Fig. 1


Extracellular Loop 1
CLDN6 (SEQ ID NO: 2) MASAGMQILGVVLTLLGWVNGLVSCALPMWKVTAFIGNSIVVAQVVWEGLWMSCVVQSTG 60
CLDN9 (SEQ ID NO: 9) MASTGLELLGMTLAVLGWLGTLVSCALPLWKVTAFIGNSIVVAQVVWEGLWMSCVVQSTG 60
CLDN4 (SEQ ID NO: 10) MASMGLQVMGIALAVLGWLAVMLCCALPMWRVTAFIGSNIVTSQTIWEGLWMNCVVQSTG 60
CLDN3 (SEQ ID NO: 11) -MSMGLEITGTALAVLGWLGTIVCCALPMWRVSAFIGSNIITSQNIWEGLWMNCVVQSTG 59
CLDN6 (SEQ ID NO: 2) QMQCKVYDSLLALPQDLQAARALCVIALLVALFGLLVYLAGAKCTTCVEEKDSKARLVLT 120
CLDN9 (SEQ ID NO: 9) QMQCKVYDSLLALPQDLQAARALCVIALLLALLGLLVAITGAQCTTCVEDEGAKARIVLT 120
CLDN4 (SEQ ID NO: 10) QMQCKVYDSLLALPQDLQAARALVIISIIVAALGVLLSVVGGKCTNCLEDESAKAKTMIV 120
CLDN3 (SEQ ID NO: 11) QMQCKVYDSLLALPQDLQAARALIVVAILLAAFGLLVALVGAQCTNCVQDDTAKAKITIV 119
Extracellular Loop 2
CLDN6 (SEQ ID NO: 2) SGIVFVISGVLTLIPVCWTAHAIIRDFYNPLVAEAQKRELGASLYLGWAASGLLLLGGGL 180
CLDN9 (SEQ ID NO: 9) AGVILLLAGILVLIPVCWTAHAIIQDFYNPLVAEALKRELGASLYLGWAAAALLMLGGGL 180
CLDN4 (SEQ ID NO: 10) AGVVFLLAGLMVIVPVSWTAHNIIQDFYNPLVASGQKREMGASLYVGWAASGLLLLGGGL 180
CLDN3 (SEQ ID NO: 11) AGVLFLLAALLTLVPVSWSANTIIRDFYNPVVPEAQKREMGAGLYVGWAAAALQLLGGAL 179
CLDN6 (SEQ ID NO: 2) LCCTCPSGGSQGPSHYMARYSTSAPAISRGPSEYP-----TKNYV 220
CLDN9 (SEQ ID NO: 9) LCCTCPPPQVERPRG--PRLGYSIPSRS-GASGLD-----KRDYV 217
CLDN4 (SEQ ID NO: 10) LCCNCPPRT---DKPYSAK---YSAARSAAASN----------YV 209
CLDN3 (SEQ ID NO: 11) LCCSCPPR----EKKYTATKVVYSAPRSTGPGASLGTGYDRKDYV 220

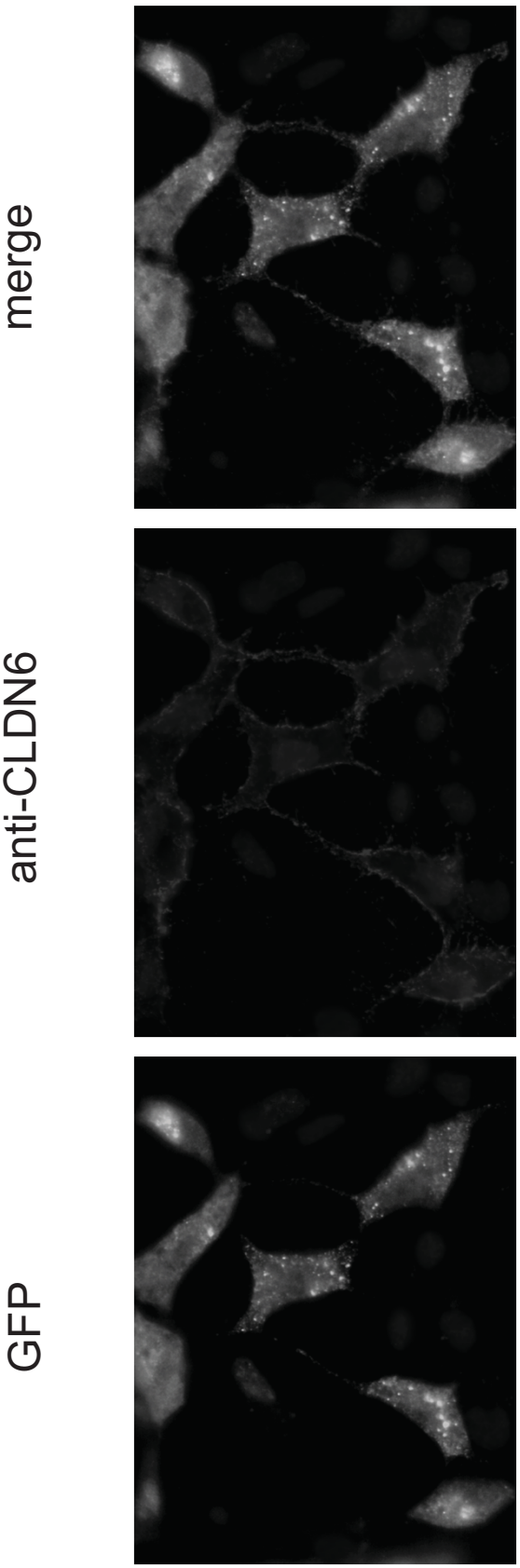


Fig. 2A

Fig. 2B

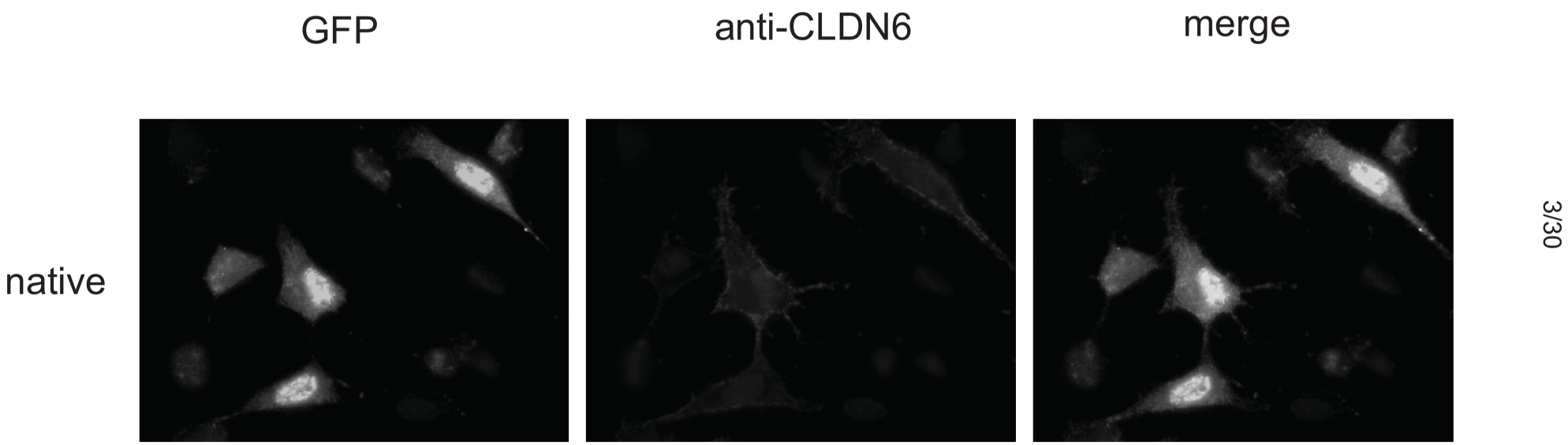


Fig. 3

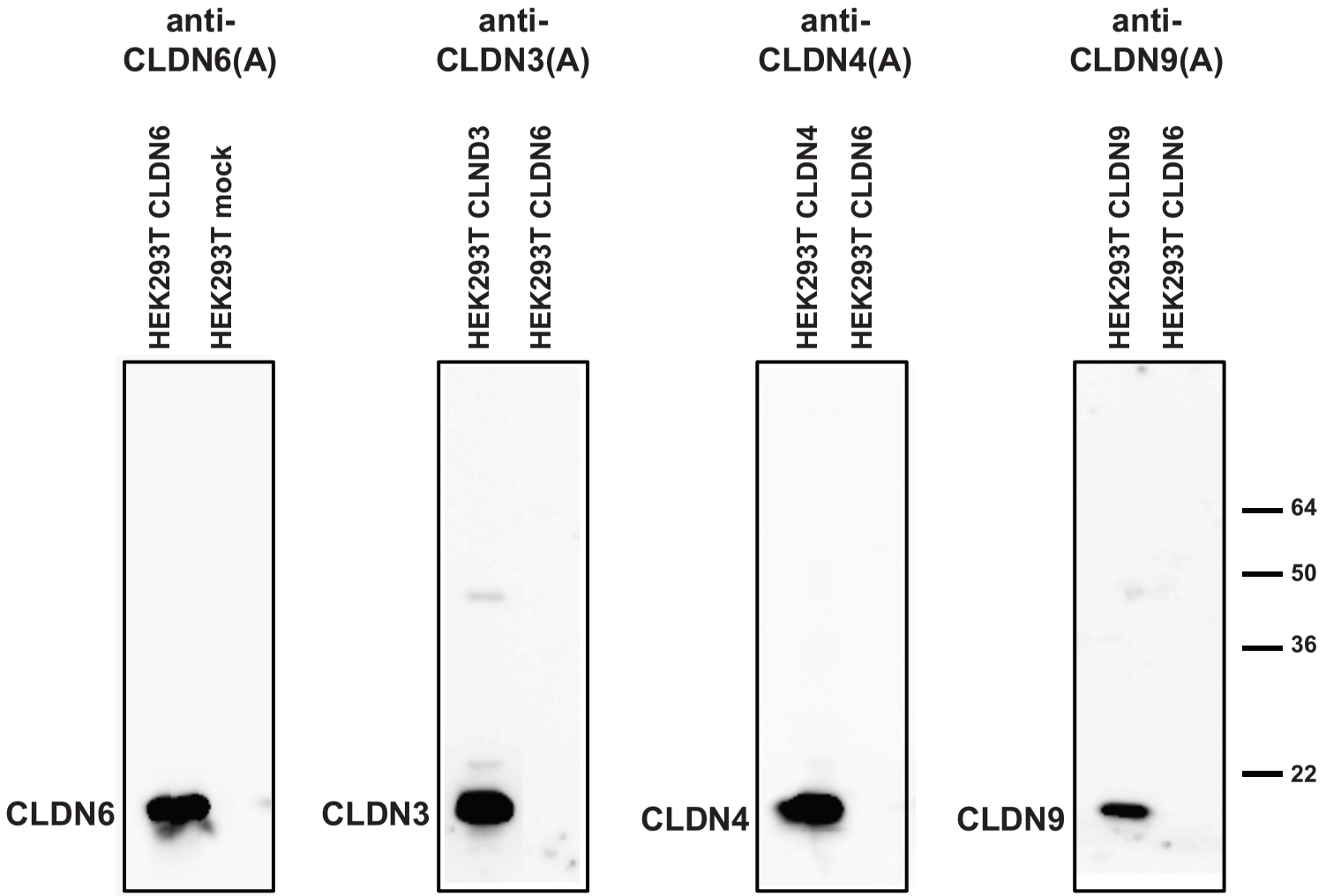

anti-
CLDN6(A)
HEK293T CLDN6
HEK293T mock
CLDN6
anti-
CLDN3(A)
HEK293T CLND3
HEK293T CLDN6
CLDN3
anti-
CLDN4(A)
HEK293T CLDN4
HEK293T CLDN6
CLDN4
anti-
CLDN9(A)
HEK293T CLDN9
HEK293T CLDN6
CLDN9
64
50
36
22

Fig. 4

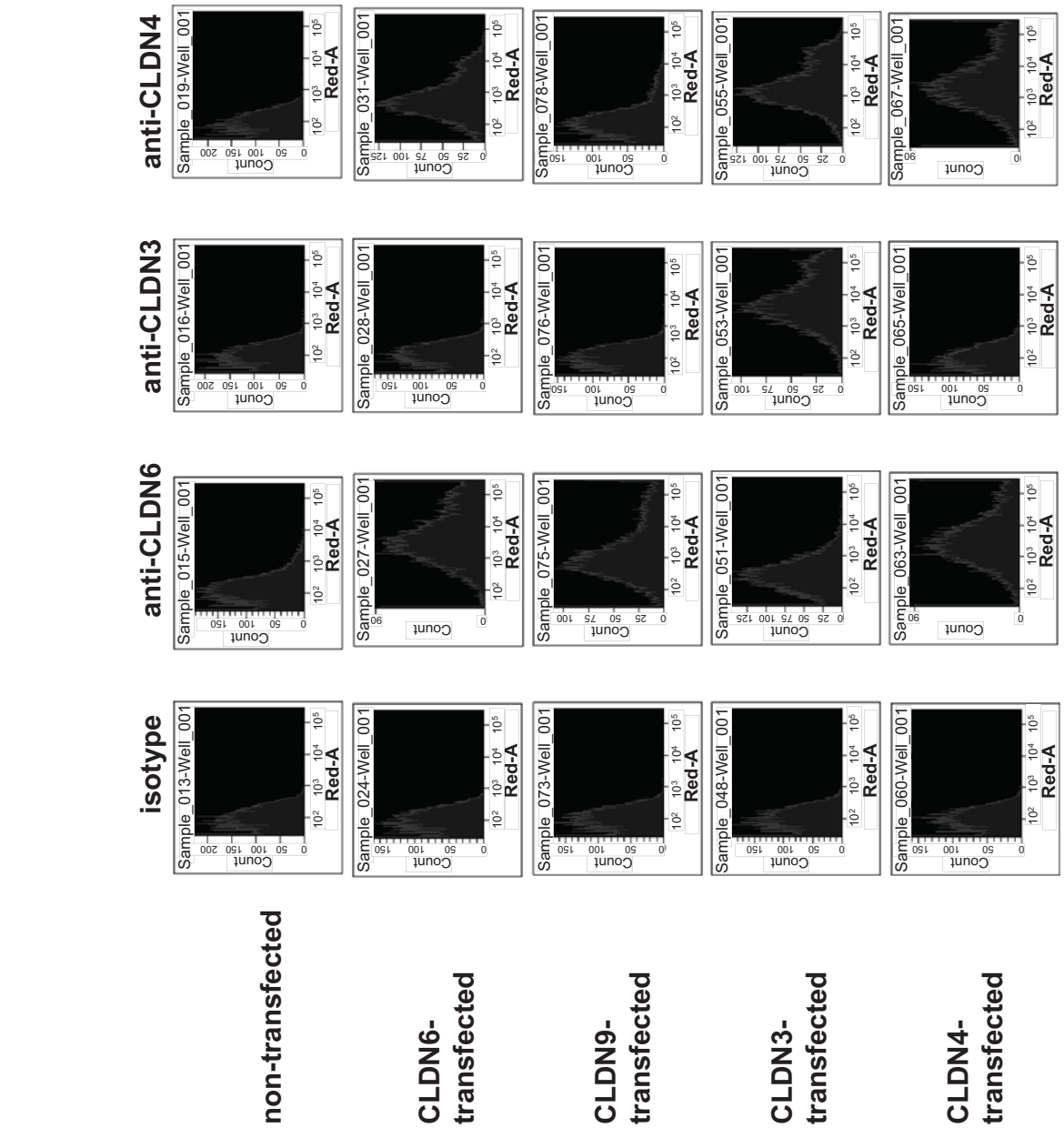

isotype
anti-CLDN6
anti-CLDN3
anti-CLDN4
non-transfected
CLDN6-transfected
CLDN9-transfected
CLDN3-transfected
CLDN4-transfected
Count
Red-A

