.667	0.043	0.118	0.202	>20	>20	>20		0.761	2.378
B185	156,250		1.839	5.152	ND	ND	ND	ND	ND	ND		29.538	>50
B191	349,386		2.508	7.031	ND	ND	ND	ND	ND	ND		4.038	22.995
B193	10,687		12.007	>50	ND	ND	ND	ND	ND	ND		>50	>50
B194	91,376		0.370	0.998	ND	ND	ND	ND	ND	ND		ND	ND
B195	69,877		11.939	28.190	ND	ND	ND	ND	ND	ND		18.174	>50
B196	349,386		>50	>50	ND	ND	ND	ND	ND	ND		0.894	4.257
B197	5,108,049		3.031	9.205	ND	ND	ND	ND	ND	ND		4.455	16.567
B199	2,284,389		3.206	8.671	ND	ND	ND	ND	ND	ND		22.494	>50
B200	781,250		0.411	0.790	0.081	0.181	1.677	>20	>20	>20		16.690	48.076
B211	781,250		>20	>20	0.402	2.413	>20	>20	>20	>20		1.999	7.921
B212	69,877		0.655	2.207	0.390	1.304	1.504	>20	0.332	1.112		22.229	>50
B214	69,877		0.941	2.424	0.130	0.598	0.071	1.454	0.257	0.859		3.615	8.300
B219	13,975		0.417	1.099	1.257	>20	7.569	>20	0.718	>20		ND	ND
B220	31,250		3.423	10.461	0.083	0.222	>20	>20	0.796	3.767		ND	ND
B221	18,275		0.641	2.913	0.072	0.241	0.003	0.008	>20	>20		1.918	7.202
B224	226,527		0.385	1.301	0.022	0.061	0.007	0.028	0.543	4.403		0.637	3.417
B226	1,746,928		6.001	>20	0.198	0.443	0.011	0.036	1.149	4.489		23.098	>50
B228	91,376		>20	>20	0.084	0.293	0.003	0.029	>20	>20		>50	>50
B229	597,441		0.271	2.094	0.021	0.056	ND	ND	ND	ND		0.648	3.395
B236	10,687		0.735	2.532	0.320	1.105	0.010	0.038	>20	>20		4.646	20.046
B244	53,437		0.315	1.063	1.174	4.106	13.120	>20	0.512	1.490		1.726	5.295
B248	781,250		>20	>20	0.355	0.981	>20	>20	>20	>20		>50	>50
B254	53,437		0.324	1.091	0.028	0.122	2.800	>20	0.459	1.779		1.049	3.644
B258	556,278		1.385	5.319	0.816	3.346	0.005	0.018	0.197	0.793		8.095	23.494
B261	33,397,968		3.162	10.403	>50	>50	ND	ND	ND	ND		9.516	29.529
B266	33,397,968		0.927	3.324	0.399	1.395	0.366	>20	10.475	>20		5.548	17.350
B277	13,975		0.513	>50	2.736	7.640	ND	ND	ND	ND		ND	ND
B283	53,437		9.211	>50	0.370	1.577	ND	ND	ND	ND		ND	ND
B289	285,548,607		0.768	3.765	4.171	41.812	ND	ND	ND	ND		5.652	20.323
B296	156,250		0.136	0.301	1.164	3.092	ND	ND	ND	ND		ND	ND
B297	6,679,594		0.266	0.986	0.415	1.580	ND	ND	ND	ND		1.438	6.770

Supplementary Table 1. Virus outgrowth culture neutralization screen. IC50 and IC80 neutralization titers from Tzm-bl assays of screening virus outgrowth culture supernatants against antibodies 3BNC117<sup>4</sup>, 10-1074<sup>5</sup>, PG16<sup>6</sup>, G52K5<sup>7</sup> and VRC01<sup>8</sup>. Color indicates antibody titer (low to high, red to green). For 3BNC117 and VRC01, participants satisfying our screen-in criterion of a culture IC50 < 2.0 µg/ml are denoted by bright red boxes. ND, not determined.



Supplementary Table 2. Participants demographic and baseline clinical characteristics.

Study ID	Age (yrs)	Gender	Race	Year of HIV diagnosis	Years since HIV diagnosis	Year ART started	Years on ART	CD4 nadir	IC50 of outgrowth culture (µg/ml)	ART regimen at enrollment*	Months VL <50 cp/ml	Switched ART regimen*	Clade	CD4 count on day 0	# of 3BNC117 Infections	Weeks to VL >50 cp/ml	Weeks to VL >75 cp/ml	Weeks to VL >200 cp/ml	
<b>Group A</b>																			
701	62	M	Black	1999	16	1999	16	209	0.077	RAL/TDF/FTC	>12	-	B	638	2	6	6	6	
702	26	M	White/hisp	2011	4	2011	4	310	0.248	EVG/CobI/TDF/FTC	>12	-	B	720	2	5	5	5	
703	41	M	White/hisp	1997	18	1997	18	500	0.572	EVG/CobI/TDF/FTC	>12	-	B	689	2	5	5	5	
704	29	M	Black	2009	6	2010	5	400	0.239	RPV/TDF/FTC	>12	DTG/TDF/FTC	B	761	2	5	5	6	
707	50	M	White	1988	27	2004	11	500	1.989	NVP/TDF/FTC	>12	DTG/TDF/FTC	B	779	2	8	9	9	
708	43	M	White	2002	13	2003	12	280	0.37	EVG/CobI/TDF/FTC	>12	-	B	958	2	8	9	9	
<b>Mean</b>	<b>41.8</b>				<b>14.0</b>		<b>11.0</b>	<b>366.5</b>	<b>0.6</b>					<b>757.5</b>		<b>6.2</b>	<b>6.3</b>	<b>6.7</b>	
705**	61	M	Black	1989	26	early 1990s	about 25	400s	0.904	RAL/DRV/r/TDF/FTC	>12	-	B	713	NA	NA	NA	NA	
706**	60	M	White	2003	12	2009	6	200	0.499	RAL/TDF/FTC	>12	-	B	592	NA	NA	NA	NA	
<b>Group B</b>																			
709	44	M	Pac Islander	2003	12	2003	12	800	0.941	LPV/r/TDF/FTC	>12	-	B	1031	3	5	5	5	
710	31	M	Black	2012	3	2014	1	500	0.187	RPV/TDF/FTC	>12	DTG/TDF/FTC	B	928	4	18	19	19	
711	30	M	Black	2014	1	2014	1	637	0.075	ATV/r/TDF/FTC	>12	-	B	1000	2	3	3	3	
712	57	F	Black	2004	11	2009	6	277	0.315	EFV/TDF/FTC	>12	DTG/TDF/FTC	B	597	4	15	15	16	
713	31	M	Black	2003	12	2014	1	500	0.417	EVG/cobI/TDF/FTC	>12	-	B	358	3	5	5	5	
714	28	M	White	2013	2	2014	1	420	0.365	RPV/TDF/FTC	>12	DTG/TDF/FTC	B	590	4	9	10	10	
715	27	M	Black	2008	7	2008	7	390	0.346	RPV/TDF/FTC	>12	DTG/TDF/FTC	B	687	4	11	11	11	
<b>Mean</b>	<b>35.4</b>				<b>6.9</b>		<b>4.1</b>	<b>541.2</b>	<b>0.4</b>					<b>738.7</b>		<b>9.4</b>	<b>9.6</b>	<b>9.9</b>	

\*1NNRTI based regimens were switched four weeks before HAART interruption due to longer half lives of NNRTIs

\*\* Participants 705 and 706's (baseline) day 0 HIV-1 RNA levels were 8,730 and 50 copies/ml, respectively. These participants were not included in the analysis given lack of viral suppression at baseline, but safety data was collected.

