

Supplementary Materials for

A V_H1-69 antibody lineage from an infected Chinese donor potently neutralizes HIV-1 by targeting the V3 glycan supersite

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Table S1A. Neutralizing breadth and potency of sera from an HIV-1-infected Chinese donor (CBJC438) on the global panel of HIV-Env strains. ^a

Global Panel			CBJC438						
Clade	Tier	Pseudovirus	2005-07-12	2006-04-06	2007-04-10	2008-03-20	2009-06-13	2009-12-15	2012-07-31
A	2	398-F1	1277	893	102	829	1575	2038	254
	2	TRO.11	260	348	54	358	334	492	122
B	2	X2278	737	601	111	670	703	879	161
	2	25710	498	294	72	323	308	241	129
C	2	Ce0217	408	427	51	331	236	378	102
	2	Ce1176	341	303	25	496	318	385	126
G	2	X1632	101	91	23	214	116	138	91
CRF01_AE	2	CNE55	114	93	31	138	63	77	82
	2	CNE8	143	94	75	191	75	151	125
CRF07_BC	2	BJOX2000	414	400	22	248	298	621	150
	2	CH119	208	207	46	217	304	533	135
AC	2	246	162	150	81	253	205	224	138
Potency (GMTs)			292	253	50	311	258	352	129
Breadth% (>20)			100	100	100	100	100	100	100

^aGlobal panel was developed by the Montefiori group at Duke University Medical Center.
The serum dilution values >1000 are highlighted in red, 200~1000 in orange, and 20~200 in green.

Table S1B. Neutralizing breadth and potency of monoclonal antibodies (mAbs) from an HIV-1-infected Chinese donor (CBJC438) on the global panel of HIV-Env strains. ^a

Global Panel			mAbs				
Clade	Tier	Pseudovirus	438-B11	438-D5	438-D6	438-F11	VRC01
A	2	398-F1	0.02	0.03	>50	>50	0.41
B	2	TRO.11	0.07	0.14	>50	>50	0.77
	2	X2278	0.09	0.08	>50	>50	0.35
C	2	25710	0.64	0.55	>50	>50	0.87
	2	Ce0217	4.53	1.67	>50	>50	0.42
	2	Ce1176	0.34	0.33	>50	>50	4.88
G	2	X1632	>50	>50	>50	>50	0.31
CRF01_AE	2	CNE55	>50	>50	>50	>50	0.64
	2	CNE8	>50	>50	>50	>50	0.56
CRF07_BC	2	BJOX2000	0.06	0.07	>50	>50	>50
	2	CH119	0.14	0.22	>50	>50	1.56
AC	2	246	>50	>50	>50	>50	0.51
Potency (GMTs)			0.18	0.19	n/a	n/a	0.69
Breadth% (<50µg/ml)			67	67	0	0	92

^aGlobal panel was developed by the Montefiori group at Duke University Medical Center.

The neutralizing potency of the mAbs was measured as IC₅₀ in µg/ml. Values < 0.2 µg/ml are highlighted in red, 0.2~2 µg/ml in yellow, and 2~50 µg/ml in green.

AG	928.28	>10.0	>10.0	>10.0	>10.0	>10.0	>10.0
AG	T211.9	>10.0	2.920	0.029	>10.0	>10.0	0.114
AG	T235.47	0.014	0.062	>10.0	0.056	0.248	>10.0
AG	T250.4	>10.0	0.001	0.001	>10.0	0.005	0.005
AG	T251.18	>10.0	>10.0	5.689	>10.0	>10.0	>10.0
AG	T255.34	>10.0	>10.0	>10.0	>10.0	>10.0	>10.0
AG	T257.31	>10.0	>10.0	>10.0	>10.0	>10.0	>10.0
AG	T263.8	>10.0	3.310	0.133	>10.0	>10.0	0.533
B	89.6	0.024	0.009	0.002	0.098	0.036	0.009
B	6535.3	0.011	0.003	0.003	0.043	0.011	0.013
B	1006.11.C3.1601	0.018	0.002	0.005	0.074	0.007	0.021
B	1012.11.TC21.3257	0.314	0.012	0.006	1.255	0.049	0.022
B	1054.07.TC4.1499	0.488	0.081	0.018	1.952	0.324	0.073
B	1056.10.TA11.1826	>10.0	0.035	0.003	>10.0	0.140	0.010
B	62357.14.D3.4589	>10.0	9.600	0.326	>10.0	>10.0	1.305
B	6240.08.TA5.4622	0.028	0.028	0.012	0.111	0.112	0.048
B	6244.13.B5.4567	0.043	0.072	0.014	0.174	0.290	0.058
B	92BR020	0.010	0.011	0.004	0.040	0.045	0.018
B	AC10.0.29	0.014	0.042	0.003	0.058	0.168	0.013
B	ADA	0.019	0.014	0.013	0.078	0.055	0.052
B	BaL.26	0.026	0.017	0.026	0.104	0.069	0.104
B	CAAN5342.A2	0.025	0.010	0.031	0.099	0.039	0.122
B	DH12	0.036	0.002	0.006	0.142	0.006	0.025
B	HxB2	>10.0	>10.0	>10.0	>10.0	>10.0	>10.0
B	JRCSF	0.034	0.063	0.006	0.137	0.253	0.022
B	JRFL	0.056	0.088	0.011	0.223	0.352	0.044
B	MN	>10.0	>10.0	>10.0	>10.0	>10.0	>10.0
B	PVO.4	4.419	0.126	0.004	>10.0	0.504	0.014
B	QHO692.42	>10.0	6.984	0.021	>10.0	>10.0	0.083
B	REJO.67	>10.0	>10.0	>10.0	>10.0	>10.0	>10.0
B	RHPA4.7	0.051	0.020	0.016	0.203	0.080	0.064
B	SC05.8C11.2344	0.014	0.022	0.007	0.058	0.087	0.027
B	SC422661.8	0.016	0.059	0.121	0.065	0.237	0.485
B	SF162	0.008	0.003	0.002	0.030	0.013	0.010
B	SS1196.1	0.009	0.004	0.004	0.038	0.016	0.015
B	TRJO.58	>10.0	9.008	0.011	>10.0	>10.0	0.043
B	TRO.11	0.023	0.008	0.006	0.092	0.032	0.023
B	WEAU.d15.410.787	0.026	0.026	0.005	0.104	0.102	0.022
B	WITO.33	>10.0	0.653	>10.0	>10.0	2.611	>10.0
B	YU2	0.047	0.089	0.035	0.190	0.356	0.139

BC	CNE17	>10.0	4.341	0.051	>10.0	>10.0	0.206
BC	CNE19	>10.0	0.012	>10.0	>10.0	0.050	>10.0
BC	CNE20	>10.0	4.89E-04	3.98E-04	>10.0	0.002	0.002
BC	CNE21	6.052	0.007	0.005	>10.0	0.027	0.018
BC	CNE30	1.196	0.049	0.245	4.782	0.197	0.981
BC	CNE52	>10.0	4.939	>10.0	>10.0	>10.0	>10.0
BC	CNE53	0.020	0.010	0.009	0.082	0.040	0.035
BC	CNE58	>10.0	>10.0	0.977	>10.0	>10.0	3.909
C	1394C9G1(Rev.)	>10.0	0.457	0.007	>10.0	1.828	0.026
C	7030102001E5(Rev.)	0.012	0.007	0.004	0.047	0.028	0.015
C	93IN905	0.009	0.003	0.004	0.036	0.010	0.016
C	BF1266.431a	>10.0	>10.0	>10.0	>10.0	>10.0	>10.0
C	CAP210.2.00.E8	>10.0	>10.0	>10.0	>10.0	>10.0	>10.0
C	CAP45.2.00.G3	>10.0	8.529	>10.0	>10.0	>10.0	>10.0
C	Ce0393 C3	>10.0	>10.0	>10.0	>10.0	>10.0	>10.0
C	Ce1172 H1	2.686	0.004	0.015	>10.0	0.015	0.059
C	Ce1176 A3	0.038	0.015	0.009	0.154	0.061	0.035
C	Ce2010 F5	>10.0	>10.0	>10.0	>10.0	>10.0	>10.0
C	Ce2060 G9	>10.0	>10.0	>10.0	>10.0	>10.0	>10.0
C	Ce703010054 2A2	>10.0	>10.0	>10.0	>10.0	>10.0	>10.0
C	Ce704809221 1B3	>10.0	0.031	0.013	>10.0	0.123	0.052
C	Du156.12	0.016	0.006	0.010	0.065	0.024	0.039
C	Du172.17	0.898	0.021	0.014	3.593	0.082	0.055
C	Du422.1	0.061	0.038	0.032	0.245	0.151	0.130
C	HIV-0013095.2.11	5.028	0.057	>10.0	>10.0	0.227	>10.0
C	HIV-001428.2.42	6.188	0.018	0.024	>10.0	0.074	0.097
C	HIV-16055.2.3	>10.0	0.626	>10.0	>10.0	2.502	>10.0
C	IAVIC22	0.008	0.001	0.003	0.033	0.006	0.010
C	ZM109F.PB4	>10.0	>10.0	>10.0	>10.0	>10.0	>10.0
C	ZM135M.PL10a	>10.0	1.260	7.496	>10.0	5.041	>10.0
C	ZM197M.PB7	>10.0	>10.0	>10.0	>10.0	>10.0	>10.0
C	ZM214M.PL15	>10.0	0.475	0.768	>10.0	1.898	3.071
C	ZM233M.PB6	>10.0	4.532	>10.0	>10.0	>10.0	>10.0
C	ZM246F.D5	>10.0	0.067	0.004	>10.0	0.268	0.014
C	ZM247F.F7	>10.0	0.028	0.016	>10.0	0.112	0.065
C	ZM249M.B10	>10.0	>10.0	1.238	>10.0	>10.0	4.950
C	ZM249M.PL1	>10.0	>10.0	1.235	>10.0	>10.0	4.941
C	ZM53M.PB12	>10.0	0.003	>10.0	>10.0	0.011	>10.0
CD	3817.v2.c59	>10.0	>10.0	0.007	>10.0	>10.0	0.030
CD	6480.v4.c25	0.006	0.005	>10.0	0.025	0.021	>10.0

CD	6811.v7.c18	0.012	0.002	0.013	0.048	0.008	0.054
CD	6952.v1.c20	>10.0	0.040	>10.0	>10.0	0.161	>10.0
CD	89.F1 2 25	>10.0	>10.0	>10.0	>10.0	>10.0	>10.0
D	231965.c01	>10.0	>10.0	>10.0	>10.0	>10.0	>10.0
D	3016.v5.c45	>10.0	>10.0	>10.0	>10.0	>10.0	>10.0
D	A07412M1.vrc12	>10.0	0.032	6.744	>10.0	0.127	>10.0
G	P0402 c2 11	0.316	0.004	0.006	1.263	0.015	0.026
G	P1981 C5 3	0.006	0.001	0.011	0.024	0.005	0.043
G	X1193 c1	>10.0	0.033	0.010	>10.0	0.132	0.041
G	X1254 c3	0.090	0.039	0.015	0.360	0.156	0.062
G	X1632 S2 B10	>10.0	>10.0	>10.0	>10.0	>10.0	>10.0
G	X2088 c9	0.015	0.005	7.559	0.059	0.020	>10.0
G	X2131 C1 B5	>10.0	0.010	0.009	>10.0	0.040	0.037
-	aMLV	>10.0	>10.0	>10.0	>10.0	>10.0	>10.0
-	VSV	>10.0	>10.0	>10.0	>10.0	>10.0	>10.0

The neutralizing potency of the mAbs was measured as IC50/ IC80 in µg/ml. Values < 0.1 µg/ml are highlighted in red, 0.1-1 µg/ml in orange, 1-5 µg/ml in yellow, and 5-10 µg/ml in green.

