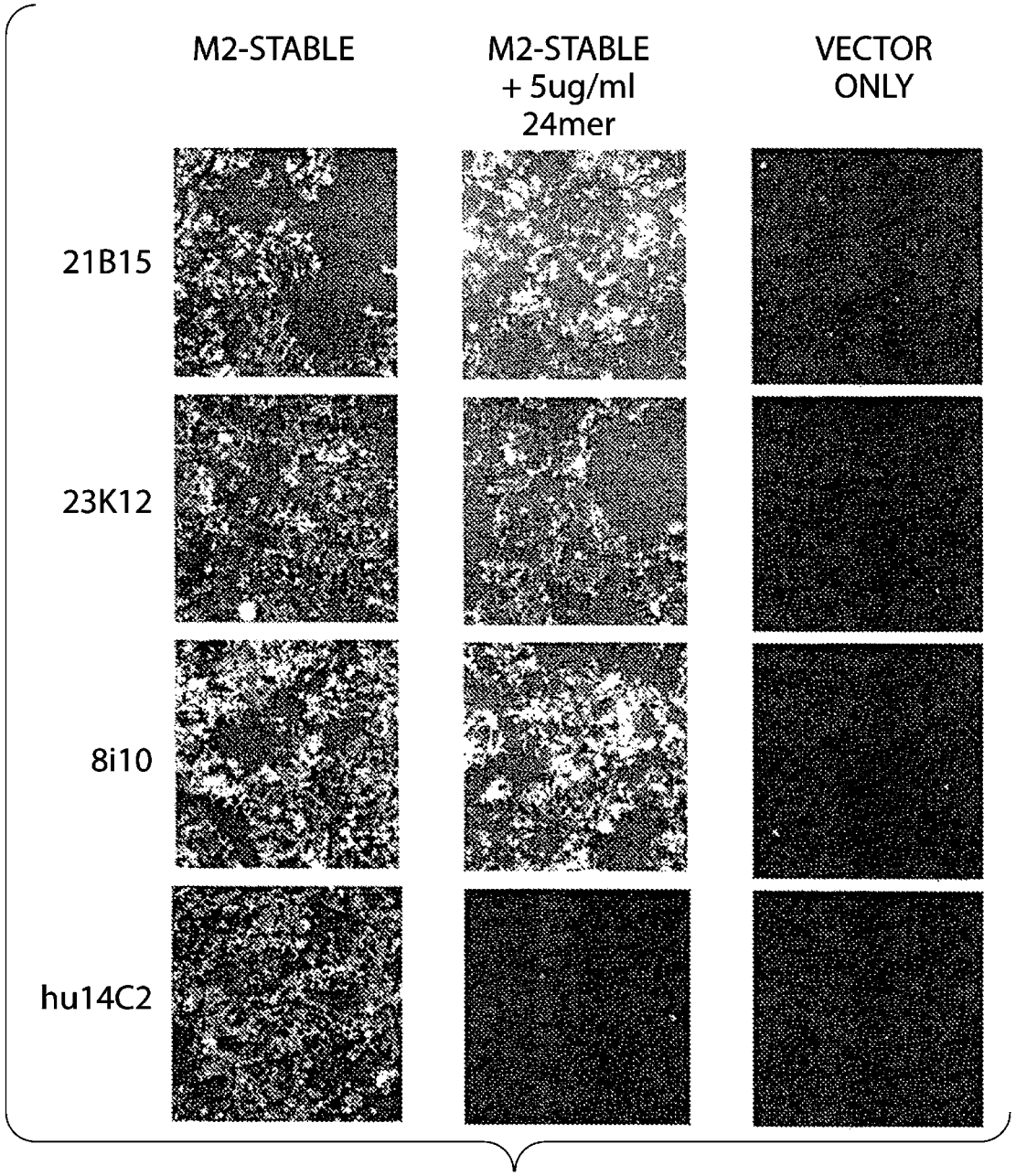

M2-STABLE
M2-STABLE + 5ug/ml 24mer
VECTOR ONLY
21B15
23K12
8i10
hu14C2

FIG. 1

VIRAL BINDING

INFLUENZA A/PR/8/32 ELISA

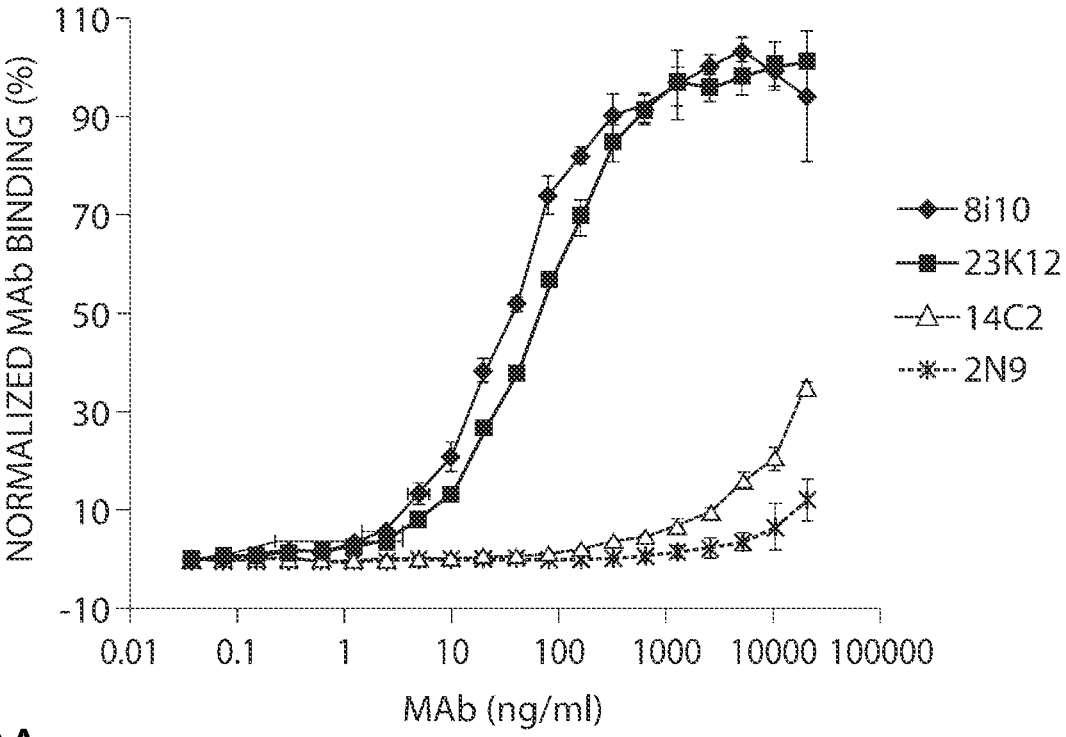


FIG. 2A

VIRAL BINDING (with Z3G1)

INFLUENZA A/PR/8/32 ELISA

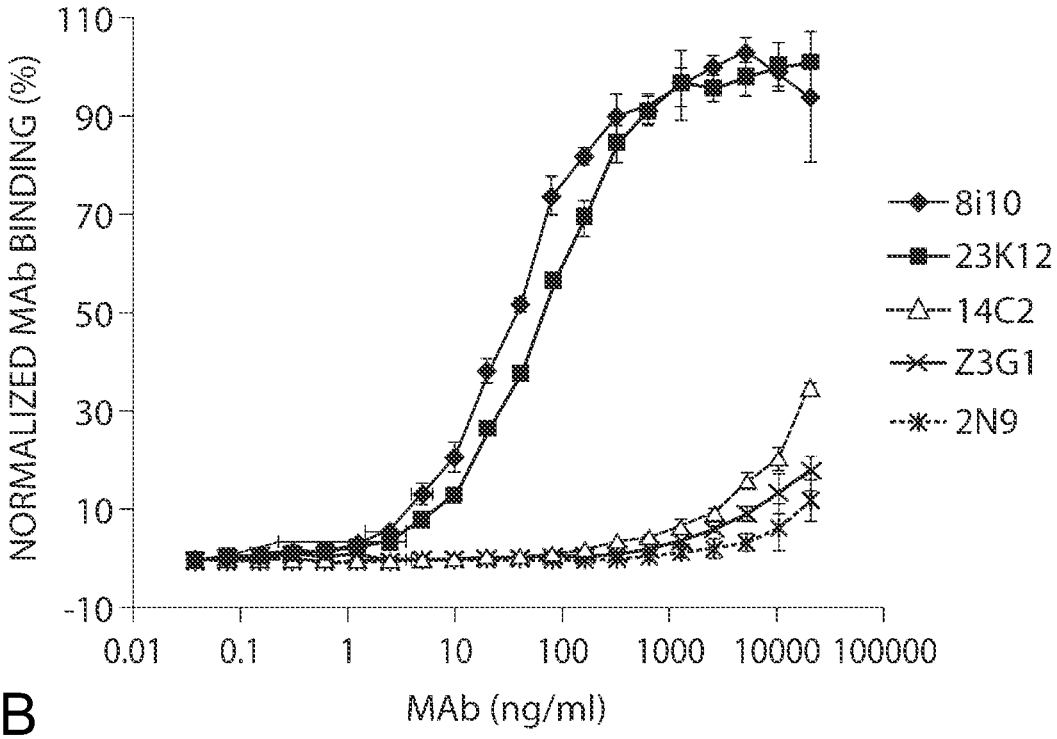


FIG. 2B

FIG. 3A

FULL-LENGTH M2 VARIANT BINDING

AMINO ACID SEQUENCES OF EXTRACELLULAR DOMAINS OF M2 VARIANTS.

SEQ ID: No:									10								20							
1	A.Brevig Mission.1.1918.H1N1	M	S	L	L	T	E	V	E	T	P	T	R	N	E	W	G	C	R	C	N	D	S	S	D
2	A.Fort Monmouth.1.1947.H1N1	M	S	L	L	T	E	V	E	T	P	T	K	N	E	W	E	C	R	C	N	D	S	S	D
3	A.Singapore.02.2005.H3N2	M	S	L	L	T	E	V	E	T	P	I	R	N	E	W	E	C	R	C	N	D	S	S	D
679	A.Wisconsin.10.98.H1N1	M	S	L	L	T	E	V	E	T	P	I	K	N	G	W	E	C	K	C	N	D	S	S	D
5	A.Wisconsin.301.1976.H1N1	M	S	L	L	T	E	V	E	T	P	I	R	S	E	W	G	C	R	C	N	D	S	S	D
6	A.Panama.1.66.H2N2	M	S	F	L	P	E	V	E	T	P	I	R	N	E	W	G	C	R	C	N	D	S	S	D
7	A.New York.321.1999.H3N2	M	S	L	L	T	E	V	E	T	P	I	R	N	E	W	G	C	R	C	N	D	S	S	N
8	A.Caracas.1.71.H3N2	M	S	L	L	T	E	V	E	T	P	I	R	K	E	W	G	C	R	C	N	D	S	S	D
9	A.Taiwan.3.71.H3N2	M	S	F	L	T	E	V	E	T	P	I	R	N	E	W	G	C	R	C	N	D	S	S	D
10	A.Wuhan.359.95.H3N2	M	S	L	P	T	E	V	E	T	P	I	R	S	E	W	G	C	R	C	N	D	S	S	D
11	A.Hong Kong.1144.99.H3N2	M	S	L	L	P	E	V	E	T	P	I	R	N	E	W	G	C	R	C	N	D	S	S	D
12	A.Hong Kong.1180.99 H3N2	M	S	L	L	P	E	V	E	T	P	I	R	N	G	W	G	C	R	C	N	D	S	S	D
13	A.Hong Kong.1774.99 H3N2	M	S	L	L	T	E	V	E	T	P	T	R	N	G	W	E	C	R	C	S	G	S	S	D
14	A.New York.217.02 H1N2	M	S	L	L	T	E	V	E	T	P	I	R	N	E	W	E	Y	R	C	N	D	S	S	D
15	A.New York.300.2003.H1N2	M	S	L	L	T	E	V	E	T	P	I	R	N	E	W	E	Y	R	C	S	D	S	S	D
16	A.swine.Spain.54008.2004.H3N2	M	S	L	L	T	E	V	E	T	P	T	R	N	G	W	E	C	R	Y	S	D	S	S	D
17	A.Guangzhou.333.99.H9N2	M	S	F	L	T	E	V	E	T	L	T	R	N	G	W	E	C	R	C	S	D	S	S	D
18	A.Hong Kong.1073.99.H9N2	M	S	L	L	T	E	V	E	T	L	T	R	N	G	W	E	C	K	C	R	D	S	S	D
19	A.Hong Kong.1.68.H3N2	M	S	L	L	T	E	V	E	T	P	I	R	N	E	W	G	C	R	C	N	D	S	S	D
20	A.swine.Hong Kong.126.1982.H3N2	M	S	L	L	T	E	V	E	T	P	I	R	S	E	W	G	C	R	C	N	D	S	G	D
21	A.New York.703.1995.H3N2	M	S	L	L	T	E	V	E	T	P	I	R	N	E	W	E	C	R	C	N	G	S	S	D
22	A.swine.Quebec.192.81 H1N1	M	S	L	P	T	E	V	E	T	P	I	R	N	E	W	G	C	R	C	N	D	S	S	D
23	A.Puerto Rico.8.34.H1N1	M	S	L	L	T	E	V	E	T	P	I	R	N	E	W	G	C	R	C	N	G	S	S	D
24	A.Hong Kong.485.97.H5N1	M	S	L	L	T	E	V	D	T	L	T	R	N	G	W	G	C	R	C	S	D	S	S	D
25	A.Hong Kong.542.97.H5N1	M	S	L	L	T	E	V	E	T	L	T	K	N	G	W	G	C	R	C	S	D	S	S	D
26	A.silky chicken.Shantou.1826.2004.H	M	S	L	L	T	E	V	E	T	P	T	R	N	G	W	E	C	K	C	S	D	S	S	D
27	A,chicken.Taiwan.0305.04.H6N1	M	S	L	L	T	E	V	E	T	H	T	R	N	G	W	E	C	K	C	S	D	S	S	D
28	A.Quail.Arkansas.16309-7.94.H7N3	M	S	L	L	T	E	V	K	T	P	T	R	N	G	W	E	C	K	C	S	D	S	S	D
29	A.Hong Kong.486.97.H5N1	M	S	L	L	T	E	V	E	T	L	T	R	N	G	W	G	C	R	C	S	D	S	S	D
30	A.Chicken.Pennsylvania.13552-1.98	M	S	L	L	T	E	V	E	T	P	T	R	D	G	W	E	C	K	C	S	D	S	S	D
31	A.chicken.Heilongjiang.48.01.H9N2	M	S	L	L	T	E	V	E	T	P	T	R	N	G	W	G	C	R	C	S	D	S	S	D
32	A.swine.Korea.S5.2005.H1N2	M	S	L	L	T	E	V	E	T	P	T	R	N	G	W	E	C	K	C	N	D	S	S	D
33	A.Hong Kong.1073.99.H9N2	M	S	L	L	T	E	V	E	T	L	T	R	N	G	W	E	C	K	C	S	D	S	S	D
34	A.Wisconsin.3523.88.H1N1	M	S	L	L	T	E	V	E	T	P	I	R	N	E	W	G	C	K	C	N	D	S	S	D
35	A.X-31 Vaccine strain H3N2	M	S	F	L	T	E	V	E	T	P	I	R	N	E	W	G	C	R	C	N	G	S	S	D
36	A.Chicken.Rostock.8.1934.H7N1	M	S	L	L	T	E	V	E	T	P	T	R	N	G	W	E	C	R	C	N	D	S	S	D
37	A.environment.New York. 16326-1.2	M	S	L	L	T	E	V	E	T	P	I	R	K	G	W	E	C	N	C	S	D	S	S	D
38	A.Indonesia.560H.2006.H5N1	M	S	L	L	T	E	V	E	T	P	T	R	N	E	W	E	C	R	C	S	D	S	S	D
39	A.Chicken.Hong Kong.SF1.03.H9N2	M	S	L	L	T	G	V	E	T	H	T	R	N	G	W	G	C	K	C	S	D	S	S	D
40	A.chicken.Hong Kong YU427.03.H9N	M	S	L	L	P	E	V	E	T	H	T	R	N	G	W	G	C	R	C	S	D	S	S	D

EXTRACELLULAR SEQUENCE OF D20 IS IDENTICAL TO #19, HK483 TO #29, AND VN1203 TO #38.