**Supplementary Table 2. Participants demographic and baseline clinical characteristics.** RAL-raitegravir, DTG-dolutegravir, FTC-emtricitabine, TDF-tenofovir disoproxil fumarate, EVG-elvitegravir, Cobi-Cobicistat, RPV-Rilpivirine, NVP-Nevirapine, DRV-Darunavir, RTV-Ritonavir.

Supplementary Table 3. Viral outgrowth culture neutralization of study participants.

701	3BNC117	10-1074	PG16	G52K5	709	3BNC117	10-1074	PG16	G52K5
<b>Culture</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>	<b>Culture</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>
Screen	0.077 0.221	0.128 0.292	0.014 0.068	4.268 47.764	Screen	0.941 2.424	0.130 0.598	0.071 1.454	0.257 0.859
Day 0	0.208 0.545	0.354 0.749	0.013 0.034	7.498 >20	Day 0 A	1.165 4.111	0.100 2.097	ND ND	ND ND
Wk6	0.147 0.720	0.069 0.155	0.005 0.016	7.078 >20	Day 0 C	1.214 4.022	>50 >50	ND ND	ND ND
Wk7	0.801 41.036	0.054 0.260	0.003 0.015	>20 >20	Wk6 A	4.615 47.525	0.271 5.531	ND ND	ND ND
Wk10	3.040 >20	0.067 0.192	0.004 0.014	>20 >20	Wk6 B	6.477 >50	0.207 8.213	ND ND	ND ND
Wk12	0.076 0.300	0.213 0.500	0.106 16.544	>20 >20	Wk6 C	7.261 >50	0.401 4.016	ND ND	ND ND
Wk14 A	0.001 0.017	0.056 0.209	ND ND	ND ND					
Wk14 B	0.121 0.404	0.184 0.602	ND ND	ND ND					
Wk14 C	0.507 2.143	0.028 0.135	ND ND	ND ND					
<b>Culture</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>	<b>Culture</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>
Screen	0.248 0.908	0.126 0.366	>50 >50	0.372 2.098	Screen	0.187 0.667	0.043 0.118	0.202 >20	>20 >20
Day 0	0.640 1.781	0.230 0.516	>20 >20	>20 >20	Wk19	0.438 1.327	0.126 0.284	2.302 >50	>50 >50
Wk5	2.082 7.632	0.229 0.658	1.118 >20	1.296 5.443	Wk20	0.495 2.116	0.196 0.427	6.043 >50	>50 >50
Wk6	2.441 8.767	0.229 0.644	0.929 >20	0.742 5.226					
Wk9	1.759 8.586	0.229 0.597	0.485 >20	0.895 5.318					
Wk11	2.191 6.573	0.382 0.857	1.393 >20	0.825 5.832					
Wk14 B	1.771 6.186	0.187 0.643	ND ND	ND ND					
Wk14 C	0.568 1.549	0.431 1.262	ND ND	ND ND					
<b>Culture</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>	<b>Culture</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>
Screen	0.572 2.833	1.395 14.138	0.016 0.051	>50 >50	Screen	0.315 1.063	1.174 4.106	13.120 >20	0.512 1.490
Day 0	ND ND	ND ND	ND ND	ND ND	Wk12	0.657 1.785	2.095 4.427	2.777 >50	0.317 0.727
Wk6	2.659 20.019	2.419 >20	0.007 0.033	7.098 >20					
Wk11	1.561 4.217	>20 >20	0.011 0.048	0.753 2.587					
<b>Culture</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>	<b>Culture</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>
Screen	0.239 1.032	0.175 0.739	0.004 0.014	>50 >50	Screen	0.417 1.099	1.257 >20	7.569 >20	0.718 >20
D0	0.195 0.557	0.223 0.625	0.014 0.062	>20 >20	Wk6	45.053 >50	>50 >50	0.021 0.155	46.969 >50
Wk5	4.268 >20	0.131 0.352	0.061 0.351	>20 >20					
Wk6	4.184 >20	0.125 0.42	0.069 0.573	>20 >20					
Wk12	0.269 0.906	0.280 0.778	0.013 0.054	>20 >20					
Wk14 B	15.495 >50	0.093 0.340	ND ND	ND ND					
Wk14 C	0.378 1.616	0.206 0.895	ND ND	ND ND					
<b>Culture</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>	<b>Culture</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>
Screen	1.989 5.285	>50 >50	0.027 0.303	0.515 1.714	Screen	0.346 1.605	0.246 0.843	0.002 0.008	1.799 6.078
Day 0	2.004 >20	>20 >20	0.028 >20	0.663 7.37	Wk11	0.208 0.537	0.232 0.498	0.005 0.034	0.765 1.990
Wk10	1.577 4.561	>20 >20	0.024 0.172	0.860 2.482					
Wk12	ND ND	ND ND	ND ND	ND ND					
Wk14 B	1.967 6.530	>50 >50	ND ND	ND ND					
<b>Culture</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>	<b>Culture</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>	<b>IC50</b> <b>IC80</b>
Screen	0.370 0.998	ND ND	ND ND	ND ND	Screen	0.346 1.605	0.246 0.843	0.002 0.008	1.799 6.078
Day 0	0.143 0.695	0.116 0.447	0.076 >20	>20 >20	Wk11	0.208 0.537	0.232 0.498	0.005 0.034	0.765 1.990
Wk9 #8	0.074 0.274	0.083 0.452	ND ND	ND ND					
Wk9 #9	>50 >50	0.017 0.114	ND ND	ND ND					
Wk10 #4	>50 >50	0.021 0.176	ND ND	ND ND					
Wk10 #5	>50 >50	0.038 0.144	ND ND	ND ND					
Wk10	>20 >20	0.142 0.661	0.004 0.020	>20 >20					
Wk12	0.379 2.051	0.052 0.231	0.022 0.171	>20 >20					

**Supplementary Table 3. Viral Outgrowth Culture Neutralization by 3BNC117 and other bNAbs.** IC50 and IC80 neutralization titers from Tzm-bl assays of study participant viral outgrowth culture supernatants against antibodies 3BNC117<sup>4</sup>, 10-1074<sup>5</sup>, PG16<sup>6</sup> and G52K5<sup>7</sup>. Color indicates antibody titer (low to high, red to green). Wk-study week, ND-not determined.

