Fig. 1

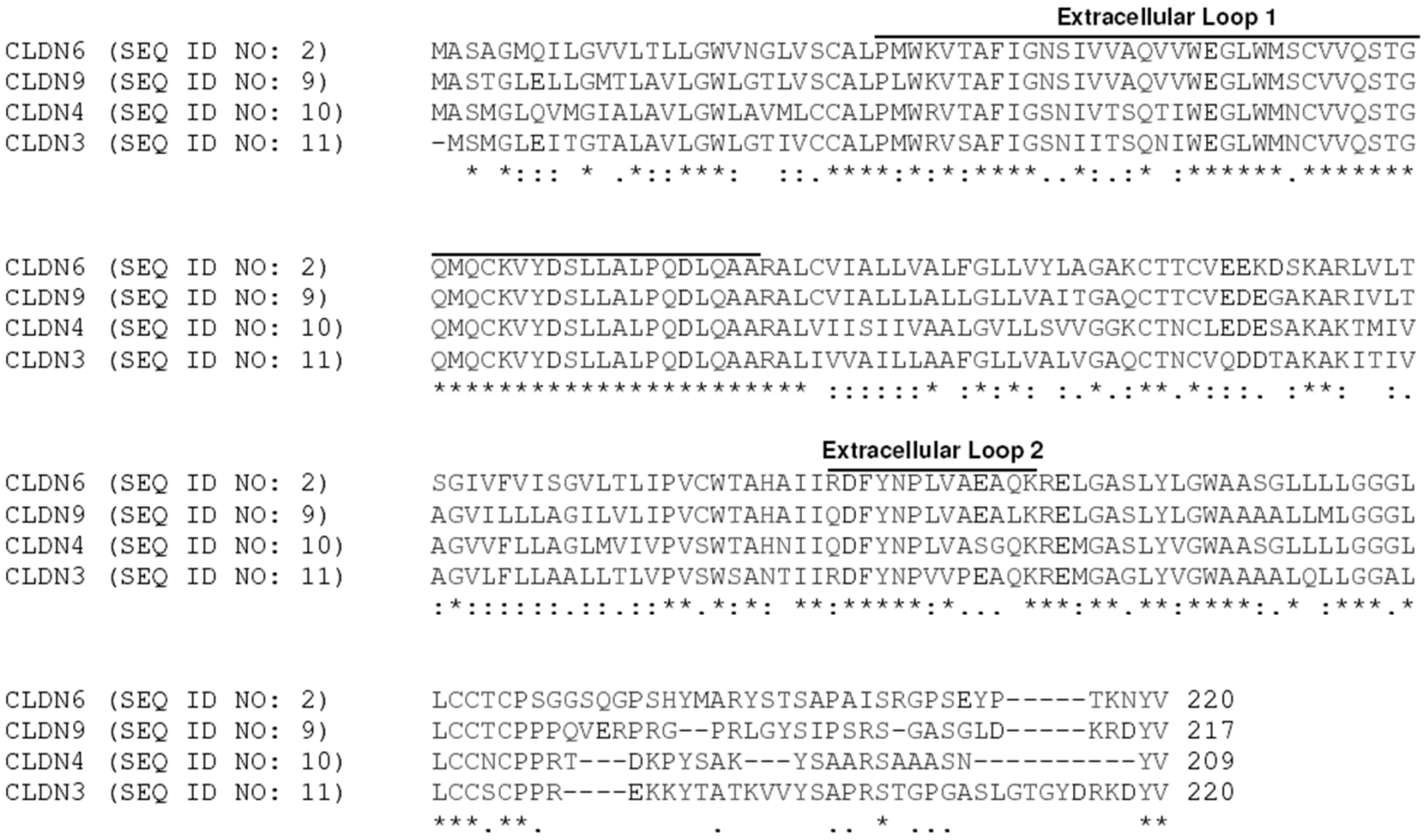

Extracellular Loop 1
CLDN6 (SEQ ID NO: 2) MASAGMQILGVVLTLLGWVNGLVSCALPMWKVTAFIGNSIVVAQVVWEGLWMSCVVQSTG 60
CLDN9 (SEQ ID NO: 9) MASTGLELLGMTLAVLGWLGTLVSCALPLWKVTAFIGNSIVVAQVVWEGLWMSCVVQSTG 60
CLDN4 (SEQ ID NO: 10) MASMGLQVMGIALAVLGWLAVMLCCALPMWRVTAFIGSNIVTSQTIWEGLWMNCVVQSTG 60
CLDN3 (SEQ ID NO: 11) -MSMGLEITGTALAVLGWLGTIVCCALPMWRVSAFIGSNIITSQNIWEGLWMNCVVQSTG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

Fig. 2A

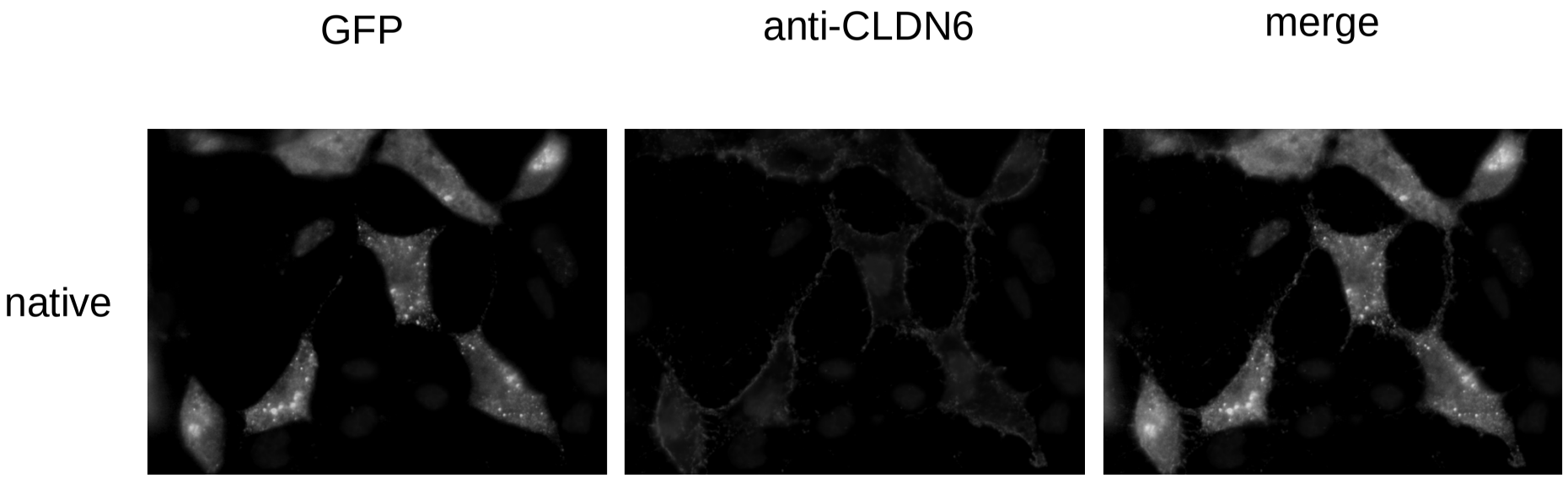


Fig. 2B

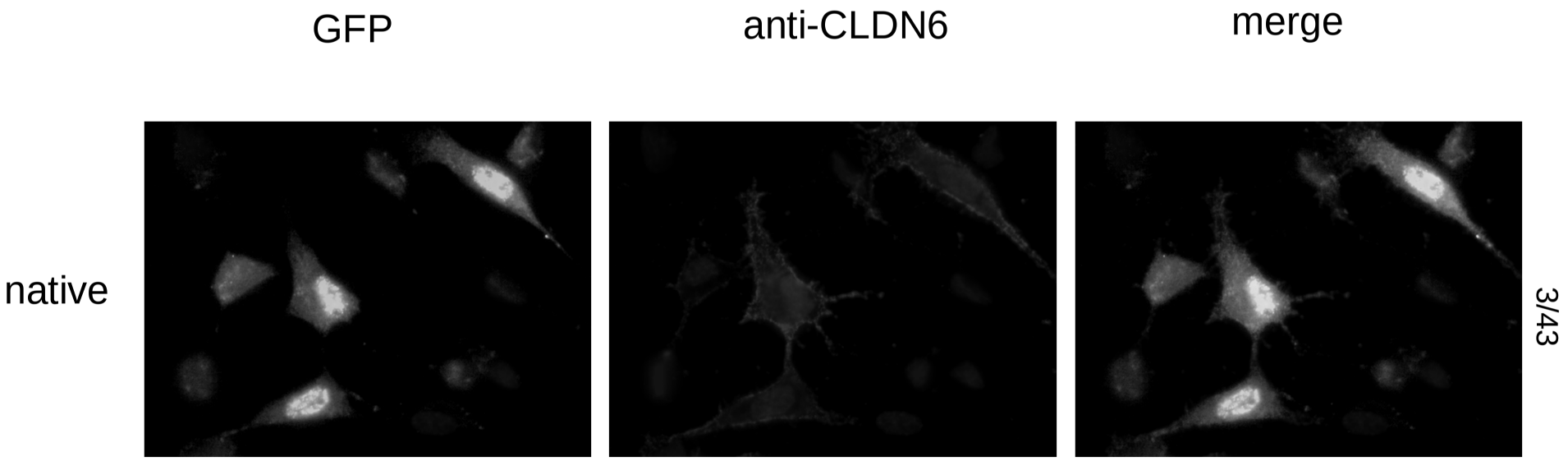


Fig. 3

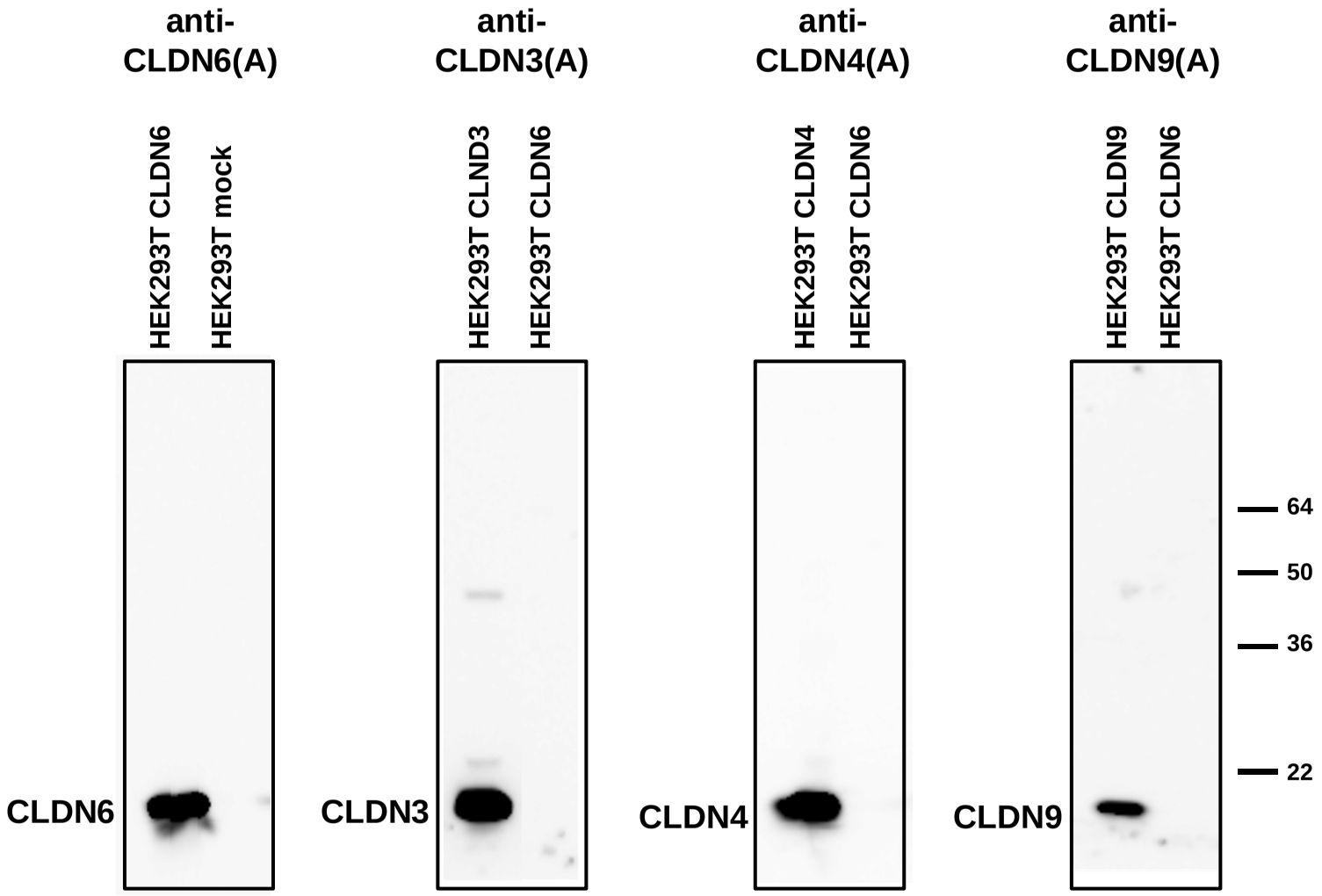

anti-
CLDN6(A)
HEK293T CLDN6
HEK293T mock
CLDN6
anti-
CLDN3(A)
HEK293T CLND3
HEK293T CLDN6
CLDN3
anti-
CLDN4(A)
HEK293T CLDN4
HEK293T CLDN6
CLDN4
anti-
CLDN9(A)
HEK293T CLDN9
HEK293T CLDN6
CLDN9
64
50
36
22

Fig. 4

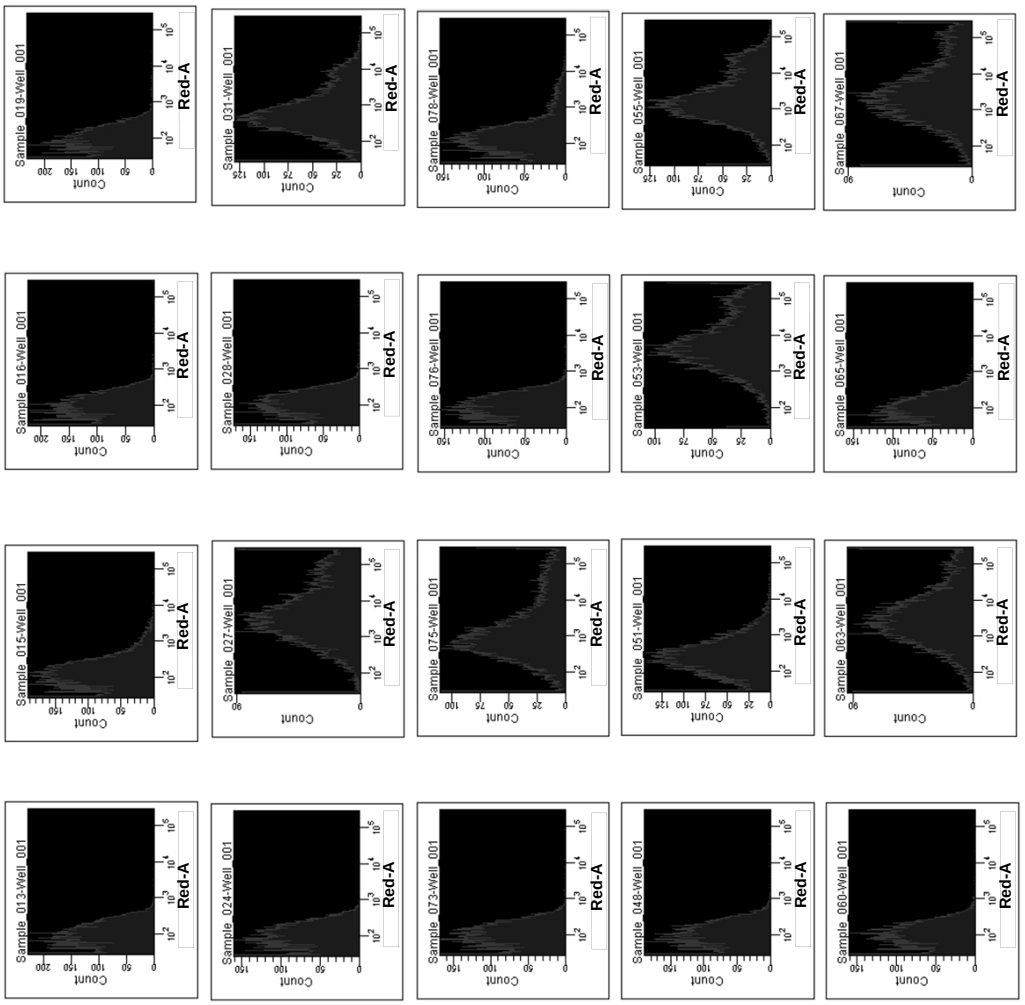

isotype
anti-CLDN6
anti-CLDN3
anti-CLDN4
non-transfected
CLDN6-transfected
CLDN9-transfected
CLDN3-transfected
CLDN4-transfected
Sample_013-Well_001
Sample_015-Well_001
Sample_016-Well_001
Sample_019-Well_001
Sample_024-Well_001
Sample_027-Well_001
Sample_028-Well_001
Sample_031-Well_001
Sample_073-Well_001
Sample_075-Well_001
Sample_076-Well_001
Sample_078-Well_001
Sample_048-Well_001
Sample_051-Well_001
Sample_053-Well_001
Sample_055-Well_001
Sample_060-Well_001
Sample_063-Well_001
Sample_065-Well_001
Sample_067-Well_001
Count
Red-A

Fig. 5A

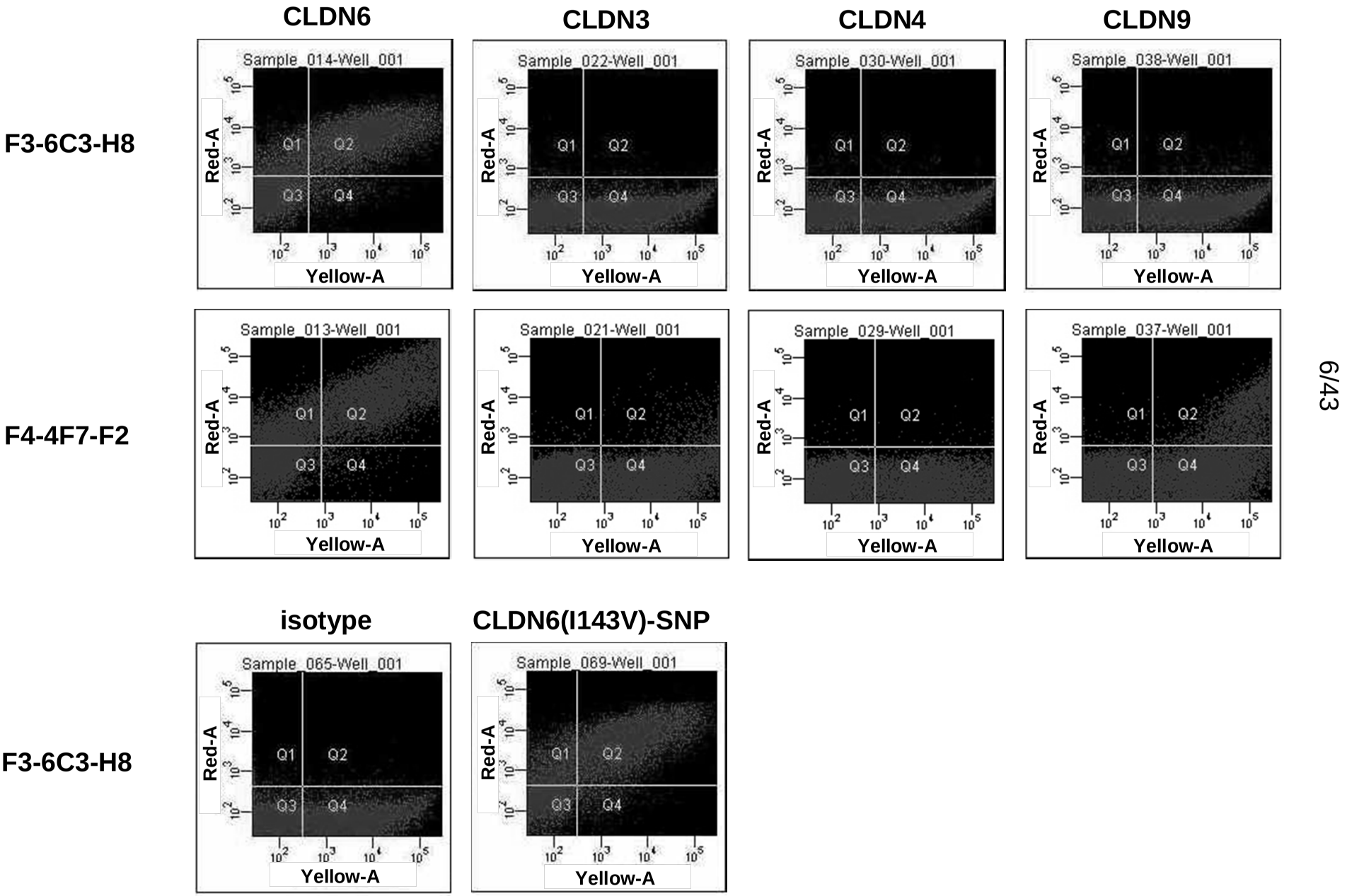

CLDN6
CLDN3
CLDN4
CLDN9
F3-6C3-H8
F4-4F7-F2
isotype
CLDN6(I143V)-SNP
F3-6C3-H8
Sample_014-Well_001
Sample_022-Well_001
Sample_030-Well_001
Sample_038-Well_001
Sample_013-Well_001
Sample_021-Well_001
Sample_029-Well_001
Sample_037-Well_001
Sample_065-Well_001
Sample_069-Well_001
Red-A
Yellow-A
Q1
Q2
Q3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

