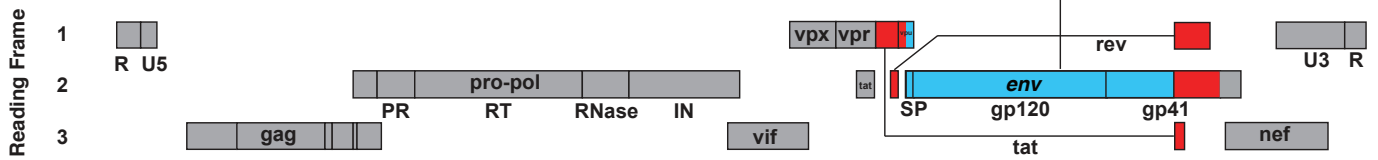


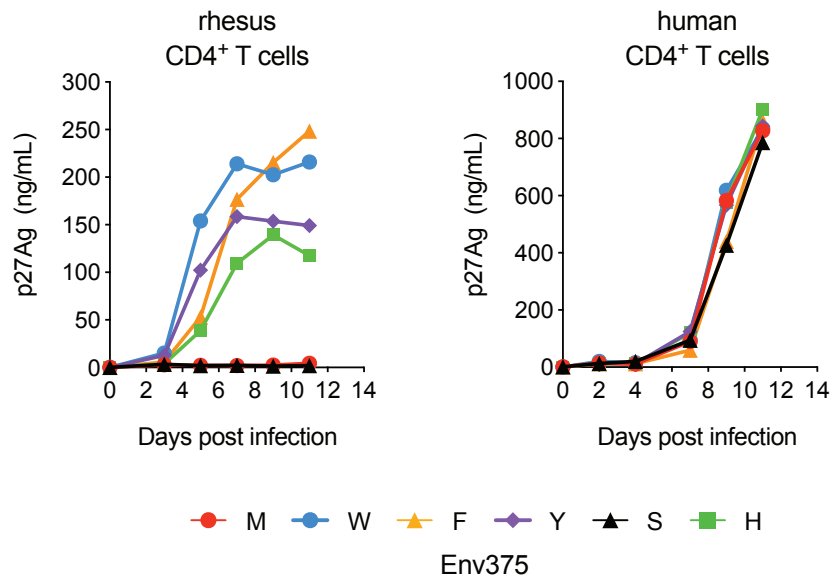
A*SHIV.CAP256SU.dCT***B**

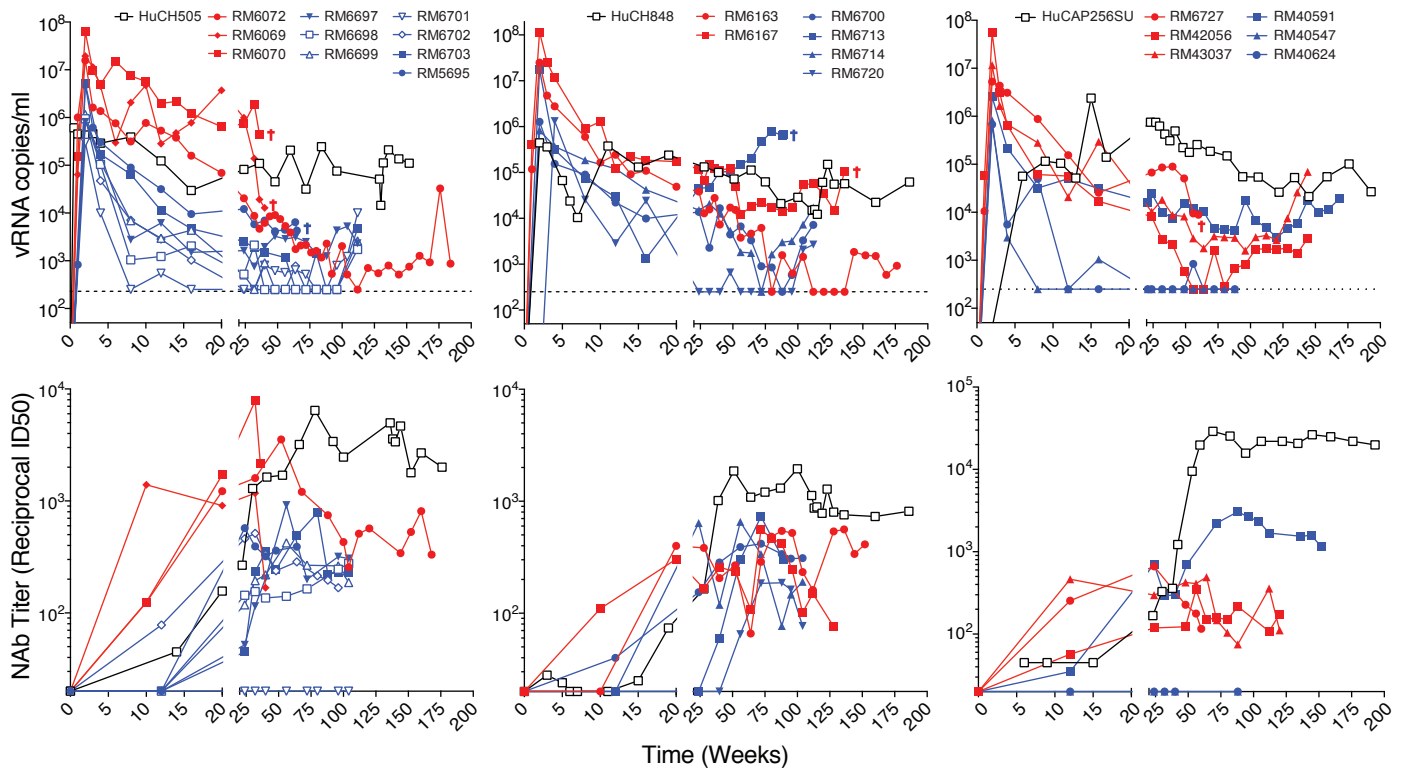
SHIV.CAP256SU Env375 variant

	375S	375M	375Y	375H	375W	375F
PGT121	0.051	0.042	0.046	0.044	0.036	0.031
8ANC195	13.3	16.3	13.9	17.3	22.4	17.3
10E8	5.9	6.9	9.2	12.6	10.6	5.2
VRC01	0.11	0.14	0.22	0.21	0.52	0.77
PG9	0.038	0.050	0.053	0.048	0.063	0.038
PGDM1400	0.005	0.007	0.005	0.006	0.010	0.006
VRC26.25	0.0003	0.0004	0.0004	0.0006	0.0006	0.0003
447-52D	>25	>25	>25	>25	>25	>25
17b	>25	>25	>25	>25	>25	>25

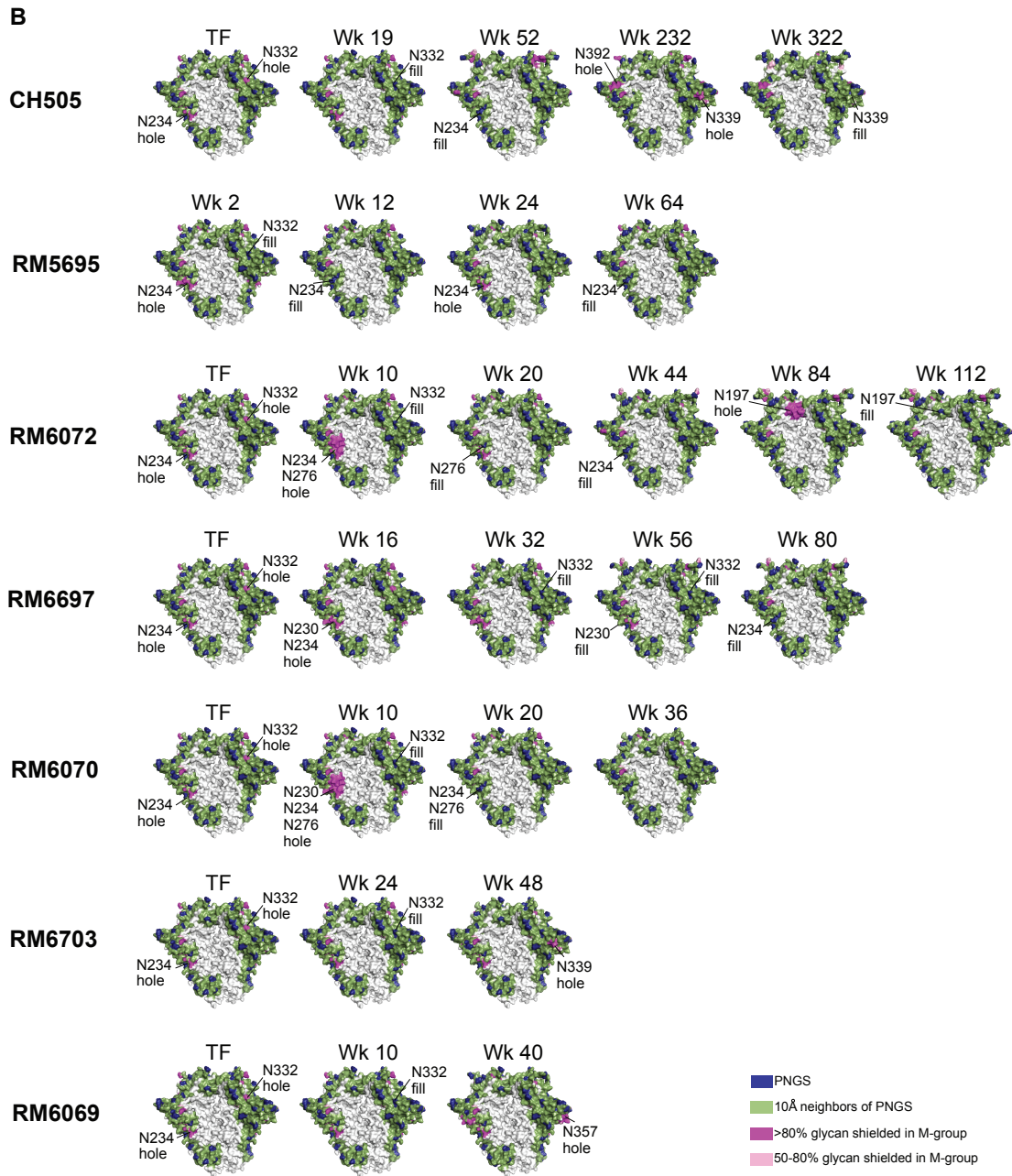
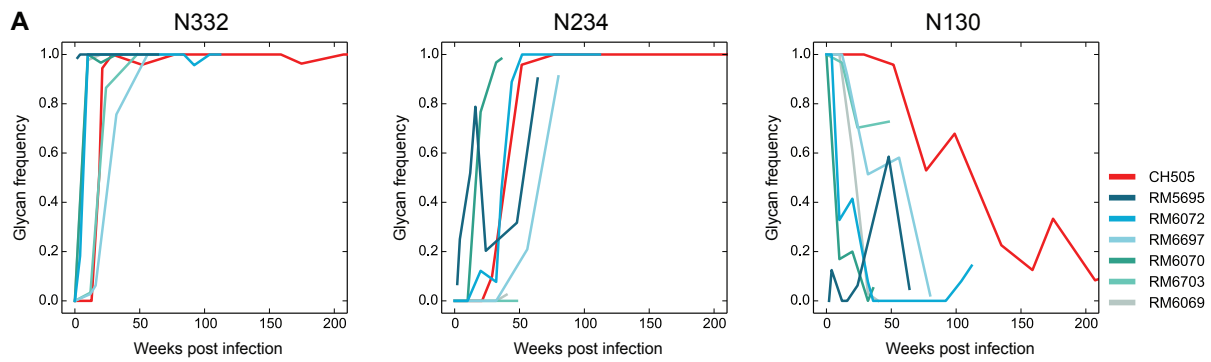


