Supplementary Notes

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Supplementary Figure 1

Virus ID	Clade	VRC26.01	VRC26.03	VRC26.06	VRC26.08
0260.v5.c36	A	>50	>50	>50	>50
0330.v4.c3	A	>50	>50	>50	>50
0439.v5.c1	A	>50	>50	>50	>50
3365.v2.c20	A	>50	20.8	>50	0.100
3415.v1.c1	A	>50	>50	>50	>50
3718.v3.c11	A	>50	0.377	>50	0.105
398-F1_F6_20	A		>50	>50	>50
BB201.B42	A	>50	0.001	1.38	0.001
BB539.2B13	A	>50	35.7	>50	0.194
BI369.9A	A	1.01	0.051	28.6	0.008
BS208.B1	A	16.7	0.009	>50	0.003
KER2008.12	A	0.308	>50	>50	>50
KER2018.11	A	5.95	0.014	42.7	0.003
KNH1209.18	A	>50	>50	>50	>50
MB201.A1	A	>50	>50	>50	>50
MB539.2B7	A	>50	>50	>50	31.9
MI369.A5	A	>50	7.88	>50	0.039
MS208.A1	A	>50	19.0	>50	0.115
Q23.17	A	>50	0.867	>50	0.010
Q259.17	A	>50	0.002	>50	0.001
Q769.d22	A	>50	>50	>50	>50
Q769.h5	A	>50	>50		
Q842.d12	A	>50	>50	>50	>50
QH209.14M.A2	A	>50	>50	>50	>50
RW020.2	A	>50	>50	>50	>50
UG037.8	A	>50	>50	>50	>50
3301.V1.C24	AC	2.78	0.047	2.92	0.013
3589.V1.C4	AC	>50	>50	>50	>50
6540.v4.c1	AC	>50	0.892	>50	0.077
6545.V4.C1	AC	>50	6.14	>50	0.026
0815.V3.C3	ACD	>50	>50	>50	>50
6095.V1.C10	ACD	2.32	0.434	>50	0.0007
3468.V1.C12	AD	>50	>50	>50	>50
Q168.a2	AD	>50	>50	>50	0.148
Q461.e2	AD	>50	>50	>50	0.502
620345.c1	AE	42.9	0.394	>50	0.001
BJOX009000.02.4	AE	>50	>50	>50	>50
BJOX010000.06.2	AE	>50	>50	>50	>50
BJOX025000.01.1	AE	>50	>50	>50	>50
BJOX028000.10.3	AE		>50	>50	>50
C1080.c3	AE	>50	0.006	>50	0.023
C2101.c1	AE	>50	>50	>50	>50
C3347.c11	AE		>50	>50	>50
C4118.09	AE	3.64	0.010	>50	0.002
CM244.ec1	AE		0.0007	6.90	0.002
CNE3	AE	>50	>50	>50	>50
CNE5	AE	2.21	0.004	>50	0.020
CNE55	AE	>50	0.019	>50	0.026
CNE56	AE	>50	>50	>50	>50
CNE59	AE	>50	>50	>50	>50

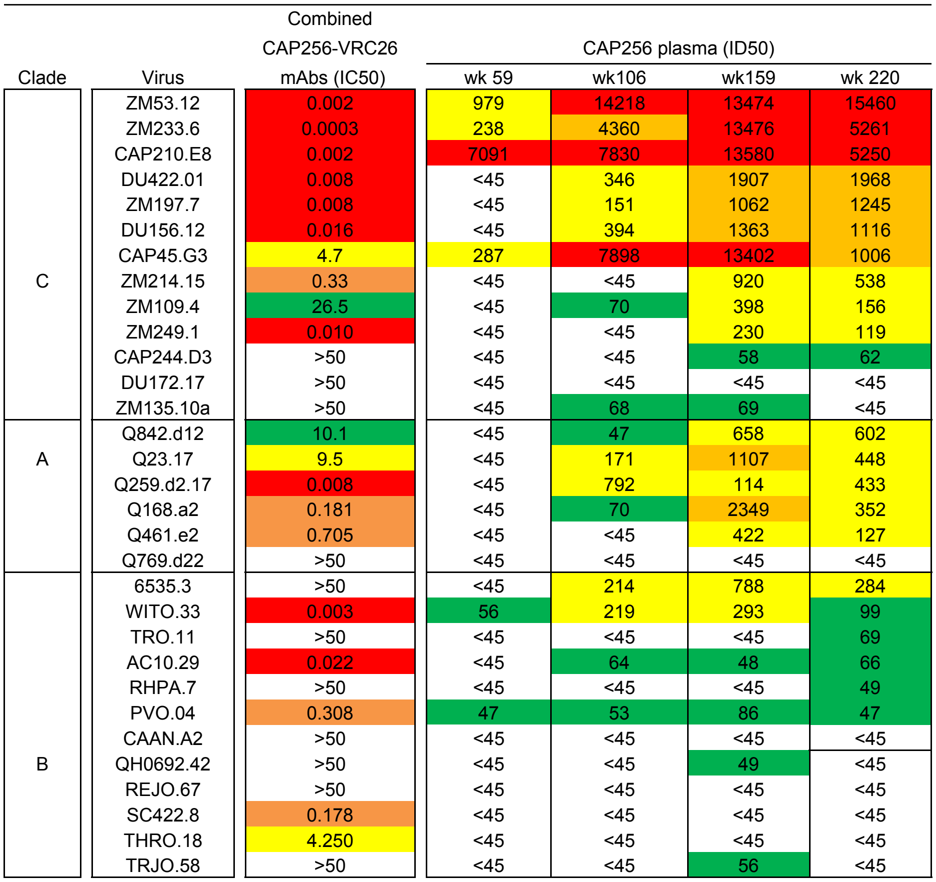
Virus ID	Clade	VRC26.01	VRC26.03	VRC26.06	VRC26.08
CNE8	AE		>50	>50	2.46
M02138	AE	>50	>50	>50	>50
R1166.c1	AE	>50	>50	>50	>50
R2184.c4	AE	>50	>50	>50	19.8
R3265.c6	AE		>50	>50	>50
TH023.6	AE		>50	>50	26.4
TH966.8	AE	>50	0.016	>50	0.036
TH976.17	AE	>50	2.95	>50	>50
235-47	AG	>50	>50	>50	0.265
242-14	AG	>50	0.062	>50	*0.0003*
263-8	AG	>50	>50	>50	0.031
269-12	AG	>50	>50	>50	>50
271-11	AG	>50	>50	>50	>50
928-28	AG	>50	3.60	>50	0.097
DJ263.8	AG	1.16	0.138	>50	0.031
T250-4	AG	0.018	0.0004	4.74	0.001
T251-18	AG	>50	>50	>50	>50
T253-11	AG	>50	>50	>50	49.5
T255-34	AG	>50	>50	>50	>50
T257-31	AG	11.0	0.004	>50	0.009
T266-60	AG	>50	0.943	>50	1.78
T278-50	AG	>50	>50	>50	>50
T280-5	AG	>50	>50	>50	>50
T33-7	AG	>50	>50	>50	>50
3988.25	B	>50	>50	>50	>50
5768.04	B	>50	>50	>50	>50
6101.10	B	>50	>50	>50	>50
6535.3	B	>50	>50	>50	>50
7165.18	B	>50	>50	>50	>50
45_01dG5	B		>50	0.877	>50
89.6.DG	B	>50	>50	>50	>50
AC10.29	B	>50	>50	0.030	>50
ADA.DG	B	>50	>50	12.5	>50
Bal.01	B	>50	>50	>50	>50
BaL.26	B	>50	>50	>50	>50
BG1168.01	B	>50	>50	>50	>50
BL01.DG	B	>50	>50	>50	>50
BR07.DG	B	>50	>50	>50	>50
BX08.16	B	>50	>50	12.6	>50
CAAN.A2	B	>50	>50	>50	>50
CNE10	B	>50	>50	>50	>50
CNE12	B	>50	>50	>50	>50
CNE14	B	>50	>50	>50	>50
CNE4	B	>50	>50	>50	>50
CNE57	B	>50	>50	>50	>50
HO86.8	B	>50	>50	>50	>50
HT593.1	B	>50	>50	>50	>50
HXB2.DG	B	>50	>50	>50	>50
JRCSF.JB	B	>50	>50	>50	>50
JRFL.JB	B	>50	>50	>50	>50

Supplementary Figure 1. Neutralization by CAP256-VRC26 antibodies of 194 Env-pseudoviruses.

Supplementary Figure 1

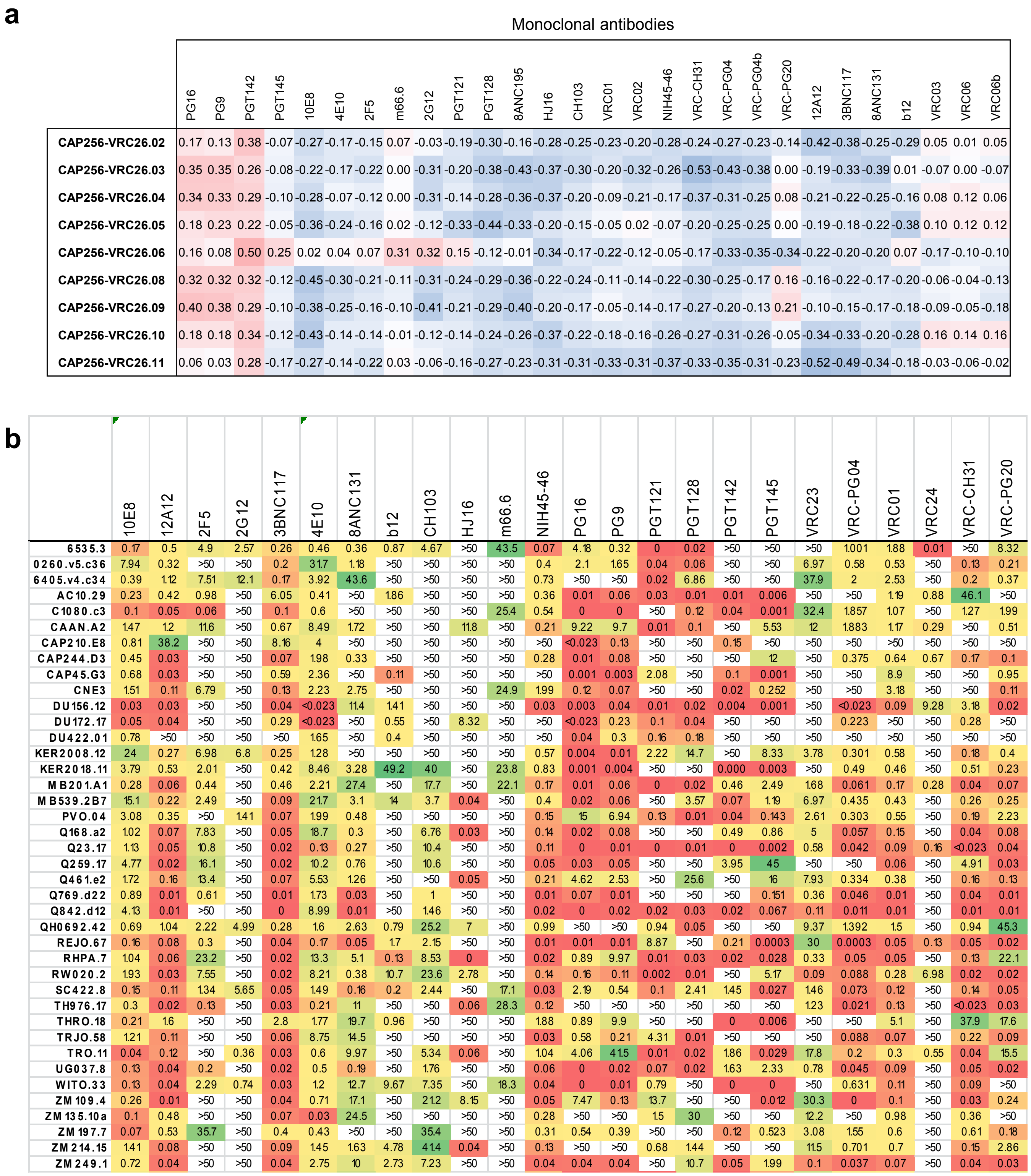
Virus ID	Clade	VRC26.01	VRC26.03	VRC26.06	VRC26.08
MN.3	B	>50	>50	>50	>50
PVO.04	B	>50	>50	0.947	11.8
QH0515.01	B	>50	>50	>50	>50
QH0692.42	B	>50	>50	>50	>50
REJO.67	B	>50	>50	>50	>50
RHPA.7	B	>50	>50	>50	>50
SC422.8	B	>50	>50	0.439	>50
SF162.LS	B	>50	>50	>50	>50
SS1196.01	B	>50	>50	>50	>50
THRO.18	B	>50	>50	3.30	>50
TRJO.58	B	>50	>50	>50	>50
TRO.11	B	>50	>50	>50	>50
WITO.33	B	>50	>50	0.005	>50
YU2.DG	B	>50	>50	>50	>50
CH038.12	BC	9.82	0.020	1.44	0.009
CH070.1	BC	>50	0.553	>50	0.039
CH117.4	BC	15.8	0.002	0.741	0.003
CH181.12	BC	0.017	0.001	0.049	0.001
CNE15	BC	>50	>50	>50	>50
CNE19	BC			>50	11.1
CNE20	BC	>50	>50	>50	>50
CNE21	BC	>50	0.021	>50	0.001
CNE40	BC	>50	>50	>50	>50
CNE7	BC	10.2	0.829	>50	0.003
286.36	C	0.281	0.008	0.559	0.004
288.38	C	>50	>50	>50	>50
0013095-2.11	C	>50	>50	>50	0.021
001428-2.42	C	>50	0.010	>50	30.9
0077_V1.C16	C	10.8	0.032	>50	0.001
00836-2.5	C	>50	>50	>50	>50
0921.V2.C14	C	>50	0.048	>50	0.036
16055-2.3	C	0.016	0.004	0.504	0.004
16845-2.22	C	>50	>50	>50	>50
16936-2.21	C	>50	0.748	>50	0.250
25710-2.43	C	>50	0.017	>50	0.006
25711-2.4	C	>50	>50	>50	>50
25925-2.22	C	>50	0.021	>50	0.013
26191-2.48	C	13.3	0.004	>50	0.001
3168.V4.C10	C	>50	>50	>50	>50
3637.V5.C3	C	>50	>50	>50	>50
3873.V1.C24	C	0.677	0.017	>50	0.004
6322.V4.C1	C	16.5	0.007	>50	0.003
6471.V1.C16	C	>50	>50	>50	>50
6631.V3.C10	C	>50	>50	>50	>50
6644.V2.C33	C	>50	>50	>50	>50
6785.V5.C14	C	1.68	0.005	2.54	0.005
6838.V1.C35	C	>50	0.006	>50	0.001
96ZM651.02	C	>50	>50	>50	2.63
BR025.9	C	>50	>50	>50	>50
CAP210.E8	C	0.166	0.011	1.20	0.030
CAP244.D3	C	>50	>50	>50	46.0
CAP45.G3	C	31.8	10.7	>50	4.69
CNE30	C	>50	>50	>50	>50
CNE31	C	>50	>50	>50	>50
CNE53	C	>50	>50	>50	>50
CNE58	C	0.749	0.100	>50	0.006
DU123.06	C	>50	>50	>50	0.015
DU151.02	C	>50	0.361	>50	0.006
DU156.12	C	>50	0.090	>50	0.006
DU172.17	C	>50	>50	>50	>50
DU422.01	C	>50	0.224	>50	1.12
MW965.26	C	14.9	0.218	>50	0.003
SO18.18	C	0.046	0.004	0.046	0.002
TV1.29	C		>50	>50	>50
TZA125.17	C	>50	>50	>50	0.018
TZBD.02	C	>50	0.014	>50	0.036
ZA012.29	C	>50	>50	>50	>50
ZM106.9	C	>50	0.015	>50	0.010
ZM109.4	C	>50	>50	>50	>50
ZM135.10a	C	>50	>50	>50	>50
ZM176.66	C	>50	0.017	>50	0.029
ZM197.7	C	22.1	0.302	>50	0.002
ZM214.15	C	>50	0.100	>50	3.23
ZM215.8	C	>50	>50	>50	>50
ZM233.6	C	0.701	0.032	22.6	0.0003
ZM249.1	C	>50	0.004	>50	0.0009
ZM53.12	C	0.036	0.017	0.082	0.004
ZM55.28a	C	40.9	0.027	>50	0.005
3326.V4.C3	CD	0.029	0.011	0.226	0.007
3337.V2.C6	CD	>50	0.012	>50	0.044
3817.v2.c59	CD	>50	>50	>50	>50
191821.E6.1	D	>50	1.50	>50	0.003
231965.c1	D	>50	>50	>50	>50
247-23	D	>50	>50	>50	0.005
3016.v5.c45	D	16.4	0.450	>50	0.005
57128.vrc15	D	>50	>50	>50	>50
6405.v4.c34	D	>50	>50	>50	>50
A03349M1.vrc4a	D	>50	>50	>50	2.68
A07412M1.vrc12	D		33.7	>50	0.068
NKU3006.ec1	D	>50	>50	>50	>50
UG024.2	D	>50	>50	>50	0.843
P0402.c2.11	G		0.100	>50	0.006
P1981.C5.3	G	>50	0.045	>50	0.008
X1193.c1	G	>50	9.68	>50	0.343
X1254.c3	G	>50	>50	>50	>50
X1632.S2.B10	G	>50	0.034	>50	0.010
X2088.c9	G	>50	>50	>50	>50
% of viruses neutralized		18%	38%	12%	47%
median IC50 for neutralized viruses		2.55	0.032	1.20	0.013
geometric mean IC50 for neutralized viruses		1.74	0.065	1.06	0.029

