

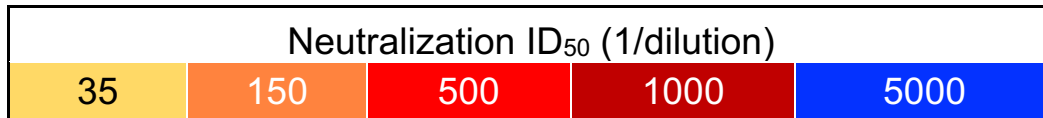
S1 Table: Neutralization ID₅₀ titers are shown for IgG purified from sera tested against murine leukemia virus (MLV) for all four cows over the course of immunization. ID₅₀ values are shown as 1/dilution.

MLV				
ID₅₀ (1/dilution)	Group 1		Group 2	
Day	Cow-485	Cow-16157	Cow-488	Cow-491
59	<35	<35	<35	<35
65	<35	<35	<35	<35
72	<35	<35	<35	<35
80	<35	37	<35	<35
85	<35	<35	<35	<35
150	<35	303	<35	<35
157	<35	70	<35	<35
164	<35	49	<35	<35
171	<35	50	<35	<35
234	<35	175	<35	<35
346	<35	<35	<35	<35
352	<35	<35	<35	<35
359	<35	<35	<35	<35

Neutralization ID₅₀ (1/dilution)		
35	150	300

S2 Table: Neutralization ID₅₀ titers are shown for IgG purified from sera from Day 359 of all four cows. Geomean ID₅₀ values and percent breadth are shown at the bottom of the graph. ID₅₀ values are shown as 1/dilution.

ID ₅₀ (1/dilution)		Group1		Group2	
Virus	Clade	Cow-485	Cow-16157	Cow-488	Cow-491
246F3	AC	<35	<35	297	<35
25710	C	1521	76	15193	<35
398F1	A	231	<35	234	118
BJOX2000	BC	<35	<35	718	<35
CE1176	C	68	72	672	<35
CE0217	C	45	<35	437	<35
CH119	BC	<35	<35	143	<35
CNE55	AE	4258	228	11923	70
CNE8	AE	581	131	4048	1094
Tro.11	B	<35	74	59	47
X1632	G	169	<35	461	46
X2278	B	<35	<35	65	<35
Geomean ID ₅₀		333	104	612	114
% Breadth		58%	42%	100%	42%



S3 Table: Neutralization IC₅₀ (µg/ml) and ID₅₀ (1/dilution) titers are shown for ID₅₀ (1/dilution) and IgG purified from sera from Day 359 for cow-485 and cow-488. Geomean IC₅₀ and ID₅₀ values are shown at the bottom of the graph.

