Figure S1. Rabbit mAb Binding to BG505 gp120 and SOSIP.664 Immunogen, Related to Figure 1.

Binding of rabbit mAbs was assayed by ELISA using streptavidin-coated plates to capture avi-tagged biotinylated (A-F) BG505 SOSIP.664 or (G-L) BG505 gp120. 96-well plates were coated overnight at 4°C with streptavidin (Jackson Immunoresearch) at 2 µg/ml in PBS. Plates were washed 4 times with PBS, 0.05% (v/v) Tween, and blocked with 3% (w/v) BSA PBS for 1 h. Subsequently, 1 µg/ml of purified BG505 SOSIP.664 specifically biotinylated via a C-terminal Avi-tag was added for 2 h. Plates were washed four times and incubated with serial dilutions of rabbit mAbs for 1 h, then washed again and binding detected with anti-rabbit Fc conjugated to alkaline phosphatase (Jackson Immunoresearch) at 1:1000 for 1 h. The gp120 and gp41 proteins were directly coated onto the ELISA plates and the 2 h antigen capture step omitted. The positive control was the anti-V3 mAb R56 (PDB: 4JO1) and the negative control was a hybrid using the heavy chain of R56 and light chain of R20, which cannot bind HIV envelope (PDB: 4JO3).



Figure S2. Reproducible 241-Dependent Neutralization Activity Induced by BG505 SOSIP.664 Immunization, Related to Figure 2.

(A) ID_{s0} values calculated in the TZM-bl assay for serum samples taken 2 weeks after the final boost in the studies described in Sanders et al., 2015). Neutralization curves from which the ID_{s0} values were generated, serum samples were titrated 3-fold from 1:20, except for rabbits 1410, 1411 and 1412 where serum samples were titrated 3-fold from 1:100. Potent neutralization categorized as an ID_{s0} >2000 is shaded red, intermediate neutralization categorized as an ID_{s0} of >200 <2000 is shaded pink, weak neutralization categorized as an IC_{s0} of >20 <200 is shaded pale pink. No neutralization activity is indicated by an ID_{s0} of <lowest serum dilution tested. (B) In a separate study 3 groups of New Zealand White rabbits (4 animals per group) were immunized according to the outlined scheme. For liposome formation, BG505 SOSIP.664 was reacted with SPDP crosslinker to achieve approximately 1 linker per SOSIP trimer. The protein was desalted into 100 mM sodium acetate (pH 5.5) to preserve the disulfide bonds in the protein in the next step. Following a 10-minute incubation with 25 mM DTT, protein was again desalted and immediately reacted overnight with maleimide-PEG₂₀₀₀-DSPE (NOF America). The following day, conjugated protein was isolated by running over a Sephadex G100 column. Lipid-conjugated BG505 SOSIP was then used to hydrate dried lipids to make liposomes made as previously described (Macauley et al., 2013) that consisted of 5 mol% MPLA (Avanti) as adjuvant and 0.1 mol% of the of the protein immunogen. (C) ID_{s0} values calculated in the TZM-bl assay for plasma samples taken 2 weeks after the final boost against the indicated viruses. (C) Neutralization curves from which the ID_{s0} values were generated, plasma samples from the study described in (B) were titrated 2-fold from a 1:100.

С

Α	Immunogen	Rabbit	BG505	MG505	MG505 K241S	
	BG505 SOSIP.664 293S GnT -/-	1256	3452	<20	2688	e
	BG505 SOSIP.664 293S GnT -/- EndoH	1284	2653	309	>4860	suod
	BG505 SOSIP.664 293S GnT -/-	1257	1874	585	3453	res
	BG505 SOSIP.664 293S GnT -/-	1279	1519	121	3719	rum
	BG505 SOSIP.664 293T	1411	877	<100	1981	it se
	BG505 SOSIP.664 293S GnT -/- EndoH	1285	835	226	4613	nden
	BG505 SOSIP.664 293S GnT -/-	1278	805	92	4631	eper
	BG505 SOSIP.664 293S GnT -/- EndoH	1283	564	<20	>4860	41-d
	BG505 SOSIP.664 293T	1410	298	<100	230	2,
	BG505 SOSIP.664 293T	1274	3660	108	173	ы t
	BG505 SOSIP.664 293S GnT -/-	1254	508	54	138	lo 2₄ ∋ffec
	BG505 SOSIP.664 293T	1412	340	178	264	ZΨ