Fig. 5B

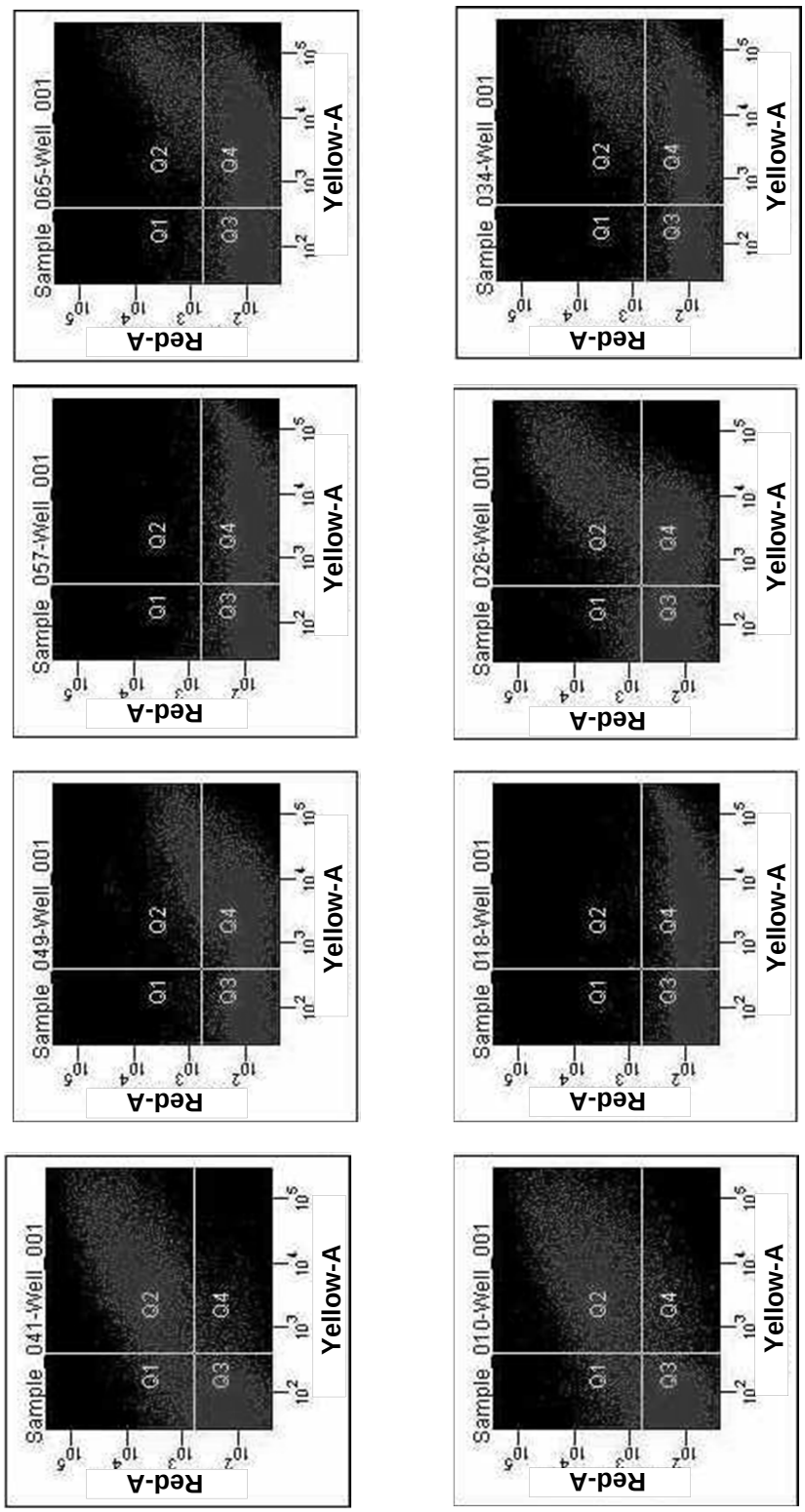
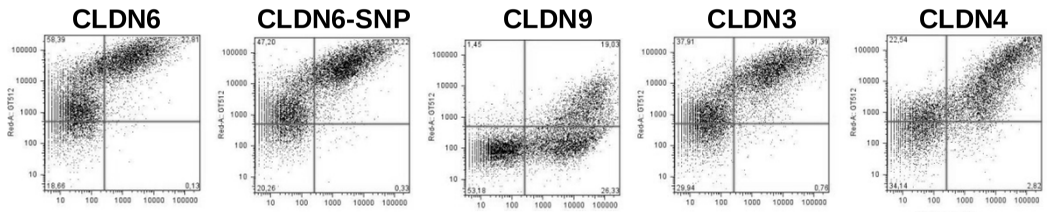
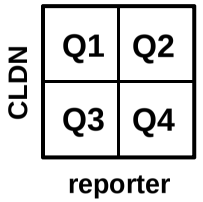
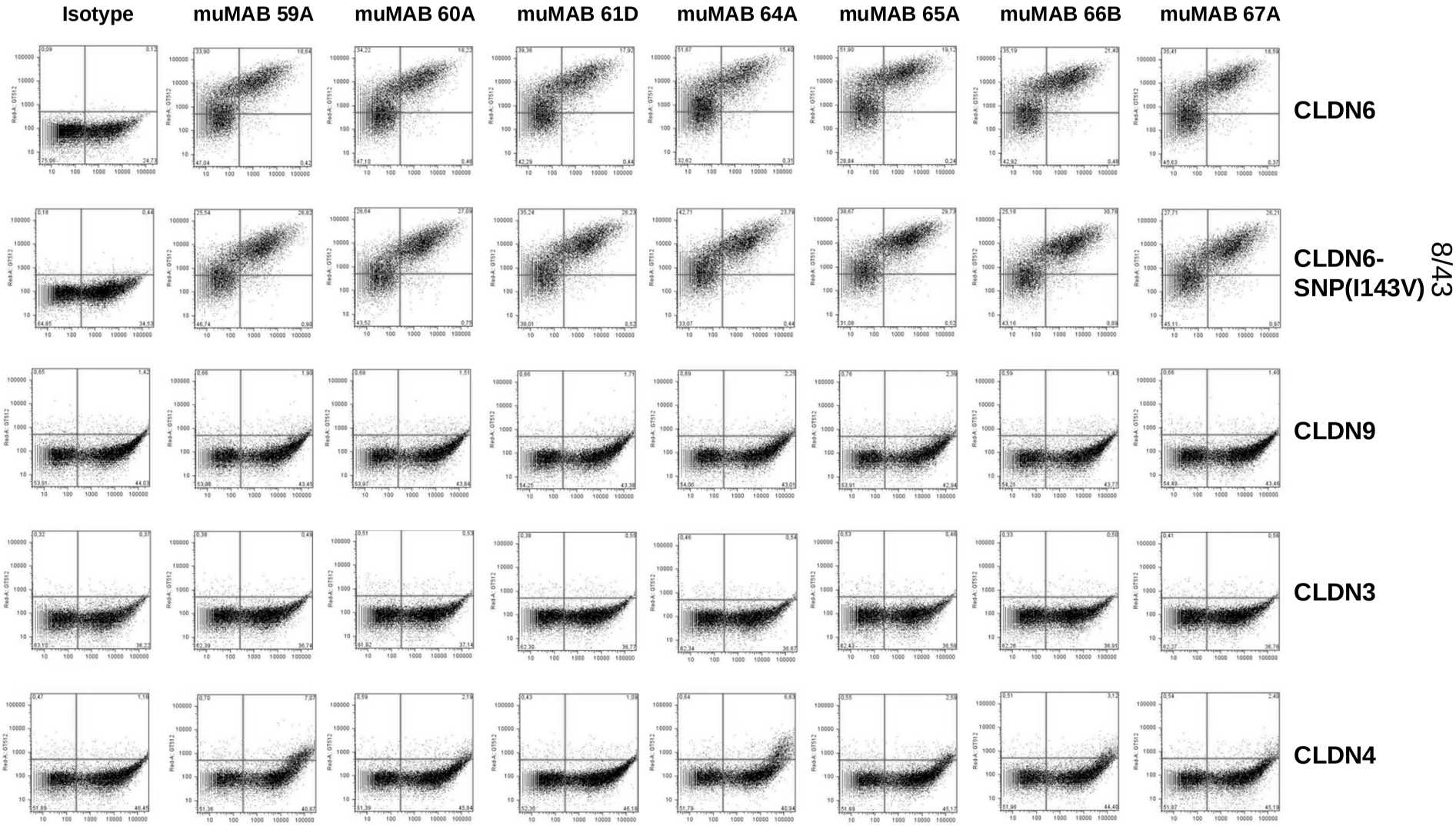

CLDN6
CLDN3
CLDN4
CLDN9
F3-7B3-B4
F3-3F7-A5
Sample_041-Well_001
Sample_049-Well_001
Sample_057-Well_001
Sample_065-Well_001
Sample_010-Well_001
Sample_018-Well_001
Sample_026-Well_001
Sample_034-Well_001
Q1
Q2
Q3
Q4
Red-A
Yellow-A

Fig. 6

positive controls







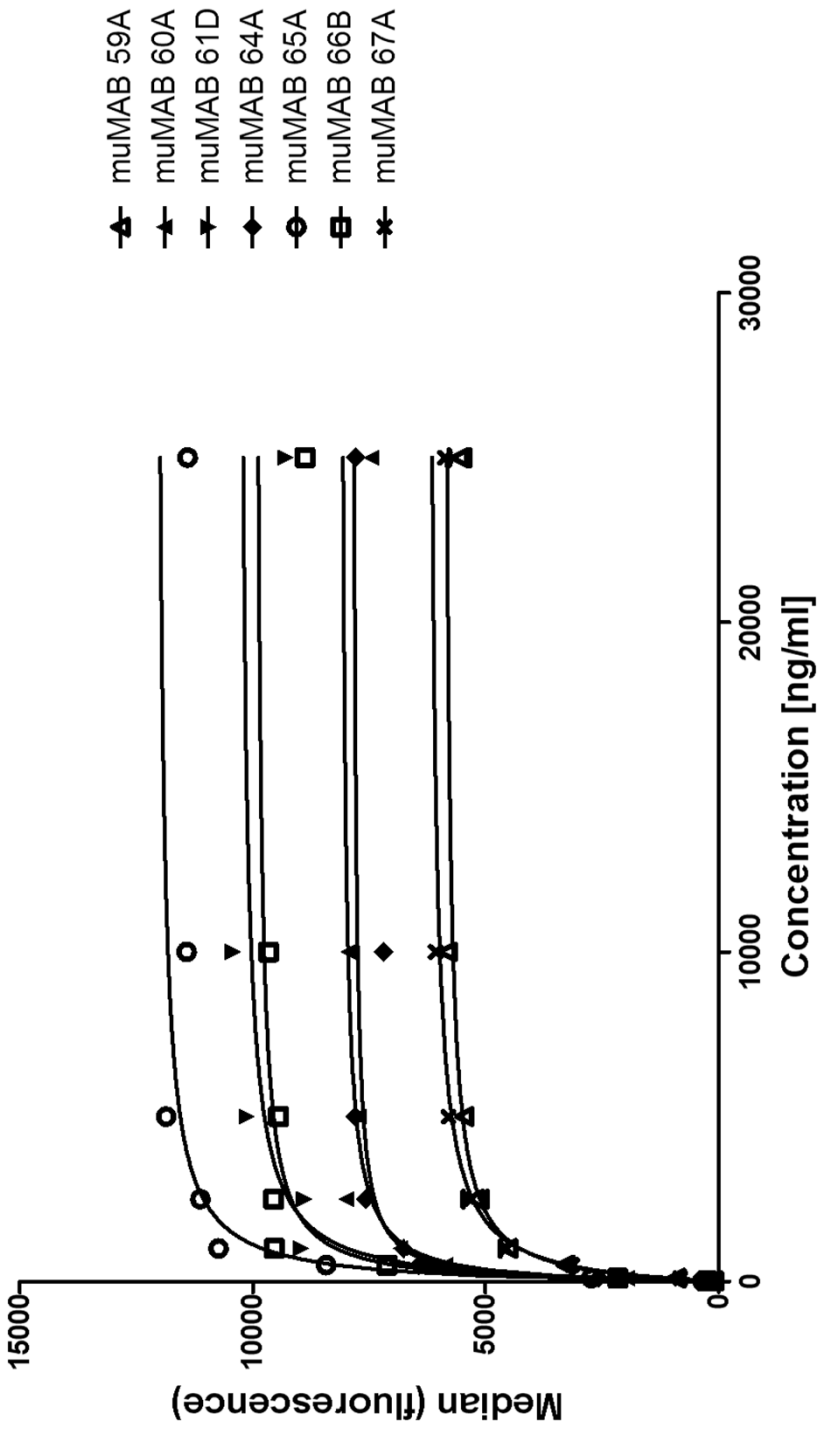

muMAB 59A
muMAB 60A
muMAB 61D
muMAB 64A
muMAB 65A
muMAB 66B
muMAB 67A
Median (fluorescence)
15000
10000
5000
0
0
10000
20000
30000
Concentration [ng/ml]

Fig. 7

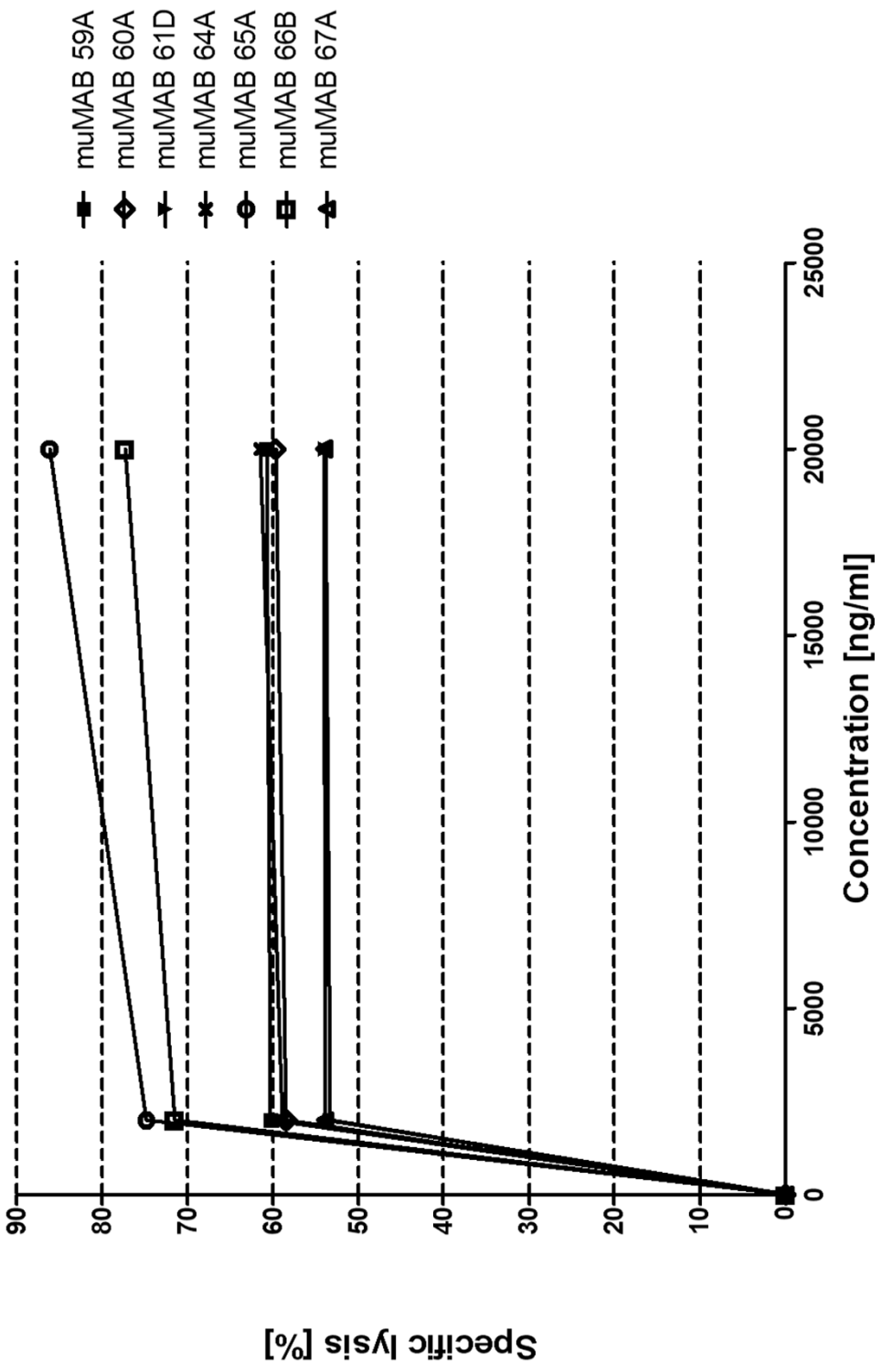
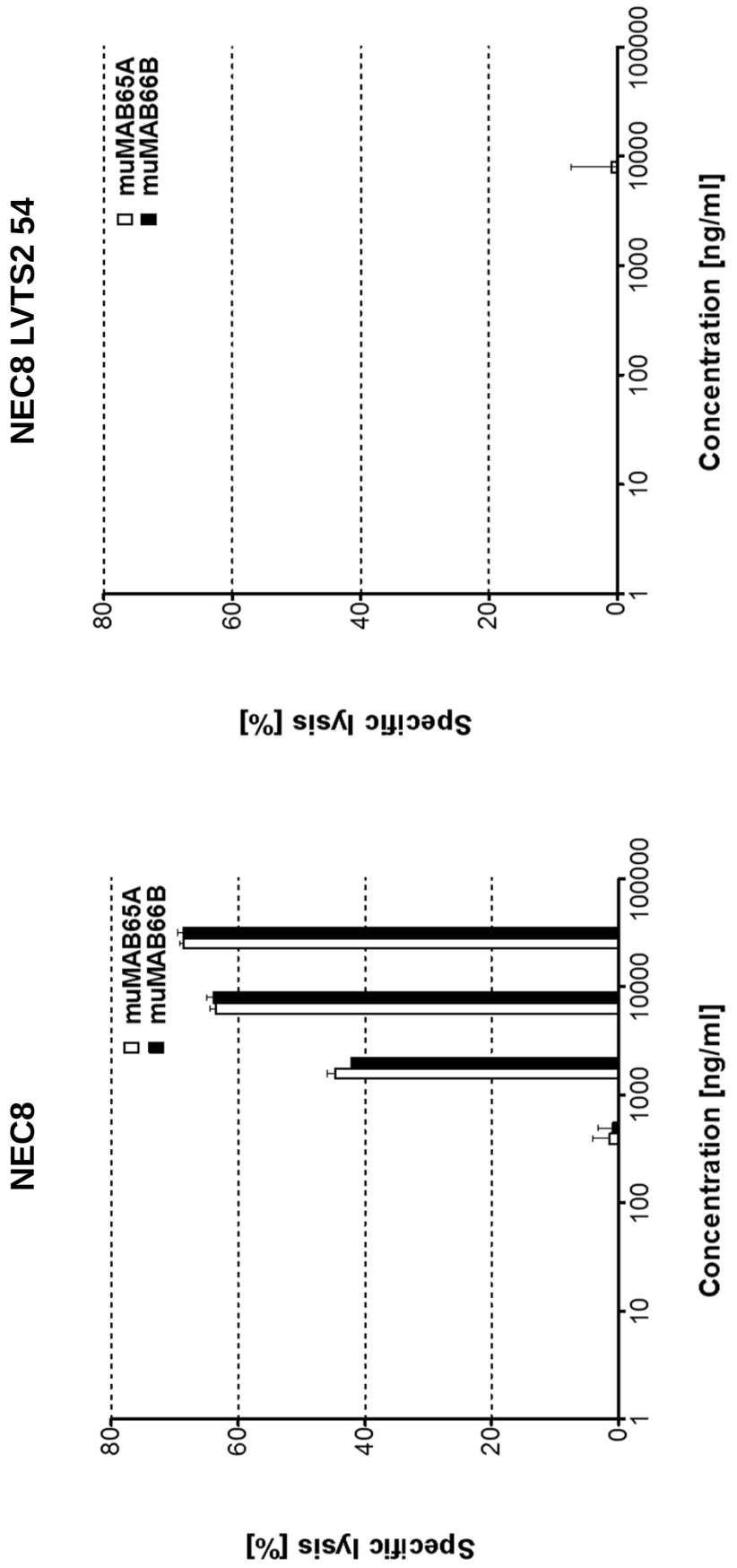

muMAB 59A
muMAB 60A
muMAB 61D
muMAB 64A
muMAB 65A
muMAB 66B
muMAB 67A
Specific lysis [%]
0
10
20
30
40
50
60
70
80
90
0
5000
10000
15000
20000
25000
Concentration [ng/ml]