Virus Strain	Clade	Bess1	Bess2	Bess4	ElsE1	ElsE2	Cow-485	Cow-488
6535.3	B	>50	>50	>50	>50	>50	<35	122
SC422661.8	B	>50	>50	>50	>50	>50	36	<35
PVO.4	B	>50	>50	>50	>50	>50	<35	<35
TRO.11	B	>50	>50	>50	>50	>50	<35	<35
AC10.0.29	B	>50	>50	>50	>50	>50	<35	<35
RHPA4259.7	B	>50	>50	>50	>50	>50	<35	<35
TRJO4551.58	B	>50	>50	>50	>50	>50	<35	<35
WITO4160.33	B	>50	>50	>50	>50	>50	<35	94
CAAN5342.A2	B	>50	>50	>50	>50	>50	<35	<35
WEAU_d15_410_5017	B (T/F)	>50	>50	>50	>50	>50	<35	<35
1006_11_C3_1601	B (T/F)	>50	>50	>50	>50	>50	<35	<35
1056_10_TA11_1826	B (T/F)	>50	>50	>50	>50	>50	<35	43
1012_11_TC21_3257	B (T/F)	>50	>50	>50	>50	>50	<35	56
6240_08_TA5_4622	B (T/F)	>50	>50	>50	>50	>50	<35	<35
6244_13_B5_4576	B (T/F)	>50	>50	>50	>50	>50	<35	<35
62357_14_D3_4589	B (T/F)	>50	>50	>50	>50	>50	<35	<35
Du156.12	C	0.016	0.084	0.006	0.004	0.001	120	11126
ZM197M.PB7	C	>50	20	>50	36	0.607	<35	114
ZM214M.PL15	C	>50	>50	>50	>50	>50	318	<35
ZM233M.PB6	C	>50	5	0.508	0.119	0.100	95	264
ZM249M.PL1	C	0.014	0.029	0.015	0.450	0.032	92	318
ZM53M.PB12	C	>50	>50	0.014	10	0.049	98	280
ZM109F.PB4	C	>50	0.496	0.056	0.084	0.020	224	1485
ZM135M.PL10a	C	>50	>50	>50	>50	>50	<35	<35
CAP45.2.00.G3	C	0.001	0.002	0.0006	0.027	0.0006	2126	5804
CAP210.2.00.E8	C	>50	13	0.026	0.289	0.078	<35	154
HIV-0013095-2.11	C	>50	>50	0.023	0.043	0.007	38	6901
HIV-16055-2.3	C	0.001	0.014	0.0006	0.004	0.0006	1017	14435
Ce0393_C3	C (T/F)	>50	0.302	0.008	0.387	0.033	241	25670
Ce1176_A3	C (T/F)	>50	>50	0.049	8	0.004	68	672
Ce2010_F5	C (T/F)	>50	>50	>50	>50	>50	<35	<35
Ce0682_E4	C (T/F)	>50	>50	>50	>50	>50	<35	40
Ce1172_H1	C (T/F)	>50	>50	0.045	0.968	0.033	50	358
Ce2060_G9	C (T/F)	0.190	50	>50	>50	2	412	218
Ce703010054_2A2	C (T/F)	>50	>50	>50	>50	>50	<35	<35
246F C1G	C (T/F)	0.001	0.003	>50	>50	>50	<35	58
249M B10	C (T/F)	0.028	0.118	0.044	1	0.083	69	345
ZM247v1(Rev-)	C (T/F)	11	6	5	>50	>50	<35	39
7030102001E5(Rev-)	C (T/F)	>50	>50	>50	>50	>50	<35	<35
1394C9G1(Rev-)	C (T/F)	0.551	0.168	0.249	2	0.004	2034	1345
Ce704809221_1B3	C (T/F)	>50	>50	>50	>50	>50	<35	<35
CNE19	BC	>50	>50	>50	>50	0.147	72	932
CNE20 (CRF07_BC)	BC	>50	>50	0.319	>50	0.299	<35	135
CNE17	BC	0.517	0.517	0.016	0.085	0.017	140	851

CNE30	BC	>50	>50	>50	>50	>50	<35	<35
CNE52	BC	0.290	0.290	>50	0.937	0.020	<35	498