Supplementary Table 4. Laboratory values for Study Participants.

**a**

<b>701</b>	<b>CD4 abs (cells/mm<sup>3</sup>)</b>	<b>CD4 %</b>	<b>CD8 abs (cells/mm<sup>3</sup>)</b>	<b>CD8 %</b>	<b>VL (copies/ml)</b>	<b>3BNC117 (ug/ml)</b>
Screen	836	38	964	44	<20D	
Day 0	638	42.5	647	43.1	<20ND	0
Day 1						207.4
Wk 1					<20D	77.65
Wk 2	690	36.3	870	45.8	<20D	52.2
Wk 3	703	37	865	45.5	30	35.15
Day 22						194.7
Wk 4	714	35.7	906	45.3	<20ND	105.3
Wk 5					<20D	71.85
Wk 6	607	33.7	796	44.2	1,586	48.15
Wk 7					99,600	35.75
Wk 8	669	30.4	1188	54	4,070	24.3
Wk 9					340	17.25
Wk 10	504	33.6	1025	46.6	50	13.16
Wk 11					30	9.85
Wk 12	623	34.6	799	44.4	<20ND	7.93
Wk 14	627	36.9	743	43.7	<20D	4.35
Wk 24					<20ND	<0.50
Wk 36	632	39.5	669	41.8	<20ND	<0.50

<b>702</b>	<b>CD4 abs (cells/mm<sup>3</sup>)</b>	<b>CD4 %</b>	<b>CD8 abs (cells/mm<sup>3</sup>)</b>	<b>CD8 %</b>	<b>VL (copies/ml)</b>	<b>3BNC117 (ug/ml)</b>
Screen	668	32	907	43	<20D	
Day 0	720	37.9	775	40.8	<20ND	0
Day 1						213.4
Wk 1					<20D	99.5
Wk 2	568	29.9	808	42.5	<20D	55.35
Wk 3	579	36.2	613	38.3	40	32.3
Day 22						312.3
Wk 4	513	34.2	630	42	<20ND	118.1
Wk 5					650	66.55
Wk 6	492	25.9	882	46.5	7,910	45.65
Wk 7					1,020	18.27
Wk 8	521	27.4	889	46.8	120	20.67
Wk 9					20	13.99
Wk 10	680	30.9	972	44.2	20	11
Wk 11					<20D	7.38
Wk 12	477	29.8	688	43	<20D	5.34
Wk 14	539	24.5	1036	47	<20D	2.21
Wk 24					<20ND	<0.50
Wk 36	624	31.2	802	40.1	<20ND	<0.50

<b>703</b>	<b>CD4 abs (cells/mm<sup>3</sup>)</b>	<b>CD4 %</b>	<b>CD8 abs (cells/mm<sup>3</sup>)</b>	<b>CD8 %</b>	<b>VL (copies/ml)</b>	<b>3BNC117 (ug/ml)</b>
Screen	1104	36	1243	40	<20ND	
Day 0	689	32.8	928	44.2	<20ND	0
Day 1						330.4
Wk 1					<20ND	146.35
Wk 2	1240	33.5	1654	44.7	<20ND	88.95
Wk 3	924	33	1310	46.8	<20D	53.1
Day 22						290.9
Wk 4	963	32.1	1278	42.6	40	120.95
Wk 5					360	123.3
Wk 6	633	33.3	804	42.3	8,490	104.1
Wk 7					1,900	61.25
Wk 8	1040	28.9	1663	46.2	<20D	37.85
Wk 9					<20ND	25.05
Wk 10	808	32.3	1105	44.2	<20ND	18.5
Wk 11					<20ND	10.5
Wk 12	1163	32.3	1685	46.8	<20ND	12.91
Wk 14	696	29	1106	46.1	<20ND	7.7
Wk 24					<20ND	<0.50
Wk 36	826	30.6	1153	42.7	<20ND	<0.50

<b>704</b>	<b>CD4 abs (cells/mm<sup>3</sup>)</b>	<b>CD4 %</b>	<b>CD8 abs (cells/mm<sup>3</sup>)</b>	<b>CD8 %</b>	<b>VL (copies/ml)</b>	<b>3BNC117 (ug/ml)</b>
Screen	621	39	523	33	<20ND	
Day 0	761	42.3	589	32.7	<20ND	0
Day 1						319
Wk 1					<20ND	98.9
Wk 2	707	37.2	570	30	<20D	82.45
Wk 3	581	44.7	361	27.8	<20D	58.3
Day 22						338.7
Wk 4	645	40.3	478	29.9	<20D	148.15
Wk 5					100	109.95
Wk 6	584	41.7	407	29.1	6,900	94.2
Wk 7					38,730	14.66
Wk 8	584	39	543	36.2	2,100	16.4
Wk 9					70	17.21
Wk 10	637	39.8	491	30.7	<20D	31.2
Wk 11					<20D	13.81
Wk 12	732	38.5	587	30.9	30	14.07
Wk 14	725	40.3	535	29.7	40	13.58
Wk 24					<20ND	1.66
Wk 36	799	47	488	28.7		<0.50

<b>707</b>	<b>CD4 abs (cells/mm<sup>3</sup>)</b>	<b>CD4 %</b>	<b>CD8 abs (cells/mm<sup>3</sup>)</b>	<b>CD8 %</b>	<b>VL (copies/ml)</b>	<b>3BNC117 (ug/ml)</b>
Screen	958	36	1167	45	<20ND	
Day 0	779	35.4	1005	45.7	<20ND	0
Day 1						171.4
Wk 1					<20ND	83.5
Wk 2	923	34.2	1239	45.9	<20ND	49.55
Wk 3	804	38.3	916	43.6	<20ND	35.15
Day 22						167.3
Wk 4	883	35.3	1133	45.3	<20ND	102.85
Wk 5					<20ND	76.1
Wk 6	864	32	1310	48.5	<20ND	53.3
Wk 7					<20D	54.8
Wk 8	815	30.2	1307	48.4	50	39.2
Wk 9					1,140	18.26
Wk 10	644	32.2	984	49.2	4,060	17.42
Wk 11					20	13.00
Wk 12	818	30.3	1377	51	<20D	8.94
Wk 14	896	30.9	1433	49.3	<20ND	5.91
Wk 24					<20ND	0.90
Wk 36	718	34.2	1010	48.1	<20ND	<0.50