Fig. 8

Fig. 9



error bars: SEM

Fig. 10

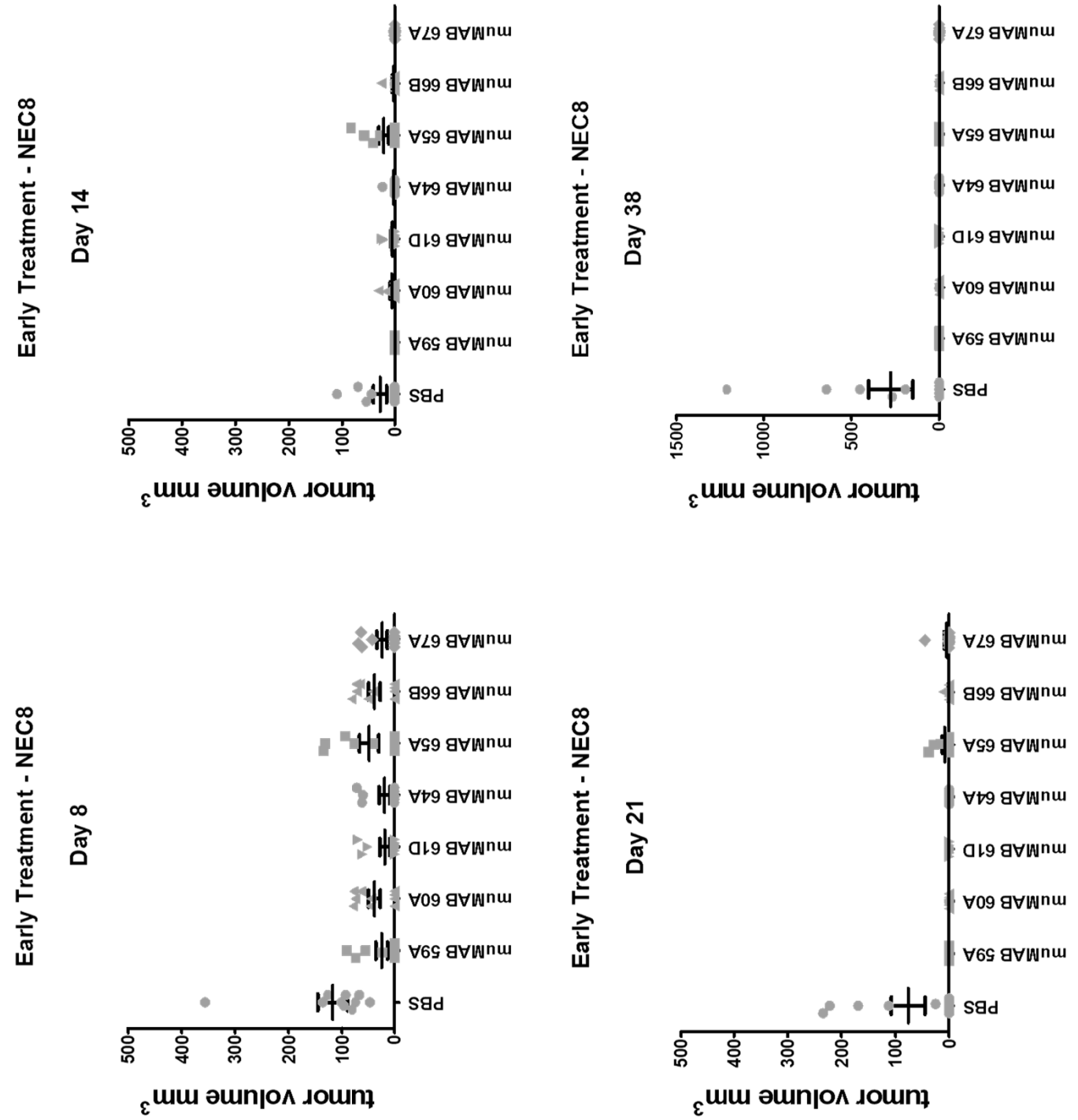
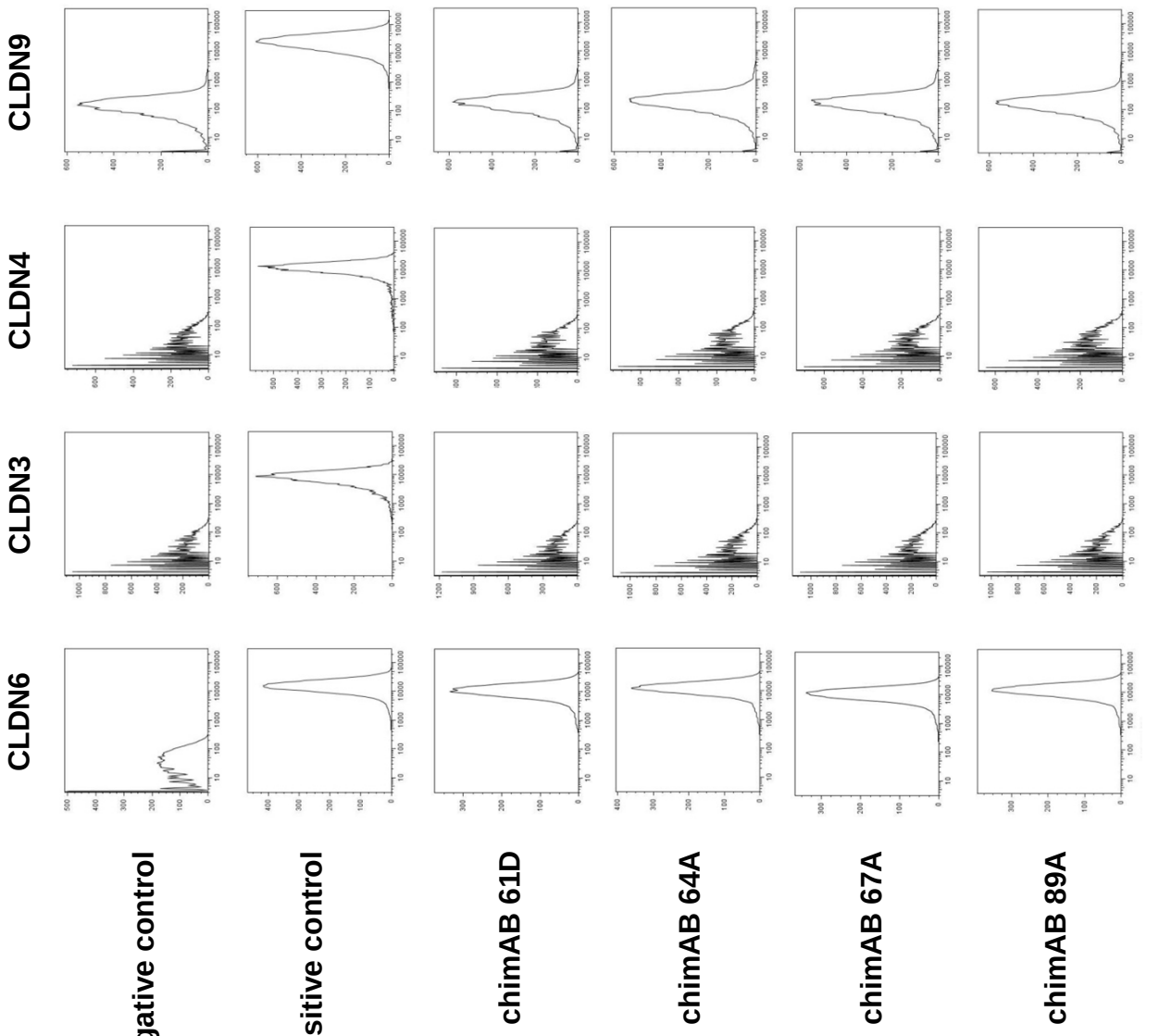

Early Treatment - NEC8
Day 8
tumor volume mm3
0
100
200
300
400
500
PBS
muMAB 59A
muMAB 60A
muMAB 61D
muMAB 64A
muMAB 65A
muMAB 66B
muMAB 67A
Early Treatment - NEC8
Day 14
tumor volume mm3
0
100
200
300
400
500
PBS
muMAB 59A
muMAB 60A
muMAB 61D
muMAB 64A
muMAB 65A
muMAB 66B
muMAB 67A
Early Treatment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


CLDN6
CLDN3
CLDN4
CLDN9
negative control
positive control
chimAB 61D
chimAB 64A
chimAB 67A
chimAB 89A
cell number
APC

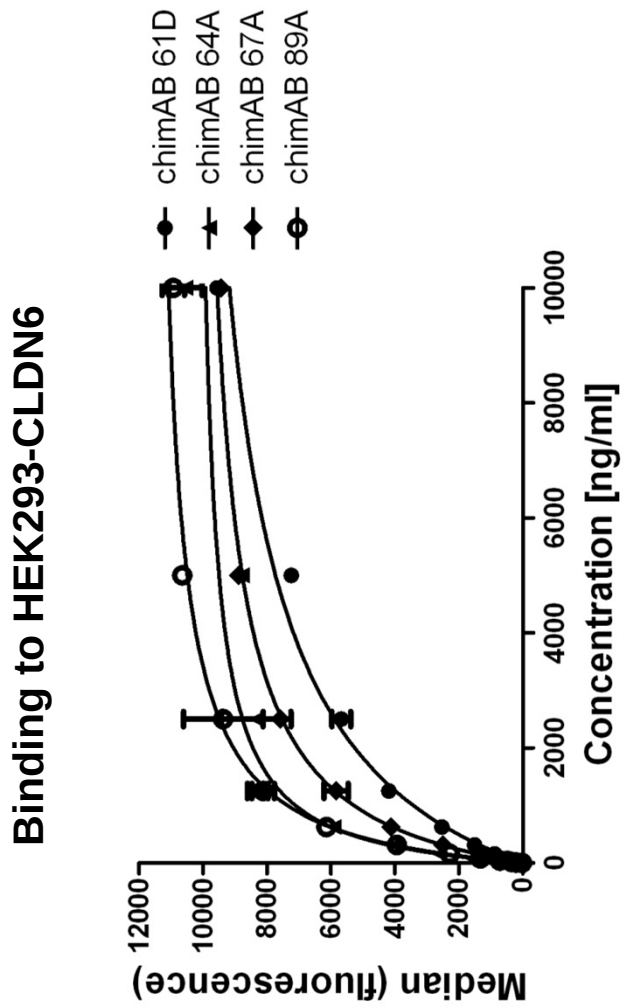

Binding to HEK293-CLDN6
chimAB 61D
chimAB 64A
chimAB 67A
chimAB 89A
Median (fluorescence)
0
2000
4000
6000
8000
10000
12000
0
2000
4000
6000
8000
10000
Concentration [ng/ml]

Fig. 12

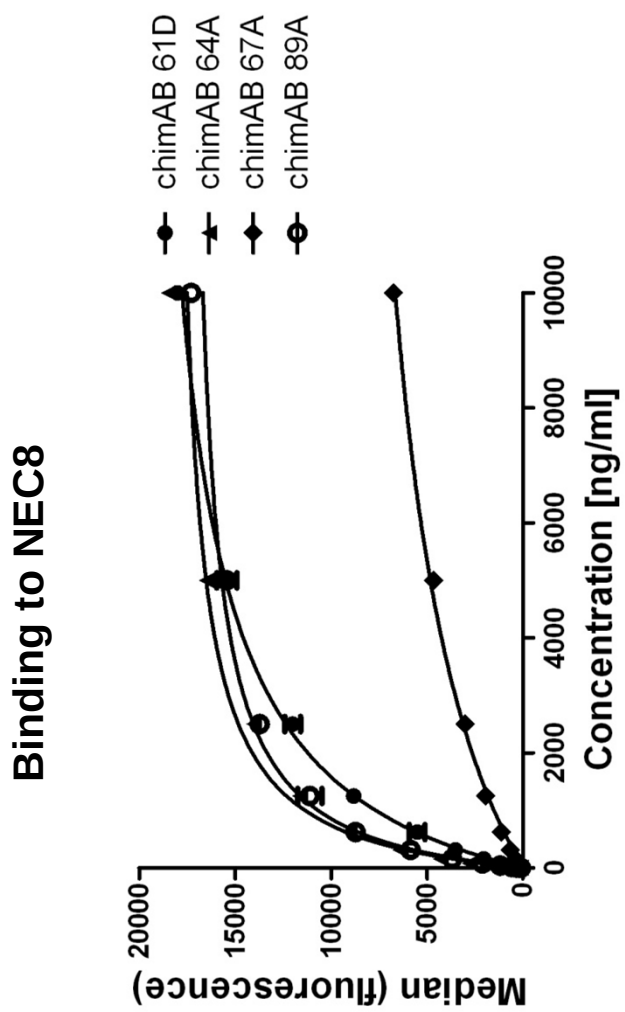

Binding to NEC8
chimAB 61D
chimAB 64A
chimAB 67A
chimAB 89A
Median (fluorescence)
20000
15000
10000
5000
0
0
2000
4000
6000
8000
10000
Concentration [ng/ml]

Fig. 13

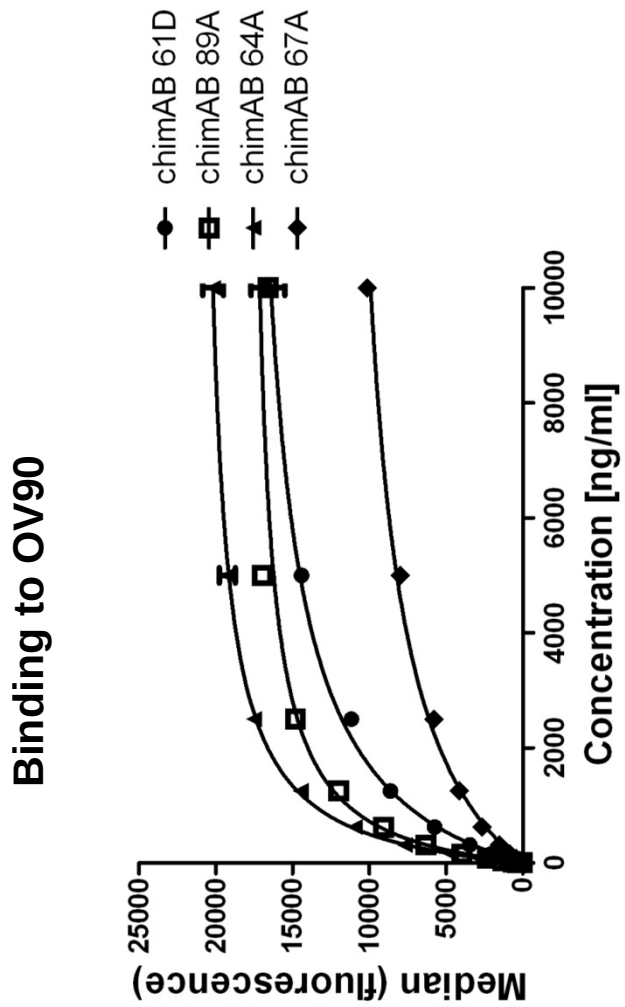

Binding to OV90
chimAB 61D
chimAB 89A
chimAB 64A
chimAB 67A
Median (fluorescence)
25000
20000
15000
10000
5000
0
0
2000
4000
6000
8000
10000
Concentration [ng/ml]

Fig. 14

Fig. 15

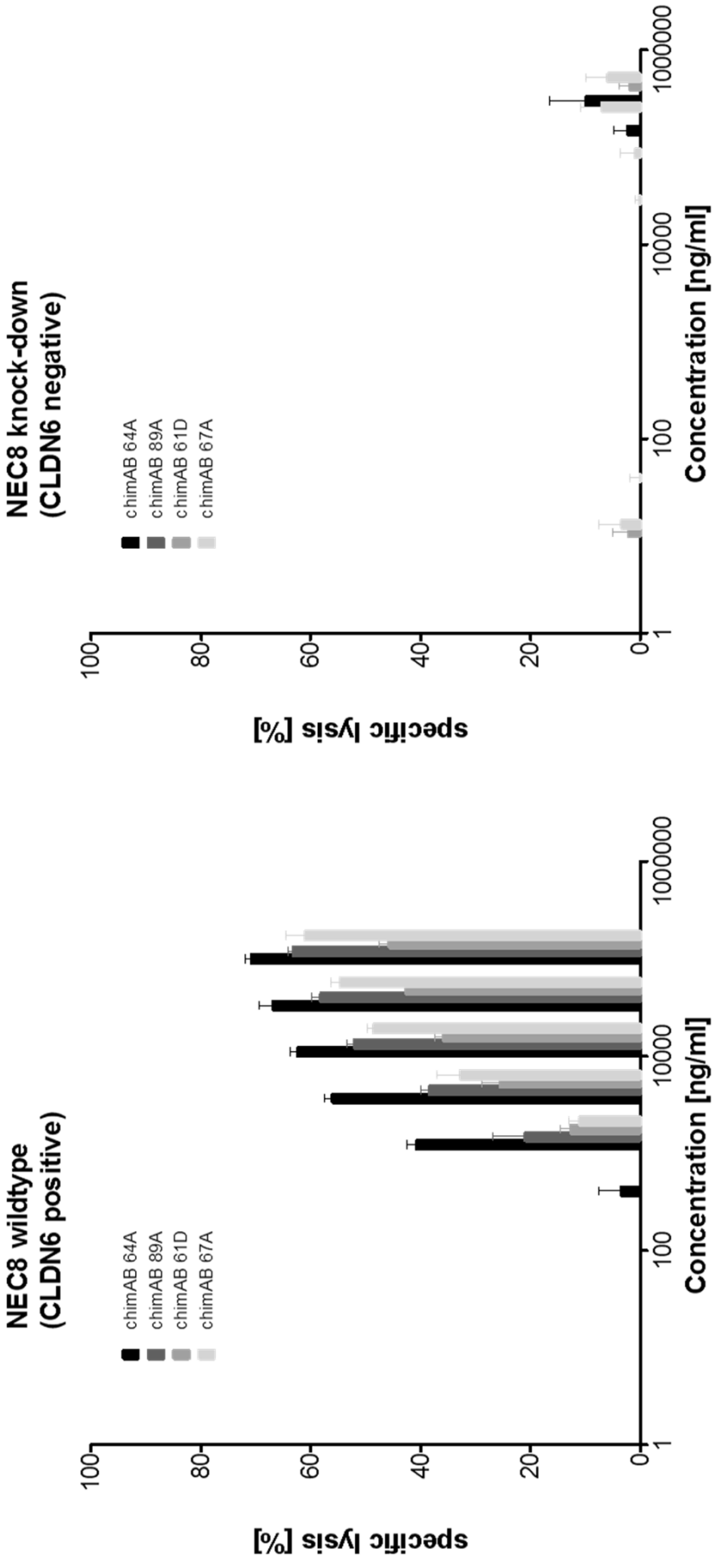

NEC8 wildtype
(CLDN6 positive)
chimAB 64A
chimAB 89A
chimAB 61D
chimAB 67A
specific lysis [%]
0
20
40
60
80
100
1
100
10000
1000000
Concentration [ng/ml]
NEC8 knock-down
(CLDN6 negative)
chimAB 64A
chimAB 89A
chimAB 61D
chimAB 67A
specific lysis [%]
0
20
40
60
80
100
1
100
10000
1000000
Concentration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

Fig. 16

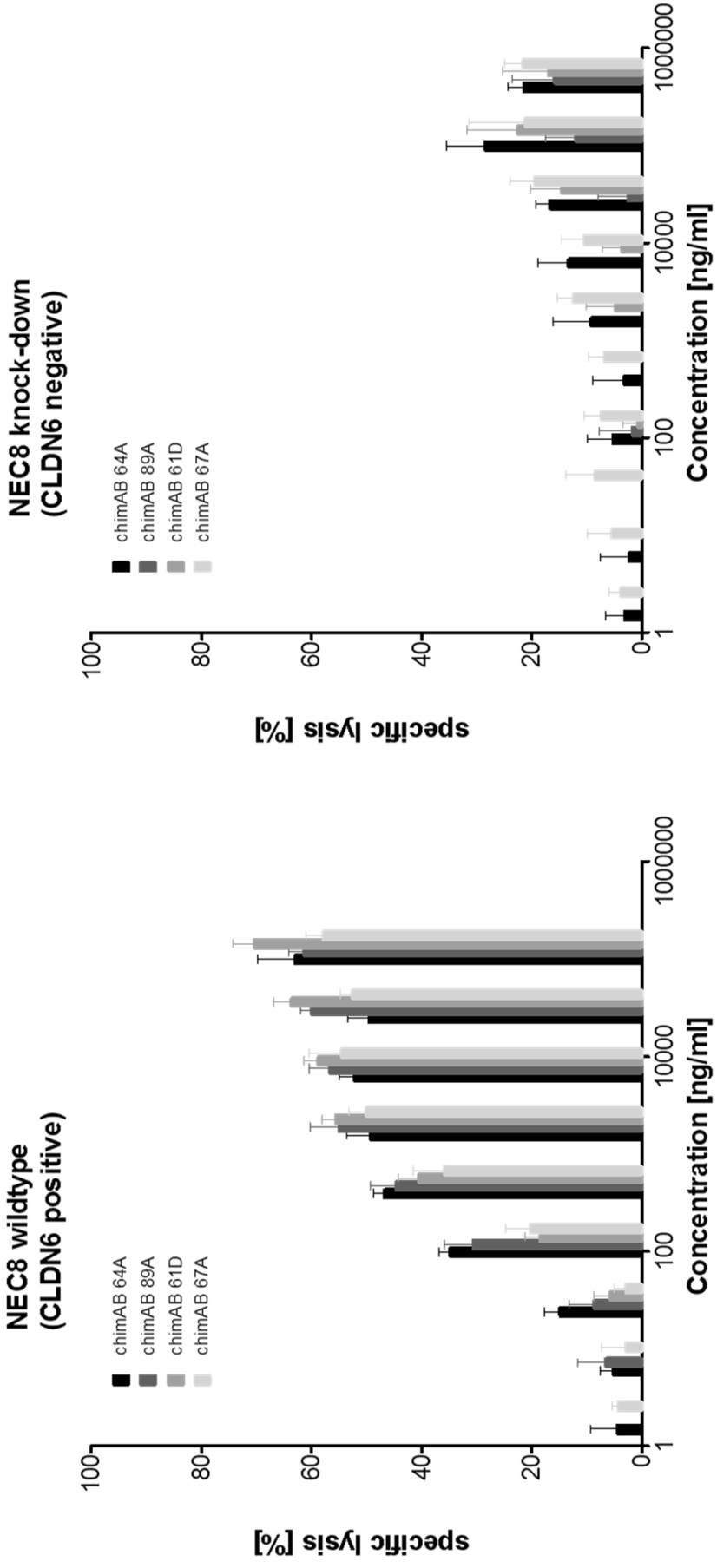

NEC8 wildtype
(CLDN6 positive)
chimAB 64A
chimAB 89A
chimAB 61D
chimAB 67A
specific lysis [%]
0
20
40
60
80
100
1
100
10000
1000000
Concentration [ng/ml]
NEC8 knock-down
(CLDN6 negative)
chimAB 64A
chimAB 89A
chimAB 61D
chimAB 67A
specific lysis [%]
0
20
40
60
80
100
1
100
10000
1000000
Concentration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