Fig. 5A

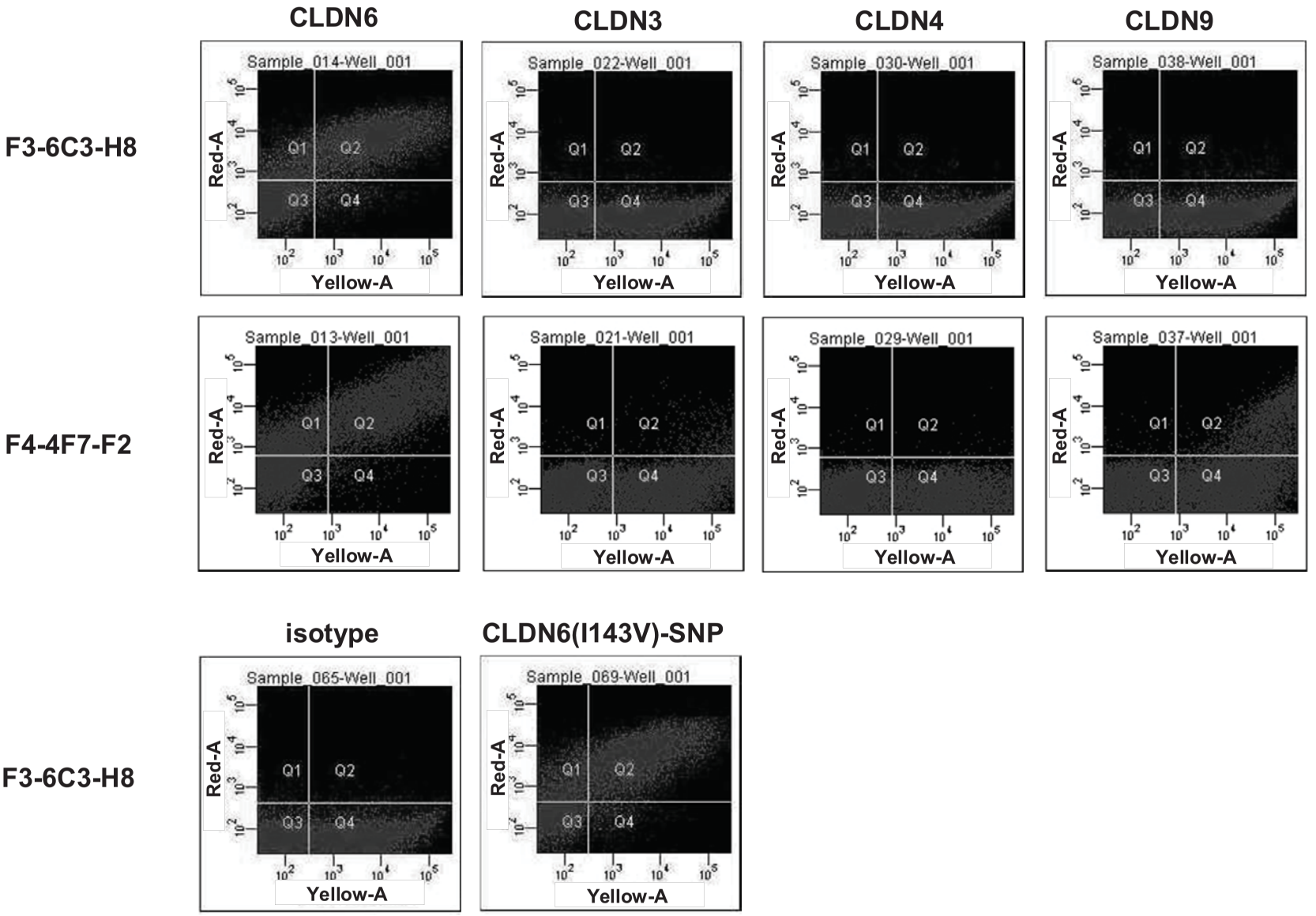
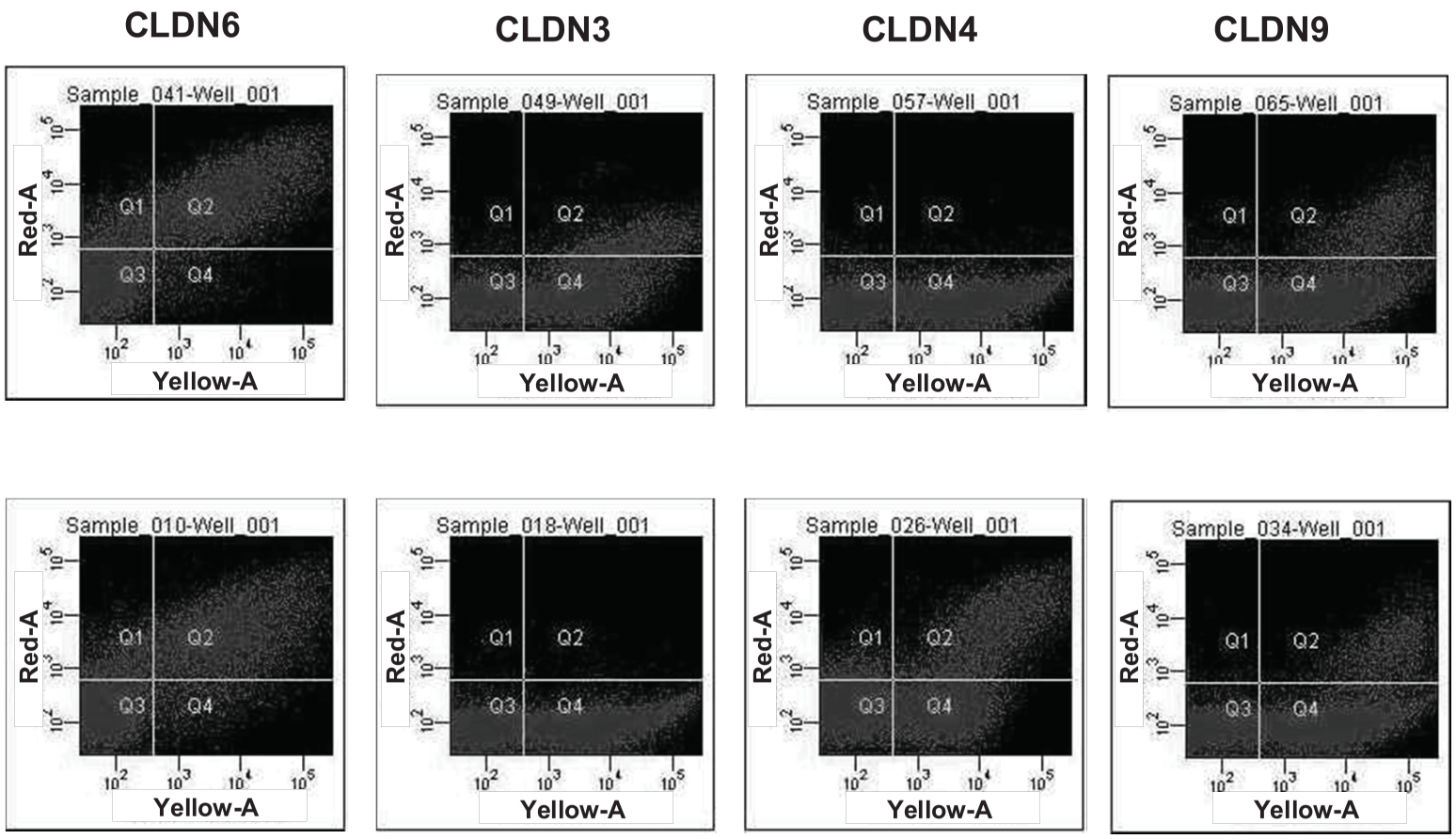

CLDN6
CLDN3
CLDN4
CLDN9
F3-6C3-H8
F4-4F7-F2
isotype
CLDN6(I143V)-SNP
F3-6C3-H8
Sample_014-Well_001
Sample_022-Well_001
Sample_030-Well_001
Sample_038-Well_001
Sample_013-Well_001
Sample_021-Well_001
Sample_029-Well_001
Sample_037-Well_001
Sample_065-Well_001
Sample_069-Well_001
Red-A
Yellow-A
Q1
Q2
Q3
Q4

Fig. 5B


CLDN6
CLDN3
CLDN4
CLDN9
F3-7B3-B4
F3-3F7-A5
Sample_041-Well_001
Sample_049-Well_001
Sample_057-Well_001
Sample_065-Well_001
Sample_010-Well_001
Sample_018-Well_001
Sample_026-Well_001
Sample_034-Well_001
Red-A
Yellow-A
Q1
Q2
Q3
Q4

CLDN	Q1	Q2
	Q3	Q4

reporter

Fig. 6

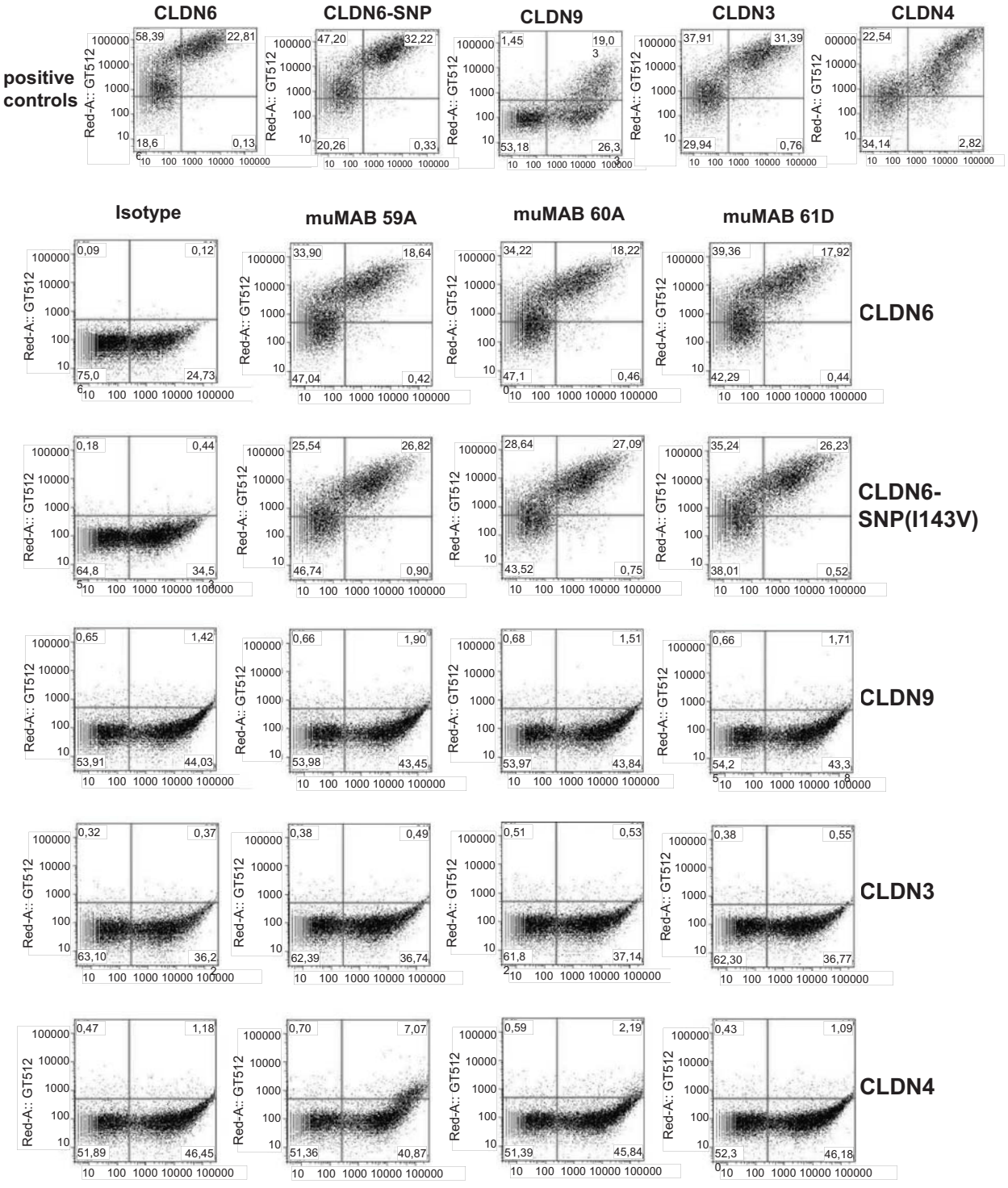


Fig. 6 (cont.)