Supplementary Figure 2



Clade	Virus	Combined CAP256-VRC26 mAbs (IC50)	CAP256 plasma (ID50)			
			wk 59	wk106	wk159	wk 220
C	ZM53.12	0.002	979	14218	13474	15460
	ZM233.6	0.0003	238	4360	13476	5261
	CAP210.E8	0.002	7091	7830	13580	5250
	DU422.01	0.008	<45	346	1907	1968
	ZM197.7	0.008	<45	151	1062	1245
	DU156.12	0.016	<45	394	1363	1116
	CAP45.G3	4.7	287	7898	13402	1006
	ZM214.15	0.33	<45	<45	920	538
	ZM109.4	26.5	<45	70	398	156
	ZM249.1	0.010	<45	<45	230	119
	CAP244.D3	>50	<45	<45	58	62
	DU172.17	>50	<45	<45	<45	<45
	ZM135.10a	>50	<45	68	69	<45
A	Q842.d12	10.1	<45	47	658	602
	Q23.17	9.5	<45	171	1107	448
	Q259.d2.17	0.008	<45	792	114	433
	Q168.a2	0.181	<45	70	2349	352
	Q461.e2	0.705	<45	<45	422	127
	Q769.d22	>50	<45	<45	<45	<45
B	6535.3	>50	<45	214	788	284
	WITO.33	0.003	56	219	293	99
	TRO.11	>50	<45	<45	<45	69
	AC10.29	0.022	<45	64	48	66
	RHPA.7	>50	<45	<45	<45	49
	PVO.04	0.308	47	53	86	47
	CAAN.A2	>50	<45	<45	<45	<45
	QH0692.42	>50	<45	<45	49	<45
	REJO.67	>50	<45	<45	<45	<45
	SC422.8	0.178	<45	<45	<45	<45
	THRO.18	4.250	<45	<45	<45	<45
	TRJO.58	>50	<45	<45	56	<45

Supplementary Figure 2. Neutralization of heterologous viruses by CAP256 plasma and mAbs. Neutralization of 31 viruses by CAP256-VRC26 antibodies and by plasma from CAP256 sampled at 4 timepoints. Plasma data are from ref. 25. Antibody values are shown as 50% inhibitory concentration (IC50) of a theoretical combination of all 12 antibodies (calculated as the lowest IC50 for each virus). Plasma is shown as 50% inhibitory dilution (ID50) with a starting dilution of 1:45.



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Monoclonal antibodies

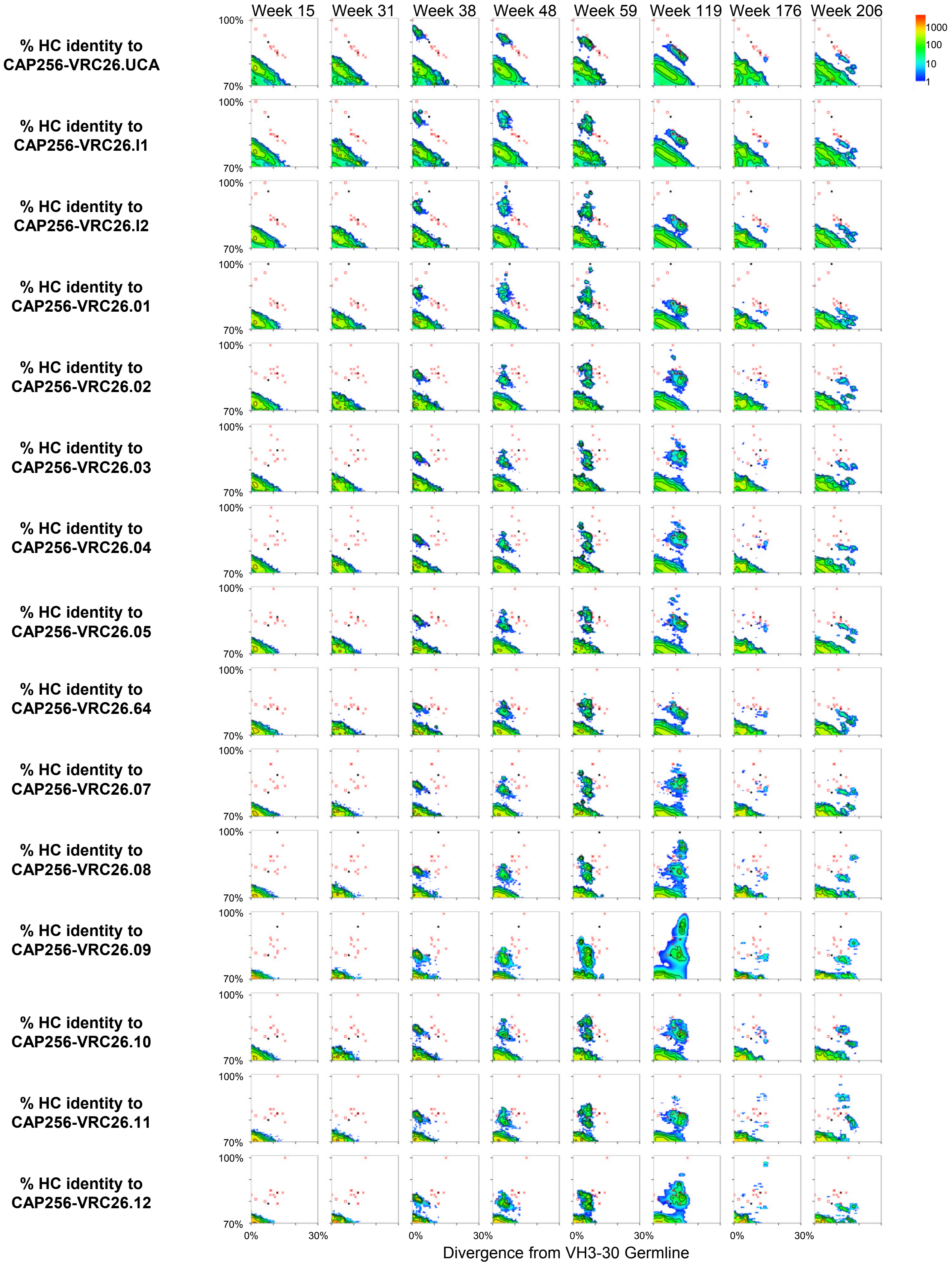
	PG16	PG9	PGT142	PGT145	10E8	4E10	2F5	m66.6	2G12	PGT121	PGT128	8ANC195	HJ16	CH103	VRC01	VRC02	NIH45-46	VRC-CH31	VRC-PG04	VRC-PG04b	VRC-PG20	12A12	3BNC117	8ANC131	b12	VRC03	VRC06	VRC06b
CAP256-VRC26.02	0.17	0.13	0.38	-0.07	-0.27	-0.17	-0.15	0.07	-0.03	-0.19	-0.30	-0.16	-0.28	-0.25	-0.23	-0.20	-0.28	-0.24	-0.27	-0.23	-0.14	-0.42	-0.38	-0.25	-0.29	0.05	0.01	0.05
CAP256-VRC26.03	0.35	0.35	0.26	-0.08	-0.22	-0.17	-0.22	0.00	-0.31	-0.20	-0.38	-0.43	-0.37	-0.30	-0.20	-0.32	-0.26	-0.53	-0.43	-0.38	0.00	-0.19	-0.33	-0.39	0.01	-0.07	0.00	-0.07
CAP256-VRC26.04	0.34	0.33	0.29	-0.10	-0.28	-0.07	-0.12	0.00	-0.31	-0.14	-0.28	-0.36	-0.37	-0.20	-0.09	-0.21	-0.17	-0.37	-0.31	-0.25	0.08	-0.21	-0.22	-0.25	-0.16	0.08	0.12	0.06
CAP256-VRC26.05	0.18	0.23	0.22	-0.05	-0.36	-0.24	-0.16	0.02	-0.12	-0.33	-0.44	-0.33	-0.20	-0.15	-0.05	0.02	-0.07	-0.20	-0.25	-0.25	0.00	-0.19	-0.18	-0.22	-0.38	0.10	0.12	0.12
CAP256-VRC26.06	0.16	0.08	0.50	0.25	0.02	0.04	0.07	0.31	0.32	0.15	-0.12	-0.01	-0.34	-0.17	-0.22	-0.12	-0.05	-0.17	-0.33	-0.35	-0.34	-0.22	-0.20	-0.20	0.07	-0.17	-0.10	-0.10
CAP256-VRC26.08	0.32	0.32	0.32	-0.12	-0.45	-0.30	-0.21	-0.11	-0.31	-0.24	-0.29	-0.36	-0.22	-0.24	-0.11	-0.14	-0.22	-0.30	-0.25	-0.17	0.16	-0.16	-0.22	-0.17	-0.20	-0.06	-0.04	-0.13
CAP256-VRC26.09	0.40	0.38	0.29	-0.10	-0.38	-0.25	-0.16	-0.10	-0.41	-0.21	-0.29	-0.40	-0.20	-0.17	-0.05	-0.14	-0.17	-0.27	-0.20	-0.13	0.21	-0.10	-0.15	-0.17	-0.18	-0.09	-0.05	-0.18
CAP256-VRC26.10	0.18	0.18	0.34	-0.12	-0.43	-0.14	-0.14	-0.01	-0.12	-0.14	-0.24	-0.26	-0.37	-0.22	-0.18	-0.16	-0.26	-0.27	-0.31	-0.26	-0.05	-0.34	-0.33	-0.20	-0.28	0.16	0.14	0.16
CAP256-VRC26.11	0.06	0.03	0.28	-0.17	-0.27	-0.14	-0.22	0.03	-0.06	-0.16	-0.27	-0.23	-0.31	-0.31	-0.33	-0.31	-0.37	-0.33	-0.35	-0.31	-0.23	-0.52	-0.49	-0.34	-0.18	-0.03	-0.06	-0.02