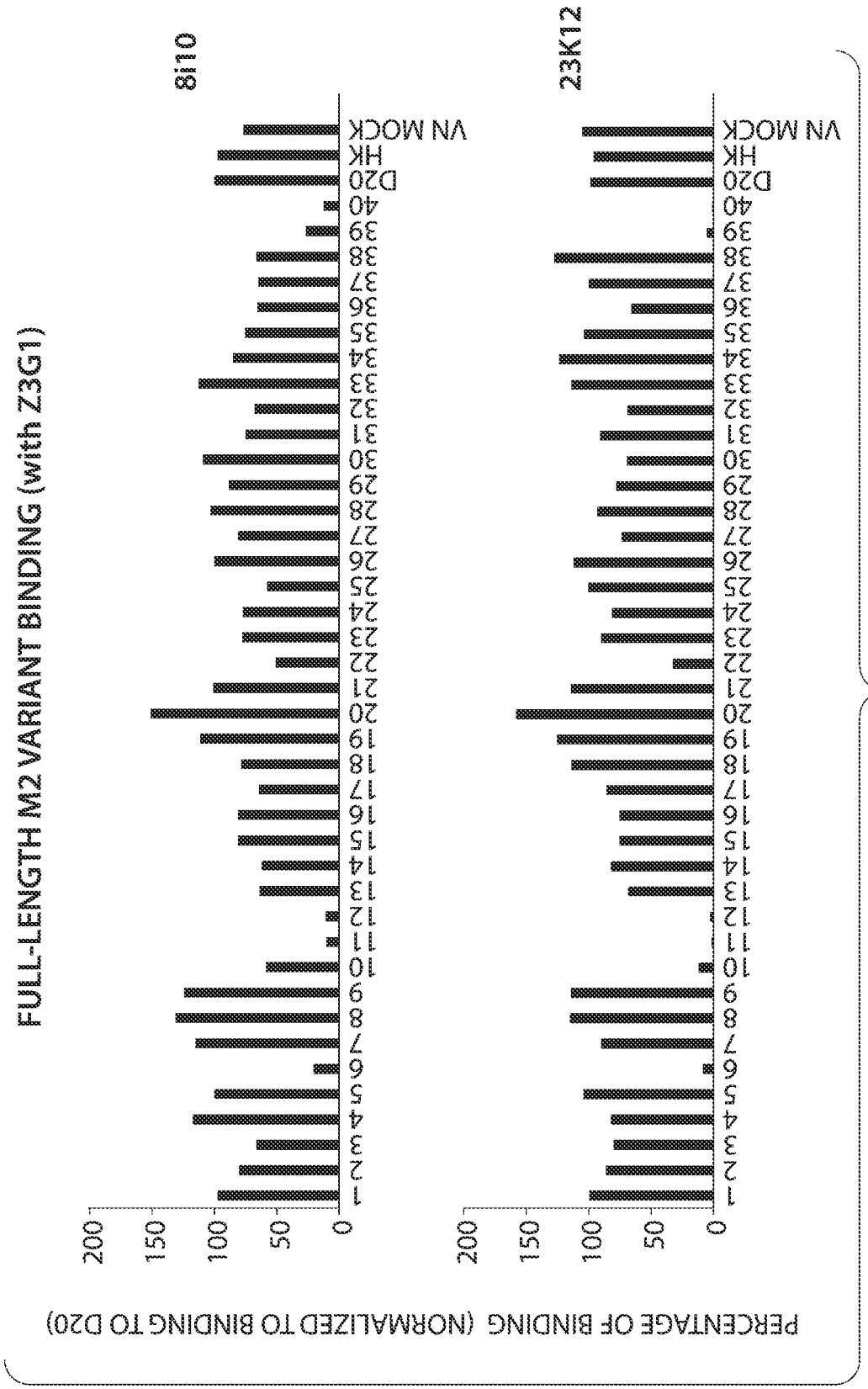

FULL-LENGTH M2 VARIANT BINDING (with Z3G1)
8i10
23K12
PERCENTAGE OF BINDING (NORMALIZED TO BINDING TO D20)
200
150
100
50
0
VN MOCK
HK
D20
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40

FIG. 3B-1

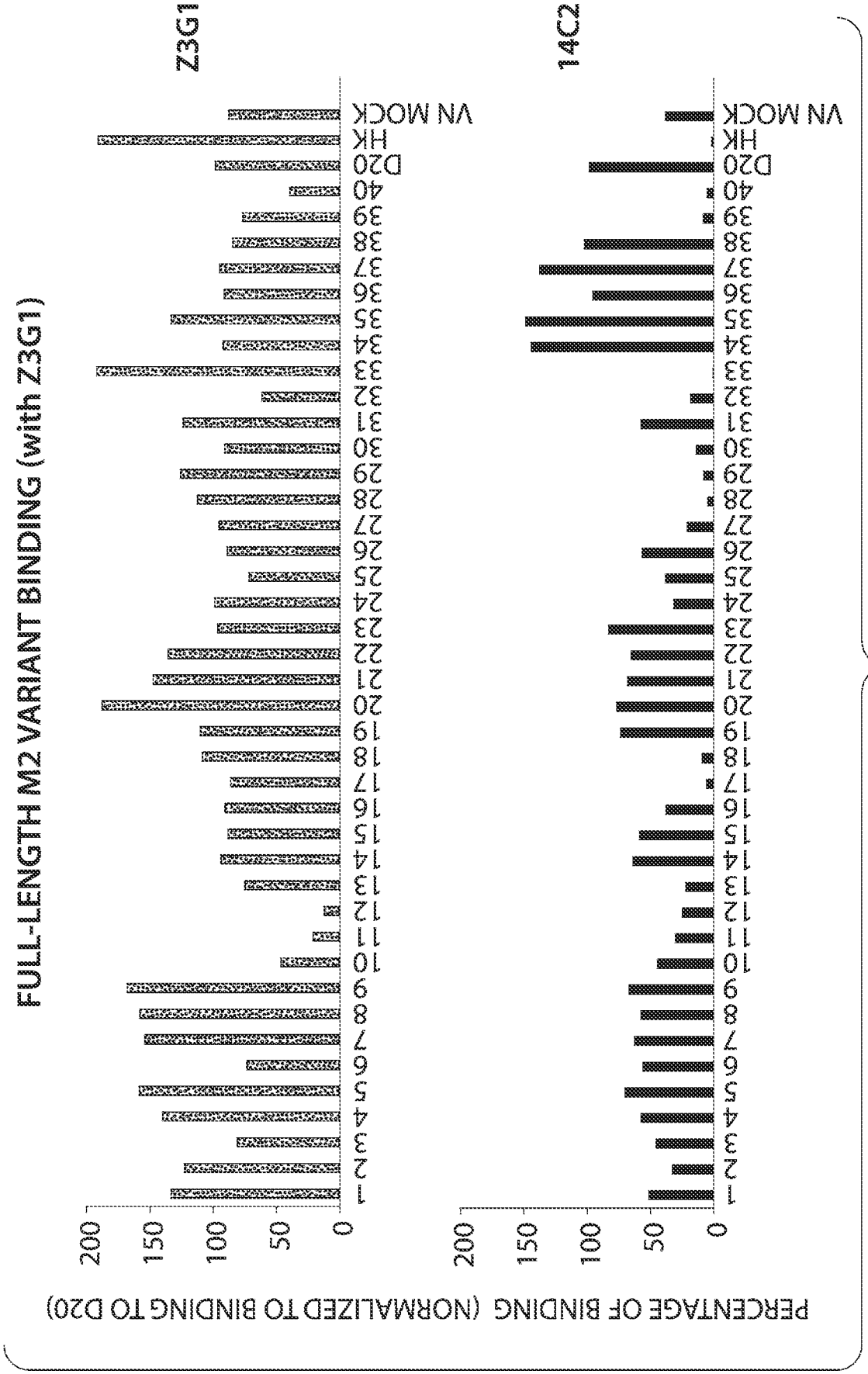

Z3G1
14C2
FULL-LENGTH M2 VARIANT BINDING (with Z3G1)
PERCENTAGE OF BINDING (NORMALIZED TO BINDING TO D20)
200
150
100
50
0
VN MOCK
HK
D20
40
39
38
37
36
35
34
33
32
31
30
29
28
27
26
25
24
23
22
21
20
19
18
17
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1

FIG. 3B-2

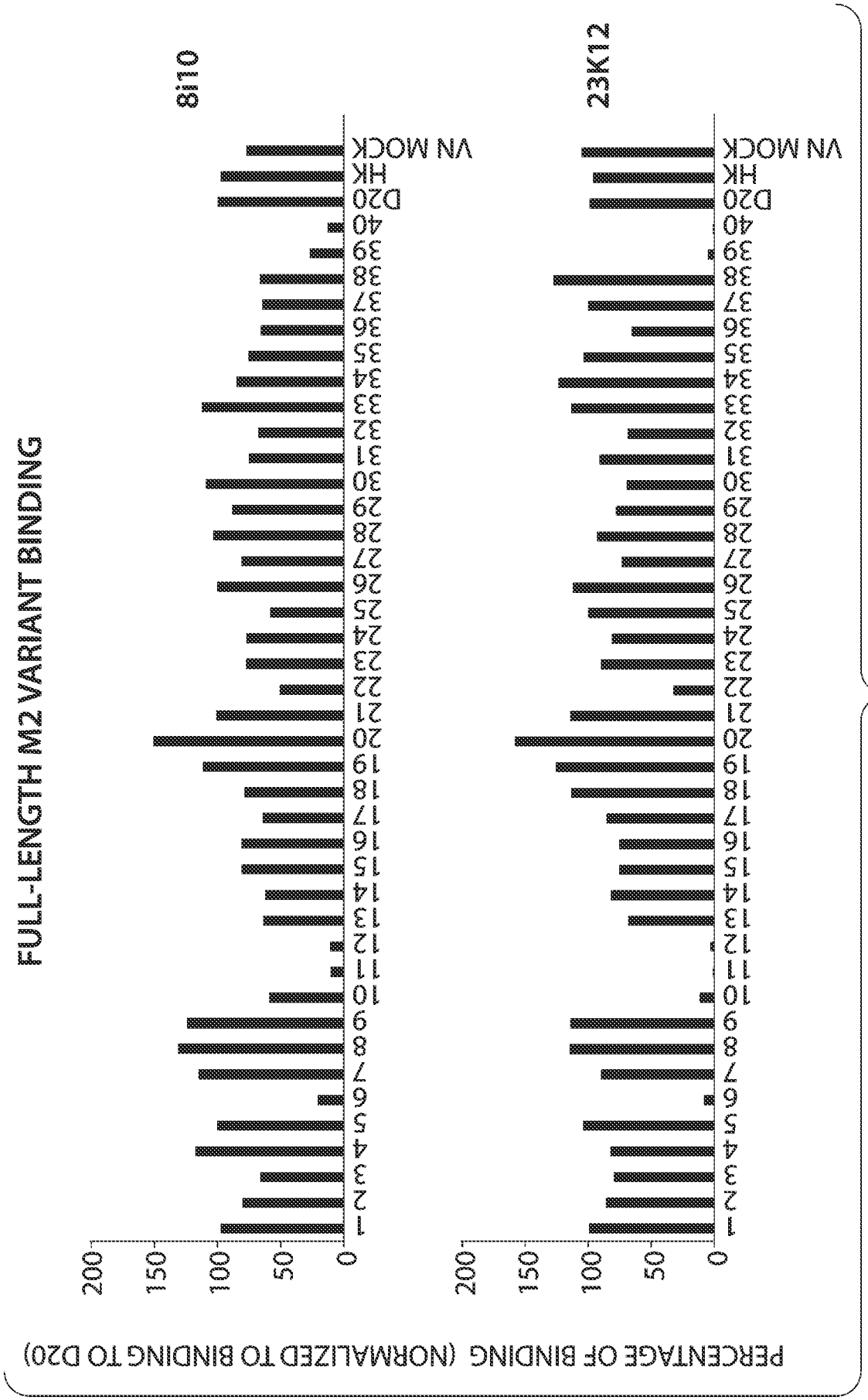

FULL-LENGTH M2 VARIANT BINDING
8i10
23K12
PERCENTAGE OF BINDING (NORMALIZED TO BINDING TO D20)
200
150
100
50
0
VN MOCK
HK
D20
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40

FIG. 3C-1

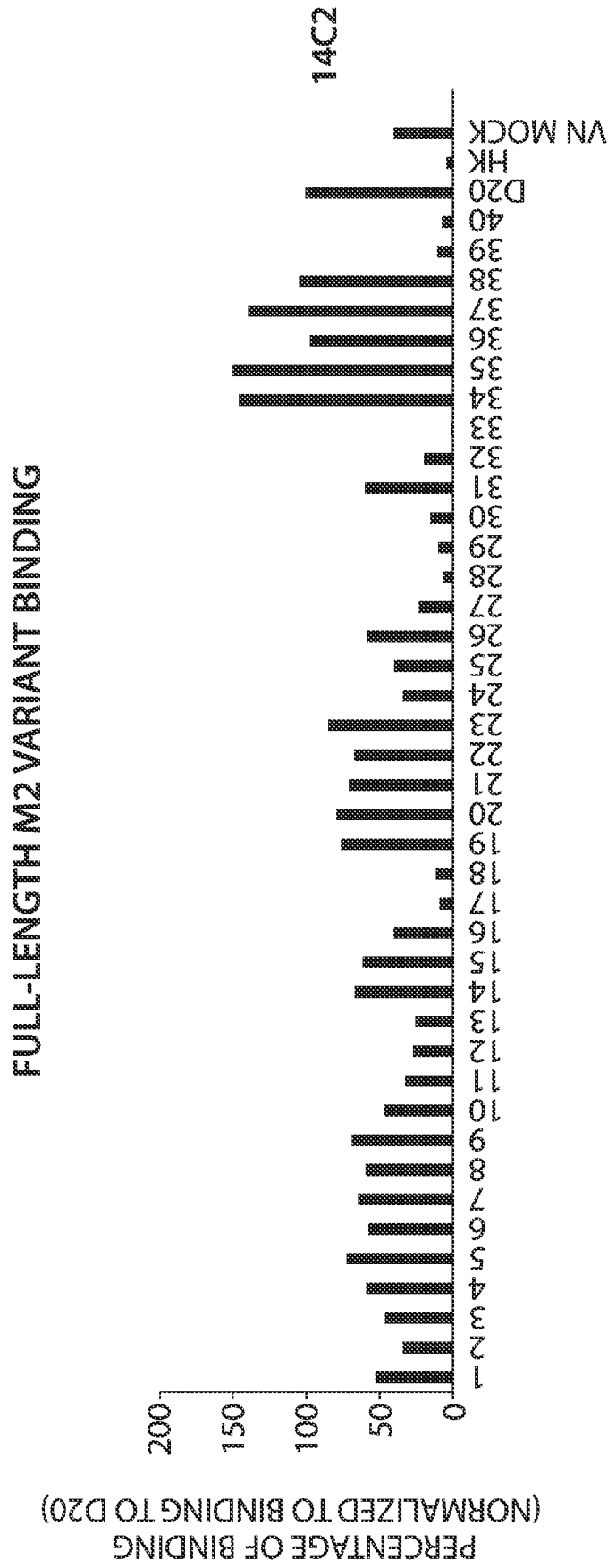

14C2
FULL-LENGTH M2 VARIANT BINDING
PERCENTAGE OF BINDING
(NORMALIZED TO BINDING TO D20)
200
150
100
50
0
VN MOCK
HK
D20
40
39
38
37
36
35
34
33
32
31
30
29
28
27
26
25
24
23
22
21
20
19
18
17
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1

FIG. 3C-2

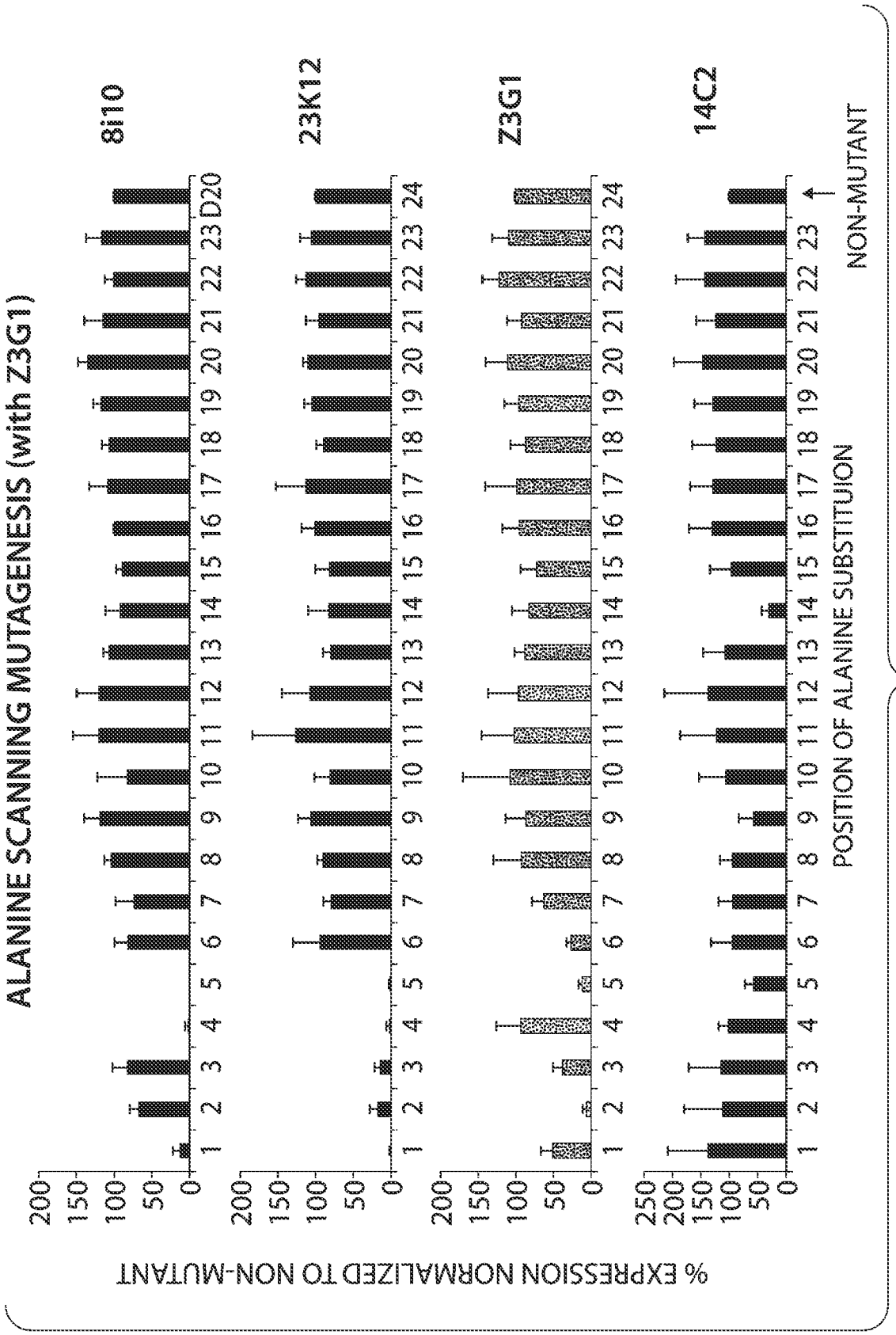

ALANINE SCANNING MUTAGENESIS (with Z3G1)
8i10
23K12
Z3G1
14C2
% EXPRESSION NORMALIZED TO NON-MUTANT
POSITION OF ALANINE SUBSTITUION
NON-MUTANT
D20