CNE53	BC	>50	>50	>50	>50	>50	<35	<35
CNE58	BC	0.458	1	0.087	4	0.044	494	904
MS208.A1	A	>50	>50	18	0.566	0.082	<35	582
Q23.17	A	1	0.163	0.006	36	2	48	<35
Q461.e2	A	0.025	0.172	0.075	1	0.105	<35	321
Q769.d22	A	>50	>50	0.001	1	0.078	112	277
Q259.d2.17	A	0.009	0.016	0.127	7	0.024	<35	606
0330.v4.c3	A	11	0.167	0.105	0.145	0.0006	<35	4512
0260.v5.c36	A	>50	0.373	0.091	39	18	<35	<35
191955_A11	A (T/F)	0.005	0.007	0.374	1	0.001	1773	780
T257-31	CRF02_AG	0.035	0.057	0.003	0.027	0.001	2845	84
263-8	CRF02_AG	0.025	0.335	0.040	0.186	0.024	506	<35
T250-4	CRF02_AG	0.0006	0.002	0.067	0.005	0.006	6756	10458
T251-18	CRF02_AG	>50	>50	>50	>50	>50	<35	<35
T278-50	CRF02_AG	>50	>50	>50	14	1	<35	<35
T255-34	CRF02_AG	>50	>50	>50	>50	>50	<35	<35
211-9	CRF02_AG	>50	>50	>50	>50	>50	<35	<35
235-47	CRF02_AG	>50	>50	>50	24	3	<35	<35
620345.c01	CRF01_AE	0.080	0.055	0.001	0.087	0.006	160	2238
C1080.c03	CRF01_AE	>50	5	0.014	0.0006	0.0006	15010	145536
R2184.c04	CRF01_AE	0.062	0.654	0.007	0.481	0.024	168	547
R1166.c01	CRF01_AE	>50	>50	>50	>50	>50	393	151
R3265.c06	CRF01_AE	>50	1	0.014	0.096	0.016	671	611
C3347.c11	CRF01_AE	12	0.545	>50	>50	>50	<35	<35
C4118.c09	CRF01_AE	0.005	0.021	0.0006	0.0006	0.0006	1403	11276
CNE8	CRF01_AE	0.386	0.057	0.263	0.029	0.005	581	4048
CNE5	CRF01_AE	0.001	0.010	0.184	0.027	0.0006	2300	5281
BJOX009000.02.4	CRF01_AE	>50	>50	>50	>50	>50	<35	58
BJOX015000.11.5	CRF01_AE (T/F)	>50	>50	>50	>50	>50	293	63
BJOX010000.06.2	CRF01_AE (T/F)	>50	>50	>50	>50	>50	<35	<35
BJOX025000.01.1	CRF01_AE (T/F)	>50	>50	2	>50	>50	268	53
X1193_C1	G	>50	>50	>50	>50	>50	<35	<35
P0402_C2_11	G	>50	>50	16	>50	26	<35	103
X1254_C3	G	>50	>50	>50	>50	>50	<35	<35
X2088_C9	G	>50	>50	0.017	0.087	0.022	456	2122
X2131_C1_B5	G	>50	>50	>50	>50	>50	<35	<35
P1981_C5_3	G	0.119	3	0.031	0.112	0.007	78	1945
X1632_S2_B10	G	11	>50	>50	0.231	0.024	169	461
3016.v5.c45	D	>50	26	>50	37	0.384	<35	35
A07412M1.vrc12	D	0.582	0.993	50	3	0.237	41	261
231965.c01	D	>50	>50	0.040	>50	0.088	<35	327
231966.c02	D	>50	>50	>50	>50	>50	<35	108
3817.v2.c59	CD	0.034	2	0.018	0.401	0.0006	197	7236
6480.v4.c25	CD	>50	>50	>50	>50	>50	<35	<35
6952.v1.c20	CD	>50	>50	>50	>50	>50	<35	<35
6811.v7.c18	CD	0.035	0.059	>50	>50	>50	<35	<35
89-F1_2_25	CD	>50	>50	>50	>50	7	<35	<35

