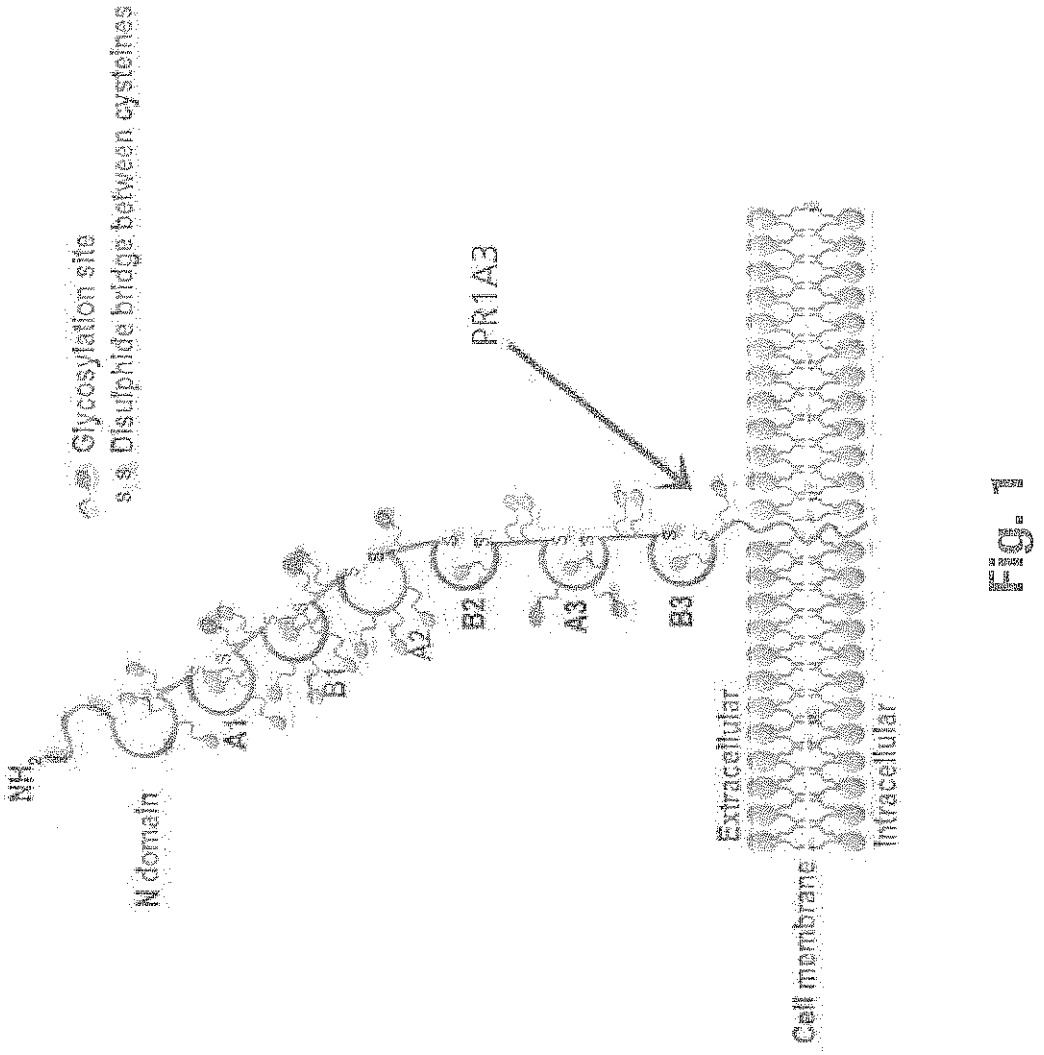

Glycosylation site
s. s. Disulphide bridge between cysteines
PR1A3
N domain
Extracellular
Cell membrane
Intracellular
A1
B1
A2
B2
A3
B3

FIG. 1

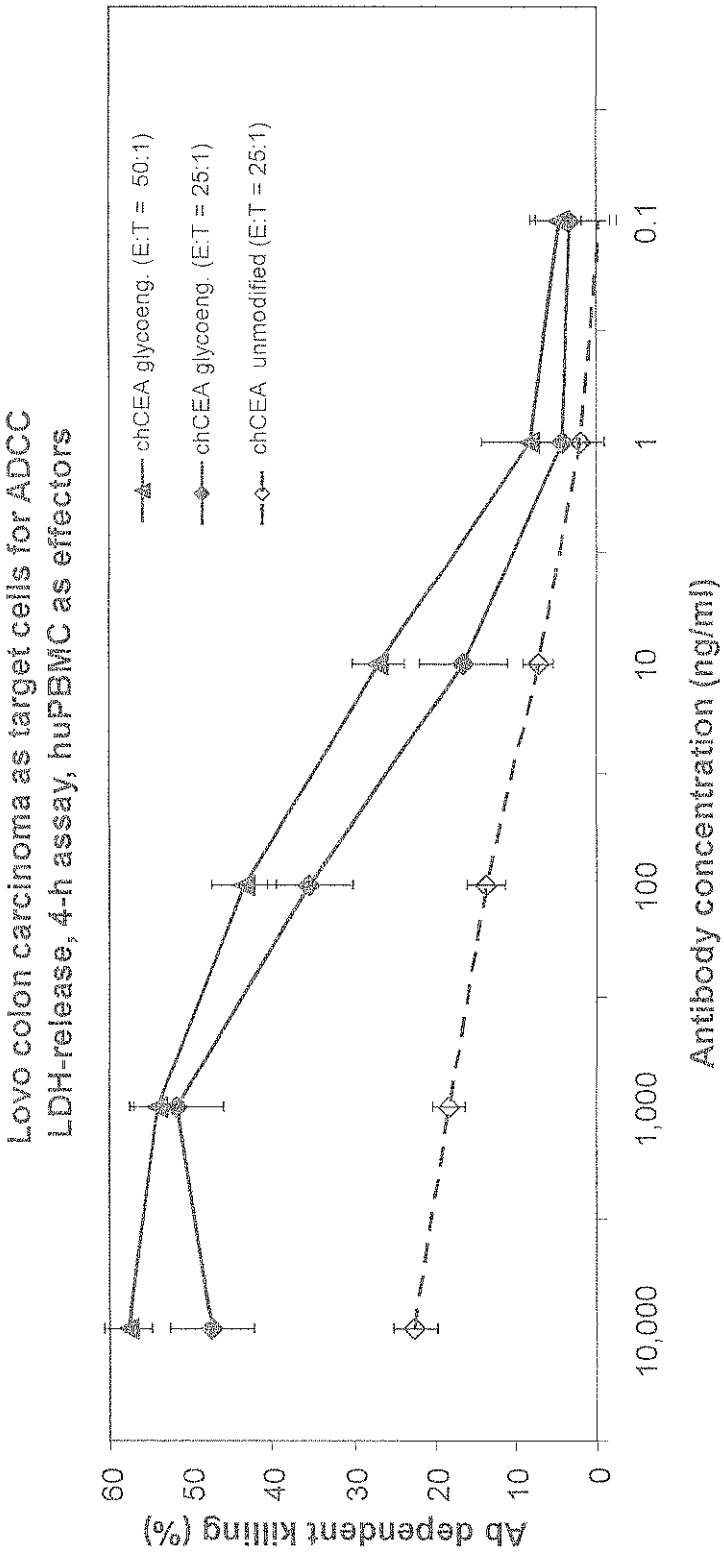

Lovo colon carcinoma as target cells for ADCC
LDH-release, 4-h assay, huPBMC as effectors
chCEA glycoeng. (E:T = 50:1)
chCEA glycoeng. (E:T = 25:1)
chCEA unmodified (E:T = 25:1)
Ab dependent killing (%)
0
10
20
30
40
50
60
Antibody concentration (ng/ml)
10,000
1,000
100
10
1
0.1