FIG. 4A

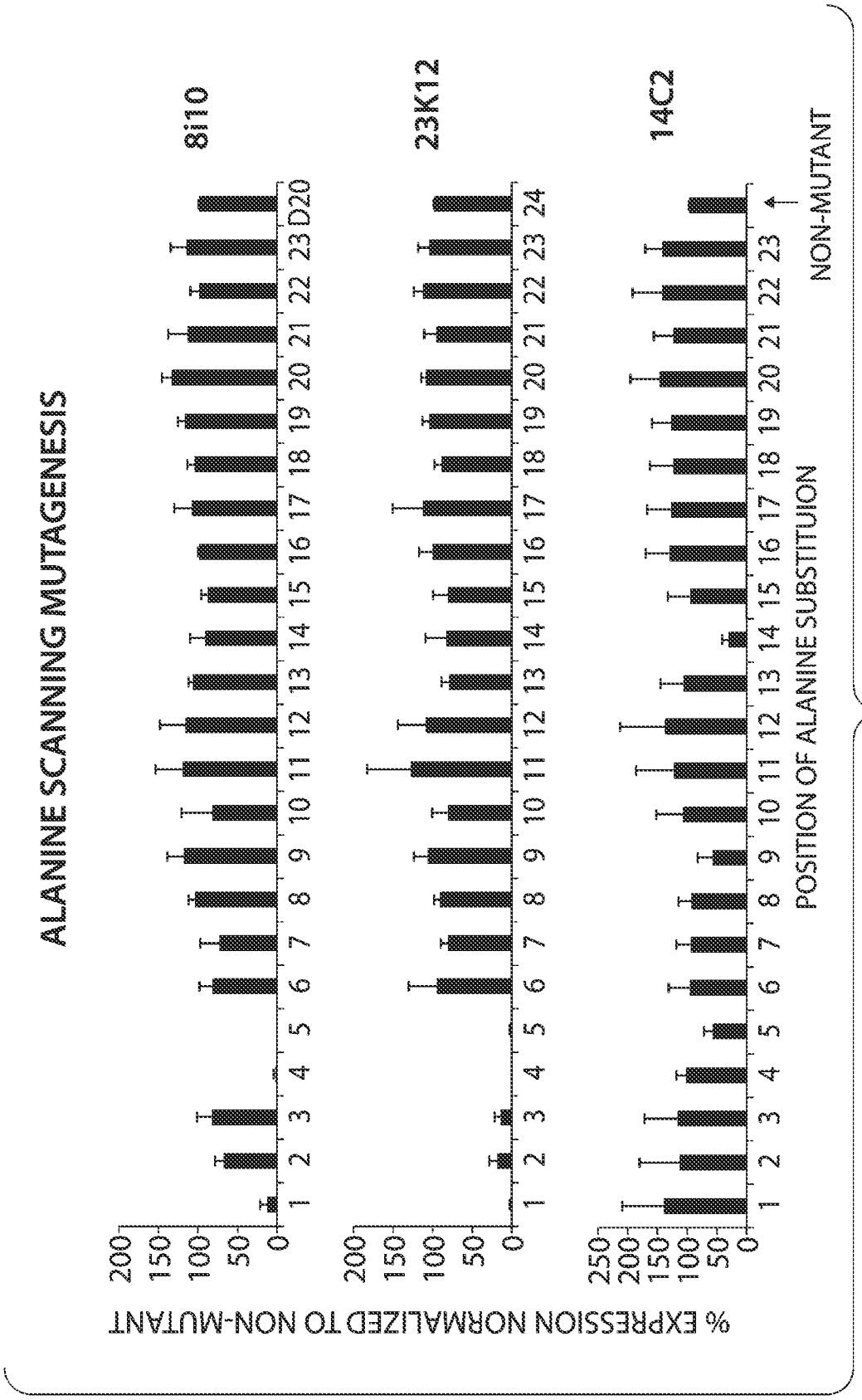

ALANINE SCANNING MUTAGENESIS
8i10
23K12
14C2
% EXPRESSION NORMALIZED TO NON-MUTANT
POSITION OF ALANINE SUBSTITUION
NON-MUTANT

FIG. 4B

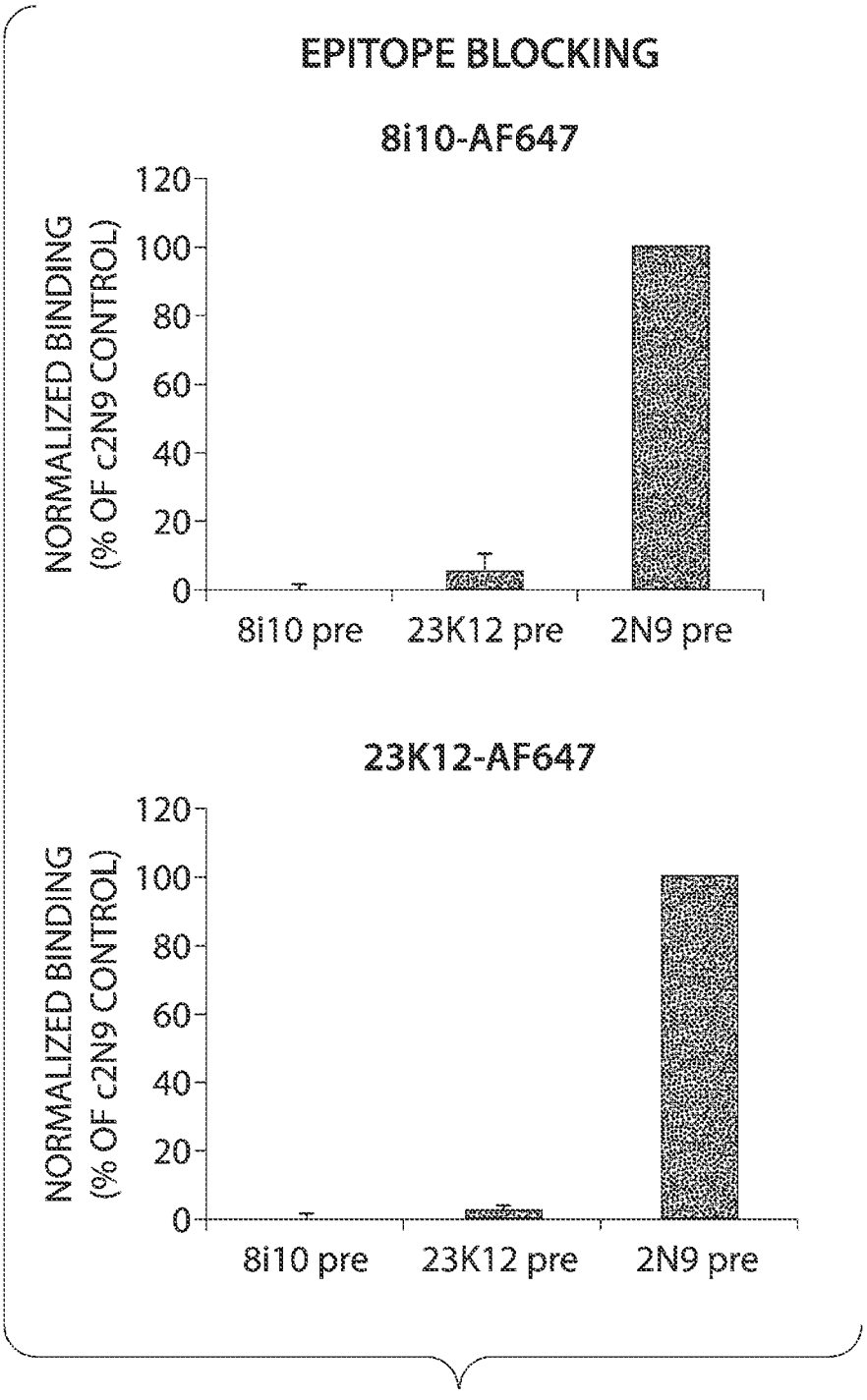

EPITOPE BLOCKING
8i10-AF647
NORMALIZED BINDING
(% OF c2N9 CONTROL)
120
100
80
60
40
20
0
8i10 pre
23K12 pre
2N9 pre
23K12-AF647
NORMALIZED BINDING
(% OF c2N9 CONTROL)
120
100
80
60
40
20
0
8i10 pre
23K12 pre
2N9 pre

FIG. 5

CROSS REACTIVITY BINDING OF ANTI-M2 ANTIBODIES TO VARIANT M2 PEPTIDES

				ELISA (OD 450)			
seqNo	Name	Size	Description	14C2	8i10	23K12	2N9
680	M2	23 aa	SLLTEVETPIRNEWGCRCNDSSD	+	-	-	-
681	M2SG	23 aa	SLLTEVETPIRSEWGCRCNDSGD	+	-	-	-
682	M2EG	23 aa	SLLTEVETPIRNEWECRCNGSSD	+	-	-	-
683	M2P	23 aa	SLPTEVETPIRNEWGCRCNDSSD	+	-	-	-
684	M2G	23 aa	SLLTEVETPIRNEWGCRCNGSSD	+	-	-	-
685	M2DLTGS	23 aa	SLLTEVDTLTRNGWGCRCSDSSD	-	-	+	-
686	M2KNS	23 aa	SLLTEVETPIRKEWGCNCSDSSD	+	-	-	-
687	M2LGS	23 aa	SLLTEVETLIRNGWGCRCSDSSD	-	-	-	-
688	M2LTKGS	23 aa	SLLTEVETLTKNGWGCRCSDSSD	-	-	-	-
689	M2SY	23 aa	SLLTEVETPIRSEWGCRYNDSSD	+	-	-	-
690	M2TGEKS	23 aa	SLLTEVETPTRNGWECKCSDSSD	+	-	-	-
691	M2HTGEKS	23 aa	SLLTEVETHTRNGWECKCSDSSD	-	-	-	-
692	M2KTGEKS	23 aa	SLLTEVKTPTRNGWECKCSDSSD	-	-	-	-
693	M2LTGS	23 aa	SLLTEVETLTRNGWGCRCSDSSD	-	-	+	-
694	M2TDGEKS	23 aa	SLLTEVETPTRDGWECKCSDSSD	+	-	-	-
695	M2TGS	23 aa	SLLTEVETPTRNGWGCRCSDSSD	+	-	W	-
696	M2TGEK	23 aa	SLLTEVETPTRNGWECKCNDSSD	+	-	-	-
697	M2LTGEKS	23 aa	SLLTEVETLTRNGWECKCSDSSD	-	-	W	-
698	M2K	23 aa	SLLTEVETPIRNEWGCKCNDSSD	+	W	+	-
699	M2FG	23 aa	SFLTEVETPIRNEWGCRCNGSSD	+	W	-	-
700	M2TGE	23 aa	SLLTEVETPTRNGWECRCNDSSD	+	-	-	-
701	M2KGENS	23 aa	SLLTEVETPIRKGWECNCSDSSD	+	-	-	-
702	M2TES	23 aa	SLLTEVETPTRNEWECRCSDSSD	+	-	-	-
703	M2GHTGKS	23 aa	SLLTGVETHTRNGWGCKCSDSSD	-	-	-	-
704	M2PHTGS	23 aa	SLLPEVETHTRNGWGCRCSDSSD	-	-	-	-

PERCENTAGE COMPARED RELATIVE TO BINDING TO WILD-TYPE PEPTIDE (Seq 1) NOTE: mAbs WERE TESTED AT 5 µg/mL

>25 %	-	NO BINDING
25 - 40 %	W	WEAK BINDING
> 40 %	+	POSITIVE BINDING

FIG. 6A

BINDING ACTIVITY OF M2 ANTIBODIES TO TRUNCATED M2 PEPTIDES

seqNo	Name	Size	Description	14C2	8i10	23K12	2N9
680	M2	23 aa	SLLTEVETPIRNEWGCRCNDSSD	3.85	0.11	0.22	0.06
705	M16	16 aa	LLTEVETPIRNEWGCR	3.94	0.09	0.21	0.09
706	M15	15 aa	LTEVETPIRNEWGCR	3.95	0.09	0.21	0.09
707	M12	12 aa	VETPIRNEWGCR	0.15	0.09	0.20	0.09
708	CM17	17 aa	ETPIRNEWGCRCNDSSD	0.19	0.11	0.34	0.11
709	CM16	16 aa	TPIRNEWGCRCNDSSD	0.23	0.13	0.35	0.12
710	CM15	15 aa	PIRNEWGCRCNDSSD	0.19	0.12	0.34	0.11
711	CM14	14 aa	IRNEWGCRCNDSSD	0.23	0.14	0.36	0.13
712	CM13	13 aa	RNEWGCRCNDSSD	0.22	0.14	0.34	0.13
713	CM12	12 aa	NEWGCRCNDSSD	0.27	0.14	0.39	0.14
714	NM17	17 aa	SLLTEVETPIRNEWGCR	3.99	0.26	0.58	0.10
715	NM16	16 aa	SLLTEVETPIRNEWGC	3.90	0.29	0.62	0.09
716	NM15	15 aa	SLLTEVETPIRNEWG	3.97	0.12	0.30	0.11
717	NM14	14 aa	SLLTEVETPIRNEW	3.97	0.11	0.24	0.09
718	NM13	13 aa	SLLTEVETPIRNE	0.18	0.11	0.25	0.10
719	NM12	12 aa	SLLTEVETPIRN	0.20	0.10	0.24	0.09
720	NM11	11 aa	SLLTEVETPIR	0.21	0.13	0.30	0.12
721	NM10	10 aa	SLLTEVETPI	0.17	0.10	0.24	0.10
722	NM8	8 aa	SLLTEVET	0.15	0.10	0.20	0.09
723	NM7	7 aa	SLLTEVE	0.14	0.10	0.20	0.08
724	NM9	9 aa	SLLTEVETP	0.21	0.12	0.30	0.19
19	M2e	24 aa	MSLLTEVETPIRNEWGCRCNDSSD	3.98	0.13	0.43	0.10
CMV	HVIR1			0.16	0.11	0.21	3.99

NOTE: mAbs WERE TESTED AT 5 µg/mL

FIG. 6B

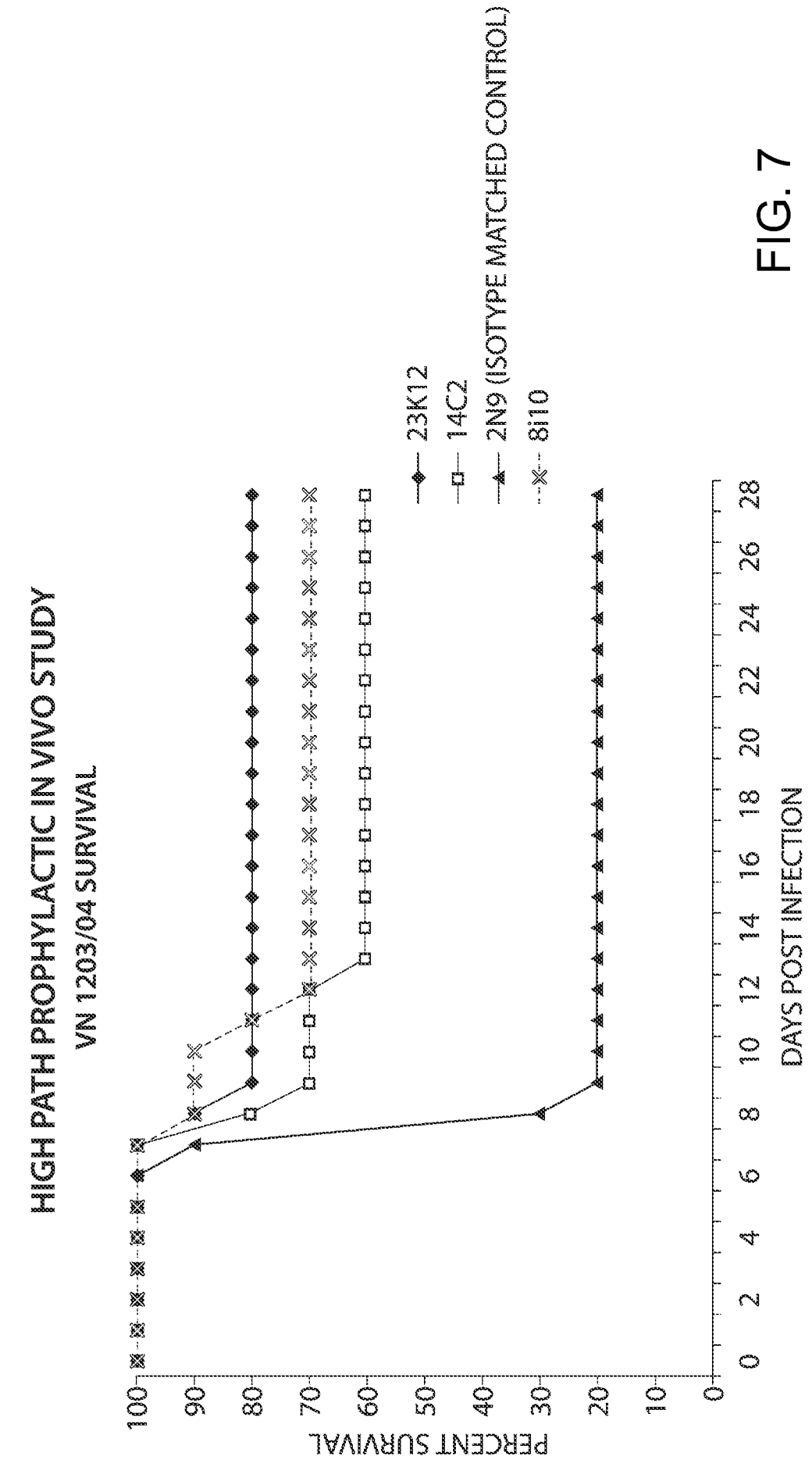

HIGH PATH PROPHYLACTIC IN VIVO STUDY
VN 1203/04 SURVIVAL
PERCENT SURVIVAL
DAYS POST INFECTION
23K12
14C2
2N9 (ISOTYPE MATCHED CONTROL)
8i10
0
10
20
30
40
50
60
70
80
90
100
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28