b

	10E8	12A12	2F5	2G12	3BNC117	4E10	8ANC131	b12	CH103	HJ16	m66.6	NIH45-46	PG16	PG9	PGT121	PGT128	PGT142	PGT145	VRC23	VRC-PG04	VRC01	VRC24	VRC-CH31	VRC-PG20
6535.3	0.17	0.5	4.9	2.57	0.26	0.46	0.36	0.87	4.67	>50	43.5	0.07	4.18	0.32	0	0.02	>50	>50	>50	1.001	1.88	0.01	>50	8.32
0260.v5.c36	7.94	0.32	>50	>50	0.2	31.7	1.18	>50	>50	>50	>50	0.4	2.1	1.65	0.04	0.06	>50	>50	6.97	0.58	0.53	>50	0.13	0.21
6405.v4.c34	0.39	1.12	7.51	12.1	0.17	3.92	43.6	>50	>50	>50	>50	0.73	>50	>50	0.02	6.86	>50	>50	37.9	2	2.53	>50	0.2	0.37
AC10.29	0.23	0.42	0.98	>50	6.05	0.41	>50	1.86	>50	>50	>50	0.36	0.01	0.06	0.03	0.01	0.01	0.006	>50	>50	1.19	0.88	46.1	>50
C1080.c3	0.1	0.05	0.06	>50	0.1	0.6	>50	>50	>50	>50	25.4	0.54	0	0	>50	0.12	0.04	0.001	32.4	1.857	1.07	>50	1.27	1.99
CAAN.A2	1.47	1.2	11.6	>50	0.67	8.49	1.72	>50	>50	11.8	>50	0.21	9.22	9.7	0.01	0.1	>50	5.53	12	1.883	1.17	0.29	>50	0.51
CAP210.E8	0.81	38.2	>50	>50	8.16	4	>50	>50	>50	>50	>50	>50	<0.023	0.13	>50	>50	0.15	>50	>50	>50	>50	>50	>50	>50
CAP244.D3	0.45	0.03	>50	>50	0.07	1.98	0.33	>50	>50	>50	>50	0.28	0.01	0.08	>50	>50	>50	12	>50	0.375	0.64	0.67	0.17	0.1
CAP45.G3	0.68	0.03	>50	>50	0.59	2.36	>50	0.11	>50	>50	>50	>50	0.001	0.003	2.08	>50	0.1	0.001	>50	>50	8.9	>50	>50	0.95
CNE3	1.51	0.11	6.79	>50	0.13	2.23	2.75	>50	>50	>50	24.9	1.99	0.12	0.07	>50	>50	0.02	0.252	>50	>50	3.18	>50	>50	0.11
DU156.12	0.03	0.03	>50	>50	0.04	<0.023	11.4	1.41	>50	>50	>50	0.03	0.003	0.04	0.01	0.02	0.004	0.001	>50	<0.023	0.09	9.28	3.18	0.02
DU172.17	0.05	0.04	>50	>50	0.29	<0.023	>50	0.55	>50	8.32	>50	>50	<0.023	0.23	0.1	0.04	>50	>50	>50	0.223	>50	>50	0.28	>50
DU422.01	0.78	>50	>50	>50	>50	1.65	>50	0.4	>50	>50	>50	>50	0.04	0.3	0.16	0.18	>50	>50	>50	>50	>50	>50	>50	>50
KER2008.12	24	0.27	6.98	6.8	0.25	1.28	>50	>50	>50	>50	>50	0.57	0.004	0.01	2.22	14.7	>50	8.33	3.78	0.301	0.58	>50	0.18	0.4
KER2018.11	3.79	0.53	2.01	>50	0.42	8.46	3.28	49.2	40	>50	23.8	0.83	0.001	0.004	>50	>50	0.000	0.003	>50	0.49	0.46	>50	0.51	0.23
MB201.A1	0.28	0.06	0.44	>50	0.46	2.21	27.4	>50	17.7	>50	22.1	0.17	0.01	0.06	0	0.02	0.46	2.49	1.68	0.061	0.17	0.28	0.04	0.07
MB539.2B7	15.1	0.22	2.49	>50	0.09	21.7	3.1	14	3.7	0.04	>50	0.4	0.02	0.06	>50	3.57	0.07	1.19	6.97	0.435	0.43	>50	0.26	0.25
PVO.04	3.08	0.35	>50	1.41	0.07	1.99	0.48	>50	>50	>50	>50	0.15	15	6.94	0.13	0.01	0.04	0.143	2.61	0.303	0.55	>50	0.19	2.23
Q168.a2	1.02	0.07	7.83	>50	0.05	18.7	0.3	>50	6.76	0.03	>50	0.14	0.02	0.08	>50	>50	0.49	0.86	5	0.057	0.15	>50	0.04	0.08
Q23.17	1.13	0.05	10.8	>50	0.02	0.13	0.27	>50	10.4	>50	>50	0.11	0	0.01	0	0.01	0	0.002	0.58	0.042	0.09	0.16	<0.023	0.04
Q259.17	4.77	0.02	16.1	>50	0.02	10.2	0.76	>50	10.6	>50	>50	0.05	0.03	0.05	>50	>50	3.95	45	>50	>50	0.06	>50	4.91	0.03
Q461.e2	1.72	0.16	13.4	>50	0.07	5.53	1.26	>50	>50	0.05	>50	0.21	4.62	2.53	>50	25.6	>50	16	7.93	0.334	0.38	>50	0.16	0.13
Q769.d22	0.89	0.01	0.61	>50	0.01	1.73	0.03	>50	1	>50	>50	0.01	0.07	0.01	>50	>50	>50	0.151	0.36	0.046	0.01	>50	0.04	0.01
Q842.d12	4.13	0.01	>50	>50	0	8.99	0.01	>50	1.46	>50	>50	0.02	0	0.02	0.02	0.03	0.02	0.067	0.11	0.011	0.01	>50	0.01	0.01
QH0692.42	0.69	1.04	2.22	4.99	0.28	1.6	2.63	0.79	25.2	7	>50	0.99	>50	>50	0.94	0.05	>50	>50	9.37	1.392	1.5	>50	0.94	45.3
REJO.67	0.16	0.08	0.3	>50	0.04	0.17	0.05	1.7	2.15	>50	>50	0.01	0.01	0.01	8.87	>50	0.21	0.0003	30	0.0003	0.05	0.13	0.05	0.02
RHPA.7	1.04	0.06	23.2	>50	0.02	13.3	5.1	0.13	8.53	0	>50	0.02	0.89	9.97	0.01	0.03	0.02	0.028	0.33	0.05	0.05	>50	0.13	22.1
RW020.2	1.93	0.03	7.55	>50	0.02	8.21	0.38	10.7	23.6	2.78	>50	0.14	0.16	0.11	0.002	0.01	>50	5.17	0.09	0.088	0.28	6.98	0.02	0.02
SC422.8	0.15	0.11	1.34	5.65	0.05	1.49	0.16	0.2	2.44	>50	17.1	0.03	2.19	0.54	0.1	2.41	1.45	0.027	1.46	0.073	0.12	>50	0.14	0.05
TH976.17	0.3	0.02	0.13	>50	0.03	0.21	11	>50	>50	0.06	28.3	0.12	>50	>50	>50	>50	>50	>50	1.23	0.021	0.13	>50	<0.023	0.03
THRO.18	0.21	1.6	>50	>50	2.8	1.77	19.7	0.96	>50	>50	>50	1.88	0.89	9.9	>50	>50	0	0.006	>50	>50	5.1	>50	37.9	17.6
TRJO.58	1.21	0.11	>50	>50	0.06	8.75	14.5	>50	>50	>50	>50	0.03	0.58	0.21	4.31	0.01	>50	>50	>50	0.088	0.07	>50	0.22	0.09
TRO.11	0.04	0.12	>50	0.36	0.03	0.6	9.97	>50	5.34	0.06	>50	1.04	4.06	41.5	0.01	0.02	1.86	0.029	17.8	0.2	0.3	0.55	0.04	15.5
UG037.8	0.13	0.04	0.2	>50	0.02	0.5	0.19	>50	1.76	>50	>50	0.06	0	0.02	0.07	0.02	1.63	2.33	0.78	0.045	0.09	>50	0.05	0.02
WITO.33	0.13	0.04	2.29	0.74	0.03	1.2	12.7	9.67	7.35	>50	18.3	0.04	0	0.01	0.79	>50	0	0	>50	0.631	0.11	>50	0.09	>50
ZM109.4	0.26	0.01	>50	>50	0.04	0.71	17.1	>50	21.2	8.15	>50	0.05	7.47	0.13	13.7	>50	>50	0.012	30.3	0	0.1	>50	0.03	0.24
ZM135.10a	0.1	0.48	>50	>50	0.07	0.03	24.5	>50	>50	>50	>50	0.28	>50	>50	1.5	30	>50	>50	12.2	>50	0.98	>50	0.36	>50
ZM197.7	0.07	0.53	35.7	>50	0.4	0.43	>50	>50	35.4	>50	>50	0.31	0.54	0.39	>50	>50	0.12	0.523	3.08	1.55	0.6	>50	0.61	0.18
ZM214.15	1.41	0.08	>50	>50	0.09	1.45	1.63	4.78	41.4	0.04	>50	0.13	>50	>50	0.68	1.44	>50	>50	11.5	0.701	0.7	>50	0.15	2.86
ZM249.1	0.72	0.04	>50	>50	0.04	2.75	10	2.73	7.23	>50	>50	0.04	0.04	0.04	>50	10.7	0.05	1.99	0.1	0.037	0.07	>50	0.04	0.03

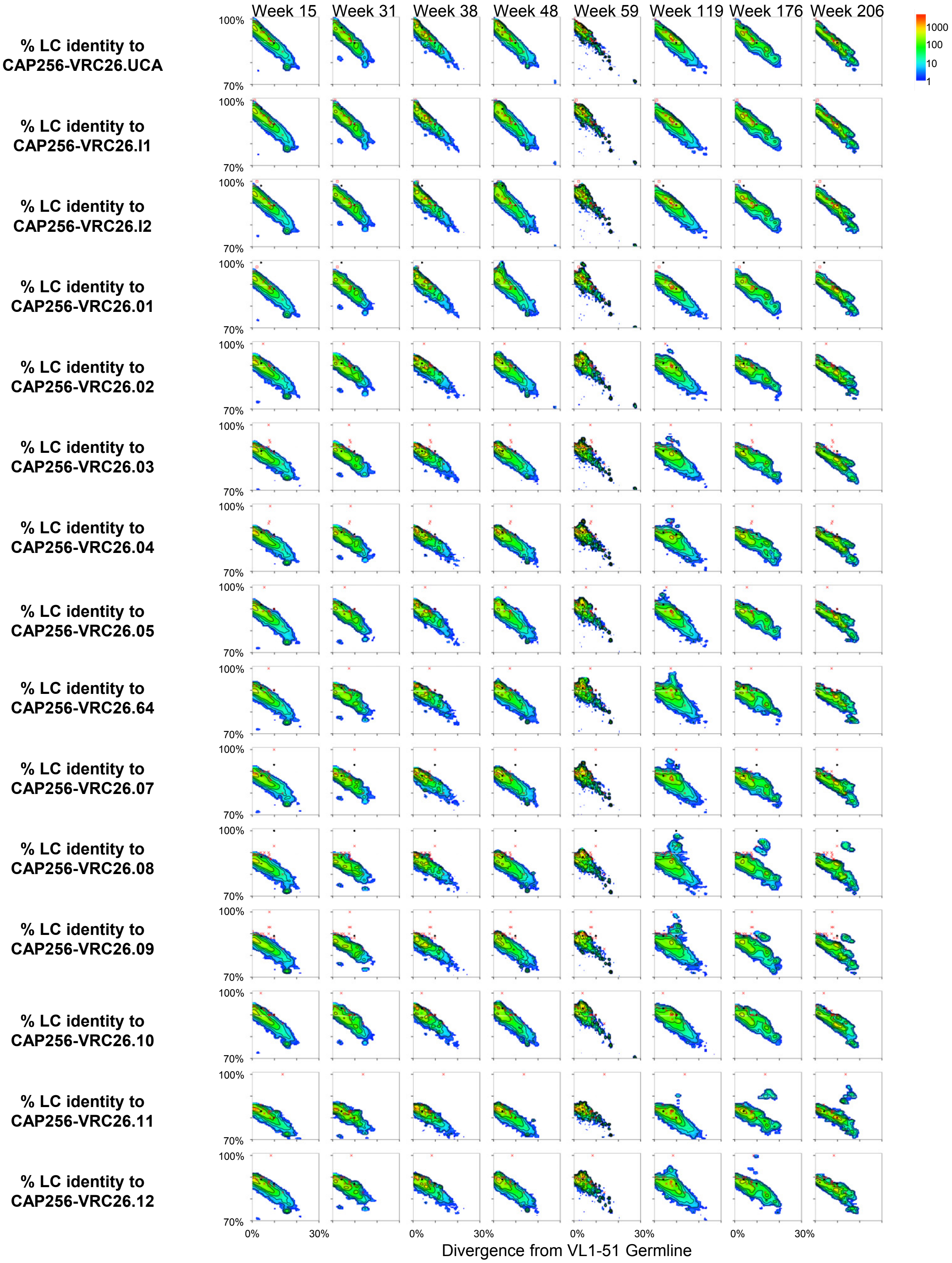
Supplementary Figure 3. Correlations of neutralization fingerprints. a, Correlation of neutralization fingerprints between CAP256-VRC26 antibodies and a panel of HIV-1 broadly neutralizing antibodies. VRC26.01, .07, and .12 were excluded due to low breadth. **b**. The neutralization data used to generate correlations shown in panel A. Data from Extended Data Figure 2A was also used.

Supplementary Figure 4A



Supplementary Figure 4A. Longitudinal heavy chain identity-divergence plots for all 12 isolated antibodies, UCA, and inferred intermediates I1 and I2. CAP256-VRC26.01 and CAP256-VRC26.08 are shown as black dots; all other isolated antibodies are shown as red Xes; UCA, I1, and I2 are shown as open red squares.