	IC ₅₀ (µg/ml)			IC ₈₀ (µg/ml)			
	438-B11	PGT121	PGT128	438-B11	PGT121	PGT128	
Total Number of Viruses Tested	129	129	129	129	129	129	
Total Number of Viruses Neutralized	IC ₅₀ / IC ₈₀ >10.0 (µg/ml)	54	81	88	48	71	82
	IC ₅₀ / IC ₈₀ >1.0 (µg/ml)	46	70	79	41	66	74
	IC ₅₀ / IC ₈₀ >0.1 (µg/ml)	41	64	69	25	38	57
Percent of Viruses Neutralized	IC ₅₀ / IC ₈₀ >10.0 (µg/ml)	41.9	62.8	68.2	37.2	55.0	63.6
	IC ₅₀ / IC ₈₀ >1.0 (µg/ml)	35.7	54.3	61.2	31.8	51.2	57.4
	IC ₅₀ / IC ₈₀ >0.1 (µg/ml)	31.8	49.6	53.5	19.4	29.5	44.2
Median IC ₅₀ / IC ₈₀ (µg/ml)	0.027	0.028	0.013	0.098	0.080	0.046	
Geometric IC ₅₀ / IC ₈₀ Mean (µg/ml)	0.058	0.037	0.024	0.136	0.072	0.065	

Antibody ID	Geometric IC ₅₀ Mean			
	Subtype A	Subtype B	Subtype C	Subtypes A, B, and C
438-B11	0.079	0.035	0.138	0.056
PGT121	0.045	0.039	0.049	0.043
PGT128	0.054	0.010	0.031	0.019

Table S1D. Characterization of four monoclonal antibodies isolated from an HIV-1-infected Chinese donor (CBJC438).

mAbs	Heavy chain					Light chain			
	IGHV	IGHD	IGHJ	CDR3 (aa)	SHM (%)	IGκ/λ V	IGκ/λ J	CDR3 (aa)	SHM (%)
438-B11	1-69*01	3-3*01	3*01	21	25.4 (73/288)	3-20*01 ^a	3*01 ^a	9	12.7 (34/267)
438-D5	1-69*01	3-3*01	3*01	21	24.7 (71/288)	3-20*01 ^a	3*01 ^a	9	13.5 (36/267)
438-D6	3-48*02	1-20*01	4*02	8	8.7 (25/288)	2-11*01 ^b	3*02 ^b	10	2.6 (7/270)
438-F11	7-4-1*02	2-21*02	6*04	20	10.1 (29/288)	1-40*01 ^b	2*01 ^b	11	7.8 (21/270)

^a438-B11 and 438-D5 use Kappa chains.

^b438-D6 and 438-F11 use Lambda chains.

Table S1E. Next-generation sequencing and antibodyomics pipeline processing of CBJC438 B -cell repertoires. ^a

Time point	N _{Raw}	N _{Assign}	Chain	N _{Chain}	<Length> (nt)	N _{Usable}	Perc _{Usable} (%)
2005	4,755,711	3,727,420	H	1,509,712	597.5	1,022,678	67.7%
			κ	1,106,927	600.5	617,666	55.8%
			λ	1,110,781	605.8	704,904	63.5%
2008	5,138,283	4,148,887	H	1,864,778	583.9	1,261,262	67.6%
			κ	1,135,577	567.7	672,894	59.3%
			λ	1,148,532	591.6	714,059	62.2%
2012	4,802,280	3,991,951	H	1,954,169	579.0	1,404,745	71.9%
			κ	1,016,963	591.0	647,514	63.7%
			λ	1,020,819	595.6	675,578	66.2%

^a Listed items include the time point, total number of raw reads (N_{Raw}), number of reads with assigned germline V genes using a cutoff E-value of 10⁻³ (N_{Assign}), antibody chain type (Chain: H, κ, and λ), number of antibody chains (N_{Chain}), average read length (<length>), number of antibody chains after pipeline processing and removing sequences with a V-gene alignment of 250 bp or shorter (N_{Usable}), and percentage of the usable reads (Perc_{Usable}=N_{Usable}/N_{Chain}×100). 5'-RACE PCR was used in library preparation. After template preparation on Ion Chef, the pooled antibody chain libraries were sequenced on Ion GeneStudio S5.

Table S2A. Expression of antibodies with selected 2005 heavy chain variants paired with the 438-D5 light chain.

No.	Chain type	Sequence index	Yield (mg/L culture sup)	Neutralization (%)	Sequence identity (%)	Amino acid sequence of variable domain
1 ^a	H	656611	2.4	36	81.3	QVGLLQSGAEVKEPGSSVTVSCKPSGGTFTNYAISWVRQAPGQGRSSSEGGRRVPIISGISKYAEQFQGRVRLYEDDSTKTVYLDLRLSLTSDDTGVYYCARWRGCLDCHYDTGAYYNDASDIWGQTMVTVSA
2 ^a	H	3252240	0.8	14	81.5	QVRLVQSGGAEVKKPGSSVTVSCKPSGGTFTFRNYAITGVRQAPGQGLQWMMGGVPIIGGISKYAEQFQGRVRLYEDDSTKTVYLDLRLSLTSDDTGVYYCARWRGCLDCHYDTGAYYNDASDIWGQTMVTVSA
3 ^a	H	4088606	1.0	42	77.9	QVRLVQSGAEVKEPGSSVTVSCKPSGGTFTNYAMHWVRQAPGQGLQWMMGGVPIIGVYKYAEQFQGRVRLYEDDSTKTVYLDLRLSLTSDDTGVYYCARWRGCLDCHYDTGAYYNDASDIWGQTMVTVSA
4 ^a	H	2771371	1.0	17	81.8	RWRLVQSGAEVKEPGSSVTVSCKPFWRHLHQLHWYLPVPPGWRTRRRSGDGGRRVPIIGVYKYAEQFQGRVRLYEDDSTKTVYLDLRLSLTSDDTGVYYCARWRGCLDCHYDTGAYYNDASDIWGQTMVTVSA
5 ^a	H	4071948_dN	0.7	33	80.3	VAGLLQVVAEVRKPGSSVTVSCKPSGGTFTNYAMHWVRQAPGQGLQWMMGGVPIIGVYKYAEQFQGRVRLYEDDSTKTVYLDLRLSLTSDDTGVYYCARWRGCLDCHYDTGAYYNDASDIWGQTMVTVSA
6 ^b	H	1018124	1.5	0	66.9	QVQLVQSGAEVKKPGSSVTVSCKPSGGTFTNYAMHWVRQAPGQGLQWMMGGIIPLLGITDYAQKQGRVTTITADDSTSTAYMDLSSLTSEDVAVYYCARAAPPDLRGIYVAYNYMDVWGKTTVTVSS
7 ^b	H	2859064	2.0	0	66.9	EVHLVQSGAEVKKPGSSVTVSCKPSGGTFTNYAMHWVRQAPGQGLQWMMGGIIPLLGITDYAQKQGRVTTITADDSTSTAYMDLSSLTSEDVAVYYCARAAPPDLRGIYVAYNYMDVWGKTTVTVSS
8 ^b	H	3069562	—	n/a	66.4	RVQLVQSGAEVKKPGSSVTVSCKPSGGTFTNYAMHWVRQAPGQGLQWMMGGIIPLLGITDYAQKQGRVTTITADDSTSTAYMDLSSLTSEDVAVYYCARAAPPDLRGIYVAYNYMDVWGKTTVTVSS
9 ^b	H	2438418	—	n/a	66.4	RWQLVQSGAEVKKPGSSVTVSCKPSGGTFTNYAMHWVRQAPGQGLQWMMGGIIPSLAITDYAQKQGRVTTITADDSTSTAYMDLSSLTSEDVAVYYCARAAPPDLRGIYVAYNYMDVWGKTTVTVSS
10 ^b	H	3749771	—	n/a	65.1	QVSRGCELVQVVAEVRKPGSSVTVSCKPSGGTFTNYAMHWVRQAPGQGLQWMMGGIIPLLGITDYAQKQGRVTTITADDSTSTAYMDLSSLTSEDVAVYYCARAAPPDLRGIYVAYNYMDVWGKTTVTVSS

Listed items include sequence number, antibody chain type, sequence index in the PGM data set, protein yield, neutralization, sequence identity to 438-B11 heavy chain determined during the pipeline processing, and amino acid sequence. No expression (—) denotes protein yield less than 0.5 mg/L. Neutralizing activity was tested against viruses on Global Panel. n/a, not available.

^a Heavy chains are related to 438-D5/B11 but cover a wide range of sequence identity and HCDR3 motifs.

^b All sequences have a similar HCDR3 loop length of 20-23 aa.

Table S2B. Expression of antibodies with selected 2005 light chain variants paired with the 438-D5 heavy chain.

No.	Chain type	Sequence index	Yield (mg/L culture sup)	Neutralization (%)	Sequence identity (%)	Amino acid sequence of variable domain
1 ^a	K	1020383	8.3	67	89.2	EIVLTQSPGTLSSSGERGLTSCRASNISAYLAWYQQKRGQTPRLLIYAASSRATATPDRFSGSGSGTDFTLTINRLEPEDFAVYYCQHYGGSFFSFGPGTQVDVK
2 ^a	K	1031879	—	n/a	88.3	EIVLTQSPGTLSSSGERGLTSCRASNISAYLAWYQQKRGQTPRLLIYAASSRATATPDRFSGSGSGTDFTLTINRLEPEGFVAVYYCQHYGGSFFSFGPGTQVDVF
3 ^a	K	158500	6.5	67	88.9	KIVLTQSPGTLSSSGERGLTSCRASNISAYLAWYQQKRGQTPRLLIYAASSRATATPDRFSGSGSGTDFTLTINRLEPEDFAVYYCQHYGGSFFSFGPGTQVDVK
4 ^a	K	1965944	7.2	67	88.6	KLIVLTQSPGTLSSSGERGLTSCRASHNISAYLAWYQQKRGQTPRLLIYAASSRATATPDRFSGSGSGTDFTLTINRLEPEDFAVYYCQHYGGSFFSFGPGTQVDVK
5 ^a	K	1043810	—	n/a	89.5	EIVLTQSPGTLSSSGERGLTSCRASNISAYLAWYQQKRGQTPRLLIYAASSRATATPDRFSGSGSGTDFTLTINRLEPEGFVAVYYCQHYGGSFFSFGPGTQVDVF

Listed items include sequence number, antibody chain type, sequence index in the PGM data set, protein yield, neutralization, sequence identity to 438-B11 light chain determined during the pipeline processing, and amino acid sequence. No expression (—) denotes protein yield less than 0.5 mg/L. Neutralizing activity was tested against viruses on Global Panel. n/a, not available.

^a Kappa chains are related to 438-D5/B11 but cover a wide range of sequence identity and KCDR3 motifs.

Table S2C. Expression of antibodies with selected 2008 heavy chain variants paired with the 438-D5 light chain.