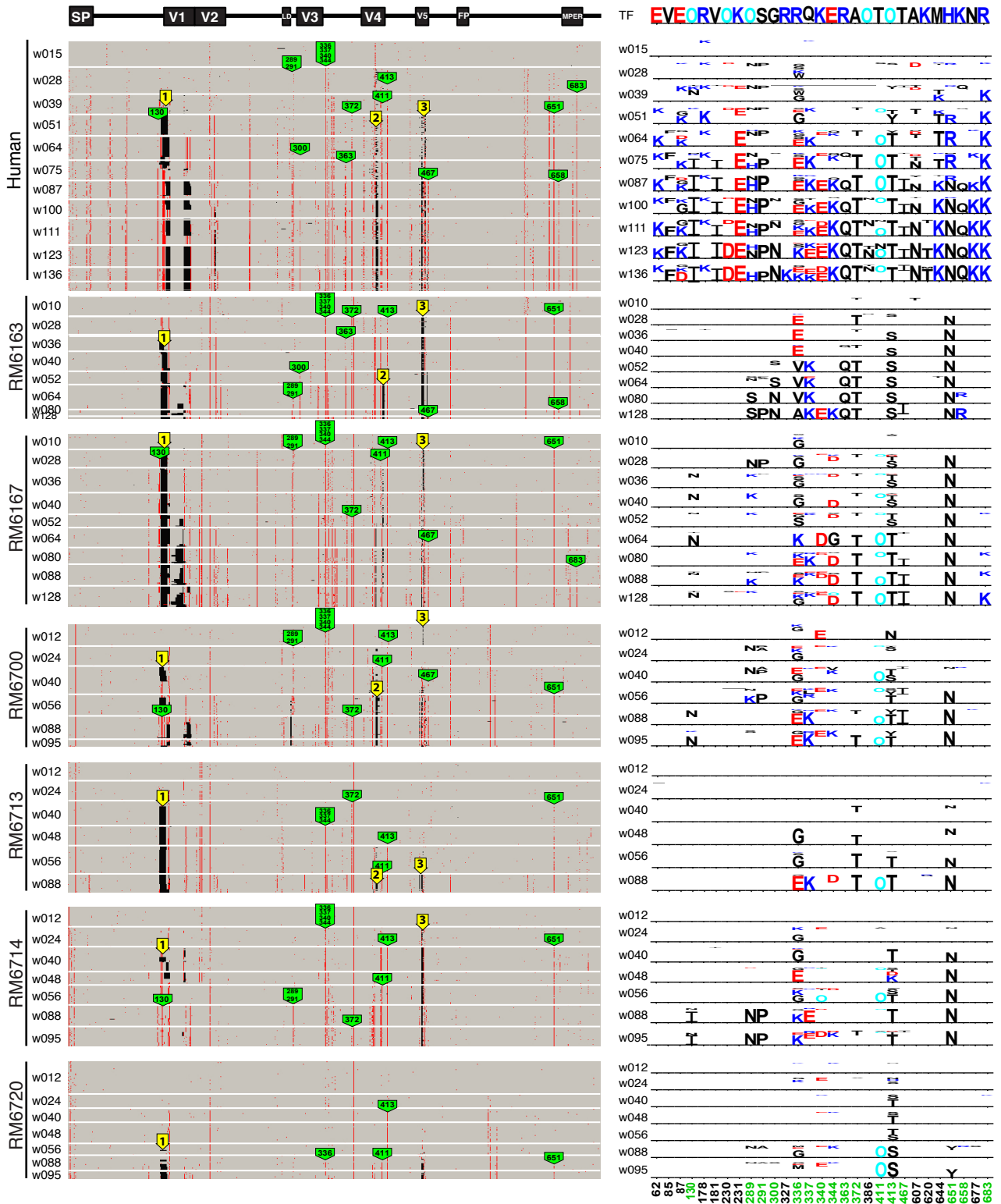
IC50 ug/mL

C

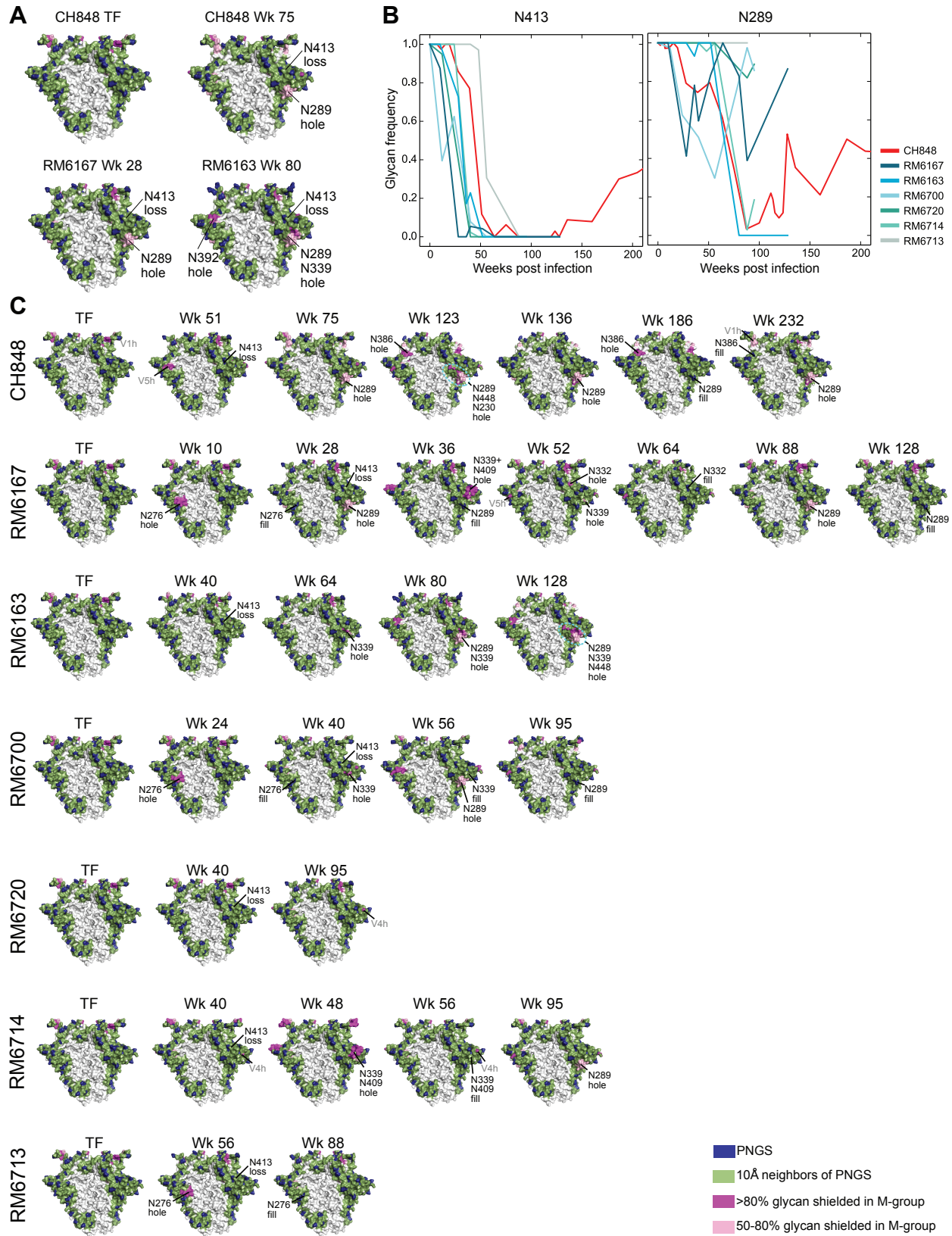


Supplemental Figure S2

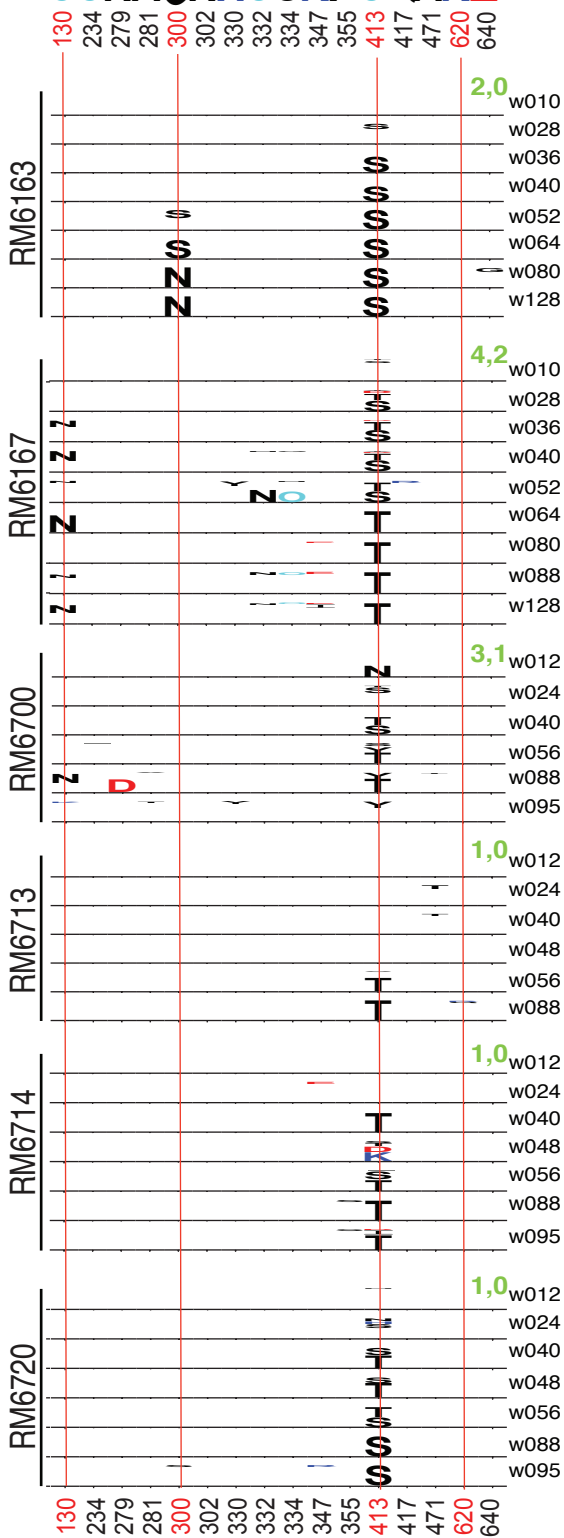




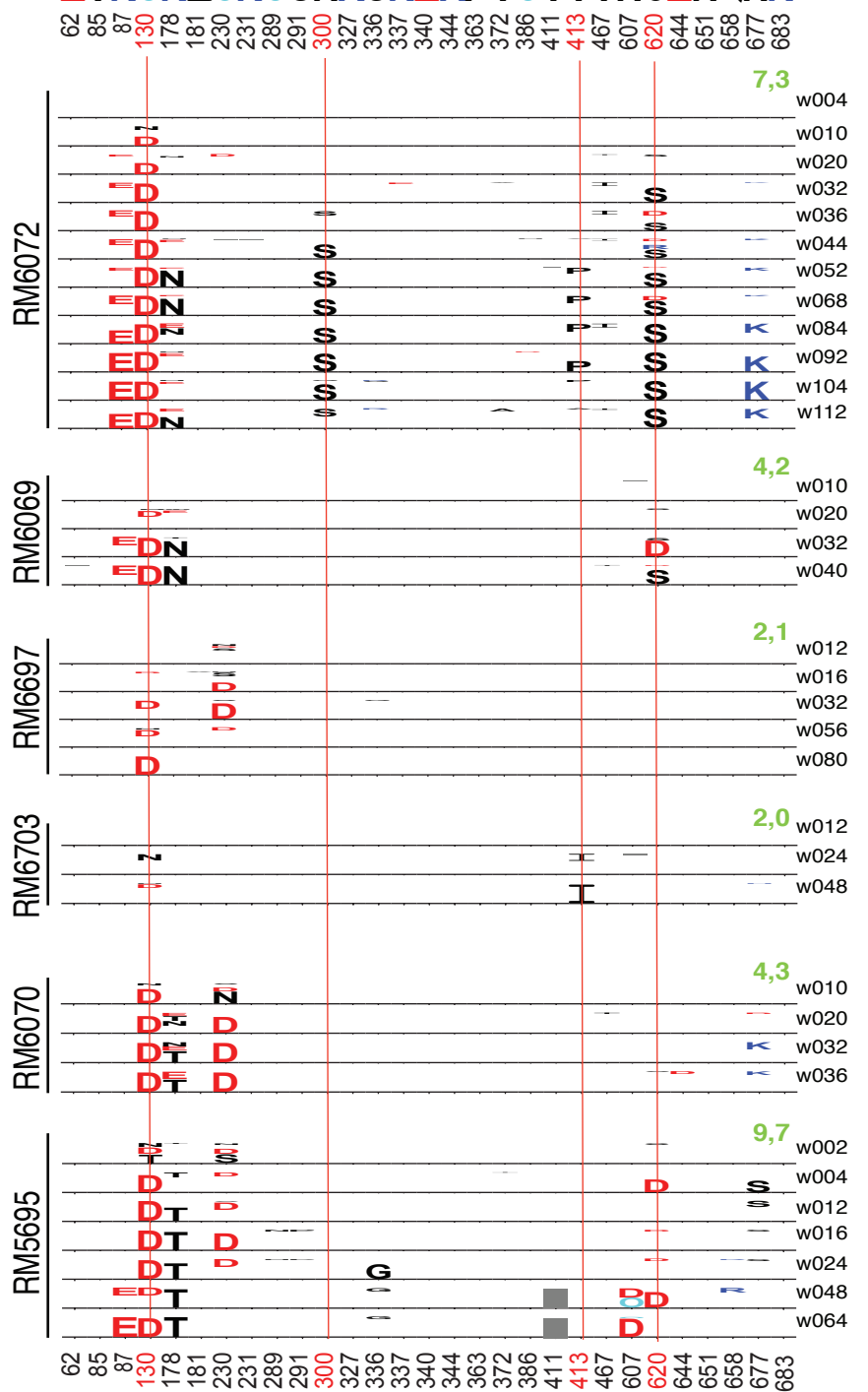
Supplementary Figure S4



Supplemental Figure S5