Supplementary Figure 4B



Supplementary Figure 4B. Longitudinal light chain identity-divergence plots for all 12 isolated antibodies, UCA, and inferred intermediates I1 and I2. CAP256-VRC26.01 and CAP256-VRC26.08 are shown as black dots; all other isolated antibodies are shown as red Xes; UCA, I1, and I2 are shown as open red squares. Unlike the heavy chain plots, most of the light chain plots do not show distinct islands, likely because light chains do not have the added junctional diversity of a D gene and thus share greater overall sequence homology, even among unrelated sequences.

Supplementary Figure 5

a

```
IGHV3-30*18      CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCTGAGACTCTCCTGTGCAGCCTCTGGA
IGHD3-3*01       ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
IGHJ3*02         ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
UCA_heavy        ..............................................................................

IGHV3-30*18      TTCACCTTCAGTAGCTATGGCATGCACTGGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGGTGGCAGTTATATCA
IGHD3-3*01       ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
IGHJ3*02         ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
UCA_heavy        ..............................................................................

IGHV3-30*18      TATGATGGAAGTAATAAATACTATGCAGACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCCAAGAACACG
IGHD3-3*01       ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
IGHJ3*02         ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
UCA_heavy        ..............................................................................

IGHV3-30*18      CTGTATCTGCAAATGAACAGCCTGAGAGCTGAGGACACGGCTGTGTATTACTGTGCGAAAGA~~~~~~~~~~~~~~~~
IGHD3-3*01       ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
IGHJ3*02         ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
UCA_heavy        ..............................................................TCTGGGAGAAAGCGAA

IGHV3-30*18      ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
IGHD3-3*01       ~~~~~~~~~~~~~~~~~~~~~GTATTACGATTTTTGGAGTGGTTATTATACC~~~~~~~~~~~~~~~~~~~~~~~~~~
IGHJ3*02         ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
UCA_heavy        AATGAAGAGTGGGCGACGGAT-.............C..T......-------CCCTGGCCAAGACCCACGGGGCGTGG

IGHV3-30*18      ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
IGHD3-3*01       ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
IGHJ3*02         ~~~~~TGATGCTTTTGATATCTGGGGCCAAGGGACAATGGTCACCGTCTCTTCA
UCA_heavy        TTGGA----.............................................
```

b

```
IGLV1-51*02      CAGTCTGTGTTGACGCAGCCGCCCTCAGTGTCTGCGGCCCCAGGACAGAAGGTCACCATCTCCTGCTCTGGAAGCAGC
IGLJ1*01         ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
UCA_light        ..............................................................................

IGLV1-51*02      TCCAACATTGGGAATAATTATGTATCCTGGTACCAGCAGCTCCCAGGAACAGCCCCCAAACTCCTCATCTATGAAAAT
IGLJ1*01         ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
UCA_light        ..............................................................................

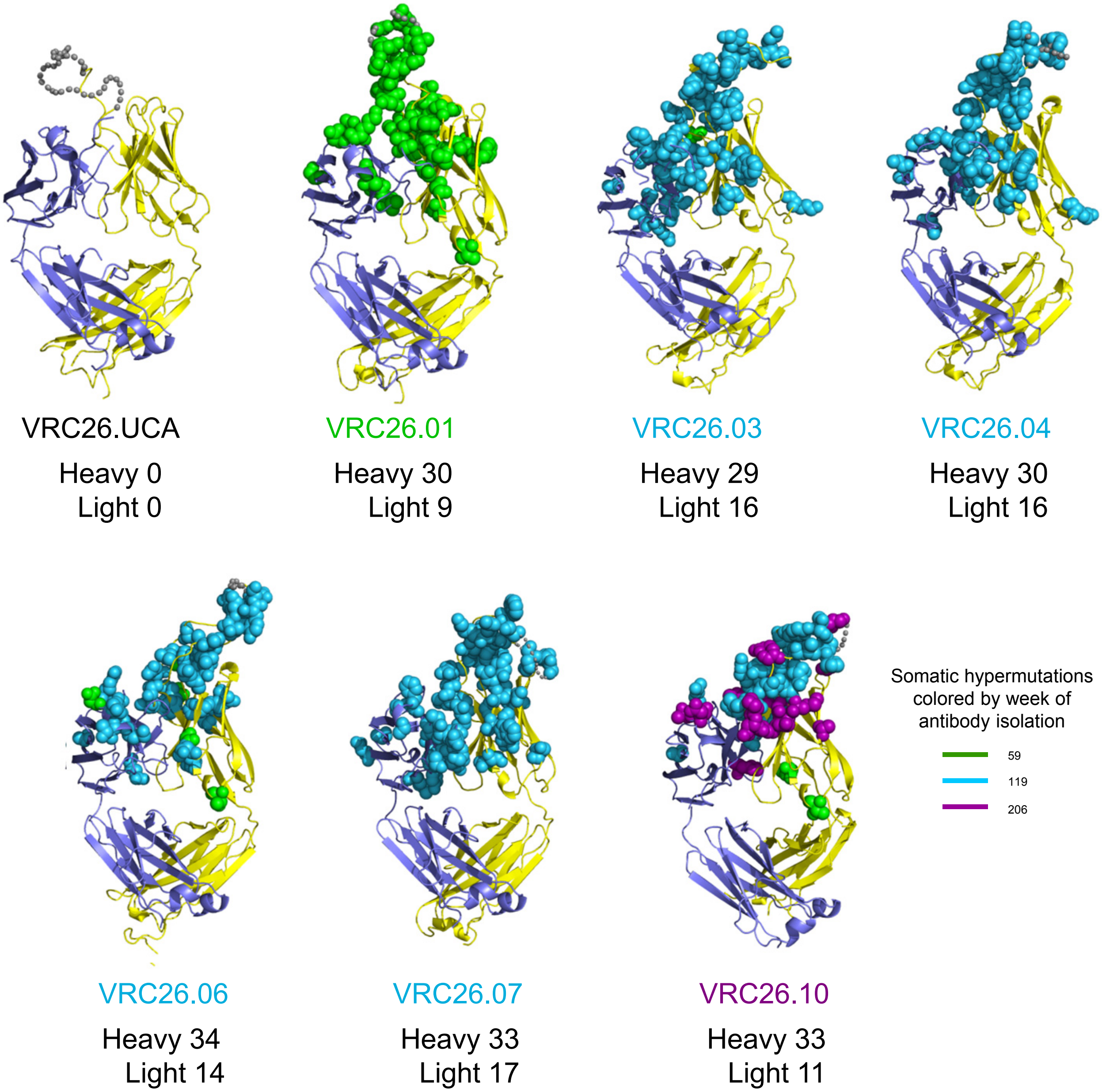
IGLV1-51*02      AATAAGCGACCCTCAGGGATTCCTGACCGATTCTCTGGCTCCAAGTCTGGCACGTCAGCCACCCTGGGCATCACCGGA
IGLJ1*01         ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
UCA_light        ..............................................................................

IGLV1-51*02      CTCCAGACTGGGGACGAGGCCGATTATTACTGCGGAACATGGGATAGCAGCCTGAGTGCTGG---~~~~~~~~~~~~~
IGLJ1*01         ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~TTATGTCTTCGGA
UCA_light        ..............................................................CGG---..........

IGLV1-51*02      ~~~~~~~~~~~~~~~~~~~~~~~~
IGLJ1*01         ACTGGGACCAAGGTCACCGTCCTA
UCA_light        ........................
```

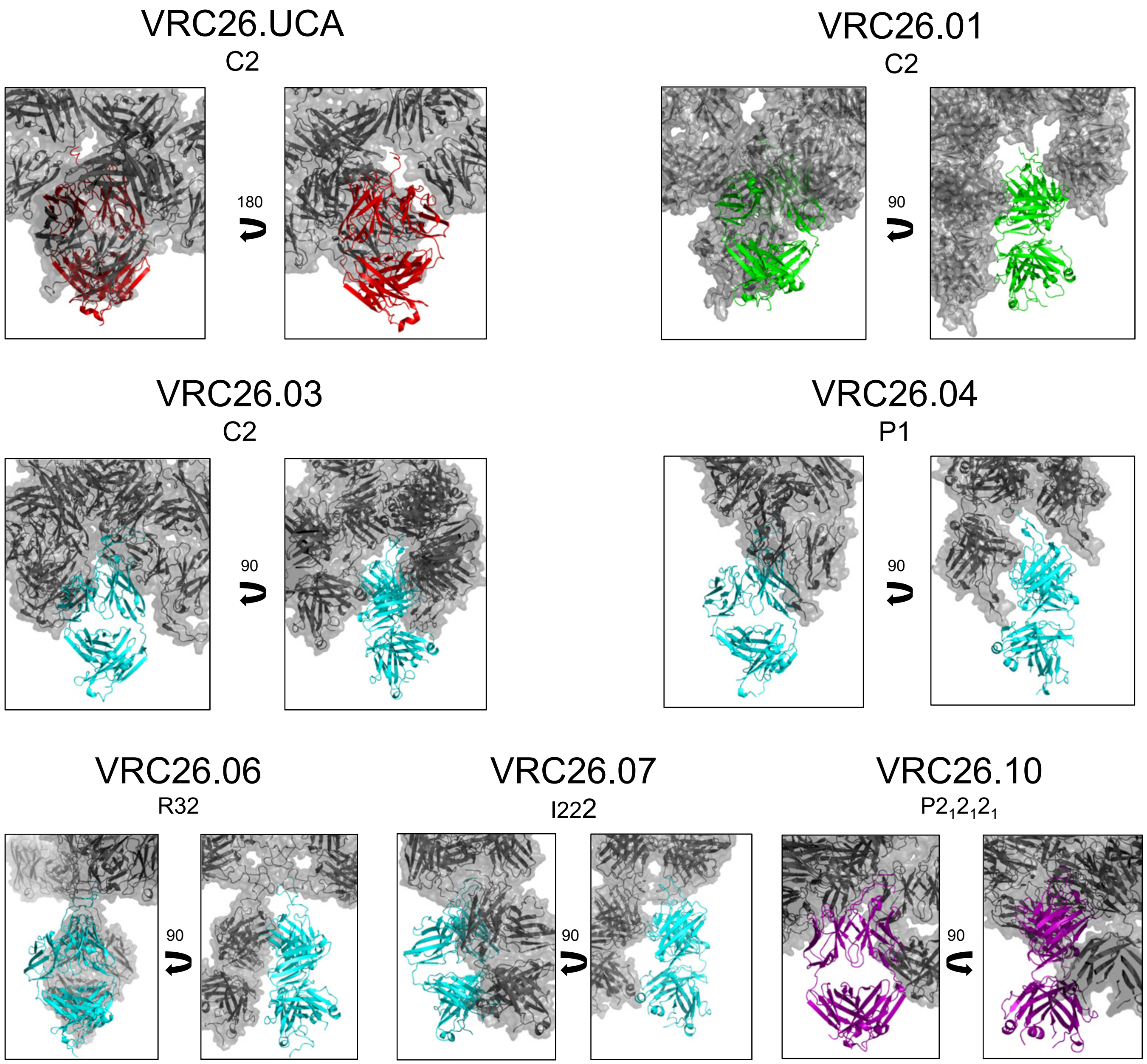
Supplementary Figure 5. VDJ recombination analysis for CAP256-VRC26 lineage. Nucleotide sequence and recombination analysis of the calculated unmutated common ancestor (UCA) of the CAP256-VRC26 lineage. **a**, heavy chain. **b**, light chain. Nucleotides that were excised from the germline genes by recombination are indicated by red italics. Predicted P-insertions are in bold font and N-insertions are underlined. The heavy chain UCA had a complete 35 amino acid CDR H3, formed from a single D gene and N-insertions of 34 and 31 nucleotides in length.

Supplementary Figure 6A



Supplementary Figure 6A. Full Fab structures of CAP256-VRC26 antibodies highlighting somatic hypermutation by week of appearance. The structures of antigen-binding fragments of CAP256-VRC26 antibodies are depicted in ribbon diagram representation with heavy chains in yellow and light chains in blue. Somatic hypermutations are shown in all atom representation, and colored according to the week post-infection from which they first appeared in isolated antibodies VRC26.01-12 (week 59, green; week 119, cyan; week 206, purple). Grey dashes indicate disordered regions of the CDR H3. The numbers of heavy and light chain mutations from the UCA are shown below the structures. See Fig. 4 for phylogenetic placement.