Fig. 2

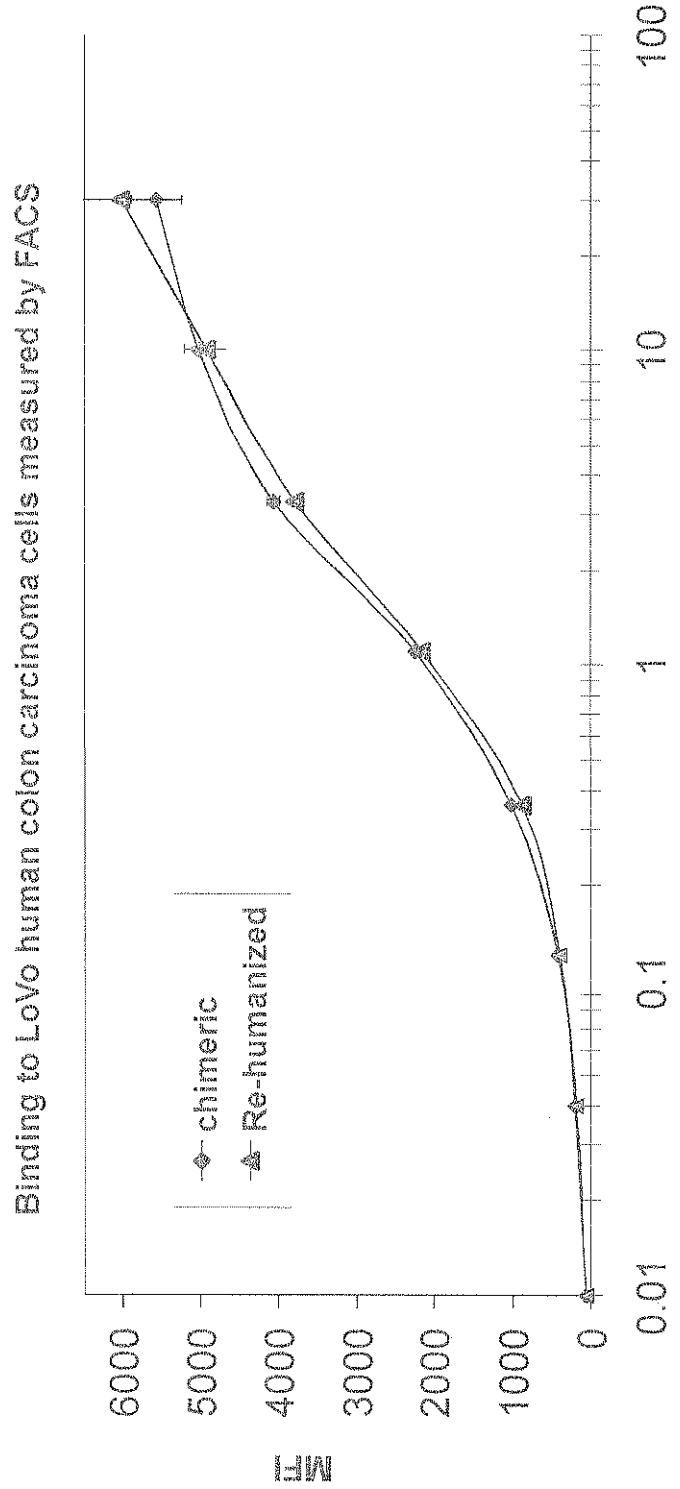

Binding to LoVo human colon carcinoma cells measured by FACS
MFI
6000
5000
4000
3000
2000
1000
0
0.01
0.1
1
10
100
Antibody concentration (µg/ml)
chimeric
Re-humanized