3301.v1.c24	AC	0.245	>50	0.269	8	0.454	<35	45	
6041.v3.c23	AC	0.018	0.086	>50	>50	>50	<35	<35	
6545.v4.c1	AC	0.014	0.065	0.003	0.005	0.001	35	4006	
0815.v3.c3	ACD	>50	>50	>50	>50	>50	<35	<35	
3103.v3.c10	ACD	>50	>50	>50	>50	>50	<35	<35	
Geomean IC ₅₀		0.061	0.238	0.047	0.352	0.031	Geomean ID ₅₀	276	557

Neutralization IC ₅₀ (µg/ml)				
50	1	0.5	0.05	0.005

Neutralization ID ₅₀ (1/Dilution)				
35	150	500	1000	5000

S4 Table: Table of recovered heavy chains tested with native and universal light chains.

Sort Stats and Summary of Screening			Sort 1	Sort 2	Sort 3	Sort 4	Short CDRH3 (0-24 AA)	Long CDRH3 (25-49 AA)	Ultralong CDRH3 (50+ AA)
Cow 485	All	Cells Sorted	108	453	559	438	NA	NA	NA
		PCR Wells Positive for Heavy Chains	34	75	169	52	NA	NA	NA
		Heavy Chain Sequences Recovered	13	43	47	49	42	72	38
	Universal Light Chain	Tested IGHV-1*7 Heavy Chains	10	40	30	NT	0	52	28
		Expressed in Screen	9	22	25	NT	0	32	24
		Positive for BG505 Binding	8	13	12	NT	0	14	19
		Monoclonals with Cross-Clade Neutralization	1	1	4	2	0	0	8
	Native Light Chain	Heavy Chain/Light Chain Pairs	12	32	41	49	41	63	30
		Expressed in Screen	9	24	34	45	34	53	25
		Positive for BG505 Binding	7	12	12	20	13	22	16
		Monoclonals with Cross-Clade Neutralization	1	0	3	2	0	0	6
	Cow 488	All	Cells Sorted	33	342	636	283	NA	NA
PCR Wells Positive for Heavy Chains			6	13	58	54	NA	NA	NA
Heavy Chain Sequences Recovered			1	6	17	49	34	4	35
Universal Light Chain		IGHV-1*7 Heavy Chains	0	2	1	NT	1	2	0
		Expressed in Screen	0	2	0	NT	0	2	0
		Positive for BG505 Binding	0	2	0	NT	0	2	0
		Monoclonals with Cross-Clade Neutralization	0	0	0	11	0	0	0
Native Light Chains		Heavy Chain/Light Chain Pairs	1	5	16	49	33	3	35
		Expressed in Screen	1	5	10	44	25	3	32
		Positive for BG505 Binding	0	3	3	33	8	3	28

S5 Table: ElsE and Bess antibodies were tested for their ability to neutralize the 12-virus global panel. IC₅₀ (µg/ml), IC₈₀ (µg/ml), and MPN (%) are shown for all antibodies whose IC₅₀ reach at least 50% neutralization. MPN= Maximum Percent Neutralized.