ACH505 TF
CH848 TF


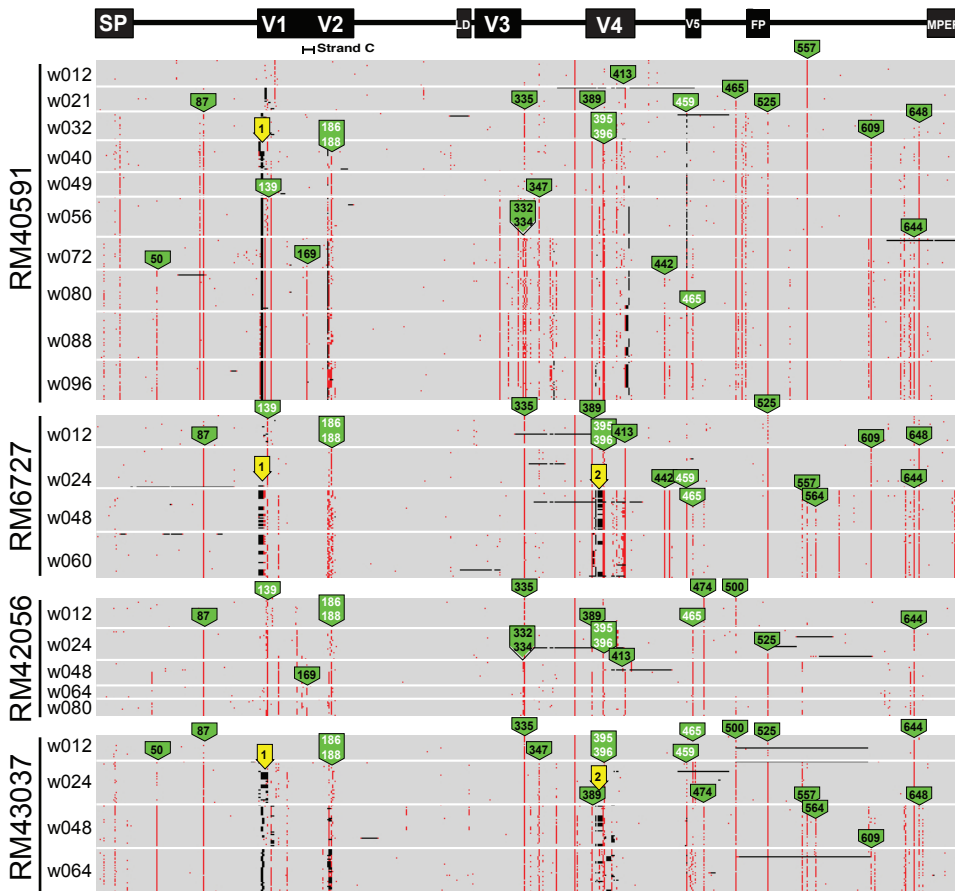
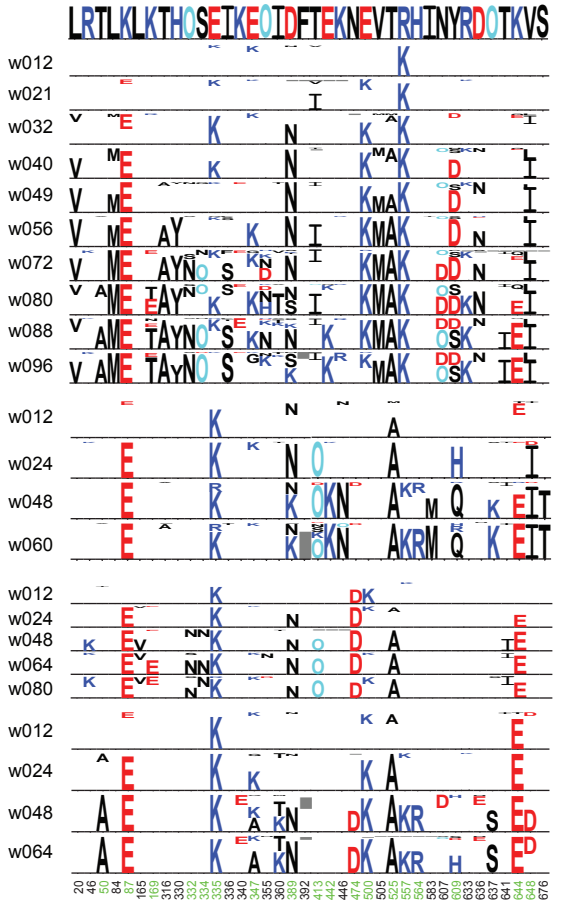
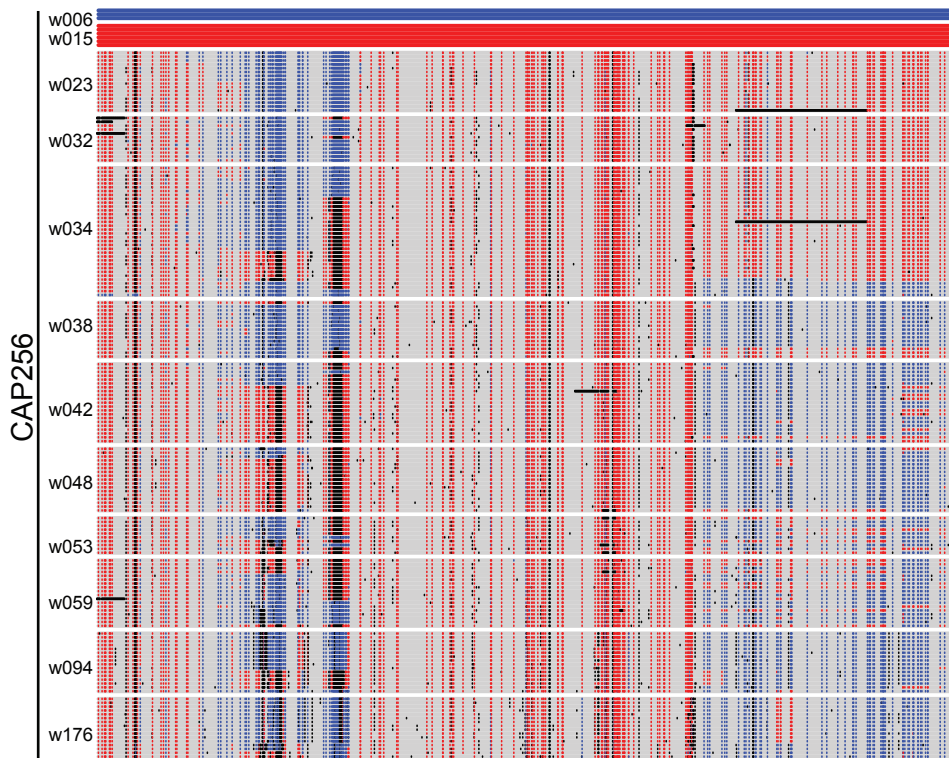
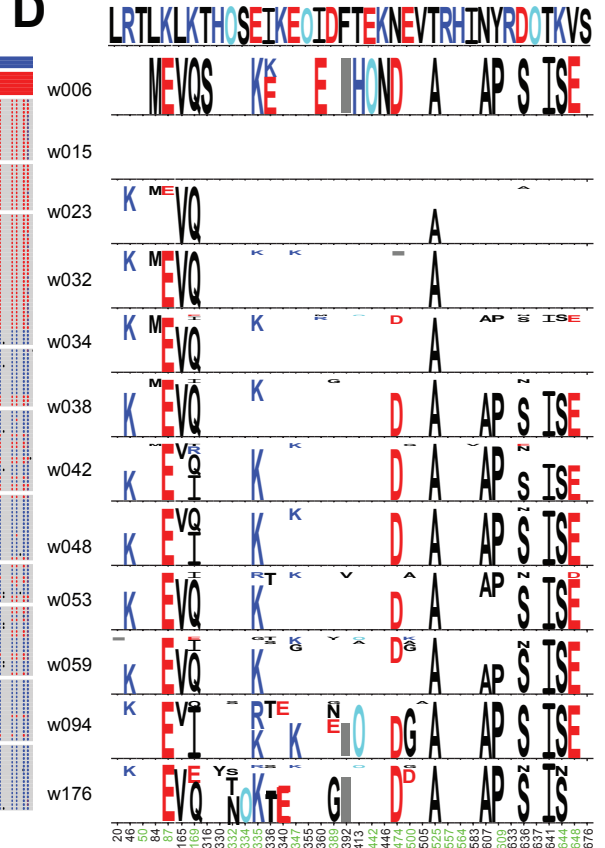
The human CH505 sites identified by LASSIE applied to SHIV CH848 infected macaques