FIG. 3

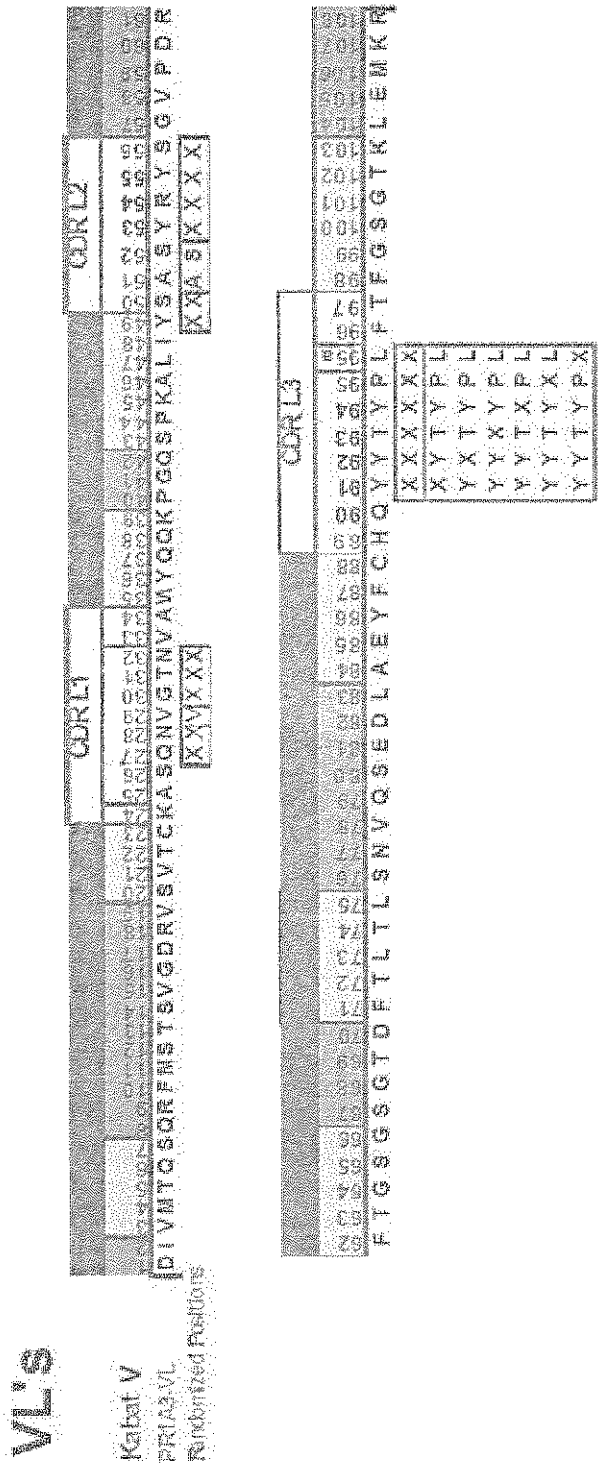


Fig. 4

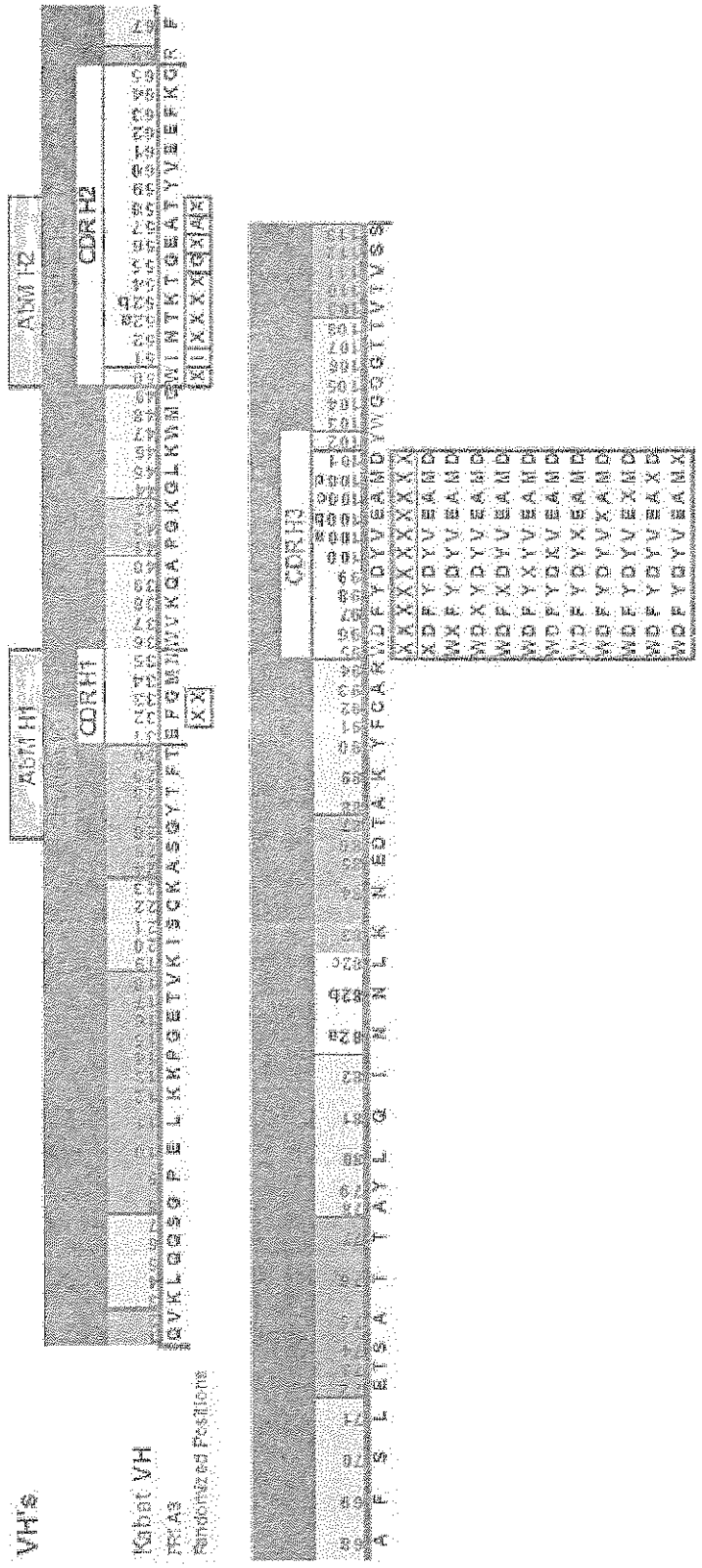


FIG 5

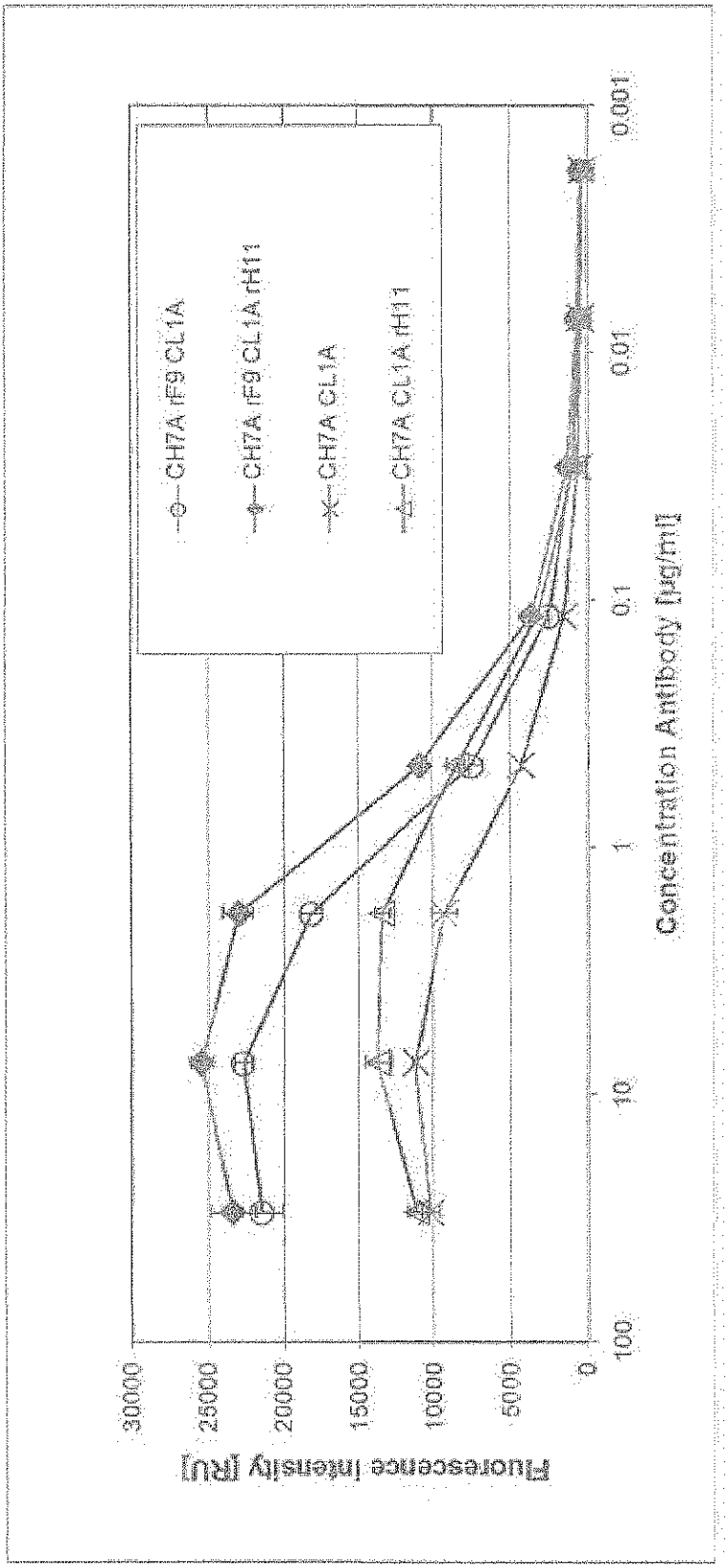

Fluorescence Intensity RFU
30000
25000
20000
15000
10000
5000
0
100
10
1
0.1
0.01
0.001
Concentration Antibody [µg/ml]