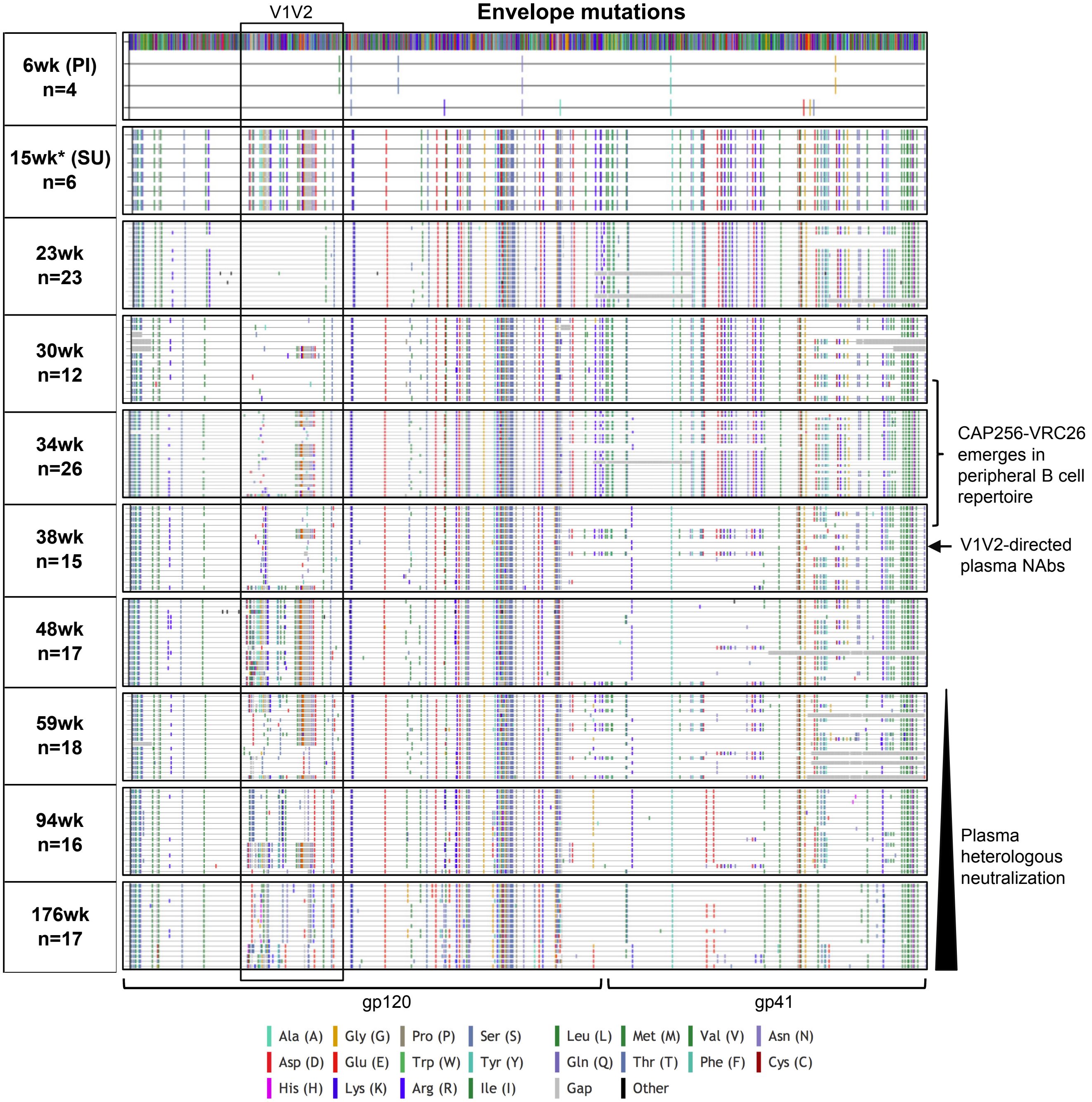
Supplementary Figure 6B



Supplementary Figure 6B. Crystal packing of CAP256-VRC26 structures. Each of the VRC26 Fab crystal structures are shown as ribbon diagrams. Neighboring molecules which pack close to the CDR H3 are displayed as grey ribbon diagrams with transparent surface representations. The space group for each structure is noted. Despite the variety of space groups and packing contacts, the five structures from later time points (cyan and purple) all display CDR H3 loops that protrude over the heavy chain.

Supplementary Figure 7

Supplementary Figure 7. Logograms of CDR H3 sequences extracted from the heavy chain phylogenetic tree in Fig. 3c, segregated by time point and subfamily. The letters in each stack represent the amino acids observed at that position, and the height of each letter is proportional to its frequency in the population. The cysteine residues that are part of a conserved disulfide bond are shown in yellow. Grey bars indicate gaps. **a,** CDR H3 sequences from the branch of the tree that includes CAP256-VRC26.01. **b,** CDR H3 sequences from the branch of the tree that includes all of the other isolated antibodies, CAP256-VRC26.02-12.



Supplementary Figure 8. HIV-1 envelope gp160 sequences amplified from CAP256 donor, shown in highlighter format. The primary infecting virus (PI) is designated as master (amino acid colors indicated in key) and the V1V2 region is boxed. The development of the CAP256-VRC26 antibody lineage, V1V2 plasma directed neutralizing antibodies, and plasma heterologous neutralization, are indicated on the right. Asterisk denotes sequences amplified with strain-specific primers matching the SU virus.

Supplementary Figure 9

```
 6     CAP256.1mo.C7J    CVKLTPLCVT LNCTTAK-G- -IN------S TDNANAT-KK PNEEIKNCSF NTITEVRDKQ KKEYALFYRL DLVSLNEGDS EGNSSRSGNF STYRLINC
week   CAP256.1mo.F7J    .......... .......-.- -..------. .......-.. .......... .......... .......... .......... .......... ........
       CAP256.1mo.1      .......... .......-.- -..------. .......-.. .......... .......... .......... .......... .......... ........
       CAP256.1mo.F1     .......... .......-.- -..------. .......-.. .......... .......... .......... .......... .......... ........

 15    CAP256.3mo.C9     .......... ...SD..VN- -..------A .Y.G------ TR........ .AT..L...K .......... .I.P..KEG- -------N.N .E......
week   CAP256.3mo.B3     .......... ...SD..VN- -..------A .Y.G------ TR........ .AT..L...K .......... .I.P..KEG- -------N.N .E......
       CAP256.3mo.C7     .......... ...SD..VN- -..------A .Y.G------ TR........ .AT..L...K .......... .I.P..KEG- -------N.N .E......
       CAP256.3mo.C4     .......... ...SD..VN- -..------A .Y.G------ TR........ .AT..L...K .......... .I.P..KEG- -------N.N .E......
       CAP256.3mo.C1     .......... ...SD..VN- -..------A .Y.G------ TR........ .AT..L...K .......... .I.P..KEG- -------N.N .E......
       CAP256.3mo.A5     .........X ...SD..VN- -..------A .Y.G------ XR........ .AT..L...K .......... .I.P..KEG- -------N.N .E......

       CAP256.5mo.14     .......... .......-.- -..------. .......-.. .......... .......... .......... .......... .......... ........
       CAP256.5mo.19     .......... .......-.- -..------. .......-.. .......... .......... .......... .......... .......... ........
       CAP256.5mo.17     .......... .......-.- -..------. .......-.. .......... .......... .......... .......... .......... ........
       CAP265.5mo.10     .......... .......-.- -..------. .......-.. .......... .......... .......... .......... .......... ........
       CAP256.5mo.23     .......... .......-.- -..------. .......-.. .......... .......... .......... .......... .......... ........
       CAP256.5mo.21     .......... .......-.- -..------. .......-.. .......... .......... .......... .......... .......... ........
       CAP256.5mo.13     .......... .......-.- -..------. .......-.. .......... .......... .......... .......... .......... ........
 23    CAP256.5mo.11     .......... .......-.- -..------. .......-.. .......... .......... .......... .......... .......... ........
week   CAP256.5mo.7      .......... .......-.- -..------. .......-.. .......... .......... .......... .......... .......... ........
       CAP256.5mo.22     .......... .......-.- -..------. .......-.. .......... .......... .......... .......... .......... ........
       CAP256.5mo.24     .......... .......-.- -..------. .......-.. .......... .......... .......... .......... .......... ........
       CAP256.5mo.16     .......... .......-.- -..------. .......-.. .......... .......... .......... .......... .......... ........
       CAP256.5mo.20     .......... .......-.- -..------. .......-.. .........L .......... .......... .......... .......... ........
       CAP256.5mo.2      .......... .......-.- -..------. .......-.. .......... .......... .......... .......... .......... ........
       CAP256.5mo.12     .......... .......-.- -..------. .......-.. .......... .......... .......... .......... .......... ........
       CAP256.5mo.9      .......... .......-.- -..------. .......-.. .......... .......... .......... .......... .......... ........
       CAP256.5mo.6      .......... .......-.- -..------. .......-.. .......... .......... .......... .......... .......... ........
       CAP256.5mo.1      .......... .......-.- -..------. .......-.. .......... .......... .......... .......... .......... ........
       CAP256.5mo.18     .......... .......-.- -..------. .......-.. .......... .......... .......... .......... .......... ........
       CAP256.5mo.4      .......... .......-.- -..------. .......-.. S......... .......... .......... .......... .......... ........
       CAP256.5mo.15     .......... .......-.- -..------. .......-.. .......... .......... .......... .......... .......... ........

       CAP256.6mo.1      .......... .......-.- -..------. .......-.. .......... .......... .......... .......... ....N..... ........
       CAP256.6mo.9      .......... .......-.- -V.------. ......A-.. .......... .......... .......... .......... .......... ........
       CAP256.6mo.3      .......... .......-.- -.S------. .......-.. .......... .......... .......... .......... .......... ........
       CAP256.6mo.2      .......... .......-.- -..------. .......-.. .......... .......... .......... .......... .......... ........
 30    CAP256.6mo.1.JM   .......... .......-.- -..------. .......-.. .......... .......... .......... .......... .......... ........
week   CAP256.6mo.3.JM   .......... .......-.- -..------. .......-.. .......... .......... .......... .......... .......... ........
       CAP256.6mo.4.JM   .......... .......-D- -..------. .......-.. .......... .......... .......... .......... .......... ........
       CAP256.6mo.5.JM   .......... .......-.- -..------. .......-.. .......... .......... .......... .......... ......Y... ........
       CAP256.6mo.6.JM   .......... .......-.- -..------. I......-.. .......... .......... .......... .......... .......... ........
       CAP256.6mo.7.JM   .......... .......-.- -..------. ..K....-.. .......... .......... .......... .......... .......... ........
       CAP256.6mo.4      .......... .......-.- -..------. .....T.-.. .......... .......... .......... .I.P..KEG- -------N.N .E......
       CAP256.6mo.8      .......... .......-.- -..------. .......-.. .......... .......... .R........ .I.P..KEG- -------N.N .E...T..

       CAP256.8mo.4      .......... .......-.- -..------. .....T.-.. .......... .......... .......... .......... ...Y...... ........
       CAP256.8mo.5      .......... .......-.- -..------. ....Y..-.. .......... .......... .......... .I.P.SGEG- -------N.N .E......
       CAP256.8mo.1      .......... .......-.- -..------. I......-.. .......... .......... .......... .I.P.SGEG- -------N.N .E......
       CAP256.8mo.2      .......... I......-.- -..------. .....V.-.. .......... .......... .......... .I.P.SGEG- -------N.N .E......
       CAP256.8mo.6      .......... .......-.- -..------. .....D.-.. .......... .......... .......... .I.P.SGEG- -------N.N .E......
       CAP256.8mo.9      .......... .......-.- -..------. ..K....-.. .......... .......... .......... .......... K......... ........
       CAP256.8mo.20     .......... .......-.- -..------. ....K..K.- .......... .......... .......... .........A .......... ........
       CAP256.8mo.25     .......... .......-.- -..------. .......K.- .......... .......... .......... .......... .....K.... ........
       CAP256.8mo.18     .......... .......-.- -..------. ..K....-.. .......... .......... .......... .......... ....N..... ........
       CAP256.8mo.15     .......... .......-.- -..------. .......-.. .......... .......... .......... .......... ...F...... ........
       CAP256.8mo.27     .......... .......D-- -..------. .......-.. .......... .......... .......... .......... ...F...... ........
 34    CAP256.8mo.14     .......... .......-.- -..------. A......-.. .......... .......... .......... .......... ...Y...... ........
week   CAP256.8mo.33     .......... .......-.- -T.------. ..D....-.. .......... .......... .......... ........N. .......... ........
       CAP256.8mo.32     .......... .......-.- -..------. ....D..-.. .......... .......... .......... ........N. .......... ........
       CAP256.8mo.11     .......... .......-.- -..------. .......-.. .......... .......... .......... .I.P.SGEG- -------N.N .E......
       CAP256.8mo.13     .......... .......-.- -..------. .......-.. .......... .......... .......... .I.P.SGEG- -------N.N .E......
       CAP256.8mo.19     .......... .......-.- -..------. ....Y..-.. .......... .......... .......... .I.P.SGEG- -------N.N .E......
       CAP256.8mo.16     .......... .......-.- -..------. I......-.. .......... .......... .......... .I.P.SGEG- -------N.N .K......
       CAP256.8mo.21     .......... .......-.- -..------. I......-.. .......... .......... .......... .I.P.SGEG- -------N.N .E......
       CAP256.8mo.22     .......... .......-.- -..------. N......-.. .......... .......... .......... .I.P.SGEG- -------N.N .K......
       CAP256.8mo.23     .......... .......-.- -..------. N......-.. .......... .......... .......... .I.P.SGEG- -------N.N .K......
       CAP256.8mo.29     .......... .......-.- -..------ ......D.-.. .......... .......... .......... .I.P.SGEG- -------N.N .E......
       CAP256.8mo.30     .......... .......-.- -..------ ........-.. .......... .......... .......... .I.P.SGEG- -------N.N .E......
       CAP256.8mo.8      .......... .......-.- -..------ ........-.. .......... .......... .......... .I.P.SGEG- -------N.N .E......
       CAP256.8mo.26     .......... .......-.- -..------ .....K..K.- .......... .......... .......... .I.P..KEG- -------N.N .E......
       CAP256.8mo.31     .......... ...SD..VN- -.D------ A.Y.G------ TR........ .AT..L...I .......... .I.P..KEG- -------N.N .E......
```

Supplementary Figure 9. HIV-1 envelope V1V2 sequences amplified from CAP256 donor, by week, with the primary infecting virus (PI) designated as master. Sequences cloned for neutralization assays are underlined. The location of key residues between 160 and 169 is highlighted.