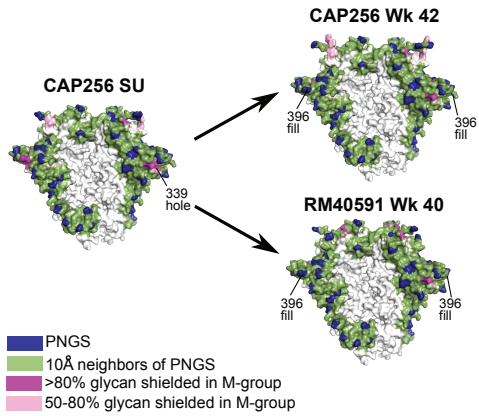
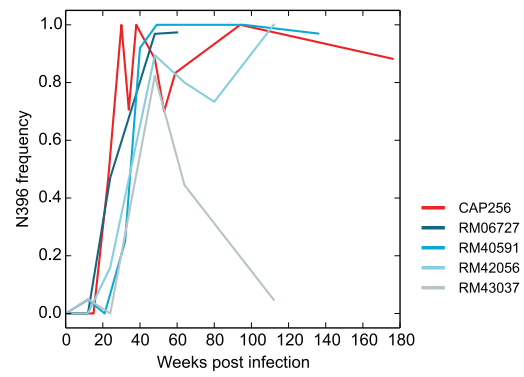
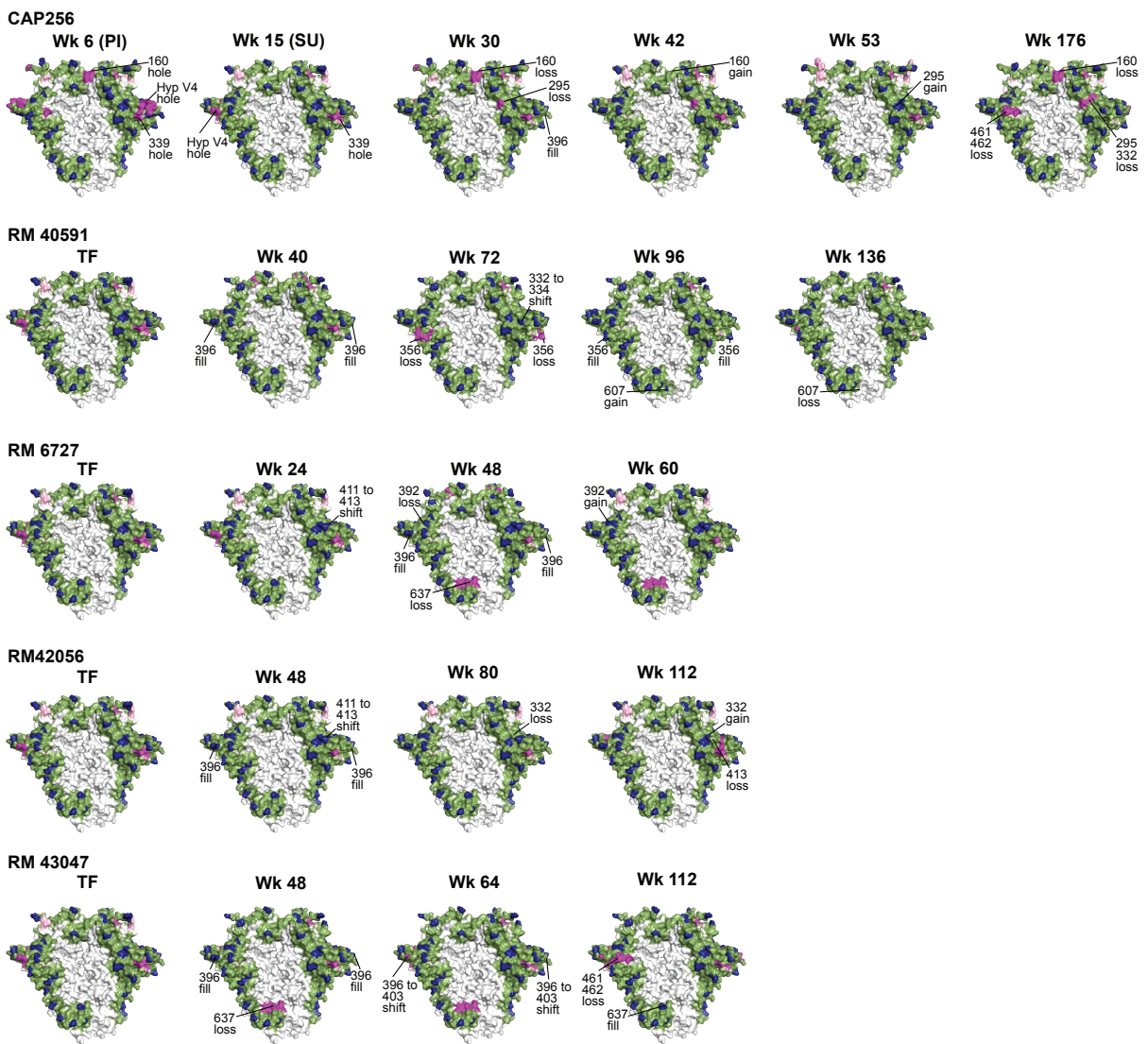
BCH848 TF
CH505 TF


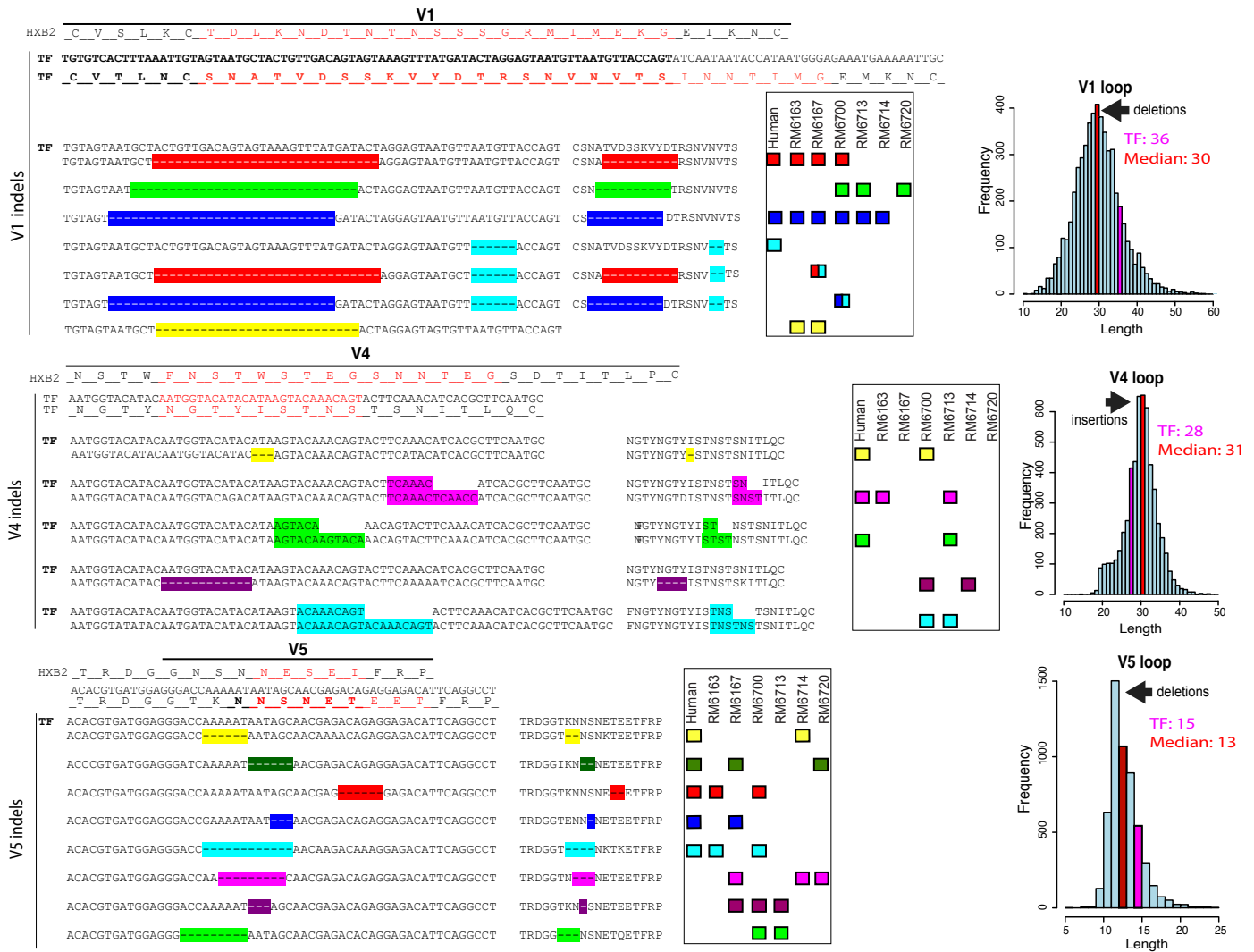
The human CH848 sites identified by LASSIE applied to SHIV CH505 infected macaques