398F1 TRO.11 X2278 25710 CE0217 Ce1176 X1632 246F3 CNE55 CNE8 BJOX CH119

		A	B	B	C	C	C	G	AC	AE	AE	BC	BC
Bess1	IC ₅₀ (µg/ml)	>50	>50	>50	<0.005	>50	>50	11	0.054	<0.005	0.386	0.066	>50
	IC ₈₀ (µg/ml)	>50	>50	>50	0.013	>50	>50	>50	0.215	<0.005	2	0.315	>50
	MPN	<50	<50	<50	100%	<50	<50	58%	94%	100%	90%	94%	<50
Bess2	IC ₅₀ (µg/ml)	>50	>50	>50	0.014	0.355	>50	>50	0.03	<0.005	0.057	0.232	>50
	IC ₈₀ (µg/ml)	>50	>50	>50	0.057	1	>50	>50	0.121	0.019	0.229	0.928	>50
	MPN	<50	<50	<50	99%	88%	<50	<50	99%	100%	99%	98%	<50
Bess3	IC ₅₀ (µg/ml)	>50	>50	>50	0.067	>50	>50	6	0.063	0.042	0.603	0.067	>50
	IC ₈₀ (µg/ml)	>50	>50	>50	0.268	>50	>50	>50	0.250	0.170	2	0.270	>50
	MPN	<50	<50	<50	100%	<50	<50	62%	99%	100%	97%	99%	<50
Bess4	IC ₅₀ (µg/ml)	>50	>50	>50	0.064	0.127	0.049	>50	0.245	0.015	0.263	0.025	>50
	IC ₈₀ (µg/ml)	>50	>50	>50	0.258	0.509	0.195	>50	0.982	0.061	1	0.098	>50
	MPN	<50	<50	<50	98%	95%	93%	<50	92%	100%	100%	99%	<50
Bess5	IC ₅₀ (µg/ml)	>50	>50	>50	>50	24	13	>50	>50	0.02	0.093	14	>50
	IC ₈₀ (µg/ml)	>50	>50	>50	>50	>50	>50	>50	>50	0.079	1	>50	>50
	MPN	<50	<50	<50	<50	50%	56%	<50	<50	97%	91%	62%	<50
Bess6	IC ₅₀ (µg/ml)	>50	>50	49	41	>50	17	>50	>50	>50	>50	>50	>50
	IC ₈₀ (µg/ml)	>50	>50	>50	>50	>50	34	>50	>50	>50	>50	>50	>50
	MPN	<50	<50	52%	58%	<50	87%	<50	<50	<50	<50	<50	<50
Bess7	IC ₅₀ (µg/ml)	>50	>50	>50	0.477	>50	>50	>50	>50	<0.005	>50	31	>50
	IC ₈₀ (µg/ml)	>50	>50	>50	<50	>50	>50	>50	>50	0.02	>50	<50	>50
	MPN	<50	<50	<50	80%	<50	<50	<50	<50	98%	<50	50%	<50
Bess8	IC ₅₀ (µg/ml)	>50	>50	>50	0.009	>50	>50	>50	2	0.007	9	0.21	>50
	IC ₈₀ (µg/ml)	>50	>50	>50	0.525	>50	>50	>50	7	0.029	>50	0.839	>50
	MPN	<50	<50	<50	97%	<50	<50	<50	72%	97%	59%	84%	<50
ElsE1	IC ₅₀ (µg/ml)	>50	>50	>50	<0.005	2	8	0.231	0.058	<0.005	0.029	0.033	>50
	IC ₈₀ (µg/ml)	>50	>50	>50	0.019	>50	>50	0.924	0.233	0.019	0.116	0.133	>50
	MPN	<50	<50	<50	99%	74%	66%	81%	88%	99%	100%	100%	<50
ElsE2	IC ₅₀ (µg/ml)	>50	>50	>50	0.006	0.009	<0.005	0.024	0.007	<0.005	0.005	0.023	>50
	IC ₈₀ (µg/ml)	>50	>50	>50	0.023	0.037	0.018	0.096	0.027	0.014	0.022	0.091	>50
	MPN	<50	<50	<50	100%	94%	94%	84%	96%	99%	100%	100%	<50
ElsE3	IC ₅₀ (µg/ml)	>50	>50	>50	<0.005	0.009	0.062	0.161	0.153	0.007	0.009	0.026	>50
	IC ₈₀ (µg/ml)	>50	>50	>50	0.015	0.035	0.249	0.643	0.611	0.027	0.034	0.103	>50
	MPN	<50	<50	<50	100%	97%	92%	84%	90%	98%	100%	100%	<50
ElsE4	IC ₅₀ (µg/ml)	>50	>50	>50	0.016	23	>50	1	2	<0.005	0.011	0.035	>50
	IC ₈₀ (µg/ml)	>50	>50	>50	0.062	>50	>50	>50	>50	0.012	0.042	0.139	>50
	MPN	<50	<50	<50	98%	54%	<50	74%	78%	98%	100%	100%	<50
ElsE5	IC ₅₀ (µg/ml)	>50	>50	>50	0.008	26	>50	3	3	0.008	0.011	0.031	>50
	IC ₈₀ (µg/ml)	>50	>50	>50	0.032	>50	>50	>50	>50	0.031	0.044	0.123	>50
	MPN	<50	<50	<50	99%	52%	<50	68%	74%	98%	100%	99%	<50
ElsE6	IC ₅₀ (µg/ml)	>50	>50	>50	0.06	>50	>50	5	>50	0.033	0.023	0.013	>50
	IC ₈₀ (µg/ml)	>50	>50	>50	0.238	>50	>50	>50	>50	0.13	0.093	0.051	>50
	MPN	<50	<50	<50	91%	<50	<50	68%	<50	95%	99%	99	<50
ElsE7	IC ₅₀ (µg/ml)	>50	>50	>50	0.007	0.77	5	0.022	2	<0.005	0.007	0.019	>50
	IC ₈₀ (µg/ml)	>50	>50	>50	0.028	3	>50	0.087	>50	0.019	0.026	0.076	>50
	MPN	<50	<50	<50	99%	80%	68%	91%	78%	99%	99%	100%	<50
ElsE8	IC ₅₀ (µg/ml)	>50	>50	>50	0.023	3	10	0.654	0.056	0.024	0.023	0.067	>50
	IC ₈₀ (µg/ml)	>50	>50	>50	0.094	>50	>50	>50	0.223	0.096	0.092	0.267	>50
	MPN	<50	<50	<50	99%	71%	60%	74%	90%	97%	99%	100%	<50
ElsE9	IC ₅₀ (µg/ml)	>50	>50	>50	0.017	0.723	3	0.067	0.047	0.006	0.019	0.043	>50
	IC ₈₀ (µg/ml)	>50	>50	>50	0.067	>50	>50	0.269	0.188	0.022	0.077	0.172	>50
	MPN	<50	<50	<50	99%	75%	69%	81%	92%	99%	100%	100%	<50
ElsE10	IC ₅₀ (µg/ml)	>50	>50	>50	0.025	>50	17	11	>50	0.009	0.063	0.093	>50
	IC ₈₀ (µg/ml)	>50	>50	>50	0.102	>50	>50	>50	>50	0.12	0.167	0.372	>50
	MPN	<50	<50	<50	93%	<50	60%	62%	<50	96%	98%	93%	<50
ElsE11	IC ₅₀ (µg/ml)	>50	>50	>50	0.033	>50	>50	0.772	>50	0.016	0.031	0.027	>50
	IC ₈₀ (µg/ml)	>50	>50	>50	0.134	>50	>50	>50	>50	0.064	0.161	0.283	>50
	MPN	<50	<50	<50	93%	<50	<50	72%	<50	96%	98%	99%	<50

S6 Table: X-ray data collection and refinement statistics for Bess and ElsE Fabs.