No.	Chain type	Sequence index	Yield (mg/L culture sup)	Neutralization (%)	Sequence identity (%)	Amino acid sequence of variable domain
1 ^a	H	1066709	30.2	67	97.7	QVRLQSGAEVKKPGSSVTISCKPVGDTFTNFAIHWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKQDRRLRYEDDPMKTVFLELRSLTSDDTGVVYCTRWRGCGMCPYDTSYNDASDVWGPQTKVIVSA
2 ^a	H	2437629	—	n/a	97.2	QVRLQSGAEWTKPGSSVDNAPCKPVGDTFTNFAIHWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKFHDRRLRYEDDPMKTVFLELRSLTSDDTGVVYCTRWRGCGMCPYDTSYNDASDVWGPQTKVIVSA
3 ^a	H	3954697	—	n/a	93.8	QVRLLRSGAEVKKPGSSVSIKCPVGGTFTNFAITWVQAPGGQLEWVGGRRVPPVGIYKYGKFKQDRRLRYEDDPMKTVFLELRSLTSDGTGVVYCTRWRGCGMCPYDTSYNDASDVWGPQTKVIVSA
4 ^a	H	1067269	6.5	67	81.5	QVRLVQSGAVVKKPGSSVTISCKPVGDTFTNFAIHWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKQDRMLWEDDPAKTVFLDLRSLTPDDTGVVYCARWRGCGDCLYDTAAYNDASDIWGGQTMVIVSA
5 ^a	H	3795269	—	n/a	80.8	QVRLQSGAVVKKPGSSVTISCKPVGDTFTNFAIHWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKQDRMLWEDDPAKTVFLDLRSLTPDDTGVVYCARWRGCGDCLYDTAAYNDASDIWGGQTMVIVSA
6 ^a	H	4500127	—	n/a	81.3	QVRLQSGAVVKKPGSSVTISCKPVGDTFTNFAIHWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKQDRMLWEDDPAKTVFLDLRSLTPDDTGVVYCARWRGCGDCLYDTAAYNDASDIWGGQTMVIVSA
7 ^a	H	881629	—	n/a	80.3	QVRLVQSGAVVKKPGSSVTISCKPVGDTFTNFAISWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKQDRMLWEDDPAKTVFLDLRSLTPDDTGVVYCARWRGCGDCLYDTAAYNDASDIWGGQTMVIVSA
8 ^a	H	1021217	4.7	75	82.1	QVRLQSGAEVKKPGSSVRSCKPLGGFTFNHAIHWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKQDRMLWEDDPAKTVFLDLRSLTSDDTGVVYCTRWRGCGDCLYDTAAYNDASDIWGGQTMVIVSA
9 ^a	H	1071291	—	n/a	81.5	QVRLQSGAEVKKPGSSVRSCKPLGGFTFNHAIHWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKQDRMLWEDDPAKTVFLDLRSLTSDDTGVVYCTRWRGCGDCLYDTAAYNDASDIWGGQTMVIVSA
10 ^a	H	2032465	—	n/a	81.8	QVRLQSGAEVKKPGSSVRSCKPLGGFTFNHAIHWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKQDRMLWEDDPAKTVFLDLRSLTSDDTGVVYCTRWRGCGDCLYDTAAYNDASDIWGGQTMVIVSA
11 ^a	H	1141564	—	n/a	79.7	RVRLQSGAVVKKPGSSVTISCKPVGDTFTNFAISWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKQDRMLWEDDPAKTVFLDLRSLTPDDTGVVYCARWRGCGDCLYDTAAYNDASDIWGGQTMVIVSA
12 ^a	H	4521170	—	n/a	79.0	RVRLQSGAVVKKPGSSVTISCKPVGDTFTNFAISWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKQDRMLWEDDPAKTVFLDLRSLTPDDTGVVYCARWRGCGDCLYDTAAYNDASDIWGGQTMVIVSA
13 ^a	H	1577295_dN	—	n/a	94.9	VAGLLQSGAEVKKPGSSLDISCKPVGDTFTNFAIHWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKFHDRRLRYEDDPMKTVFLELRSLTSDDTGVVYCTRWRGCGMCPYDTSYNDASDIWGGQTKVIVSA
14 ^a	H	3385754_dN	—	n/a	95.6	GRVLQSGAEWTKPGSTVDNAPCKTVGGTFTKFAIHWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKFHDRRLRYEDDPMKTVFLELRSLTSDDTGVVYCTRWRGCGMCPYDTSYNDASDIWGGQTKVIVSA
15 ^a	H	552047	—	n/a	96.7	RCVPRRLLQSGADGWNPEFGSSVTISCKPVGDTFTNFAIHWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKFHDRRLRYEDDPMKTVFLELRSLTSDDTGVVYCTRWRGCGMCPYDTSYNDASDIWGGQTKVIVSA
16 ^a	H	1759061	—	n/a	94.6	HVRLQSGAEVKKPGSSVTISCKPVGDTFTNFAIHWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKFHDRRLRYEDDPMKTVFLELRSLTSDDTGVVYCTRWRGCGMCPYDTSYNDASDIWGGQTKVIVSA
17 ^a	H	1278991	—	n/a	95.9	HVRLQSGADGWNKPKGSSVTISCKPVGDTFTNFAIHWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKFHDRRLRYEDDPMKTVFLELRSLTSDDTGVVYCTRWRGCGMCPYDTSYNDASDIWGGQTKVIVSA
18 ^a	H	2288360	2.7	67	97.4	HVRLQSGAEAKKPGSSVTISCKPVGDTFTNFAIHWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKFHDRRLRYEDDPMKTVFLELRSLTSDDTGVVYCTRWRGCGMCPYDTSYNDASDIWGGQTKVIVSA
19 ^a	H	1797956	6.4	33	82.8	TVRLQSGAEVKKPGSSVRSCKPLGGFTFNHAIHWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKQDRMLWEDDPAKTVFLDLRSLTSDDTGVVYCTRWRGCGDCLYDTAAYNDASDIWGGQTMVIVSA
20 ^a	H	1719278_dN	—	n/a	97.9	VAGLLQSGAEVKKPGSSVTISCKPVGDTFTNFAIHWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKFHDRRLRYEDDPMKTVFLELRSLTSDDTGVVYCTRWRGCGMCPYDTSYNDASDIWGGQTKVIVSA
21 ^a	H	3140010	—	n/a	96.4	PVRLVQSGAEVKKPGSSVTISCKPVGDTFTNFAIHWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKFHDRRLRYEDDPMKTVFLELRSLTSDDTGVVYCTRWRGCGMCPYDTSYNDASDIWGGQTKVIVSA
22 ^a	H	364904	—	n/a	95.9	PVLLQSGAEVKKPGSSVTISCKPVGDTFTNFAIHWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKQDRMLWEDDPMKTVFLELRSLTSDDTGVVYCTRWRGCGMCPYDTSYNDASDIWGGQTKVIVSA
23 ^a	H	3656520	2.8	0	97.9	TVRLVQSGAEVKKPGSSVTISCKPVGDTFTNFAIHWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKFHDRRLRYEDDPMKTVFLELRSLTSDDTGVVYCTRWRGCGMCPYDTSYNDASDIWGGQTKVIVSA
24 ^a	H	3639936	6.1	8	97.9	QVRLQSGAEVKKPGSSVTISCKPVGDTFTNFAIHWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKFHDRRLRYEDDPMKTVFLELRSLTSDDTGVVYCTRWRGCGMCPYDTSYNDASDIWGGQTKVIVSA
25 ^a	H	2534625_dN	—	n/a	96.7	VAGLLQSGAEVKKPGSSVTISCKPVGDTFTNFAIHWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKFHDRRLRYEDDPMKTVFLELRSLTSDDTGVVYCTRWRGCGMCPYDTSYNDASDIWGGQTKVIVSA
26 ^b	H	3162349	1.0	0	69.0	QVQLVQSGAEVKKPGSSVKSCKASGDTFSSYAIHWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKFHDRRLRYEDDPMKTVFLELRSLTSDDTGVVYCTRWRGCGMCPYDTSYNDASDIWGGQTKVIVSA
27 ^b	H	1064503	1.7	0	65.9	QVHLVQSGAEVKKPGSSVKSCKASGDTFSSYAIHWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKFHDRRLRYEDDPMKTVFLELRSLTSDDTGVVYCTRWRGCGMCPYDTSYNDASDIWGGQTKVIVSA
28 ^b	H	1201231	—	n/a	70.3	QVQLVQSGAEVKKPGSSVKSCKASGDTFSSYAIHWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKFHDRRLRYEDDPMKTVFLELRSLTSDDTGVVYCTRWRGCGMCPYDTSYNDASDIWGGQTKVIVSA
29 ^b	H	1047823	—	n/a	67.7	QVQLVQSGAEVKKPGSSVKSCKASGDTFSSYAIHWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKFHDRRLRYEDDPMKTVFLELRSLTSDDTGVVYCTRWRGCGMCPYDTSYNDASDIWGGQTKVIVSA
30 ^b	H	1041439	—	n/a	63.6	QVQLVESGAEVKKPGSSVAVSCKASGDTFSSYAIHWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKFHDRRLRYEDDPMKTVFLELRSLTSDDTGVVYCTRWRGCGMCPYDTSYNDASDIWGGQTKVIVSA
31 ^b	H	129610	—	n/a	67.7	QVQLVQSGAEVKKPGSSVKSCKASGDTFSSYAIHWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKFHDRRLRYEDDPMKTVFLELRSLTSDDTGVVYCTRWRGCGMCPYDTSYNDASDIWGGQTKVIVSA
32 ^b	H	103511	—	n/a	66.4	QAQLHLVQSGAEVKKPGSSVRSCKASGDTFSSYAIHWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKFHDRRLRYEDDPMKTVFLELRSLTSDDTGVVYCTRWRGCGMCPYDTSYNDASDIWGGQTKVIVSA
33 ^b	H	1006836	4.7	33	70.0	RVQLVQSGPEVKKPGSSVKSCKAAGDTFSSYAIHWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKFHDRRLRYEDDPMKTVFLELRSLTSDDTGVVYCTRWRGCGMCPYDTSYNDASDIWGGQTKVIVSA
34 ^b	H	1730326	—	n/a	67.2	QVRLQSGAEVQKPGSSVKSCKASGDTFSSYAIHWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKFHDRRLRYEDDPMKTVFLELRSLTSDDTGVVYCTRWRGCGMCPYDTSYNDASDIWGGQTKVIVSA
35 ^b	H	1168805	—	n/a	69.0	QVQLVQSGAEVKKPGSSVKSCKASGDTFSSYAIHWVRQAPGGQLEWVGGRRVPPVGIYKYGKFKFHDRRLRYEDDPMKTVFLELRSLTSDDTGVVYCTRWRGCGMCPYDTSYNDASDIWGGQTKVIVSA

Listed items include sequence number, antibody chain type, sequence index in the PGM data set, protein yield, neutralization, sequence identity to 438-B11 heavy chain determined during the pipeline processing, and amino acid sequence. No expression (—) denotes protein yield less than 0.5 mg/L. Neutralizing activity was tested against viruses on Global Panel. n/a, not available.

^a Heavy chains are related to 438-D5/B11 but cover a wide range of sequence identity and HCDR3 motifs.

^b All sequences have a similar HCDR loop length of 20-23 aa

Table S2D. Expression of antibodies with selected 2008 light chain variants paired with the 438-D5 heavy chain.

No.	Chain type	Sequence index	Yield (mg/L culture sup)	Neutralization (%)	Sequence identity (%)	Amino acid sequence of variable domain
1 ^a	K	1181460	2.1	67	97.2	DIVLTQSPVTLSSSGEAGTLCRASQNISSSWIAWYQRRGQVPRLLISAASARAAGIPDRFTGRGSGTDFTLTISRLEPEDFGVYSCQYGGFFSFGPGTQVDVK
2 ^a	K	1611025	8.6	67	87.3	DIVLTQSPGTLSSSGETGTLSCRASQNISSSWIAWYHRRGQVPRLLIYAASSRAGGIPDRFSGSGSGTDFTLTISRLEHGFGLYCYQYGGFFFTFGPGTPVDVK
3 ^a	K	3391100	—	n/a	96.0	HIVLTQSPVTLSSSGKTGTLSCRASQNISSSWIAWYQRRGQSPRLLISAASARAAGIPDRFTGRGSGTDFTLTITRLEPEDFGVYSCQYGGFFFTFGPGTQVDVK
4 ^a	K	1540803	22.4	67	86.1	TIVLTQSPGTLSSSGETGTLSCRASQNISSSWIAWYHRRGQVPRLLIYATSSRAGGIPDRFSGSGSGTDFTLTISRLEHGFGLYCYQYGGFFFTFGPGTPVDVK
5 ^a	K	1093646	3.2	67	96.9	TIVLTQSPVTLSSSGETGTLSCRASQNISSSWIAWYQRRGQVPRLLISAASARAAGIPDRFTGRGSGTDFTLTISRLEPEDFGVYSCQYGGFFSFGPGTQVDVK

Listed items include sequence number, antibody chain type, sequence index in the PGM data set, protein yield, neutralization, sequence identity to 438-B11 light chain determined during the pipeline processing, and amino acid sequence. No expression (—) denotes protein yield less than 0.5 mg/L. Neutralizing activity was tested against viruses on Global Panel. n/a, not available.

^a Cover a wide range of sequence identity and KCDR3 motifs.

Table S2E. Expression of antibodies with selected 2012 heavy chain variants paired with the 438-D5 light chain.

No.	Chain type	Sequence index	Yield (mg/L culture sup)	Neutralization (%)	Sequence identity (%)	Amino acid sequence of variable domain
1 ^a	H	1273901	5.0	67	97.4	QVRLQSGAEVKKPGSSVTLSCKPVGDTFTNFALHWVRQAPQGQLEWVGRVVPVVGIIYKYGKKFQDRRLRYEDDPMKAVFLELRSLTSDDTGVYYCTRWRGCGMCPYDTSYNDASDVWGPVKTVIVSA
2 ^a	H	2070251	—	n/a	80.3	QVRLQSGAEVKKPGSSVRVSKPLGGFIHNHALHWVRQAPQGQLEWVGRVVPVVGIIYKYGKKFQDRRLTFEDDPMKIVYLELSGLTSDDTGVYYCTRWRGCLDCHADTTPYNDASEIWPVTMTIVSA
3 ^{b,c}	H	1128948	—	n/a	68.7	QVQLVQSGAEVKKPGSSLLKVSCKASGGTFNSYALSWVRQAPQGQLEWLGIIIPVFGTVNYAQKFKQGRVTITADEFTSTAYMELSSLTSEDVAVYYCARAYCTQSSCYPEWGYYYYYMDVWKGTTVTASS
4 ^{b,c}	H	1802268	2.4	8	69.2	QVQLVQSGAEVKKPGSFVKVSKASGGTFNSYALSWVRQAPQGQLEWLGIIIPVFGTVNYAQKFKQGRVTITADEFTSTAYMELSSLTSEDVAVYYCARAYCTQSSCYPEWGYYYYYMDVWKGTTVTASS
5 ^b	H	130290	32.2	0	69.0	QVLLVQSGAEVKKPGSSVKVSKASGGTFNFGNFAIHWVRQAPQGQLEWVGIIIPVYGSADYADKFKGRVTMTADDSTSTAYLEVSSLRSDDSAVYYCARGSQSTKVSMPAAVITYSYSDVWKGTTVTIVSS
6 ^b	H	1044069	1.3	0	69.5	QVQLVQSGAEVKKPGSSVKVSKASGGTLSNPFVLSWVRQAPQGQLEWLGFIPIGDI SNSAQNFQGRVTITADESNNTAYMDLSSLKFEDTAIYYCAIKTLTEAYYDDGLYYYYMDVWKGTTVTIVSS
7 ^b	H	1023928	19.5	8	69.5	QVQLVQSGAEVKKPGSSVKVSKASGGTFNNSMNVWRQAPQGQLEWVGRIIPVFGTVNYAQKFKQGRVTITADKSTRTRAYMELSTLKSSEDVAVYYCARDSSEYVNFWSGTYMTRRGAFLMGQGTMTIVSS
8 ^{b,c}	H	2390299	—	n/a	61.5	QVQLVQSGPEVNEPSSVKVSKASGGTFKFLLSWVRSGPQQIDWVGKIIPVFGTGHYAPKFKQGRVSI TADTSTNTVYMAMSVSGSEDVAVYYCATLGDCSRSSCLFPVVRDGYMDVWKGTTIVSS
9 ^{b,c}	H	3171013	—	n/a	64.4	QVQLVQSGPEVKKPGSSVKVSKASGGTFKISISWVRQAPQGQLEWVGKIIPLPFGTGHYAPKFKQGRVSI TADTSTNTVYMAMSVSGSEDVAVYYCATLGDCSRSSCLFPVVRAYMDVWKGTTIVSS

Listed items include sequence number, antibody chain type, sequence index in the PGM data set, protein yield, neutralization, sequence identity to 438-B11 heavy chain determined during the pipeline processing, and amino acid sequence. No expression (—) denotes protein yield less than 0.50 mg/L. Neutralizing activity was tested against viruses on Global Panel. n/a, not available.