CH7A rF9 CL1A
CH7A rF9 CL1A rH11
CH7A CL1A
CH7A CL1A rH11

Fig. 6

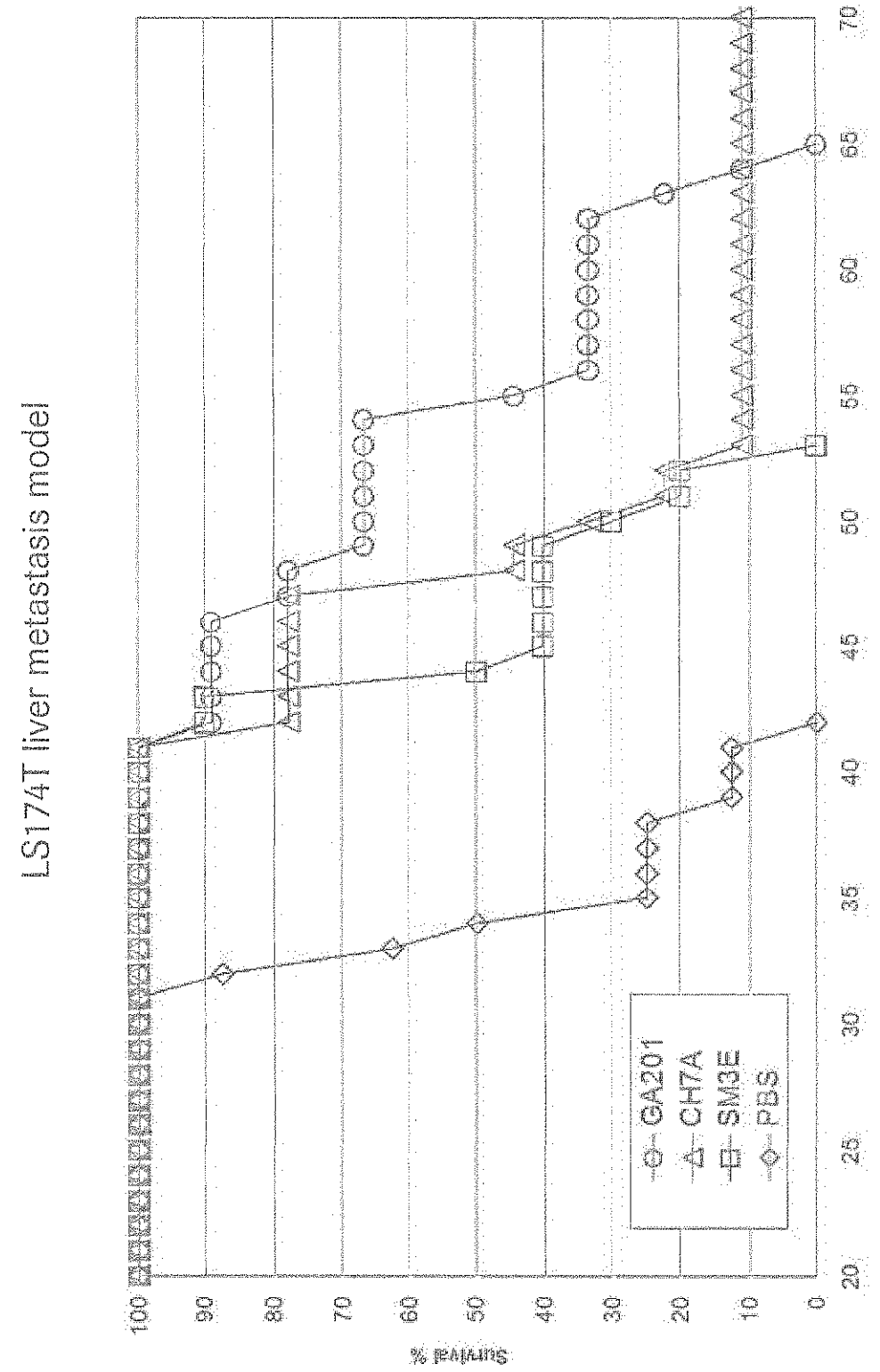

LS174T liver metastasis model
Survival %
100
90
80
70
60
50
40
30
20
10
0
20
25
30
35
40
45
50
55
60
65
70
Study day
GA201
CH7A
SM3E
PBS