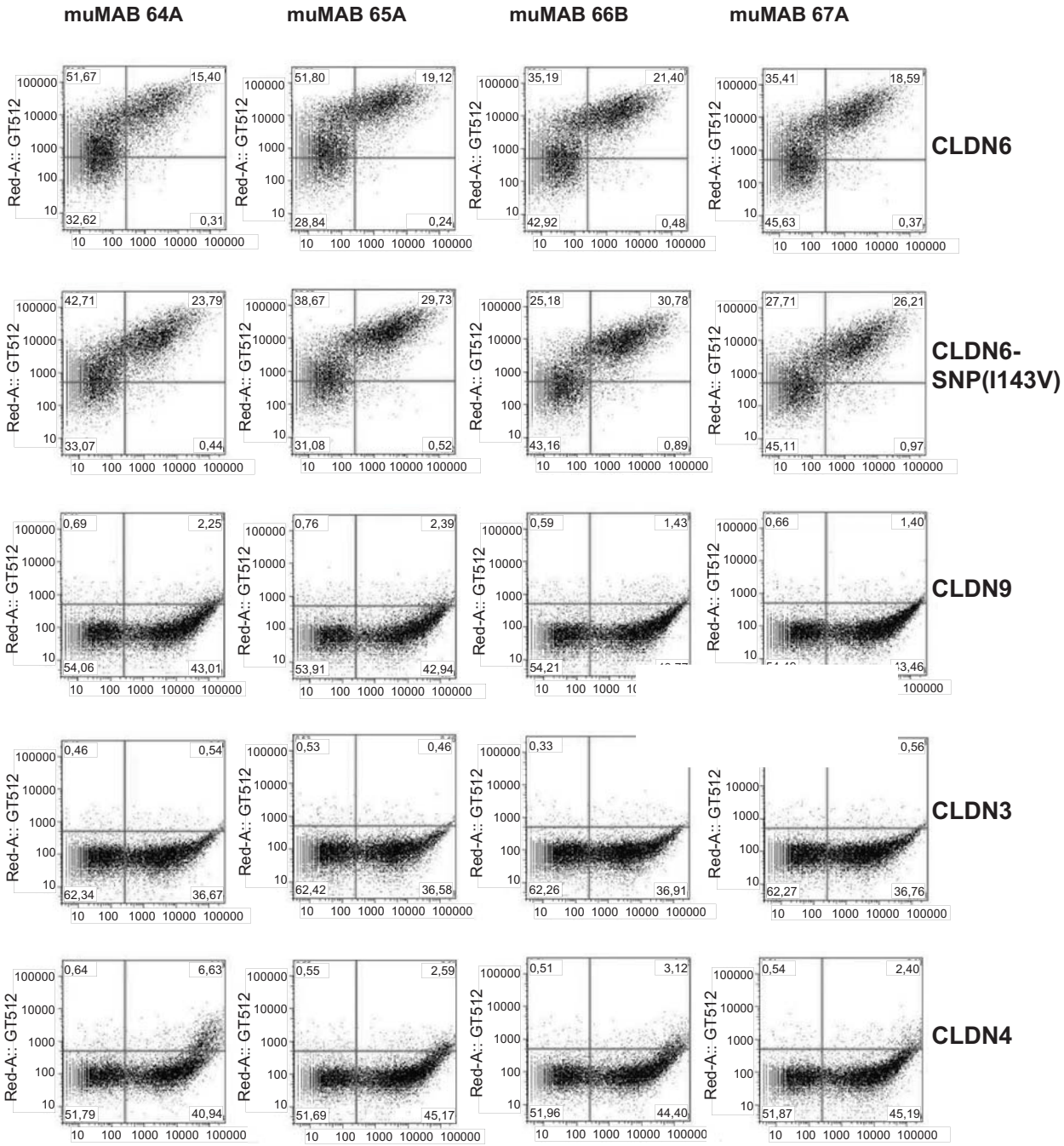

muMAB 64A
muMAB 65A
muMAB 66B
muMAB 67A
CLDN6
CLDN6-SNP(I143V)
CLDN9
CLDN3
CLDN4
Red-A:: GT512
51,67
15,40
32,62
0,31
51,80
19,12
28,84
0,24
35,19
21,40
42,92
0,48
35,41
18,59
45,63
0,37
42,71
23,79
33,07
0,44
38,67
29,73
31,08
0,52
25,18
30,78
43,16
0,89
27,71
26,21
45,11
0,97
0,69
2,25
54,06
43,01
0,76
2,39
53,91
42,94
0,59
1,43
54,21
0,66
1,40
0,46
0,54
62,34
36,67
0,53
0,46
62,42
36,58
0,33
62,26
36,91
0,56
62,27
36,76
0,64
6,63
51,79
40,94
0,55
2,59
51,69
45,17
0,51
3,12
51,96
44,40
0,54
2,40
51,87
45,19
10 100 1000 10000 100000

Fig. 7

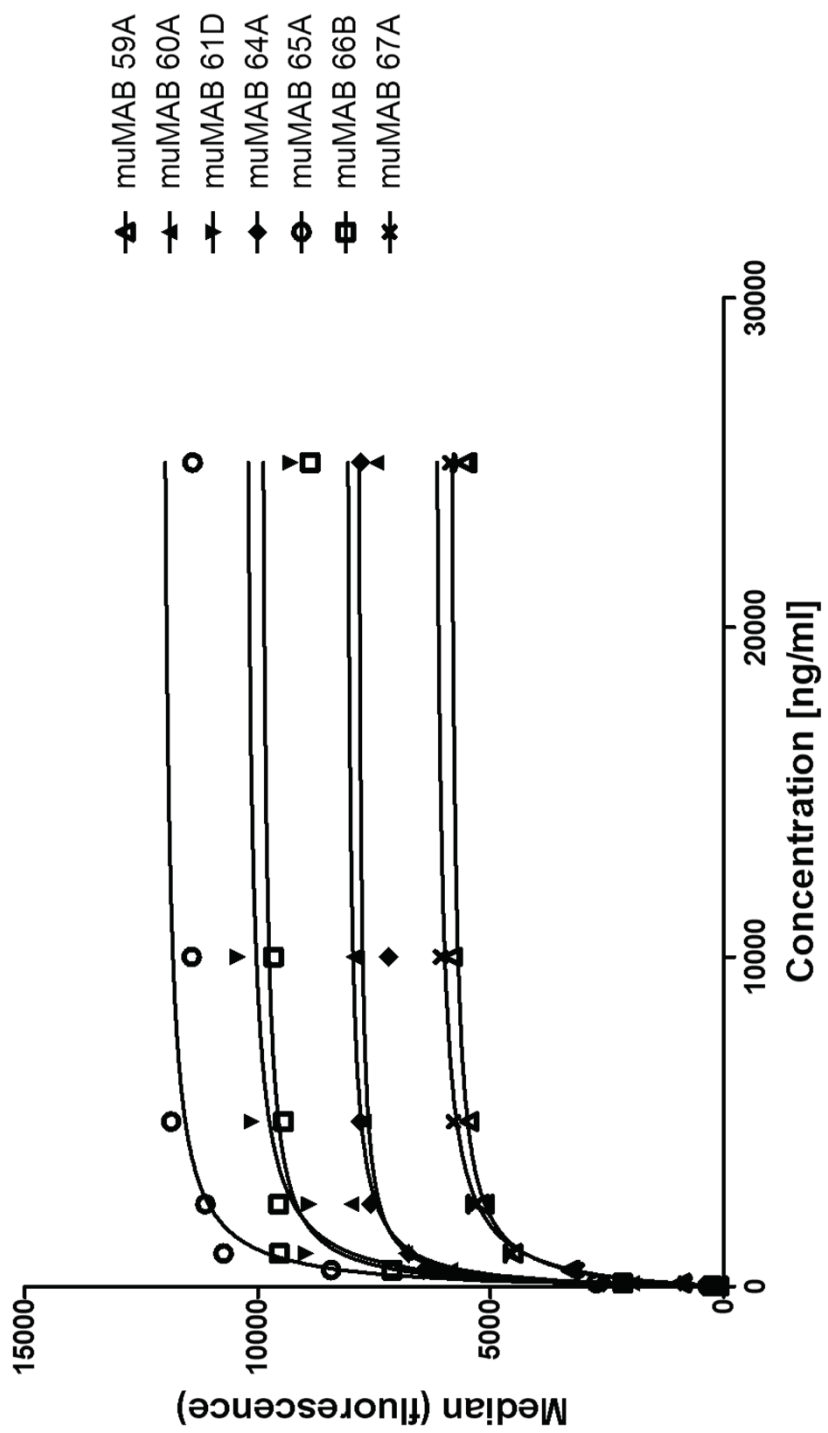
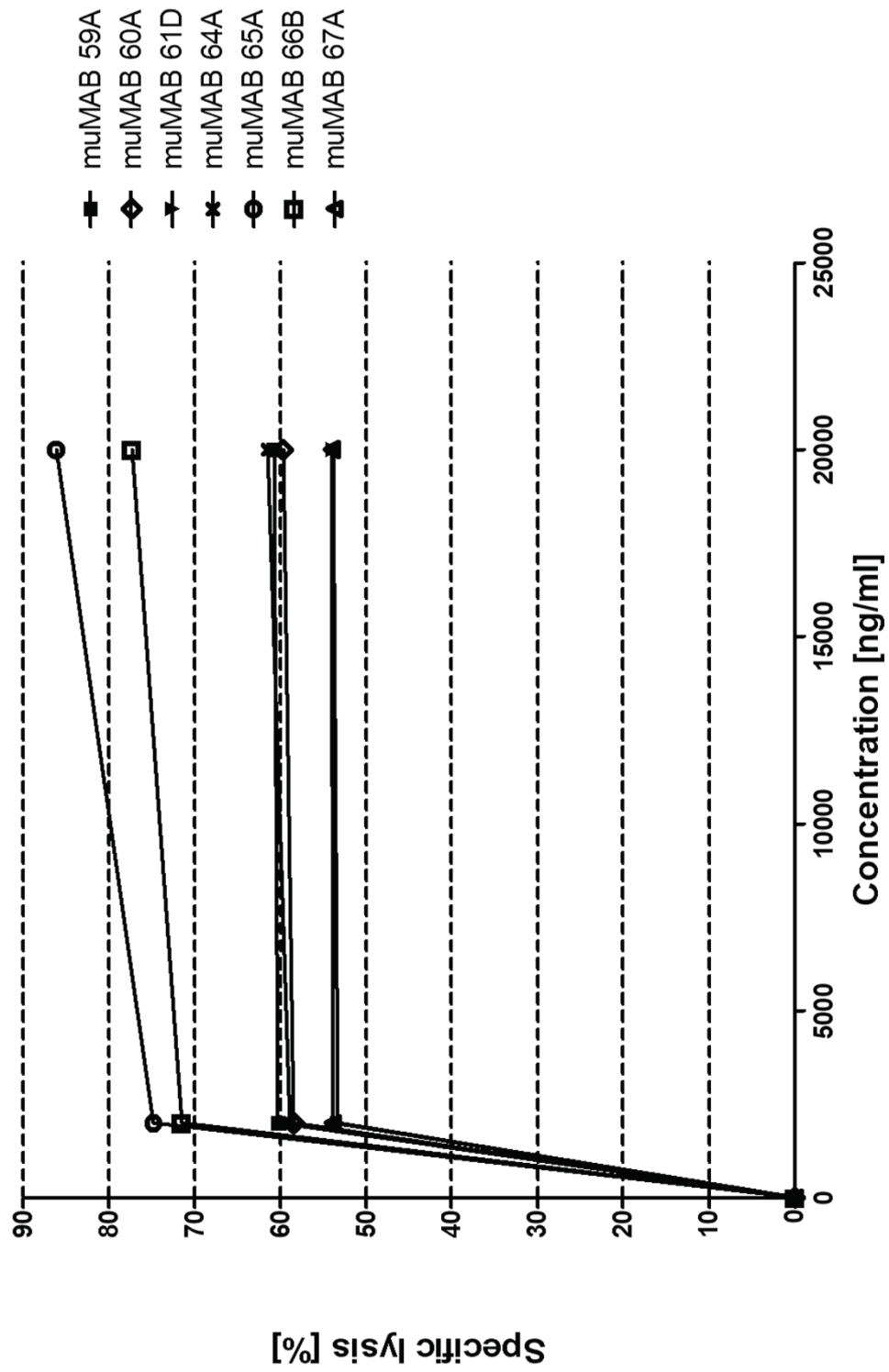

muMAB 59A
muMAB 60A
muMAB 61D
muMAB 64A
muMAB 65A
muMAB 66B
muMAB 67A
Median (fluorescence)
15000
10000
5000
0
0
10000
20000
30000
Concentration [ng/ml]

Fig. 8


muMAB 59A
muMAB 60A
muMAB 61D
muMAB 64A
muMAB 65A
muMAB 66B
muMAB 67A
Specific lysis [%]
0
10
20
30
40
50
60
70
80
90
0
5000
10000
15000
20000
25000
Concentration [ng/ml]