Original study described in (Sanders et al., 2015)

3	Week	0	4	8	12	16
	Dose	20 µg protein liposome I.D	20 µg protein liposome I.M	20 µg protein iscomatrix I.M	20 µg protein iscomatrix I.M	100 µg protein
	Group I	empty	empty	В	В	В
	Group II	A	A	В	В	В
	Group III	В	В	В	В	В
	(A) SF162 g	pp41 post fusior	n trimer (Li et a	I., 2015)		

(B) BG505 SOSIP.664 293F (Sanders et al., 2013)

.M	=	In	trai	mu	scu	lar;	I.D	=	Int	trad	lern	nal	

Rabbit	Group	BG505	MG505	MG505 K241S	
3409	Ι	300	<100	392	mu
3412	I	673	<100	842	seri
3414	Ш	144	<100	126	dent ons€
3415	=	343	<100	150	pend espo
3417	Ш	645	<100	1082	l-de
3420	Ш	555	<100	612	24
3410	Ι	168	<100	<100	241 ect
3416	=	162	<100	<100	No eff
3411	Ι	<100	<100	<100	ß
3413	=	<100	<100	<100	on Nizir
3419	III	<100	<100	<100	N. eutra
3418	Ш	<100	<100	<100	Ъ

Figure S3. Negative-stain EM Data, Related to Figure 3 and 4.

(A) Reference-free 2D class averages, (B) 2D back-projections of the final model, (C) 3D reconstructions (top and side views), and (D) FSC curves with estimated resolution for rabbit mAbs in complex with BG505 SOSIP.664. All samples were stained using 2% (w/v) uranyl formate. The total particles included in the final reconstruction and the estimated resolution using a Fourier shell correlation (FSC) cutoff of 0.5 are as follow: BG505+10A Fab – 7,050 particles (~ 20 Å); BG505+11A – 5,072 particles (~ 20 Å); BG505+11B Fab – 8,586 particles (~ 22 Å); BG505+12A – 6,798 particles (~ 22 Å). Complexes containing Fabs 10A, 11A, and 11B were refined with C3 symmetry imposed, while the complex with Fab 12A, where the most common 2D classes showed 1 or 2 Fabs per trimer, was refined asymmetrically. An initial common-lines model was generated using 2D class averages in EMAN2 (Tang et al., 2007) followed by refinement against all particles in Sparx (Penczek et al., 1994). 2D back projections were calculated using EMAN2.



Figure S4. Rabbit mAb Binding Kinetics as Measured by Biolayer Interferometry, related to Figure 3.

BG505 SOSIP.664 trimers containing a C-terminal 8x-HisTag and either a Ser or Asn at position 241 (HXB2 numbering) were loaded onto Ni-NTA biosensors and dipped into varying concentrations of rabbit Fabs (1000, 500, 250, 125, 62.5, 32.25, 16 nM). All samples were previously diluted in 1X kinetics buffer. Anti-HIV Fabs b6 and PGT151 were included as negative and positive controls, respectively, to ensure trimer integrity. A 1:1 binding model (assumes first order kinetics and that binding rates to each ligand site are equal) was fit to the data (red lines) and antibody concentrations with best overall fit as judged by proper alignment association and dissociation curves were used to determine kinetics parameters. As the highest and lowest Fab concentrations (minimum of three) that resulted in the best overall fit as judged by proper alignment to association and dissociation curves ($R^2 > 0.98$) were used to determine kinetics parameters by averaging the calculated Kd, on- and off-rates. No binding was observed for 11B and BG505 SOSIP.664 S241N. Assays were conducted at 25°C.



Figure S5. Frequency and Incidence of Combinations of ≥50% Conserved Glycan Sites, Related to Figure 5.