Fig. 7

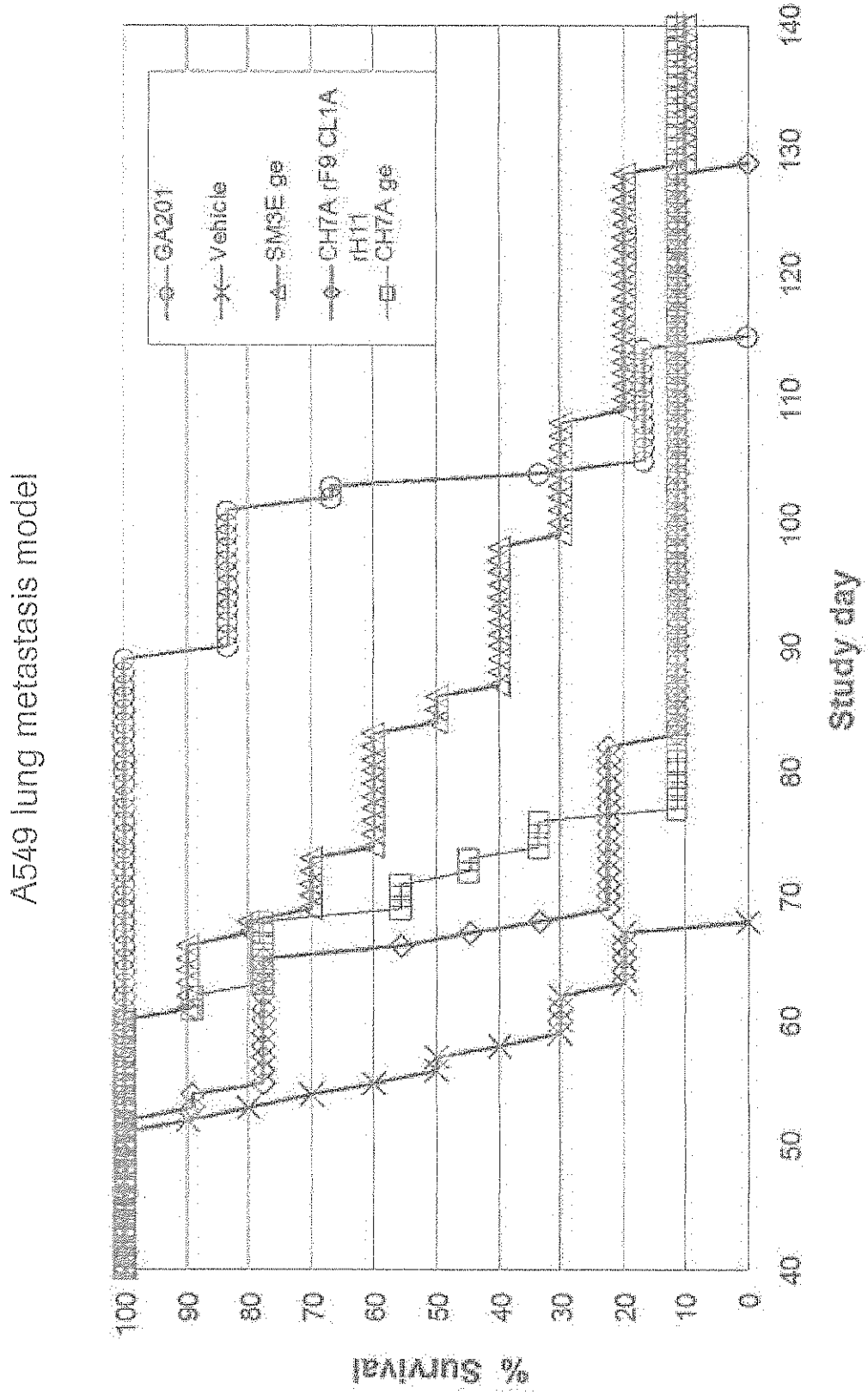

A549 lung metastasis model
% Survival
Study day
GA201
Vehicle
SM3E ge
CH7A rF9 CL1A
IH11
CH7A ge
100
90
80
70
60
50
40
30
20
10
0
40
50
60
70
80
90
100
110
120
130
140

Fig. 8

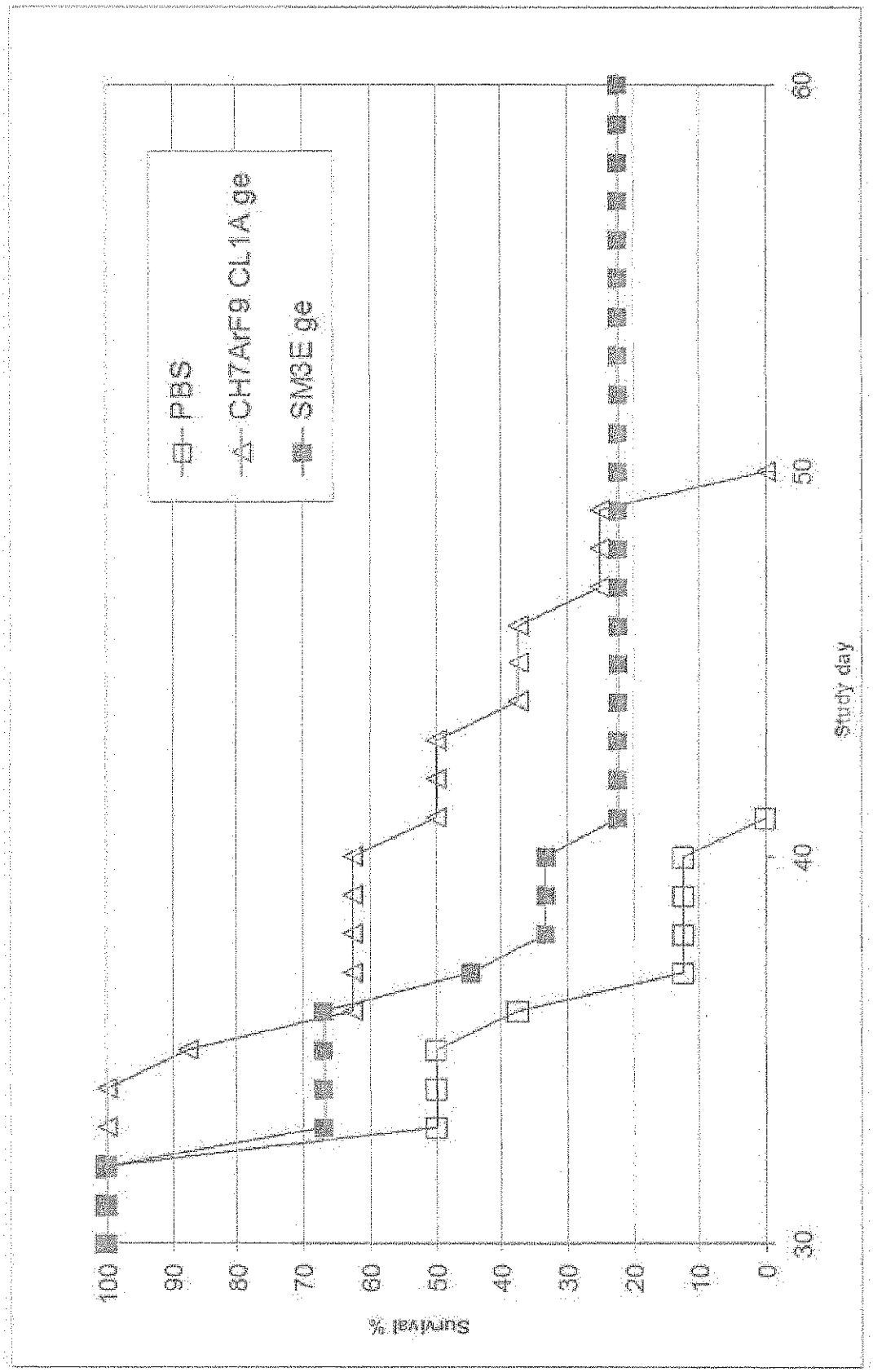

MKN45 liver metastasis model
PBS
CH7ArF9 CL1A ge
SM3E ge
Survival %
100
90
80
70
60
50
40
30
20
10
0
30
40
50
60
Study day