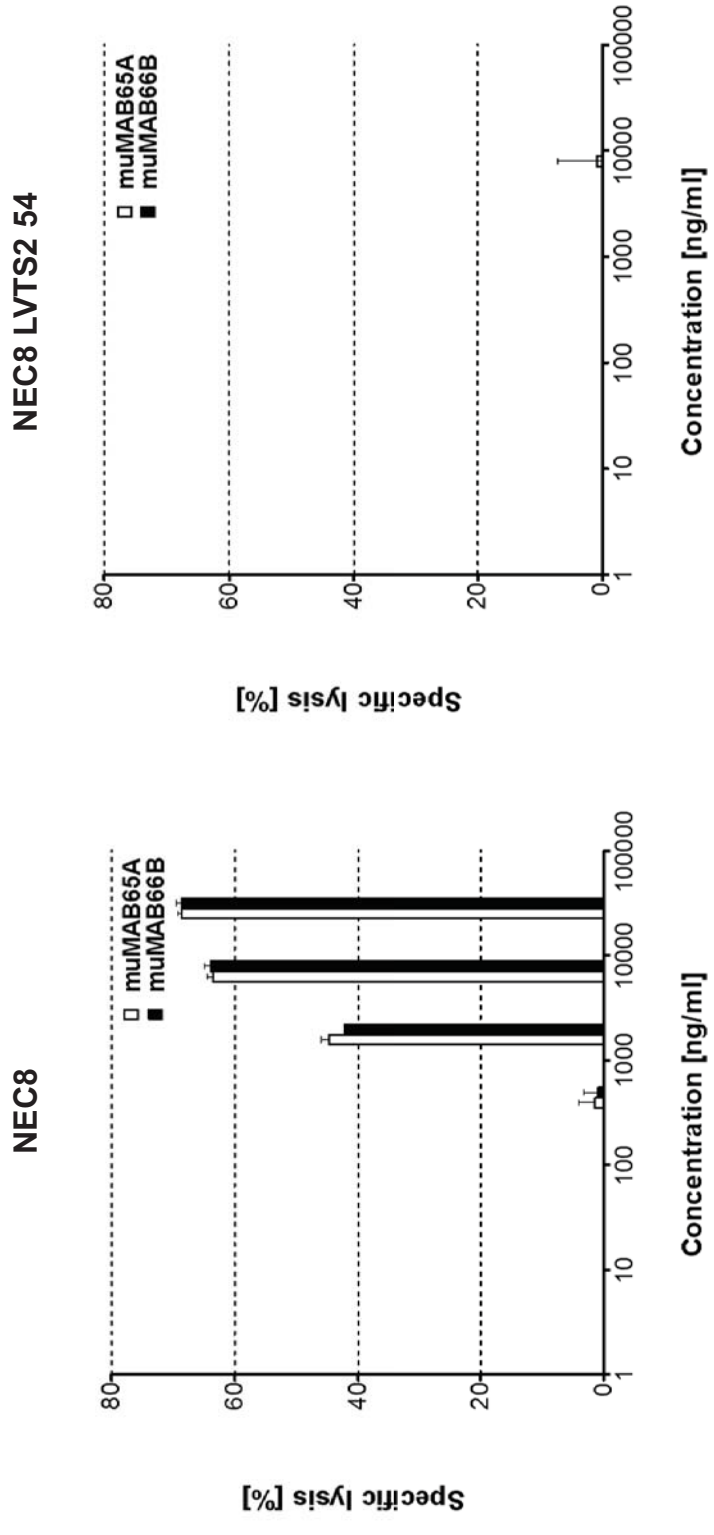

NEC8
muMAB65A
muMAB66B
Specific lysis [%]
0
20
40
60
80
1
10
100
1000
10000
100000
Concentration [ng/ml]
NEC8 LVTS2 54
muMAB65A
muMAB66B
Specific lysis [%]
0
20
40
60
80
1
10
100
1000
10000
100000
Concentration [ng/ml]

Fig. 9

Fig. 10

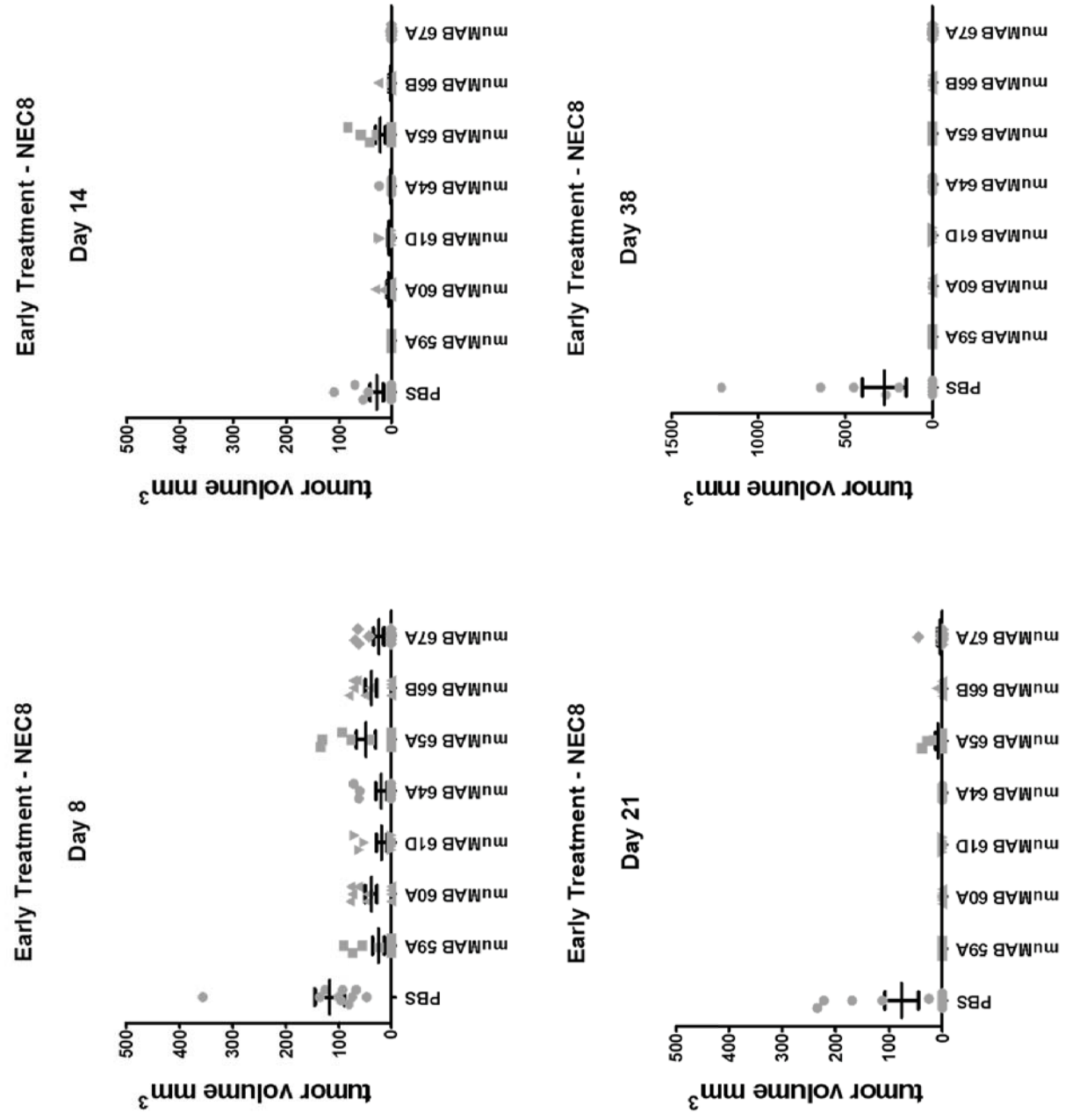
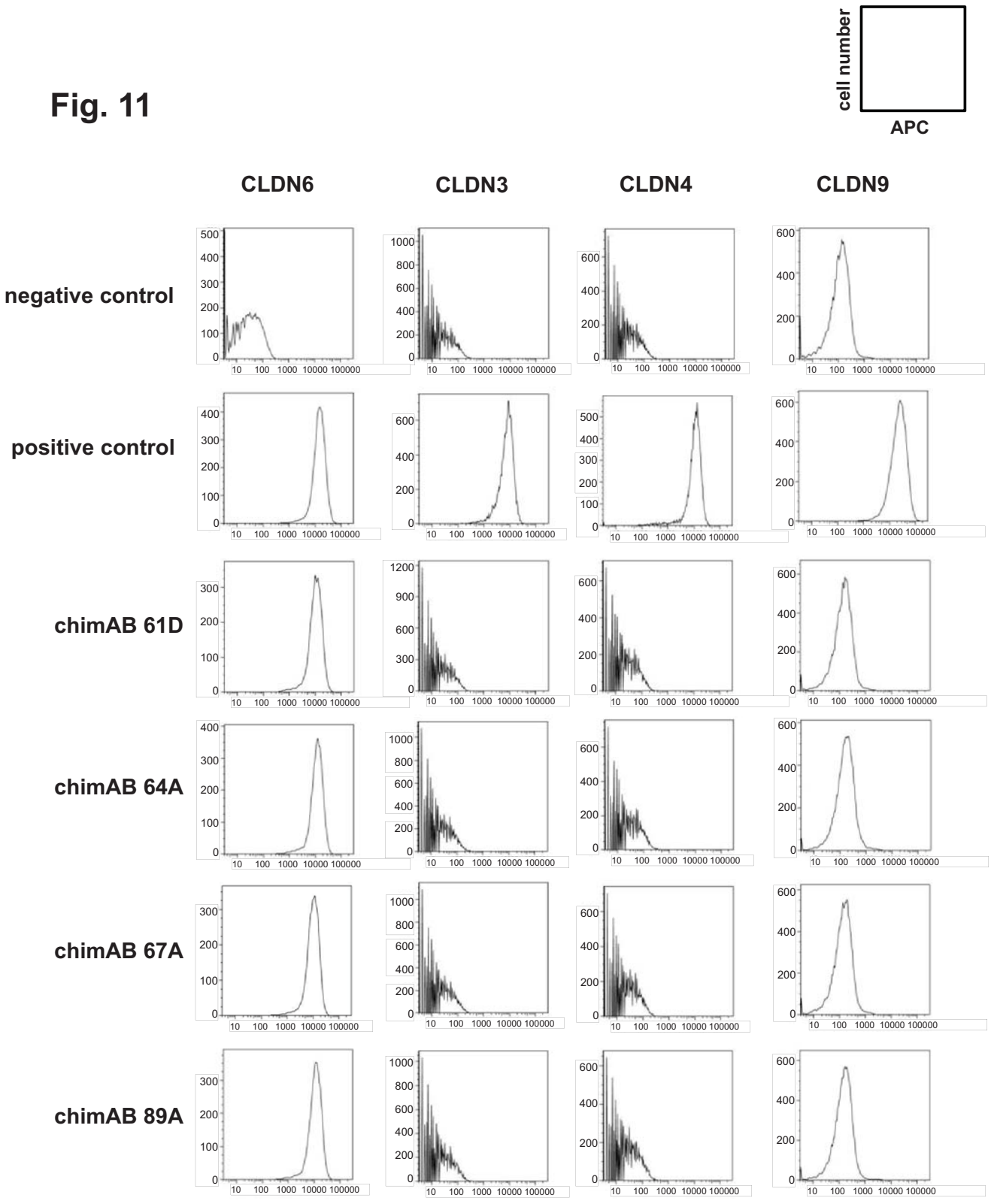

Early Treatment - NEC8
Day 8
tumor volume mm3
0
100
200
300
400
500
PBS
muMAB 59A
muMAB 60A
muMAB 61D
muMAB 64A
muMAB 65A
muMAB 66B
muMAB 67A
Early Treatment - NEC8
Day 14
tumor volume mm3
0
100
200
300
400
500
PBS
muMAB 59A
muMAB 60A
muMAB 61D
muMAB 64A
muMAB 65A
muMAB 66B
muMAB 67A
Early Treatment - NEC8
Day 21
tumor volume mm3
0
100
200
300
400
500
PBS
muMAB 59A
muMAB 60A
muMAB 61D
muMAB 64A
muMAB 65A
muMAB 66B
muMAB 67A
Early Treatment - NEC8
Day 38
tumor volume mm3
0
500
1000
1500
PBS
muMAB 59A
muMAB 60A
muMAB 61D
muMAB 64A
muMAB 65A
muMAB 66B
muMAB 67A

Fig. 11


cell number
APC
CLDN6
CLDN3
CLDN4
CLDN9
negative control
positive control
chimAB 61D
chimAB 64A
chimAB 67A
chimAB 89A
10 100 1000 10000 100000

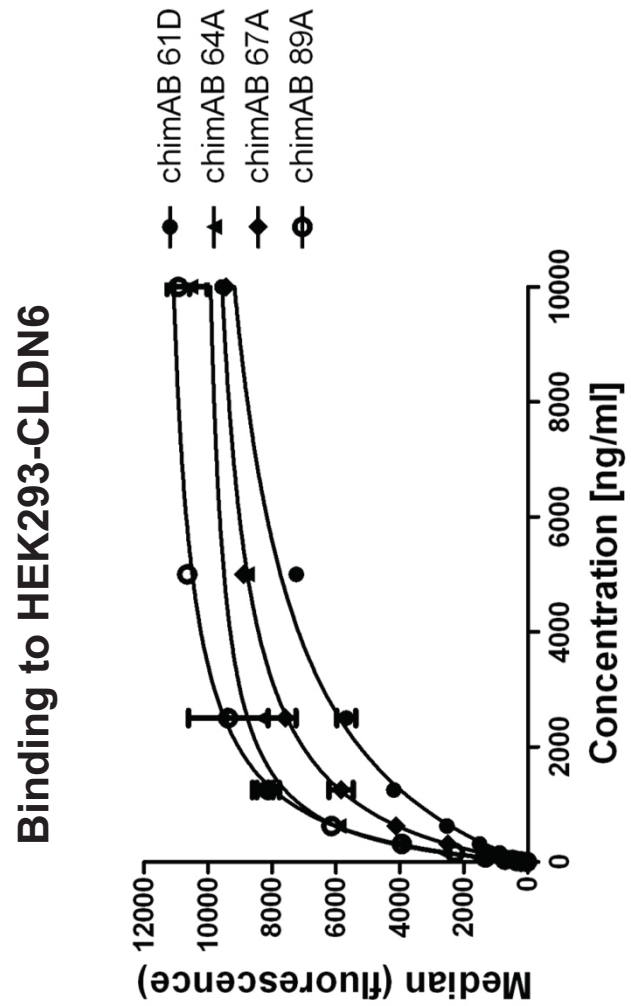

Binding to HEK293-CLDN6
chimAB 61D
chimAB 64A
chimAB 67A
chimAB 89A
Median (fluorescence)
0
2000
4000
6000
8000
10000
12000
0
2000
4000
6000
8000
10000
Concentration [ng/ml]