FIG. 7

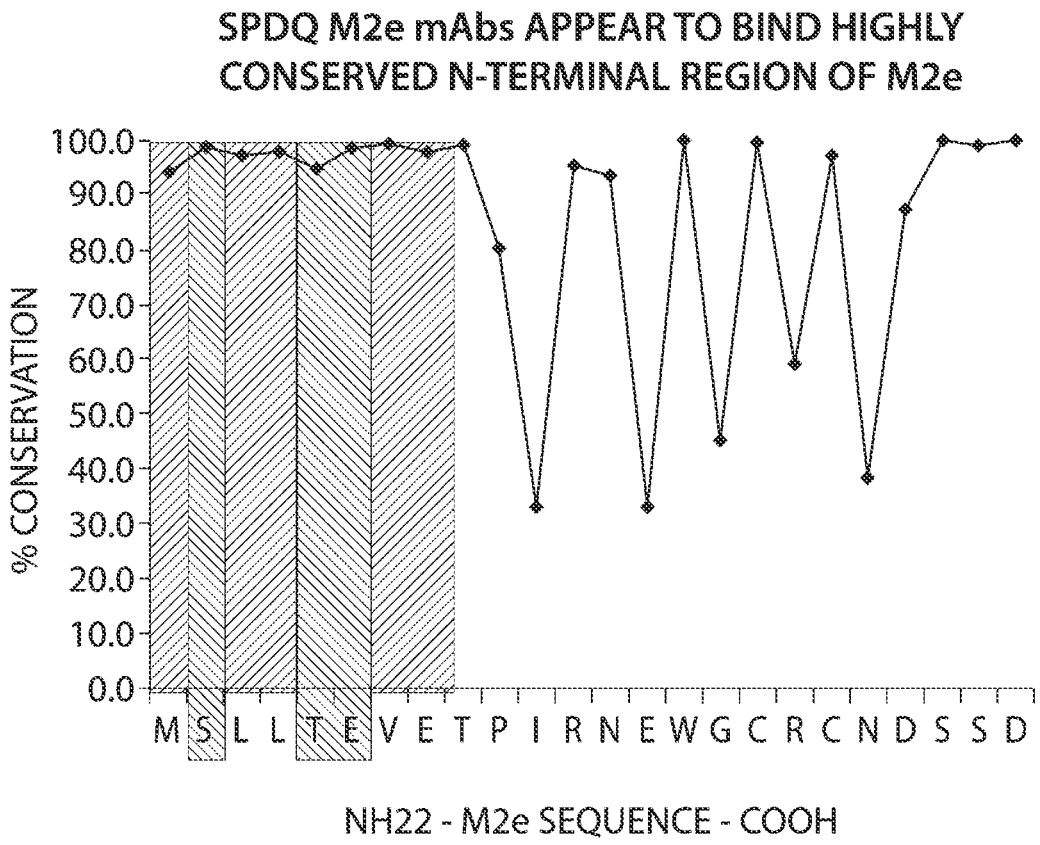

SPDQ M2e mAbs APPEAR TO BIND HIGHLY CONSERVED N-TERMINAL REGION OF M2e
% CONSERVATION
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
M S L L T E V E T P I R N E W G C R C N D S S D
NH22 - M2e SEQUENCE - COOH

FIG. 8

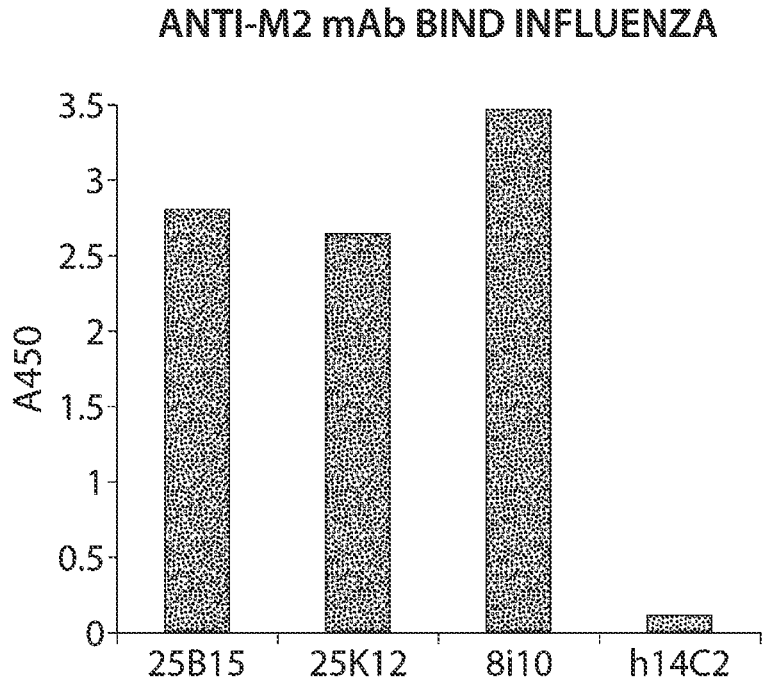

ANTI-M2 mAb BIND INFLUENZA
A450
3.5
3
2.5
2
1.5
1
0.5
0
25B15
25K12
8i10
h14C2

FIG. 9

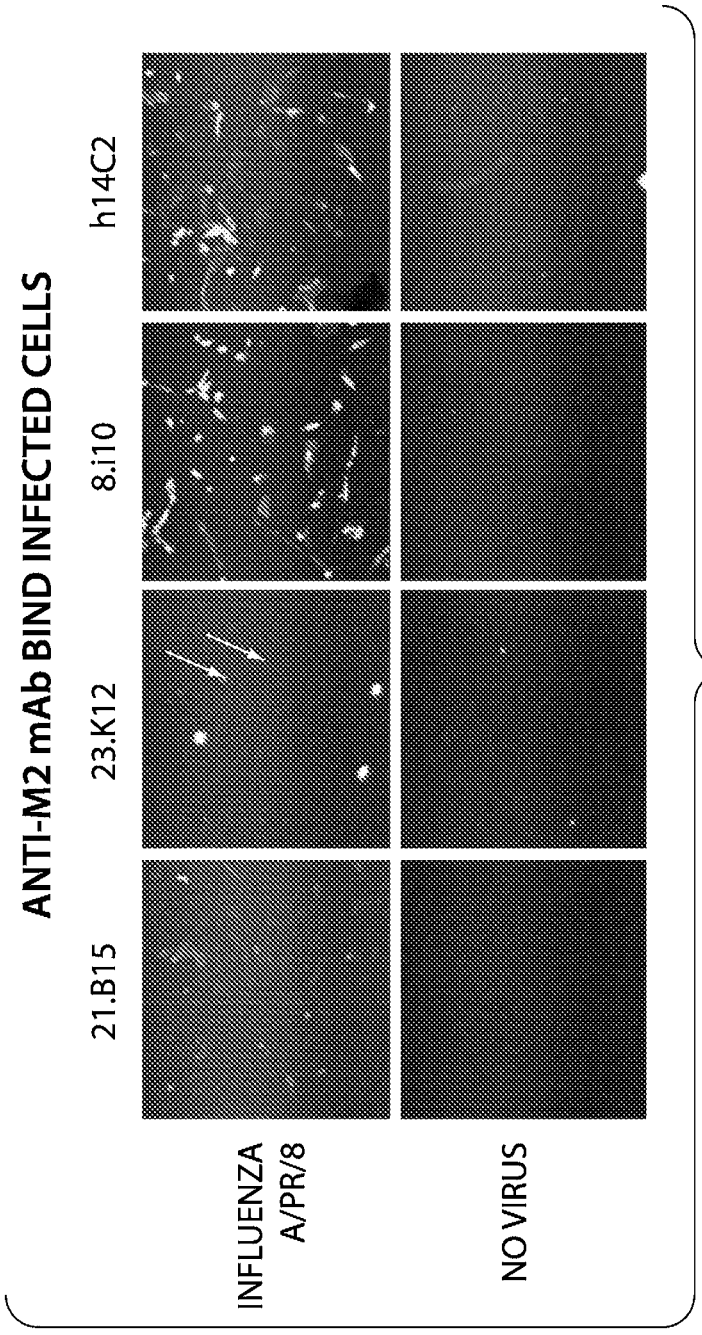

ANTI-M2 mAb BIND INFECTED CELLS
21.B15
23.K12
8.i10
h14C2
INFLUENZA A/PR/8
NO VIRUS

FIG. 10

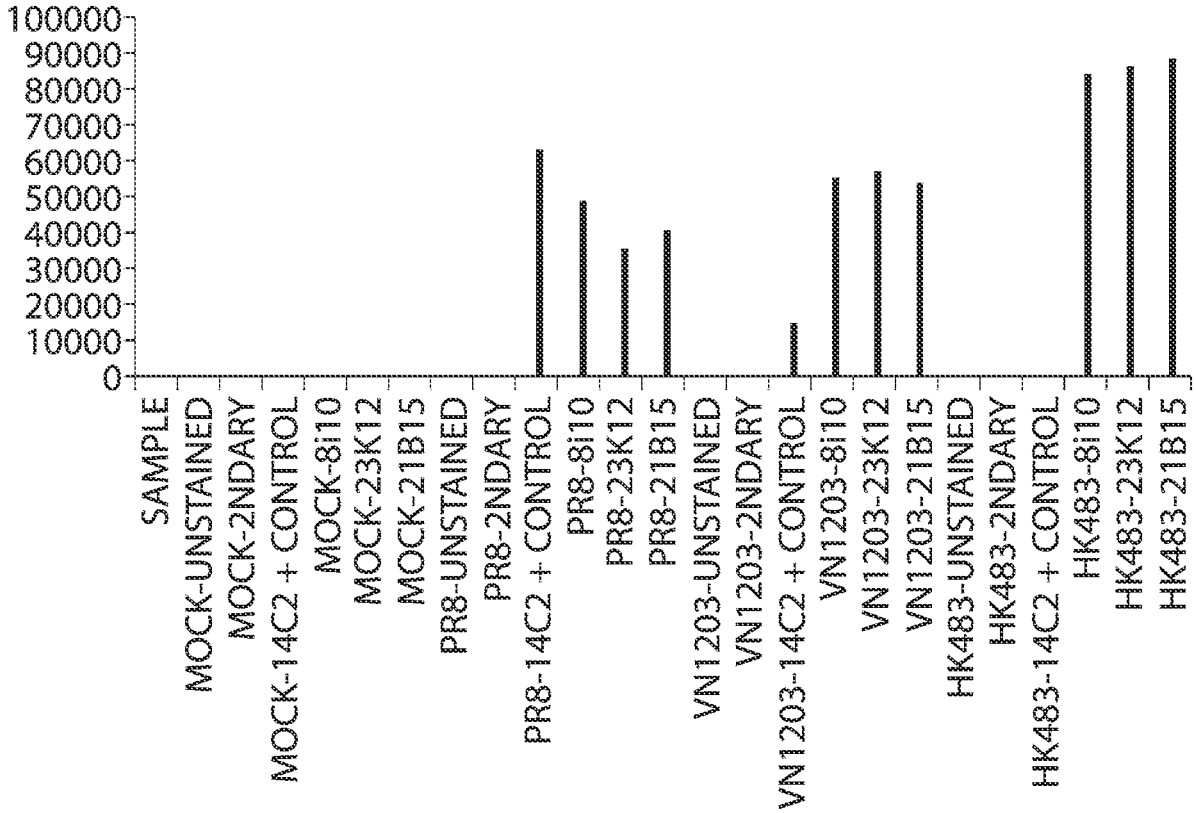

100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
SAMPLE
MOCK-UNSTAINED
MOCK-2NDARY
MOCK-14C2 + CONTROL
MOCK-8i10
MOCK-23K12
MOCK-21B15
PR8-UNSTAINED
PR8-2NDARY
PR8-14C2 + CONTROL
PR8-8i10
PR8-23K12
PR8-21B15
VN1203-UNSTAINED
VN1203-2NDARY
VN1203-14C2 + CONTROL
VN1203-8i10
VN1203-23K12
VN1203-21B15
HK483-UNSTAINED
HK483-2NDARY
HK483-14C2 + CONTROL
HK483-8i10
HK483-23K12
HK483-21B15

FIG. 11

FIG. 12A

Heavy Chain

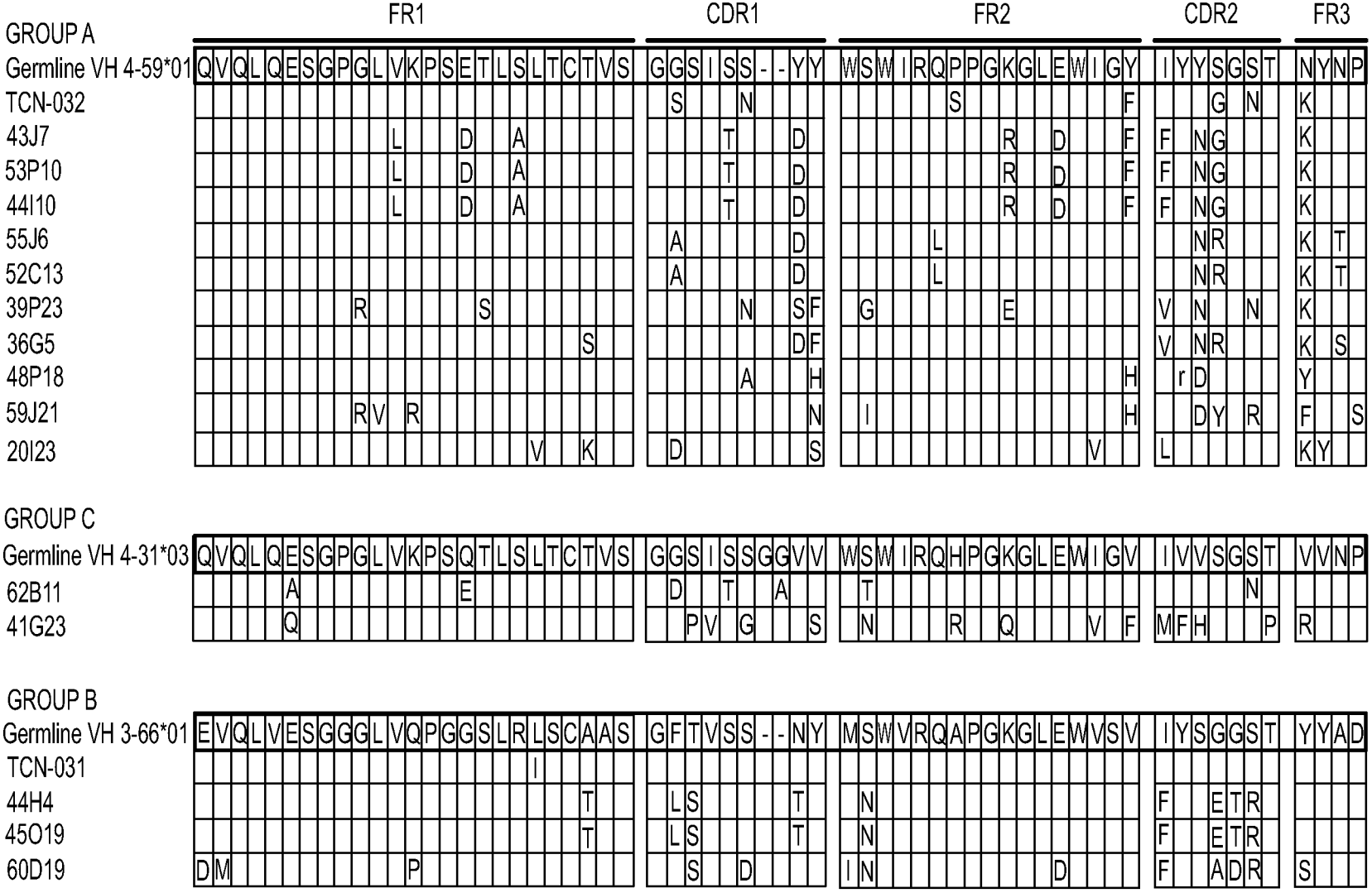


FIG. 12A (continued)