Fig 9

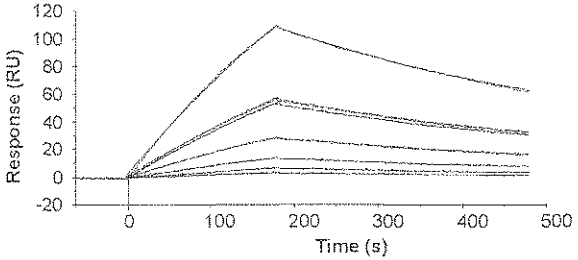
Sensorgram of anti-CEA Fabs

CH7A H4E9 CL1A

k_{on}: 0.527 x 10^3

k_{off}: 0.0027

KD: 518 nM

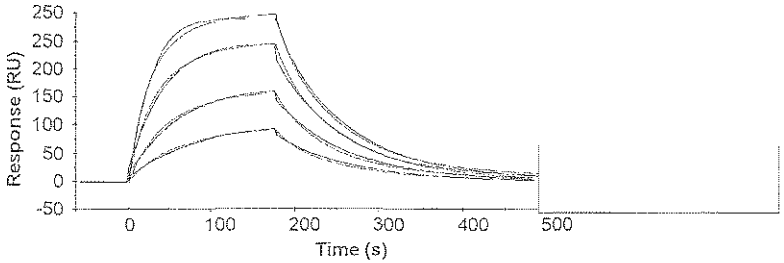


CH7A CL1A pAC18

k_{on}: 9.57 x 10^4

k_{off}: 0.0206

KD: 216 nM



CH7A H4E9 CL1A pAC18

k_{on}: 3.64 x 10^4

k_{off}: 0.0035

KD: 96 nM

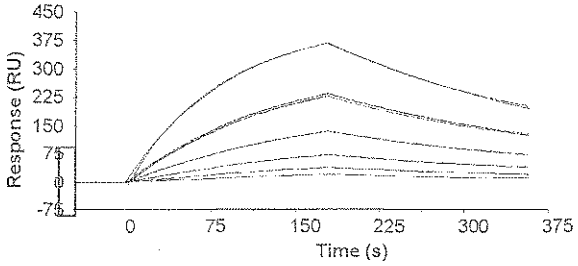


Fig. 10

randomization CDR1 and CDR2 VH (CH7A)

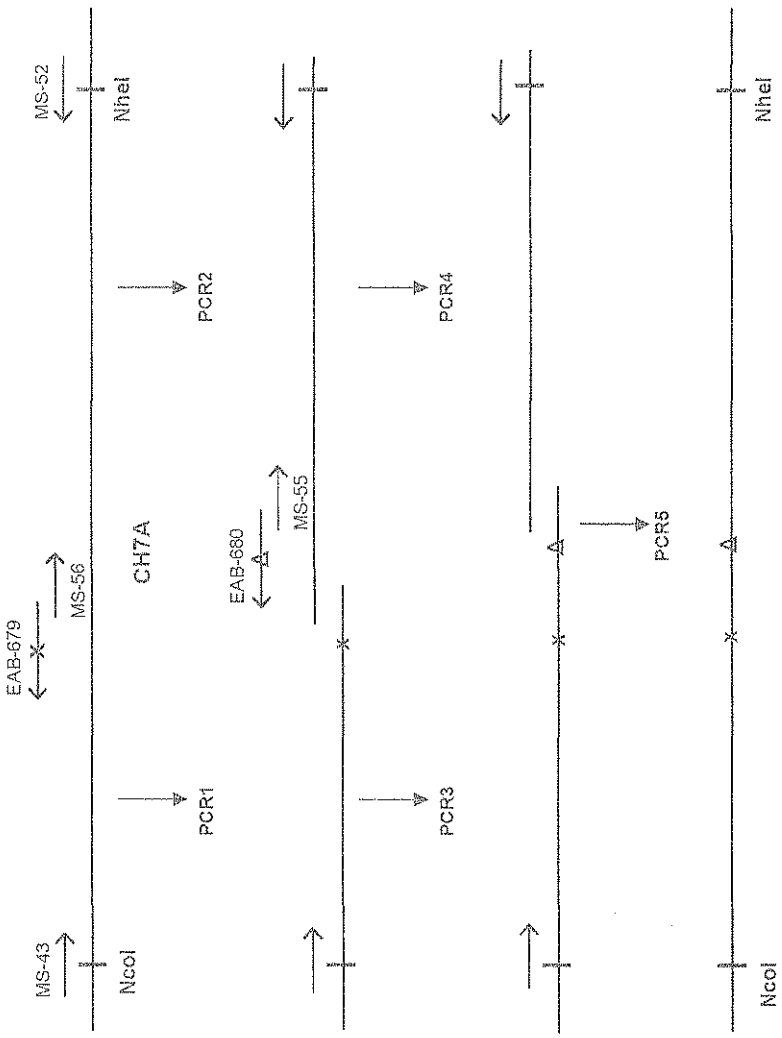


FIG. 11

randomization CDR1 and CDR2 VL(CL1A)