Fig. 17

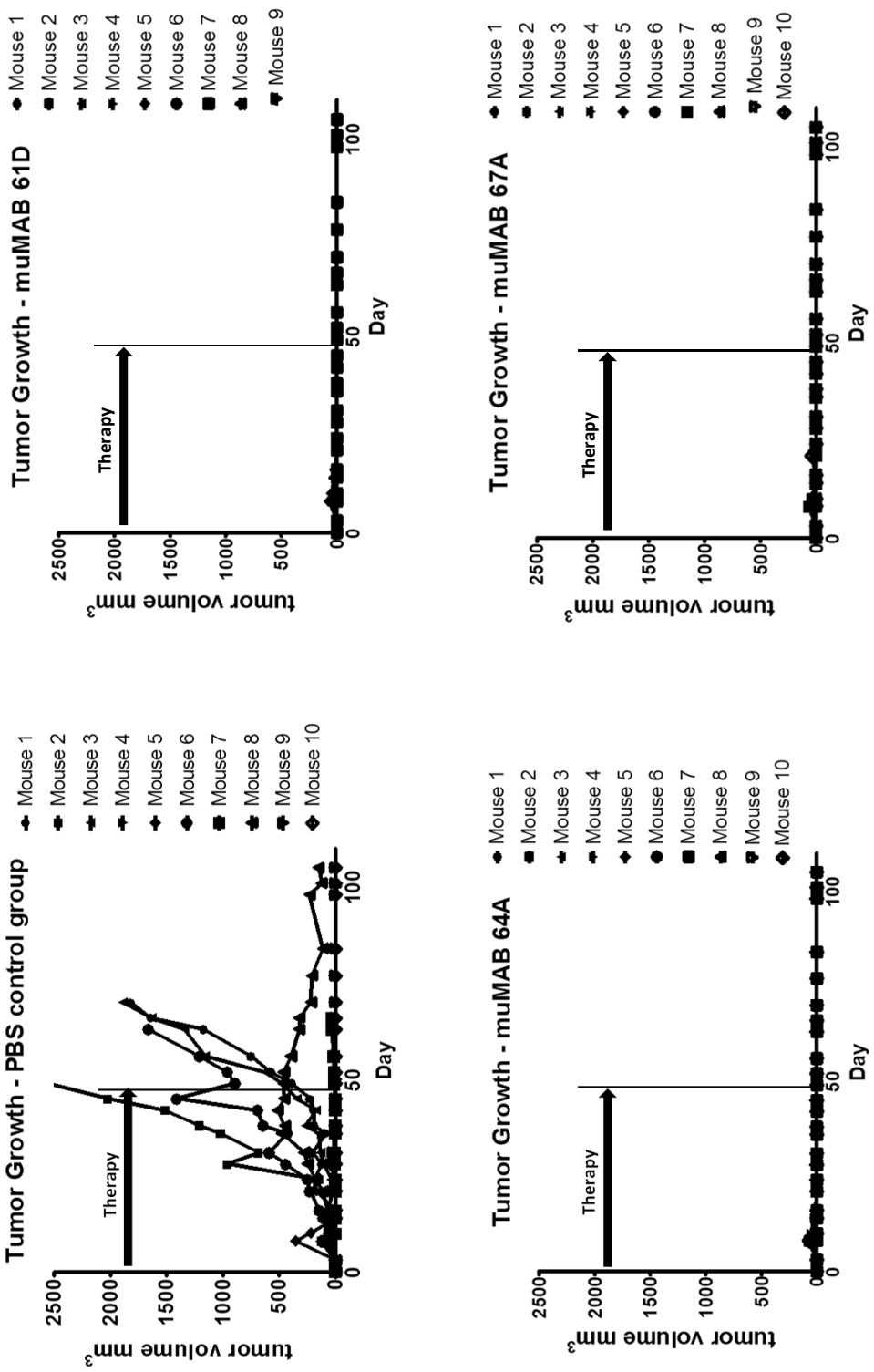

Tumor Growth - PBS control group
Therapy
tumor volume mm³
Day
Mouse 1
Mouse 2
Mouse 3
Mouse 4
Mouse 5
Mouse 6
Mouse 7
Mouse 8
Mouse 9
Mouse 10
Tumor Growth - muMAB 61D
Tumor Growth - muMAB 67A
Tumor Growth - muMAB 64A

Fig. 18

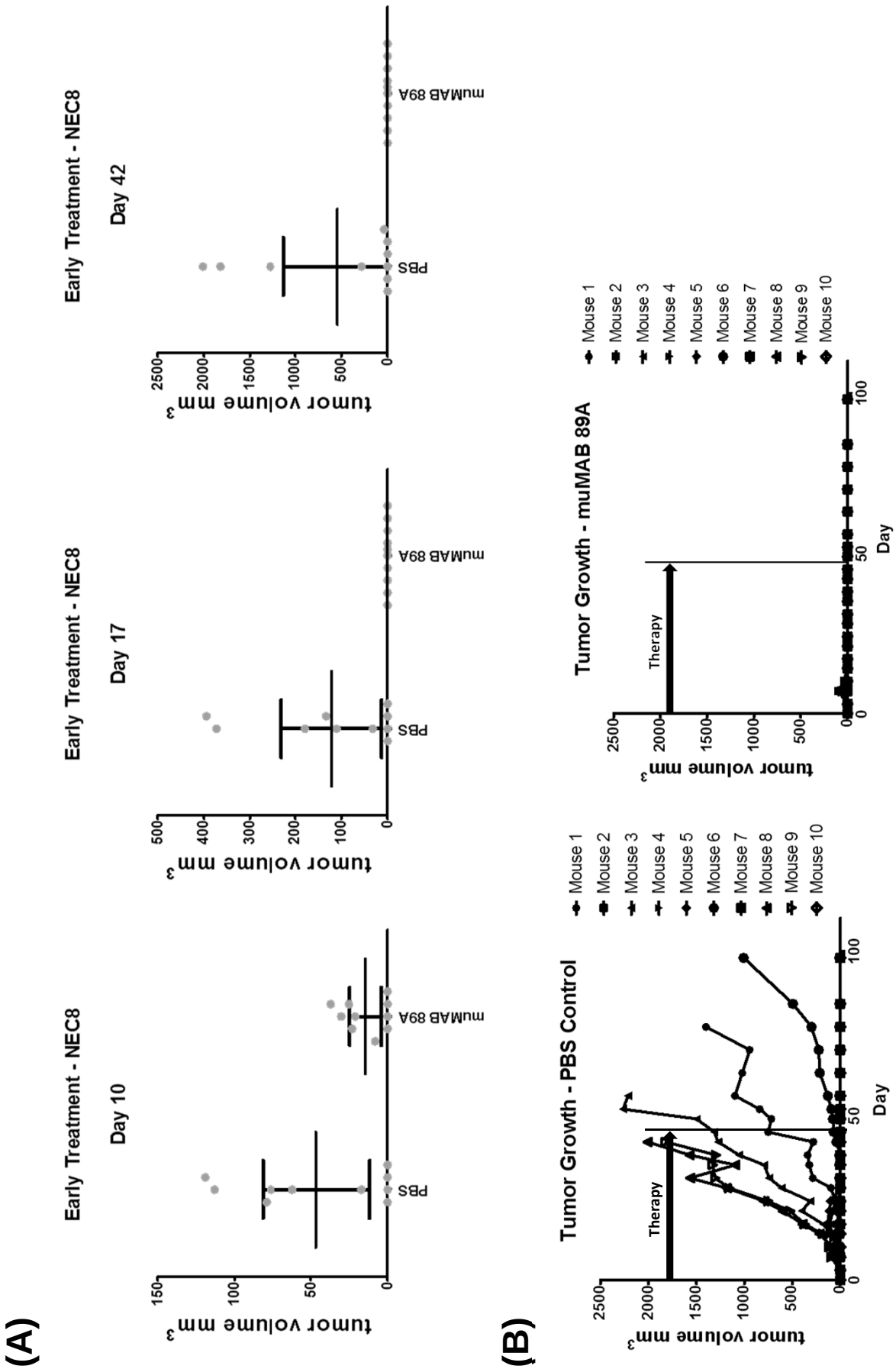

(A)
Early Treatment - NEC8
Day 10
tumor volume mm³
PBS
muMAB 89A
Early Treatment - NEC8
Day 17
tumor volume mm³
PBS
muMAB 89A
Early Treatment - NEC8
Day 42
tumor volume mm³
PBS
muMAB 89A
(B)
Tumor Growth - PBS Control
Therapy
tumor volume mm³
Day
Mouse 1
Mouse 2
Mouse 3
Mouse 4
Mouse 5
Mouse 6
Mouse 7
Mouse 8
Mouse 9
Mouse 10
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
Mouse 9
Mouse 10

Fig. 19

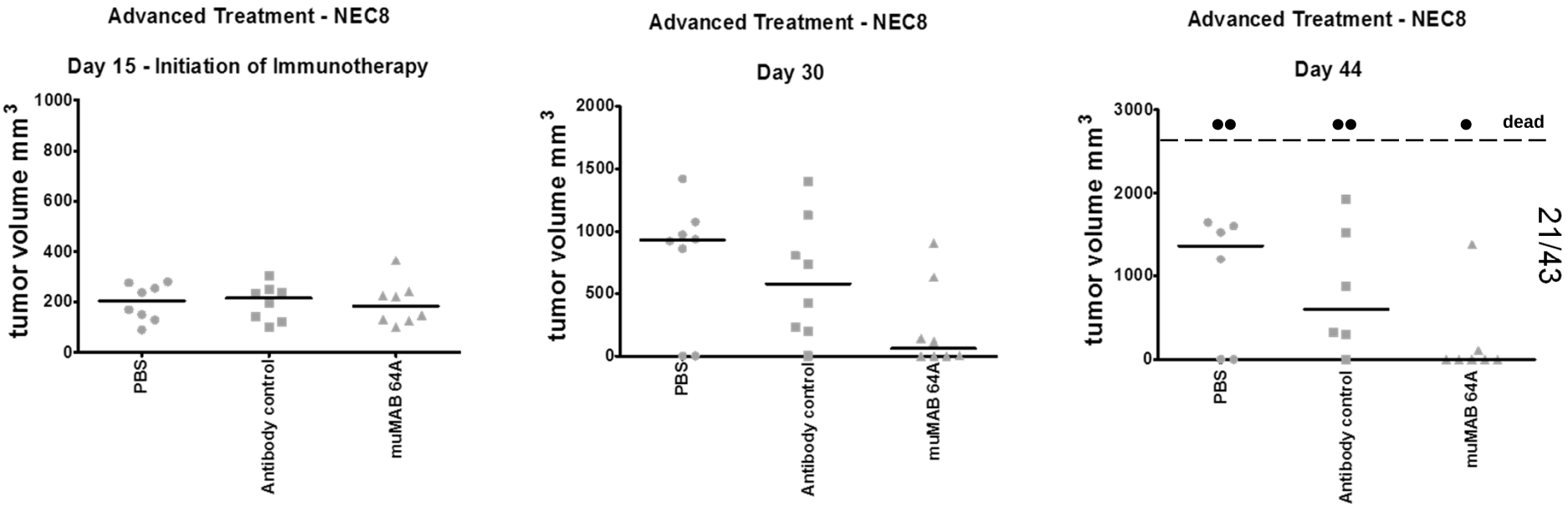
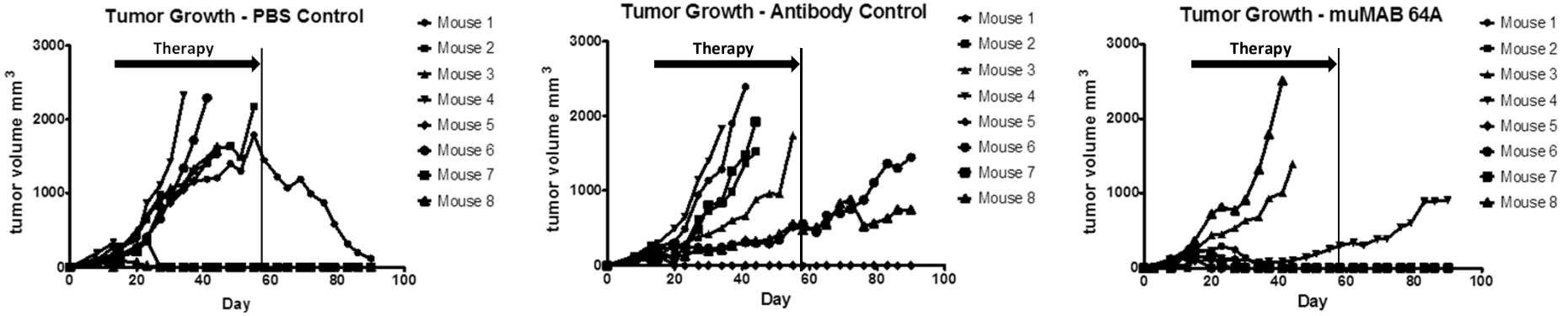

Advanced Treatment - NEC8
Day 15 - Initiation of Immunotherapy
tumor volume mm3
1000
800
600
400
200
0
PBS
Antibody control
muMAB 64A
Advanced Treatment - NEC8
Day 30
tumor volume mm3
2000
1500
1000
500
0
PBS
Antibody control
muMAB 64A
Advanced Treatment - NEC8
Day 44
tumor volume mm3
3000
2000
1000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

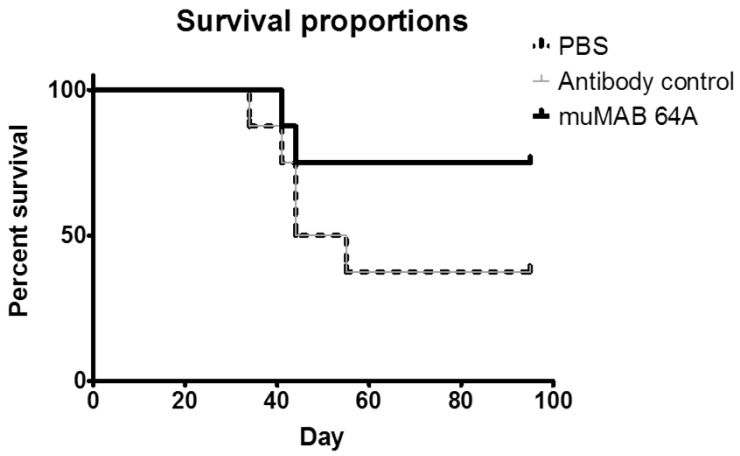

Survival proportions
PBS
Antibody control
muMAB 64A
Percent survival
Day

Fig. 21

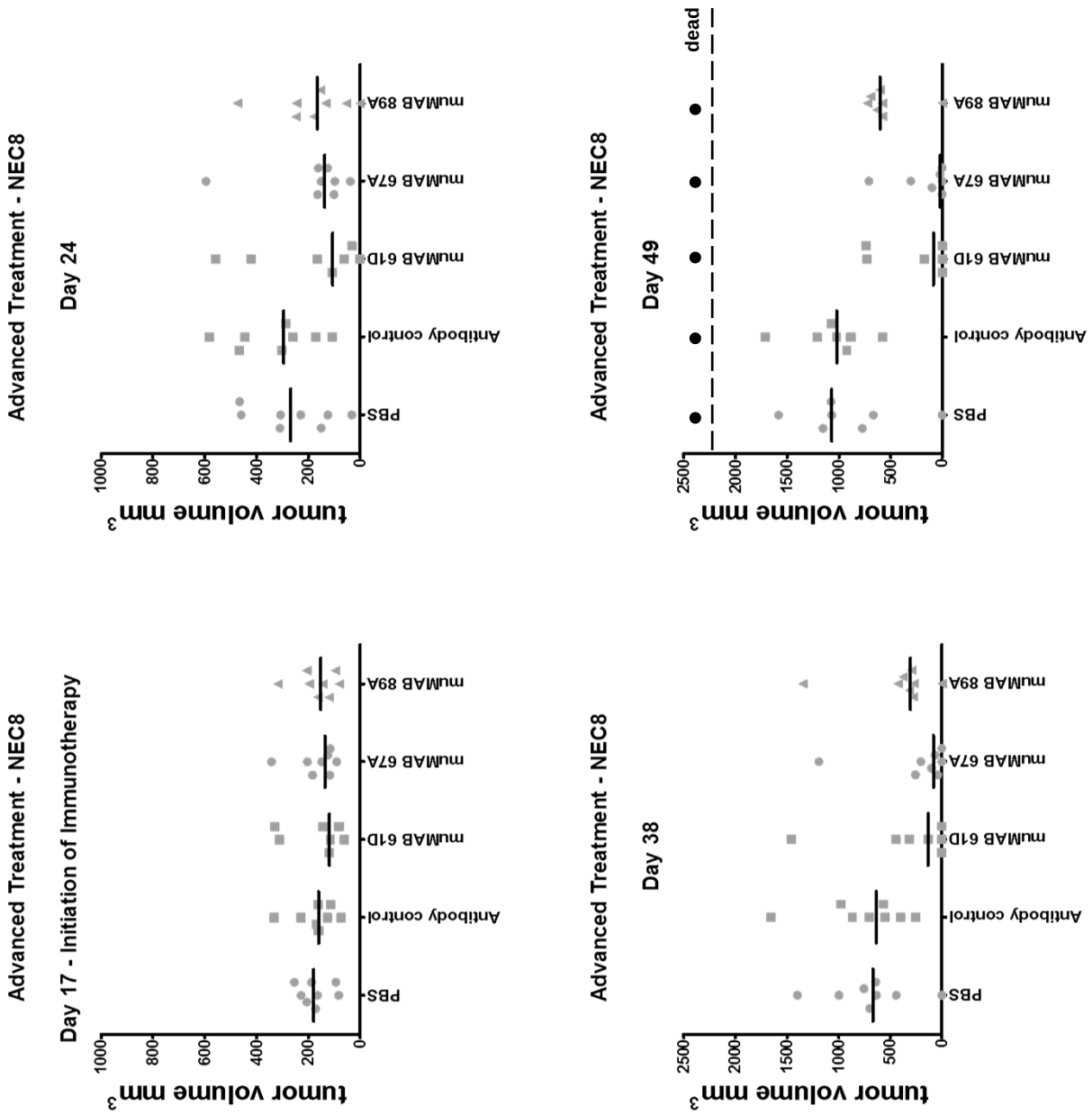
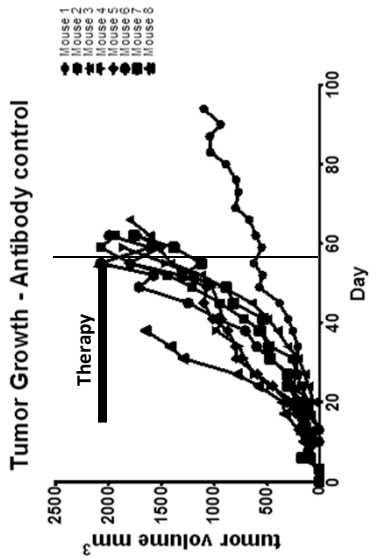
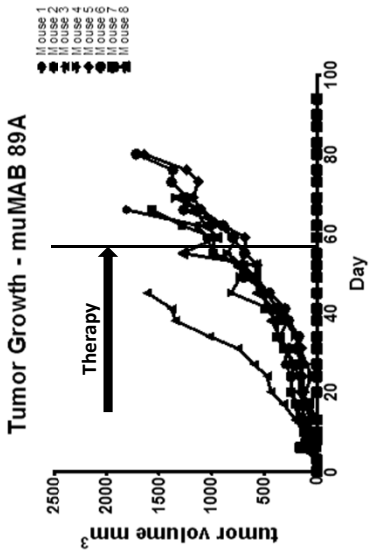
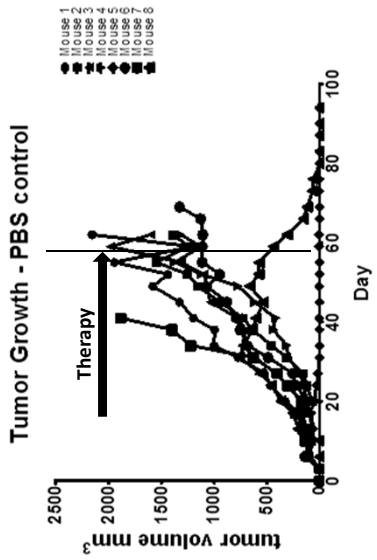

Advanced Treatment - NEC8
Day 17 - Initiation of Immunotherapy
Day 24
Day 38
Day 49
dead
tumor volume mm3
0
200
400
600
800
1000
500
1000
1500
2000
2500
PBS
Antibody control
muMAB 61D
muMAB 67A
muMAB 89A

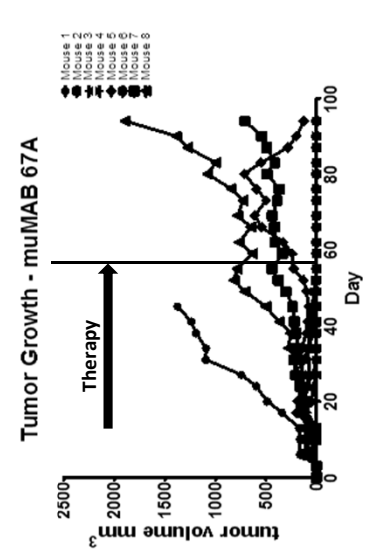
Fig. 22

(A)