Supplementary Figure 9

6 week

```
CAP256.1mo.C7J     CVKLTPLCVT LNCTTAK-G- -IN------S TDNANAT-KK PNEEIKNCSF NTITEVRDKQ KKEYALFYRL DLVSLNEGDS EGNSSRSGNF STYRLINC
```

15 week

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CAP256.3mo.C9      .......... ...SD..VN- -..------A .Y.G------ TR........ .AT..L...K .......... .I.P..KEG- -------N.N .E......
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38 week

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CAP256.9mo.26      .......... .......-.- -..------ ....T.T.K.- .......... .......... .......... .......... ....N..... ........
CAP256.9mo.39      .......... .......-.- -..------ ...K....R.- .......... .......... .......... .......... ....N..... ........
CAP256.9mo.19      .......... .......-.- -..------ R....V.K.- .......... .......... .......... .......... ....N..... ........
CAP256.9mo.14      .......... .......-.- -..------ .....E..K.- .......... .......... .......... .......... ...F...... ........
CAP256.9mo.6       .......... .......-.- -..------ .....E..K.- .......... .......... .......... .......... ...F...... ........
CAP256.9mo.20      .......... .......-.- -..------ .....E..K.- .......... .......... .......... .......... ...F...... ........
CAP256.9mo.8       .......... .......-.- -..------ ........K.- .......... .......... .......... .......... ...F...... ........
CAP256.9mo.21      .......... .......-.- -..------ .....S..K.- .......... .......... .......... .......... ----...... ........
CAP256.9mo.38      .......... .......-.- -..------ ...T..T.K.- .......... .......... .......... ........E. .......... ........
CAP256.9mo.10      .......... .......-.- -..------ ......T.K.- .......... .......... .......... ........N. .......... ........
CAP256.9mo.34      .......... .......-.- -..------ ......V.K.- .......... .......... .......... ........N. .......... ........
CAP256.9mo.40      .......... .......-.- -..------ ......V.K.- .......... .......... .......... .........Y .......... ........
CAP256.9mo.16      .......... .......-.- -..------ ......V.K.- .......... .......... .......... .I.P.SGEG- -------N.N .E......
CAP256.9mo.17      .......... .......-.- -.D------ ......V.K.- .......... .......... .......... .I.P.SGEG- -------N.N .E......
CAP256.9mo.43      .......... ...SD..VN- -.S------ A.Y.G------ TR........ .AT..L...I .......... .I.P..KEG- -------N.N .E......
```

48 week

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CAP256.12mo.17     .......... .....----- -..------ .....E..-.. .......... .......... .......... .I.P.SGEG- -------N.N .E......
CAP256.12mo.10     .......... .......-.- -.DSTDN-- A.A-----T.. .......... ..T....... .......... .I.P.SGEG- -------N.N .E......
CAP256.12mo.13     .....X.... .......-.- -..STDNAN AIY.G------ TR........ .AT..L...I .......... .I.P.SGEG- -------N.N .E......
CAP256.12mo.12     .......... ...SD..VN- -VT------ A.Y.G------ TR........ .AT..L.... .......... .I.P.SGEG- -------N.N .E......
CAP256.12mo.9      .......... ...SD..VN- --------- A.Y.G------ TR........ .AT....... .......... .I.P.SGEG- -------N.N .E......
CAP256.12mo.2      .......... ...SD.--N- -..------ A.Y.G------ TR........ .AT..L...I .......... .I.P.SGEG- -------N.N .E......
CAP256.12mo.14     .......... ...SD..VN- --------- A.Y.G------ TR........ .AT..L...I .......... .I.P.SGEG- -------N.N .E......
CAP256.12mo.15     .......... ...SD..VN- -.S------ A.Y.G------ TR........ .AT..L...I .......... .I.P.SGEG- -------N.N .E......
CAP256.12mo.16     .......... ...SD..VN- -.S------ A.Y.G------ TR........ .AT..L...I .......... .I.P.SGEG- -------N.N .E......
CAP256.12mo.18     .......... ...SD..VN- -.S------ A.Y.G------ TR........ .AT..L...I .......... .I.P.SGEG- -------N.N .E......
CAP256.12mo.1      .......... ...SD..VN- --------- A.Y.G------ TR........ .AT..L...I R......... .I.P.SGEG- -------N.N .E......
CAP256.12mo.11     .......... ...SD..VN- --------- A.Y.G------ TR........ .AT..L...I R......... .I.P.SGEG- -------N.N .E......
CAP256.12mo.19     .......... ...SD..VN- --------- A.Y.G------ TR........ .AT..L...I R......... .I.P.SGEG- -------N.N .E......
CAP256.12mo.5      .......... ...SD..VN- --------- A.Y.G------ TR........ .AT..L...I R......... .I.P.SGEG- -------N.N .E......
CAP256.12mo.8      .......... ...SD..VN- --------- A.Y.G------ TR........ .AT..L...I R......... .I.P.SGEG- -------N.N .E......
CAP256.12mo.5      .......... ...SD..VN- -.T------ AIH.G------ TR........ .AT....... .R........ .I.P.SGEG- -------N.N .E......
CAP256.12mo.3      .......... ...SD..GNE N-------- V.Y.G------ TR........ .AT.....I R......... .I.P.SGEG- -------N.N .E......
CAP256.12mo.4      .......... ...SD..VNE S-------- A.Y.G------ TR........ ...A...... .......... .I.P.SGEG- -------N.N .E......
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59 week

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CAP256.14mo.10a    ........I. .......-.- -..------ ....T..-.. .......... ..T....... .......... .......... -...N..... ........
CAP256.14mo.4a     ........I. ....I..-.- -..------ ..G..T..-.. .......... ..T....... .......... ........N. ....N..... ........
CAP256.14mo.6a     .......... .....IN--- --------- ...T....-.. .......... T......... .......... ........E. ....N..... ........
CAP256.14mo.11a    .......... ....------ -..------ ...T....-.. .......... .......... .......... ........E. ....N..... ........
CAP256.14mo.5a     .......... ....------ -..------ ...T....-.. .......... .......... .......... ........E. ....N..... ........
CAP256.14mo.7a     .......... ....------ -..------ ...T....-.. .......... .......... .......... ........E. ....N..... ........
CAP256.14mo.12a    .......... .......-D- -..------ ......V.-.. .......... .......... .......... .I.P.SGEG- -------D.N .E......
CAP256.14mo.9a     .......... .......-D- -..------ ........-I. .T........ ..T....... .......... .I.P.SGEG- -------N.N .E......
CAP256.14mo.2b     .......... .......-D- -..------ ....S..-.. .......... D......... .......... .I.P.SGEG- -------N.N .E......
CAP256.14mo.5b     .......... .......-D- -..------ ........-I. .T........ ..T....... .......... .I.P.SGEG- -------N.N .E......
CAP256.14mo.7b     .......... .......-D- -..------ ....I..-.. .......... ..T..L...I .......... .I.P.SGKG- -------N.N .E......
CAP256.14mo.6b     .......... .......-D- -..------ ........-I. .......... ..T....... .......... .I.P.SGEG- -------N.N .E......
CAP256.14mo.13B    .......... .......-D- -..------ ........-I. .......... ..T....... .......... .I.P.SGEG- -------N.N .E......
CAP256.14mo.10b    .......... ...SD.N--- -..------ A.Y.G------ TR........ .AT.....I .......... .I.P.SGEG- -------N.N .E......
CAP256.14mo.4b     .......... ...SD.N--- --------- A.Y.G------ TR........ .AT....... .......... .I.P.SGEG- -------N.N .E......
CAP256.14mo.2a     .......... ...SDVN--- -..------ A.Y.G------ TR........ .ATS.L...E .......... .I.P.SGEG- -------N.N .E......
CAP256.14mo.1a     .......... ...SD.N--- -..------ A.Y.G------ TR........ SAT..L...I .......... .I.P.SGEG- -------N.N .E......
CAP256.14mo.8b     .......... ...SD.NV-- --.------ A.Y.G------ TR........ .......... .E........ .I.P.SGEG- -------N.N .E......
```

Supplementary Figure 9

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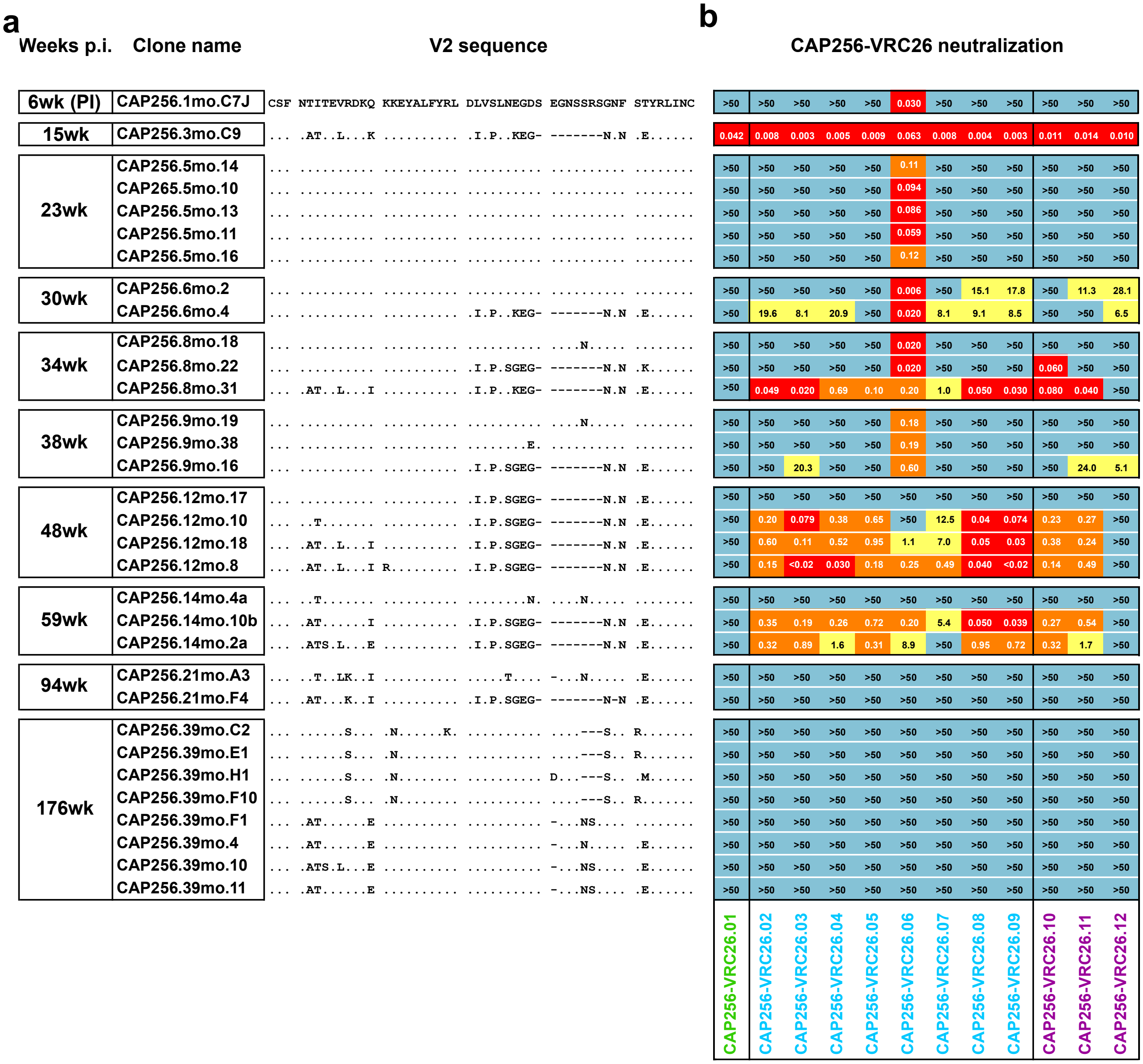
6 week
CAP256.1mo.C7J     CVKLTPLCVT LNCTTAK-G- -IN------S TDNANAT-KK PNEEIKNCSF NTITEVRDKQ KKEYALFYRL DLVSLNEGDS EGNSSRSGNF STYRLINC

15 week
CAP256.3mo.C9      .......... ...SD..VN- -..------A .Y.G------ TR........ .AT..L...K .......... .I.P..KEG- -------N.N .E......

94 week
CAP256.21mo.D12    .......... .....IN-ST T..------ ........-I. .......... ..T..LK..I .......... .......... -...N..... .E......
CAP256.21mo.A11b   .......... .....IN-ST T..------ ...T....-I. .......... .IT......I .......... .......... -...N..... .E......
CAP256.21mo.A3     .......... .....IN-ST T..------ ........-I. .......... ..T..LK..I .......... .....T.... -...N..... .E......
CAP256.21mo.A6     .......... .....IN-ST T..------ ........-I. .......... ..T..LK..I .......... .....T.... -...N..... .E......
CAP256.21mo.A1     .......... .....IN-ST T..------ ........-I. .D........ ..T..LK..I .......... .......... -...N..... .E......
CAP256.21mo.F1     .......... .....IN-ST T..------ ........-I. .......... ..T..LK..I .......... .......... -...N..... .E......
CAP256.21mo.C4     .......... .....IN-ST T..------ ........-I. .......... ..T..LK..I .......... .......... -...N..... .E......
CAP256.21mo.B2     .......... .....IN-ST T..------ ........-I. .......... ..T..LK..I .......... .......... -...N..... .E......
CAP256.21mo.E12    .......... .....IN-ST T..------ ........-I. .......... ..T..LK..I .......... .......... -...N..... .E......
CAP256.21mo.B10    .......... .....IN-ST T..------ ........-I. .......... ..T..LK..I .......... .......... -...N..... .E......
CAP256.21mo.F4     .......... ...SD.N--- ---------- T.Y.G------ TR..T..... .AT...K..I .......... .I.P.SGEG- -------N-N .E......
CAP256.21mo.C1     .......... ...SD.N--- ---------- T.Y.G------ TR..T..... .AT...K..I .......... .I.P.SGEG- -------N-N .E......
CAP256.21mo.D6     .......... ...SD.N--- -.T------ VAY.G------ TR........ .AT...K..I .......... .I.P.SGEG- -------N-N .E......
CAP256.21mo.C2     .......... ...SD.N--- ---------- T.Y.G------ TR..T..... .AT...K..I .......... .I.P.SGEG- -------N-N .E......
CAP256.21mo.A1     .......... ...SD.N--- ---------- T.Y.G------ TR..T..... .AT...K... .......... .I.P.SGEG- -------K.N .E......
CAP256.21mo.A11    .......... .......-D- -..------ ......V.--- T......... .......... .N........ .......... ....---S.. R.......