Fig. 12

Fig. 13

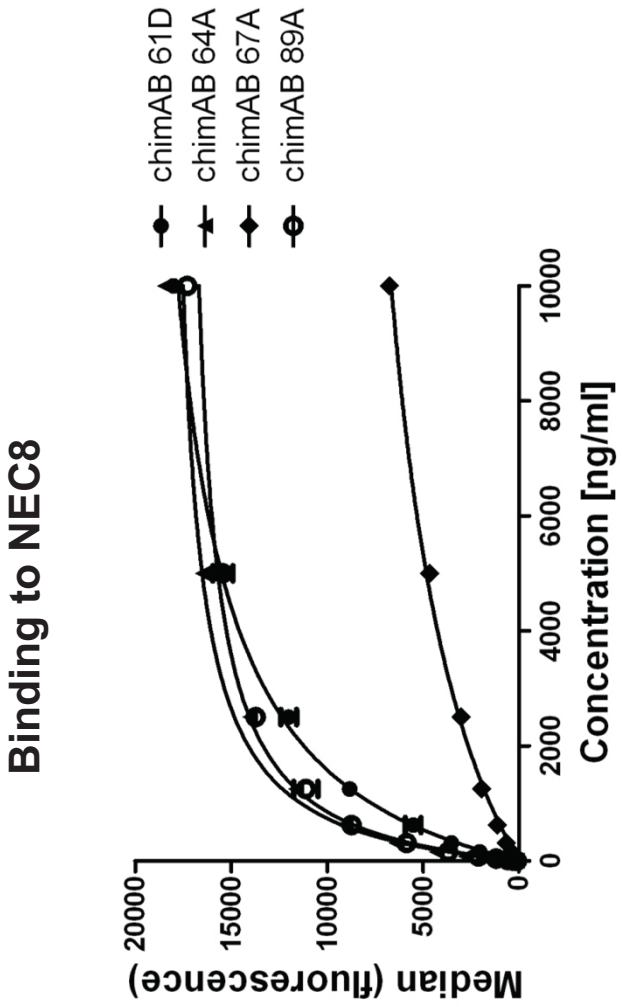

Binding to NEC8
chimAB 61D
chimAB 64A
chimAB 67A
chimAB 89A
Median (fluorescence)
20000
15000
10000
5000
0
0
2000
4000
6000
8000
10000
Concentration [ng/ml]

Fig. 14

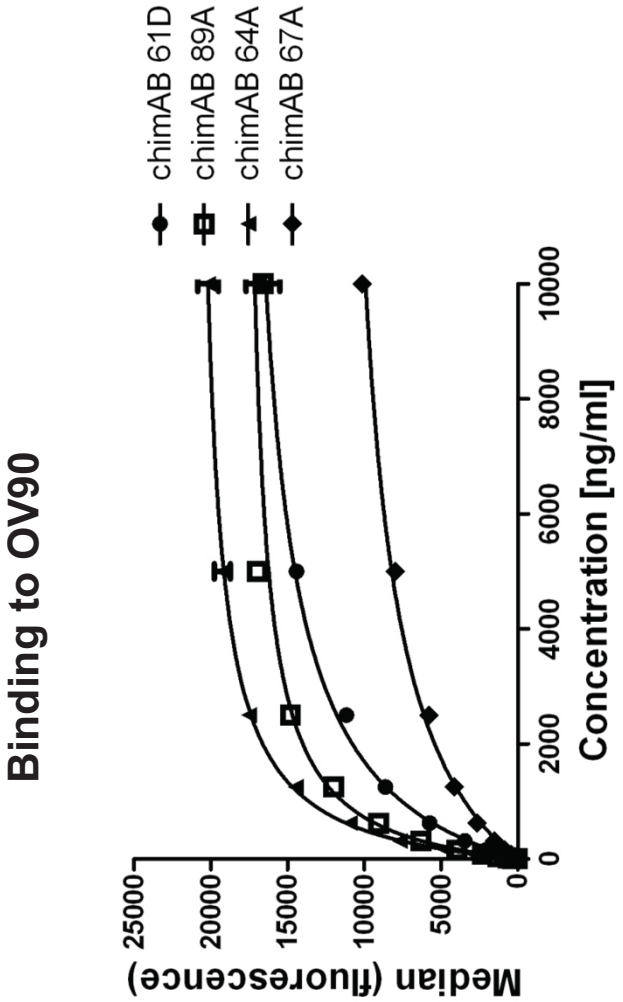

Binding to OV90
chimAB 61D
chimAB 89A
chimAB 64A
chimAB 67A
Median (fluorescence)
25000
20000
15000
10000
5000
0
0
2000
4000
6000
8000
10000
Concentration [ng/ml]

Fig. 15

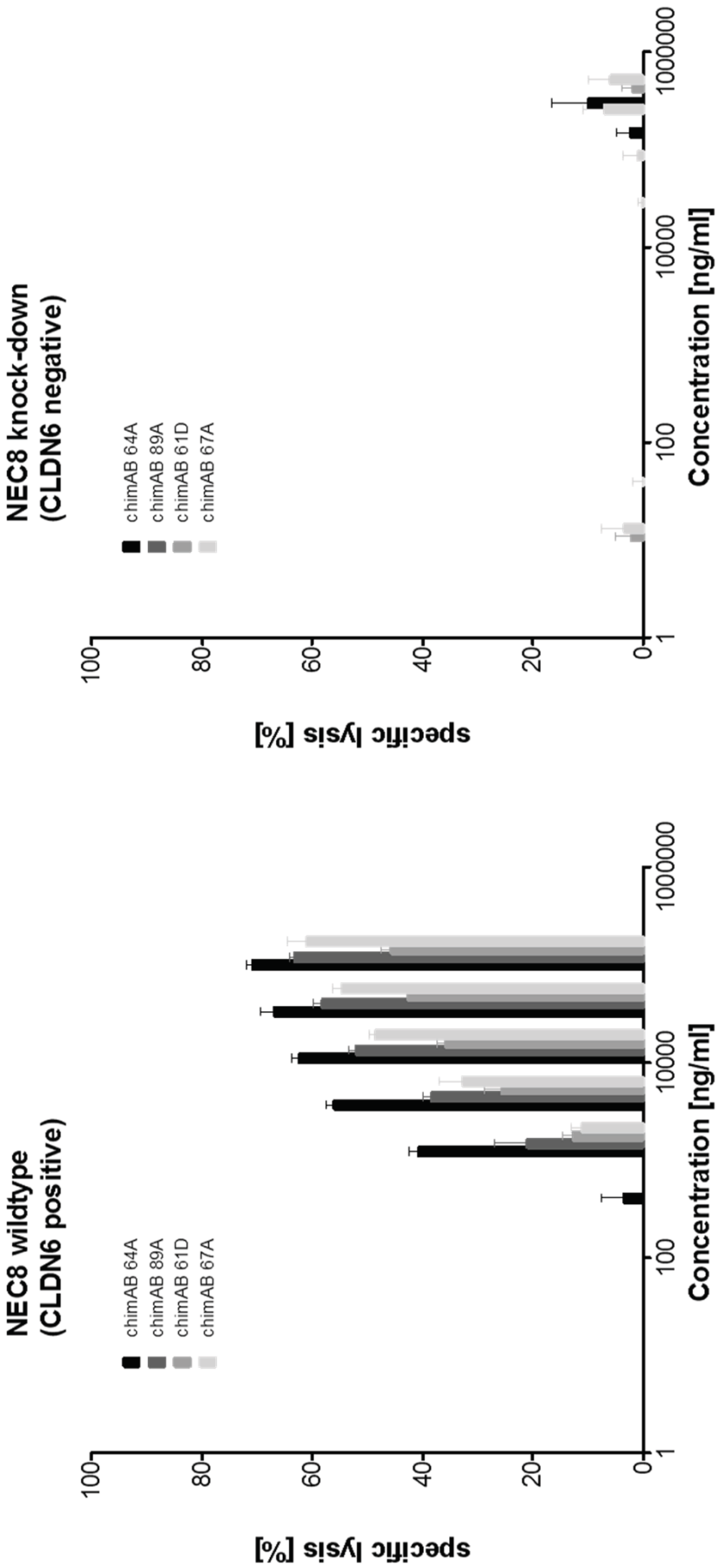

NEC8 knock-down
(CLDN6 negative)
chimAB 64A
chimAB 89A
chimAB 61D
chimAB 67A
specific lysis [%]
0
20
40
60
80
100
1
100
10000
1000000
Concentration [ng/ml]
NEC8 wildtype
(CLDN6 positive)
chimAB 64A
chimAB 89A
chimAB 61D
chimAB 67A
specific lysis [%]
0
20
40
60
80
100
1
100
10000
1000000
Concentration [ng/ml]

Fig. 16

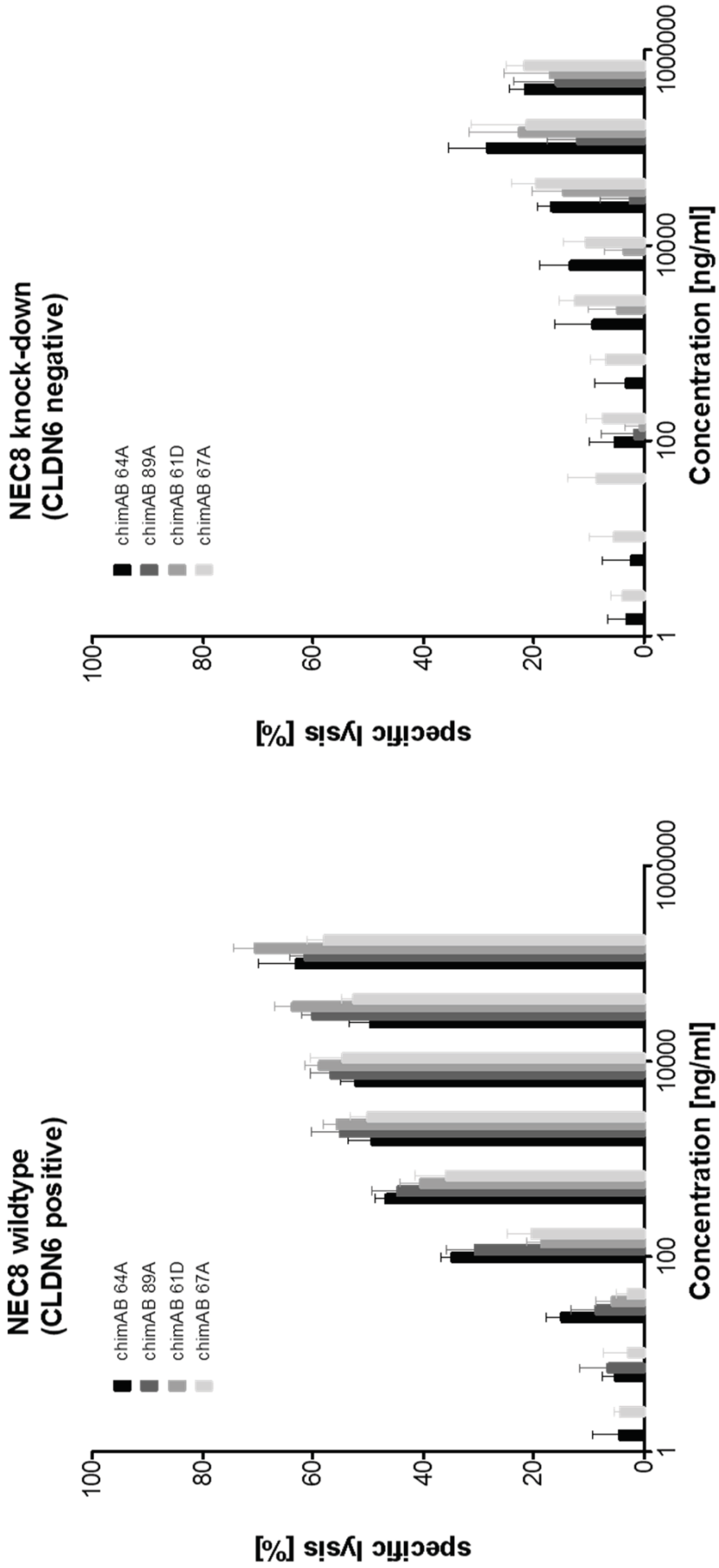
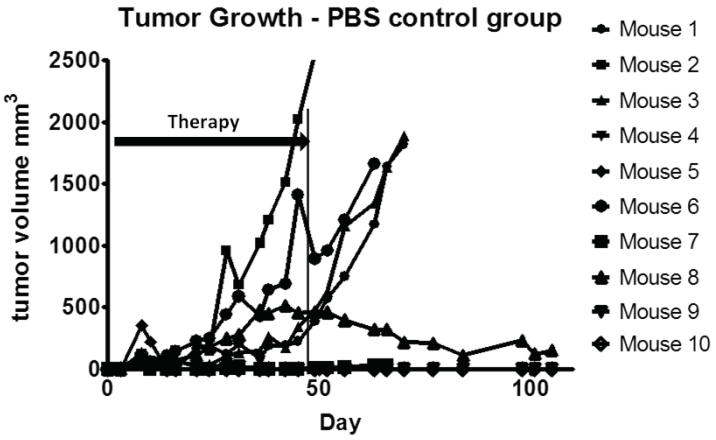
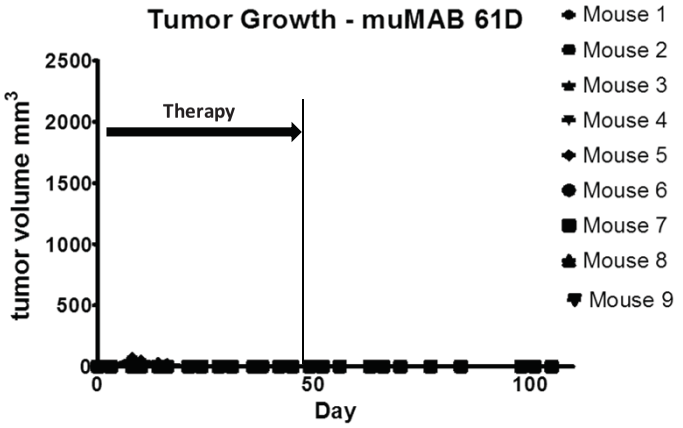
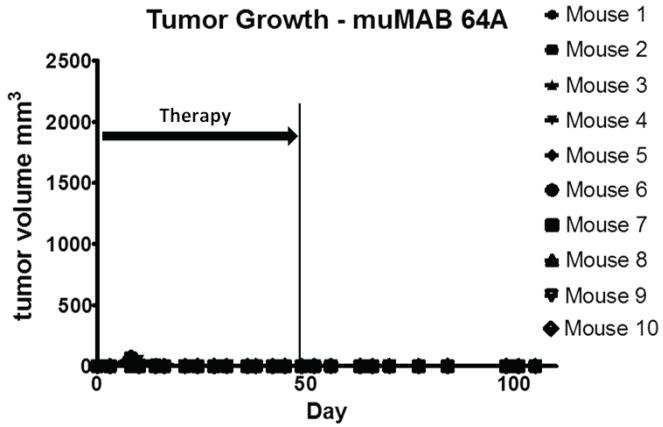