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


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

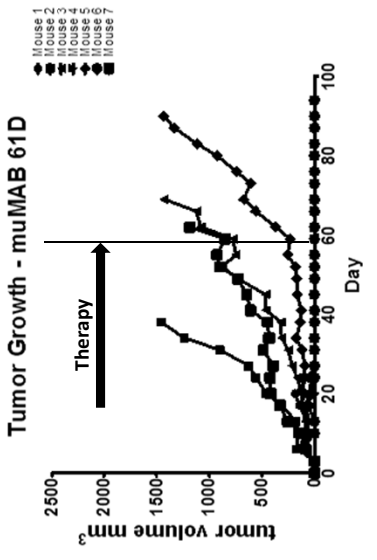

Tumor Growth - muMAB 61D
Therapy
tumor volume mm3
Day
Mouse 1
Mouse 2
Mouse 3
Mouse 4
Mouse 5
Mouse 6
Mouse 7

Fig. 22

(B)

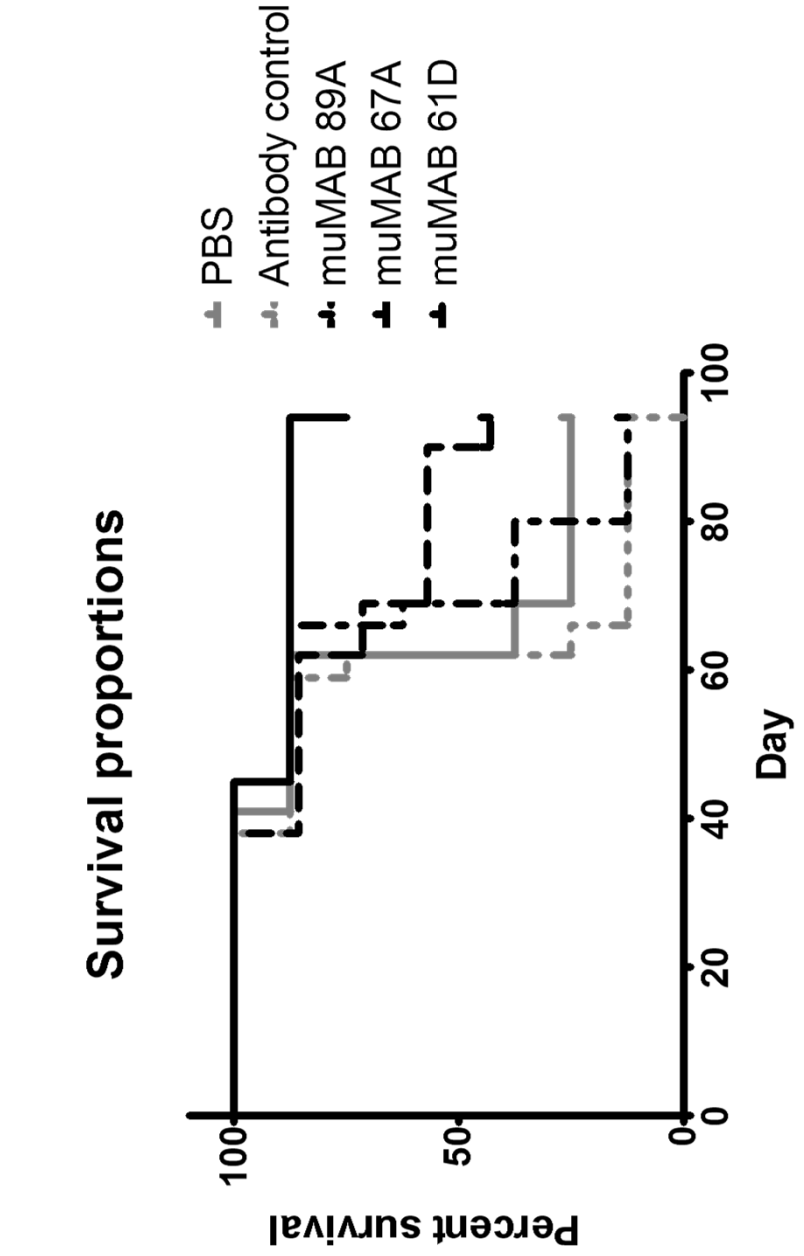

Survival proportions
PBS
Antibody control
muMAB 89A
muMAB 67A
muMAB 61D
Percent survival
100
50
0
0
20
40
60
80
100
Day

Fig. 23

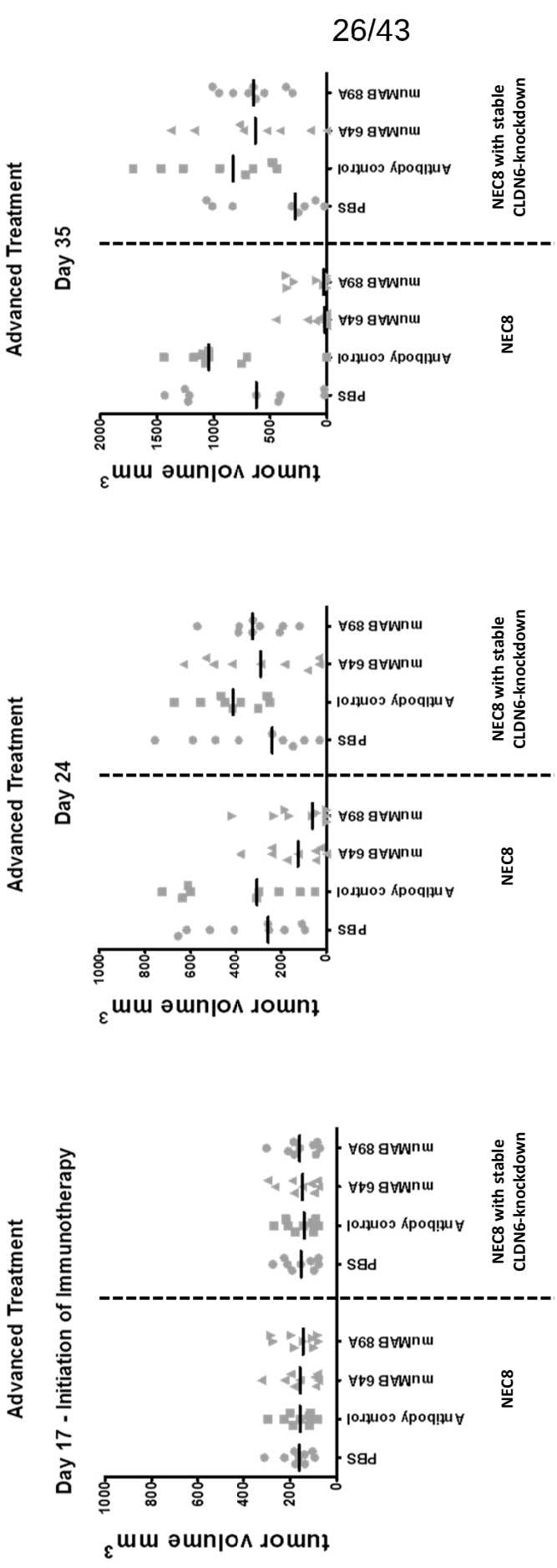

Advanced Treatment
Day 17 - Initiation of Immunotherapy
Day 24
Day 35
tumor volume mm3
0
200
400
600
800
1000
500
1000
1500
2000
PBS
Antibody control
muMAB 64A
muMAB 89A
NEC8
NEC8 with stable CLDN6-knockdown

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
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
GT512chimAB 61D		X		X																			X	X	X			X
GT512chimAB 64A		X		X																			X	X	X			X
GT512chimAB 67A		X		X																			X	X	X			X
GT512chimAB 89A		X		X																			X	X	X			X
R&D		X		X																			X	X	X			X

	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	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																	
GT512chimAB 64A										X																	
GT512chimAB 67A										X																	
GT512chimAB 89A										X																	
R&D										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
no influence on antibody binding
contributes to antibody binding
essential for antibody binding

Fig. 25

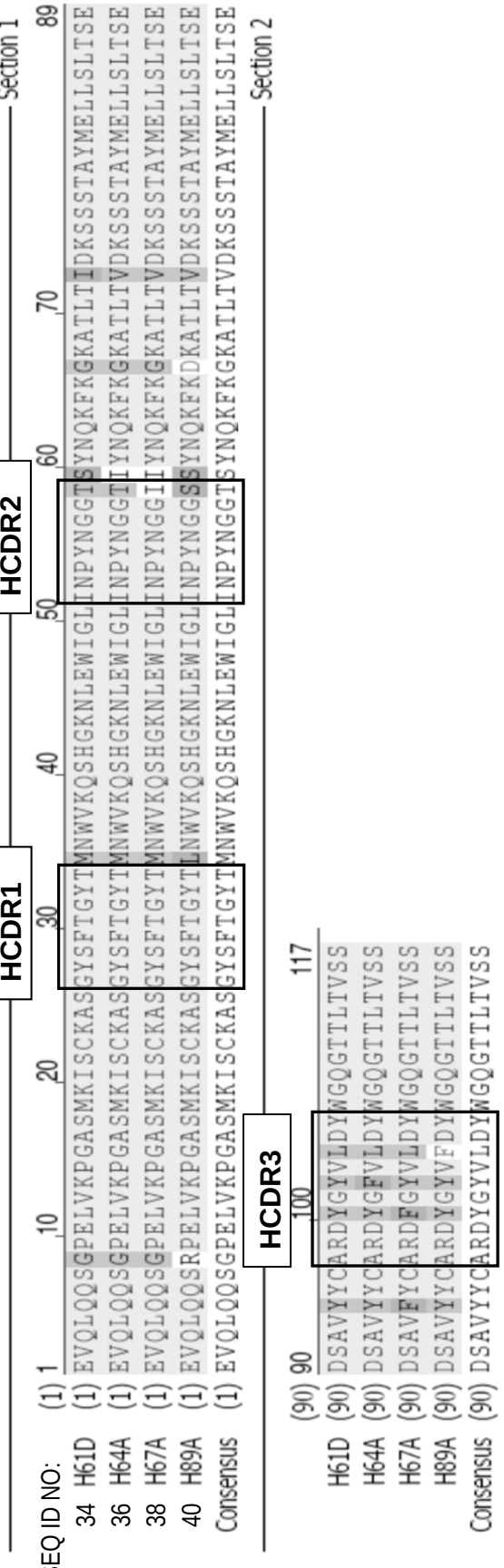

Section 1
Section 2
HCDR1
HCDR2
HCDR3
SEQ ID NO:
34 H61D
36 H64A
38 H67A
40 H89A
Consensus
(1) EVQLQQSGPELVKPGASMKISCKASGYSFTGYTMNWVKQSHGKNLEWIGLINPYNGGTSYNQKFKGKATLTIDKSSSTAYMELLSLTSE
(1) EVQLQQSGPELVKPGASMKISCKASGYSFTGYTMNWVKQSHGKNLEWIGLINPYNGGTIYNQKFKGKATLTVDKSSSTAYMELLSLTSE
(1) EVQLQQSGPELVKPGASMKISCKASGYSFTGYTMNWVKQSHGKNLEWIGLINPYNGGIIYNQKFKGKATLTVDKSSSTAYMELLSLTSE
(1) EVQLQQSRPELVKPGASMKISCKASGYSFTGYTLNWVKQSHGKNLEWIGLINPYNGGSSYNQKFKDKATLTVDKSSSTAYMELLSLTSE
(1) EVQLQQSGPELVKPGASMKISCKASGYSFTGYTMNWVKQSHGKNLEWIGLINPYNGGTSYNQKFKGKATLTVDKSSSTAYMELLSLTSE
(90) DSAVYYCARDYGYVLDYWGQGTTLTVSS
(90) DSAVYYCARDYGFVLDYWGQGTTLTVSS
(90) DSAVFYCARDFGYVLDYWGQGTTLTVSS
(90) DSAVYYCARDYGYVFDYWGQGTTLTVSS
(90) DSAVYYCARDYGYVLDYWGQGTTLTVSS

Fig. 26

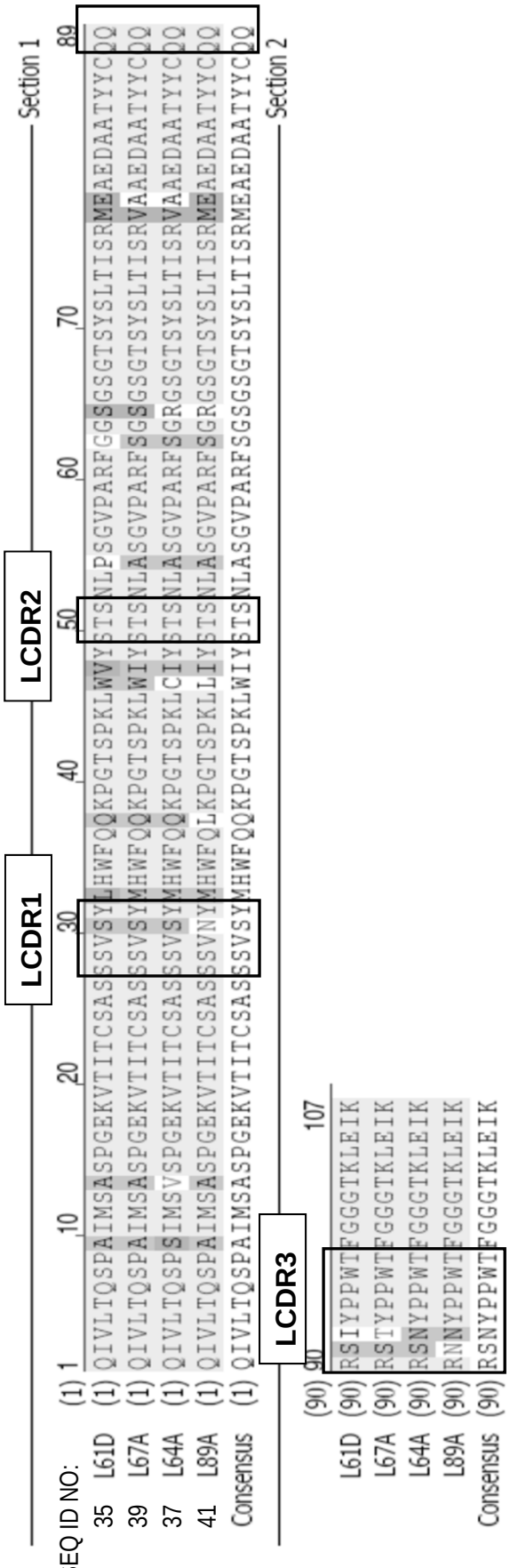
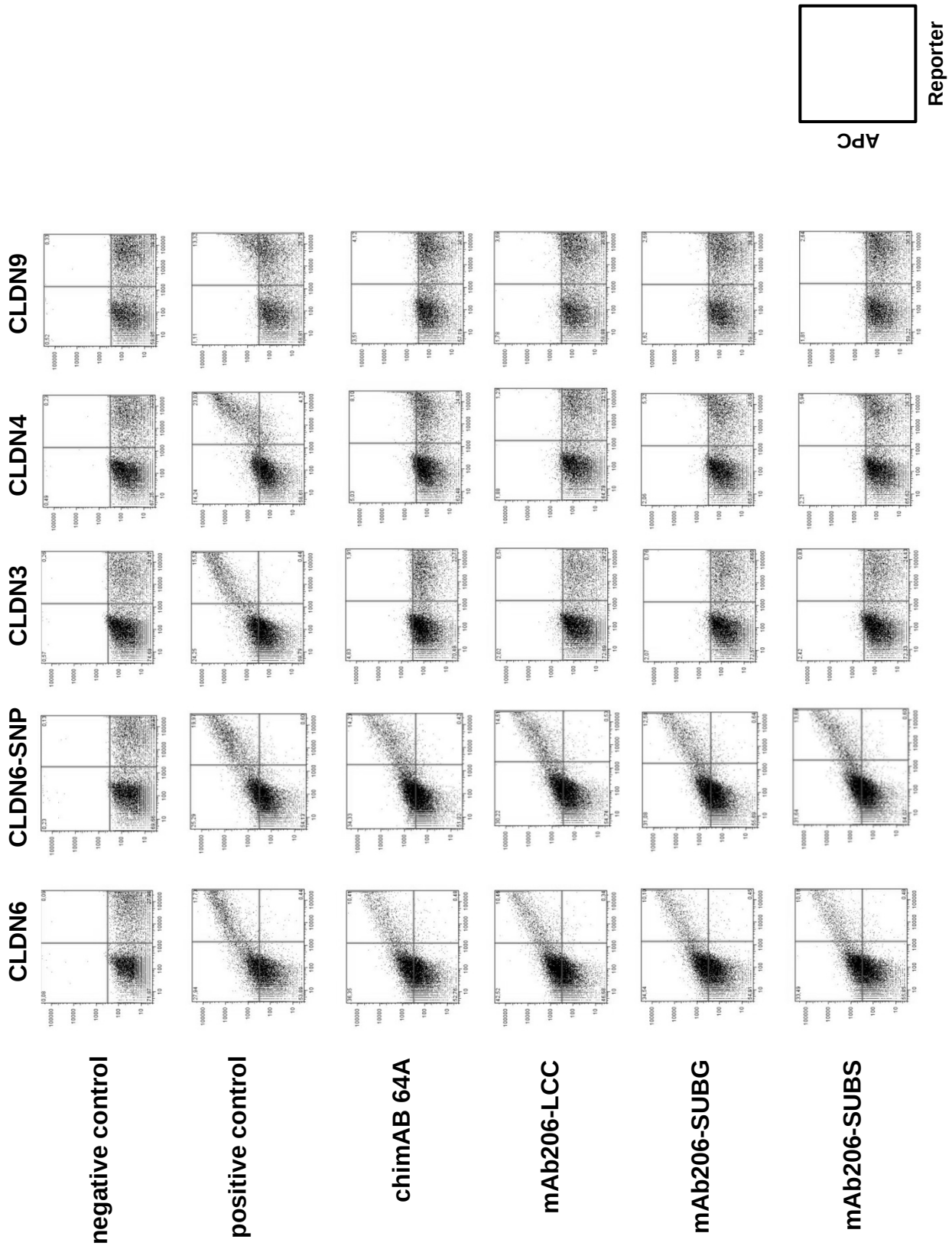

Section 1
Section 2
LCDR1
LCDR2
LCDR3
SEQ ID NO:
35 L61D
39 L67A
37 L64A
41 L89A
Consensus
(1) QIVLTQSPAIMSASPGEKVTITCSASSSVSYMHWFQQKPGTSPKLWIYSTSNLASGVPARFSGSGSGTSYSLTISRMEAEDAATYYCQQ 89
(90) RSIYPPWTFGGGTKLEIK 107
(90) RSTYPPWTFGGGTKLEIK
(90) RSNYPPWTFGGGTKLEIK
(90) RNNYPPWTFGGGTKLEIK
(90) RSNYPPWTFGGGTKLEIK

Fig. 27


CLDN6
CLDN6-SNP
CLDN3
CLDN4
CLDN9
negative control
positive control
chimAB 64A
mAb206-LCC
mAb206-SUBG
mAb206-SUBS
APC
Reporter

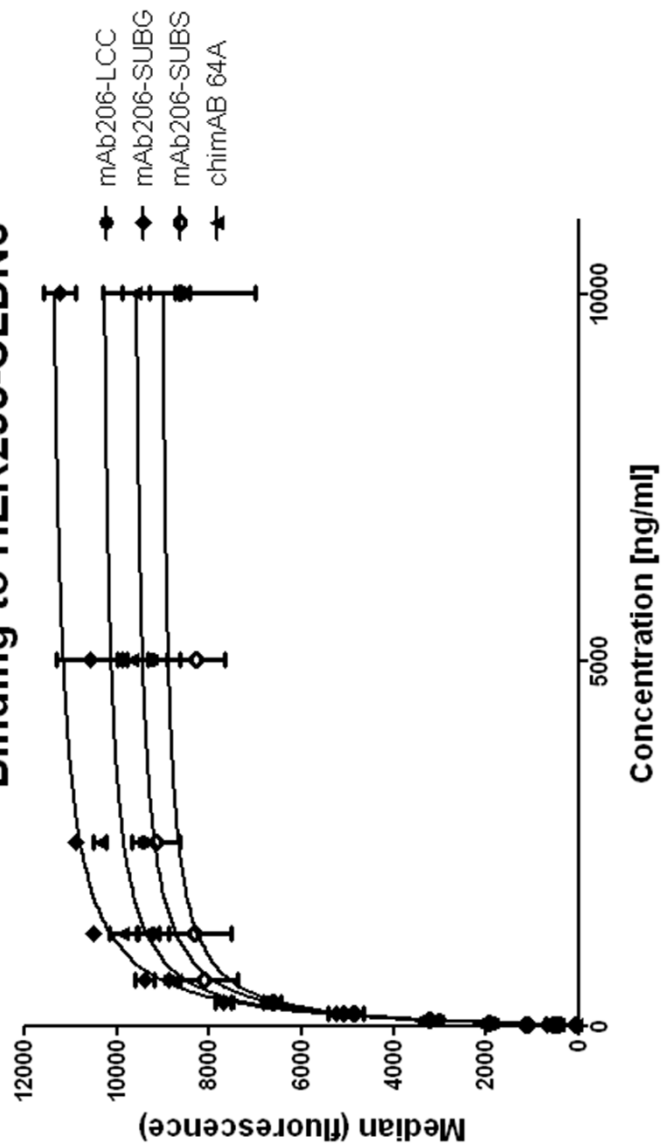

Binding to HEK293-CLDN6
mAb206-LCC
mAb206-SUBG
mAb206-SUBS
chimAB 64A
Median (fluorescence)
12000
10000
8000
6000
4000
2000
0
0
5000
10000
Concentration [ng/ml]