TF Loss:

Total number of sites, followed by selected sites not shared between CH848 and CH505

A**B****C****D**

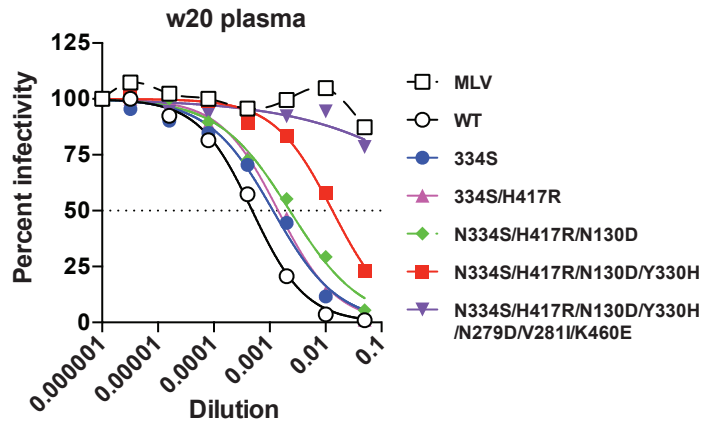
A**B****C**



A

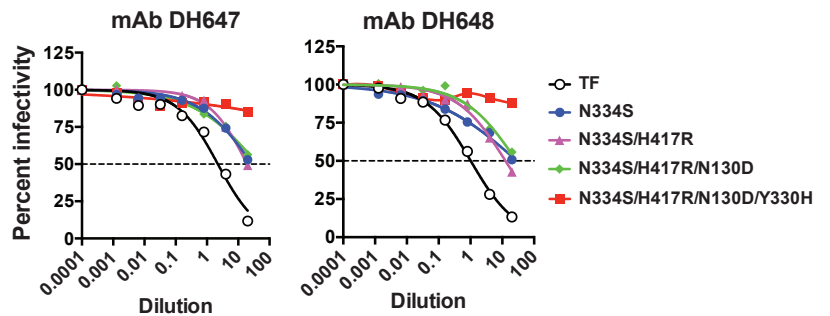
Virus	Mutation Location	RM6072 plasma	
		w10	w20
TF_ID50		286	2,397
TF_RID50 (ID50 _{mut} /ID50 _{TF})		1	1
N130D	V1	0.3	0.6
T234N	C2	0.3	1.2
N279D	Loop-D	<0.1	0.7
V281I	Loop-D	<0.1	0.7
K302N	V3	224.3	51.9
Y330H	V3	0.7	1.5
N334S	V3C3	0.2	0.4
H417R	V4	1.1	1.2
K460E	V5	<0.1	1.8

>3 fold resistant >3 fold sensitive



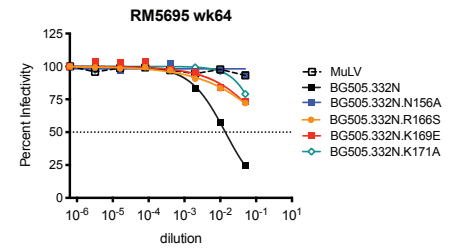
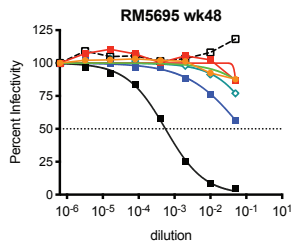
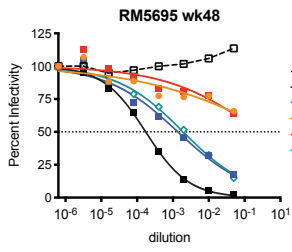
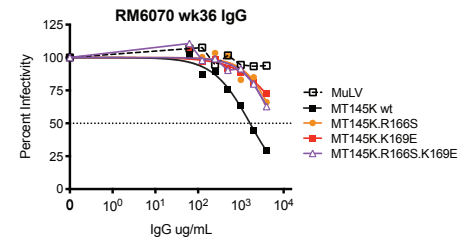
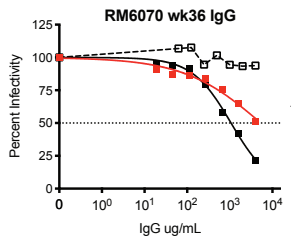
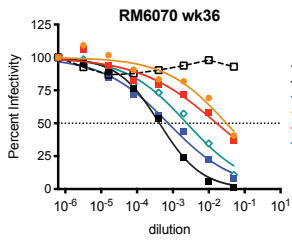
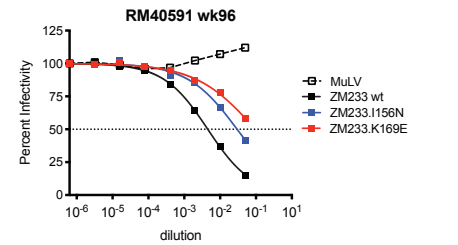
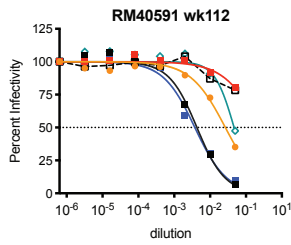
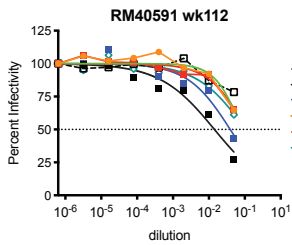
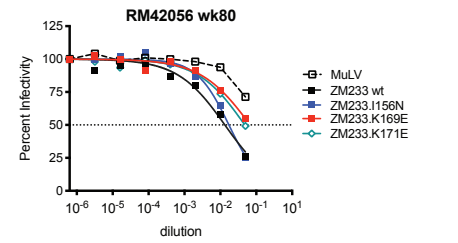
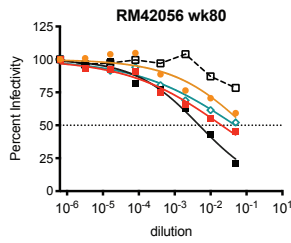
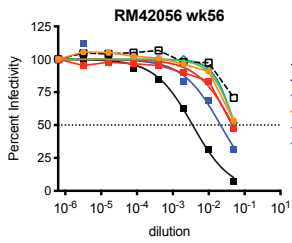
B

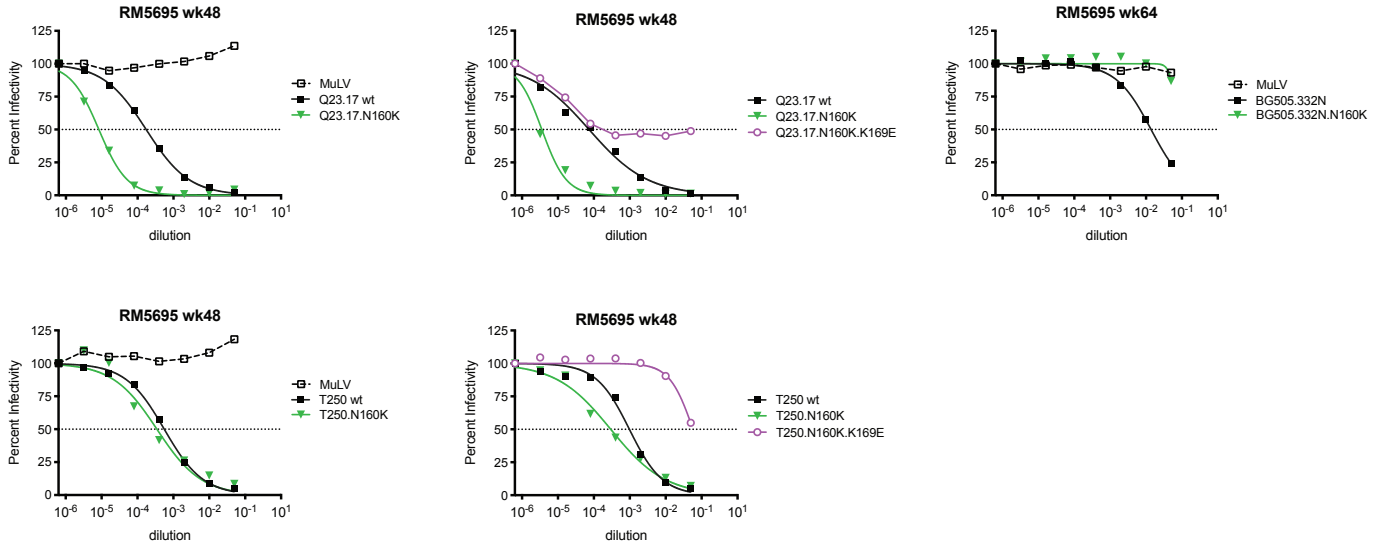
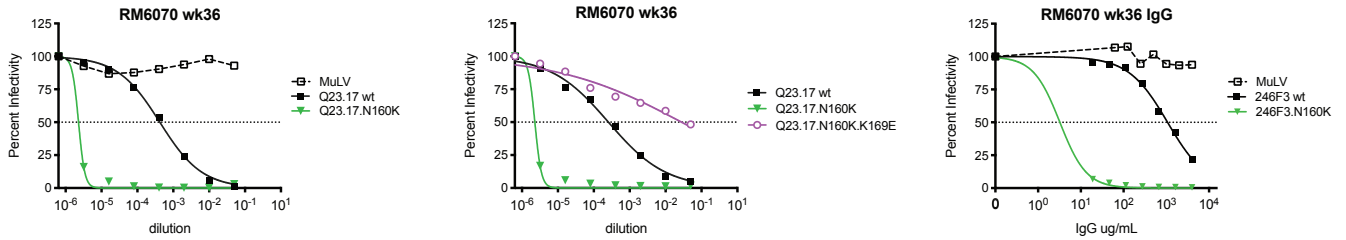
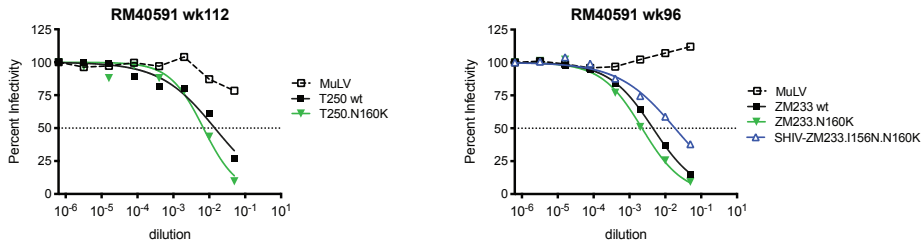
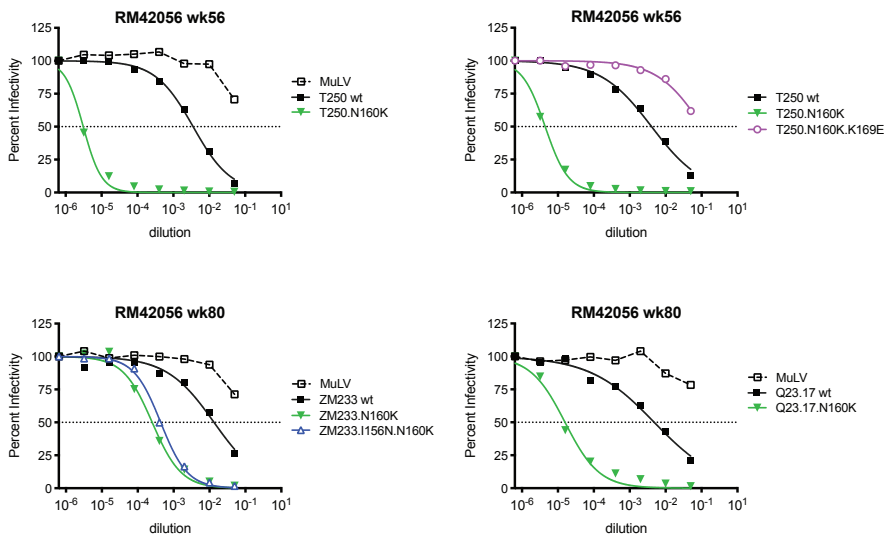
Virus	Mutation Location	RM6072 V3 mAbs	
		DH647	DH648
TF_IC ₅₀ (ug/ml)		2.2	1.0
N130D	V1	3.3	0.9
K302N	V3	15.5	>20
Y330H	V3	2.5	1.8
N334S	V3C3	>20	>20
H417R	V4	2.0	2.0