NEC8 knock-down
(CLDN6 negative)
chimAB 64A
chimAB 89A
chimAB 61D
chimAB 67A
specific lysis [%]
0
20
40
60
80
100
1
100
10000
1000000
Concentration [ng/ml]
NEC8 wildtype
(CLDN6 positive)
chimAB 64A
chimAB 89A
chimAB 61D
chimAB 67A
specific lysis [%]
0
20
40
60
80
100
1
100
10000
1000000
Concentration [ng/ml]

Fig. 17


Tumor Growth - PBS control group
tumor volume mm3
2500
2000
1500
1000
500
0
Therapy
0
50
100
Day
Mouse 1
Mouse 2
Mouse 3
Mouse 4
Mouse 5
Mouse 6
Mouse 7
Mouse 8
Mouse 9
Mouse 10


Tumor Growth - muMAB 61D
tumor volume mm3
2500
2000
1500
1000
500
0
Therapy
0
50
100
Day
Mouse 1
Mouse 2
Mouse 3
Mouse 4
Mouse 5
Mouse 6
Mouse 7
Mouse 8
Mouse 9


Tumor Growth - muMAB 64A
tumor volume mm3
2500
2000
1500
1000
500
0
Therapy
0
50
100
Day
Mouse 1
Mouse 2
Mouse 3
Mouse 4
Mouse 5
Mouse 6
Mouse 7
Mouse 8
Mouse 9
Mouse 10

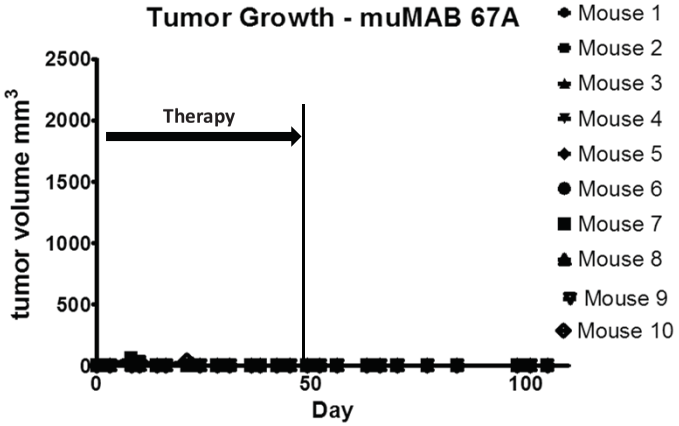
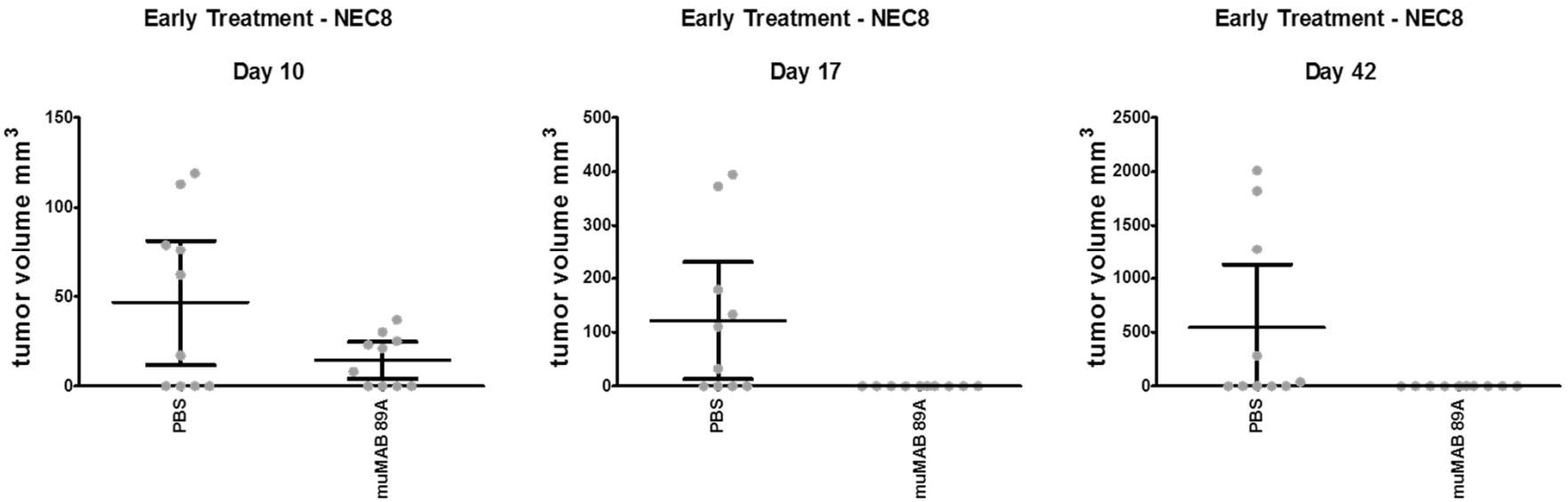

Tumor Growth - muMAB 67A
tumor volume mm3
2500
2000
1500
1000
500
0
Therapy
0
50
100
Day
Mouse 1
Mouse 2
Mouse 3
Mouse 4
Mouse 5
Mouse 6
Mouse 7
Mouse 8
Mouse 9
Mouse 10

Fig. 18

(A)


Early Treatment - NEC8
Day 10
tumor volume mm3
150
100
50
0
PBS
muMAB 89A
Early Treatment - NEC8
Day 17
tumor volume mm3
500
400
300
200
100
0
PBS
muMAB 89A
Early Treatment - NEC8
Day 42
tumor volume mm3
2500
2000
1500
1000
500
0
PBS
muMAB 89A

(B)

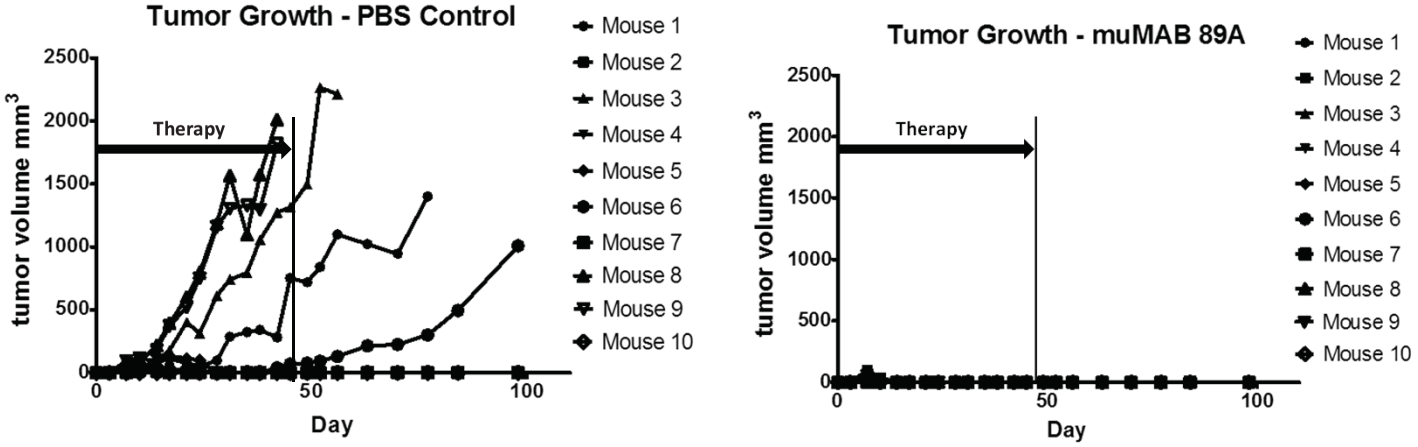

Tumor Growth - PBS Control
tumor volume mm3
2500
2000
1500
1000
500
0
Therapy
0
50
100
Day
Mouse 1
Mouse 2
Mouse 3
Mouse 4
Mouse 5
Mouse 6
Mouse 7
Mouse 8
Mouse 9
Mouse 10
Tumor Growth - muMAB 89A
tumor volume mm3
2500
2000
1500
1000
500
0
Therapy
0
50
100
Day
Mouse 1
Mouse 2
Mouse 3
Mouse 4
Mouse 5
Mouse 6
Mouse 7
Mouse 8
Mouse 9
Mouse 10

Fig. 19

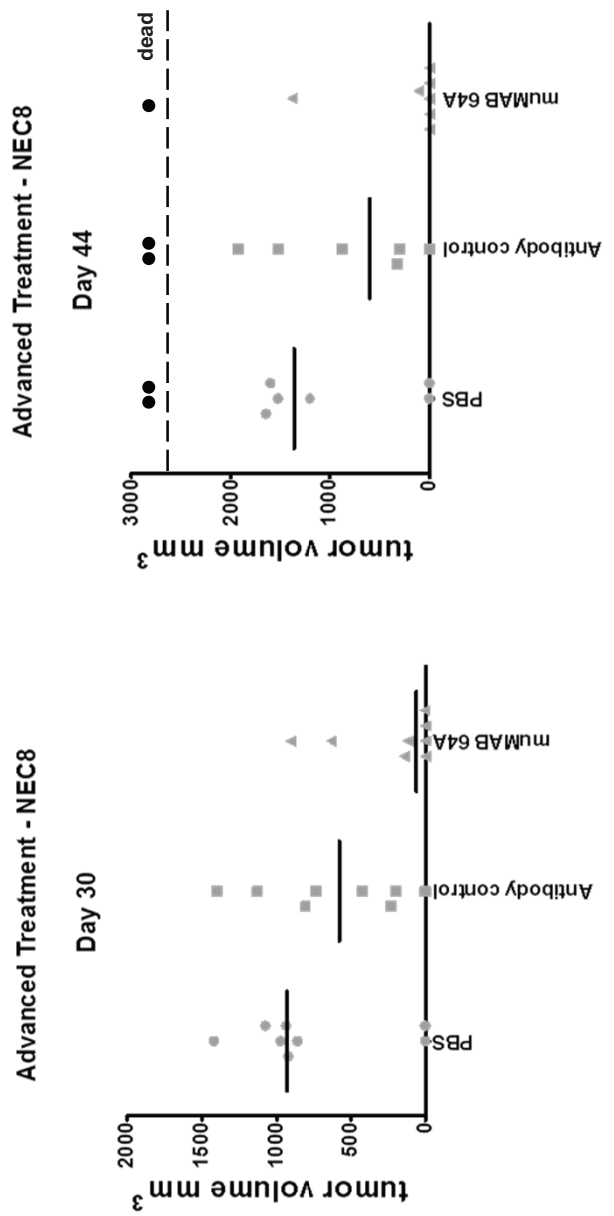
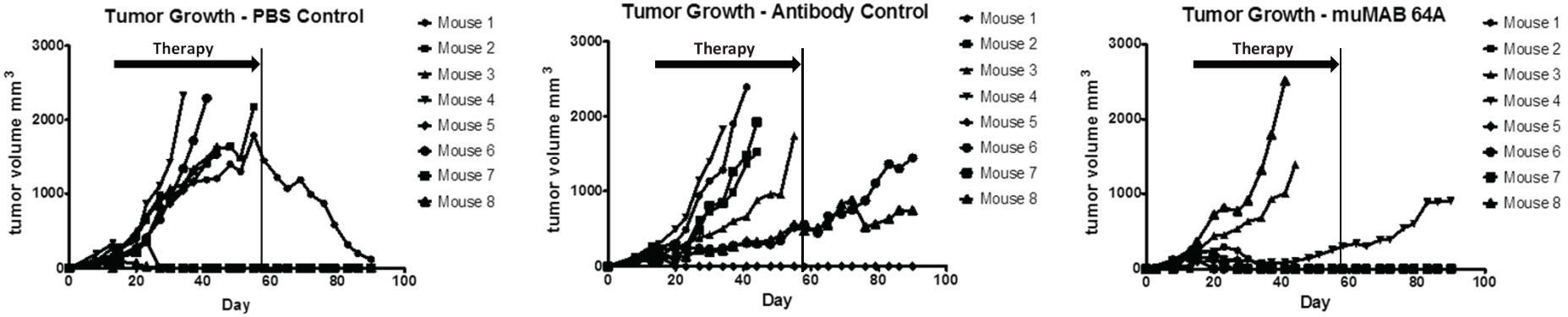

Advanced Treatment - NEC8
Day 15 - Initiation of Immunotherapy
tumor volume mm3
1000
800
600
400
200
0
PBS
Antibody control
muMAB 64A
Advanced Treatment - NEC8
Day 30
tumor volume mm3
2000
1500
1000
500
0
PBS
Antibody control
muMAB 64A
Advanced Treatment - NEC8
Day 44
tumor volume mm3
3000
2000
1000
0
dead
PBS
Antibody control
muMAB 64A

Fig. 20

(A)