(A) The % conservation of each indicated glycan site by sequence alignment to HXB2 across the set of 3792 filtered unique sequences. (B) The independent frequency of glycan pairs was computed by multiplying the observed frequencies of each glycan pair. The dependent frequency was then determined by calculating the frequency of isolates containing both glycosylation sites. For each glycan pair, the ratio of dependent frequency and independent frequency is shown. A ratio greater than 1.0 for a glycan pair indicates the glycans are more frequently found together than would be expected if the glycans occurred independently. (C) The number of unique patient Env sequences missing two or more \geq 50% conserved glycan sites, when one of the missing sites is 289, is shown in the third row. The number of unique patient Env sequences for those strains missing two or more \geq 50% conserved glycan sites, where one missing site is 289, are shown stratified for each \geq 50% conserved glycan site.

A Glycan residue number (HXB2)	88	156	160	197	234	241	262	276	289	295	301	332	339	355	386	392	448	611	616	625	637
% conservation	98.8%	95.7%	91.5%	98.7%	78.6%	97.3%	99.6%	94.5%	72.0%	62.5%	92.0%	67.0%	64.2%	76.0%	86.8%	80.9%	88.5%	98.3%	92.9%	96.3%	96.7%
						<u> </u>						1		I	ļ		<u> </u>	<u> </u>			<u> </u>
R 88															umber o	of HIV st	rains				3792
156															rains m	issing 2	2+ glyca 2+ glyca	ns ns inclu	idina 28	20	3407 1030
160												1.10		S	rains m	issing 2	241 and	289		,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	33
100																<u> </u>					
197													Ŧ								
234													Ratic		、 —			T			
241													of		ו	miss	ing 289		Nu	umber o	of
262												1.05	dep			and gl	ycan si	te	HI	v strain	s
276													ben				88			15	
													den				156			35	
													t fre				100 197			<u>92</u> 12	
												1.00	ique				234			291	
												1.00	ency				241			33	
Ö ³³²													/to				262			3	
													ind				295			456	
355													epe				301			45	
386												0.05	nde				332			241	
392												0.95	int f				339			277	
448													req				335 386			160	
448													uen				392			186	
611													cy				448			90	
616												0.00					611			18	
625												0.90					625			70	
637																	637			88	

88 156 160 197 234 241 262 276 289 295 301 332 339 355 386 392 448 611 616 625 637 Glycosylation site

Table S1. Rabbit Single-Cell PCR, Related to Figure 1.

cDNA was generated using Superscript III Reverse Transcription (Invitrogen) as previously described (Sok et al., 2014). First round PCR products were produced using 2.5 µl of cDNA and Hotstart Taq Master mix (Qiagen) for 50 cycles using the primers below designated "PCR 1". Subsequently, 2.5 µl of first round PCR product was used as template for the second round using the primers below designated "PCR 2". PCR products were sequenced and lineages identified using Clonify (Briney et al., 2016). Heavy and light chain variable regions were then amplified by PCR with primers containing homology arms specific for the expression vector. The final PCR products and vector were ligated using high fidelity assembly mix (NEB) and individual clones isolated and sequence verified.

PCR step	Primer name	5'-3' sequence
Kappa PCR 1	RVK1	GCGCCGGAGCTCGTGATGACCCAGACTCCA
Kappa PCR 1	RVK2	GCGCCGGAGCTCGATATGACCCAGACTCCA
Kappa PCR 1	RCK1	GCGCCGTCTAGACTAACAGTCACCCCTATTGAAGC
Kappa PCR 1	RCK2	GCGCCGTCTAGACTAACAGTTCTTCCTACTGAAGC
Kappa PCR 1	IGк	GATGCCAGTTGTTTGGGTGGT
Kappa PCR 2	kEcoRIA	ACGAATTCGGACATCGTGATGACCCAGACTCCA
Kappa PCR 2	RkRBamhl	GGAGGACAGAAGGCGCAACTGGATCACCTTTGACC
Heavy PCR 1	RHFout	ATGGAGACTGGGCTGCGCTGGCTTC
Heavy PCR 1	RHRout1	GTCCTTGGGTTTTGGGGGAAAGATGAA
Heavy PCR 1	RHRout2	GTCCCCGCAGCAGGGGGCCAGTGGGAA
Heavy PCR 1	RHRout3	CTCCTCCCGGGGAGGGCCCATGGTGTA
Heavy PCR 2	RHFin	CTGGCTTCTCCTGGTCGCTGTGCTCAAAG
Heavy PCR 2	RHRin1	ACAGACGGTCCCCCAAGAGTTC
Heavy PCR 2	RHRin2	GACTGATGGAGCCTTAGGTTGCCC
Heavy PCR 2	RHRin3	ACCTTCGGCTCCAGGGGCTGCCC

Table S2. Rabbit mAb Neutralization Activity, Related to Figure 2 and 4.