^a Heavy chains are related to 438-D5/B11 but cover a wide range of sequence identity and HCDR3 motifs.

^b All sequences have a similar HCDR3 loop length of 20-23 aa.

^c The HCDR3 loop has the same characteristic disulfide bond as 438-B11.

Table S2F. Expression of antibodies with selected 2012 light chain variants paired with the 438-D5 heavy chain.

No.	Chain type	Sequence index	Yield (mg/L culture sup)	Neutralization (%)	Sequence identity (%)	Amino acid sequence of variable domain
1 ^a	K	1720240	0.6	17	82.7	EIVLTQSPGTLSSLSPGERATLSCRASQTVNNDYLAWYQQKPGQAPRLLIYGASSRPTGIPDRFSGSGSGTDFTLTISRLPEPEFVAVYCCQVASSLPFTFGQGTTRLVIK
2 ^a	K	3926609	—	n/a	86.7	EIVLTQSPGTLSSLSPGERATLSCRASQSVSASYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGSASGTDFTLTISRLPEPEFVAVYHCQQYGGSPLPFTFGQGTKVDIK

Listed items include sequence number, antibody chain type, sequence index in the PGM data set, protein yield, neutralization, sequence identity to 438-B11 light chain determined during the pipeline processing, and amino acid sequence. No expression (—) denotes protein yield less than 0.5 mg/L. Neutralizing activity was tested against viruses on Global Panel. n/a, not available.

^a Germline-like kappa chains.

Table S3A. Neutralizing and binding activity of selected NGS-derived 438-B11/D5 somatic heavy variants paired with 438-D5 light chain.

Tier-1 virus and global panel			2005					2008						2012			control			
Clade	Tier	Pseudovirus	05HC-01	05HC-02	05HC-03	05HC-04	05HC-05	08HC-01	08HC-04	08HC-08	08HC-18	08HC-19	08HC-24	08HC-33	12HC-01	12HC-04	12HC-07	438-B11	438-D5	VRC01
B	1A	SF162	>50	>50	4.05	>50	9.52	0.01	0.01	0.04	0.01	1.74	>50	5.61	0.04	16.12	35.23	0.02	0.02	0.48
C	1A	MW965	50.0 0	>50	>50	>50	37.04	0.11	1.14	21.50	0.25	>50	>50	>50	11.69	>50	>50	1.19	1.75	0.07
A	2	398-F1 ^a	23.8 1	41.67	20.83	37.04	--	0.02	0.03	0.13	0.01	25.78	41.08	11.57	0.18	19.05	47.38	0.02	0.03	0.41
B	2	TRO.11 ^a	>50	>50	27.78	--	--	0.09	0.08	0.92	0.03	>50	>50	>50	0.93	>50	>50	0.07	0.14	0.77
	2	X2278 ^a	45.4 5	--	33.33	--	--	0.03	0.03	0.08	0.04	14.22	>50	18.13	1.33	>50	>50	0.09	0.08	0.35
C	2	25710 ^a	>50	>50	>50	>50	>50	0.23	0.53	10.16	0.18	>50	>50	>50	6.06	>50	>50	0.64	0.55	0.87
	2	Ce0217 ^a	>50	>50	>50	>50	20.41	0.39	0.34	3.99	0.17	>50	>50	>50	24.39	>50	>50	4.53	1.67	0.42
	2	Ce1176 ^a	>50	>50	>50	>50	>50	0.13	0.18	0.48	0.08	>50	>50	20.15	0.92	>50	>50	0.34	0.33	4.88
G	2	X1632 ^a	>50	--	>50	--	--	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	0.31
CRF01_AE	2	CNE55 ^a	>50	--	>50	--	--	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	0.64
	2	CNE8 ^a	>50	--	>50	--	--	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	0.56
CRF07_BC	2	BJOX2000 ^a	41.6 7	>50	47.62	>50	--	0.03	0.04	0.13	0.02	2.53	>50	>50	0.21	>50	>50	0.06	0.07	>50
	2	CH119 ^a	37.0 4	>50	23.81	>50	--	0.10	0.21	0.57	0.05	17.93	>50	20.92	0.62	>50	>50	0.14	0.22	1.56
AC	2	246 ^a	--	--	>50	--	--	>50	>50	20.66	>50	>50	>50	>50	>50	>50	>50	>50	>50	0.51
Binding to BG505 probe ^b			+	+/-	++++	+	+++	++++	++++	++++	++++	++++	+++	++++	++++	++	++	++++	++++	++++
Potency on global panel			35.9 5	41.67	29.37	37.04	20.41	0.08	0.11	0.87	0.05	11.36	41.08	17.24	1.19	19.05	47.38	0.18	0.19	0.69
Breadth% on global panel			36	14	42	17	33	67	67	75	67	33	8	33	67	8	8	67	67	92

The neutralizing potency of the mAbs was measured as IC₅₀ in µg/ml. Values < 0.2 µg/ml are highlighted in red, 0.2~2 µg/ml in yellow, 2~50 µg/ml in green.

The neutralizing breadth was calculated as the percentage of viruses neutralized with IC₅₀ < 50 µg/ml.

"--": not tested.

^aGlobal panel of 12 HIV-1 Env strains.

^bBinding capacity was tested to the sorting probe BG505 by ELISA and categorized based on the OD₄₅₀ value at the 10 µg/ml of antibody tested.

"++++": OD₄₅₀ ≥ 3.0; "+++": 2.0 ≤ OD₄₅₀ < 3.0; "++": 1.0 ≤ OD₄₅₀ < 2.0; "+": 0.2 ≤ OD₄₅₀ < 1.0; "+/-": 0.1 ≤ OD₄₅₀ < 0.2; "-": OD₄₅₀ < 0.1.

Table S3B. Neutralizing and binding activity of selected NGS-derived 438-B11/D5 somatic light variants paired with 438-D5 heavy chain.

Tier-1 virus and global panel			2005			2008				2012	control		
Clade	Tier	Pseudovirus	05KC-01	05KC-03	05KC-04	08KC-01	08KC-02	08KC-04	08KC-05	12KC-01	438-B11	438-D5	VRC01
B	1A	SF162	0.02	0.02	0.02	0.01	0.01	0.03	0.02	7.40	0.02	0.02	0.48
C	1A	MW965	0.40	0.24	0.08	2.04	6.19	8.07	1.80	>50	1.19	1.75	0.07
A	2	398-F1 ^a	0.03	0.02	0.03	0.01	0.03	0.04	0.02	41.67	0.02	0.03	0.41
B	2	TRO.11 ^a	0.20	0.22	0.22	0.08	0.15	0.19	0.11	>50	0.07	0.14	0.77
	2	X2278 ^a	0.15	0.09	0.06	0.07	0.17	0.18	0.04	>50	0.09	0.08	0.35
C	2	25710 ^a	1.26	0.90	1.23	0.36	2.38	4.13	0.73	>50	0.64	0.55	0.87
	2	Ce0217 ^a	9.96	8.43	6.14	3.65	4.43	12.53	1.88	>50	4.53	1.67	0.42
	2	Ce1176 ^a	0.20	0.21	0.27	0.13	0.19	0.24	0.11	>50	0.34	0.33	4.88
G	2	X1632 ^a	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	0.31
CRF01_AE	2	CNE55 ^a	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	0.64
	2	CNE8 ^a	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	0.56
CRF07_BC	2	BJOX2000 ^a	0.06	0.06	0.06	0.02	0.04	0.03	0.02	45.00	0.06	0.07	>50
	2	CH119 ^a	0.23	0.20	0.23	0.10	0.19	0.22	0.13	>50	0.14	0.22	1.56
AC	2	246 ^a	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	0.51
Binding to BG505 probe^b			++++	++++	++++	++++	++++	++++	++++	++++	++++	++++	++++
Potency on global panel			0.27	0.23	0.24	0.11	0.24	0.32	0.12	43.30	0.18	0.19	0.69
Breadth% on global panel			67	67	67	67	67	67	67	17	67	67	92

The neutralizing potency of the mAbs was measured as IC₅₀ in µg/ml. Values < 0.2 µg/ml are highlighted in red, 0.2~2 µg/ml in yellow, 2~50 µg/ml in green.

The neutralizing breadth was calculated as the percentage of viruses neutralized with IC₅₀ < 50 µg/ml.

"-": not tested.

^aGlobal panel of 12 HIV-1 Env strains.

^b Binding capacity was tested to the sorting probe (HR1-redesigned BG505 trimer) by ELISA and categorized based on OD₄₅₀ value at 10 µg/ml of antibody tested.

"++++": OD₄₅₀ ≥ 3.0; "+++": 2.0 ≤ OD₄₅₀ < 3.0; "++": 1.0 ≤ OD₄₅₀ < 2.0; "+": 0.2 ≤ OD₄₅₀ < 1.0; "+/-": 0.1 ≤ OD₄₅₀ < 0.2; "-": OD₄₅₀ < 0.1.