176 week
CAP256.39mo.C2     .......... .......-D- -..------ ....V.V.--- T......... ......S... .N......K. .......... ....---S.. R.......
CAP256.39mo.B1     .......... .......-D- -..------ ....V.V.--- T......... ......S... .N......K. .......... ....---S.. R.......
CAP256.39mo.E1     .......... .......-D- -T.------ ...K..V.--- T......... ......S... .N........ .......... ....---S.. R.......
CAP256.39mo.H1     .......... .......-D- -..------ ...HV.V.--- T......... ......S... .N........ .......... D...---S.. .M......
CAP256.39mo.F10    .......... .......-D- -S.------ ...H..V.--- T......... ......S... .N........ .......... ....---S.. R.......
CAP256.39mo.6      .......... .......-D- -N.------ ...H..V.--- T......... ......S... .N........ .......... ....---S.. R.......
CAP256.39mo.8      .......... .......-D- -T.------ ...H..V.--- T......... ......S... .N........ .......... ....---S.. R.......
CAP256.39mo.12     .......... .......-D- -..------ G..H..V.--- T......... ......S... .N........ .......... ....---S.. R.......
CAP256.39mo.13     .......... .......-D- -..------ ..G...V.--- T......... ......S... .N........ .......... ....---S.. R.......
CAP256.39mo.17     .......... .......-D- -..------ ......V.--- T......... ......S... .N........ .......... D...---S.. .M......
CAP256.39mo.18     .......... .......-D- -..------ ..N...V.--- T......... ......S... .N........ .......... D...---S.. .M......
CAP256.39mo.20     .......... .......-D- --.------ ...H..V.--- TK........ ......S... .N........ .......... ....---S.. R.......
CAP256.39mo.F1     .......... ....HIN-ST T..------ ...TV..YNG AR........ .AT......E .......... .......... -...NS.... ........
CAP256.39mo.4      .......... ....HIN-ST T..------ ...TV..YNG AR........ .AT......E .......... .......... -...N..... .E......
CAP256.39mo.22     .......... ...SDV.--- -..------ V.Y.G------ TK...R.... .AT......E .......... .......... -...NS.... .E......
CAP256.39mo.10     .......... ...SEV.--- -..------ V.Y.G------ TK...R.... .ATS.L...E .......... .......... -...NS.... .E......
CAP256.39mo.11     .......... ...SD.N--- -RT------ VAY.G------ TR........ .AT......E .......... .......... -...NS.... .E......
```

Supplementary Figure 10

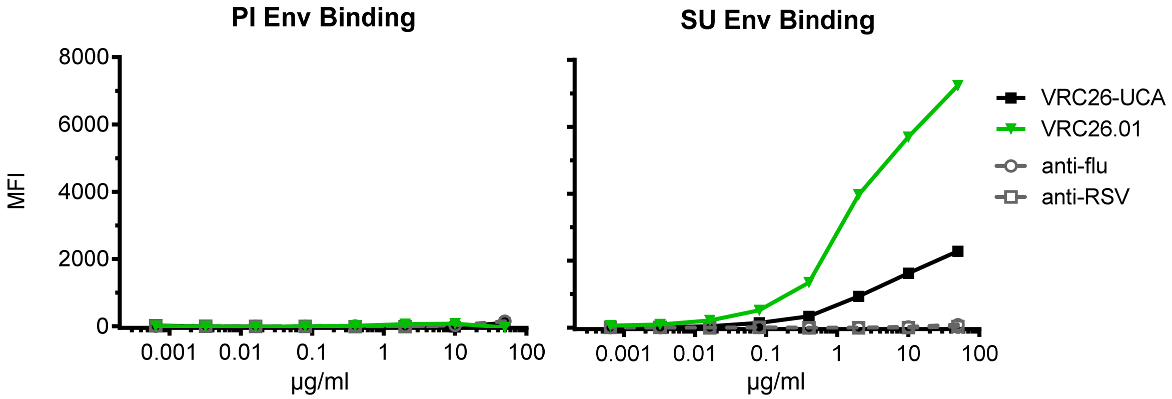


a

b

Weeks p.i.	Clone name	V2 sequence	CAP256-VRC26 neutralization											
			CAP256-VRC26.01	CAP256-VRC26.02	CAP256-VRC26.03	CAP256-VRC26.04	CAP256-VRC26.05	CAP256-VRC26.06	CAP256-VRC26.07	CAP256-VRC26.08	CAP256-VRC26.09	CAP256-VRC26.10	CAP256-VRC26.11	CAP256-VRC26.12
6wk (PI)	CAP256.1mo.C7J	`CSF NTITEVRDKQ KKEYALFYRL DLVSLNEGDS EGNSSRSGNF STYRLINC`	>50	>50	>50	>50	>50	0.030	>50	>50	>50	>50	>50	>50
15wk	CAP256.3mo.C9	`... .AT..L...K .......... .I.P..KEG- -------N.N .E......`	0.042	0.008	0.003	0.005	0.009	0.063	0.008	0.004	0.003	0.011	0.014	0.010
23wk	CAP256.5mo.14	`... .......... .......... .......... .......... ........`	>50	>50	>50	>50	>50	0.11	>50	>50	>50	>50	>50	>50
	CAP265.5mo.10	`... .......... .......... .......... .......... ........`	>50	>50	>50	>50	>50	0.094	>50	>50	>50	>50	>50	>50
	CAP256.5mo.13	`... .......... .......... .......... .......... ........`	>50	>50	>50	>50	>50	0.086	>50	>50	>50	>50	>50	>50
	CAP256.5mo.11	`... .......... .......... .......... .......... ........`	>50	>50	>50	>50	>50	0.059	>50	>50	>50	>50	>50	>50
	CAP256.5mo.16	`... .......... .......... .......... .......... ........`	>50	>50	>50	>50	>50	0.12	>50	>50	>50	>50	>50	>50
30wk	CAP256.6mo.2	`... .......... .......... .......... .......... ........`	>50	>50	>50	>50	>50	0.006	>50	15.1	17.8	>50	11.3	28.1
	CAP256.6mo.4	`... .......... .......... .I.P..KEG- -------N.N .E......`	>50	19.6	8.1	20.9	>50	0.020	8.1	9.1	8.5	>50	>50	6.5
34wk	CAP256.8mo.18	`... .......... .......... .......... ....N..... ........`	>50	>50	>50	>50	>50	0.020	>50	>50	>50	>50	>50	>50
	CAP256.8mo.22	`... .......... .......... .I.P.SGEG- -------N.N .K......`	>50	>50	>50	>50	>50	0.020	>50	>50	>50	0.060	>50	>50
	CAP256.8mo.31	`... .AT..L...I .......... .I.P..KEG- -------N.N .E......`	>50	0.049	0.020	0.69	0.10	0.20	1.0	0.050	0.030	0.080	0.040	>50
38wk	CAP256.9mo.19	`... .......... .......... .......... ....N..... ........`	>50	>50	>50	>50	>50	0.18	>50	>50	>50	>50	>50	>50
	CAP256.9mo.38	`... .......... .......... ........E. .......... ........`	>50	>50	>50	>50	>50	0.19	>50	>50	>50	>50	>50	>50
	CAP256.9mo.16	`... .......... .......... .I.P.SGEG- -------N.N .E......`	>50	>50	20.3	>50	>50	0.60	>50	>50	>50	>50	24.0	5.1
48wk	CAP256.12mo.17	`... .......... .......... .I.P.SGEG- -------N.N .E......`	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50
	CAP256.12mo.10	`... ..T....... .......... .I.P.SGEG- -------N.N .E......`	>50	0.20	0.079	0.38	0.65	>50	12.5	0.04	0.074	0.23	0.27	>50
	CAP256.12mo.18	`... .AT..L...I .......... .I.P.SGEG- -------N.N .E......`	>50	0.60	0.11	0.52	0.95	1.1	7.0	0.05	0.03	0.38	0.24	>50
	CAP256.12mo.8	`... .AT..L...I R......... .I.P.SGEG- -------N.N .E......`	>50	0.15	<0.02	0.030	0.18	0.25	0.49	0.040	<0.02	0.14	0.49	>50
59wk	CAP256.14mo.4a	`... ..T....... .......... ........N. ....N..... ........`	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50
	CAP256.14mo.10b	`... .AT......I .......... .I.P.SGEG- -------N.N .E......`	>50	0.35	0.19	0.26	0.72	0.20	5.4	0.050	0.039	0.27	0.54	>50
	CAP256.14mo.2a	`... .ATS.L...E .......... .I.P.SGEG- -------N.N .E......`	>50	0.32	0.89	1.6	0.31	8.9	>50	0.95	0.72	0.32	1.7	>50
94wk	CAP256.21mo.A3	`... ..T..LK..I .......... .....T.... -...N..... .E......`	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50
	CAP256.21mo.F4	`... .AT...K..I .......... .I.P.SGEG- -------N-N .E......`	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50
176wk	CAP256.39mo.C2	`... ......S... .N......K. .......... ....---S.. R.......`	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50
	CAP256.39mo.E1	`... ......S... .N........ .......... ....---S.. R.......`	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50
	CAP256.39mo.H1	`... ......S... .N........ .......... D...---S.. .M......`	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50
	CAP256.39mo.F10	`... ......S... .N........ .......... ....---S.. R.......`	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50
	CAP256.39mo.F1	`... .AT......E .......... .......... -...NS.... ........`	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50
	CAP256.39mo.4	`... .AT......E .......... .......... -...N..... .E......`	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50
	CAP256.39mo.10	`... .ATS.L...E .......... .......... -...NS.... .E......`	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50
	CAP256.39mo.11	`... .AT......E .......... .......... -...NS.... .E......`	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50

Supplementary Figure 10. Sequences of individual Env clones tested in Figure 5d. a, HIV-1 envelope clones by week, from 6 to 176 weeks post infection, with the amino acid sequence of the V1V2 region shown. **b,** Neutralization (IC_{50} values) by each of the 12 CAP256-VRC26 mAbs tested against Env clones. The CAP256 mAbs are colored to indicate the time point when the sequences were first detected by next generation sequencing (as in Fig 3).



Supplementary Figure 11. CAP256-VRC26 UCA does not bind to PI Env. CAP256-VRC26 UCA and the early antibody CAP256-VRC26.01 bind to cell-surface expressed Env from the superinfecting virus (SU) but not the primary infecting virus (PI). Assay performed as in Figure 6. Assay shown is representative of 3 independent experiments. MFI, median fluorescence intensity.

Supplementary Table 1. Statistics for heavy-light chain paired deep sequencing.

Time point	V-gene primers	PBMC recovered (viable/nonviable)	PBMC viability	Viable CD27+ B cells recovered*	Est. CD27+ B cells analyzed*	VRC-26 paired HC reads	250bp reads post-QF (R1+R2)
wk34	FR1**	12 m / 8 m	60%	30k	13 k	0	5,558,841
	LP**	*same as above*	*above*	*above*	13 k	0	6,174,263
wk48	FR1	2.9 m / 12.2 m	19%	9 k	8.1 k	17762	2,233,614
wk59	FR1	6.7 m / 5.9 m	53%	4.5 k	4 k	14	5,623,331
wk69	FR1	6.2 m / 5.0 m	55%	31 k	28 k	158	2,486,745
wk119	FR1	5.1 m / 0.5 m	89%	50 k	23 k	735	5,523,921
	LP	*same as above*	*above*	*above*	23 k	18	4,259,354

*CD27+ hemocytometer estimates
** Primers shown in Supplementary Table 5

Supplementary Table 2

Supplementary Table 2. Crystallographic data collection and refinement statistics
Values in parentheses are for highest-resolution shell

	VRC26.UCA	VRC26.01	VRC26.03	VRC26.04	VRC26.06	VRC26.07	VRC26.10