<b>708</b>	<b>CD4 abs (cells/mm<sup>3</sup>)</b>	<b>CD4 %</b>	<b>CD8 abs (cells/mm<sup>3</sup>)</b>	<b>CD8 %</b>	<b>VL (copies/ml)</b>	<b>3BNC117 (ug/ml)</b>
Screen	990	45	796	36	<20ND	
Day 0	958	45.6	767	36.5	<20D	0
Day 1						181.1
Wk 1		42.2	657	36.5	<20ND	96.9
Wk 2	760				<20ND	53.9
Wk 3	966	46	773	36.8	<20ND	41
Day 22						200.3
Wk 4	887	46.7	654	34.4	<20ND	118.75
Wk 5					<20ND	89
Wk 6	953	45.4	762	36.3	<20ND	65.15
Wk 7					<20ND	57.45
Wk 8	742	41.2	704	39.1	140	45.05
Wk 9					4,920	16.44
Wk 10	687	40.4	792	46.6	7,100	14.89
Wk 11					<20D	15.51
Wk 12	682	37.9	837	46.5	<20ND	15.48
Wk 14	758	42.1	731	40.6	<20D	7.32
Wk 24					<20D	<0.50
Wk 36	926	44.1	809	38.5	<20ND	<0.50



Supplementary Table 4 continued. Laboratory values for Study Participants.

**c**

<b>705</b>	<b>CD4 abs (cells/mm<sup>3</sup>)</b>	<b>CD4 %</b>	<b>CD8 abs (cells/mm<sup>3</sup>)</b>	<b>CD8 %</b>	<b>VL (copies/ml)</b>	<b>3BNC117 (ug/ml)</b>	<b>706</b>	<b>CD4 abs (cells/mm<sup>3</sup>)</b>	<b>CD4 %</b>	<b>CD8 abs (cells/mm<sup>3</sup>)</b>	<b>CD8 %</b>	<b>VL (copies/ml)</b>	<b>3BNC117 (ug/ml)</b>
Screen	905	34	872	32	<20		Screen	504	19	1633	63	40	
Day 0	713	32.4	733	33.3	8730	<0.5	Day 0	592	26.9	1217	55.3	50	<0.5
Day 1					393.2		Day 1						264.3
Wk 1					6140	148.85	Wk 1					<20 D	130.6
Wk 2	701	29.2	866	36.1	50,150	61.9	Wk 2	420	20	1258	59.9	80	66.15
Wk 3							Wk 3	418	20.9	1114	55.7	110	36.1
Day 22							Day 22						314.7
Wk 4					184,100	17.5	Wk 4	386	22.7	1017	59.8	1060	138.35
Wk 5							Wk 5					4780	91.4
Wk 6							Wk 6	281	18.7	944	62.9	6970	42.55
Wk 7							Wk 7					130	28.3
Wk 8	682	23.5	1520	52.4	115,590	2.84	Wk 8					<20 ND	18.55
Wk 9							Wk 9					<20 D	13.37
Wk 10							Wk 10	387	17.6	1355	61.6	<20 ND	8.77
Wk 11							Wk 11					<20 ND	6.5
Wk 12	848	21.2	1888	47.2	450		Wk 12	442	22.1	1030	51.5	<20 ND	4.8
Wk 13							Wk 13						
Wk 14							Wk 14	520	20.8	1378	55.1	<20 ND	1.99
Wk 24							Wk 24						<0.5
Wk 36	949	27.1	1407	40.2			Wk 36						<0.5

**Supplementary Table 4. Laboratory values for Study Participants.** Absolute CD4+ T cell counts (CD4 abs), CD4+ T cell per cent among CD3+T cells (CD4%), absolute CD8+ T cell counts (CD8 abs), CD8+ T cell per cent among CD3+T cells (CD8%), viral loads (VL) as well as 3BNC117 concentration in serum during the study period for each study participant in Group A (a), Group B (b) and two additional participants (c). The latter were excluded from further analysis as their viral levels were not <20 copies/ml at day 0. Participant 705 chose not to restart ART and therefore remained viraemic for several weeks. Blue shaded areas indicate time points after re-initiation of ART, green font indicates time points of 3BNC117 infusion; Wk-study week. <20ND-viral load below 20 copies/ml and undetected, <20D-viral load below 20copies/ml but detected.

Supplementary Table 5. Adverse events reported during study follow up in study groups A and B

Group A						Group B					
Adverse Events	No. AEs	No. Mild	No. Moderate	No. Severe	No. of participants (n=8)	Adverse Events	No. AEs	No. Mild	No. Moderate	No. Severe	No. of participants (n=7)
<b>Within 2 weeks of last infusion *</b>						<b>Within 2 weeks of last infusion *</b>					
Anemia	1	1	-	-	1	Asthma exacerbation #	1	-	-	1	1
Chest tightness	2	2	-	-	2	Diarrhea	1	1	-	-	1
Headache	2	2	-	-	2	Dizziness	1	1	-	-	1
Hyperbilirubinemia †	1	-	-	1	1	Ear ache	1	1	-	-	1
Low back pain	1	-	1	-	1	Hyperhydrosis	2	2	-	-	1
Muscle cramps	2	2	-	-	2	Nausea	1	1	-	-	1
Paresthesia upper extremity	2	2	-	-	2	Pain at infusion site	1	1	-	-	1
Skin abscess	1	-	1	-	1	URI	4	3	1	-	4
Upper respiratory tract infection	3	3	-	-	3						
<b>Total reported AEs</b>	<b>15</b>	<b>12</b>	<b>2</b>	<b>1</b>	<b>5</b>	<b>Total reported AEs</b>	<b>12</b>	<b>10</b>	<b>1</b>	<b>1</b>	<b>5</b>
<b>Follow up period - 36 weeks after first 3BNC117 infusion **</b>						<b>Follow up period - 8 to 14 weeks after first 3BNC117 infusion **</b>					
<b>Related to 3BNC117</b>						<b>Related to 3BNC117</b>					
Chest tightness	2	2	-	-	2	Diarrhea	1	1	-	-	1
Chills	1	1	-	-	1	Hyperhydrosis	2	2	-	-	1
Feverishness	2	1	1	-	2	Nausea	1	1	-	-	1
Headache	7	4	3	-	6	Pain at infusion site	1	1	-	-	1
Malaise/fatigue	1	1	-	-	1	URI	2	2	-	-	2
Paresthesia upper extremity	3	3	-	-	3						
Restlessness	1	1	-	-	1	<b>Any related AE</b>	<b>7</b>	<b>7</b>	<b>0</b>	<b>0</b>	<b>5</b>
Upper respiratory tract infection	2	2	-	-	2						
<b>Any related AE</b>	<b>19</b>	<b>15</b>	<b>4</b>	<b>0</b>	<b>6</b>	<b>Not related to 3BNC117</b>	<b>1</b>	<b>-</b>	<b>-</b>	<b>1</b>	<b>1</b>
<b>Not related to 3BNC117</b>						<b>Not related to 3BNC117</b>					
Anal dysplasia	1	1	-	-	1	Asthma exacerbation #	1	-	-	1	1
Anemia	1	1	-	-	1	Bacterial pneumonia #	1	-	-	1	1
Arthralgia (mono-articular)	1	1	-	-	1	Back pain	1	1	-	-	1
Hyperbilirubinemia †	1	-	-	1	1	Dizziness	1	1	-	-	1
Low back pain	1	-	1	-	1	Ear ache	1	1	-	-	1
Muscle cramps	2	2	-	-	2	Feverishness	1	1	-	-	1
Skin abscess	1	-	1	-	1	Headache	2	2	-	-	2
Syphilis	1	1	-	-	1	Transaminitis	1	1	-	-	1
Upper respiratory tract infection	3	3	-	-	3	Upper respiratory tract infection	5	5	-	-	4
<b>Any non-related AE</b>	<b>12</b>	<b>9</b>	<b>2</b>	<b>1</b>	<b>6</b>	<b>Any non-related AE</b>	<b>14</b>	<b>12</b>	<b>0</b>	<b>2</b>	<b>6</b>
<b>Total reported AEs</b>	<b>31</b>	<b>24</b>	<b>6</b>	<b>1</b>	<b>6</b>	<b>Total reported AEs</b>	<b>21</b>	<b>19</b>	<b>0</b>	<b>2</b>	<b>6</b>