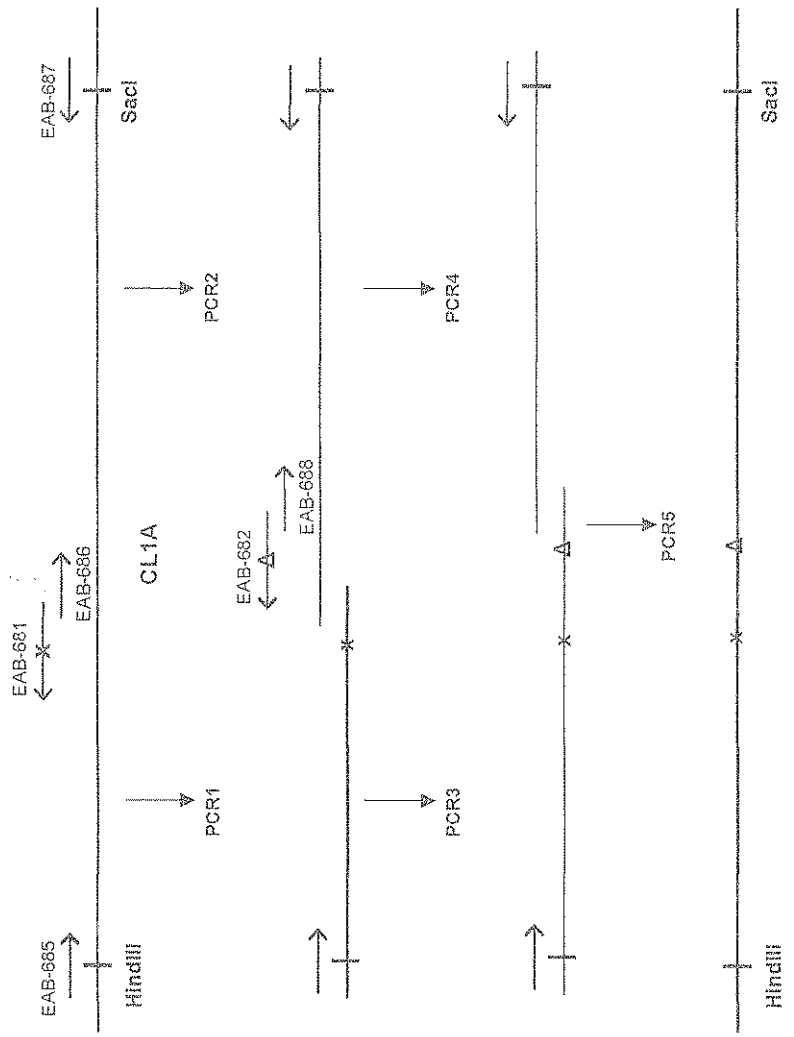


Fig. 12

randomization CDR3 VHH Qi17A3

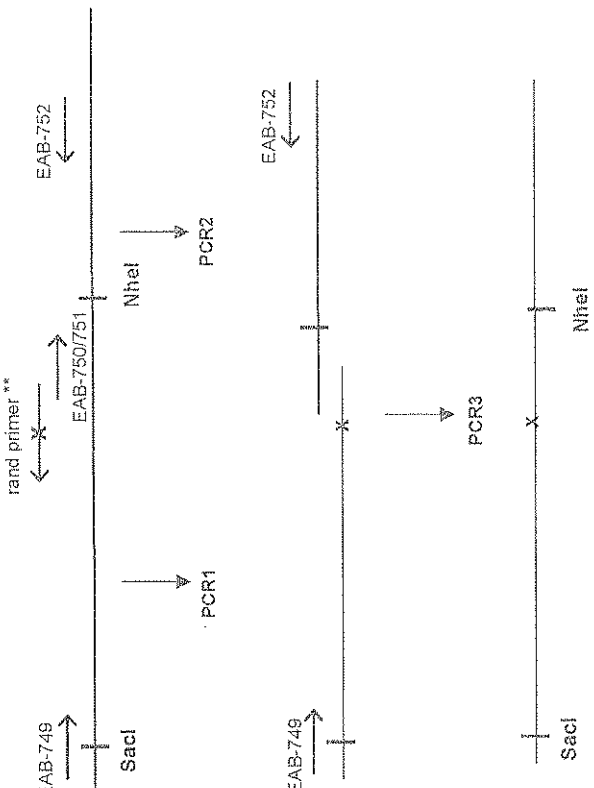


Fig. 13

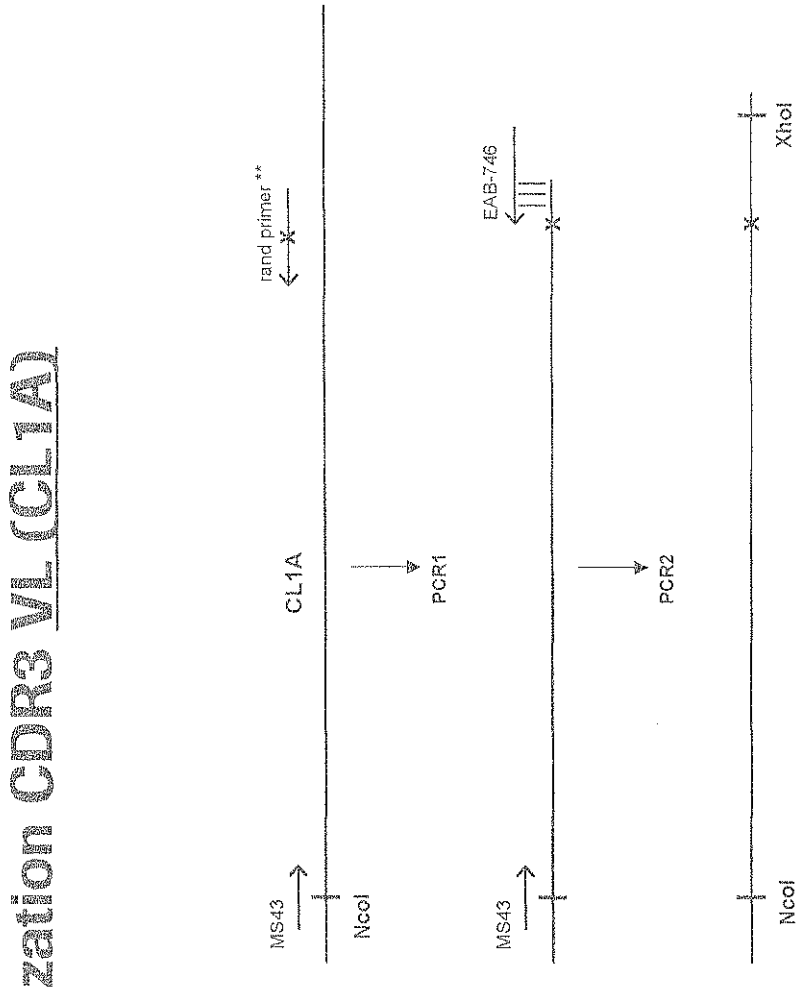
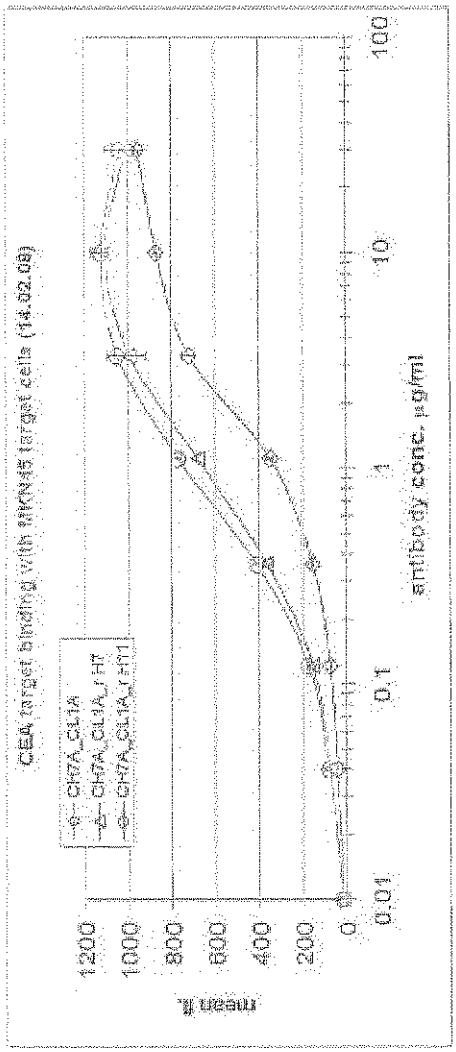

randomization CDR3 VL (CL1A)
CL1A
rand primer **
MS43
NcoI
PCR1
EAB-746
MS43
PCR2
NcoI
XhoI