Data collection							
Space group	C2	C2	C2	P1	R32:H	I222	P212121
Cell constants							
a, b, *c* (Å)	85.5, 81.2, 69.2	104.4 71.2 82.9	99.2, 80.9, 87.6	68.0, 85.5, 103.3	253.5, 253.5, 70.1	70.1, 87.3, 224.4	43.4, 46.2, 232.5
a, b, g (°)	90.0, 124.0, 90.0	90.0, 93.3, 90	90.0, 116.7, 90.0	97.9, 107.7, 91.7	90.0, 90.0, 120.0	90.0, 90.0, 90.0	90,0, 90.0, 90.0
Wavelength (Å)	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Resolution (Å)	50.0-2.90 (3.0-2.9)	50.0-1.90 (1.93-1.90)	50.0-2.70 (2.75-2.70)	50.0-3.15 (3.20-3.15)	50.0-3.0 (3.11-3.0)	40-2.6 (2.64-2.60)	50-1.91 (1.94-1.91)
R_{merge}	11 (37)	8 (54)	15(44)	14(39)	13(54)	13(51)	13(46)
I / sI	5.9 (1.8)	16.3 (2.1)	6.9(1.8)	5.8(1.8)	16.6(2.1)	12.5(1.7)	8.4(2.5)
Completeness (%)	85.7 (82.8)	100 (99.8)	88.4 (51.1)	95.9 (79.6)	98.8 (88.5)	93.9 (53.0)	65.2 (50)
Redundancy	2.3 (2.2)	3.7 (3.2)	2.9(1.7)	1.9(1.8)	10.0(5.0)	6.5(3.9)	4.1(3.9)
Molecules/ASU	1	1	1	4	1	1	1
Refinement							
Resolution (Å)	33.1-2.9 (3.0-2.9)	34.7-1.90 (1.96-1.90)	40.1-2.69 (2.79-2.69)	35.63-3.12 (3.2-3.12)	40.9-3.0 (3.1-3.0)	30.0-2.6 (2.71-2.62)	32.77-1.90 (1.97-1.91)
Unique reflections	7,500 (660)	48,060 (3,241)	13,071(641)	36,806(2,685)	16,997(1,487)	19,901(1,816)	24,684(2,029)
R_{work} / R_{free} (%)	21.1/24.6	18/19.9	20.3/24.5	25.6/28.5	19.3/23.3	22.1/24.5	21.0, 24.1
No. atoms							
Protein	3249	3324	3447	13,508	3477	3361	3323
Water	17	197	47	0	0	17	267
B-factors (Å^2)							
Protein	55.0	33.3	47.8	51.3	66.3	36.2	22.2
Water	27.5	43.7	39	na	na	33.2	25.1
R.m.s. deviations							
Bond lengths (Å)	0.004	0.008	0.003	0.009	0.003	0.005	0.005
Bond angles (°)	.885	1.22	0.82	1.15	0.79	1.01	.96
Ramachandran							
Most favored regions (%)	90.2	98.2	92.0	91.0	96.0	92.5	96.5
Additional allowed regions (%)	9.4	1.8	7.8	8.4	3.8	7.5	3.3
Disallowed regions (%)	0.6	0.0	0.2	0.6	0.2	0.0	0.2

Supplementary Table 3

Supplementary Table 3. Signals of selective pressure within in the V2 epitope (residues 160-171) of primary infecting (PI)-like and superinfecting (SU)-like viruses. Signals of selective pressure were detected at each site using MEME (to detect episodic diversifying selection, with p values >0.05 considered significant) and DEPS (directional selection; maximum Bayes Factor >20 considered significant, with the preferred amino acid selected for indicated in parentheses).

HXB2 position	Analysis* †	Output	PI	SU
160	Directional (DEPS)	Max BF	ns	ns
	Diversifying (MEME)	P value	ns	ns
161	Directional (DEPS)	Max BF	ns	ns
	Diversifying (MEME)	P value	ns	ns
162	Directional (DEPS)	Max BF	ns	ns
	Diversifying (MEME)	P value	ns	ns
163	Directional (DEPS)	Max BF	ns	ns
	Diversifying (MEME)	P value	ns	ns
164	Directional (DEPS)	Max BF	ns	ns
	Diversifying (MEME)	P value	ns	ns
165	Directional (DEPS)	Max BF (Preferred residues)	ns	**191 (V)**
	Diversifying (MEME)	P value	ns	ns
166	Directional (DEPS)	Max BF (Preferred residues)	**3403 (S)**	ns
	Diversifying (MEME)	P value	ns	ns
167	Directional (DEPS)	Max BF	ns	ns
	Diversifying (MEME)	P value	ns	ns
168	Directional (DEPS)	Max BF	ns	ns
	Diversifying (MEME)	P value	ns	ns
169	Directional (DEPS)	Max BF (Preferred residues)	ns	**77095 (IQ)**
	Diversifying (MEME)	P value	ns	**0.0001**
170	Directional (DEPS)	Max BF	ns	ns
	Diversifying (MEME)	P value	ns	ns
171	Directional (DEPS)	Max BF (Preferred residues)	**290 (K)**	ns
	Diversifying (MEME)	P value	ns	ns

*DEPS ns = <20; †MEME ns = >0.05; BF = Bayes Factor

Supplementary Table 4

Supplementary Table 4. PCR Primers used to prepare amplicon for 454 pyrosequencing.

For all timepoints except week 176

Heavy Chain: VH3 only	**5' pool**	
	XLR-A_VH3 LEADER-A	CCATCTCATCCCTGCGTGTCTCCGACTCAG TAAAAGGTGTCCAGTGT
	XLR-A_VH3 LEADER-B	CCATCTCATCCCTGCGTGTCTCCGACTCAG TAAGAGGTGTCCAGTGT
	XLR-A_VH3 LEADER-C	CCATCTCATCCCTGCGTGTCTCCGACTCAG TAGAAGGTGTCCAGTGT
	XLR-A_VH3 LEADER-D	CCATCTCATCCCTGCGTGTCTCCGACTCAG GCTATTTTTAAAGGTGTCCAGTGT
	XLR-A_VH3 LEADER-E	CCATCTCATCCCTGCGTGTCTCCGACTCAG TACAAGGTGTCCAGTGT
	XLR-A_VH3 LEADER-F	CCATCTCATCCCTGCGTGTCTCCGACTCAG TTAAAGCTGTCCAGTGT
	3' pool	
	XLR-B_3xwCgammaCH1-2	CCTATCCCCTGTGTGCCTTGGCAGTCTCAG GG GGA AGA CCG ATG GGC CCT TGG T
	XLR-B_3CmuCH1	CCTATCCCCTGTGTGCCTTGGCAGTCTCAG GGGAATTCTCACAGGAGACGA
Lambda Chain	**5' pool**	
	XLR-A_5L-VL1/2	CCATCTCATCCCTGCGTGTCTCCGACTCAG GCACAGGGTCCTGGGCCCAGTCTG
	XLR-A_5L-VL3	CCATCTCATCCCTGCGTGTCTCCGACTCAG GCTCTGTGACCTCCTATGAGCTG
	XLR-A_5L-VL4/5	CCATCTCATCCCTGCGTGTCTCCGACTCAG GGTCTCTCTCSCAGCYTGTGCTG
	XLR-A_5L-VL6	CCATCTCATCCCTGCGTGTCTCCGACTCAG GTTCTTGGGCCAATTTTATGCTG
	XLR-A_5L-VL7/8	CCATCTCATCCCTGCGTGTCTCCGACTCAG GAGTGGATTCTCAGACTGTGGTG
	XLR-A_5MP-VL1	CCATCTCATCCCTGCGTGTCTCCGACTCAG GCTCACTGCACAGGGTCCTGGGCC
	XLR-A_5MP-VL3-1	CCATCTCATCCCTGCGTGTCTCCGACTCAG GCTTACTGCACAGGATCCGTGGCC
	XLR-A_5MP-VL3-19	CCATCTCATCCCTGCGTGTCTCCGACTCAG ACTCTTTGCATAGGTTCTGTGGTT
	XLR-A_5MP-VL3-21	CCATCTCATCCCTGCGTGTCTCCGACTCAG TCTCACTGCACAGGCTCTGTGACC
	XLR-A_5MP-VL7-43	CCATCTCATCCCTGCGTGTCTCCGACTCAG ACTTGCTGCCCAGGGTCCAATTC
	3' primer	
	XLR-B_3CL	CCTATCCCCTGTGTGCCTTGGCAGTCTCAG CACCAGTGTGGCCTTGTTGGCTTG

Used for week 176 sample only

Heavy Chain: Vh_all	**5' pool**	
	XLR-A_5L-VH1	CCATCTCATCCCTGCGTGTCTCCGACTCAG ACAGGTGCCCACTCCCAGGTGCAG
	XLR-A_5L-VH3	CCATCTCATCCCTGCGTGTCTCCGACTCAG AAGGTGTCCAGTGTGARGTGCAG
	XLR-A_5L-VH4/6	CCATCTCATCCCTGCGTGTCTCCGACTCAG CCCAGATGGGTCCTGTCCCAGGTGCAG
	XLR-A_5L-VH5	CCATCTCATCCCTGCGTGTCTCCGACTCAG CAAGGAGTCTGTTCCGAGGTGCAG
	XLR-A_5xwL-VH1	CCATCTCATCCCTGCGTGTCTCCGACTCAG GCAGCCACAGGTGCCCACTCC
	XLR-A_5xwL-VH1-24	CCATCTCATCCCTGCGTGTCTCCGACTCAG CAGCAGCTACAGGCACCCACGC
	XLR-A_5xwL-VH1-69	CCATCTCATCCCTGCGTGTCTCCGACTCAG GGCAGCAGCTACAGGTGTCCAGTCC
	XLR-A_VH3-L1-MP	CCATCTCATCCCTGCGTGTCTCCGACTCAG GCTATTTTAAAAGGTGTCCAATGT
	XLR-A_VH3/4-L1-MP	CCATCTCATCCCTGCGTGTCTCCGACTCAG GTGGCAGCTCCCAGATGGGTCCTGTC
	XLR-A_VH3/4-L3-MP	CCATCTCATCCCTGCGTGTCTCCGACTCAG GTTGCAGTTTTAAAAGGTGTCCAGTG
	XLR-A_VH5-L1-MP	CCATCTCATCCCTGCGTGTCTCCGACTCAG GCTGTTCTCCAAGGAGTCTGTTCC
	3' pool	
	XLR-B_3xwCgammaCH1	CCTATCCCCTGTGTGCCTTGGCAGTCTCAG GGGGAAGACCGATGGGCCCTTGGTGG
	XLR-B_3CmuCH1	CCTATCCCCTGTGTGCCTTGGCAGTCTCAG GGGAATTCTCACAGGAGACGA
Light Chains (kappa+lambda)	**5' pool**	
	XLR-A_5xwL-VK1/2	CCATCTCATCCCTGCGTGTCTCCGACTCAG ATGAGGSTCCCYGCTCAGCTCCTGGG
	XLR-A_5L-VK3	CCATCTCATCCCTGCGTGTCTCCGACTCAG CTCTTCCTCCTGCTACTCTGGCTCCCAG
	XLR-A_5L-VK4	CCATCTCATCCCTGCGTGTCTCCGACTCAG ATTTCTCTGTTGCTCTGGATCTCTG
	XLR-A_5L-VL1/2	CCATCTCATCCCTGCGTGTCTCCGACTCAG GCACAGGGTCCTGGGCCCAGTCTG
	XLR-A_5L-VL3	CCATCTCATCCCTGCGTGTCTCCGACTCAG GCTCTGTGACCTCCTATGAGCTG
	XLR-A_5L-VL4/5	CCATCTCATCCCTGCGTGTCTCCGACTCAG GGTCTCTCTCSCAGCYTGTGCTG
	XLR-A_5L-VL6	CCATCTCATCCCTGCGTGTCTCCGACTCAG GTTCTTGGGCCAATTTTATGCTG
	XLR-A_5L-VL7/8	CCATCTCATCCCTGCGTGTCTCCGACTCAG GAGTGGATTCTCAGACTGTGGTG
	XLR-A_5MP-VL1	CCATCTCATCCCTGCGTGTCTCCGACTCAG GCTCACTGCACAGGGTCCTGGGCC
	XLR-A_5MP-VL3-1	CCATCTCATCCCTGCGTGTCTCCGACTCAG GCTTACTGCACAGGATCCGTGGCC
	XLR-A_5MP-VL3-19	CCATCTCATCCCTGCGTGTCTCCGACTCAG ACTCTTTGCATAGGTTCTGTGGTT
	XLR-A_5MP-VL3-21	CCATCTCATCCCTGCGTGTCTCCGACTCAG TCTCACTGCACAGGCTCTGTGACC
	XLR-A_5MP-VL7-43	CCATCTCATCCCTGCGTGTCTCCGACTCAG ACTTGCTGCCCAGGGTCCAATTC
	3' pool	
	XLR-B_3xwCK1	CCTATCCCCTGTGTGCCTTGGCAGTCTCAG CAGCAGGCACACAACAGAGGCAGTTCC
	XLR-B_3CL	CCTATCCCCTGTGTGCCTTGGCAGTCTCAG CACCAGTGTGGCCTTGTTGGCTTG

Supplementary Table 5. Additional primers used in Heavy-light chain paired deep sequencing.

Conc (nM)	Primer ID	Primer Sequence
40	VH1_LP	tattcccatcgcggcgcACAGGTGCCCACTCCCAGGTGCAG
40	VH3_LP	tattcccatcgcggcgcAAGGTGTCCAGTGTGARGTGCAG
40	VH4/6_LP	tattcccatcgcggcgcCCCAGATGGGTCCTGTCCCAGGTGCAG
40	VH5_LP	tattcccatcgcggcgcCAAGGAGTCTGTTCCGAGGTGCAG
40	hVλ1for_LP	gcgccgcgatgggaataNNNNNNNNNNNNNNNNTCTGCTCGAGTTCGGTCAGGTCCTGGGCCCAGTCTGTGCTG
40	hVλ2for_LP	gcgccgcgatgggaataNNNNNNNNNNNNNNNNTCTGCTCGAGTTCGGTCAGGTCCTGGGCCCAGTCTGCCCTG
40	hVλ3for-2_LP	gcgccgcgatgggaataNNNNNNNNNNNNNNNNTCTGCTCGAGTTCGGTCAYWCTGCACAGGCTCTGTGACCTCCTAT
40	hVλ4/5for_LP	gcgccgcgatgggaataNNNNNNNNNNNNNNNNTCTGCTCGAGTTCGGTCAGGTCTCTCTCSCAGCYTGTGCTG
40	hVλ6for_LP	gcgccgcgatgggaataNNNNNNNNNNNNNNNNTCTGCTCGAGTTCGGTCAGTTCTTGGGCCAATTTTATGCTG
40	hVλ7for_LP	gcgccgcgatgggaataNNNNNNNNNNNNNNNNTCTGCTCGAGTTCGGTCAGGTCCAATTCYCAGGCTGTGGTG
40	hVλ8for_LP	gcgccgcgatgggaataNNNNNNNNNNNNNNNNTCTGCTCGAGTTCGGTCAGAGTGGATTCTCAGACTGTGGTG
40	hVκ1/2for_LP	gcgccgcgatgggaataNNNNNNNNNNNNNNNNTCTGCTCGAGTTCGGTCAATGAGGSTCCCYGCTCAGCTGCTGG
40	hVκ3for_LP	gcgccgcgatgggaataNNNNNNNNNNNNNNNNTCTGCTCGAGTTCGGTCACTCTTCCTCCTGCTACTCTGGCTCCCAG
40	hVκ4for_LP	gcgccgcgatgggaataNNNNNNNNNNNNNNNNTCTGCTCGAGTTCGGTCAATTTCTCTGTTGCTCTGGATCTCTG