\* Top panels list all reported adverse events (AE) within 2 weeks of last 3BNC117 infusion, and \*\* bottom panels list all reported (related or non-related) AE during the observation period in group A (left) and group B (right).

# Participant 710, who had history of asthma, developed an episode of asthma exacerbation that required treatment with systemic steroids, symptoms began 11 days after second 3BNC117. Two months later, he was admitted to the hospital with bacterial pneumonia, which required treatment with systemic antibiotics. Both events were of grade 3 severity and considered not related to 3BNC117.

† Participant 708's total and direct bilirubin levels increased to 2.3 mg/dl and 0.8 mg/dl, respectively, 1 week after the second 3BNC117 infusion. Transaminases remained within normal limits. The elevation in direct bilirubin was of grade 3 severity according to the DAIDS v2.0 Toxicity Grading Scale. Bilirubin levels normalized by the next measurement 4 weeks later.

Supplementary Table 6. ACTG Trial Participants undergoing ATI without antibody treatment.

Subject ID	Source study	Age at ATI	Gender	Duration of ART (from first ART to ATI) (years)	Nadir CD4 cell count (categorized)	Pre-ATI CD4	pre-ATI regimen	NNRTI-based pre-ATI regimen	Weeks from ATI until VL >200cp/ml
2	A5197	42	Male	1.2758	201 - 500	821	tdf ftc rtv atv	No	1.9
11	A371	33	Male	1.2183	> 500	1713	abc d4t 3tc rtv apv	No	1.7
12	A371	36	Male	1.2293	> 500	688	abc d4t 3tc rtv apv	No	1.7
16	A371	34	Male	2.8693	201 - 500	535	abc d4t 3tc rtv apv	No	3
19	A371	38	Male	1.1554	201 - 500	919	abc d4t 3tc rtv apv	No	2
21	A371	38	Male	1.1718	> 500	748	abc d4t 3tc rtv apv	No	2.9
22	A371	31	Male	1.0924	201 - 500	582	abc d4t 3tc rtv apv	No	2.9
23	A371	31	Male	1.0267	> 500	989	abc d4t 3tc rtv apv	No	2.9
24	A371	24	Male	1.1499	201 - 500	621	abc d4t 3tc rtv apv	No	1
27	A371	38	Male	1.1882	201 - 500	773	abc d4t 3tc rtv apv	No	1
28	A371	44	Male	1.1253	201 - 500	829	abc d4t 3tc rtv apv	No	1.9
29	A5024	35	Male	5.4018	201 - 500	689	3tc zdv idv	No	2.3
31	A371	36	Male	1.1526	201 - 500	1141	abc d4t 3tc rtv apv	No	3
32	A371	37	Male	1.9986	201 - 500	951	abc d4t 3tc rtv apv	No	2.9
33	A371	41	Male	1.3388	> 500	670	abc 3tc rtv apv	No	5.7
34	A371	27	Male	1.0349	> 500	979	d4t ddi 3tc rtv apv	No	2.6
39	A371	46	Male	1.0075	201 - 500	598	abc d4t 3tc rtv apv	No	4
44	A371	47	Male	1.0951	201 - 500	759	abc d4t 3tc rtv apv	No	2
51	A5197	43	Male	7.2608	201 - 500	1294	d4t 3tc idv	No	2.3
52	A371	22	Female	1.0185	201 - 500	509	abc d4t 3tc rtv apv	No	1.9
57	A371	20	Male	1.0869	201 - 500	784	abc d4t 3tc rtv apv	No	1.9
58	A371	35	Male	1.2731	201 - 500	610	abc d4t 3tc rtv apv	No	2.6
59	A371	43	Male	1.0185	> 500	1439	abc d4t 3tc rtv apv	No	3.9
60	A371	41	Male	1.0404	> 500	1179	abc d4t 3tc rtv apv	No	6
61	A371	41	Male	1.0021	201 - 500	710	abc d4t 3tc rtv apv	No	1.9
62	A371	27	Female	1.0951	201 - 500	719	abc d4t 3tc rtv apv	No	1
63	A5068	47	Male	5.3854	> 500	1667	3tc zdv nfV	No	4.6
64	A371	29	Male	1.0431	201 - 500	536	abc d4t 3tc rtv apv	No	2.6
65	A5068	49	Male	8.9911	201 - 500	852	3tc zdv idv rtv	No	2.9
72	A371	41	Male	1.7413	> 500	846	abc d4t 3tc rtv apv	No	2.1
84	A5197	35	Male	6.1136	201 - 500	1270	d4t ddi nfV	No	1.9
88	A371	41	Male	1.0513	> 500	799	abc d4t 3tc rtv apv	No	3
89	A371	19	Male	1.0924	> 500	687	abc d4t 3tc rtv apv	No	2.9
91	A371	49	Male	1.0897	> 500	890	abc d4t 3tc rtv apv	No	3
92	A371	27	Male	1.1718	> 500	814	abc d4t 3tc rtv apv	No	2.1
94	A371	44	Male	1.0513	> 500	874	d4t ddi 3tc rtv apv	No	3.9
95	A371	40	Male	1.2266	201 - 500	1081	abc d4t 3tc rtv apv	No	1.9
101	A5024	42	Male	8.4736	201 - 500	775	3tc zdv rtv	No	2.3
102	A371	21	Male	1.0021	> 500	759	abc d4t 3tc rtv apv	No	0.9
104	A371	44	Male	1.013	> 500	821	abc 3tc tdf nfV	No	1.9
105	A5197	44	Male	4.0739	201 - 500	673	3tc zdv tdf fpv	No	4
106	A5197	47	Male	9.0924	> 500	740	3tc zdv nfV	No	2.7
107	A5197	41	Male	5.5387	201 - 500	1330	d4t 3tc atv	No	3
114	A371	29	Male	1.0185	> 500	1221	abc d4t 3tc rtv apv	No	1.9
115	A371	22	Male	1.0212	> 500	1127	abc d4t 3tc rtv apv	No	1.9
116	A371	42	Male	1.1006	> 500	844	abc d4t 3tc rtv apv	No	2.7
123	A371	48	Male	1.065	> 500	1398	3tc tdf nfV	No	2.9
124	A371	41	Male	1.0185	> 500	1285	abc d4t 3tc rtv apv	No	3.7
127	A371	40	Male	1.0157	> 500	736	abc d4t 3tc rtv apv	No	2
128	A371	48	Male	1.013	> 500	981	abc d4t 3tc rtv apv	No	2.1
134	A371	38	Male	1.0787	201 - 500	552	abc d4t 3tc rtv apv	No	1.7
139	A371	39	Male	1.1554	> 500	966	abc d4t 3tc rtv apv	No	1.9