Tumor Growth - PBS Control
Therapy
tumor volume mm3
Day
Mouse 1
Mouse 2
Mouse 3
Mouse 4
Mouse 5
Mouse 6
Mouse 7
Mouse 8
Tumor Growth - Antibody Control
Therapy
tumor volume mm3
Day
Tumor Growth - muMAB 64A
Therapy
tumor volume mm3
Day

(B)

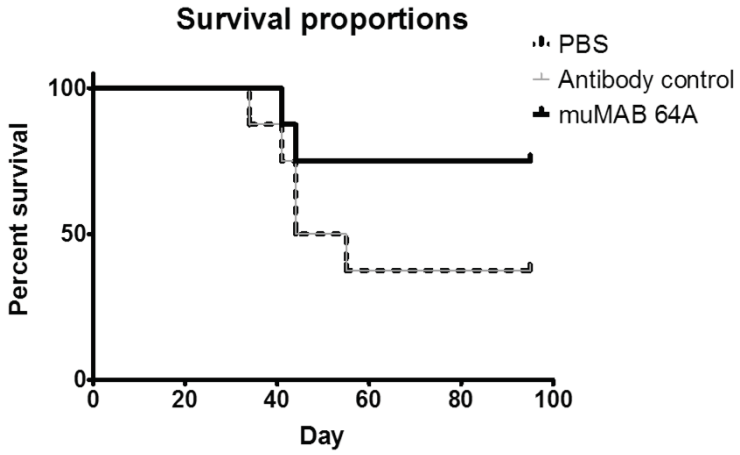
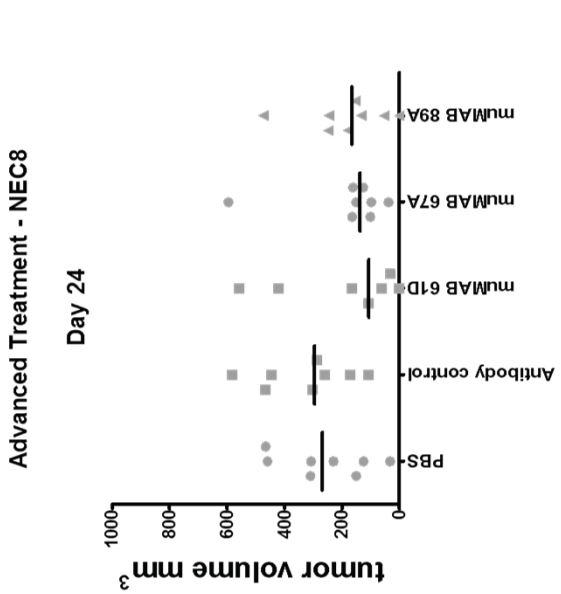
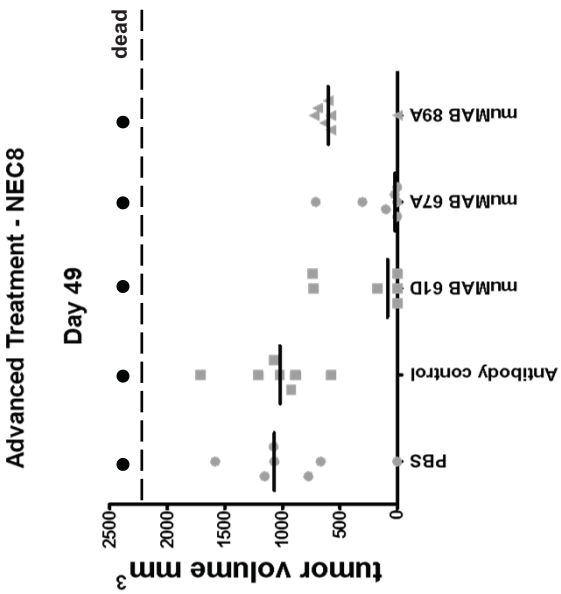
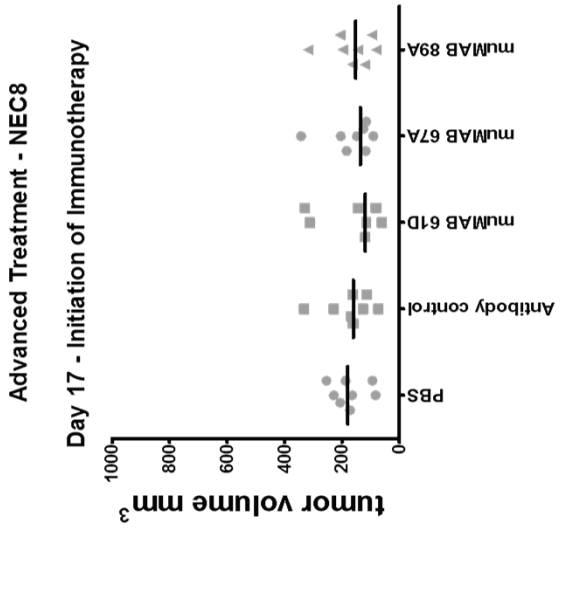

Survival proportions
PBS
Antibody control
muMAB 64A
Percent survival
Day

Fig. 21


Advanced Treatment - NEC8
Day 24
tumor volume mm3
0
200
400
600
800
1000
PBS
Antibody control
muMAB 61D
muMAB 67A
muMAB 89A


Advanced Treatment - NEC8
Day 49
dead
tumor volume mm3
0
500
1000
1500
2000
2500
PBS
Antibody control
muMAB 61D
muMAB 67A
muMAB 89A


Advanced Treatment - NEC8
Day 17 - Initiation of Immunotherapy
tumor volume mm3
0
200
400
600
800
1000
PBS
Antibody control
muMAB 61D
muMAB 67A
muMAB 89A

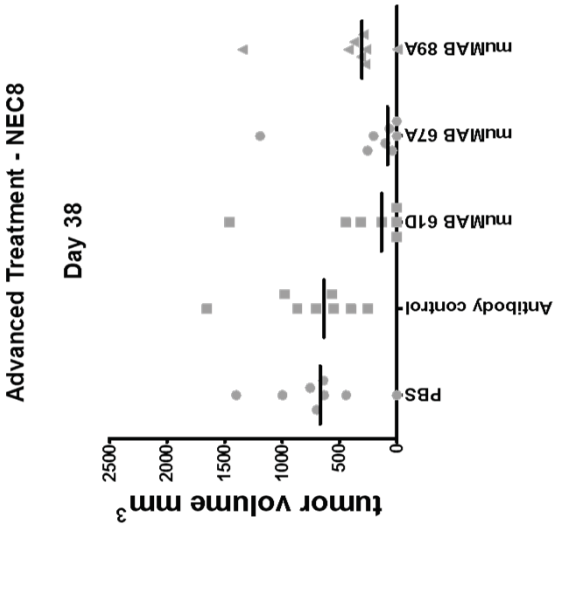
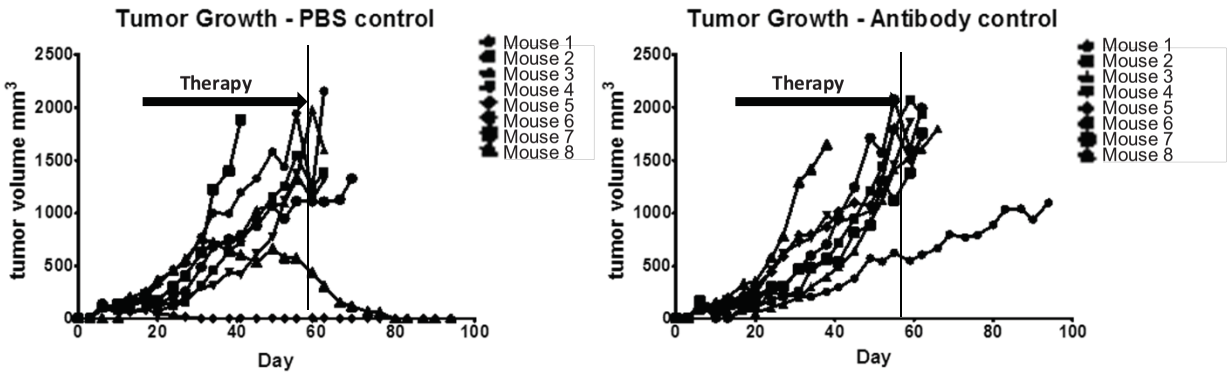
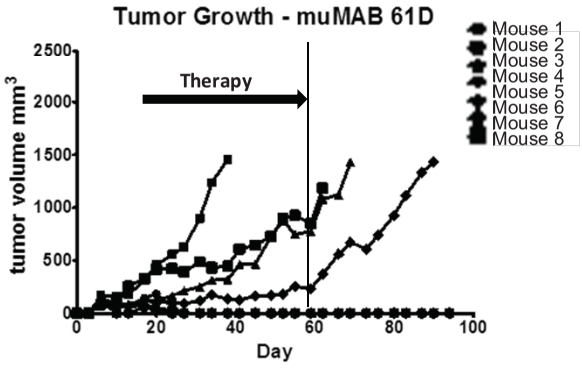

Advanced Treatment - NEC8
Day 38
tumor volume mm3
0
500
1000
1500
2000
2500
PBS
Antibody control
muMAB 61D
muMAB 67A
muMAB 89A

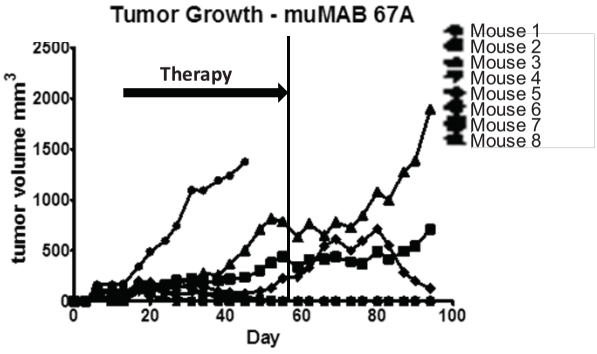
Fig. 22

(A)


Tumor Growth - PBS control
Therapy
tumor volume mm3
Day
Mouse 1
Mouse 2
Mouse 3
Mouse 4
Mouse 5
Mouse 6
Mouse 7
Mouse 8

Tumor Growth - Antibody control
Therapy
tumor volume mm3
Day
Mouse 1
Mouse 2
Mouse 3
Mouse 4
Mouse 5
Mouse 6
Mouse 7
Mouse 8


Tumor Growth - muMAB 61D
Therapy
tumor volume mm3
Day
Mouse 1
Mouse 2
Mouse 3
Mouse 4
Mouse 5
Mouse 6
Mouse 7
Mouse 8


Tumor Growth - muMAB 67A
Therapy
tumor volume mm3
Day
Mouse 1
Mouse 2
Mouse 3
Mouse 4
Mouse 5
Mouse 6
Mouse 7
Mouse 8

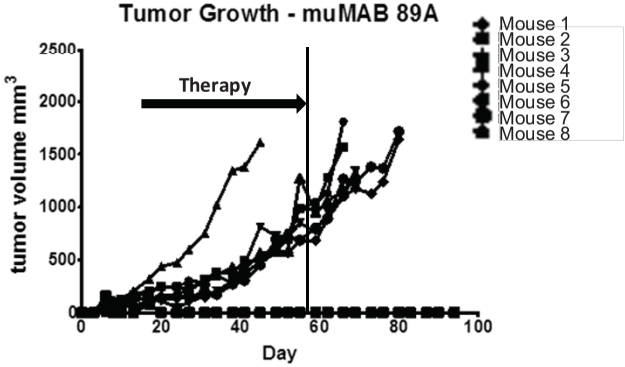

Tumor Growth - muMAB 89A
Therapy
tumor volume mm3
Day
Mouse 1
Mouse 2
Mouse 3
Mouse 4
Mouse 5
Mouse 6
Mouse 7
Mouse 8

Fig. 22

(B)

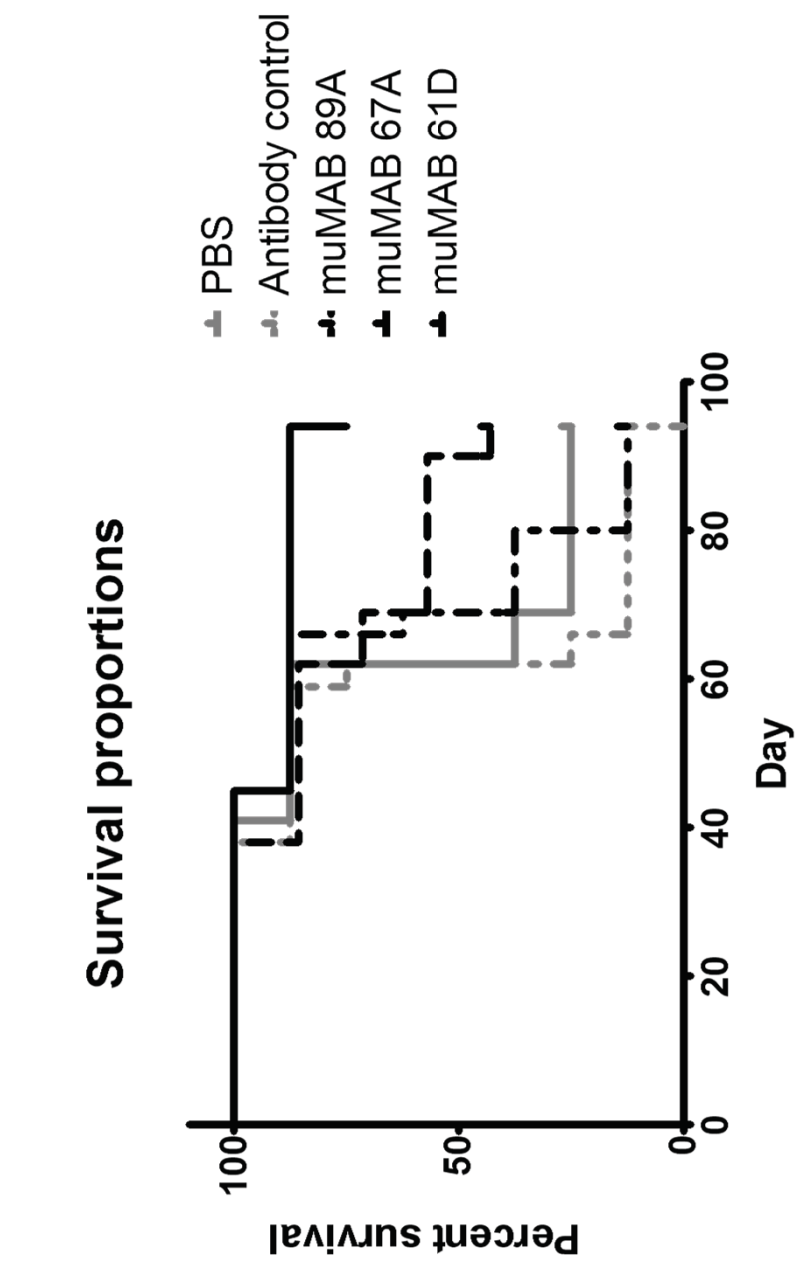

Survival proportions
PBS
Antibody control
muMAB 89A
muMAB 67A
muMAB 61D
Percent survival
100
50
0
0
20
40
60
80
100
Day