	Fab ElsE1	Fab ElsE2	Fab ElsE5	Fab ElsE6	Fab ElsE7	Fab ElsE8	Fab ElsE9	Fab ElsE11	Fab Bess4	Fab Bess7
PDB code	8V4I	8VBJ	8VBK	8VBL	8VBM	8VBN	8VBO	8VBR	8VBP	8VBQ
Crystallization condition	40% ethylene glycol, 0.1M HEPES, pH 7.5, 5% Peg3000, 20°	0.1M Tris, pH 8.5, 1.5M ammonium sulfate, 12% glycerol, 4°	0.1M sodium cacodylate, pH 6.5, 40% MPD, 5% Peg8000, 20°	0.1M Ches, pH 9.5, 50% Peg200, 20°	0.1M Ches, pH 9.5, 20% Peg 8000, 4°	20% Peg3350, 0.2M KCl, 4°	0.1M sodium cacodylate, pH 6.5, 40% MPD, 5% Peg 8000, 20°	0.1M Ches, pH 9.5, 50% Peg200, 4°	70% MPD, 0.1M Hepes, pH 7.5, 20°	0.095M sodium citrate, pH 5.6, 19% 2-propanol, 5% glycerol, 19% Peg4000, 20°
Wavelength	0.97946	0.97946	1.03317	0.97946	0.97946	0.97741	0.97946	0.97741	0.97946	0.97741
Beamline	SSRL 12-1	SSRL 12-2	APS 23-ID-B	SSRL 12-2	SSRL 12-2	ALS 5.0.1	SSRL 12-1	ALS 5.0.1	SSRL 12-1	ALS 5.0.1
Resolution range	37.89 - 1.81 (1.88 - 1.81)	45.48 - 1.90 (1.97 - 1.90)	43.86 - 1.89 (1.96 - 1.89)	46.80 - 2.35 (2.43 - 2.35)	42.23 - 2.54 (2.63 - 2.54)	46.95 - 1.83 (1.90 - 1.83)	36.30 - 2.30 (2.38 - 2.30)	49.58 - 2.65 (2.75 - 2.65)	29.94 - 2.80 (2.90 - 2.80)	48.29 - 2.10 (2.18 - 2.10)
Space group/twin law	C 2 2 2 ₁	C 2 2 2 ₁	P 2 ₁ 2 ₁ 2 ₁	P 2 ₁ 2 ₁ 2	P 2 ₁ 2 ₁ 2 ₁	P 2 ₁ 2 ₁ 2 ₁	P 2 ₁ 2 ₁ 2	P 2 ₁ 2 ₁ 2 ₁ I, h, -k	P 2 ₁ 2 ₁ 2 ₁	C 2
Unit cell (Å, °)	69.79, 84.12, 174.58, 90, 90, 90	69.96, 178.59, 105.71, 90, 90, 90	56.26, 70.02, 109.08, 90, 90, 90	117.59, 69.98, 77.32, 90, 90, 90	58.22, 70.61, 123.97, 90, 90, 90	59.22, 120.27, 150.30, 90, 90, 90	70.11, 150.89, 51.32, 90, 90, 90	70.05, 70.19, 241.83, 90, 90, 90	66.61, 70.28, 111.46, 90, 90, 90	83.00, 69.78, 87.52, 90, 103.52, 90
Total reflections	460,645 (32,773)	442,490 (44,977)	423,944 (39,845)	168,777 (17,085)	76,645 (6407)	1,219,769 (90,327)	81,165 (7982)	378,268 (10,647)	44,117 (4130)	98,588 (7823)
Unique reflections	45,028 (3292)	51,939 (5160)	34,653 (3286)	27,185 (2649)	16,971 (1511)	95,768 (9306)	24,379 (2325)	33,457 (1618)	12,710 (1143)	28,113 (2607)
Multiplicity	10.2 (10.0)	8.5 (8.7)	12.2 (12.1)	6.2 (6.4)	4.5 (4.2)	12.8 (9.8)	3.3 (3.4)	11.3 (6.6)	3.5 (3.3)	3.5 (3.0)
Completeness (%)	95.6 (70.1)	98.8 (99.2)	98.7 (94.9)	99.7 (98.8)	96.8 (84.6)	99.8 (98.2)	97.8 (95.3)	94.0 (63.9)	93.8 (87.2)	98.8 (92.4)
Mean I/sigma(I)	10.5 (0.9)	8.4 (1.4)	13.8 (2.4)	9.1 (2.4)	7.5 (1.5)	15.9 (1.3)	9.3 (2.5)	11.3 (6.6)	7.0 (3.0)	8.7 (1.2)
Wilson B-factor	34	23	27	34	44	26	44	51	38	32
R-merge (%)	15.5 (251)	22.4 (224)	11.8 (109)	19.8 (140)	16.4 (135)	11.6 (173)	9.2 (77.8)	9.0 (84.8)	19.1 (80.5)	15.2 (107)
R-meas (%)	16.2 (264)	23.8 (238)	12.3 (114)	21.7 (152)	18.6 (155)	12.0 (183)	10.8 (90.9)	9.4 (91.4)	22.4 (95.9)	17.9 (128)
R-pim (%)	4.6 (77.2)	7.9 (77.6)	3.5 (32.3)	8.6 (59.4)	8.6 (74.2)	3.3 (57.5)	5.6 (46.2)	2.7 (32.0)	11.5 (51.0)	9.3 (70.3)
CC1/2 (%)	99.6 (41.0)	99.5 (41.3)	99.8 (86.7)	99.3 (49.7)	99.0 (40.0)	99.9 (50.8)	99.5 (61.1)	99.0 (77.4)	97.3 (49.8)	99.2 (37.6)
Reflections used in refinement	44,983 (3264)	51,917 (5148)	34,637 (3277)	27,183 (2649)	16,886 (1437)	95,655 (9237)	24,379 (2325)	33,316 (2271)	12,577 (1141)	28,099 (2601)
Reflections used for R-free	2273 (190)	2580 (266)	1773 (159)	1331 (141)	783 (77)	1970 (191)	1175 (117)	1993 (138)	620 (62)	1348 (114)
R-work (%)	22.1 (41.1)	19.5 (35.0)	20.4 (33.9)	19.7 (27.7)	23.5 (37.8)	22.4 (37.5)	24.8 (34.1)	24.7 (49.7)	19.6 (26.2)	23.0 (32.5)
R-free (%)	25.7 (55.6)	22.9 (37.2)	24.5 (39.3)	24.4 (34.5)	29.0 (46.8)	25.8 (39.6)	28.0 (38.9)	26.0 (56.4)	23.2 (30.9)	26.7 (30.7)
Number of non-hydrogen atoms	3750	3889	3707	3593	3463	7146	3535	7026	3257	3715
macromolecules	3563	3555	3496	3477	3463	6755	3465	7026	3257	3569
solvent	191	334	211	116	0	681	70	0	0	142
Protein residues	479	477	473	475	472	915	469	956	441	486
RMS(bonds)	0.003	0.013	0.003	0.002	0.002	0.008	0.002	0.003	0.003	0.003