The rabbit mAbs were titrated against the indicated pseudoviruses in the TZM-bl luciferase reporter assay and the IC_{50} values shown were calculated using Prism. Potent neutralization categorized as an $IC_{50} < 1$, intermediate neutralization categorized as an IC_{50} of >1<10, weak neutralization categorized as an IC_{50} of >10<100. No neutralization activity is indicated by an IC_{50} of >100.

							Virus	strain					
		SF162	ADA	HXB2	BAL	93IN905	YU2	JRCSF	JRFL	92RW020	92BR020	94UG109	BG505
	10A	>100	>100	>100	>100	>100	>100	>100	>100	>100	>100	>100	0.37
	10B	>100	>100	>100	>100	2.62	>100	>100	>100	>100	>100	>100	>100
	10C	6.38	0.68	0.59	11.54	9.23	>100	>100	>100	>100	>100	>100	>100
	11A	>100	>100	>100	>100	>100	>100	>100	>100	>100	>100	>100	0.17
Ab	11B	>100	>100	>100	>100	>100	>100	>100	>100	>100	>100	>100	0.11
t m	11B1	>100	>100	>100	>100	>100	>100	>100	>100	>100	>100	>100	1.14
bi	11B2	>100	>100	>100	>100	>100	>100	>100	>100	>100	>100	>100	0.67
Ral	11B4	>100	>100	>100	>100	>100	>100	>100	>100	>100	>100	>100	0.35
	11B5	>100	>100	>100	>100	>100	>100	>100	>100	>100	>100	>100	0.24
	11B7	>100	>100	>100	>100	>100	>100	>100	>100	>100	>100	>100	0.23
	12A	>200	>100	>100	>100	>200	>100	>100	>100	>100	>100	>100	100.00
	12A1	>200	>100	>100	>100	>200	>100	>100	>100	>100	>100	>100	100.00

Table S3. BG505 Pseudovirus Alanine-Scanning Mutagenesis, Related to Figure 2 and 4.

The rabbit mAbs were titrated against the indicated mutated pseudoviruses in the TZM-bl luciferase reporter assay and the IC_{50} values shown were calculated using Prism. Potent neutralization categorized as an $IC_{50} < 1$, intermediate neutralization categorized as an IC_{50} of >1<10, weak neutralization categorized as an IC_{50} of >10<100. No neutralization activity is indicated by an IC_{50} of >100. Fold change in IC_{50} value for mAbs was calculated and compared to previously described fold changes in ID_{50} (Sanders et al., 2015) seen with the serum samples from the source animals. NT = not tested.

				IC ₅₀	ıg/ml				Fold change					
		10A	11A	PGT151	VRC01	PGT121	PG9	10A	1410 serum	11A	1411 serum			
	BG505	0.372	0.170	0.002	0.053	0.061	0.031	-	-	-	-			
	E87A	0.674	0.298	0.003	0.052	0.027	0.026	2	2	2	1			
	W112A	0.139	0.216	0.004	0.061	0.048	0.040	0	2	1	1			
	K121A	0.943	0.048	0.008	0.135	0.114	0.067	3	3	0	1			
	L125A	0.713	0.189	0.004	0.042	0.022	0.036	2	4	1	1			
	L165A	0.219	0.045	0.033	0.022	0.038	0.020	1	4	0	2			
	K168A	0.285	0.172	0.004	0.059	0.047	0.133	1	10	1	6			
	T198A	0.652	0.020	0.004	0.247	0.064	0.050	2	4	0	1			
strain	T257A	>100	84.790	0.003	0.059	0.023	0.027	>600	>50	499	1			
	D279A	>100	0.064	0.004	89.300	0.028	0.040	>600	2	0	1			
	Y384A	18.750	0.275	0.008	0.170	0.104	0.073	50	2	2	1			
	N386A	21.638	0.170	0.002	0.055	0.013	0.019	58	4	1	2			
sr	N392A	0.309	0.030	0.003	0.094	0.055	0.055	1	>50	0	1			
<u>'ir</u>	1396A	0.612	0.126	0.003	0.132	0.068	0.046	2	10	1	1			
~	S397A	1.719	0.334	0.004	0.092	0.058	0.046	5	10	2	1			
	N398A	6.222	0.491	0.007	0.065	0.033	0.041	17	10	3	1			
	K421A	0.376	0.095	0.005	0.044	0.040	0.032	1	9	1	7			
	Q422A	0.100	0.068	0.002	0.050	0.031	0.034	0	8	0	6			
	1424A	0.337	0.119	0.004	0.052	0.034	0.047	1	12	1	1			
	T455A	100.000	50.787	0.002	0.093	0.018	0.040	269	NT	299	NT			
	P470A	100.000	68.536	0.006	0.042	0.012	0.012	269	3	403	1			
	D474A	24.690	0.091	0.005	0.004	0.020	0.652	66	NT	1	NT			
	D477A	100.000	100.000	0.002	0.076	0.016	0.030	269	>50	588	6			
	N488A	2.955	0.545	0.003	0.103	0.206	0.066	8	NT	3	NT			