Heavy Chain

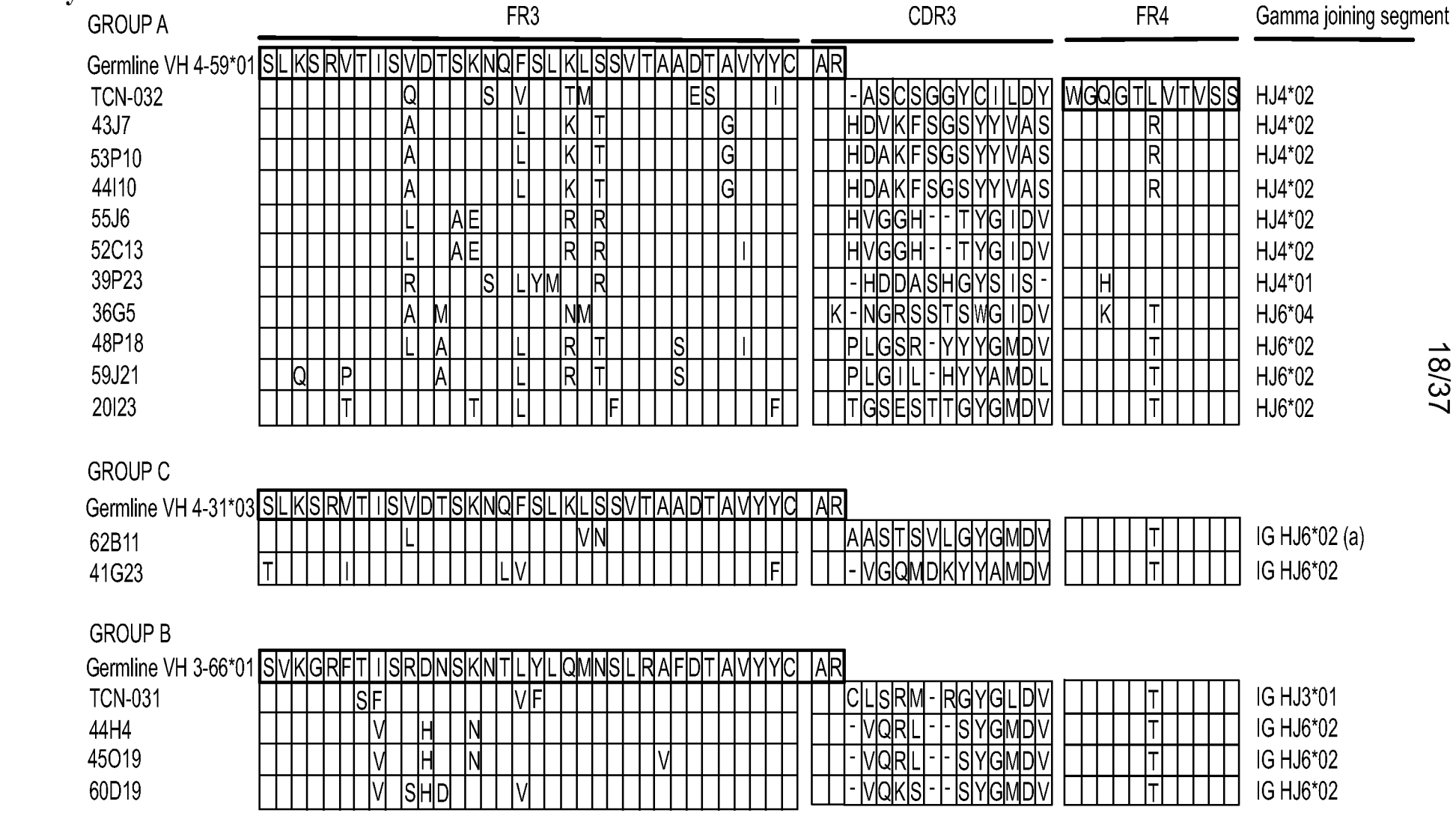


FIG. 12B

Kappa Chain

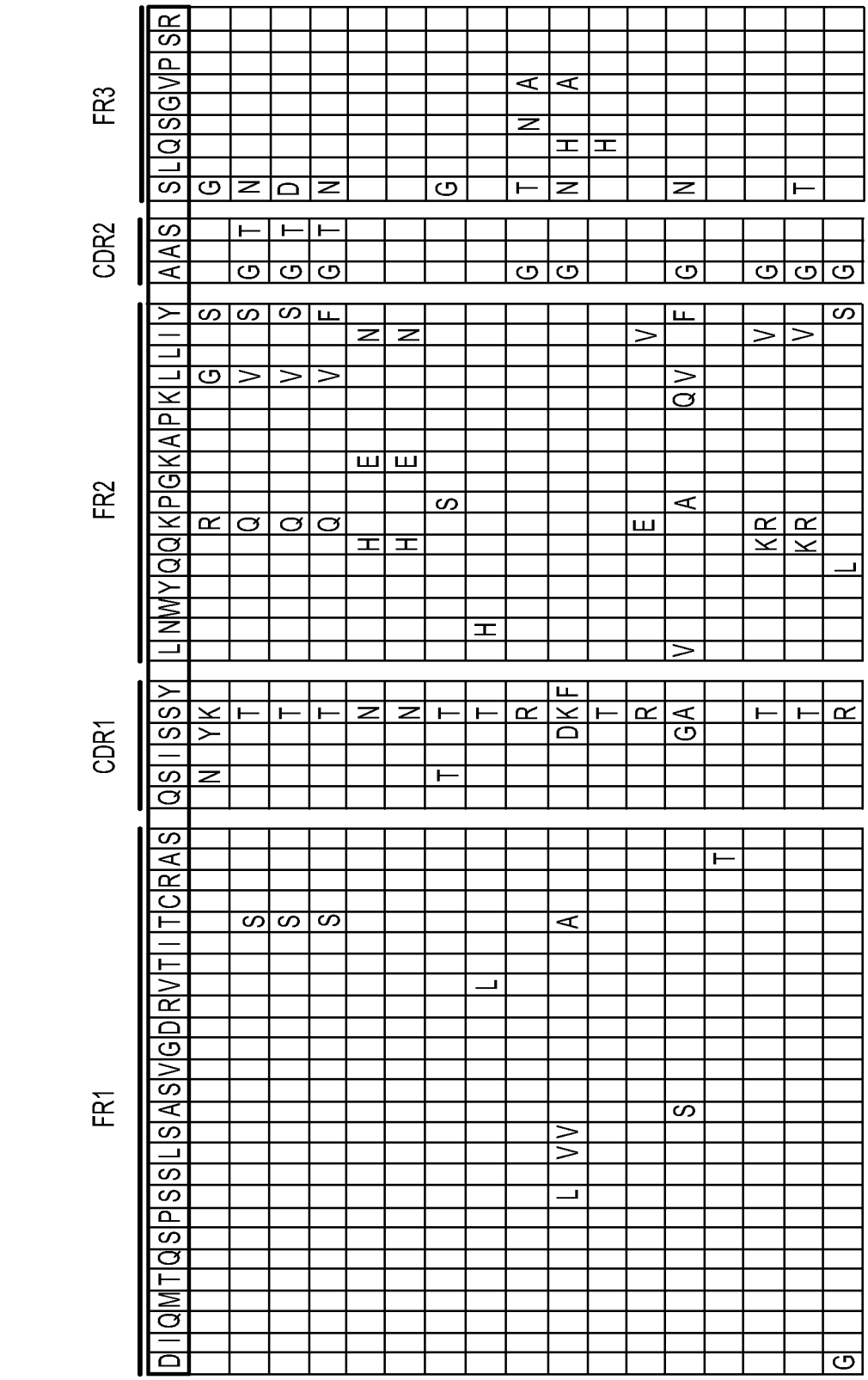
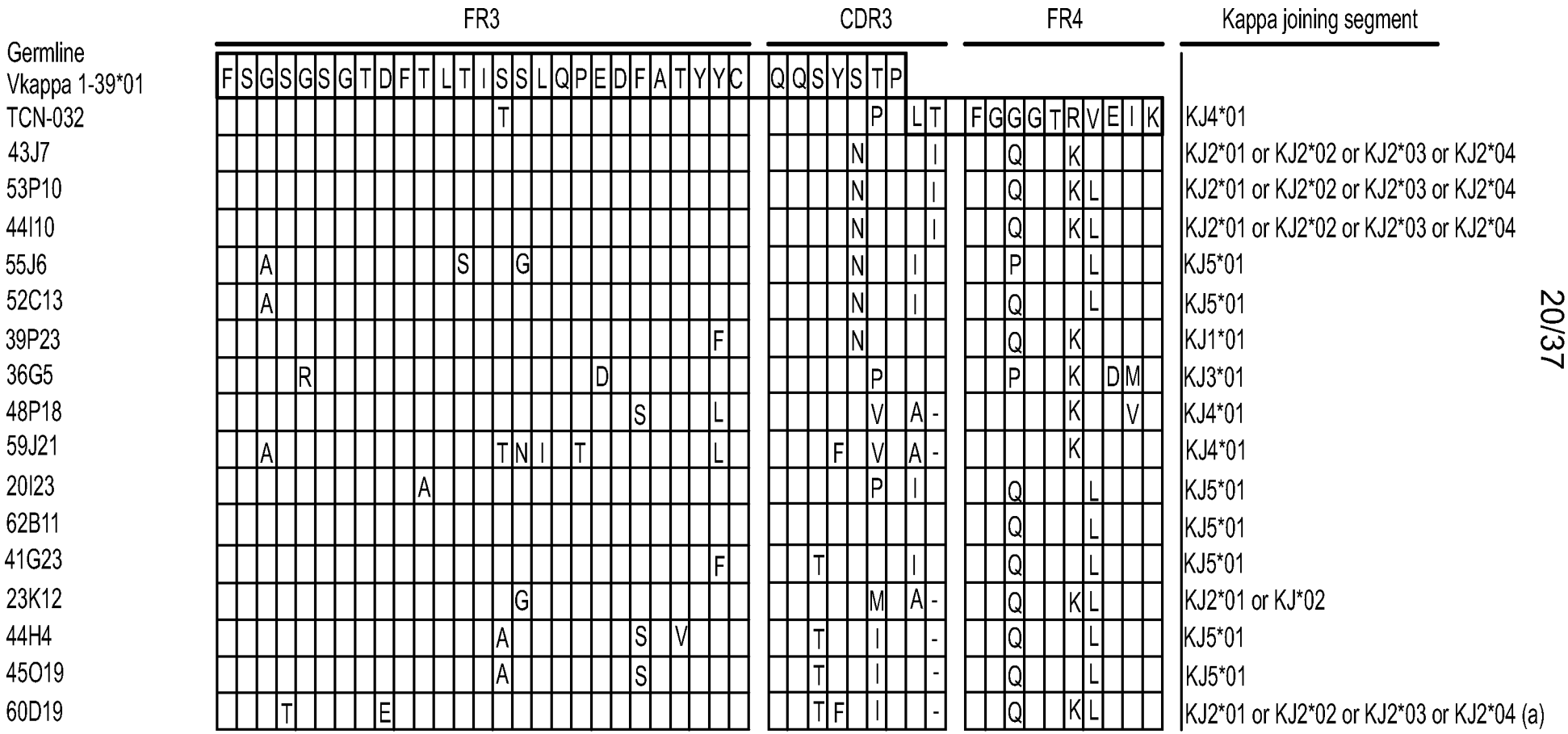


FIG. 12B (continued)



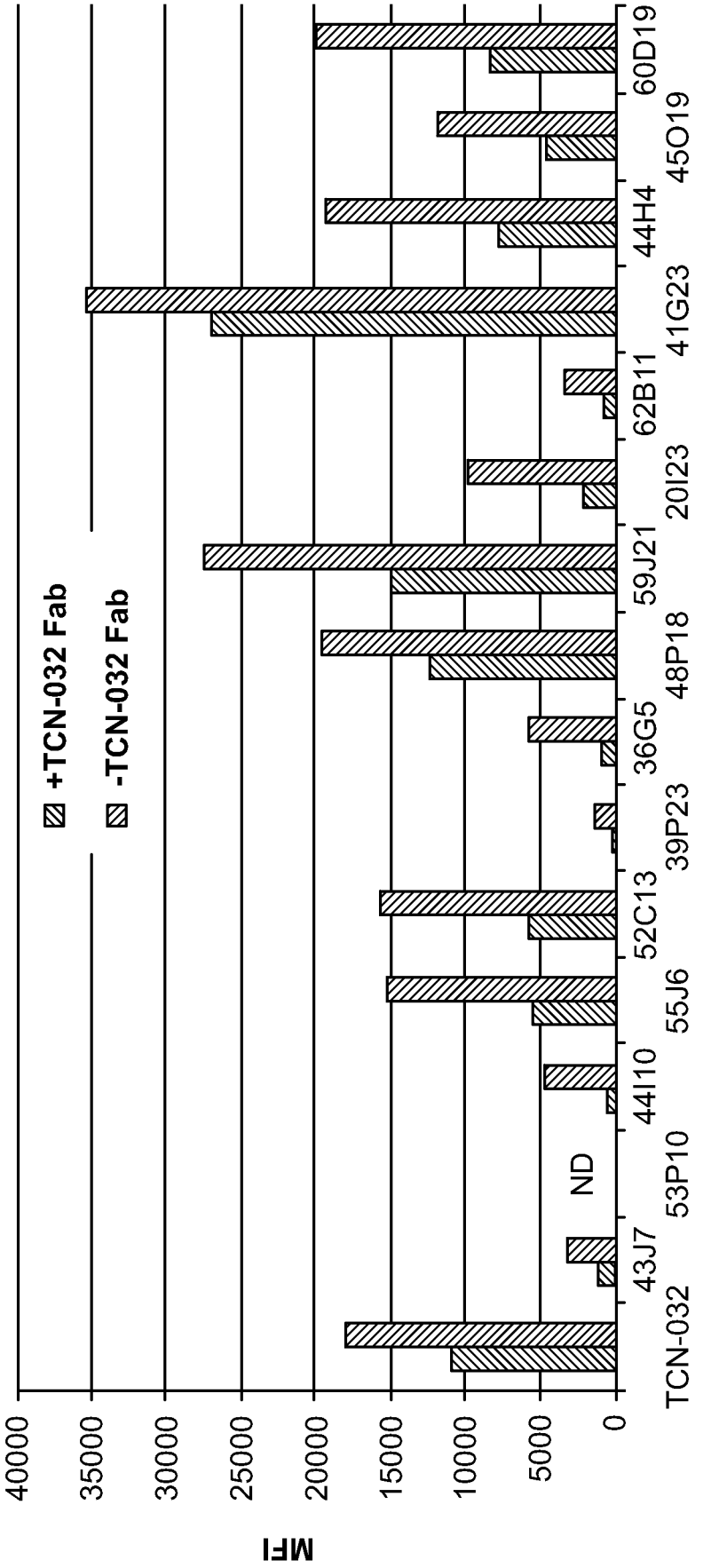

+TCN-032 Fab
-TCN-032 Fab
MFI
40000
35000
30000
25000
20000
15000
10000
5000
0
TCN-032
43J7
53P10
ND
44I10
55J6
52C13
39P23
36G5
48P18
59J21
20I23
62B11
41G23
44H4
45O19
60D19
mAb

FIG. 13

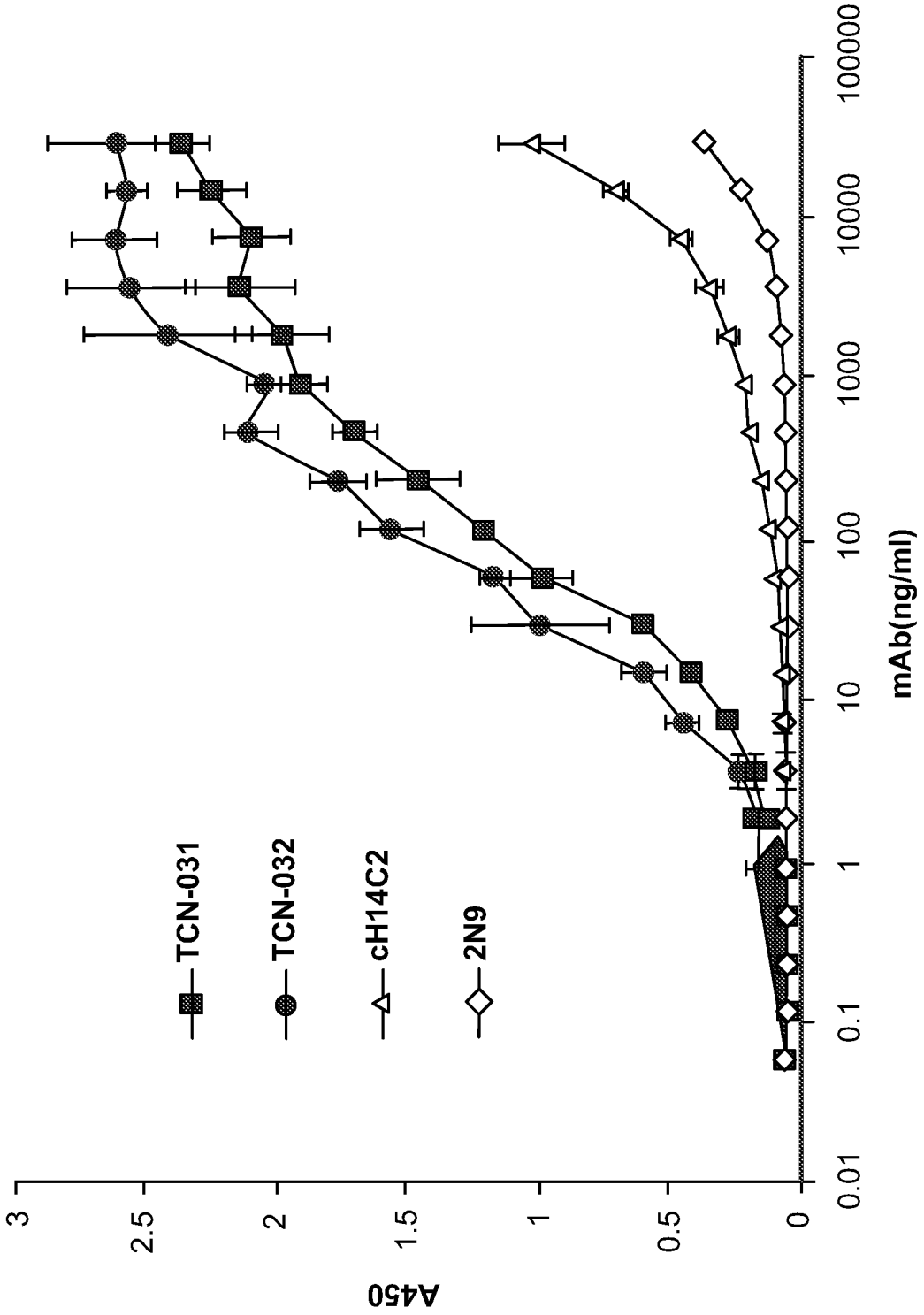

A450
mAb(ng/ml)
TCN-031
TCN-032
cH14C2
2N9
0
0.5
1
1.5
2
2.5
3
0.01
0.1
1
10
100
1000
10000
100000

FIG. 14A

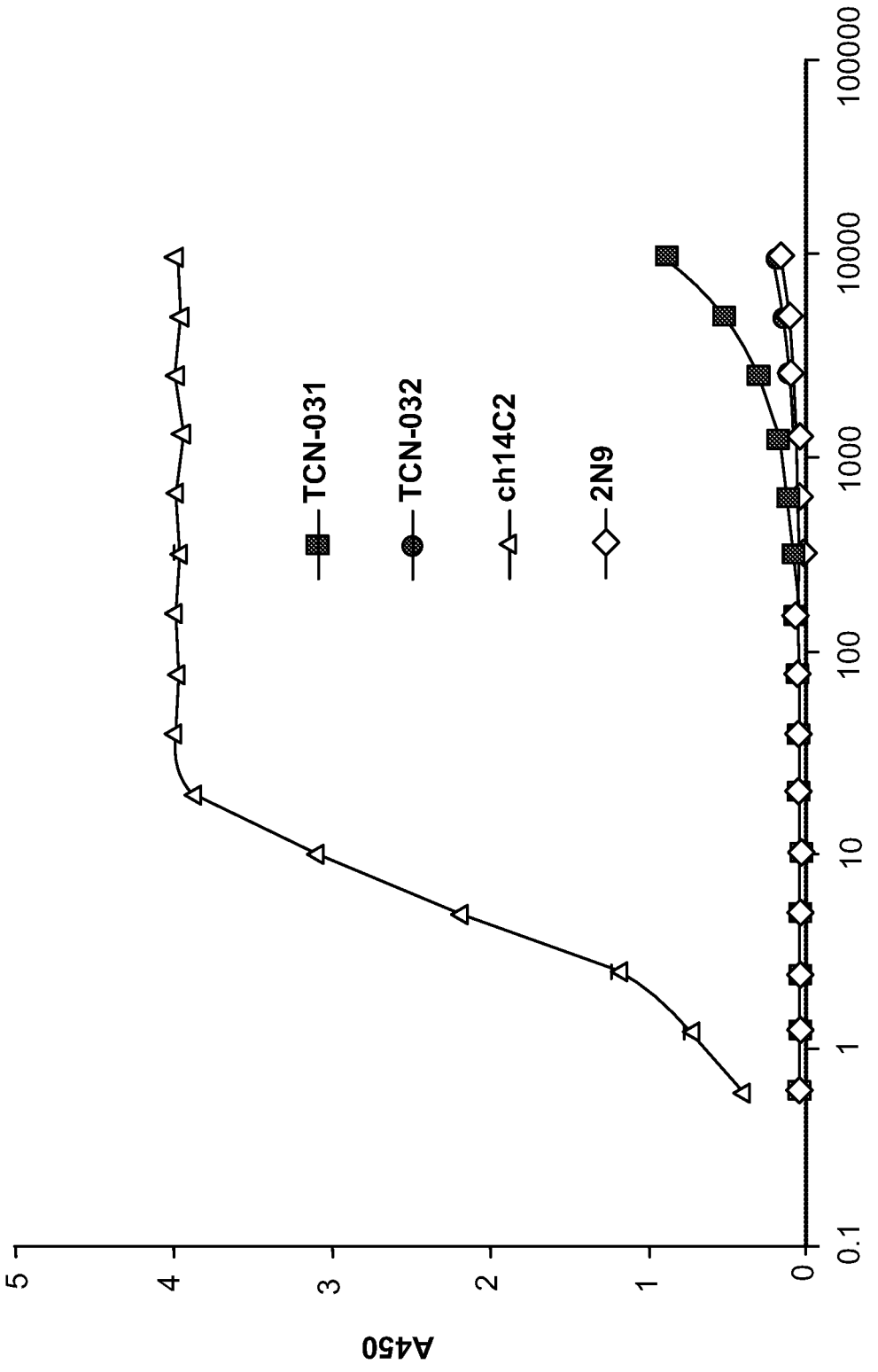

A450
mAb(ng/mL)
TCN-031
TCN-032
ch14C2
2N9
0
1
2
3
4
5
0.1
1
10
100
1000
10000
100000