Fig. 23

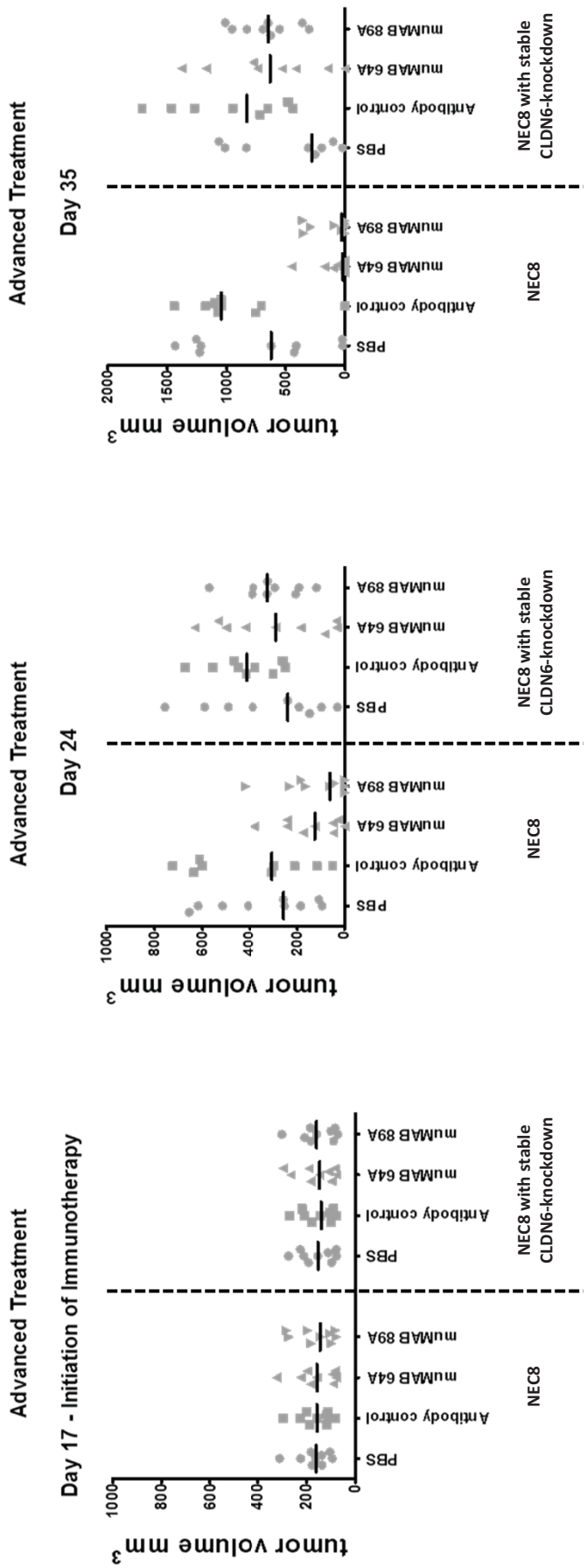

Advanced Treatment
Day 17 - Initiation of Immunotherapy
Day 24
Day 35
tumor volume mm3
0
200
400
600
800
1000
500
1000
1500
2000
PBS
Antibody control
muMAB 64A
muMAB 89A
NEC8
NEC8 with stable CLDN6-knockdown

Fig. 24

	EC1 (aa 27-81)																																																					
	L	P	M	W	K	V	T	A	F	I	G	N	S	I	V	V	A	Q	V	V	W	E	G	L	W	M	S	C	V	V	Q	S	T	G	Q	M	Q	C	K	V	Y	D	S	L	L	A	L	P	Q	D	L	Q	A	A	R
Name	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81
GT512chimAB 61D		X		X																			X	X	X			X										X																	
GT512chimAB 64A		X		X																			X	X	X			X										X																	
GT512chimAB 67A		X		X																			X	X	X			X										X																	
GT512chimAB 89A		X		X																			X	X	X			X										X																	
R&D		X		X																			X	X	X			X										X																	

	EC2 (aa 137-161)																								
	C	W	T	A	H	A	I	I	R	D	F	Y	N	P	L	V	A	E	A	Q	K	R	E	L	G
Name	137	138	139	140	141	142	143	144	145	146	147	148	149	150	151	152	153	154	155	156	157	158	159	160	161
GT512chimAB 61D																									
GT512chimAB 64A																									
GT512chimAB 67A																									
GT512chimAB 89A																									
R&D																									

- X altered transport to the membrane
- (white) no influence on antibody binding
- (grey) contributes to antibody binding
- (black) essential for antibody binding

Fig. 25

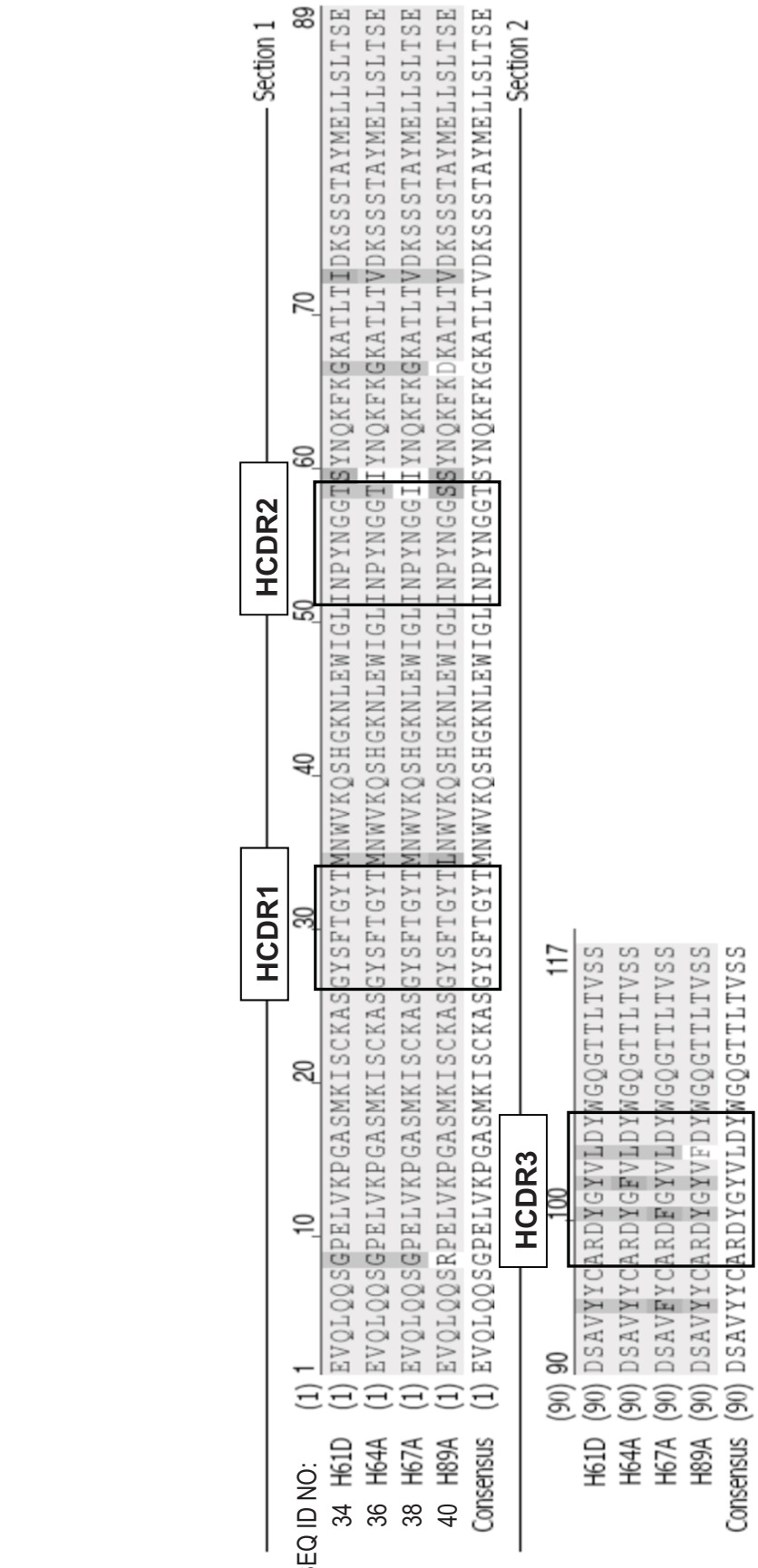
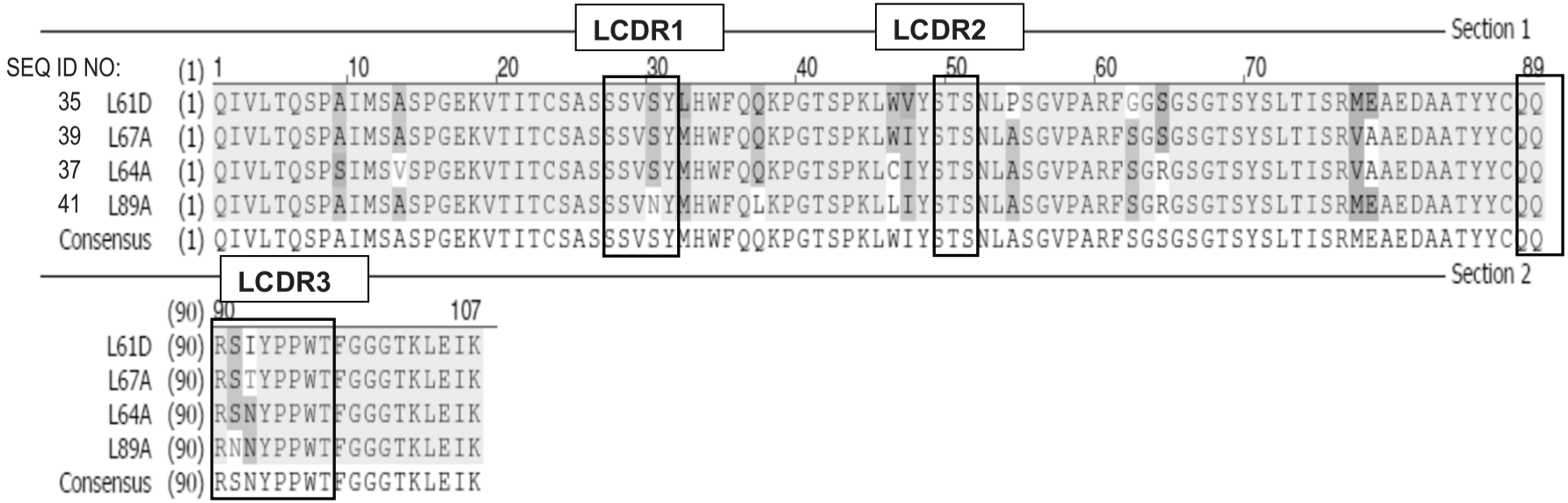

Section 1
Section 2
HCDR1
HCDR2
HCDR3
SEQ ID NO:
34 H61D
36 H64A
38 H67A
40 H89A
Consensus
(1) EVQLQQSGPELVKPGASMKISCKASGYSFTGYTMNWVKQSHGKNLEWIGLINPYNGGTSYNQKFKGKATLTVDKSSSTAYMELLSLTSE
(90) DSAVYYCARDYGYVLDYWGQGTTLTVSS

Fig. 26


LCDR1
LCDR2
Section 1
SEQ ID NO:
(1) 1 10 20 30 40 50 60 70 89
35 L61D (1) QIVLTQSPAIMSASPGEKVTITCSASSSVSYLHWFQQKPGTSPKLWVYSTSNLPSGVPARFGGSGSGTSYSLTISRMEAEDAATYYCQQ
39 L67A (1) QIVLTQSPAIMSASPGEKVTITCSASSSVSYMHWFQQKPGTSPKLWIYSTSNLASGVPARFSGSGSGTSYSLTISRVAAEDAATYYCQQ
37 L64A (1) QIVLTQSPSIMSVSPGEKVTITCSASSSVSYMHWFQQKPGTSPKLCIYSTSNLASGVPARFSGRGSGTSYSLTISRVAAEDAATYYCQQ
41 L89A (1) QIVLTQSPAIMSASPGEKVTITCSASSSVNYMHWFQLKPGTSPKLLIYSTSNLASGVPARFSGRGSGTSYSLTISRMEAEDAATYYCQQ
Consensus (1) QIVLTQSPAIMSASPGEKVTITCSASSSVSYMHWFQQKPGTSPKLWIYSTSNLASGVPARFSGSGSGTSYSLTISRMEAEDAATYYCQQ
LCDR3
Section 2
(90) 90 107
L61D (90) RSIYPPWTFGGGTKLEIK
L67A (90) RSTYPPWTFGGGTKLEIK
L64A (90) RSNYPPWTFGGGTKLEIK
L89A (90) RNNYPPWTFGGGTKLEIK
Consensus (90) RSNYPPWTFGGGTKLEIK