Table S4: Non-neutralizing rabbit mAb epitope mapping, Related to Figure 2,3 and 4.

96-well ELISA plates were coated overnight at 4°C with mouse anti-Avi-tag antibody (Genscript) at 2 µg/ml in PBS. Plates were washed 4 times with PBS, 0.05% (v/v) Tween, and blocked with 3% (w/v) BSA PBS for 1 h. Concurrently, 5-fold serial dilutions of non-biotinylated rabbit or human mAbs starting at 100 µg/ml were pre-incubated with 1 µg/ml of purified Avi-tagged BG505 SOSIP.664 protein for 1 h. The mAb-SOSIP mixture was then transferred to the blocked ELISA plates and incubated for 1 h. Plates were washed four times and incubated with 0.5 µg/ml of biotinylated mAb for 1 h, then washed again and binding detected with streptavidin-alkaline phosphatase (Jackson Immunoresearch) at 1:1000 for 1 h. mAbs were biotinylated using the NHS-micro-biotinylation kit (Pierce). Competition is expressed as percentage binding where 100% was the absorbance measured when BG505 SOSIP.664 protein only was captured on the anti-avi-tag ELISA plate. The V3-specific mAb 10B was used as a negative control for non-specific inhibition.

									Biotir	nylated	rabbit ı	mAbs							
		10A	10B	10C	10D	10H	101	10J	11A	11B	11C	11D	11E	11G	12C	12J	12M	12N	12A
	B6	92	157	19	97	70	104	101	72	72	97	99	98	103	110	96	107	105	NT
	A32	87	178	108	98	91	109	102	78	73	96	98	102	104	106	78	106	110	NT
	2F5	112	103	96	98	101	111	102	92	81	95	98	101	111	104	98	106	102	NT
	F240	114	103	66	99	92	110	102	89	85	95	99	101	102	105	92	110	108	NT
	3D6	126	107	99	100	107	111	103	94	94	94	100	102	103	100	106	110	115	NT
	PGT124	97	60	76	93	105	4	100	67	79	90	102	90	95	90	152	97	91	NT
	PGT128	97	56	57	87	100	7	97	79	75	88	92	82	87	84	163	87	89	NT
ĺ	10-1074	146	72	71	108	177	4	101	116	102	95	98	101	99	103	181	108	107	NT
٩	PGV04	122	97	27	112	126	110	103	96	103	99	104	108	104	114	211	120	109	NT
An	VRC01	88	82	21	89	100	107	100	72	91	107	96	85	93	91	193	84	87	NT
2	PG9	97	87	85	118	92	83	103	88	88	101	103	113	102	117	151	126	121	NT
it	CAP256	98	93	83	125	107	95	103	83	93	102	104	118	104	121	102	137	127	NT
be	3BC176	96	105	109	71	83	107	96	79	90	84	87	73	86	72	83	82	87	70
on	3BC315	79	94	100	34	55	92	53	62	76	49	71	32	73	29	34	35	44	24
	8ANC915	37	72	74	80	41	105	94	54	61	89	52	80	14	106	194	90	71	23
	35022	107	91	109	72	98	112	95	95	99	85	95	71	92	75	157	68	75	83
	PGT152	109	80	108	70	90	111	95	93	99	108	102	75	102	58	158	79	75	NT
	D3724	95	73	91	98	83	101	103	81	92	97	103	100	100	102	104	112	103	NT
	PGT145	102	78	112	117	91	79	104	84	101	104	103	115	98	117	114	146	123	NT
	CH03	111	86	116	99	93	93	103	96	104	99	102	98	97	102	129	107	101	NT
	SELF	13	32	19	5	32	11	5	12	5	5	4	4	3	5	22	8	6	4
	11A	12	81	85	43	90	99	51	12	5	73	73	57	97	64	161	43	46	NT
	Blank	106	99	118	100	103	101	103	110	103	100	100	100	100	100	101	100	100	96