C

Virus	Mutation Location	RM6072 CD4bs mAbs		Human CH505 CD4bs mAbs		
		DH650.UCA	DH650	CH235.UCA	CH235.IA3	CH235.9
TF_IC ₅₀ (ug/ml)		>20	2.2	>20	3.6	0.4
T234N	C2	>20	>20	>20	>20	0.6
N279D	Loop-D	>20	>20	>20	>20	0.4
V281I	Loop-D	>20	3.5	>20	5.6	0.2
K460E	V5	>20	>20	>20	13.2	1.3

A**B****C****D**

A**B****C****D**

A Autologous NAb responses to wildtype and V1 deleted variants of CH848 TF in SHIV CH848 infected RM plasma

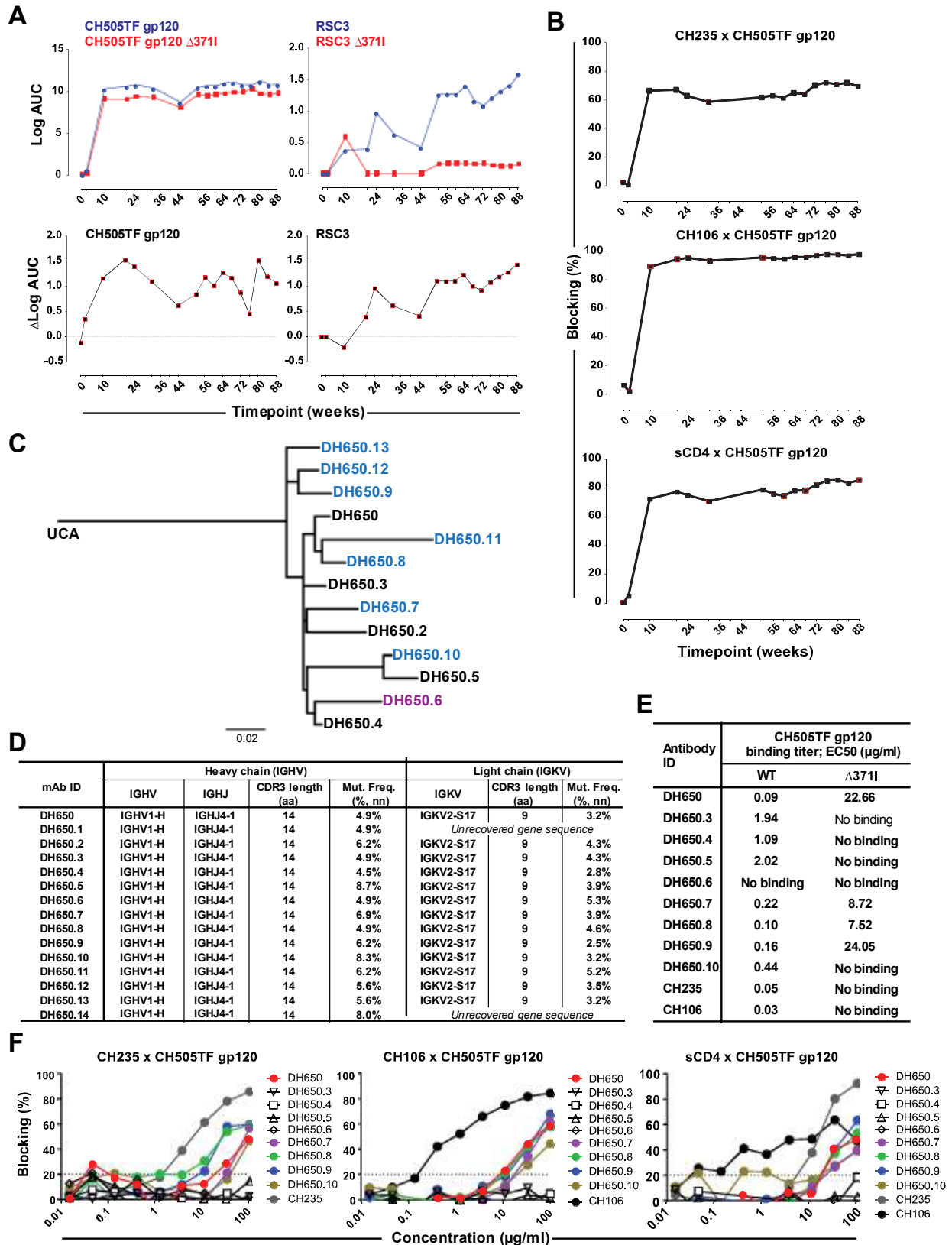
Animal ID	Plasma timepoint	CH848 TF	CH848 R336G	CH848 TFdV1 (V1Δ10aa)	w36con (V1Δ10aa+ Mut)
RM6167	w10	220	72	130	<20
	w36	435	ND	948	28

B Epitope mapping of autologous, strain-specific neutralizing mAbs from RM6163

Animal ID	Antibody ID	CH848 TF	CH848 TFdV1 (Δ10aa)	CH848 N301D	CH848 N332D
RM6163	DH898.1	2.84	11.49	3.19	>50
w52 LN	DH898.2	6.57	27.38	8.56	>50
	DH898.3	3.69	16.35	5.93	>50
	DH898.4	0.64	3.29	0.86	>50
	DH898.5	2.83	12.18	5.40	>50
	DH898.6	3.12	21.67	5.74	>50

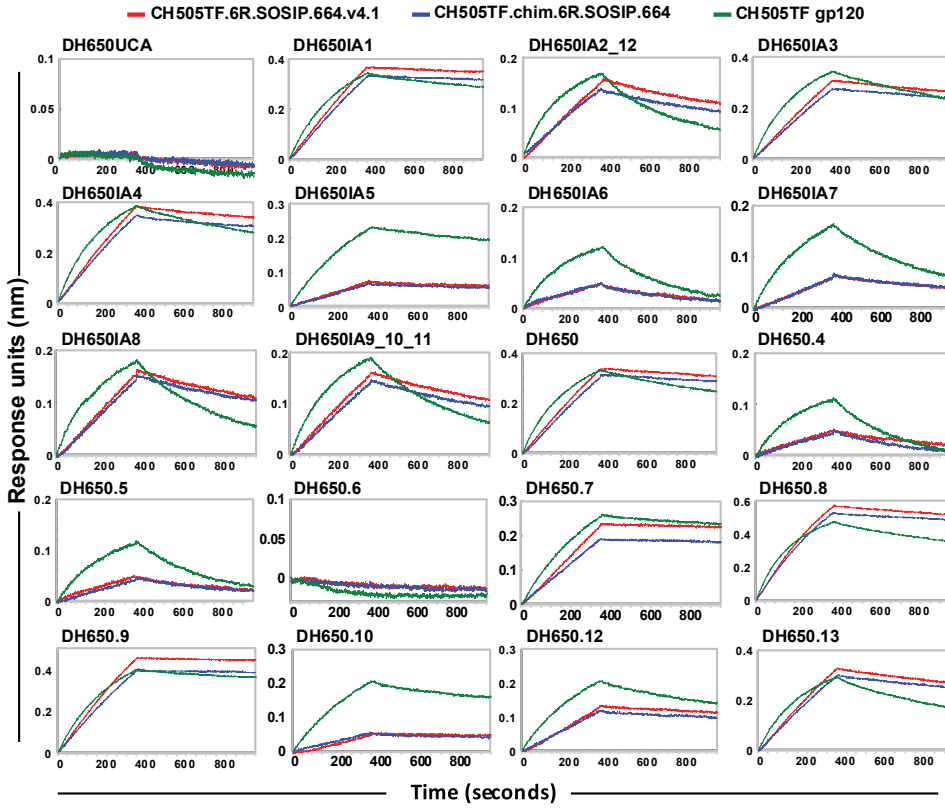
IC50, μg/mL

<1
1-10
10-50
>50



Supplemental Figure S15

A



B

IC50, µg/mL	>50	10-50	1-10	0.1-1	<0.1
Antibody ID	TF	TF gly4	MuLV		
DH650UCA	>50	>50	>50		
DH650IA1	3.8	<0.02	>50		
DH650IA2_12	>50	0.06	>50		
DH650IA3	4.2	<0.02	>50		
DH650IA4	4.6	<0.02	>50		
DH650IA5	11.4	<0.02	>50		
DH650IA6	>50	<0.02	>50		
DH650IA7	>50	<0.02	>50		
DH650IA8	20.0	<0.02	>50		
DH650IA9_10_11	20.0	0.03	>50		
DH650	2.6	<0.02	>50		
DH650.2	10.0	<0.02	>50		
DH650.3	>50	0.4	>50		
DH650.4	>50	<0.02	>50		
DH650.5	>50	0.06	>50		
DH650.6	>50	>50	>50		
DH650.7	3.3	<0.02	>50		
DH650.8	2.0	<0.02	>50		
DH650.9	3.8	<0.02	>50		
DH650.10	10.3	<0.02	>50		
DH650.12	9.6	<0.02	>50		
DH650.13	8.3	<0.02	>50		

C

IC50, µg/mL	>50	10-50	1-10	0.1-1	<0.1	
Antibody ID	HIV-1 isolate/ Tier phenotype/ IC50, µg/mL					
	CH505 TF	JRFL	Q168	Q842	BG1168	SF162 MuLV
	2	2	2	2	1	1 n/a
DH650	9.6	>50	>50	>50	>50	>50
DH650.3	>50	>50	>50	>50	>50	>50
DH650.4	>50	>50	>50	>50	>50	>50
DH650.5	>50	>50	>50	>50	>50	>50
DH650.6	>50	>50	>50	>50	>50	>50
DH650.7	5.0	>50	>50	>50	>50	>50
DH650.8	4.5	>50	>50	>50	>50	>50
DH650.9	4.4	>50	>50	>50	>50	>50
DH650.10	23.7	>50	>50	>50	>50	>50
CH235	0.58	1.7	>50	3.9	>50	>50