FIG. 14B

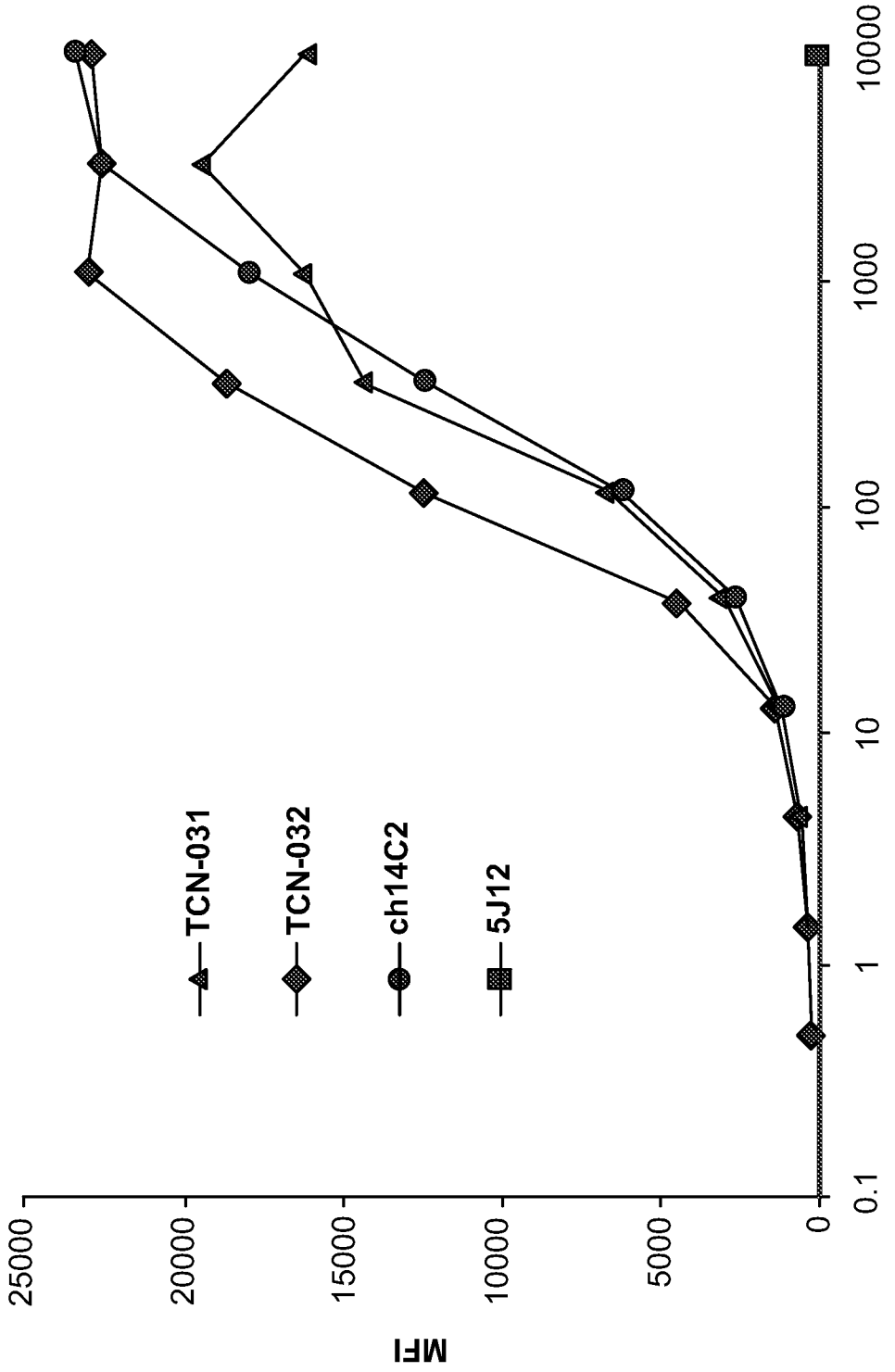

MFI
25000
20000
15000
10000
5000
0
0.1
1
10
100
1000
10000
mAb (ng/ml)
TCN-031
TCN-032
ch14C2
5J12

FIG. 14C

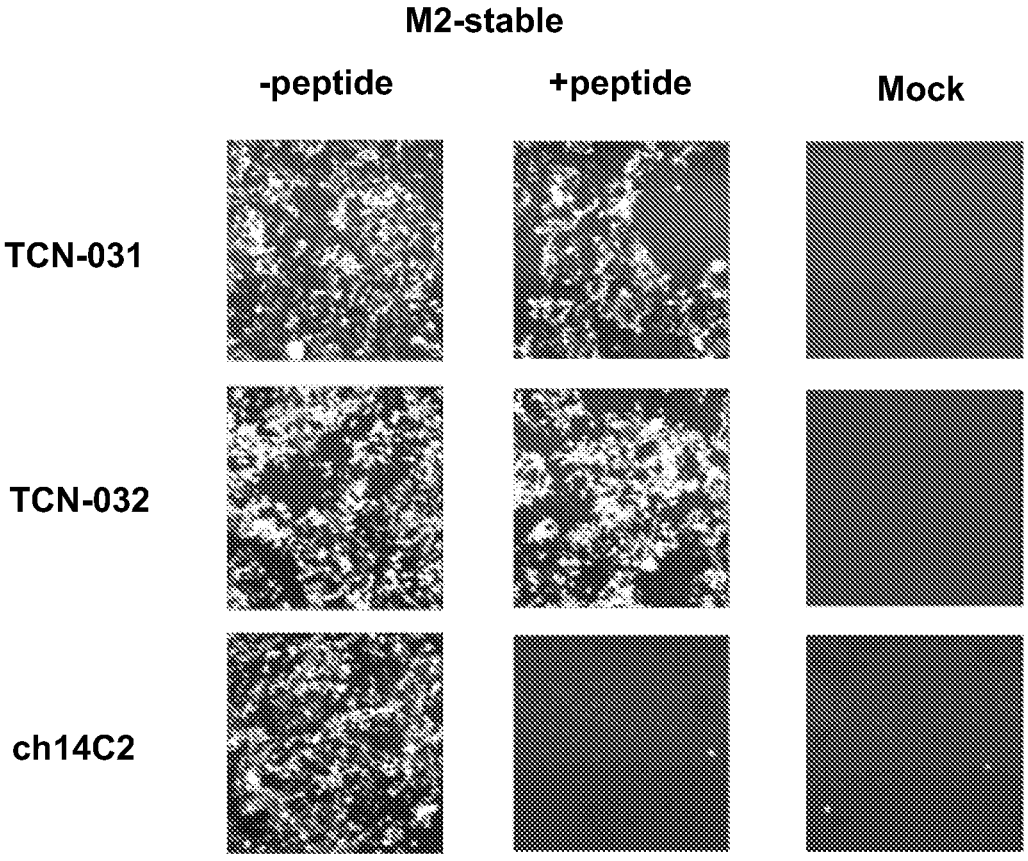


FIG. 14D

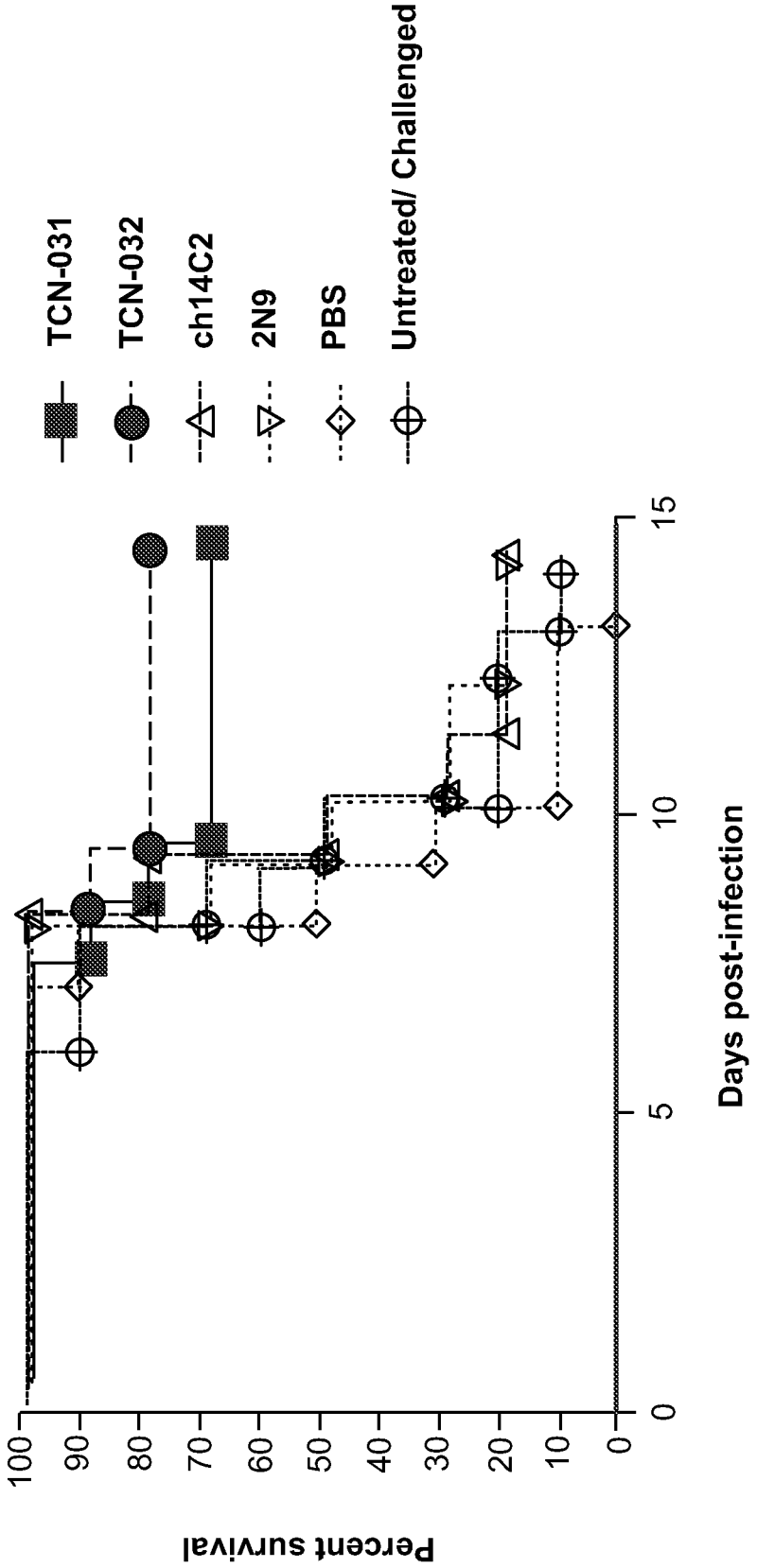

TCN-031
TCN-032
ch14C2
2N9
PBS
Untreated/ Challenged
Percent survival
100
90
80
70
60
50
40
30
20
10
0
0
5
10
15
Days post-infection

FIG. 15A

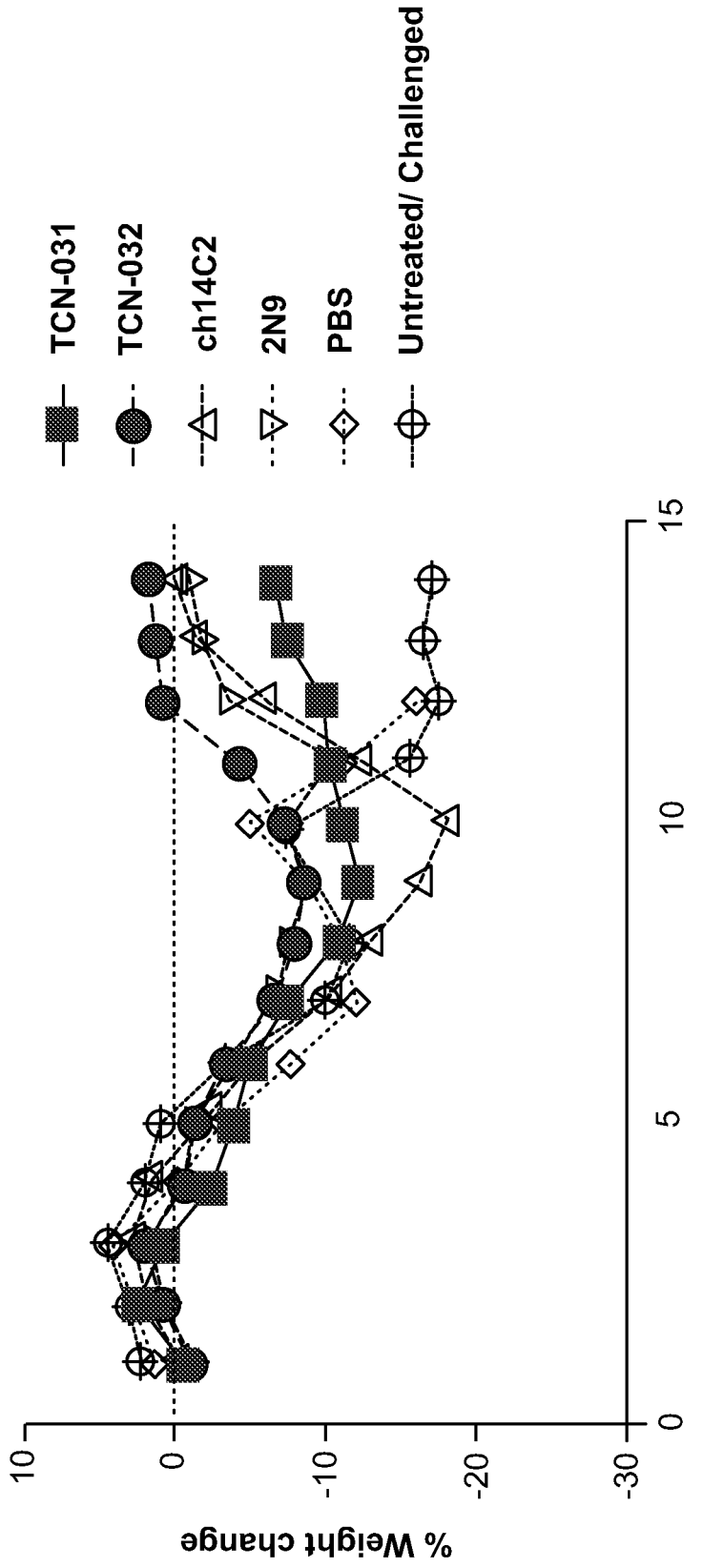

TCN-031
TCN-032
ch14C2
2N9
PBS
Untreated/ Challenged
% Weight change
10
0
-10
-20
-30
0
5
10
15
Days post-infection

FIG. 15B

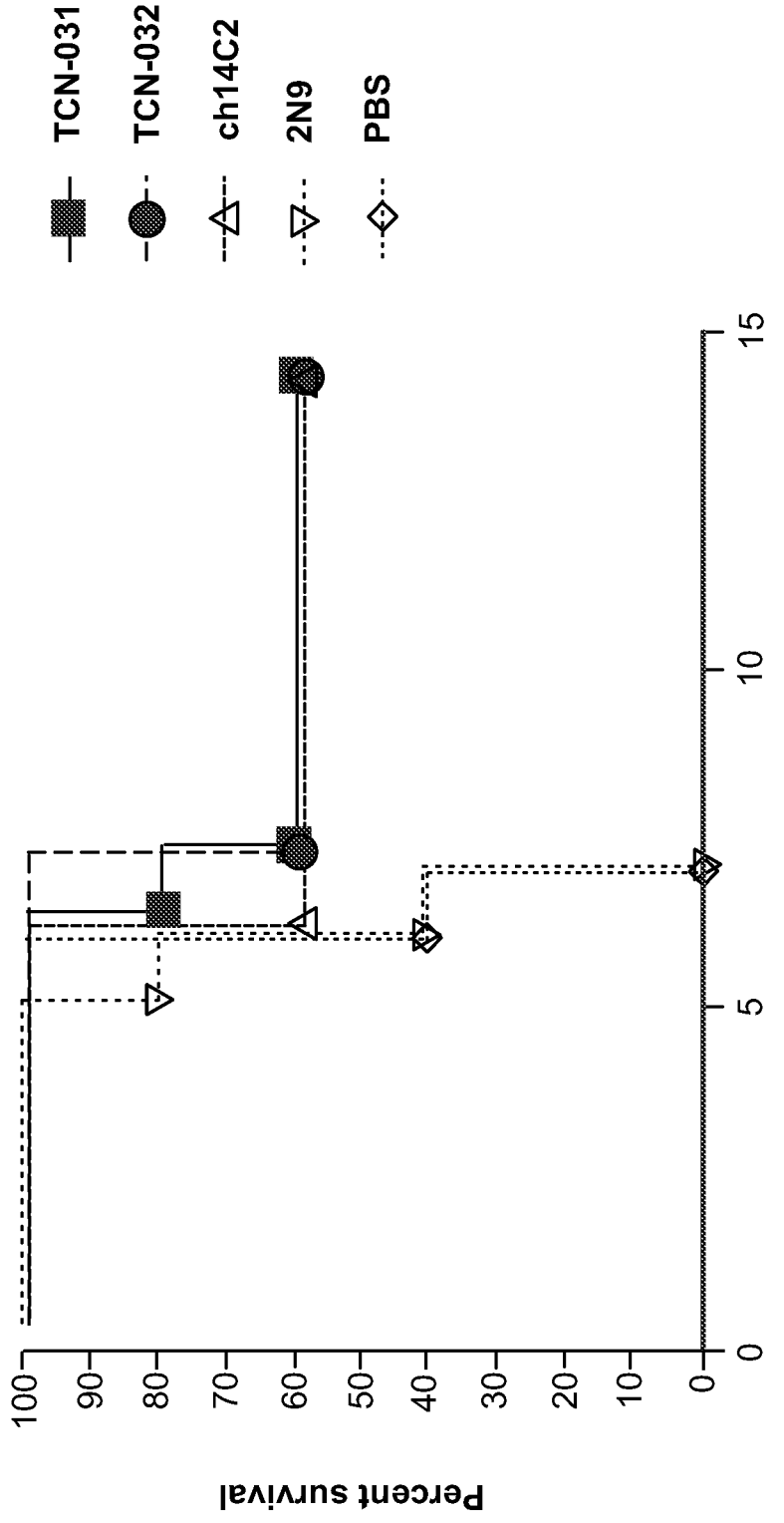

TCN-031
TCN-032
ch14C2
2N9
PBS
Percent survival
100
90
80
70
60
50
40
30
20
10
0
0
5
10
15
Days post-infection