Table S3C. Anti-viral human antibodies with intra-HCDR3 disulfide bond(s).^a

Antibody	HCDR3	Germline	PDB ID	Virus Target (epitope)
438-B11 (this study)	WRGCGMCPYDTSSYYNDASDV	IGHV1-69	6UUH *	HIV-1 Env (Glycan supersite)
438-D5 (this study)	WRGCGMCPYDTSSYYNDASDV	IGHV1-69	6UUL *	HIV-1 Env (Glycan supersite)
VRC03	VRRGSCDYCGDFPWQY	IGHV1-02	5JXA *	HIV-1 Env (RBS)
VRC03GL	ARRGSCDYCGDFPWQY	IGHV1-02	5JOF *	HIV-1 Env (RBS)
VRC06B	VRKGPSCPFCGDFHWQH	IGHV1-02	4XNZ *	HIV-1 Env (RBS)
45-VRC01.H03+06.D-001739	VRKGPSCPFCGDFHWQH	IGHV1-02	4S1Q *	HIV-1 Env (RBS)
VRC06	VRRGSSCPFCGDFHFEH	IGHV1-02	4JB9 *	HIV-1 Env (RBS)
45-VRC01.H5.F-185917	VRTADCDERDPCKGWVFPH	IGHV1-02	4S1S *	HIV-1 Env (RBS)
VRC08	VRGRSCCGRRHCNGADCFNWFQH	IGHV1-02	4XMP **	HIV-1 Env (RBS)
VRC08c	VRGKSCCNGRRYCNGADCFNWFQY	IGHV1-02	4XNY **	HIV-1 Env (RBS)
45.VRC01.H08.F-117225	VRGKSCCNGRRYCNGADCFNWFQY	IGHV1-02	4S1R **	HIV-1 Env (RBS)
CAP256-VRC26.03	AKDLREDECEEWSDYYDFGKQLPCRKSRGVAGIFDG	IGHV3-30	4OD1 *	HIV-1 Env (V1-V2)
CAP256-VRC26.04	AKDLREDECEEWSDYYDFGKQLPCRKSRGVAGIFDK	IGHV3-30	4ORG *	HIV-1 Env (V1-V2)
CAP256-VRC26.07	AKDLREDECEEWSDYYDFGKQLPCRKSRGVAGVFDK	IGHV3-30	4OD3 *	HIV-1 Env (V1-V2)
CAP256-VRC26.10	AKDMREYECEYWTSDYYDFGRPQPCIDRRGVVGI FDM	IGHV3-30	4OCS *	HIV-1 Env (V1-V2)
CAP256-VRC26.25	AKDLREDECEEWSDYYDFGKQLPCA KSRGGLVGIADN	IGHV3-30	5DT1 *	HIV-1 Env (V1-V2)
CAP256-VRC26.06	ARDLRELECEEWTL YNYYDFGSRGPCVDPRGVAGSFVDV	IGHV3-30	4OCW *	HIV-1 Env (V1-V2)
F045-092	AGPSITESHYCLDCAAKDY YGLDV	IGHV1-69	4O58 *	Influenza HA (RBS)
FluA-20	ARGTEDLG YCSGSCP NH	IGHV4-61	6OBZ *	Influenza HA (trimer interface)
F10	ARSPSY ICSGGTCVFDH	IGHV1-69	3FKU *	Influenza HA (stem region)
FLD194	HASCSARSCYWG PVDY	IGHV5-51	5A3I *	Influenza HA (RBS)
HEPC3	ARDGVRYCGGGR CYNWFDP	IGHV1-69	6MED *	Hepatitis-C E2
HEPC74	ARDLLKYCGGGN CHSLLVDP	IGHV1-69	6MEE *	Hepatitis-C E2
AR3A	VRPETPRYCSGGFCYGEFDN	IGHV1-69	6BKB *	Hepatitis-C E2
AR3C	VRSVTPRYCSGGFCYGEFDY	IGHV1-69	4MWF *	Hepatitis-C E2
ADI-19425	ARLG YCSGGSCHFDY	IGHV3-21	6APC *	RSV F
CB0002.5	ARSGFCSDDAC YRRGSWFDP	IGHV4-4/59	6BLI *	RSV G
CR9501	AACGAYVLI SNCGWFDS	IGHV4-31	6OE4 *	RSV F
8f9	ARDGKCGGGR CYSGLLDY	IGHV3-30	3EYF *	humCMV Env (AD2S1)
m336	ARVGYCSSTSCNRGAFDI	IGHV1-69	4XAK *	MERS-CoV (RBS)
CDC2-C2	AREGGHQGYCSGGSCYDFDY	IGHV1-69	6C6Z *	MERS-CoV (RBS)
R13	ASLPYCSGRICRPRTDY	IGHV4-31	6IEA *	RVFV Env Gn
CR1-10	ARLTSDCSGGNCYQAFDY	IGHV4-31	5W1K *	JUNV Env GP1 (RBS)

^a Human antibodies targeting non-viral antigens (e.g. PDB IDs: 4PTU, 4VID, 4N2U, 2HFG, 2IG2, 5IFJ, and 5BV7) are not listed in this table.

RBS = Receptor-binding site

RSV = Respiratory Syncytial Virus

HA = Hemagglutinin

humCMV = human cytomegalovirus

MERS-CoV = Middle East respiratory syndrome coronavirus

RVFV = Rift Valley fever virus

JUNV = Junin virus (causing human hemorrhagic fever)

* One intra-HCDR3 disulfide bond; ** Two intra-HCDR3 disulfide bonds

Table S3D. X-ray crystallographic data collection and refinement statistics

Data collection	BG505 UFO.664, Fabs 438-B11, 35O22	Fab 438-B11 & PG	Fab 438-B11ΔSS	Fab 438-D5
X-ray Source	APS 23ID-D	SSRL 12-2	APS 23ID-D	APS 23ID-D
Wavelength (Å)	1.033	0.979	1.033	1.033
Detector	Pilatus	Pilatus	Pilatus	Pilatus
Space group	H32	P2 ₁	P2 ₁	P2 ₁ 2 ₁ 2 ₁
Unit cell parameters	a = b = 247.3, c = 257.6 Å	a = 71.1, b = 72.7, c = 108.7 Å β = 101.1°	a = 104.1, b = 66.1, c = 108.8 Å β = 117.9°	a = 92.7, b = 97.8, c = 125.5 Å
Resolution (Å)	50.00 - 3.80 (3.87 - 3.80) ^a	50.00 - 2.70 (2.75 - 2.70) ^a	50.00 - 2.10 (2.14 - 2.10)	50.00 - 2.07 (2.14 - 2.07)
Observations	293,758	86,956	449,748	833,571
Unique reflections	29,804 (1,403) ^a	29,107 (1,479) ^a	76,942 (3,836) ^a	71,245 (6,892) ^a
Redundancy	9.9 (6.4) ^a	3.0 (3.0) ^a	5.8 (5.9) ^a	11.7 (9.7) ^a
Completeness (%)	99.6 (95.2) ^a	96.6 (97.8) ^a	99.9 (99.6) ^a	99.8 (98.2) ^a
$\langle I/\sigma \rangle^b$	13.0 (1.0) ^a	12.9 (1.4) ^a	9.1 (1.2) ^a	22.8 (1.0) ^a
R_{sym}^c	0.17 (1.19) ^a	0.10 (0.96) ^a	0.17 (1.28) ^a	0.19 (>1.0) ^a
R_{pim}^c	0.05 (0.42) ^a	0.05 (0.53) ^a	0.07 (0.52) ^a	0.05 (0.79) ^a
CC _{1/2}	0.89 (0.47) ^a	0.89 (0.54) ^a	0.84 (0.46) ^a	0.88 (0.56) ^a
Refinement statistics				
Resolution (Å)	49.44 - 3.80	48.23 - 2.70	48.08 - 2.10	46.37 - 2.07
Reflections (work)	29,787	29,094	76,912	71,132
$R_{\text{cryst}}(\%)^d / R_{\text{free}}(\%)^e$	29.9 / 31.7	22.7 / 26.0	22.9 / 26.8	20.0 / 24.5
No. atoms				
Protein	11,441	7,644	6,724	6,653
Glycan	978	110	28	52
Water	-	-	534	407
Average <i>B</i> -value (Å ²)				
Protein	163	57	37	55
Glycan	163	56	36	54
Water	-	97	94	132
Wilson <i>B</i> -value (Å ²)	132	-	40	54
		57	28	41
RMSD from ideal geometry				
Bond length (Å)	0.004	0.003	0.003	0.003
Bond angles (°)	0.77	0.67	0.58	0.59
Ramachandran statistics (%) ^f				
Favored	90.31	97.16	97.13	97.33
Allowed	8.87	2.84	2.87	2.67
Outliers	0.82	0	0	0
PDB ID	6UTK	6UUH	6UUM	6UUL

^a Numbers in parentheses refer to the highest resolution shell.^b Calculated as average(*I*)/average(σI)

^c $R_{\text{sym}} = \sum_{hkl} \sum_i |I_{hkl,i} - \langle I_{hkl} \rangle| / \sum_{hkl} \sum_i I_{hkl,i}$, where $I_{hkl,i}$ is the scaled intensity of the i^{th} measurement of reflection h, k, l , $\langle I_{hkl} \rangle$ is the average intensity for that reflection, and n is the redundancy. R_{pim} is a redundancy-independent measure of the quality of intensity measurements. $R_{\text{pim}} = \sum_{hkl} (1/(n-1))^{1/2} \sum_i |I_{hkl,i} - \langle I_{hkl} \rangle| / \sum_{hkl} \sum_i I_{hkl,i}$, where $I_{hkl,i}$ is the scaled intensity of the i^{th} measurement of reflection h, k, l , $\langle I_{hkl} \rangle$ is the average intensity for that reflection, and n is the redundancy.

^d $R_{\text{cryst}} = \sum_{hkl} |F_o - F_c| / \sum_{hkl} |F_o| \times 100$

^e R_{free} was calculated as for R_{cryst} , but on a test set comprising 5% of the data excluded from refinement.

^fThese values were calculated using MolProbity (<http://molprobity.biochem.duke.edu/>).

Table S3E. X-ray crystallographic data collection and refinement statistics

Data collection	BG505 UFO.664, Fabs 438-B11ΔSS, 35O22
X-ray Source	SSRL 12-2
Wavelength (Å)	0.979
Detector	Pilatus
Space group	H3
Unit cell parameters	a = b= 148.5, c = 843.5 Å
Resolution (Å)	50.00 – 6.51 (6.62 – 6.51) ^a
Observations	55,947
Unique reflections	13,313 (638) ^a
Redundancy	4.2 (3.2) ^a
Completeness (%)	97.5 (95.5) ^a
$\langle I/\sigma \rangle$ ^b	7.3 (1.0) ^a
R_{sym} ^c	0.19 (1.19) ^a
R_{pim} ^c	0.09 (0.64) ^a
CC _{1/2}	0.85 (0.62) ^a
Refinement statistics	
Resolution (Å)	46.71 – 6.51
Reflections (work)	13,258
R_{cryst} (%) ^d / R_{free} (%) ^e	30.7 / 35.5
No. atoms	
Protein	22820
Glycan	642
Water	-
Average <i>B</i> -value (Å ²)	282
Protein	283
Glycan	252
Water	-
Wilson <i>B</i> -value (Å ²)	234
RMSD from ideal geometry	
Bond length (Å)	0.003
Bond angles (°)	0.64
Ramachandran statistics (%) ^f	
Favored	90.44
Allowed	8.74
Outliers	0.82
PDB ID	6V6W

^a Numbers in parentheses refer to the highest resolution shell.

^b Calculated as average(*I*)/average(σI)

^c $R_{\text{sym}} = \sum_{hkl} \sum_i | I_{hkl,i} - \langle I_{hkl} \rangle | / \sum_{hkl} \sum_i I_{hkl,i}$, where $I_{hkl,i}$ is the scaled intensity of the i^{th} measurement of reflection h, k, l , $\langle I_{hkl} \rangle$ is the average intensity for that reflection, and n is the redundancy. R_{pim} is a redundancy-independent measure of the quality of intensity measurements. $R_{\text{pim}} = \sum_{hkl} (1/(n-1))^{1/2} \sum_i | I_{hkl,i} - \langle I_{hkl} \rangle | / \sum_{hkl} \sum_i I_{hkl,i}$, where $I_{hkl,i}$ is the scaled intensity of the i^{th} measurement of reflection h, k, l , $\langle I_{hkl} \rangle$ is the average intensity for that reflection, and n is the redundancy.

^d $R_{\text{cryst}} = \sum_{hkl} | F_o - F_c | / \sum_{hkl} | F_o | \times 100$

^e R_{free} was calculated as for R_{cryst} , but on a test set comprising 5% of the data excluded from refinement.

^fThese values were calculated using MolProbity (<http://molprobity.biochem.duke.edu/>).