RMS(angles)	0.66	1.05	0.64	0.56	0.51	0.98	0.53	0.56	0.58	0.56
Ramachandran favored, allowed, outliers (%)	94.3, 5.3, 0.4	97.5, 2.5, 0.0	96.8, 3.2, 0.0	96.2,3.4, 0.4	94.6, 4.7, 0.6	96.56, 3.33, 0.11	94.58, 4.34, 1.08	95.25, 4.11, 0.63	95.17, 4.37, 0.46	95.23, 4.77, 0.00
Rotamer outliers (%)	1.94	2.18	0.99	1.23	1.75	1.79	1.76	1.84	1.58	0.73
Clashscore	3.3	1.9	1.3	3.2	4.6	2.4	3.7	2.9	2.2	1.7
Average B-factor	45	31	35	43	65	35	63	59	36	47
macromolecules	45	31	35	43	65	35	63	59	36	48
solvent	44	35	36	41	NA	37	72	NA	NA	37

Statistics for the highest-resolution shell are shown in parentheses.

S7 Table: Secondary structural elements in stalk/knob regions. #=residue number, AA=residue type, and SS=secondary structure type. DSSP was used to assign the secondary structure type for residues in stalk/knob regions from the crystal structures [86]. SS are designated as: α -helix: H, 3_{10} helix :G, extended strand: E, bend: S, hydrogen bonded turn: T. Blank fields have 'coil' secondary structure. Blank AA fields indicate unmodeled residues. Residues at the tips of the two knob 'loops' (114-118 and 127 -133 in the ElsE Fabs and 114-120 and 132-137 in Bess7) are highlighted in bold; these might be expected to interact with Env.