FIG. 15C

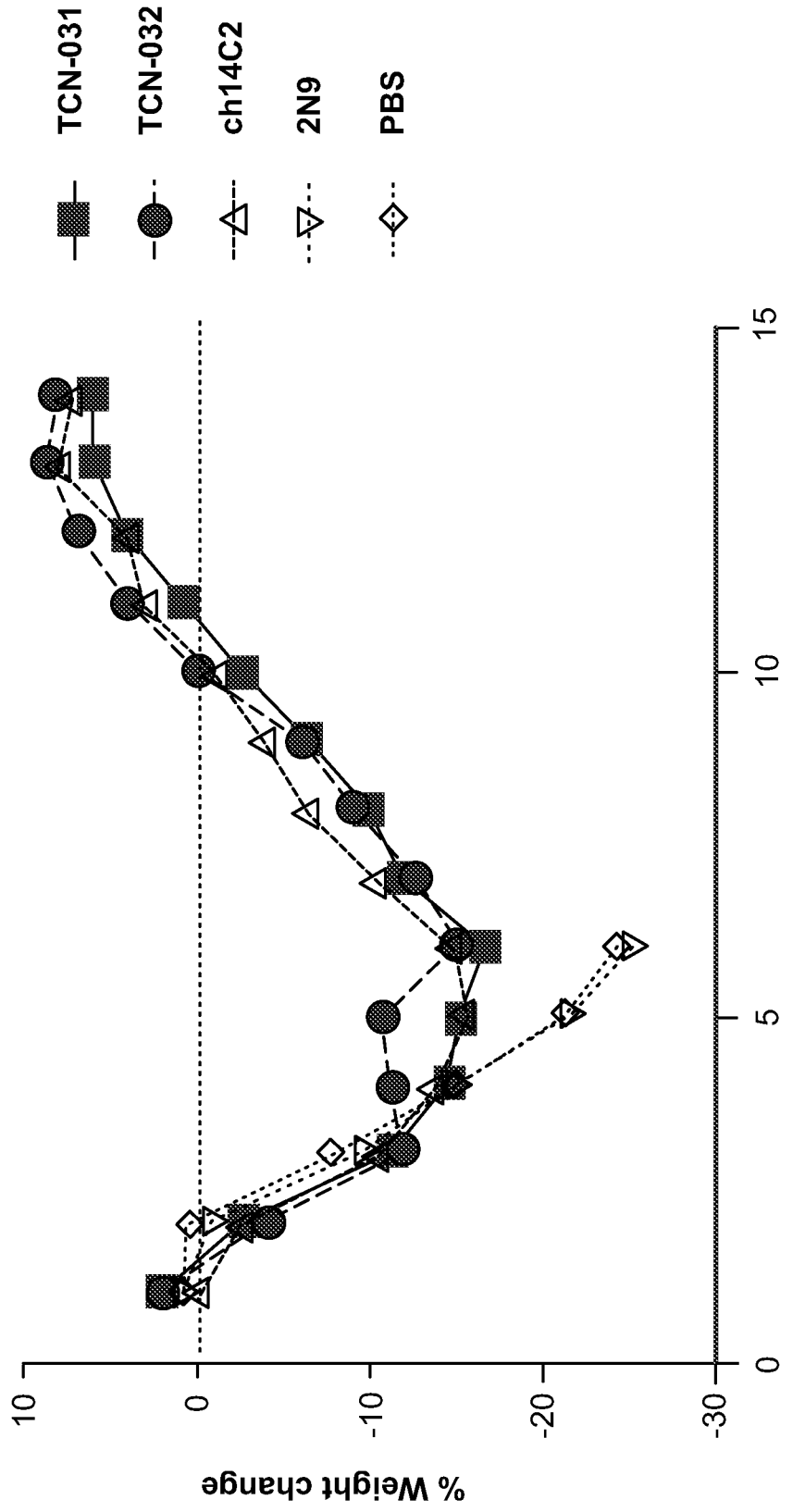

TCN-031
TCN-032
ch14C2
2N9
PBS
% Weight change
10
0
-10
-20
-30
0
5
10
15
Days post-infection

FIG. 15D

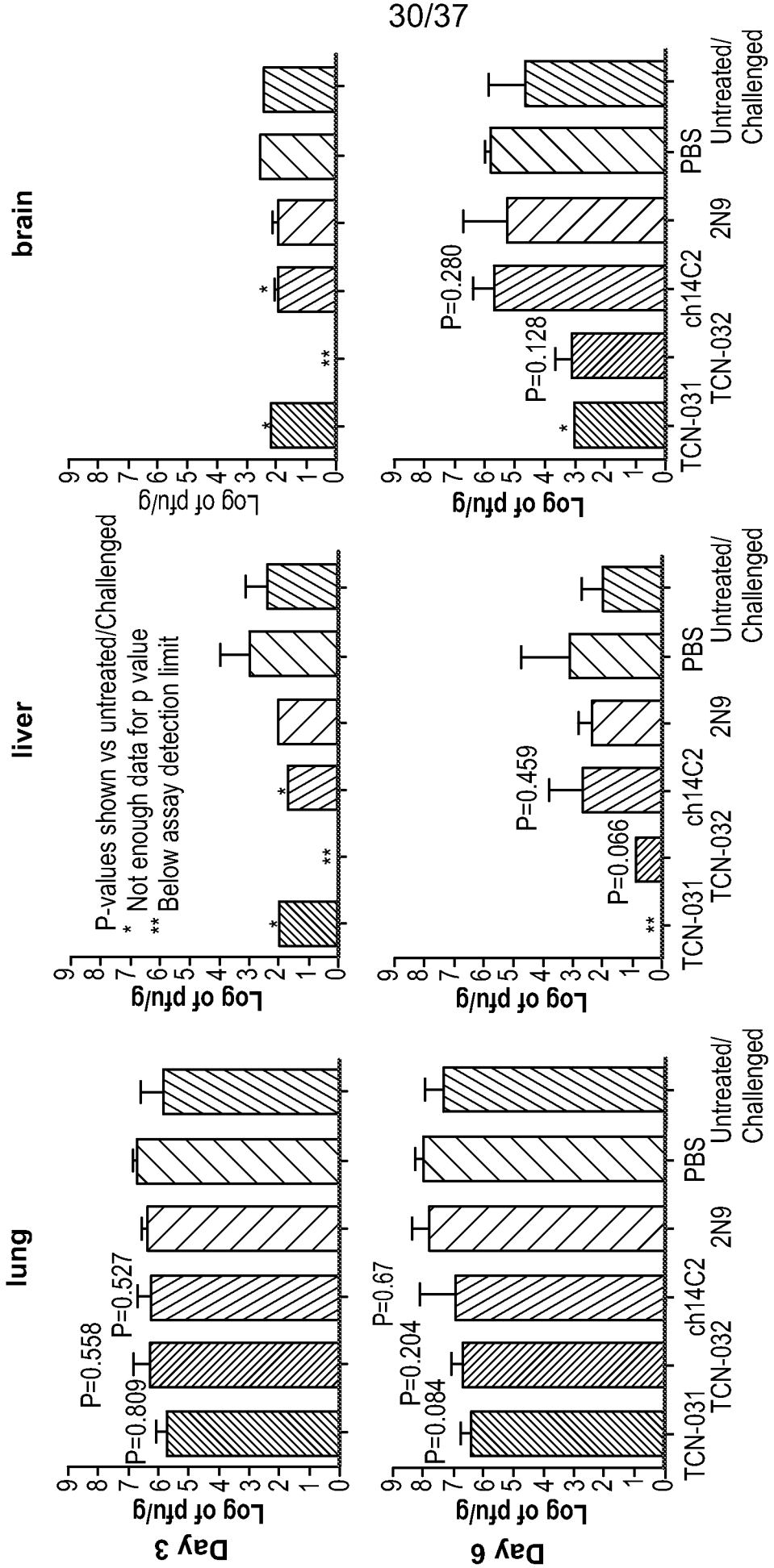

lung
liver
brain
Day 3
Day 6
Log of pfu/g
P=0.558
P=0.809
P=0.527
P=0.084
P=0.204
P=0.67
P=0.066
P=0.459
P=0.128
P=0.280
P-values shown vs untreated/Challenged
* Not enough data for p value
** Below assay detection limit
TCN-031
TCN-032
ch14C2
2N9
PBS
Untreated/
Challenged

FIG. 16

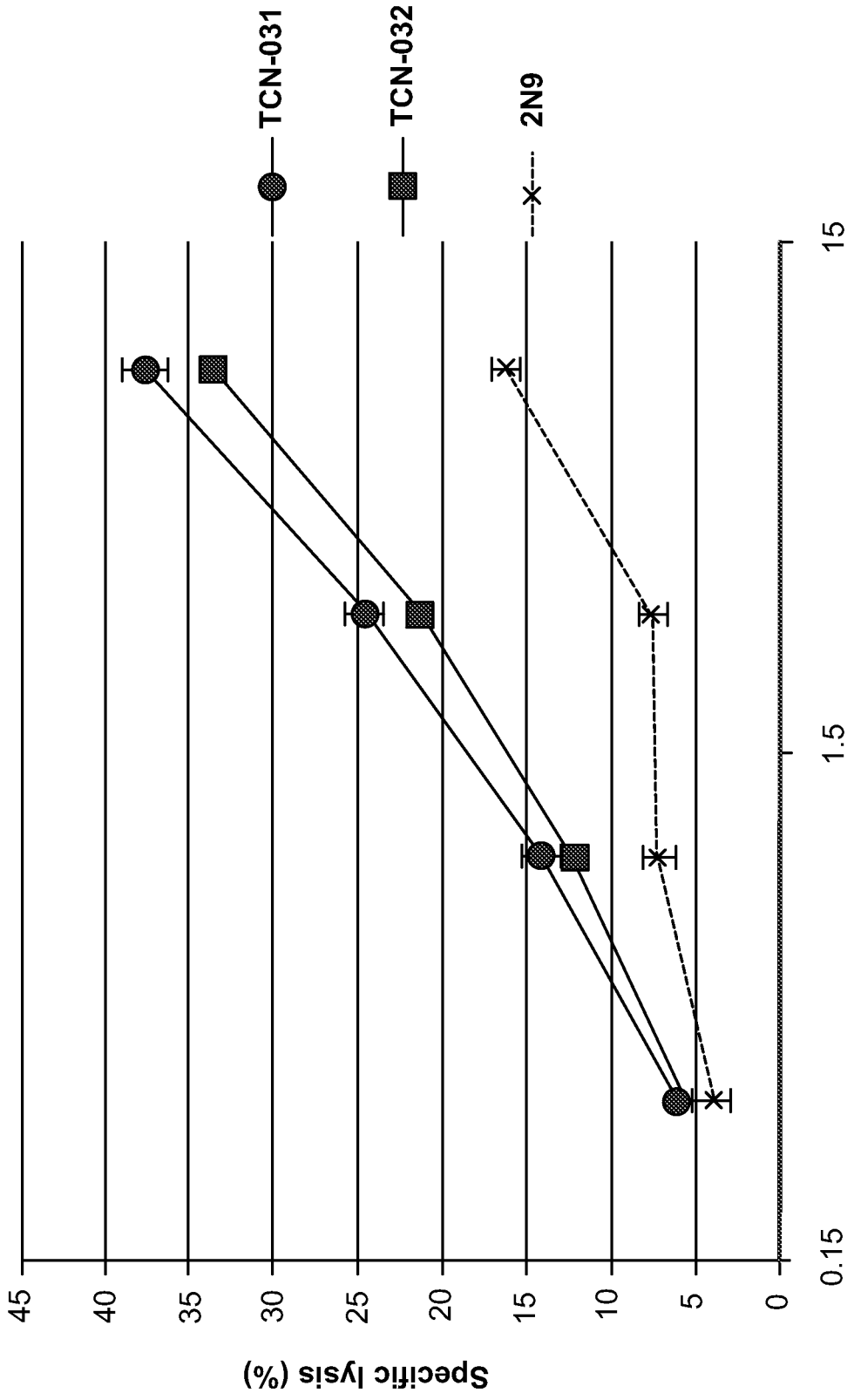

TCN-031
TCN-032
2N9
Specific lysis (%)
45
40
35
30
25
20
15
10
5
0
0.15
1.5
15
Effector:Target

FIG. 17

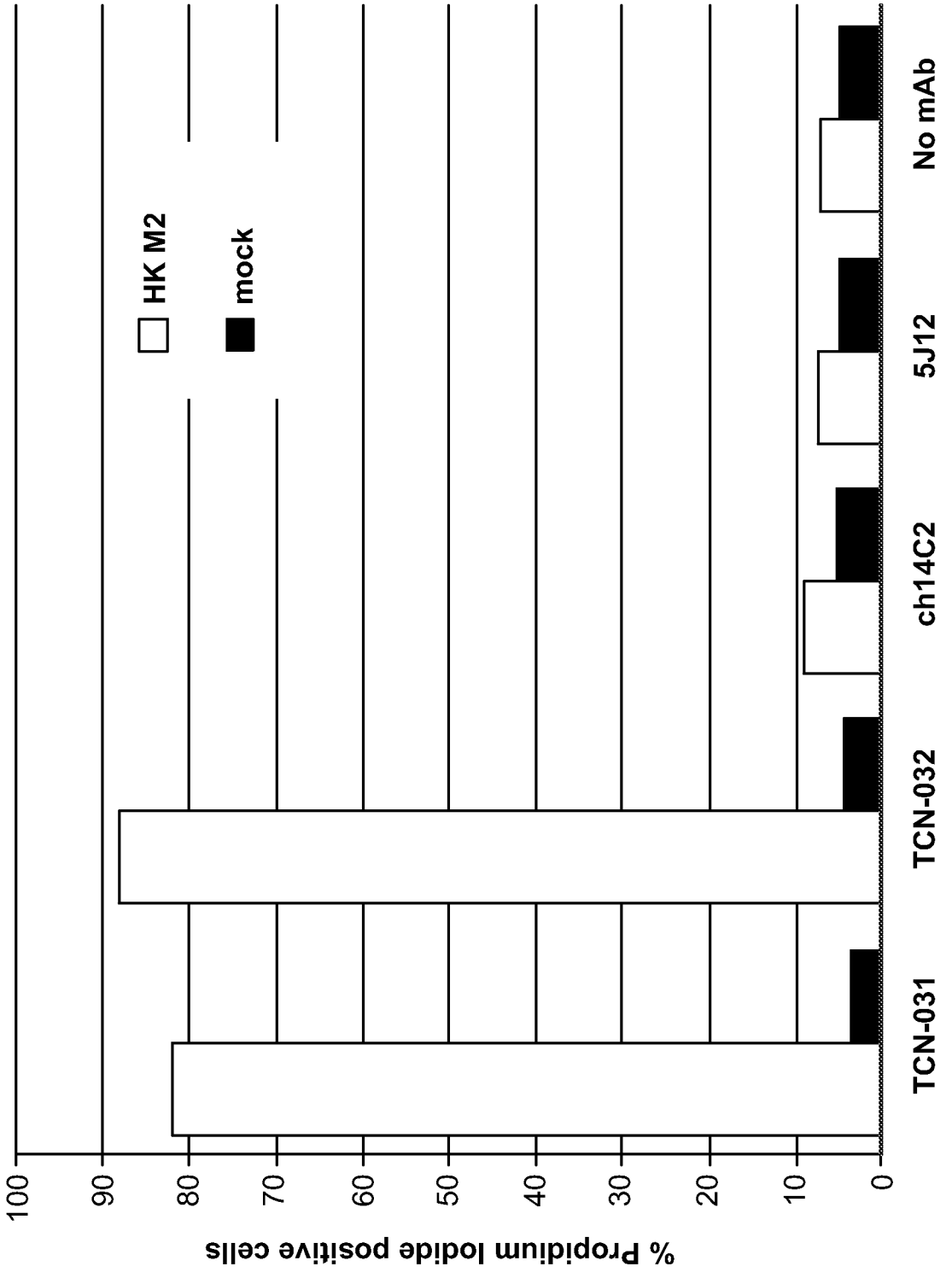

% Propidium Iodide positive cells
100
90
80
70
60
50
40
30
20
10
0
HK M2
mock
TCN-031
TCN-032
ch14C2
5J12
No mAb