Fig. 28

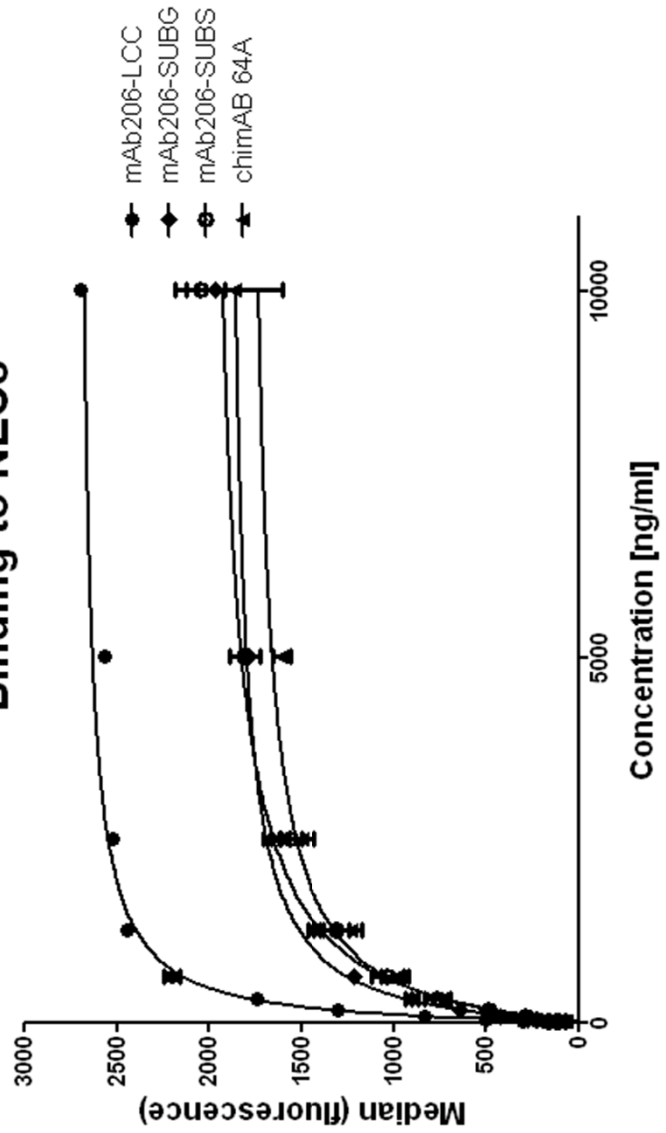

Binding to NEC8
mAb206-LCC
mAb206-SUBG
mAb206-SUBS
chimAB 64A
Median (fluorescence)
0
500
1000
1500
2000
2500
3000
0
5000
10000
Concentration [ng/ml]

Fig. 29

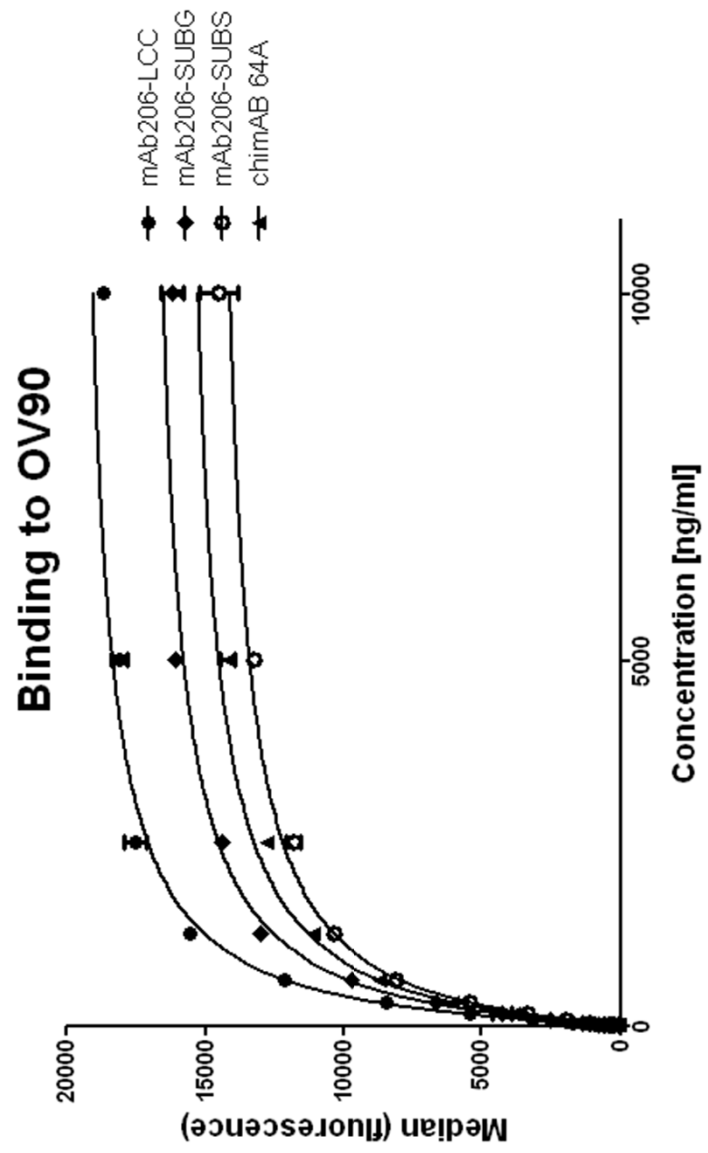
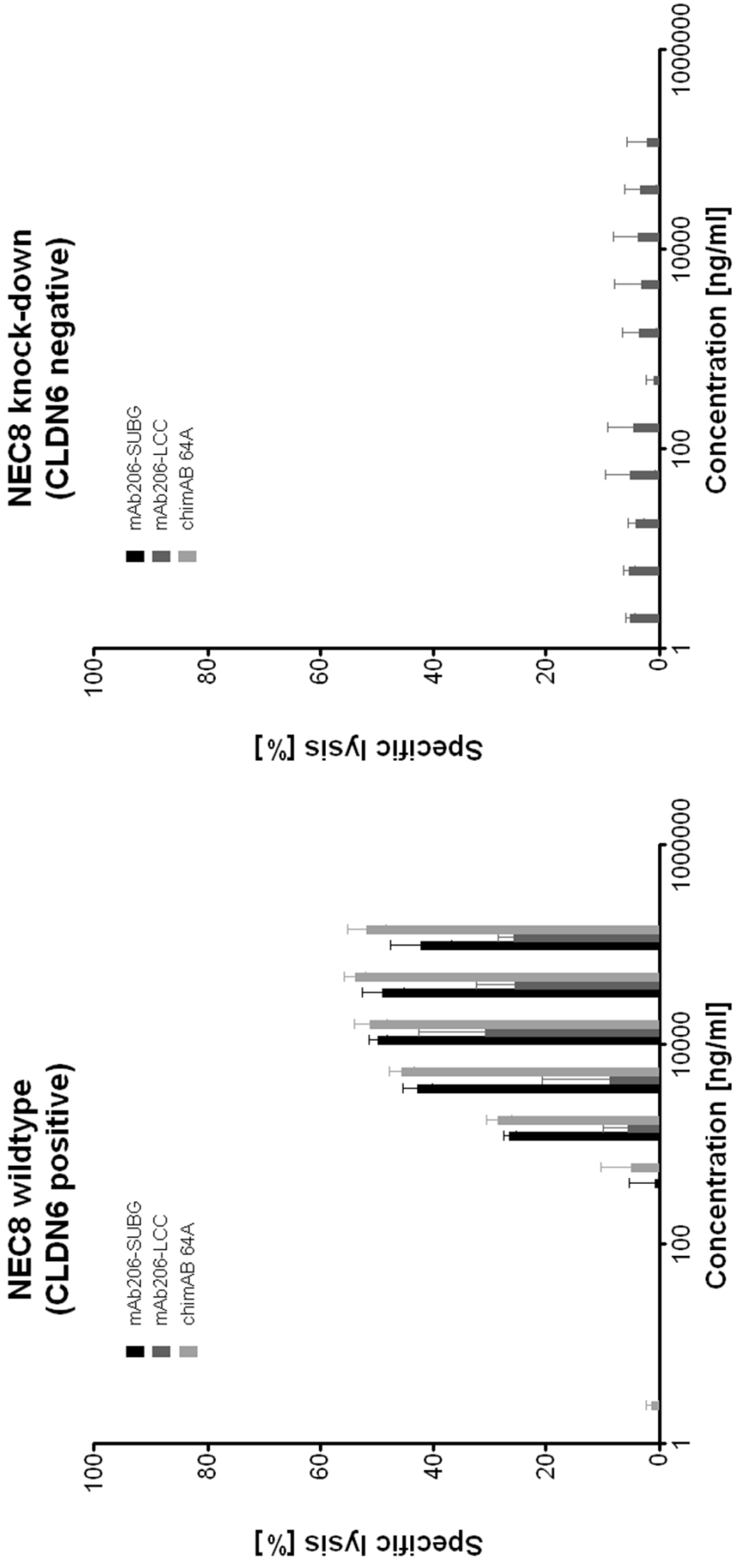

Binding to OV90
mAb206-LCC
mAb206-SUBG
mAb206-SUBS
chimAB 64A
Median (fluorescence)
20000
15000
10000
5000
0
0
5000
10000
Concentration [ng/ml]

Fig. 30

Fig. 31a


NEC8 wildtype
(CLDN6 positive)
mAb206-SUBG
mAb206-LCC
chimAB 64A
Specific lysis [%]
0
20
40
60
80
100
1
100
10000
1000000
Concentration [ng/ml]
NEC8 knock-down
(CLDN6 negative)
mAb206-SUBG
mAb206-LCC
chimAB 64A
Specific lysis [%]
0
20
40
60
80
100
1
100
10000
1000000
Concentration [ng/ml]

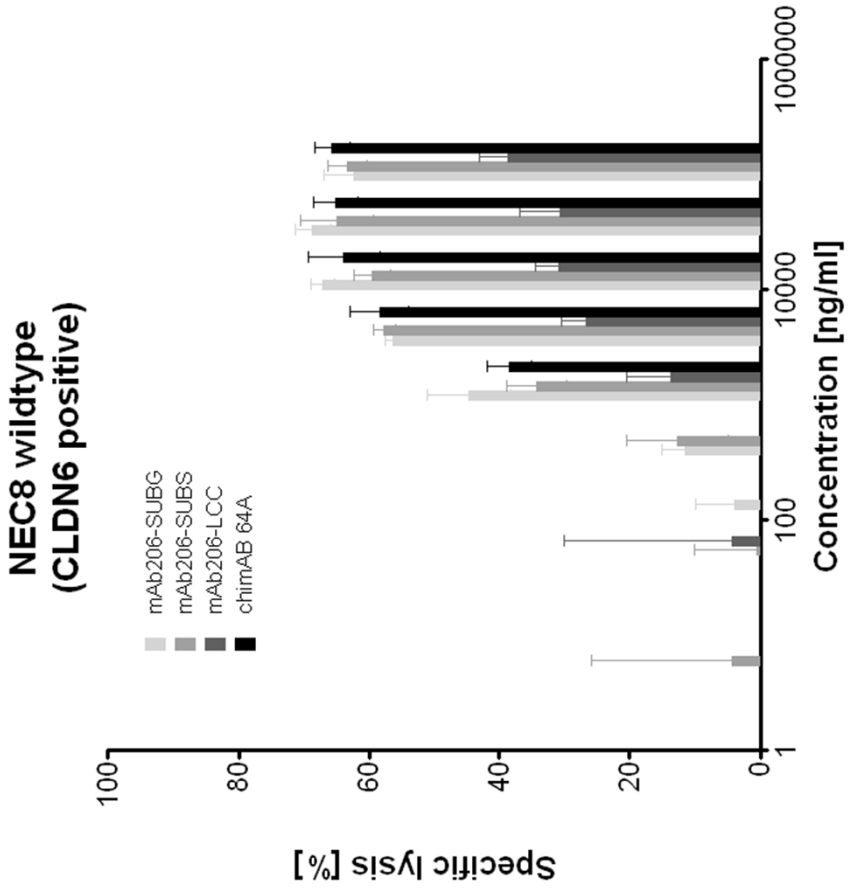

NEC8 wildtype
(CLDN6 positive)
mAb206-SUBG
mAb206-SUBS
mAb206-LCC
chimAB 64A
Specific lysis [%]
0
20
40
60
80
100
1
100
10000
1000000
Concentration [ng/ml]

Fig. 31b

Fig. 32a

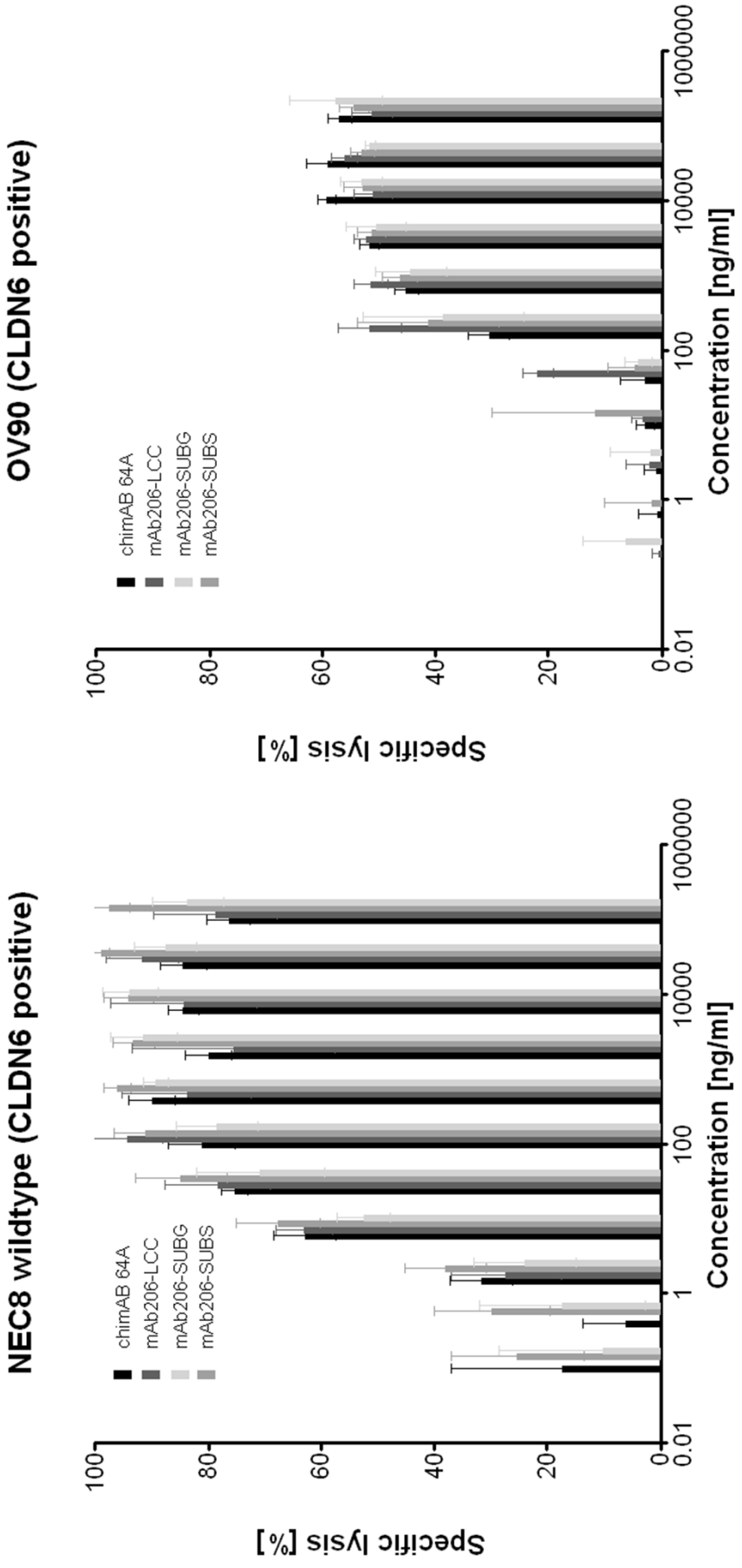

NEC8 wildtype (CLDN6 positive)
OV90 (CLDN6 positive)
chimAB 64A
mAb206-LCC
mAb206-SUBG
mAb206-SUBS
Specific lysis [%]
Concentration [ng/ml]
0
20
40
60
80
100
0.01
1
100
10000
1000000

Fig. 32b

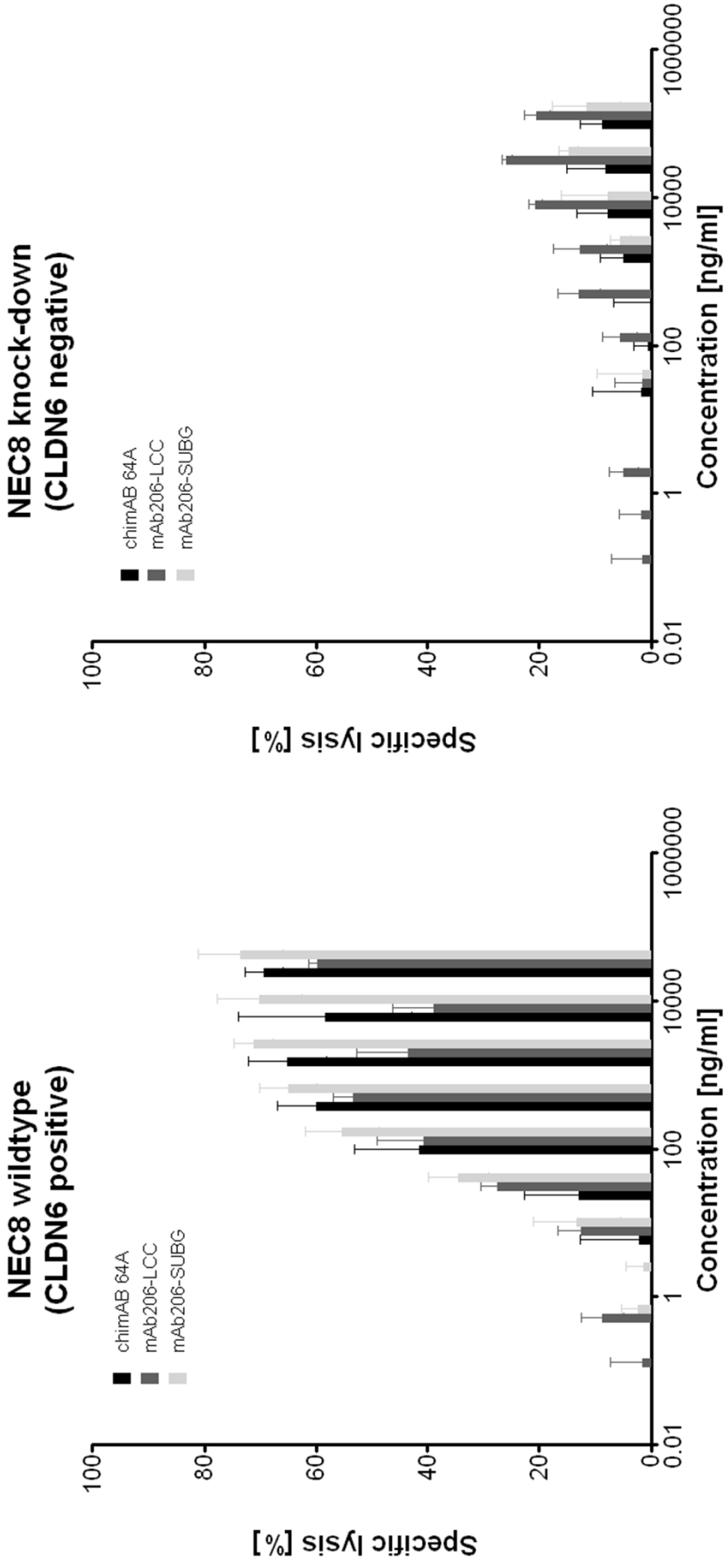

NEC8 wildtype
(CLDN6 positive)
chimAB 64A
mAb206-LCC
mAb206-SUBG
Specific lysis [%]
Concentration [ng/ml]
NEC8 knock-down
(CLDN6 negative)
chimAB 64A
mAb206-LCC
mAb206-SUBG
Specific lysis [%]
Concentration [ng/ml]