A

IGHV4-ABB-5*01_S8200
 Q V Q L Q E S G P G L V K P S E T L S L T C A V S G G G D S F G F H Y W N W I R Q P P G K G L E

RHA1.V2.01H
 CAGGTGCAGCTCGAGTGGGCCCAGGACTGGTGAAGCCTTCGGAGACCTCTCCCTCACTCGTGTCTCTGGTGGG-----TCCATCAGGGTACTACTGGAACTGGATCGCAACCCCAAGGGAAGGGCCGGAG

RHA1.V2.02H
 CAGGTGCAGCTCGAGTGGGCCCAGGACTGGTGAAGCCTTCGGAGACCTCTCCCTCACTCGTGTCTCTGGTGGG-----TCCATCAGGGTACTACTGGAACTGGATCGCAACCCCAAGGGAAGGGCCGGAG

RHA1.V2.03H
 CAGGTGCAGCTCGAGTGGGCCCAGGACTGGTGAAGCCTTCGGAGACCTCTCCCTCACTCGTGTCTCTGGTGGG-----TCCATCAGGGTACTACTGGAACTGGATCGCAACCCCAAGGGAAGGGCCGGAG

RHA1.V2.04H
 CAGGTGCAGCTCGAGTGGGCCCAGGACTGGTGAAGCCTTCGGAGACCTCTCCCTCACTCGTGTCTCTGGTGGG-----TCCATCAGGGTACTACTGGAACTGGATCGCAACCCCAAGGGAAGGGCCGGAG

IGHV4-ABB-5*01_S8200
 W I G Y I G G S S S G S T Y Y N P S L K S R V T I S T D T S K N Q F S L K L S S V T A A D T A V Y

RHA1.V2.01H
 TGGATTGGCATAATCGGTGGCAGTACGGGAGCACTAACAACCCCTCCCTCAAGAGTCAAGCACCATTCAAAGGACACCCCAAGAACCACTCTCCCTCAAGCTCAGCTCTGCAACGGCCGGACAAGCCGCTGAT

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RHA1.V2.04H
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IGHV4-ABB-5*01_S8200
 Y C A R

RHA1.V2.01H
 TCTGTGCGAGAAAAGGCGAAGACTTTTACGGAGGATACGGTCAATATTCACCCGAGGCTGGTCTCTGGTGGGCCCCTGGCACCCCAATCATCATCTCCCA

RHA1.V2.02H
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RHA1.V2.03H
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RHA1.V2.04H
 TCTGTGCGAGAAAAGGCGAAGACTTTTACGGAGGATACGGTCAATATTCACCCGAGGCTGGTCTCTGGTGGGCCCCTGGCACCCCAATCATCATCTCCCA

B

IGLV1-ACN*02
 Q S V L T Q P P S V S G A P G Q R V T I S C T G S S S N I G G Y Y V Q W Y Q Q L P G

RHA1.V2.01L
 CAGTGTGTGTGACGCGACCGCCCTCAGTGTCTGGGGCGCCCGGGCAGAGGGTACCACCTCTCCTGCACTGGGAGDAGTCCAACTTGGAGGTATTATGTCAGTGGTACCGAGAGTCCAGGA

RHA1.V2.02L
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RHA1.V2.03L
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RHA1.V2.04L
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IGLV1-ACN*02
 T A P K L L I Y E N N K R P S G V S D R F S G S Q S G T S A S L T I T G L Q S E D E

RHA1.V2.01L
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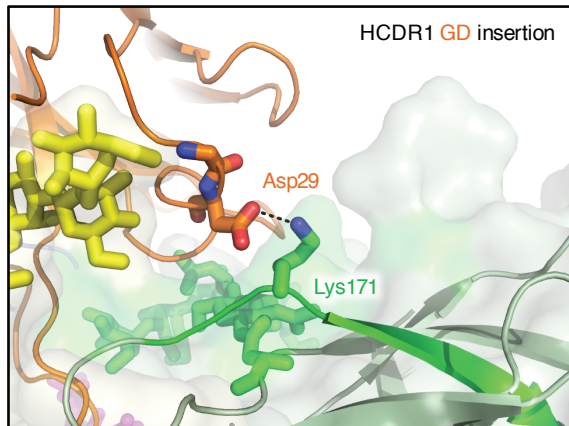
IGLV1-ACN*02
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RHA1.V2.02L
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RHA1.V2.03L
 GCTGATTATTACTGCGAGTCCATGACAGGACCTATTAATCGGAAGGGGGAACCGGCTGACCGTCCCTG

RHA1.V2.04L
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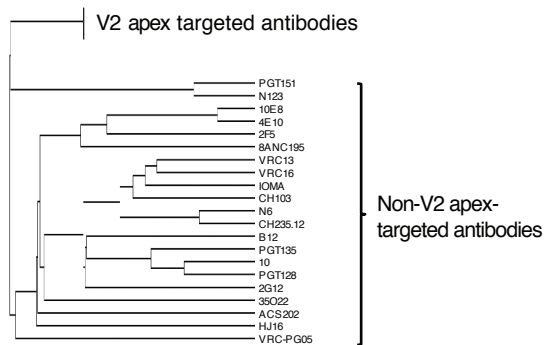
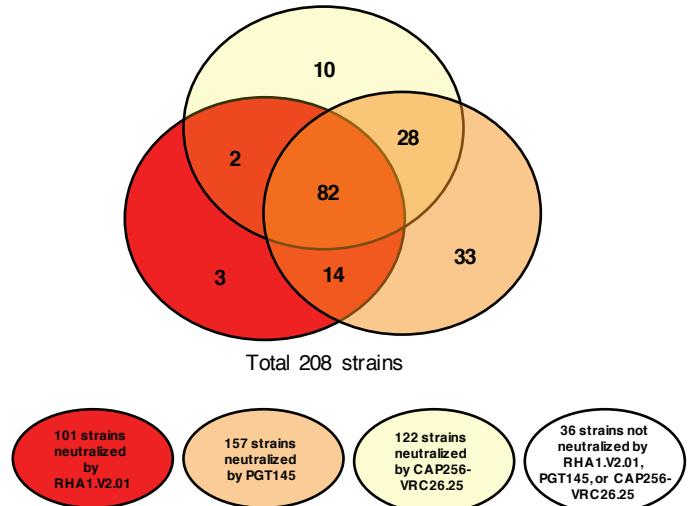
A**B**

VH4-ABB*01 CAR-----
 DH3-9 -----YYEDDYGY~~Y~~T-----
 JH2-P -----WYFDLW
 RHA1.V2.01 CARKGEDFYEDDYGQYFTAGWFFDLW
 RHA1.V2.02 CARKGEDFYEDDYGQYFTAGWYFDLW
 RHA1.V2.03 CARKGEDFYEDDYGQYFTAGWYFDLW
 RHA1.V2.04 CARKGEDFYEDDYGQYFTAGWFFDLW

VH4-ABB*01 CAR-----
 DH3-9 -----YYEDDYGY~~Y~~T-----
 JH2-P -----WYFDLW
 RHA1.V2.01 ...KGEDF.....Q.F.AG.F.....
 RHA1.V2.02 ...KGEDF.....Q.F.AG.......
 RHA1.V2.03 ...KGEDF.....Q.F.AG.......
 RHA1.V2.04 ...KGEDF.....Q.F.AG.F.....

C

PGT145	CLTGSKHRLRDYFLYNE [*] YGN [*] YEEWGDYLATLDVW
PCT64-35S	CMT---GVERGDFWSDDY [*] S-QHYNT---YLIDVW
RHA1.V2.01	CAR---KGE <u>D</u> FYEDDYG-QYFTA---GWFFDLW
RHA1.V2.02	CAR---KGE <u>D</u> FYEDDYG-QYFTA---GWYFDLW
RHA1.V2.03	CAR---KGE <u>D</u> FYEDDYG-QYFTA---GWYFDLW
RHA1.V2.04	CAR---KGE <u>D</u> FYEDDYG-QYFTA---GWFFDLW

D**E**

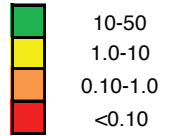
A**B****Autoantigens**

	SSA	SSB	Sm	RNP	Sci 70	Jo 1	dsDNA	Cent B	Histone
Positive control 1	-	-	-	-	-	-	-	+	-
Positive control 2	+	+	-	-	-	+	+	-	+
Positive control 3	-	-	+	+	+	-	-	-	-
CH65	-	-	-	-	-	-	-	-	-
4E10	-	+	+	-	-	+	-	+	+
RHA1.V2.01	-	-	-	-	-	-	-	-	-

Rhesus mAbs

		Rhesus mAbs				RM5695 wk56 plasma
		RHA1.V2.01	RHA1.V2.02	RHA1.V2.03	RHA1.V2.04	
Global panel	246F3	0.21	0.24	0.31	0.24	109
	X1632	0.16	0.12	0.32	0.24	465
	25710	0.74	0.33	2.18	1.76	28
	CNE55	0.35	0.63	2.75	1.45	20
	X2278	0.40	0.41	1.87	1.18	28
	BJOX0020000	1.94	0.64	1.99	2.09	22
	CNE8	4.09	1.27	6.78	5.76	179
	CE0217	3.085	1.77	>50	>50	26
	TRO.11	>50	>50	>50	>50	72
	CE1176.A3	>50	>50	>50	>50	20
	CH119.10	>50	31	>50	>50	<20
	BG505.T332N	0.05	0.11	0.11	0.10	139
	CAP256SU	0.45	0.27	0.85	0.76	65
	ZM233.6	0.01	0.43	0.02	0.01	413
WITO.33	0.03	0.04	0.04	0.03	138	
T250-4	0.01	0.01	0.02	0.01	1977	
Q23.17	0.005	0.005	0.006	0.003	5051	
MT145K	0.13	0.07	0.181	0.15	161	
autologous	CH505 TF	0.463	0.180	0.648	0.507	421

IC50 ug/mL



Plasma ID50



RHA1.V2.01

IC50 (ug/mL)