	Bess7		ElsE1		ElsE2		ElsE5		ElsE6		ElsE7		ElsE8		ElsE9		ElsE11_1		ElsE11_2	
#	AA	SS	AA	SS	AA	SS	AA	SS	AA	SS	AA	SS	AA	SS	AA	SS	AA	SS	AA	SS
92	C		C		C		C		C		C		C		C		C		C	
93	T		T		T		T		T		T		T		T		T		T	
94	T	E	T	E	T	E	T	E	T	E	T	E	A	E	T		T	E	T	
95	V	E	V	E	V	E	V	E	V	E	V	E	V	E	V	E	V	E	V	E
96	H	E	H	E	H	E	H	E	H	E	H	E	V	E	R	E	R	E	R	E
97	Q	E	Q	E	Q	E	Q	E	Q	E	Q	E	Q	E	Q	E	Q	E	Q	E
98	T	E	Q	E	Q	E	Q	E	Q	E	Q	E	E	E	Q	E	Q	E	Q	E
99	T	E	T	E	T	E	T	E	T	E	T	E	T	E	V	E	T	E	T	E
100	K	E	R	E	R	E	R	E	R	E	R	E	R	E	H	E	R	E	R	E
101	T		K	E	K	E	K	E	K	E	K	E	K	E	K	E	K	E	K	E
102	T		G	E	S	E	G	E	S	E	S	E	S	E	T	E	S	E	S	E
103	K	E	C		C		C		C		C		C		C		C		C	
104	E	E	P		P		P		P		P		P		P		P		P	
105	C		D	T	G	T	D	S	A	S	D	S	D	T	Q	S	D	T	D	T
106	P		G	T	G	T	G	S	G	S	G	S	G	T	G	S	G	T	G	T
107	E	T	W		Y		W		Y		W		W		W		W		W	
108	G	T	R	E	T	E	S	E	T	E	M	E	R	E	R	E	T	E	T	E
109	Y		F	E	F	E	F	E	L	E	F	E	F	E	F	E	L	E	L	E
110	N	E	G	H	G	G	G	T	A	T	G	S	G	T	G	H	A	H	A	H
111	W	E	W	H	Y	G	W	T	K	T	F	T	W	T	W	H	K	H	K	H
112	D		D	H	D	G	D	T	D	T	D	T	D	T	D	H	D	H	D	H
113	D	S	C	H	C	G	C	T	C	T	C		C	T	C	H	C	H	C	H
114	G		G	T	G	T	G	T	G				G	T	G	T	G	T	G	T
115	C		F		F		F						F		F		F		F	
116	G		H		H								H		H		Y		Y	
117	S	G	G	S	G	S							G	S	G	S	G	S	G	S
118	E	G	Y	T	W	T							Y	T	Y	T	Y	T	Y	T
119	L	G	G	T	G	T			G		G		G	T	G	T	G	T	G	T
120	G		Q	T	S	T	!		S	T	S		T	T	S	T	S	T	S	T
121	C		E	T	D	T	E		E	T	E	S	E	T	D	T	E	T	E	T
122	G	S	D	S	D	S	D		D	S	D	S	D	S	D	S	D		D	S
123	G	S	C	E	C	E	C	E	C	E	C	E	C	E	C	E	C	E	C	E
124	A	S	Y	E	Y	E	Y	E	Y	E	V	E	Y	E	Y	E	Y	E	Y	E
125	D	S	E	S	P	S	D	S	D	S	D	S	E	S	E	S	D	S	D	S
126	C	S	D		D	S	D		D		D		D		D	S	D		D	

S8 Table: Cryo-EM data collection, refinement and validation statistics.

	BG505 SOSIP + Bess4 Fab + RM20A3 Fab (EMD-41498) (PDB: 8TQ1)
Data collection and processing	
Microscope	TFS Krios
Magnification	130,000x
Voltage (kV)	300
Electron exposure (e-/Å ²)	55.5
Defocus range (µm)	-0.7 to -1.7
Detector	Gatan K2 Summit
Recording mode	Counting
Pixel size (Å)	1.045
Symmetry imposed	C1
Micrographs (no.)	3,871
Initial particle images (no.)	494,075
Final particle images (no.)	82,374
Map resolution (Å)	3.3
FSC threshold	0.143
Map sharpening <i>B</i> factor (Å ²)	-83.5
Map pixel size (Å)	1.045
Map resolution range (Å)	2.4-5.0
Refinement	
Initial model used (PDB code)	6x9r
Model resolution (Å)	3.3
FSC threshold	0.5
Model resolution range (Å)	2.4-4.0
EMRinger score	3.95
Model composition	
Non-hydrogen atoms	19,788
Protein residues	2,400
Ligands	79
Mean <i>B</i> factors (Å ²)	
Protein	71
Ligand	96
R.m.s. deviations	
Bond lengths (Å)	0.006
Bond angles (°)	1.125
Validation	
MolProbity score	1.11
Clashscore	1.49
Poor rotamers (%)	0.19
Ramachandran plot	
Favored (%)	96.54
Allowed (%)	3.46
Disallowed (%)	0.00