Table S5. Ability of All Isolated Rabbit mAbs to Compete in ELISA with Biotinylated nAbs 10A, 11A, 11B and 12A, Related to Figure 2, 3 and 4.

96-well ELISA plates were coated overnight at 4°C with mouse anti-Avi-tag antibody (Genscript) at 2 µg/ml in PBS. Plates were washed 4 times with PBS, 0.05% (v/v) Tween, and blocked with 3% (w/v) BSA PBS for 1 h. Concurrently, 5-fold serial dilutions of non-biotinylated rabbit mAbs starting at 100 µg/ml were pre-incubated with 1 µg/ml of purified Avi-tagged BG505 SOSIP.664 protein for 1 h. The mAb-SOSIP mixture was then transferred to the blocked ELISA plates and incubated for 1 h. Plates were washed four times and incubated with 0.5 µg/ml of biotinylated mAb for 1 h, then washed again and binding detected with streptavidin-alkaline phosphatase (Jackson Immunoresearch) at 1:1000 for 1 h. mAbs were biotinylated using the NHS-micro-biotinylation kit (Pierce). Competition is expressed as percentage binding where 100% was the absorbance measured when BG505 SOSIP.664 protein only was captured on the anti-avi-tag ELISA plate. The V3-specific mAb 10B was used as a negative control for non-specific inhibition.