Fig. 33

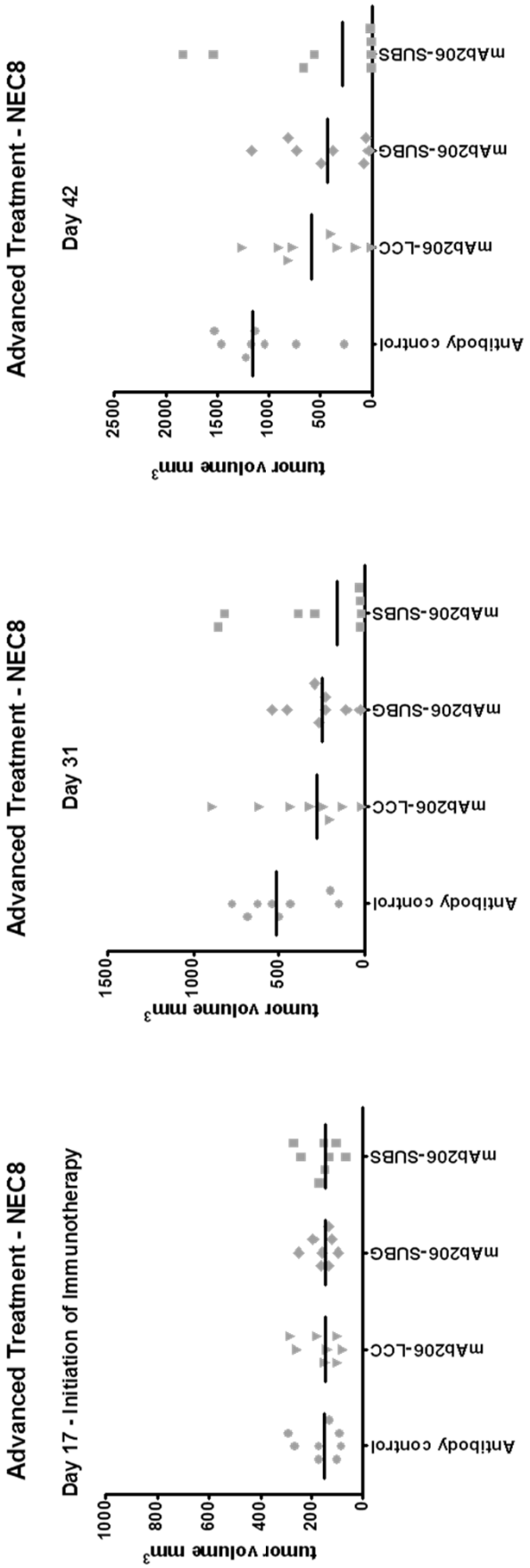
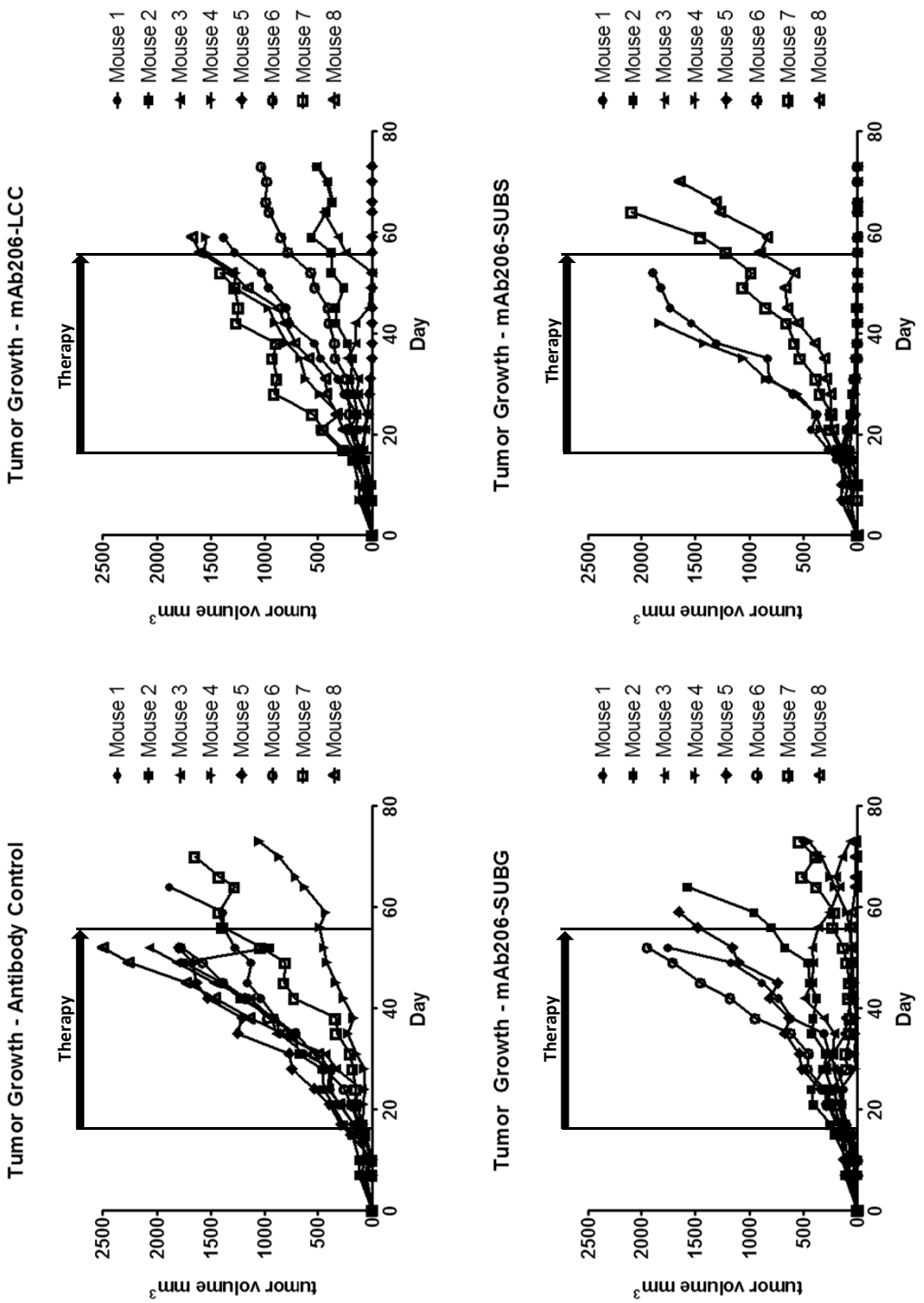

Advanced Treatment - NEC8
Day 17 - Initiation of Immunotherapy
tumor volume mm3
1000
800
600
400
200
0
Antibody control
mAb206-LCC
mAb206-SUBG
mAb206-SUBS
Advanced Treatment - NEC8
Day 31
tumor volume mm3
1500
1000
500
0
Antibody control
mAb206-LCC
mAb206-SUBG
mAb206-SUBS
Advanced Treatment - NEC8
Day 42
tumor volume mm3
2500
2000
1500
1000
500
0
Antibody control
mAb206-LCC
mAb206-SUBG
mAb206-SUBS

Fig. 34a


Tumor Growth - Antibody Control
Tumor Growth - mAb206-LCC
Tumor Growth - mAb206-SUBS
Tumor Growth - mAb206-SUBG
Therapy
Day
tumor volume mm³
Mouse 1
Mouse 2
Mouse 3
Mouse 4
Mouse 5
Mouse 6
Mouse 7
Mouse 8
0
500
1000
1500
2000
2500
0
20
40
60
80

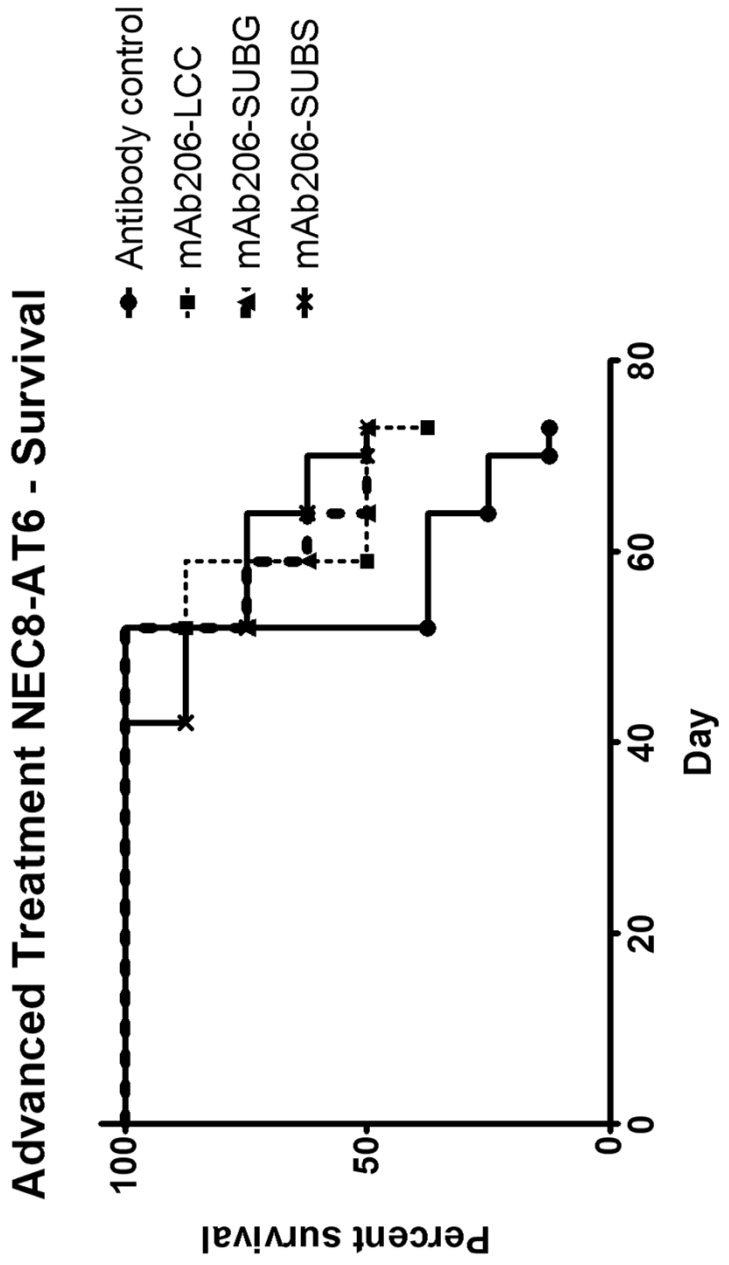

Advanced Treatment NEC8-AT6 - Survival
Antibody control
mAb206-LCC
mAb206-SUBG
mAb206-SUBS
Percent survival
100
50
0
0
20
40
60
80
Day

Fig. 34b

Fig. 35

Name	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
	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
chimAB 64A		X		X																			X	X	X			X
mAb206- LCC		X		X																			X	X	X			X
mAb206- SUBG		X		X																			X	X	X			X
mAb206- SUBS		X		X																			X	X	X			X

Name	EC1 (aa 27-81)																										
	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
	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
chimAB 64A										X																	
mAb206- LCC										X																	
mAb206- SUBG										X																	
mAb206- SUBS										X																	

Name	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
	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
chimAB 64A																									
mAb206- LCC																									
mAb206- SUBG																									
mAb206- SUBS																									

X altered transport to the membrane

no influence on antibody binding

contributes to antibody binding

essential for antibody binding

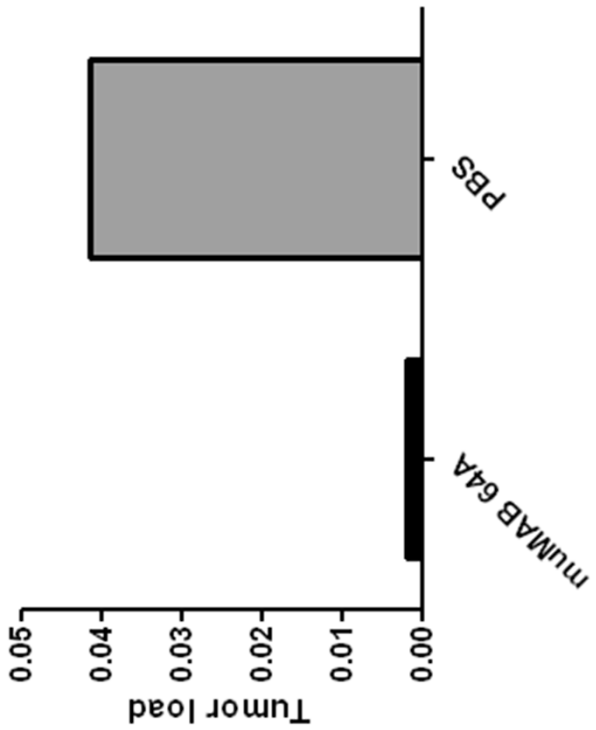


Fig. 36

Fig. 37

	mAb206-LCC	mAb206-SUBG	muMAB 64A
Cancer tissues			
OvarCA	2/2	2/2	2/2
TestisCA	1/1	1/1	4/4
Normal tissues			
Breast	0/1	0/1	-
Colon	0/1	0/1	0/4
Duodenum	0/1	0/1	-
Gall bladder	0/1	0/1	-
Heart	0/1	0/1	0/1
Kidney	0/1	0/1	0/4
Liver	0/1	0/1	0/2
Lung	0/1	0/1	-
Lymphnode	0/1	0/1	-
Oesophagus	0/1	0/1	0/1
Ovar	0/1	0/1	-
Pancreas	0/1	0/1	0/2
Placenta	0/1	0/1	-
Prostate	0/1	0/1	0/2
Sceletal muscle	0/1	0/1	-
Spleen	0/1	0/1	-
Stomach	0/1	0/1	0/2
Testis	0/4	0/4	0/2
Tube	0/1	0/1	-
Thyroidea	0/1	0/1	-
Uterus	0/2	0/2	-

SEQUENCE LISTING

<110> Ganymed Pharmaceuticals AG
Johannes Gutenberg-Universität Mainz

<120> ANTIBODIES FOR TREATMENT OF CANCER EXPRESSING CLAUDIN 6

<130> SG4105A

<150> EP 11 004 004.5
<151> 2011-05-13

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<151> 2011-05-13

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ggcctggtct cctgtgccct gcccatgtgg aaggtgaccg ctttcatcgg caacagcatc 180

gtggtggccc aggtggtgtg ggagggcctg tggatgtcct gcgtggtgca gagcaccggc 240

cagatgcagt gcaaggtgta cgactcactg ctggcgctgc cacaggacct gcaggctgca 300

cgtgccctct gtgtcatcgc cctccttgtg gccctgttcg gcttgctggt ctaccttgct 360

ggggccaagt gtaccacctg tgtggaggag aaggattcca aggcccgcct ggtgctcacc 420

tctgggattg tctttgtcat ctcaggggtc ctgacgctaa tccccgtgtg ctggacggcg 480

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ggggcctccc tctacttggg ctgggcggcc tcaggccttt tgttgctggg tgggggttg 600

ctgtgctgca cttgcccctc gggggggtcc cagggcccca gccattacat ggcccgctac 660

tcaacatctg cccctgccat ctctcggggg ccctctgagt accctaccaa gaattacgtc 720

tgacgtggag gggaatgggg gctccgctgg cgctagagcc atccagaagt ggcagtgccc 780

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atcttgacat gcccatctta gaagccagtc aagctatgga actaatgcgg aggctgcttg 1020

ctgtgctggc tttgcaacaa gacagactgt ccccaagagt tcctgctgct gctgggggct 1080

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tctcttcacc cctggaaaaa caaatgatct gttaacaaag gactgcccac ctccggaact 1200

tctgacctct gtttcctccg tcctgataag acgtccaccc cccagggcca ggtcccagct 1260

atgtagaccc ccgcccccac ctccaacact gcacccttct gccctgcccc cctcgtctca 1320

ccccctttac actcacattt ttatcaaata aagcatgttt tgttagtgc 1369

<210> 2
<211> 220
<212> PRT
<213> Homo sapiens

<400> 2

Met Ala Ser Ala Gly Met Gln Ile Leu Gly Val Val Leu Thr Leu Leu
1 5 10 15

Gly Trp Val Asn Gly Leu Val Ser Cys Ala Leu Pro Met Trp Lys Val
20 25 30

Thr Ala Phe Ile Gly Asn Ser Ile Val Val Ala Gln Val Val Trp Glu
35 40 45

Gly Leu Trp Met Ser Cys Val Val Gln Ser Thr Gly Gln Met Gln Cys
50 55 60

Lys Val Tyr Asp Ser Leu Leu Ala Leu Pro Gln Asp Leu Gln Ala Ala
65 70 75 80

Arg Ala Leu Cys Val Ile Ala Leu Leu Val Ala Leu Phe Gly Leu Leu
85 90 95

Val Tyr Leu Ala Gly Ala Lys Cys Thr Thr Cys Val Glu Glu Lys Asp
100 105 110

Ser Lys Ala Arg Leu Val Leu Thr Ser Gly Ile Val Phe Val Ile Ser
115 120 125

Gly Val Leu Thr Leu Ile Pro Val Cys Trp Thr Ala His Ala Ile Ile
130 135 140

Arg Asp Phe Tyr Asn Pro Leu Val Ala Glu Ala Gln Lys Arg Glu Leu
145 150 155 160

Gly Ala Ser Leu Tyr Leu Gly Trp Ala Ala Ser Gly Leu Leu Leu Leu
165 170 175

Gly Gly Gly Leu Leu Cys Cys Thr Cys Pro Ser Gly Gly Ser Gln Gly
180 185 190

Pro Ser His Tyr Met Ala Arg Tyr Ser Thr Ser Ala Pro Ala Ile Ser
195 200 205

Arg Gly Pro Ser Glu Tyr Pro Thr Lys Asn Tyr Val
210 215 220

<210> 3
<211> 805
<212> DNA
<213> Artificial

<220>
<223> codon-optimized nucleic acid sequence encoding human claudin 6

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agcttgccac catggccagc gccggcatgc agatcctggg agtggtgctg accctgctgg 120

gctgggtgaa cggcctggtg tcctgcgccc tgcccatgtg gaaagtgacc gccttcatcg 180

gcaacagcat cgtggtggcc caggtcgtgt gggagggcct gtggatgagc tgtgtggtgc 240

agagcaccgg ccagatgcag tgcaaggtgt acgacagcct gctggccctg cctcaggatc 300

tgcaggccgc cagagccctg tgtgtgatcg ccctgctggt cgccctgttc ggcctgctgg 360

tgtacctcgc tggcgccaag tgcaccacct gtgtggagga aaaggacagc aaggcccggc 420

tggtcctgac aagcggcatc gtgttcgtga tcagcggcgt gctgacactg atccccgtgt 480

gctggaccgc ccacgccatc atccgggact tctacaaccc tctggtggcc gaggcccaga 540

agagagagct gggcgccagc ctgtatctgg gatgggccgc ctcaggactg ctgctgctgg 600

gcggaggcct gctgtgctgt acatgtccta gcggcggctc ccagggccct agccactaca 660

tggcccggta cagcaccagc gcccctgcca tcagcagagg ccccagcgag taccccacca 720

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tcgtattacg tcgcgctcac tggcc 805

<210> 4
<211> 165
<212> DNA
<213> Artificial

<220>
<223> codon-optimized nucleic acid sequence encoding the predicted extracellular loop 2 (EC2) of human claudin 6

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ggcgcgccaa ggtaccaagc ttgccaccat ggaaaccgac accctgctgc tgtgggtgct 60

gctcctgtgg gtcccaggct ctacaggcga cgccgcccag cccagagact tctacaaccc 120

cctggtggcc gaggcccaga agctcgagtc tagagggtta attaa 165

<210> 5
<211> 38
<212> PRT
<213> Artificial

<220>
<223> predicted 2nd extracellular loop of human claudin 6 containing an Ig kappa leader sequence

<220>
<221> SIGNAL
<222> (1)..(21)
<223> Ig kappa leader sequence

<220>
<221> DOMAIN
<222> (26)..(38)
<223> predicted 2nd extracellular loop (EC2) of human claudin 6

<400> 5

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1 5 10 15

Gly Ser Thr Gly Asp Ala Ala Gln Pro Arg Asp Phe Tyr Asn Pro Leu
20 25 30

Val Ala Glu Ala Gln Lys
35

<210> 6
<211> 13
<212> PRT
<213> Homo sapiens

<400> 6

Arg Asp Phe Tyr Asn Pro Leu Val Ala Glu Ala Gln Lys
1 5 10

<210> 7
<211> 53
<212> PRT
<213> Homo sapiens

<400> 7

Pro Met Trp Lys Val Thr Ala Phe Ile Gly Asn Ser Ile Val Val Ala
1 5 10 15

Gln Val Val Trp Glu Gly Leu Trp Met Ser Cys Val Val Gln Ser Thr
20 25 30

Gly Gln Met Gln Cys Lys Val Tyr Asp Ser Leu Leu Ala Leu Pro Gln
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Asp Leu Gln Ala Ala
50

<210> 8
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<212> PRT
<213> Homo sapiens

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<222> (143)..(143)
<223> human claudin 6 I143V polymorphism

<400> 8

Met Ala Ser Ala Gly Met Gln Ile Leu Gly Val Val Leu Thr Leu Leu
1 5 10 15

Gly Trp Val Asn Gly Leu Val Ser Cys Ala Leu Pro Met Trp Lys Val
20 25 30

Thr Ala Phe Ile Gly Asn Ser Ile Val Val Ala Gln Val Val Trp Glu
35 40 45

Gly Leu Trp Met Ser Cys Val Val Gln Ser Thr Gly Gln Met Gln Cys
50 55 60

```
Lys Val Tyr Asp Ser Leu Leu Ala Leu Pro Gln Asp Leu Gln Ala Ala
65                  70                  75                  80

Arg Ala Leu Cys Val Ile Ala Leu Leu Val Ala Leu Phe Gly Leu Leu
                85                  90                  95

Val Tyr Leu Ala Gly Ala Lys Cys Thr Thr Cys Val Glu Glu Lys Asp
            100                 105                 110

Ser Lys Ala Arg Leu Val Leu Thr Ser Gly Ile Val Phe Val Ile Ser
        115                 120                 125

Gly Val Leu Thr Leu Ile Pro Val Cys Trp Thr Ala His Ala Val Ile
    130                 135                 140

Arg Asp Phe Tyr Asn Pro Leu Val Ala Glu Ala Gln Lys Arg Glu Leu
145                 150                 155                 160

Gly Ala Ser Leu Tyr Leu Gly Trp Ala Ala Ser Gly Leu Leu Leu Leu
                165                 170                 175

Gly Gly Gly Leu Leu Cys Cys Thr Cys Pro Ser Gly Gly Ser Gln Gly
            180                 185                 190

Pro Ser His Tyr Met Ala Arg Tyr Ser Thr Ser Ala Pro Ala Ile Ser
        195                 200                 205

Arg Gly Pro Ser Glu Tyr Pro Thr Lys Asn Tyr Val
    210                 215                 220


<210>  9
<211>  217
<212>  PRT
<213>  Homo sapiens

<400>  9

Met Ala Ser Thr Gly Leu Glu Leu Leu Gly Met Thr Leu Ala Val Leu
1               5                   10                  15

Gly Trp Leu Gly Thr Leu Val Ser Cys Ala Leu Pro Leu Trp Lys Val
            20                  25                  30

Thr Ala Phe Ile Gly Asn Ser Ile Val Val Ala Gln Val Val Trp Glu
        35                  40                  45

Gly Leu Trp Met Ser Cys Val Val Gln Ser Thr Gly Gln Met Gln Cys
    50                  55                  60

Lys Val Tyr Asp Ser Leu Leu Ala Leu Pro Gln Asp Leu Gln Ala Ala
65                  70                  75                  80

Arg Ala Leu Cys Val Ile Ala Leu Leu Leu Ala Leu Leu Gly Leu Leu
                85                  90                  95
```

```
Val Ala Ile Thr Gly Ala Gln Cys Thr Thr Cys Val Glu Asp Glu Gly
            100                 105                 110

Ala Lys Ala Arg Ile Val Leu Thr Ala Gly Val Ile Leu Leu Leu Ala
        115                 120                 125

Gly Ile Leu Val Leu Ile Pro Val Cys Trp Thr Ala His Ala Ile Ile
    130                 135                 140

Gln Asp Phe Tyr Asn Pro Leu Val Ala Glu Ala Leu Lys Arg Glu Leu
145                 150                 155                 160

Gly Ala Ser Leu Tyr Leu Gly Trp Ala Ala Ala Ala Leu Leu Met Leu
                165                 170                 175

Gly Gly Gly Leu Leu Cys Cys Thr Cys Pro Pro Pro Gln Val Glu Arg
            180                 185                 190

Pro Arg Gly Pro Arg Leu Gly Tyr Ser Ile Pro Ser Arg Ser Gly Ala
        195                 200                 205

Ser Gly Leu Asp Lys Arg Asp Tyr Val
    210                 215
```