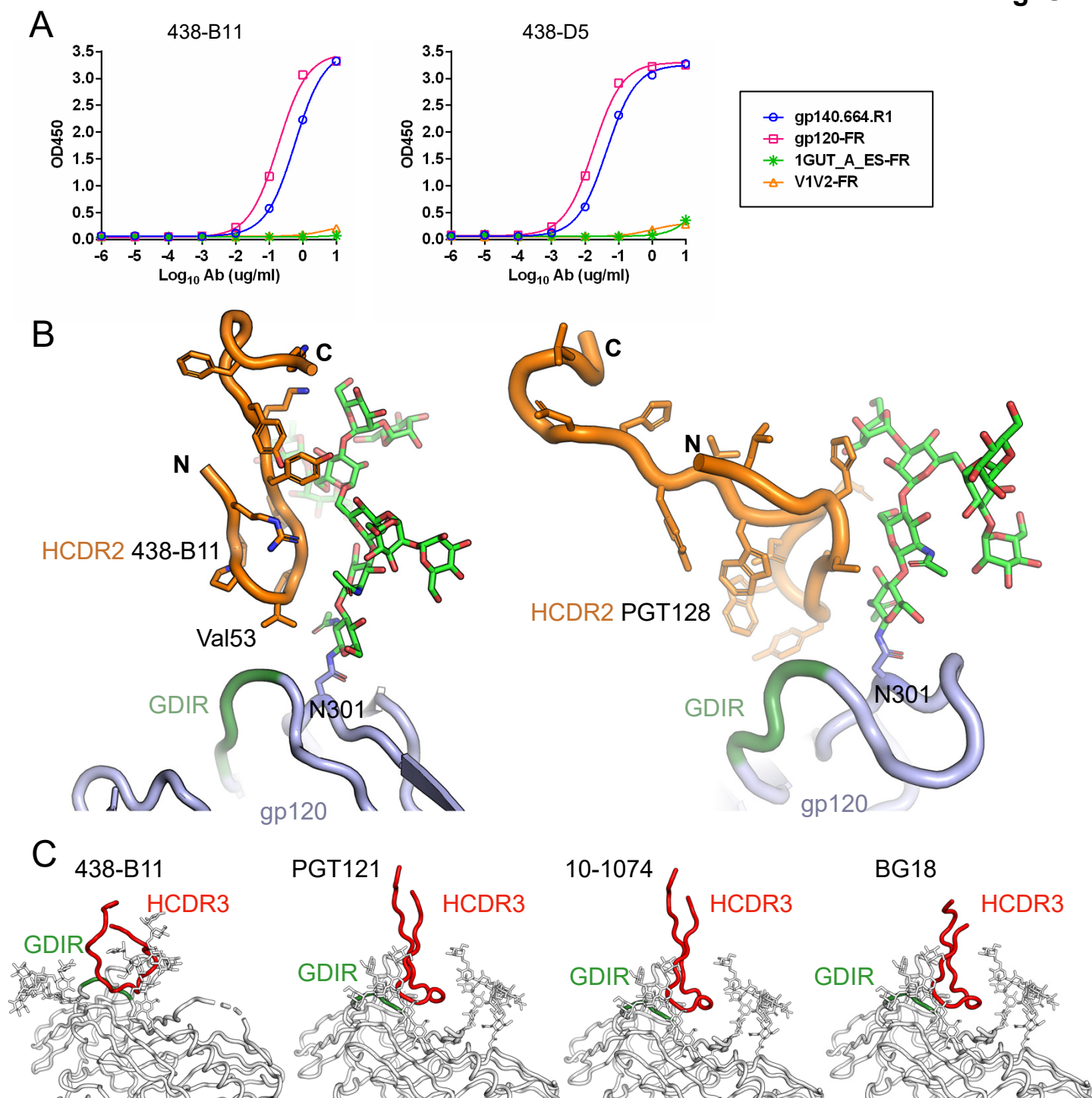


fig. S1. Binding of monoclonal antibodies (mAbs) to the HIV-1 Env. (A) 438-B11 and 438-D5 binding to the untagged HR1-redesigned trimer, BG505 gp140.664.R1, and four epitope antigens including a gp120-ferritin nanoparticle (gp120-FR), an N332 epitope-presenting ferritin nanoparticle (1GUT_A_ES-FR), and a ZM109 V1V2 ferritin nanoparticle (V1V2-FR). (B) Interaction of the apolar face of N-linked glycans at Asn301 of gp120 (blue) with HCDR2 (orange) of 438-B11 in complex with BG505 UFO.664 (left) and PGT128 with a modified gp120 (right, PDB ID: 3TYG). (C) HCDR3 (red) of different bNAbs buried in the N332 glycan pocket.

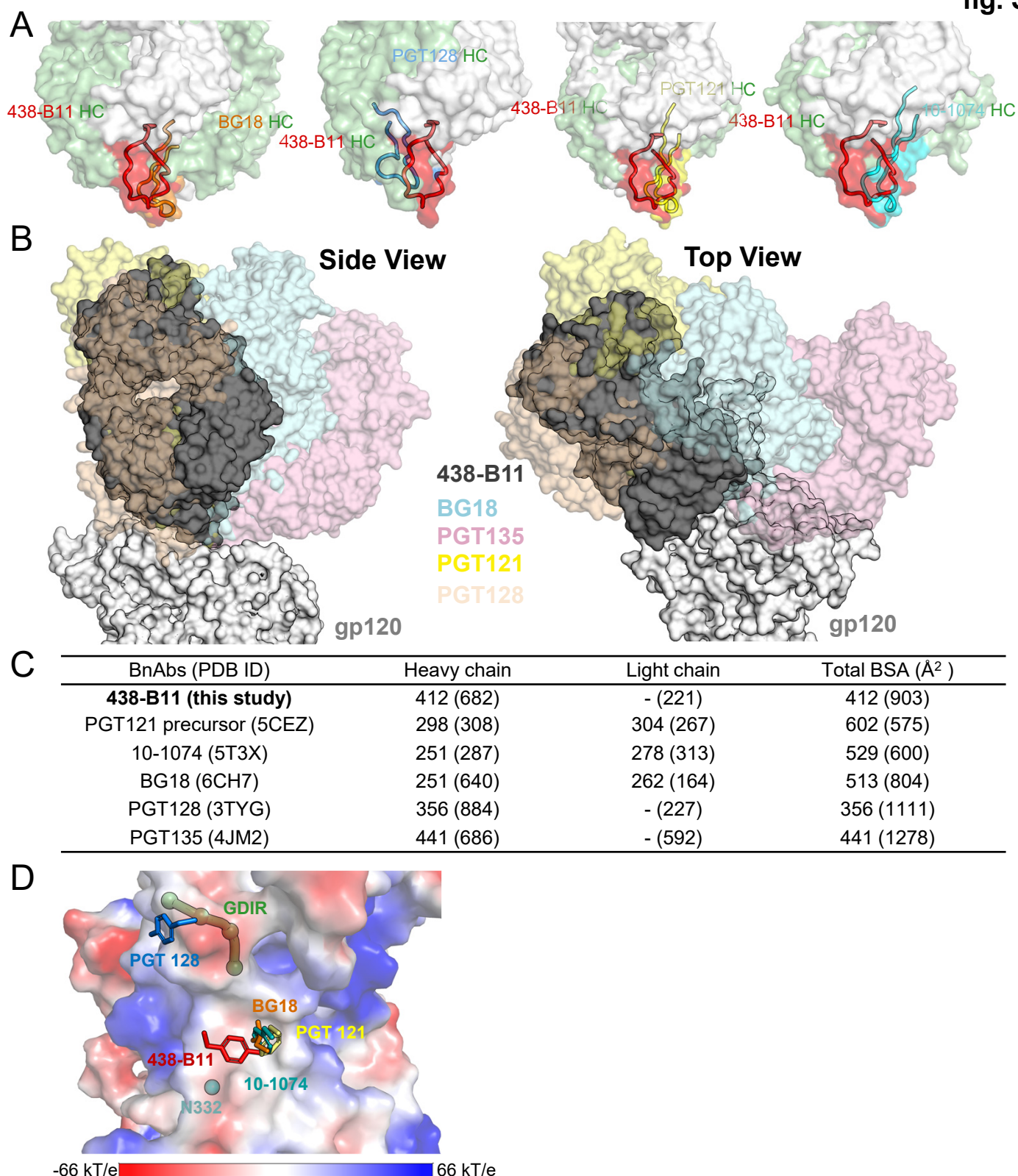
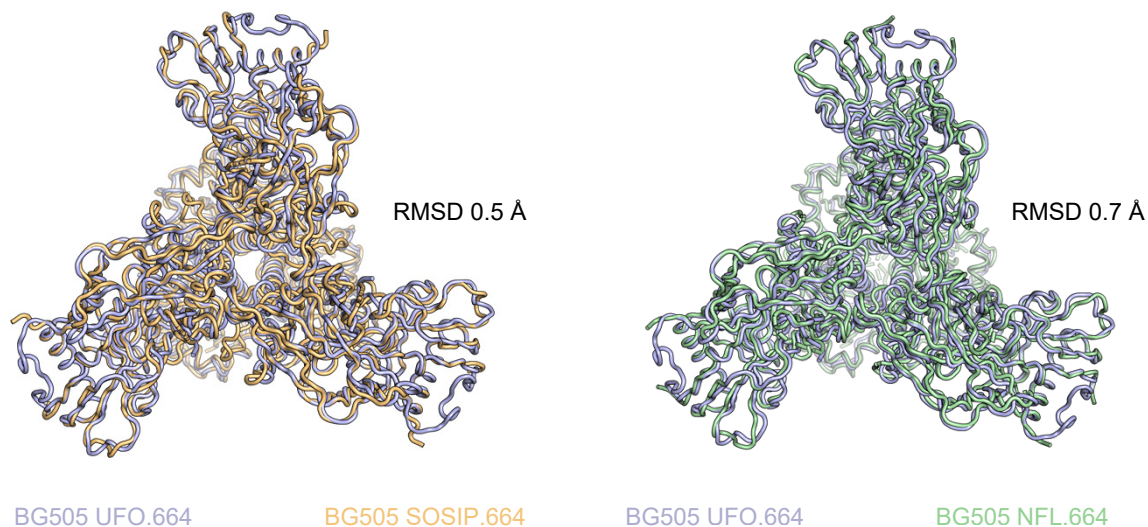


fig. S2. Analysis of bNAbs HCDR3 orientation, angle of approach, and interaction hotspots on gp120. (A) Superposition of the gp120 of Env-bound bNAbs (HC: green; and LC: grey) showing the relative HCDR3 orientation of 438-B11 (red), BG18 (orange), PGT128 (blue), PGT121 (yellow) and 10-1074 (cyan). **(B)** Side and top views of N332/V3 glycan-class bNAbs angle of approach to the gp120. **(C)** Buried surface area (BSA) in \AA^2 contributed by bNAb heavy and light chain CDRs on the protein and glycan (shown in parentheses) components of the gp120 surface. **(D)** Residue at the tip of HCDR3 (PGT128: marine; 438-B11: red; PGT121 precursor: yellow; BG18: orange; and 10-174: cyan) are shown in sticks and interact with gp120 on the Env. The electrostatic surface of gp120 is shown with the bar below indicating negatively to positively charged molecular surfaces.

A



B

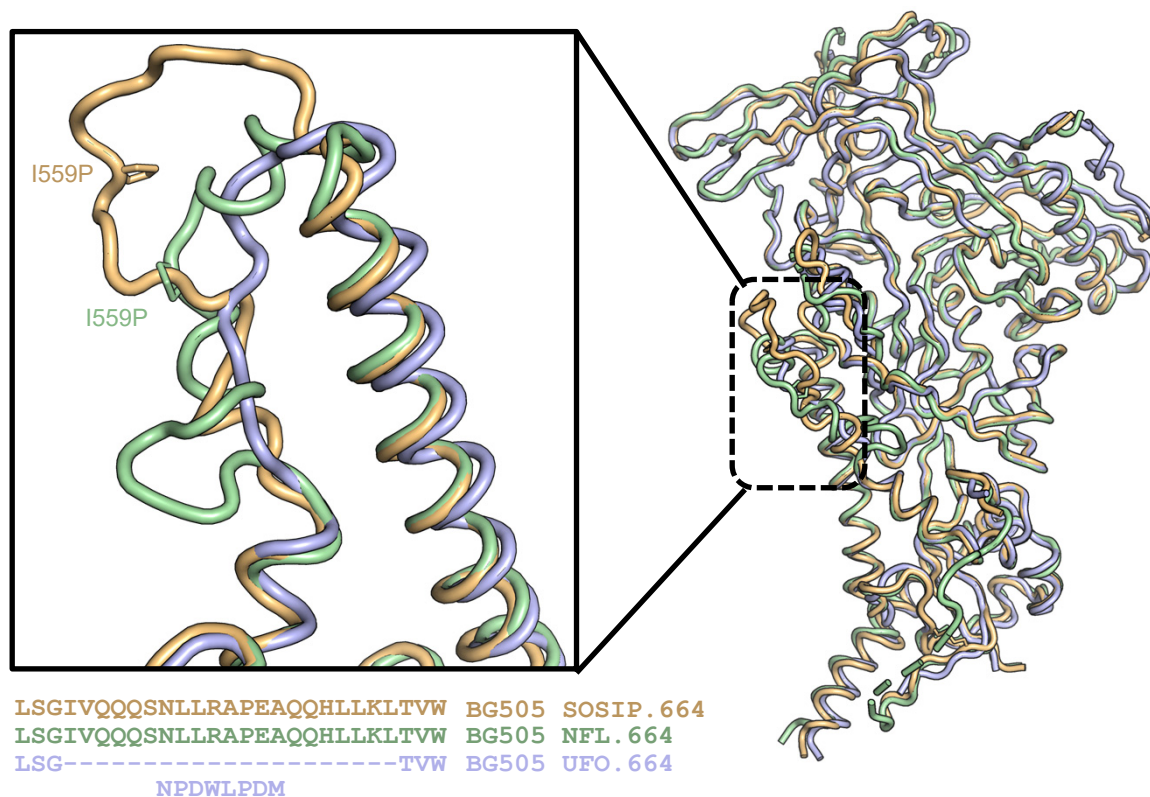


fig. S3. BG505 trimers of SOSIP, NFL, and UFO designs share a highly similar architecture. (A) Superimposition of cleaved BG505 SOSIP.664 (orange), uncleaved BG505 NFL.664 (green) and UFO.664 (blue). **(B)** Superimposition of SOSIP (orange), NFL (green) and UFO (blue) BG505 protomers. The inset on the left shows a close-up view of the superimposed heptad repeat 1 (HR1) N-terminal region (HR1_N) from the three trimer designs. The I559P mutation is labeled for SOSIP and NFL. Sequence alignment of HR1_N in three trimer designs is shown below the insert.