**Supplementary Table 6. ACTG Trial Participants undergoing ATI without antibody treatment.** 52 participants from ACTG trials who underwent ATI without antibody infusion<sup>9</sup>. Controls were selected based on similar inclusion criteria: Age 18-65, Plasma HIV-1 RNA < 50 copies/ml for at least 12 months before ATI while on combination ART, CD4 count at time of ATI >500 cells/ul, CD4 nadir >200 cells/ul, weekly viral load measurements at least until viral rebound occurred<sup>10,11</sup>. TDF/FTC (tenofovir disoproxil fumarate/emtricitabine), RTV-ritonavir, ATV-atazanavir, NFV-nelfinavir, ABC-abacavir, D4T-stavudine, 3TC-lamivudine, APV-amprenavir, ZDV/3TC (zidovudine/lamivudine), IDV-indinavir, DDI-didanosine, ABC/3TC-abacavir/lamivudine, TDF-tenofovir, FPV-fosamprenavir, ZDV-zidovudine.

## Supplementary Table 7. Statistical Analysis

**a** Baseline Statistics

	Group	Mean	sd	Unpaired Wilcoxon test
Age	ACTG	37.250	8.184	
	Group A + B	38.385	12.101	0.9803
	Group A	41.833	13.348	0.3844
	Group B	35.429	11.058	0.3979
	Group	Mean	sd	Unpaired Wilcoxon test
Years on ART	ACTG	2.134	2.250	
	Group A + B	7.308	5.950	0.0895
	Group A	11.000	5.657	<b>0.0004</b>
	Group B	4.143	4.337	0.4185
	Group	Mean	sd	Unpaired Wilcoxon test
Day 0 CD4 (cells/mm <sup>3</sup> )	ACTG	899.481	285.988	
	Group A + B	747.385	192.356	0.1192
	Group A	757.500	110.502	0.2722
	Group B	738.714	252.262	0.2273
	Group	Female	Male	Fisher's Exact test
Gender	ACTG	2	50	
	Group A + B	1	12	0.4940
	Group A	0	6	1.0000
	Group B	1	6	0.3202
	Group	201 - 500	> 500	Fisher's Exact test
CD4 Nadir (cells/mm <sup>3</sup> )	ACTG	26	26	
	Group A + B	11	2	<b>0.0302</b>
	Group A	6	0	<b>0.0281</b>
	Group B	5	2	0.4281

**b** Confounder Analysis

Case vs Control	Age	Years on ART	Gender	CD4 Nadir	Day 0 CD4
Group A vs ACTG	<b>0.0008</b>	<b>&lt; 1e-04</b>	0.0524	0.8850	0.5770
Group B vs ACTG	0.0679	0.0590	0.7040	0.7502	0.8677
Group A + B vs ACTG	<b>0.0252</b>	<b>0.0007</b>	0.8931	0.2323	0.6192

**c** Effect of bNAbs Treatment on Rebound Delay

Case vs Control	Likelihood ratio test	(Weighted) log rank test
Group A vs ACTG	<b>&lt; 1e-04</b>	<b>&lt; 1e-05</b>
Group B vs ACTG	<b>&lt; 1e-08</b>	<b>&lt; 1e-04 *</b>
Group A + B vs ACTG	<b>&lt; 1e-11</b>	<b>&lt; 1e-05</b>

**Supplementary Table 7. Statistical Analysis.** We compared the different treatment groups (Group A, Group B, Group A + B) with the control group (ACTG) regarding **a**, baseline statistics: We performed a two-sided Fisher's Exact test for categorical variables (gender and CD4 Nadir) and an unpaired Wilcoxon test (two-sided) for continuous variables (age, years on ART and CD4 count before ATI initiation). **b**, potential confounders of the treatment effect on rebound delay: We built univariate survival regression models for each potential confounder and compared those models to a null model using a likelihood ratio test. Rebound time was modeled using a log-normal distribution, which resulted in the best model fit as measured by Akaike Information Criterion (AIC) among several different distributions (see Extended Data Fig. 4). **c**, statistical significance of the treatment effect on rebound delay: To determine if there is a significant effect of the treatment on the rebound delay after adjusting for the discovered confounders, we performed a weighted log-rank test<sup>12</sup> where the variables of the log-rank statistic are re-weighted by estimated inverse probability weights of each sample, which are based on the discovered confounders (see Methods Statistical Analysis). For the comparison between Group B participants and the ACTG trial participants, no confounders were discovered. Thus, we performed a standard log-rank test in that setting (marked with a star). In addition, we built for each comparison group a multivariate survival regression model containing the treatment group label and the discovered confounders as predictors and compared this model to a model using only the confounders as predictors with a likelihood ratio test (LRT). Significant p-values at significance level  $\alpha = 0.05$  are shown in red.



Supplementary Table 8. Hamming distance calculations and Poisson Fitter values for rebound sequences.