		10A-biotin			10B-biotin				11A-biotin				11B-biotin				12A-biotin				
	µg/ml:	100	20	4	0.8	100	20	4	0.8	100	20	4	0.8	100	20	4	0.8	100	20	4	0.8
	10A	5	5	5	16	83	92	98	83	5	5	5	17	5	5	5	8	4	4	5	12
	10A1	4	4	5	80	80	77	74	85	5	5	5	86	4	4	5	56	5	5	5	39
	10B	100	99	101	112	4	4	5	10	102	104	103	113	96	96	98	102	113	103	104	71
	10C	99	99	100	113	127	126	124	123	102	104	103	115	97	99	97	101	17	106	94	113
	10D	62	64	66	72	95	82	81	80	72	76	76	84	6	6	7	23	5	49	90	64
	10E	101	101	101	112	102	100	99	85	102	105	103	119	98	97	96	99	65	103	103	117
	10F	101	102	100	107	92	87	83	85	103	105	103	111	93	97	98	99	61	107	101	97
	10H	80	79	78	89	106	101	78	102	91	92	87	95	86	87	88	92	34	63	58	81
	101	100	101	101	100	102	87	80	79	103	105	105	104	97	98	100	97	64	99	101	101
	10J	100	100	101	100	104	86	77	78	103	104	104	105	95	94	95	96	70	107	115	108
	11A	4	3	4	6	83	97	83	75	4	4	4	6	3	3	3	4	5	4	4	4
	11A1	5	4	4	5	83	84	75	81	4	4	4	6	4	4	4	6	5	4	5	5
	11A2	4	3	4	6	83	83	95	103	3	3	3	6	3	3	3	11	3	3	3	5
	11A3	13	13	14	36	85	86	103	104	13	13	14	32	27	28	31	68	10	11	11	27
	11B	4	4	4	16	77	77	77	85	4	4	5	17	4	4	4	7	4	4	5	6
	11B1	7	8	10	64	72	66	67	99	8	9	11	70	10	11	13	53	7	6	7	25
q	11B2	8	8	9	40	77	67	70	103	8	9	9	47	9	10	11	29	7	7	8	24
itor mAt	11B4	24	26	27	64	75	69	72	106	29	28	30	69	35	37	39	67	18	17	19	43
	11B5	6	6	6	20	66	65	67	105	6	6	7	22	6	6	7	14	7	6	7	13
etit	11B7	11	13	13	43	61	66	68	105	12	12	14	48	15	15	17	39	12	11	13	25
du	11C	70	73	/2	//	90	//	104	101	87	91	88	87	90	92	90	91	98	111	88	85
ပိ	11D	95	94	94	96	75	95	81	110	97	98	97	98	93	91	98	95	5	5	6	6
	11E	57	68	63	72	81	96	81	113	89	90	91	90	84	87	87	87	11	76	80	72
	11F	75	69	61	64	89	//	//	107	91	92	8/	85	89	87	84	84	40	35	19	21
	116	94	90	95	94	91	0/	91	107	100		100	98	93	95	94	93	<u>р</u>	<u>р</u>	о 7	10
	12A	75	94 02	90		04 06	112	107	107	50 52	00	93	94	67	09	93	94	5	0 5	1	6
	12A1	29	03	94	90	00 94	100	107	109	55 72	02 90	92	95	07 Q1	00	93	97	5	5	6	0
	12A2	100	9 4 100	90 101	97 103	04 85	103	107	104	07	09	101	90	01	100	94	97 102	6	6	0 8	7 20
	120	00	02		00	05	80	70	104	97	99	07	06	00	100	00	00	115	102	106	104
	120	87	82	89	106	100	101	105	105	85	86	97	103	93 Q1	95	93	100	103	84	100	94
	121	92	84	87	95	82	106	100	100	87	88	86	93	91	95	93	97	58	59	65	56
	12.1	103	101	102	120	92	100	92	85	104	102	103	113	103	90	100	103	112	116	116	107
	126 12K	86	80	77	68	97	103	91	85	79	82	79	75	91	91	87	85	75	80	67	50
	12L	90	94	99	124	82	104	86	85	84	94	100	118	90	94	96	98	83	103	119	109
	12M	70	71	71	96	94	100	93	91	62	68	76	93	81	83	83	85	58	71	81	74
	12N	64	68	71	76	105	109	115	113	56	63	65	72	82	81	89	87	45	37	39	41
	120	94	92	91	93	107	95	111	110	89	91	89	92	98	102	101	99	92	93	88	86
	12R	101	100	100	99	106	104	86	103	98	100	98	99	99	98	102	103	9	9	10	18
	Blank	101	100	100	99	111	83	109	97	100	101	100	99	98	97	105	99	117	93	98	92

Supplemental Information References

Macauley, M.S., Pfrengle, F., Rademacher, C., Nycholat, C.M., Gale, A.J., von Drygalski, A., and Paulson, J.C. (2013). Antigenic liposomes displaying CD22 ligands induce antigen-specific B cell apoptosis. The Journal of clinical investigation *123*, 3074-3083.

Penczek, P.A., Grassucci, R.A., and Frank, J. (1994). The ribosome at improved resolution: new techniques for merging and orientation refinement in 3D cryo-electron microscopy of biological particles. Ultramicroscopy 53, 251-270.

Sanders, R.W., van Gils, M.J., Derking, R., Sok, D., Ketas, T.J., Burger, J.A., Ozorowski, G., Cupo, A., Simonich, C., Goo, L., et al. (2015). HIV-1 neutralizing antibodies induced by native-like envelope trimers. Science 349, aac4223.

Sok, D., van Gils, M.J., Pauthner, M., Julien, J.P., Saye-Francisco, K.L., Hsueh, J., Briney, B., Lee, J.H., Le, K.M., Lee, P.S., *et al.* (2014). Recombinant HIV envelope trimer selects for quaternarydependent antibodies targeting the trimer apex. Proceedings of the National Academy of Sciences of the United States of America 111, 17624-17629.

Tang, G., Peng, L., Baldwin, P.R., Mann, D.S., Jiang, W., Rees, I., and Ludtke, S.J. (2007). EMAN2: an extensible image processing suite for electron microscopy. Journal of structural biology 157, 38-46.