.001-01
.01-100
100-10.0
1.00-10.0
>10.0

Virus ID	Clade	IC50 (ug/mL)
0260.v5.c36	A	13.9
0330.v4.c3	A	0.046
0439.v5.c1	A	>50
3365.v2.c20	A	0.390
3718.v3.c11	A	0.809
398-F1.F6.20	A	>50
BB201.B42	A	0.010
BB539.2B13	A	>50
BG505.W6M.C2	A	0.067
BI369.9A	A	0.083
BS208.B1	A	0.045
KER2008.12	A	0.043
KER2018.11	A	0.013
KNH1209.18	A	0.958
MB201.A1	A	14.7
MB539.2B7	A	1.36
MI369.A5	A	0.682
MS208.A1	A	>50
Q23.17	A	0.005
Q259.17	A	0.397
Q769.d22	A	>50
Q769.h5	A	>50
Q842.d12	A	0.020
QH209.14M.A2	A	>50
RW020.2	A	>50
UG037.8	A	>50
246-F3.C10.2	AC	0.179
3301.v1.c24	AC	>50
3589.v1.c4	AC	>50
6540.v4.c1	AC	0.199
6545.v4.c1	AC	0.120
0815.v3.c3	ACD	>50
6095.v1.c10	ACD	12.5
3468.v1.c12	AD	>50
Q168.a2	AD	0.069
Q461.e2	AD	>50
620345.c1	AE	23.5
BJOX009000.02.4	AE	>50
BJOX010000.06.2	AE	>50
BJOX025000.01.1	AE	>50
BJOX028000.10.3	AE	>50
C1080.c3	AE	0.001
C2101.c1	AE	>50
C3347.c11	AE	>50
C4118.09	AE	0.049
CM244.ec1	AE	0.004
CNE3	AE	0.041
CNE5	AE	0.017
CNE55	AE	1.17
CNE56	AE	>50
CNE59	AE	0.102
CNE8	AE	8.55
M02138	AE	>50
R1166.c1	AE	>50
R2184.c4	AE	>50
R3265.c6	AE	>50
TH023.6	AE	>50
TH966.8	AE	0.092
TH976.17	AE	>50
235-47	AG	0.251
242-14	AG	0.869
263-8	AG	>50
269-12	AG	>50
271-11	AG	0.018
928-28	AG	>50
DJ263.8	AG	1.06
T250-4	AG	0.010
T251-18	AG	>50
T253-11	AG	>50
T255-34	AG	0.077
T257-31	AG	30.3
T266-60	AG	13.5
T278-50	AG	9.27
T280-5	AG	>50
T33-7	AG	0.011

Virus ID	Clade	IC50 (ug/mL)
3988.25	B	11.5
5768.04	B	0.985
6101.10	B	>50
6535.3	B	4.16
45_01dG5	B	3.97
89.6.DG	B	>50
AC10.29	B	1.17
ADA.DG	B	8.96
Bal.01	B	>50
Bal.26	B	>50
BG1168.01	B	>50
BL01.DG	B	>50
BR07.DG	B	>50
BX08.16	B	0.073
CAAN.A2	B	>50
CNE10	B	>50
CNE12	B	>50
CNE14	B	>50
CNE4	B	>50
CNE57	B	>50
HO86.8	B	43.6
HT593.1	B	6.70
HXB2.DG	B	>50
JRCSF.JB	B	0.015
JRFL.JB	B	>50
MN.3	B	>50
PVO.04	B	>50
QH0515.01	B	>50
QH0692.42	B	>50
REJO.67	B	1.06
RHPA.7	B	>50
SC422.8	B	>50
SF162.LS	B	>50
SS1196.01	B	>50
THRO.18	B	>50
TRJO.58	B	>50
TRO.11	B	>50
WITO.33	B	0.019
X2278.C2.B6	B	0.133
YU2.DG	B	>50
BJOX002000.03.2	BC	0.821
CH038.12	BC	1.97
CH070.1	BC	0.052
CH117.4	BC	0.005
CH119.10	BC	21.1
CH181.12	BC	0.009
CNE15	BC	>50
CNE19	BC	>50
CNE20	BC	7.47
CNE21	BC	0.069
CNE40	BC	>50
CNE7	BC	>50

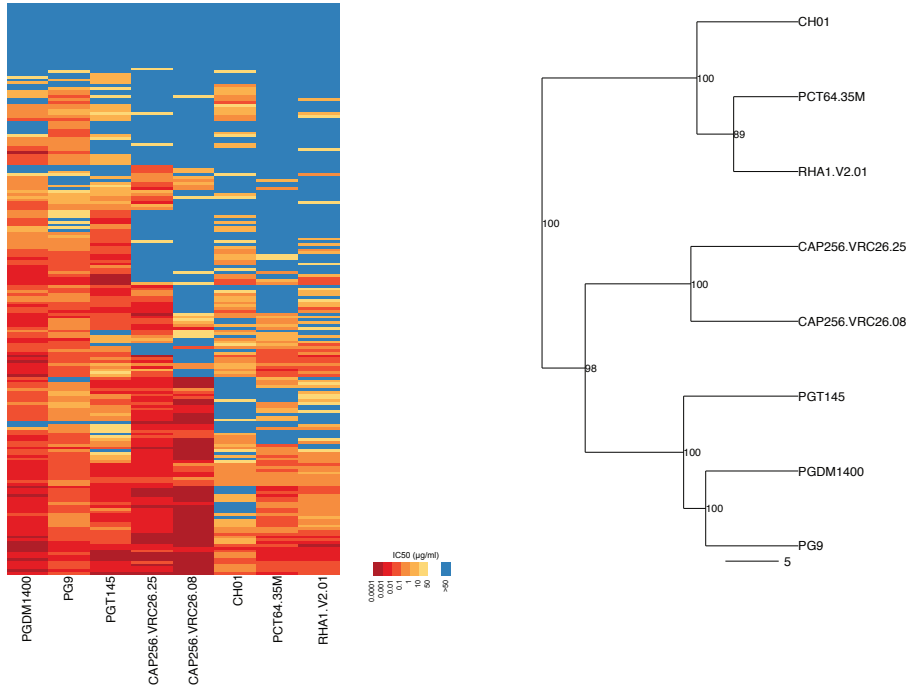
Virus ID	Clade	IC50 (ug/mL)
286.36	C	0.701
288.38	C	>50
0013095-2.11	C	>50
001428-2.42	C	0.057
00836-2.5	C	>50
0921.v2.c14	C	>50
16055-2.3	C	0.077
16845-2.22	C	>50
16936-2.21	C	>50
25710-2.43	C	0.856
25711-2.4	C	>50
25925-2.22	C	0.156
26191-2.48	C	0.404
3168.v4.c10	C	>50
3637.v5.c3	C	>50
3873.v1.c24	C	6.10
426c	C	>50
6322.v4.c1	C	>50
6471.v1.c16	C	>50
6631.v3.c10	C	>50
6644.v2.c33	C	>50
6785.v5.c14	C	0.107
6838.v1.c35	C	0.271
96ZM651.02	C	>50
BR025.9	C	0.051
CAP210.E8	C	11.2
CAP244.D3	C	>50
CAP256.206.C9	C	0.225
CAP45.G3	C	0.006
Ce1176.A3	C	>50
CE703010217.B6	C	2.19
CNE30	C	>50
CNE31	C	>50
CNE53	C	6.18
CNE58	C	0.045
DU123.06	C	0.281
DU151.02	C	1.05
DU156.12	C	0.350
DU172.17	C	>50
DU422.01	C	>50
MW965.26	C	12.6
SO18.18	C	0.205
TV1.29	C	2.28
TZA125.17	C	40.8
TZBD.02	C	4.01
ZA012.29	C	>50
ZM106.9	C	24.7
ZM109.4	C	>50
ZM135.10a	C	>50
ZM176.66	C	0.078
ZM197.7	C	43.1
ZM214.15	C	>50
ZM215.8	C	>50
ZM233.6	C	0.009
ZM249.1	C	0.324
ZM53.12	C	0.589
ZM55.28a	C	>50
3326.v4.c3	CD	0.162
3337.v2.c6	CD	>50
3817.v2.c59	CD	>50
191821.E6.1	D	48.6
231965.c01	D	>50
247-23	D	0.211
3016.v5.c45	D	0.572
57128.vrc15	D	>50
6405.v4.c34	D	>50
A03349M1.vrc4a	D	>50
A07412M1.vrc12	D	9.22
NKU3006.ec1	D	>50
UG021.16	D	>50
UG024.2	D	>50
P0402.c2.11	G	2.14
P1981.C5.3	G	>50
X1193.c1	G	>50
X1254.c3	G	>50
X1632.S2.B10	G	0.112
X2088.c9	G	>50
X2131.C1.B5	G	5.90
SIVmac251.30.SG3	NA	>50
SVA.MLV	NA	>50

RHA1.V2.01 RHA1.V2.03 RHA1.V2.04

T250-4 wt	0.012	0.019	0.017
T250-4.K169E	>25	>25	>25
T250-4.R166S	>25	>25	>25
T250-4.N160K	>25	>25	>25
246-F3 wt	0.352	0.413	0.243
246-F3.R169E	>25	>25	>25
246-F3.N160K	>25	>25	>25
BG505.332N wt	0.164	0.268	0.278
BG505.332N.K169E	>25	>25	>25
BG505.332N.R166S	>25	>25	>25
BG505.332N.N160K	>25	>25	>25
CAP256SU wt	0.412	0.791	0.428
CAP256SU.K169E	>25	>25	>25
CAP256SU.R166S	>25	>25	>25
CAP256SU.T162I	>25	>25	>25
X1632 wt	0.433	0.284	0.118
X1632.K169E	>25	>25	>25
X1632.N160K	>25	>25	>25
MT145K wt	0.16	0.25	0.23
MT145K.K169E	>25	>25	>25
MT145K.R166S	>25	>25	>25
MT145K.N160D	>25	>25	>25
Q23.17 wt	0.007	0.009	0.008
Q23.17.R169E	>25	>25	>25
Q23.17.R166S	>25	>25	>25
Q23.17.N160K	2.96	1.37	1.00

<0.10	0.10-1.0	1.0-10	10-50
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IC50 ug/mL

A**B**

	RHA1 sensitive	RHA1 resistant
PCT64-35M sensitive	72	17
PCT6-35M resistant	29	90
p=2.0x10 ⁻¹⁶ ; Odd's ratio (OR)=13.14; Accuracy (Acc) = 0.78		

	RHA1 sensitive	RHA1 resistant
CAP256.25 sensitive	84	38
CAP256.25 resistant	17	69
p=1.7x10 ⁻¹² ; OR=57.35; Acc = 0.74		

	RHA1 sensitive	RHA1 resistant
PG9 sensitive	100	68
PG9 resistant	1	39
p=2.3x10 ⁻¹² ; OR=57.35; Acc = 0.69		

	RHA1 sensitive	RHA1 resistant
PGDM1400 sensitive	99	68
PGDM1400 resistant	2	39
p=2.8x10 ⁻¹¹ ; OR=28.39; Acc = 0.66		

	RHA1 sensitive	RHA1 resistant
PGT145 sensitive	96	61
PGT145 resistant	5	46
p=4.4x10 ⁻¹¹ ; OR=14.47; Acc=0.68		

	RHA1 sensitive	RHA1 resistant
CAP256.08 sensitive	67	28
CAP256.08 resistant	34	79
p=7.3x10 ⁻⁹ ; OR=5.56; Acc=0.70		

	RHA1 sensitive	RHA1 resistant
CH01 sensitive	72	38
CH01 resistant	29	69
p=2.4x10 ⁻⁷ ; OR=4.51; Acc=0.67		

C