<210> 10
<211> 209
<212> PRT
<213> Homo sapiens

<400> 10

```
Met Ala Ser Met Gly Leu Gln Val Met Gly Ile Ala Leu Ala Val Leu
1               5                   10                  15

Gly Trp Leu Ala Val Met Leu Cys Cys Ala Leu Pro Met Trp Arg Val
            20                  25                  30

Thr Ala Phe Ile Gly Ser Asn Ile Val Thr Ser Gln Thr Ile Trp Glu
        35                  40                  45

Gly Leu Trp Met Asn Cys Val Val Gln Ser Thr Gly Gln Met Gln Cys
    50                  55                  60

Lys Val Tyr Asp Ser Leu Leu Ala Leu Pro Gln Asp Leu Gln Ala Ala
65                  70                  75                  80

Arg Ala Leu Val Ile Ile Ser Ile Ile Val Ala Ala Leu Gly Val Leu
                85                  90                  95

Leu Ser Val Val Gly Gly Lys Cys Thr Asn Cys Leu Glu Asp Glu Ser
            100                 105                 110

Ala Lys Ala Lys Thr Met Ile Val Ala Gly Val Val Phe Leu Leu Ala
        115                 120                 125
```

```
Gly Leu Met Val Ile Val Pro Val Ser Trp Thr Ala His Asn Ile Ile
    130                 135                 140

Gln Asp Phe Tyr Asn Pro Leu Val Ala Ser Gly Gln Lys Arg Glu Met
145                 150                 155                 160

Gly Ala Ser Leu Tyr Val Gly Trp Ala Ala Ser Gly Leu Leu Leu Leu
                165                 170                 175

Gly Gly Gly Leu Leu Cys Cys Asn Cys Pro Pro Arg Thr Asp Lys Pro
            180                 185                 190

Tyr Ser Ala Lys Tyr Ser Ala Ala Arg Ser Ala Ala Ala Ser Asn Tyr
        195                 200                 205

Val
```

<210> 11
<211> 220
<212> PRT
<213> Homo sapiens

<400> 11

```
Met Ser Met Gly Leu Glu Ile Thr Gly Thr Ala Leu Ala Val Leu Gly
1               5                   10                  15

Trp Leu Gly Thr Ile Val Cys Cys Ala Leu Pro Met Trp Arg Val Ser
            20                  25                  30

Ala Phe Ile Gly Ser Asn Ile Ile Thr Ser Gln Asn Ile Trp Glu Gly
        35                  40                  45

Leu Trp Met Asn Cys Val Val Gln Ser Thr Gly Gln Met Gln Cys Lys
    50                  55                  60

Val Tyr Asp Ser Leu Leu Ala Leu Pro Gln Asp Leu Gln Ala Ala Arg
65                  70                  75                  80

Ala Leu Ile Val Val Ala Ile Leu Leu Ala Ala Phe Gly Leu Leu Val
                85                  90                  95

Ala Leu Val Gly Ala Gln Cys Thr Asn Cys Val Gln Asp Asp Thr Ala
            100                 105                 110

Lys Ala Lys Ile Thr Ile Val Ala Gly Val Leu Phe Leu Leu Ala Ala
        115                 120                 125

Leu Leu Thr Leu Val Pro Val Ser Trp Ser Ala Asn Thr Ile Ile Arg
    130                 135                 140

Asp Phe Tyr Asn Pro Val Val Pro Glu Ala Gln Lys Arg Glu Met Gly
145                 150                 155                 160
```

```
Ala Gly Leu Tyr Val Gly Trp Ala Ala Ala Ala Leu Gln Leu Leu Gly
                165                 170                 175

Gly Ala Leu Leu Cys Cys Ser Cys Pro Pro Arg Glu Lys Lys Tyr Thr
            180                 185                 190

Ala Thr Lys Val Val Tyr Ser Ala Pro Arg Ser Thr Gly Pro Gly Ala
        195                 200                 205

Ser Leu Gly Thr Gly Tyr Asp Arg Lys Asp Tyr Val
    210                 215                 220
```

<210> 12
<211> 159
<212> DNA
<213> Artificial

<220>
<223> codon-optimized nucleic acid sequence encoding the predicted extracellular loop 1 (EC1) of human claudin 6

<400> 12

```
cccatgtgga aagtgaccgc cttcatcggc aacagcatcg tggtggccca ggtggtctgg       60

gagggcctgt ggatgagctg cgtggtgcag agcaccggcc agatgcagtg caaggtgtac      120

gacagcctgc tggccctgcc tcaggatctg caggctgct                             159
```

<210> 13
<211> 106
<212> PRT
<213> Artificial

<220>
<223> predicted 1st extracellular loop of human claudin 6 containing an Ig kappa leader sequence

<220>
<221> Signal
<222> (1)..(21)
<223> Ig kappa leader sequence

<220>
<221> Domain
<222> (26)..(78)
<223> predicted 1st extracellular loop (EC1) of human claudin 6

<400> 13

```
Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro
1               5                   10                  15

Gly Ser Thr Gly Asp Ala Ala Gln Pro Pro Met Trp Lys Val Thr Ala
            20                  25                  30

Phe Ile Gly Asn Ser Ile Val Val Ala Gln Val Val Trp Glu Gly Leu
        35                  40                  45

Trp Met Ser Cys Val Val Gln Ser Thr Gly Gln Met Gln Cys Lys Val
    50                  55                  60
```

```
Tyr Asp Ser Leu Leu Ala Leu Pro Gln Asp Leu Gln Ala Ala Leu Glu
65                  70                  75                  80

Ser Arg Gly Pro Phe Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Asn
                85                  90                  95

Met His Thr Gly His His His His His His
            100                 105

<210>  14
<211>  13
<212>  PRT
<213>  Homo sapiens

<400>  14

Pro Met Trp Lys Val Thr Ala Phe Ile Gly Asn Ser Ile
1               5                   10

<210>  15
<211>  15
<212>  PRT
<213>  Homo sapiens

<400>  15

Met Trp Lys Val Thr Ala Phe Ile Gly Asn Ser Ile Val Val Ala
1               5                   10                  15

<210>  16
<211>  20
<212>  DNA
<213>  Artificial

<220>
<223>  Oligonucleotide

<400>  16
tccatgacgt tcctgacgtt                                                  20

<210>  17
<211>  43
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  Oligonucleotide

<400>  17
gagaaagctt gccgccacca tgggatggag ctggatcttt ctc                         43

<210>  18
<211>  43
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  Oligonucleotide

<400>  18
gagagggccc ttggtggagg ctgaagagac tgtgagagtg gtg                         43
```

<210> 19
<211> 43
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 19
gagagggccc ttggtggagg ctgaggagac tgtgagagtg gtg 43

<210> 20
<211> 43
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 20
gagagggccc ttggtggagg ctgaggagac tgtgagagtg gtg 43

<210> 21
<211> 46
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 21
gagaaagctt gccgccacca tgcattttca agtgcagatt ttcagc 46

<210> 22
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 22
cacacgtacg tttgatttcc agcttggtgc ctc 33

<210> 23
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 23
cacacgtacg tttgatttcc agcttggtgc ctc 33

<210> 24
<211> 993
<212> DNA
<213> Homo sapiens

<400> 24
gcctccacca agggcccaag cgtgttcccc ctggccccca gcagcaagag caccagcggc 60

ggcacagccg ccctgggctg cctggtgaag gactacttcc ccgagcccgt gaccgtgagc 120

tggaacagcg gagccctgac ctccggcgtg cacaccttcc ccgccgtgct gcagagcagc 180

ggcctgtaca gcctgagcag cgtggtgacc gtgcccagca gcagcctggg cacccagacc 240

tacatctgca acgtgaacca caagcccagc aacaccaagg tggacaagag agtggagccc 300

aagagctgcg acaagaccca cacctgcccc ccctgcccag ccccagagct gctgggcgga 360

cccagcgtgt tcctgttccc ccccaagccc aaggacaccc tgatgatcag caggaccccc 420

gaggtgacct gcgtggtggt ggacgtgagc cacgaggacc cagaggtgaa gttcaactgg 480

tacgtggacg gcgtggaggt gcacaacgcc aagaccaagc ccagagagga gcagtacaac 540

agcacctaca gggtggtgtc cgtgctgacc gtgctgcacc aggactggct gaacggcaag 600

gaatacaagt gcaaggtctc caacaaggcc ctgccagccc ccatcgaaaa gaccatcagc 660

aaggccaagg gccagccacg ggagccccag gtgtacaccc tgcccccag ccgggaggag 720

atgaccaaga accaggtgtc cctgacctgt ctggtgaagg gcttctaccc cagcgacatc 780

gccgtggagt gggagagcaa cggccagccc gagaacaact acaagaccac cccccagtg 840

ctggacagcg acggcagctt cttcctgtac agcaagctga ccgtggacaa gtccaggtgg 900

cagcagggca acgtgttcag ctgcagcgtg atgcacgagg ccctgcacaa ccactacacc 960

cagaagtccc tgagcctgag ccccggcaag tag 993

<210> 25
<211> 330
<212> PRT
<213> Homo sapiens

<400> 25

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
100 105 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
115 120 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys

130 135 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145 150 155 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
165 170 175

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
180 185 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
195 200 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
210 215 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225 230 235 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
245 250 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
260 265 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
275 280 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
290 295 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305 310 315 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
325 330

<210> 26
<211> 324
<212> DNA
<213> Homo sapiens

<400> 26
cgtacggtgg ccgctcccag cgtgttcatc ttcccccca gcgacgagca gctgaagtcc 60

ggcaccgcca gcgtggtgtg cctgctgaac aacttctacc cccgggaggc caaggtgcag 120

tggaaggtgg acaacgccct gcagagcggc aacagccagg agagcgtcac cgagcaggac 180

agcaaggact ccacctacag cctgagcagc accctgaccc tgagcaaggc cgactacgag 240

aagcacaagg tgtacgcctg cgaggtgacc caccagggcc tgtccagccc cgtgaccaag 300

agcttcaaca ggggcgagtg ctag 324

<210> 27

<211> 107
<212> PRT
<213> Homo sapiens

<400> 27

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
1 5 10 15

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
20 25 30

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
35 40 45

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
50 55 60

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
65 70 75 80

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
85 90 95

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105

<210> 28
<211> 32
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<220>
<221> misc_feature
<222> (31)..(32)
<223> any nucleotide

<400> 28
ttttttttttt ttttttttttt ttttttttttt nn 32

<210> 29
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 29
aagcagtggt atcaacgcag agtacgcggg 30

<210> 30
<211> 26
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 30
ctgctcactg gatggtggga agatgg 26

<210> 31
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 31
acaggggcca gtggatagac cgatg 25

<210> 32
<211> 45
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 32
gtaatacgac tcactatagg gcaagcagtg gtatcaacgc agagt 45

<210> 33
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 33
gtaatacgac tcactatagg gc 22

<210> 34
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody VH sequence

<400> 34

Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1 5 10 15

Ser Met Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly Tyr
20 25 30

Thr Met Asn Trp Val Lys Gln Ser His Gly Lys Asn Leu Glu Trp Ile
35 40 45

Gly Leu Ile Asn Pro Tyr Asn Gly Gly Thr Ser Tyr Asn Gln Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ile Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

```
Met Glu Leu Leu Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Asp Tyr Gly Tyr Val Leu Asp Tyr Trp Gly Gln Gly Thr Thr
            100                 105                 110

Leu Thr Val Ser Ser
        115
```

<210> 35
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody VL sequence

<400> 35

```
Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
1               5                   10                  15

Glu Lys Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Leu
            20                  25                  30

His Trp Phe Gln Gln Lys Pro Gly Thr Ser Pro Lys Leu Trp Val Tyr
        35                  40                  45

Ser Thr Ser Asn Leu Pro Ser Gly Val Pro Ala Arg Phe Gly Gly Ser
    50                  55                  60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Met Glu Ala Glu
65                  70                  75                  80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Arg Ser Ile Tyr Pro Pro Trp
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
            100                 105
```

<210> 36
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody VH sequence

<400> 36

```
Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1               5                   10                  15

Ser Met Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly Tyr
            20                  25                  30

Thr Met Asn Trp Val Lys Gln Ser His Gly Lys Asn Leu Glu Trp Ile
        35                  40                  45
```

```
Gly Leu Ile Asn Pro Tyr Asn Gly Gly Thr Ile Tyr Asn Gln Lys Phe
    50                  55                  60

Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Leu Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Asp Tyr Gly Phe Val Leu Asp Tyr Trp Gly Gln Gly Thr Thr
            100                 105                 110

Leu Thr Val Ser Ser
        115
```

<210> 37
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody VL sequence

<400> 37

```
Gln Ile Val Leu Thr Gln Ser Pro Ser Ile Met Ser Val Ser Pro Gly
1               5                   10                  15

Glu Lys Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
            20                  25                  30

His Trp Phe Gln Gln Lys Pro Gly Thr Ser Pro Lys Leu Cys Ile Tyr
        35                  40                  45

Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Arg
    50                  55                  60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Ala Ala Glu
65                  70                  75                  80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Arg Ser Asn Tyr Pro Pro Trp
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
            100                 105
```

<210> 38
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody VH sequence

<400> 38

```
Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1               5                   10                  15
```

Ser Met Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly Tyr
20 25 30

Thr Met Asn Trp Val Lys Gln Ser His Gly Lys Asn Leu Glu Trp Ile
35 40 45

Gly Leu Ile Asn Pro Tyr Asn Gly Gly Ile Ile Tyr Asn Gln Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Leu Ser Leu Thr Ser Glu Asp Ser Ala Val Phe Tyr Cys
85 90 95

Ala Arg Asp Phe Gly Tyr Val Leu Asp Tyr Trp Gly Gln Gly Thr Thr
100 105 110

Leu Thr Val Ser Ser
115

<210> 39
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody VL sequence

<400> 39

Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

His Trp Phe Gln Gln Lys Pro Gly Thr Ser Pro Lys Leu Trp Ile Tyr
35 40 45

Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Ala Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Arg Ser Thr Tyr Pro Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 40
<211> 117
<212> PRT

<213> Artificial Sequence

<220>
<223> Antibody VH sequence

<400> 40

Glu Val Gln Leu Gln Gln Ser Arg Pro Glu Leu Val Lys Pro Gly Ala
1 5 10 15

Ser Met Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly Tyr
20 25 30

Thr Leu Asn Trp Val Lys Gln Ser His Gly Lys Asn Leu Glu Trp Ile
35 40 45

Gly Leu Ile Asn Pro Tyr Asn Gly Gly Ser Ser Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Leu Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Tyr Gly Tyr Val Phe Asp Tyr Trp Gly Gln Gly Thr Thr
100 105 110

Leu Thr Val Ser Ser
115

<210> 41
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody VL sequence

<400> 41

Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Asn Tyr Met
20 25 30

His Trp Phe Gln Leu Lys Pro Gly Thr Ser Pro Lys Leu Leu Ile Tyr
35 40 45

Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Arg
50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Met Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Arg Asn Asn Tyr Pro Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 42
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody VH CDR3 sequence

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Any amino acid, preferably an aromatic amino acid, more preferably Phe or Tyr, most preferably Tyr

<220>
<221> MISC_FEATURE
<222> (3)..(3)
<223> Any amino acid, preferably an aromatic amino acid, more preferably Phe or Tyr, most preferably Tyr

<220>
<221> MISC_FEATURE
<222> (5)..(5)
<223> Any amino acid, preferably Leu or Phe, more preferably Leu

<400> 42

Xaa Gly Xaa Val Xaa
1 5

<210> 43
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody VH CDR3 sequence

<220>
<221> MISC_FEATURE
<222> (2)..(2)
<223> Any amino acid, preferably an aromatic amino acid, more preferably Phe or Tyr, most preferably Tyr

<220>
<221> MISC_FEATURE
<222> (4)..(4)
<223> Any amino acid, preferably an aromatic amino acid, more preferably Phe or Tyr, most preferably Tyr

<220>
<221> MISC_FEATURE
<222> (6)..(6)
<223> Any amino acid, preferably Leu or Phe, more preferably Leu

<400> 43

Asp Xaa Gly Xaa Val Xaa
1 5

<210> 44

<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody VH CDR3 sequence

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Any amino acid, preferably an aromatic amino acid, more preferably Phe or Tyr, most preferably Tyr

<220>
<221> MISC_FEATURE
<222> (3)..(3)
<223> Any amino acid, preferably an aromatic amino acid, more preferably Phe or Tyr, most preferably Tyr

<220>
<221> MISC_FEATURE
<222> (5)..(5)
<223> Any amino acid, preferably Leu or Phe, more preferably Leu

<400> 44

Xaa Gly Xaa Val Xaa Asp
1 5

<210> 45
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody VH CDR3 sequence

<220>
<221> MISC_FEATURE
<222> (2)..(2)
<223> Any amino acid, preferably an aromatic amino acid, more preferably Phe or Tyr, most preferably Tyr

<220>
<221> MISC_FEATURE
<222> (4)..(4)
<223> Any amino acid, preferably an aromatic amino acid, more preferably Phe or Tyr, most preferably Tyr

<220>
<221> MISC_FEATURE
<222> (6)..(6)
<223> Any amino acid, preferably Leu or Phe, more preferably Leu

<400> 45

Asp Xaa Gly Xaa Val Xaa Asp
1 5

<210> 46
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody VH CDR3 sequence

<220>
<221> MISC_FEATURE
<222> (4)..(4)
<223> Any amino acid, preferably an aromatic amino acid, more preferably Phe or Tyr, most preferably Tyr

<220>
<221> MISC_FEATURE
<222> (6)..(6)
<223> Any amino acid, preferably an aromatic amino acid, more preferably Phe or Tyr, most preferably Tyr

<220>
<221> MISC_FEATURE
<222> (8)..(8)
<223> Any amino acid, preferably Leu or Phe, more preferably Leu

<400> 46

Ala Arg Asp Xaa Gly Xaa Val Xaa Asp Tyr
1 5 10

<210> 47
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Antibody VH CDR1 sequence

<400> 47

Gly Tyr Ser Phe Thr Gly Tyr Thr
1 5

<210> 48
<211> 8
<212> PRT
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<220>
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<220>
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<223> Any amino acid, preferably Thr, Ser or Ile, most preferably Thr

<400> 48

Ile Asn Pro Tyr Asn Gly Gly Xaa
1 5

<210> 49
<211> 5
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<220>
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<220>
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<223> Any amino acid, preferably Ser or Asn, most preferably Ser

<220>
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<223> Any amino acid, preferably Tyr, Ser, Ile, Asn or Thr, more preferably Tyr, Ser, or Asn, most preferably Asn

<220>
<221> MISC_FEATURE
<222> (4)..(4)
<223> Any amino acid, preferably Ser or Tyr, more preferably Tyr

<400> 49

Arg Xaa Xaa Xaa Pro
1 5

<210> 50
<211> 7
<212> PRT
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<223> Antibody VL CDR3 sequence

<220>
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<220>
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<400> 50

Gln Arg Xaa Xaa Xaa Pro Pro
1 5

<210> 51
<211> 10
<212> PRT
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<220>
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<220>
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<222> (6)..(6)
<223> Any amino acid, preferably Ser or Tyr, more preferably Tyr

<400> 51

Gln Gln Arg Xaa Xaa Xaa Pro Pro Trp Thr
1 5 10

<210> 52
<211> 5
<212> PRT
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<400> 52

Ser Ser Val Xaa Tyr
1 5

<210> 53
<211> 3
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<220>
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<400> 53

Ser Thr Ser
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<210> 54
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<400> 54

Gln Ile Val Leu Thr Gln Ser Pro Ser Ile Met Ser Val Ser Pro Gly
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Glu Lys Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

His Trp Phe Gln Gln Lys Pro Gly Thr Ser Pro Lys Leu Gly Ile Tyr
35 40 45

Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Arg
50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Ala Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Arg Ser Asn Tyr Pro Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 55
<211> 107
<212> PRT
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<220>
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<400> 55

Gln Ile Val Leu Thr Gln Ser Pro Ser Ile Met Ser Val Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

His Trp Phe Gln Gln Lys Pro Gly Thr Ser Pro Lys Leu Ser Ile Tyr
35 40 45

Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Arg
50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Ala Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Arg Ser Asn Tyr Pro Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 56
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 56
gggataattt cagctgacta aacag 25

<210> 57
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 57
ttccgtttag ttaggtgcag ttatc 25