### First Time Point Plasma SGS

	Single rebound?	# SGS	Min HD	Mean HD	Max HD	p-value	p (no APOBEC)
701	yes	9	0	2.72	7	0.3061	0.8172
702	no	9	0	10.39	16	N/A	N/A
703	no	15	0	38.82	71	N/A	N/A
704	yes	16	0	0.98	4	0.9095	0.8235
707	yes	12	0	1.33	4	0.8175	0.8175
708	yes	11	0	0.73	2	0.4264	0.4264
709	no*	7	0	0.29	1	n.d.*	n.d.*

\*second lineage detected at W006

**Supplementary Table 8. Hamming distance calculations and Poisson Fitter values for rebound sequences.** Poisson Fitter v2<sup>13</sup> was applied as described in Methods. Reported are: participant ID, number of plasma-derived single genome sequences (SGSs) from the first time point post-rebound used in the calculation, minimum/mean/maximum pairwise Hamming distances, and two p goodness of fit values (described in Methods, with and without APOBEC sites included). Participants were designated as having a single rebound virus if (i) sequences from the first time point exhibited a star-like phylogeny, (ii) sequences from the first time point yielded a nonsignificant p goodness of fit value, demonstrating a Poisson distribution of Hamming distances, and (iii) all sequences from the second time point fell within the same, monophyletic lineage. Viral sequences from participant 709 fit criteria (i) and (ii), but not (iii) (Extended Data Figs. 7 and 8).

Supplementary Table 9. SGS Derived Pseudovirus Neutralization.

Donor	Timepoint	Sample source	Sample name	3BNC117		
				IC50	IC80	MPI
701	Day 0	Culture	701A-cul-d0-06-26-G4_S16	0.011	0.041	100
701	Day 0	Culture	701B-cul-d0-06-19-A10_S92	0.010	0.034	100
701	Week 6	Plasma	701-W6-P-06-12-C11_S5	0.015	1.123	89
701	Week 6	Plasma	701-W6-P-06-12-C7_S4	5.344	>25	54
701	Week 7	Plasma	<b>701-W7-P-06-12-B3_S96</b>	0.019	0.504	89
701	Week 7	Plasma	701-W7-P-06-12-A2_S93	>25	>25	43
702	Day 0	Culture	702-cul-d0-06-19-F7_S91	0.041	0.205	100
702	Day 0	Culture	702-cul-d0-06-29-A3_S36	0.032	0.154	100
702	Week 5	Plasma	702-W5-P-06-12-C7_S18	0.111	0.794	100
702	Week 5	Plasma	702-W5-P-06-12-E2_S21	0.161	0.772	100
702	Week 6	Plasma	<b>702-W6-P-06-12-C3_S36</b>	2.453	>25	75
702	Week 6	Plasma	702-W6-P-06-12-H11_S63	0.079	0.396	100
703	Week 5	Plasma	703-W5-P-06-12-D5_S84	0.030	0.140	99
703	Week 5	Plasma	703-W5-P-06-12-H1_S90	0.107	0.586	100
703	Week 6	Plasma	703-W6-P-06-12-D7_S66	0.018	0.166	100
703	Week 6	Plasma	<b>703-W6-P-06-12-D10_S67</b>	2.971	>25	73
704	Day 0	Culture	704-cul-d0-06-26-D1_S27	0.040	0.182	98
704	Week 5	Plasma	<b>704-W5-P-06-19-A3_S59</b>	0.292	1.791	85
704	Week 6	Plasma	704-W6-P-06-19-E11_S80	0.257	>25	79
704	Week 6	Plasma	704-W6-P-06-19-G11_S87	0.127	0.740	94
707	Day 0	Culture	707-d0A-F10_S45	0.106	0.823	96
707	Day 0	Culture	707-d0A-CX-E3_S14	0.132	0.736	98
707	Week 9	Plasma	<b>707-W9-P-B6_S13</b>	0.087	0.370	96
707	Week 9	Plasma	707-W9tit-P-C5_S91	0.087	1.051	90
707	Week 10	Plasma	707-W10-P-F5_S52	0.107	0.942	95
708	Day 0	Culture	708-d0B-CX-B1_S26	0.006	0.034	99
708	Day 0	Culture	708-d0B-CX-F10_S74	0.014	0.057	99
708	Week 9	Plasma	<b>708-W9-P-H10_S81</b>	0.391	>25	61
709	Screen	Culture	709 prescreen E5	0.106	0.316	100
709	Week 5	Plasma	<b>709-W5-P-A8_S5</b>	0.748	3.432	97
709	Week 6	Plasma	709-W6-P-D5_S19	0.374	13.312	83

**Supplementary Table 9. SGS Derived Pseudovirus Neutralization.** SGS-derived pseudoviruses were tested for neutralization by 3BNC117. The SGS sequences from which these pseudoviruses were made are listed (Supplementary Fig. 2). Bold, red samples reflect the predominant genotype at rebound for each participant (Fig. 4b and Extended Data Figs. 7 and 8). Neutralization is indicated by IC50, IC80 and the maximum percent inhibition (MPI) achieved when 3BNC117 was tested up to 25 µg/ml against each virus. Color indicates antibody titer (low to high, red to green). Viruses not reaching 99% inhibition are shaded in gray.