A

B11 HC reversion (IGHV1-69*01+IGHJ3*01)

438-B11 HC QVQLVQSGAEVRKPGSSVTISCKPVGFTFTNFIAHWVRQAPGQGLEWVGGRRVPVVGIIYKYGKKFH
 438-B11 g1HC QVQLVQSGAEVKKPGSSVKVSKASGGTFSSYAISWVRQAPGQGLEWMMGGIIPIFGTANYAQQKFQ
 *****:*****.:***. ****:.:*** *****:*** :*: * :*.:**:

HCDR3

438-B11 HC DRLRLYEDDPMKTVFLELRSLTSDDTGVYYCTRWRGCGMCPYDTSSYYNDASDVWGPGTKVIVSA
 438-B11 g1HC GRVTITADESTSTAYMELSSLRSEDVAVYYCTRWRGCGMCPYDTSSYYNDASDVWQQTMTVTVSS
 .*: : *:. .*:.:** ** *:.:*****:*****:***** ** * **:

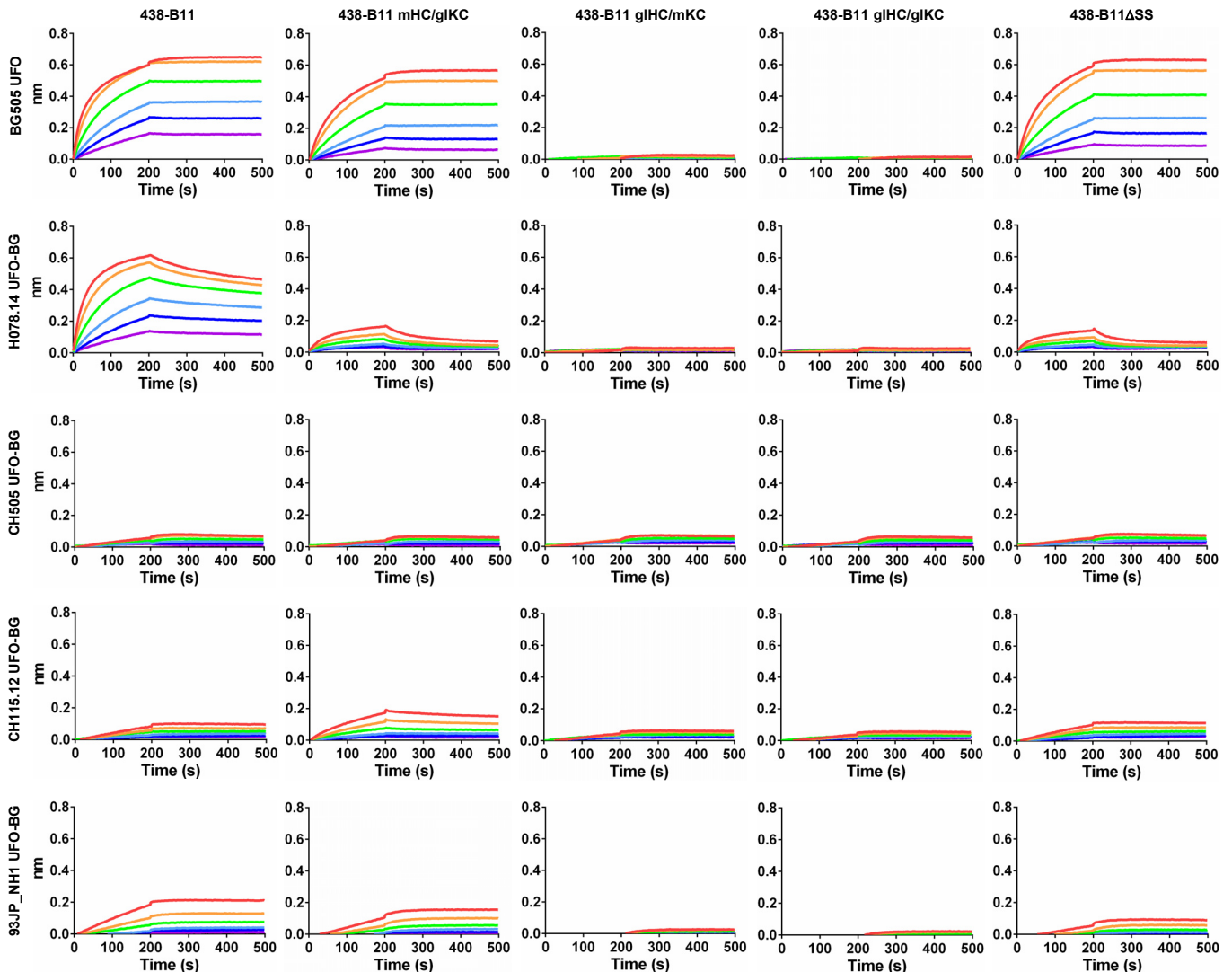
B11 KC reversion (IGKV3-20*01+IGKJ3*01)

438-B11 KC EIVLTQSPVTLTSLSSGETGTLSCRASQNISSSWIAWYQRRGQVPRLLISAASARAAGIPDRFTG
 438-B11 g1KC EIVLTQSPGTLTSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSG
 ***** *****.*.*****.:****.:*****: ** .***** .*:.:*****:*

KCDR3

438-B11 KC RSGGTDFTLTITRLEPEDFGVYSCQYVGGSSFFTFGPGTQVDVK
 438-B11 g1KC SSGGTDFTLTISRLEPEDFAVYYCQYVGGSSFFTFGPGTKVDIK
 *****:*****.* *****:*****:***:*

B



C

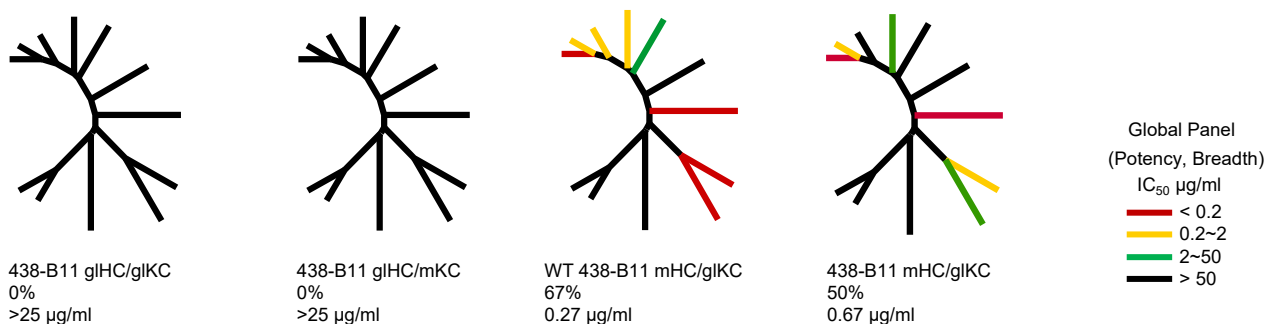


fig. S4. Characterization of 438-B11 germline revertants and 438-B11 Δ SS mutant. (A) Sequence alignment 438-B11 HC and KC revertants with their respective wildtype sequences. Putative germline genes and CDR3 regions (Kabat number) are labeled. **(B)** Binding of 438-B11 revertants and 438-B11 Δ SS mutant to UFO/UFO-BG trimers derived from five representative HIV-1 Envs, including clade-A BG505, clade-B H078.14, clade-C CH505, clade-BC CH115.12, and clade-AE 93JP_NH1. BLI sensorgrams were obtained from an Octet RED96 instrument using a titration series of six trimer concentrations (200-6.25 nM by 2-fold dilution). **(C)** Neutralization breadth (%) and potency ($\mu\text{g/ml}$) of germline revertants and mature 438-B11 against the global panel. The color-coding scheme is based on potency.

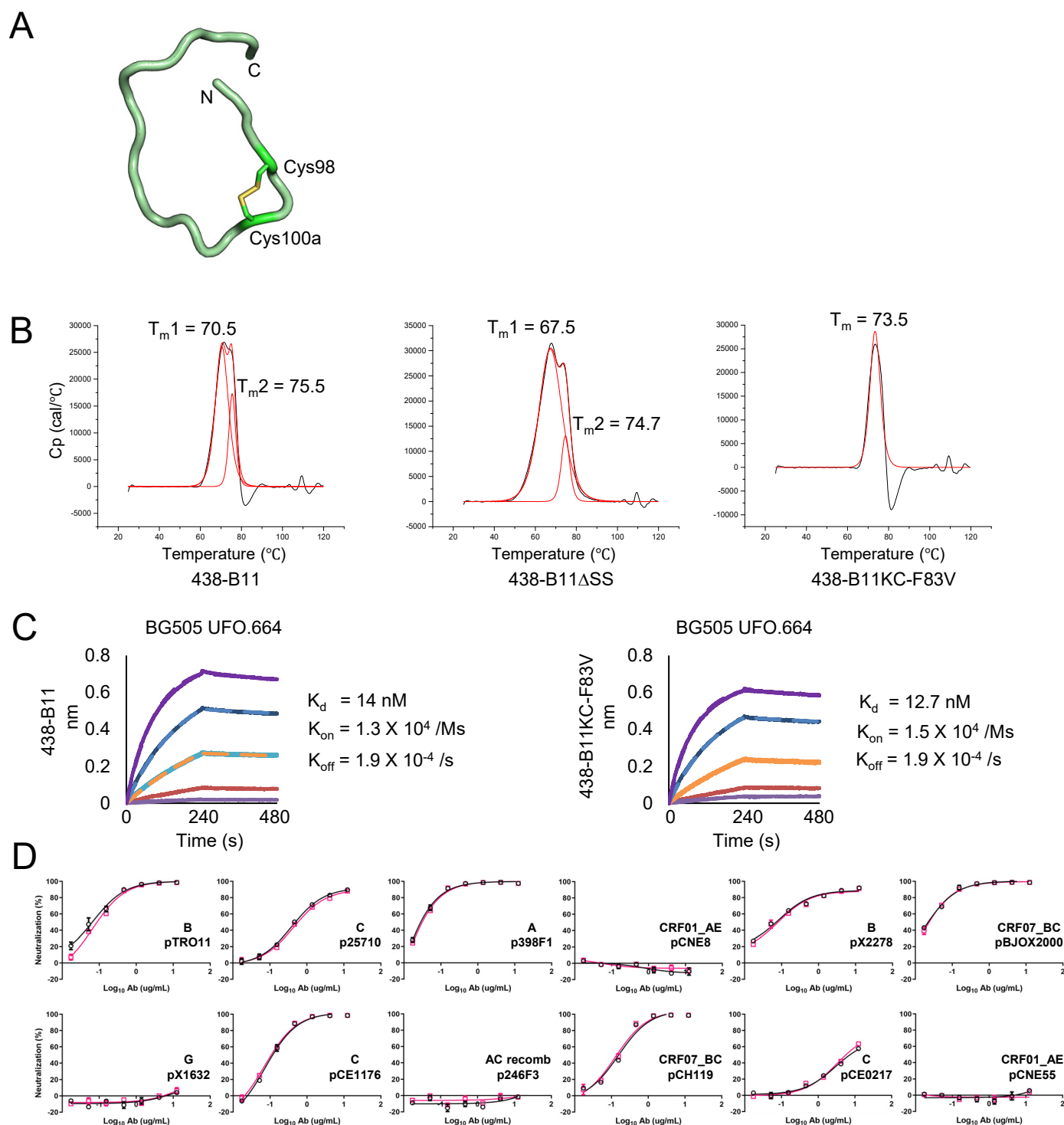


fig. S5. Structure, binding and neutralization of 438-B11, 438-B11 Δ SS, and 438-B11KC-F83V. (A) Structure of the U-shaped 438-B11 HCDR3 loop with the intra-HCDR3 disulfide bond (Cys98-Cys100a). (B) Differential scanning calorimetry (DSC) analysis of 438-B11, 438-B11 Δ SS, and 438-B11KC-F83V. Melting temperatures (T_M) are labeled after the fitting. (C) Binding of 438-B11 and 438-B11KC-F83V for BG505 UFO.664 trimer. BLI sensorgrams were obtained from an Octet RED96 instrument using a titration series of five trimer concentrations (800-50 nM by 2-fold dilution). (D) Neutralization of global panel by 438-B11 (black) and 438-B11KC-F83V (pink).