FIG. 18

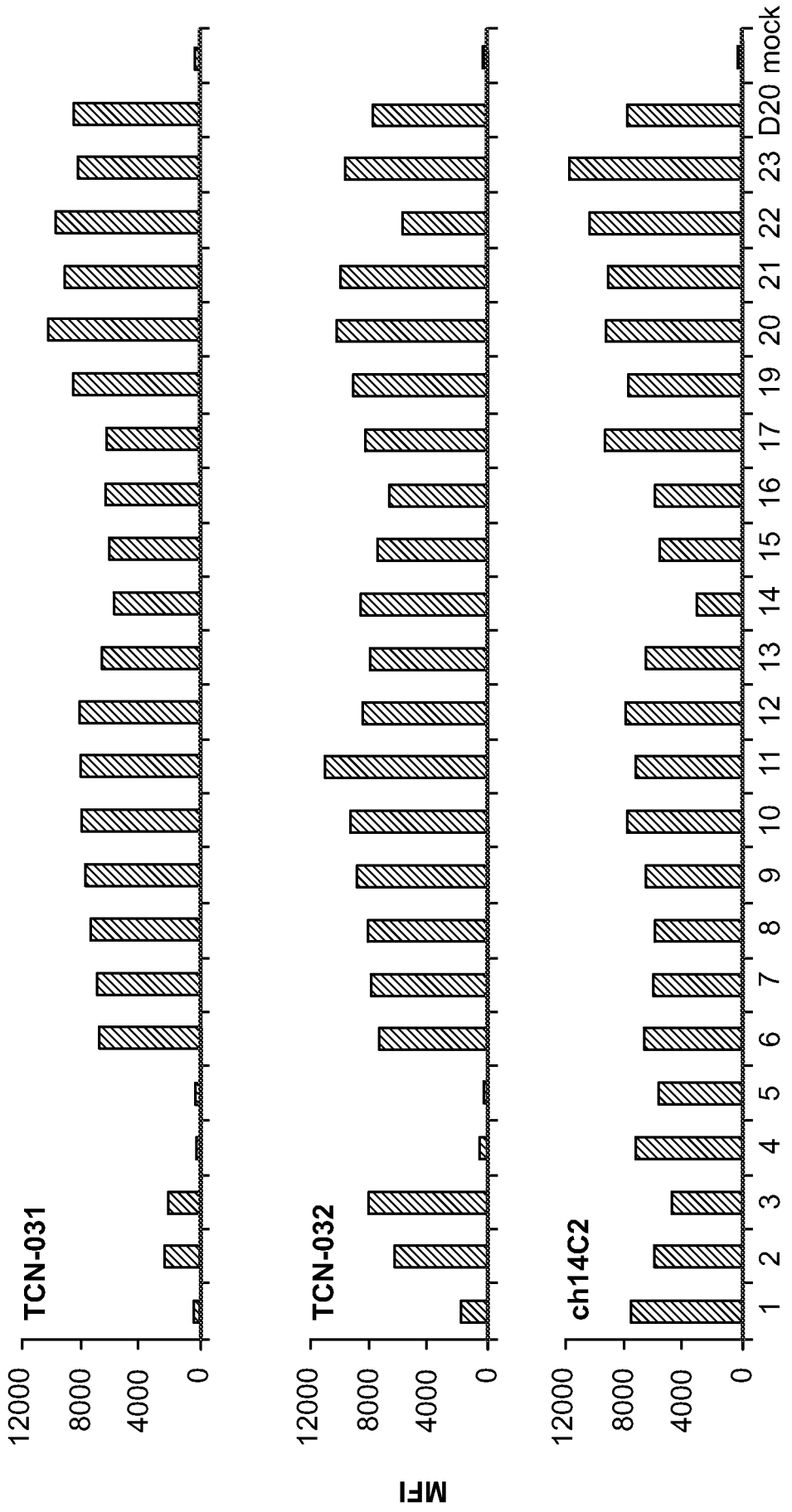

TCN-031
TCN-032
ch14C2
MFI
12000
8000
4000
0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 19 20 21 22 23 D20 mock
Position of Alanine substitution in M2e

FIG. 19A

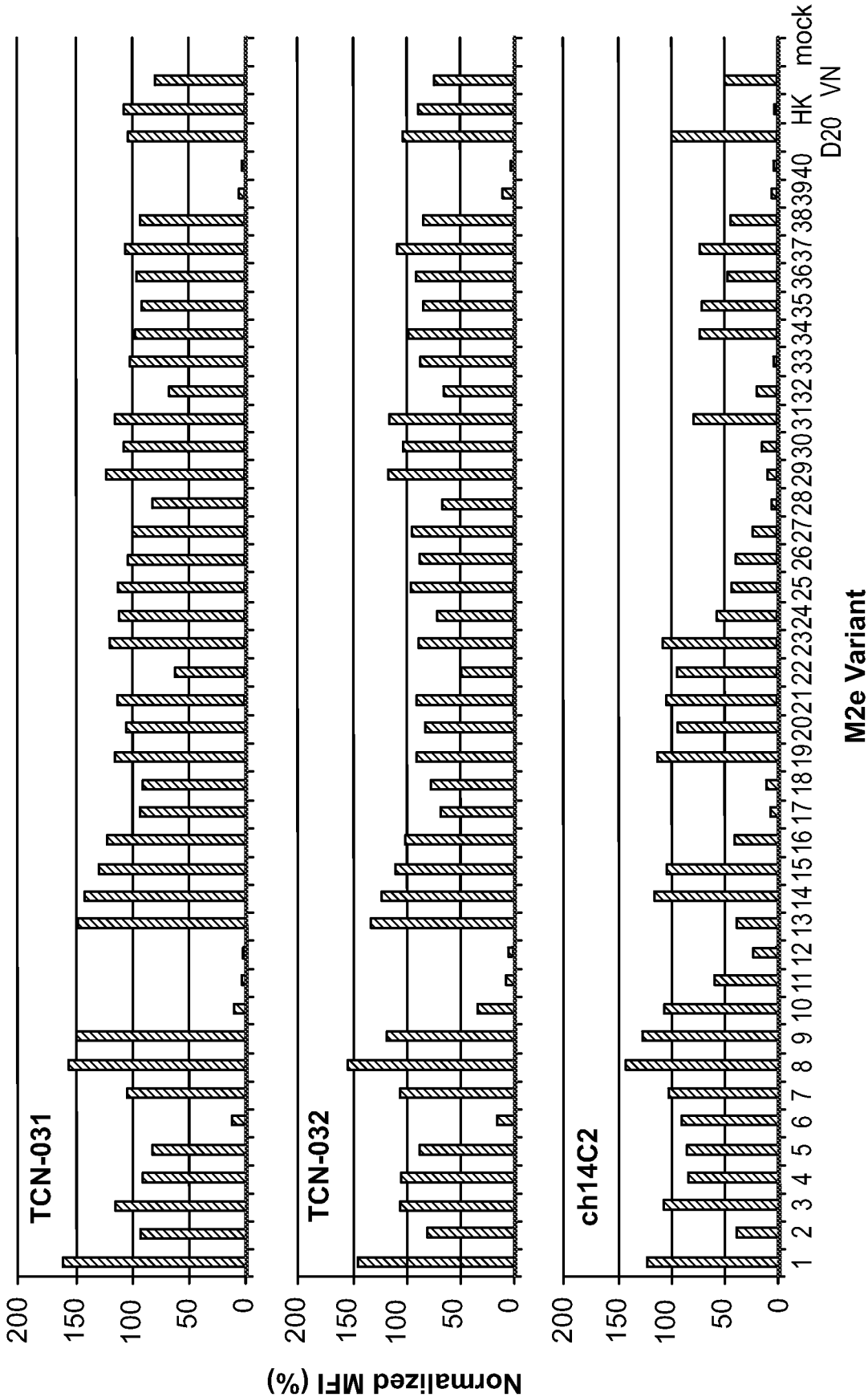

TCN-031
TCN-032
ch14C2
Normalized MFI (%)
200
150
100
50
0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 HK mock D20 VN
M2e Variant

FIG. 19B

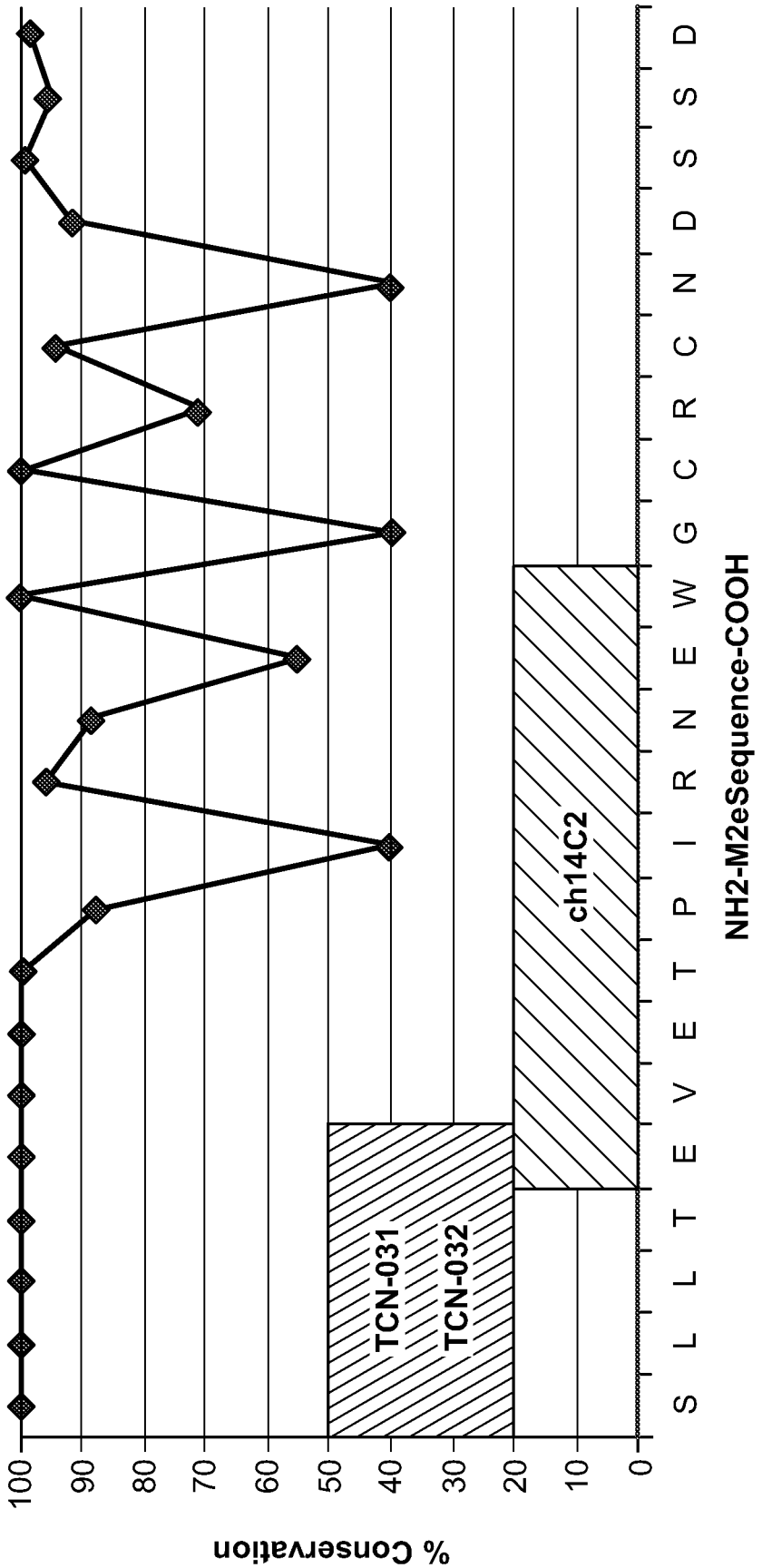

% Conservation
100
90
80
70
60
50
40
30
20
10
0
TCN-031
TCN-032
ch14C2
S L L T E V E T P I R N E W G C R C N D S S D
NH2-M2eSequence-COOH

FIG. 19C

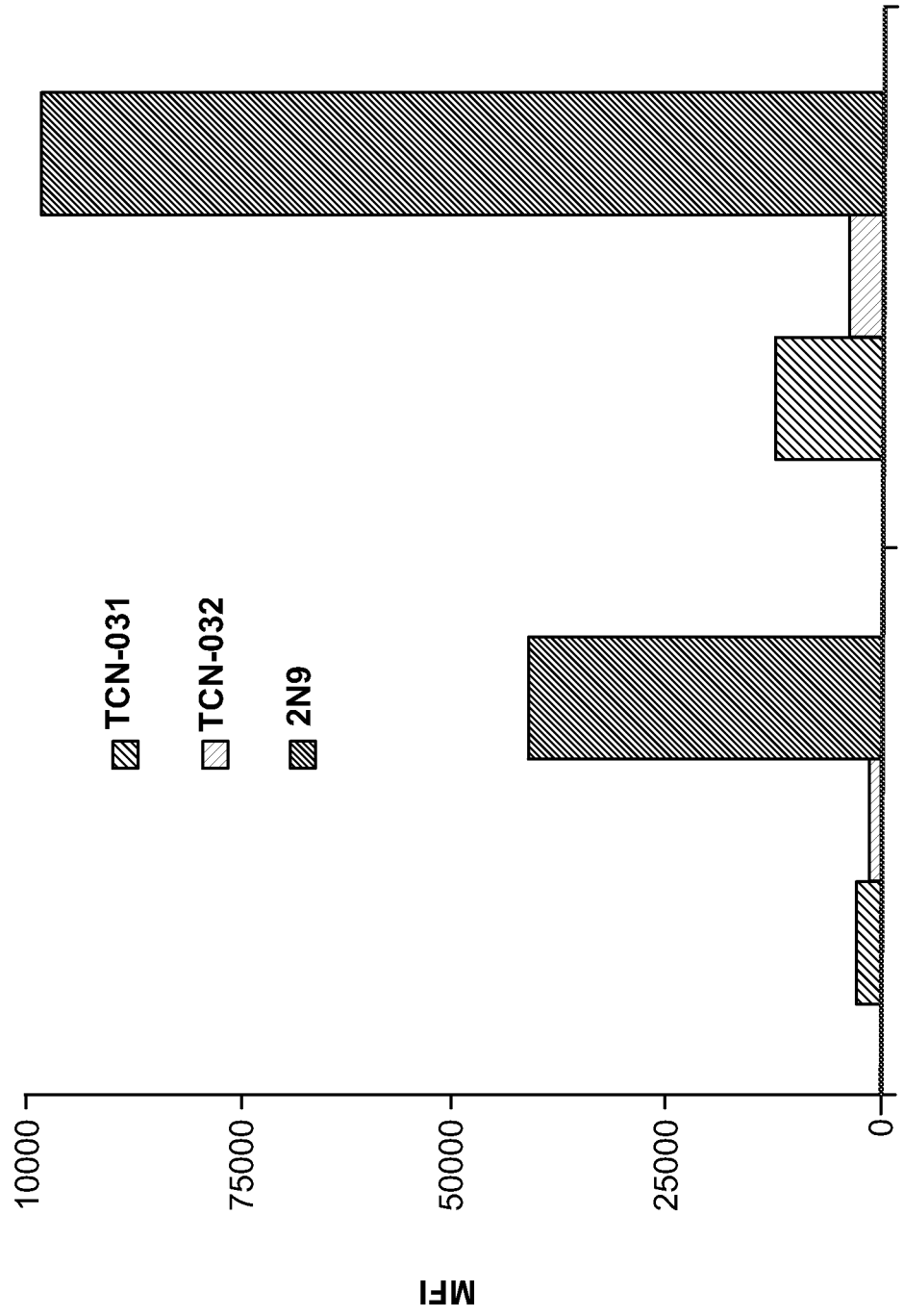
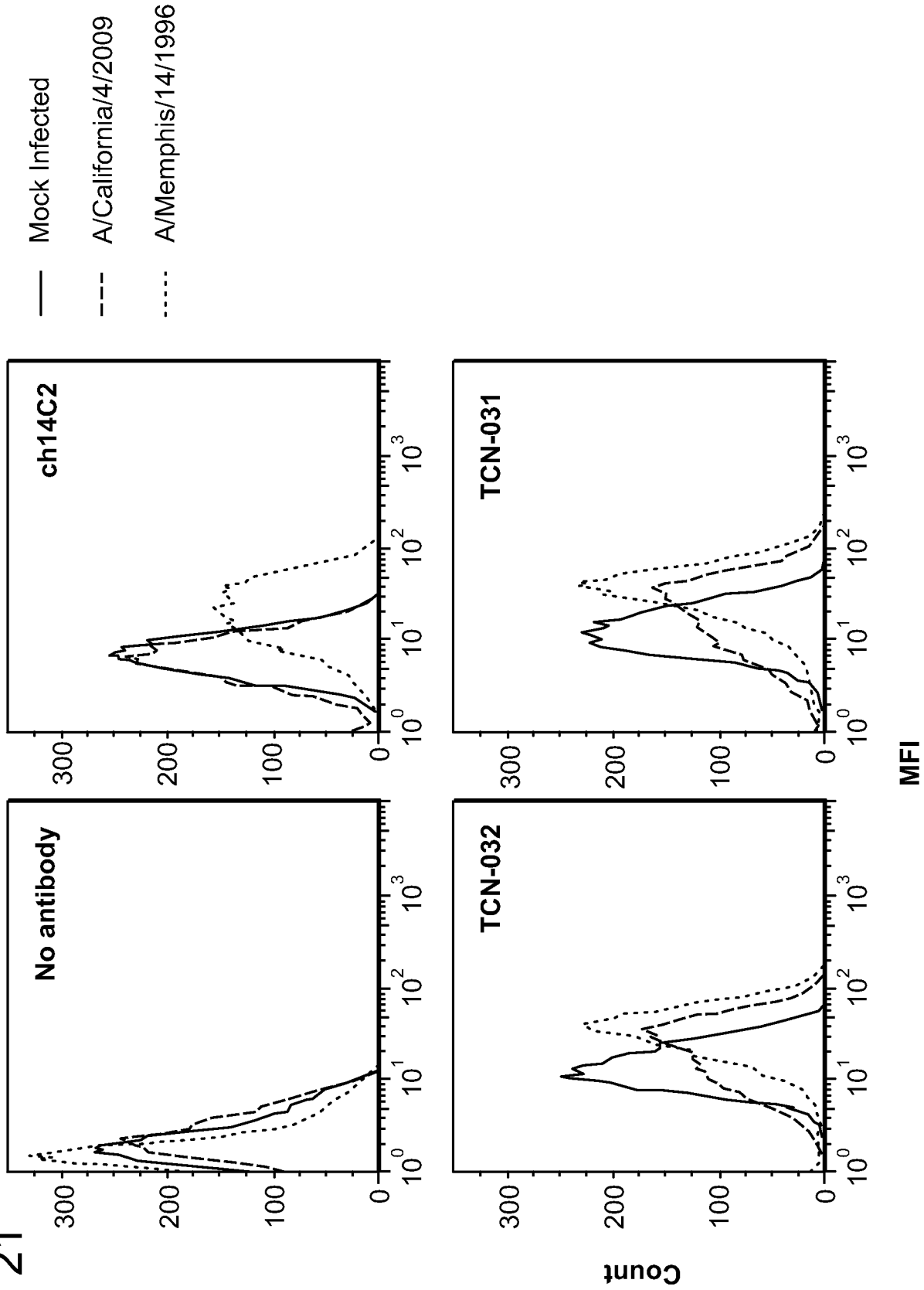

MFI
10000
7500
5000
2500
0
TCN-031
TCN-032
2N9
TCN-031 AF647
TCN-032 AF647

FIG. 20

FIG. 21


Mock Infected
A/California/4/2009
A/Memphis/14/1996
No antibody
ch14C2
TCN-032
TCN-031
Count
MFI