- 1 Kearse, M. *et al.* Geneious Basic: an integrated and extendable desktop software platform for the organization and analysis of sequence data. *Bioinformatics* **28**, 1647-1649, doi:10.1093/bioinformatics/bts199 (2012).
- 2 Zhou, T. *et al.* Structural basis for broad and potent neutralization of HIV-1 by antibody VRC01. *Science* **329**, 811-817, doi:science.1192819 [pii] 10.1126/science.1192819 (2010).
- 3 Lyumkis, D. *et al.* Cryo-EM structure of a fully glycosylated soluble cleaved HIV-1 envelope trimer. *Science* **342**, 1484-1490, doi:10.1126/science.1245627 (2013).
- 4 Scheid, J. F. *et al.* Sequence and Structural Convergence of Broad and Potent HIV Antibodies That Mimic CD4 Binding. *Science*, doi:science.1207227 [pii] 10.1126/science.1207227 (2011).
- 5 Mouquet, H. *et al.* Complex-type N-glycan recognition by potent broadly neutralizing HIV antibodies. *Proceedings of the National Academy of Sciences of the United States of America* **109**, E3268-3277, doi:10.1073/pnas.1217207109 (2012).
- 6 Walker, L. M. *et al.* Broad and potent neutralizing antibodies from an African donor reveal a new HIV-1 vaccine target. *Science* **326**, 285-289, doi:1178746 [pii] 10.1126/science.1178746 (2009).
- 7 Scharf, L. *et al.* Antibody 8ANC195 reveals a site of broad vulnerability on the HIV-1 envelope spike. *Cell reports* **7**, 785-795, doi:10.1016/j.celrep.2014.04.001 (2014).
- 8 Wu, X. *et al.* Rational design of envelope identifies broadly neutralizing human monoclonal antibodies to HIV-1. *Science* **329**, 856-861, doi:science.1187659 [pii] 10.1126/science.1187659 (2010).
- 9 Li, J. Z. *et al.* The size of the expressed HIV reservoir predicts timing of viral rebound after treatment interruption. *AIDS* **30**, 343-353, doi:10.1097/QAD.0000000000000953 (2016).
- 10 Volberding, P. *et al.* Antiretroviral therapy in acute and recent HIV infection: a prospective multicenter stratified trial of intentionally interrupted treatment. *AIDS* **23**, 1987-1995, doi:10.1097/QAD.0b013e32832eb285 (2009).
- 11 Rosenberg, E. S. *et al.* Safety and immunogenicity of therapeutic DNA vaccination in individuals treated with antiretroviral therapy during acute/early HIV-1 infection. *PloS one* **5**, e10555, doi:10.1371/journal.pone.0010555 (2010).
- 12 Xie, J. & Liu, C. Adjusted Kaplan-Meier estimator and log-rank test with inverse probability of treatment weighting for survival data. *Statistics in medicine* **24**, 3089-3110, doi:10.1002/sim.2174 (2005).
- 13 Giorgi, E. E. & Bhattacharya, T. A note on two-sample tests for comparing intra-individual genetic sequence diversity between populations. *Biometrics* **68**, 1323-1326; author reply 1326, doi:10.1111/j.1541-0420.2012.01775.x (2012).
- 14 Laird, G. M. *et al.* Rapid quantification of the latent reservoir for HIV-1 using a viral outgrowth assay. *PLoS pathogens* **9**, e1003398, doi:10.1371/journal.ppat.1003398 (2013).
- 15 Caskey, M. *et al.* Viraemia suppressed in HIV-1-infected humans by broadly neutralizing antibody 3BNC117. *Nature* **522**, 487-491, doi:10.1038/nature14411 (2015).

- 16 Shingai, M. *et al.* Antibody-mediated immunotherapy of macaques chronically infected with SHIV suppresses viraemia. *Nature* **503**, 277-280, doi:10.1038/nature12746 (2013).
- 17 Kilby, J. M. *et al.* A randomized, partially blinded phase 2 trial of antiretroviral therapy, HIV-specific immunizations, and interleukin-2 cycles to promote efficient control of viral replication (ACTG A5024). *The Journal of infectious diseases* **194**, 1672-1676, doi:10.1086/509508 (2006).
- 18 Jacobson, J. M. *et al.* Evidence that intermittent structured treatment interruption, but not immunization with ALVAC-HIV vCP1452, promotes host control of HIV replication: the results of AIDS Clinical Trials Group 5068. *The Journal of infectious diseases* **194**, 623-632, doi:10.1086/506364 (2006).
- 19 Pereyra, F. *et al.* The major genetic determinants of HIV-1 control affect HLA class I peptide presentation. *Science* **330**, 1551-1557, doi:10.1126/science.1195271 (2010).
- 20 Montefiori, D. C. Evaluating neutralizing antibodies against HIV, SIV, and SHIV in luciferase reporter gene assays. *Curr Protoc Immunol* **Chapter 12**, Unit 12 11, doi:10.1002/0471142735.im1211s64 (2005).
- 21 Li, M. *et al.* Human immunodeficiency virus type 1 env clones from acute and early subtype B infections for standardized assessments of vaccine-elicited neutralizing antibodies. *Journal of virology* **79**, 10108-10125, doi:10.1128/JVI.79.16.10108-10125.2005 (2005).
- 22 Horwitz, J. A. *et al.* HIV-1 suppression and durable control by combining single broadly neutralizing antibodies and antiretroviral drugs in humanized mice. *Proceedings of the National Academy of Sciences of the United States of America* **110**, 16538-16543, doi:10.1073/pnas.1315295110 (2013).
- 23 Salazar-Gonzalez, J. F. *et al.* Deciphering human immunodeficiency virus type 1 transmission and early envelope diversification by single-genome amplification and sequencing. *Journal of virology* **82**, 3952-3970, doi:10.1128/JVI.02660-07 (2008).
- 24 West, A. P., Jr. Computational analysis of anti-HIV-1 antibody neutralization panel data to identify potential functional epitope residues. *PNAS* (2013).
- 25 Crooks, G. E., Hon, G., Chandonia, J. M. & Brenner, S. E. WebLogo: a sequence logo generator. *Genome research* **14**, 1188-1190, doi:10.1101/gr.849004 (2004).
- 26 Kirchherr, J. L. *et al.* High throughput functional analysis of HIV-1 env genes without cloning. *Journal of virological methods* **143**, 104-111, doi:10.1016/j.jviromet.2007.02.015 (2007).
- 27 Larkin, M. A. *et al.* Clustal W and Clustal X version 2.0. *Bioinformatics* **23**, 2947-2948, doi:btm404 [pii] 10.1093/bioinformatics/btm404 (2007).
- 28 Maddison, W. P. & Maddison, D. R. *MacClade - Analysis of Phylogeny and Character Evolution - Version 4.* (Sinauer Associates, Inc., 2001).

- 29 Darriba, D., Taboada, G. L., Doallo, R. & Posada, D. jModelTest 2: more models, new heuristics and parallel computing. *Nature methods* **9**, 772, doi:10.1038/nmeth.2109 (2012).
- 30 Guindon, S. *et al.* New algorithms and methods to estimate maximum-likelihood phylogenies: assessing the performance of PhyML 3.0. *Systematic biology* **59**, 307-321, doi:10.1093/sysbio/syq010 (2010).
- 31 Chun, T. W. *et al.* Quantification of latent tissue reservoirs and total body viral load in HIV-1 infection. *Nature* **387**, 183-188, doi:10.1038/387183a0 (1997).
- 32 Parrish, N. F. *et al.* Phenotypic properties of transmitted founder HIV-1. *Proceedings of the National Academy of Sciences of the United States of America* **110**, 6626-6633, doi:10.1073/pnas.1304288110 (2013).
- 33 Maydt, J. & Lengauer, T. Recco: recombination analysis using cost optimization. *Bioinformatics* **22**, 1064-1071, doi:10.1093/bioinformatics/btl057 (2006).
- 34 Altfeld, M. A. *et al.* Identification of dominant optimal HLA-B60- and HLA-B61-restricted cytotoxic T-lymphocyte (CTL) epitopes: rapid characterization of CTL responses by enzyme-linked immunospot assay. *Journal of virology* **74**, 8541-8549 (2000).
- 35 Addo, M. M. *et al.* Comprehensive epitope analysis of human immunodeficiency virus type 1 (HIV-1)-specific T-cell responses directed against the entire expressed HIV-1 genome demonstrate broadly directed responses, but no correlation to viral load. *Journal of virology* **77**, 2081-2092 (2003).