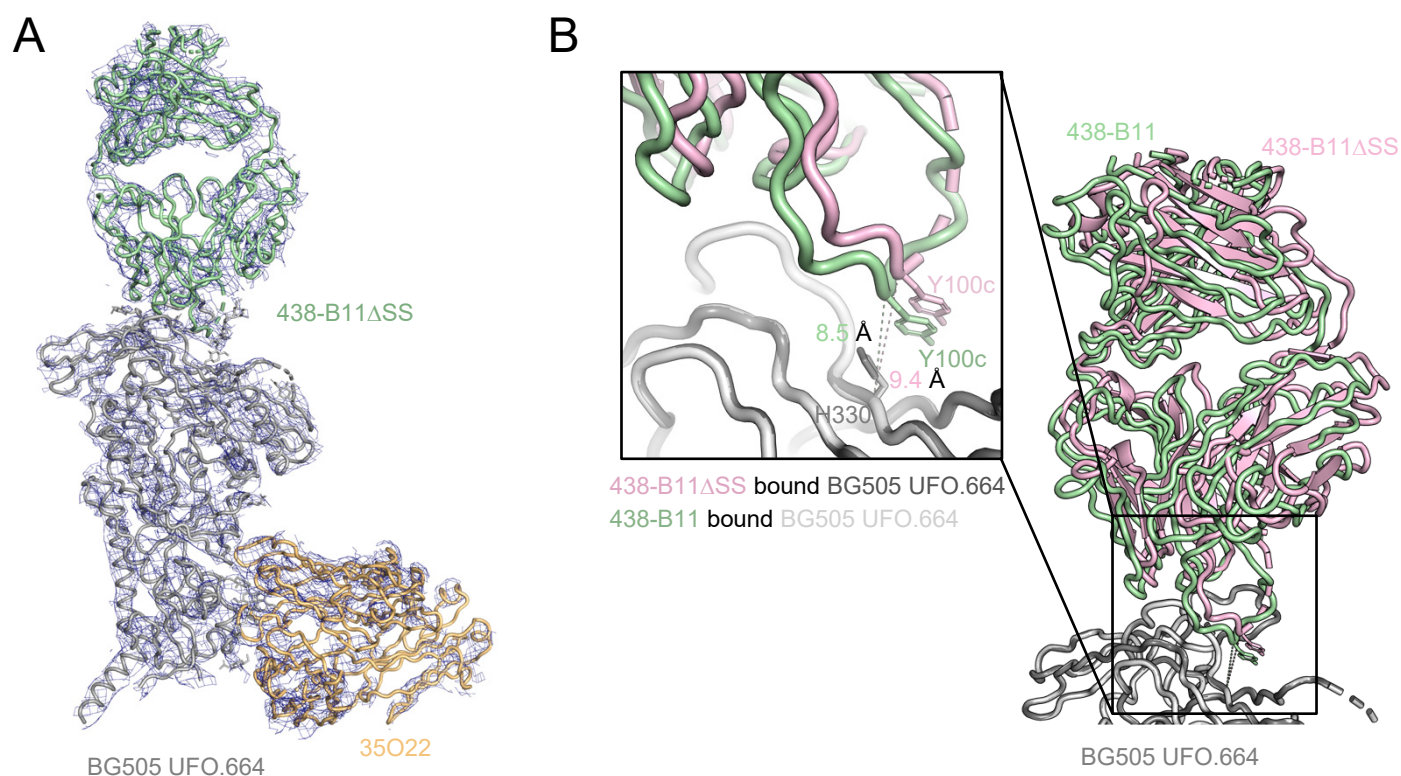


fig. S6. Crystallographic analysis of the 438-B11 disulfide bond mutant. (A) Crystal structure of the BG505 UFO.664 trimer (gp140:grey) trimer in complex with Fabs 438-B11 Δ SS (green) and 35O22 (orange) at 6.5 Å resolution. The side view of the Env protomer is shown here. **(B)** Superposition of the complex crystal structures of WT 438-B11 (green) and 438-B11 Δ SS (pink) bound to the BG505 UFO.664 trimer. The left inset shows an ~ 1 Å upward movement of Fab 438-B11 Δ SS compared to WT 438-B11 on the gp120 protein surface. The distances are measured in Å between the C α atoms of gp120 His330 and 438-B11 HCDR3 Tyr100c.

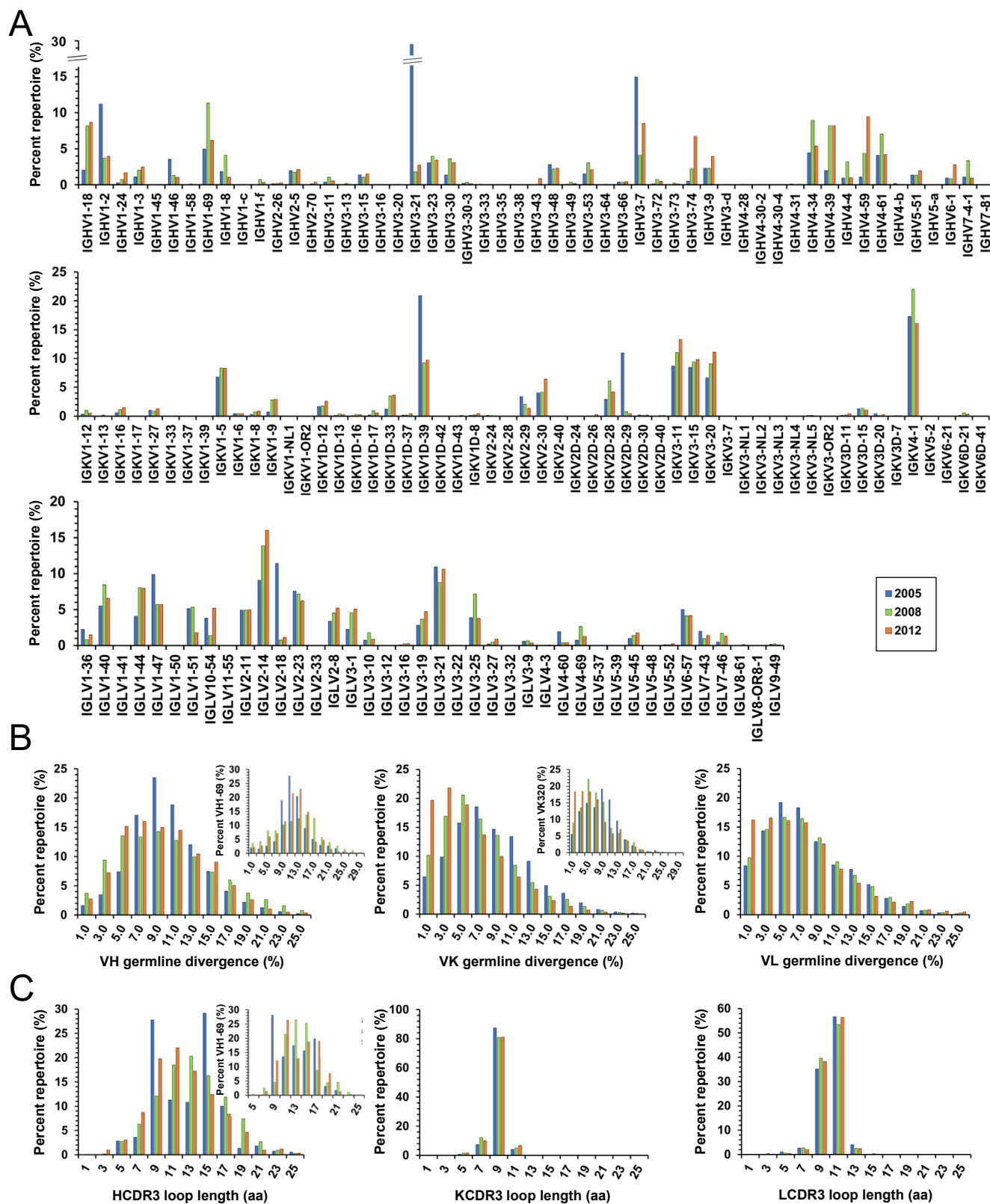


fig. S7. B cell repertoire profiles of an HIV-1-infected Chinese donor (CBJC438) at three time points. The distribution is plotted for **(A)** germline V gene usage for heavy and light (κ and λ) chains, **(B)** germline gene divergence, or degree of SHM, and **(C)** CDR3 loop length (H: heavy chain; K: κ chain; L: λ chain). Color coding denotes the time point analyzed with 2005 shown in blue, 2008 in green, and 2012 in orange.

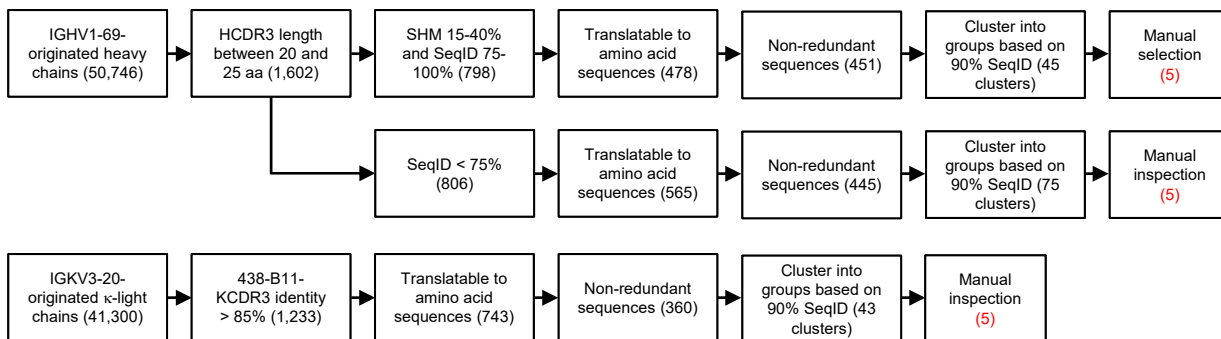
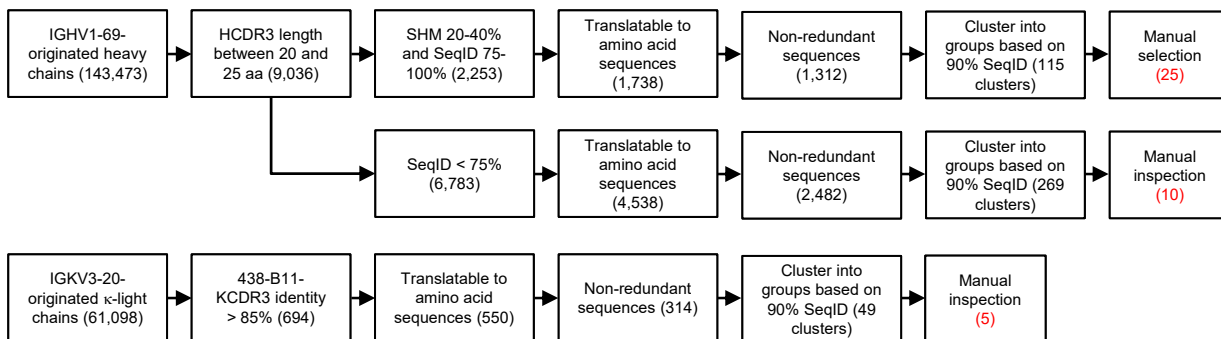
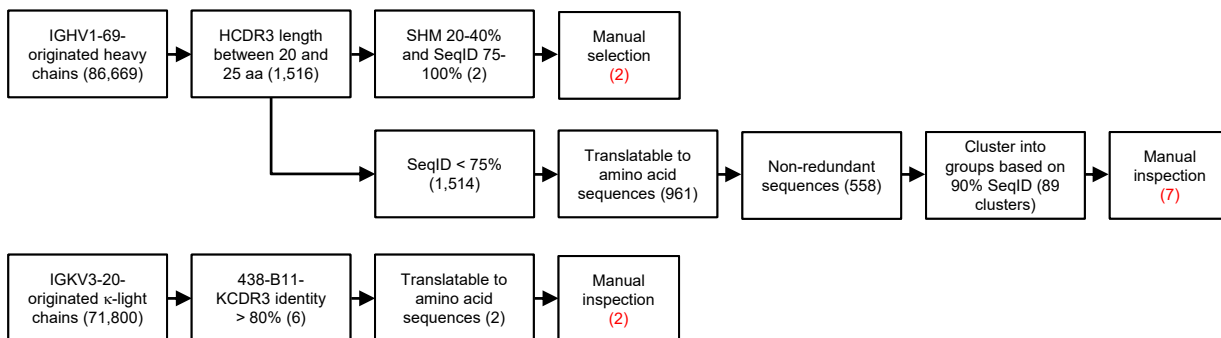
A Selection of HC and KC sequences from the 2005 donor repertoire**B Selection of HC and KC sequences from the 2008 donor repertoire****C Selection of HC and KC sequences from the 2012 donor repertoire**

fig. S8. Bioinformatics procedure used for selecting sequences from repertoire NGS data of an HIV-1-infected Chinese donor (CBJC438) for antibody synthesis and characterization. (A) 2005 repertoire. (B) 2008 repertoire. (C) 2012 repertoire. The number of remaining sequences at each step of the process is labeled.