Fig. 14


CEA target binding with MKN45 target cells (14.02.08)
CH7A_C1L1A
CH7A_C1L1A_HT
CH7A_C1L1A_HT1
mean fl.
1200
1000
800
600
400
200
0
0.01
0.1
1
10
100
antibody conc. µg/ml

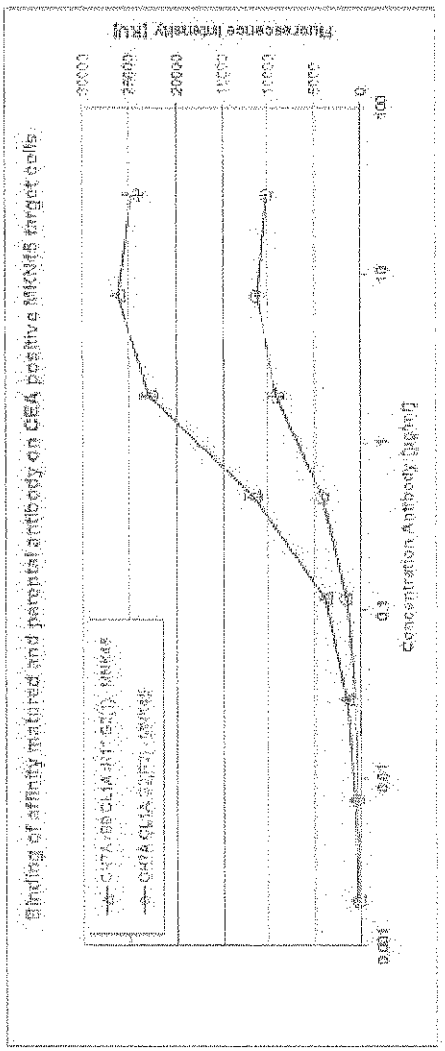

Binding of affinity matured and parental antibody on CEA positive MKN45 target cells
fluorescence intensity [FL1]
30000
25000
20000
15000
10000
5000
0
0.01
0.1
1
10
100
concentration Antibody [µg/ml]

FIG. 5

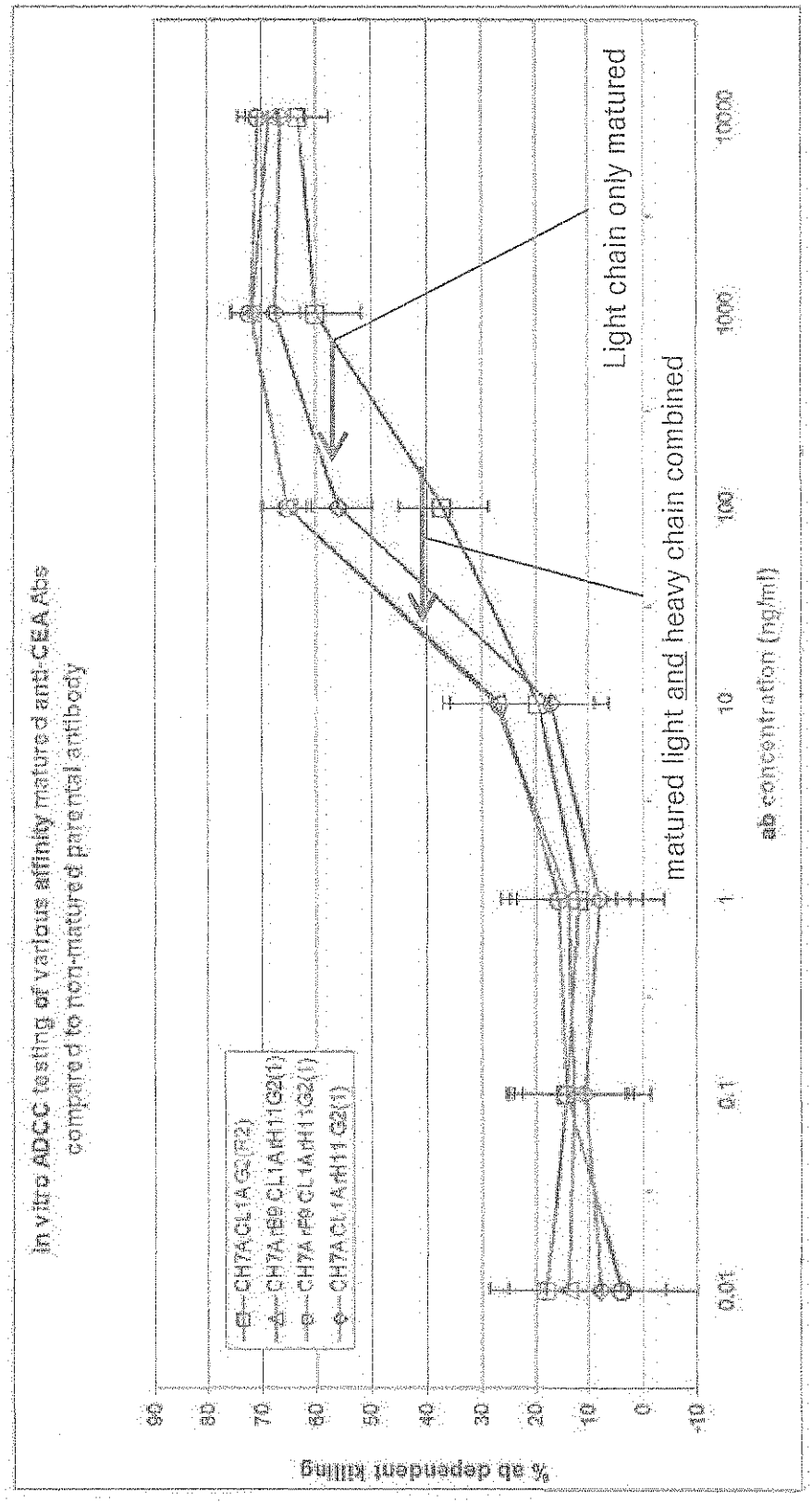

in vitro ADCC testing of various affinity matured anti-CEA Abs
compared to non-matured parental antibody
% ab dependent killing
ab concentration (ng/ml)
CH7ACL1AG4(F2)
CH7A1B9CL1AH11G2(1)
CH7A F9 CL1AH11G2(1)
CH7ACL1AH11G2(1)
Light chain only matured
matured light and heavy chain combined

FIG. 19

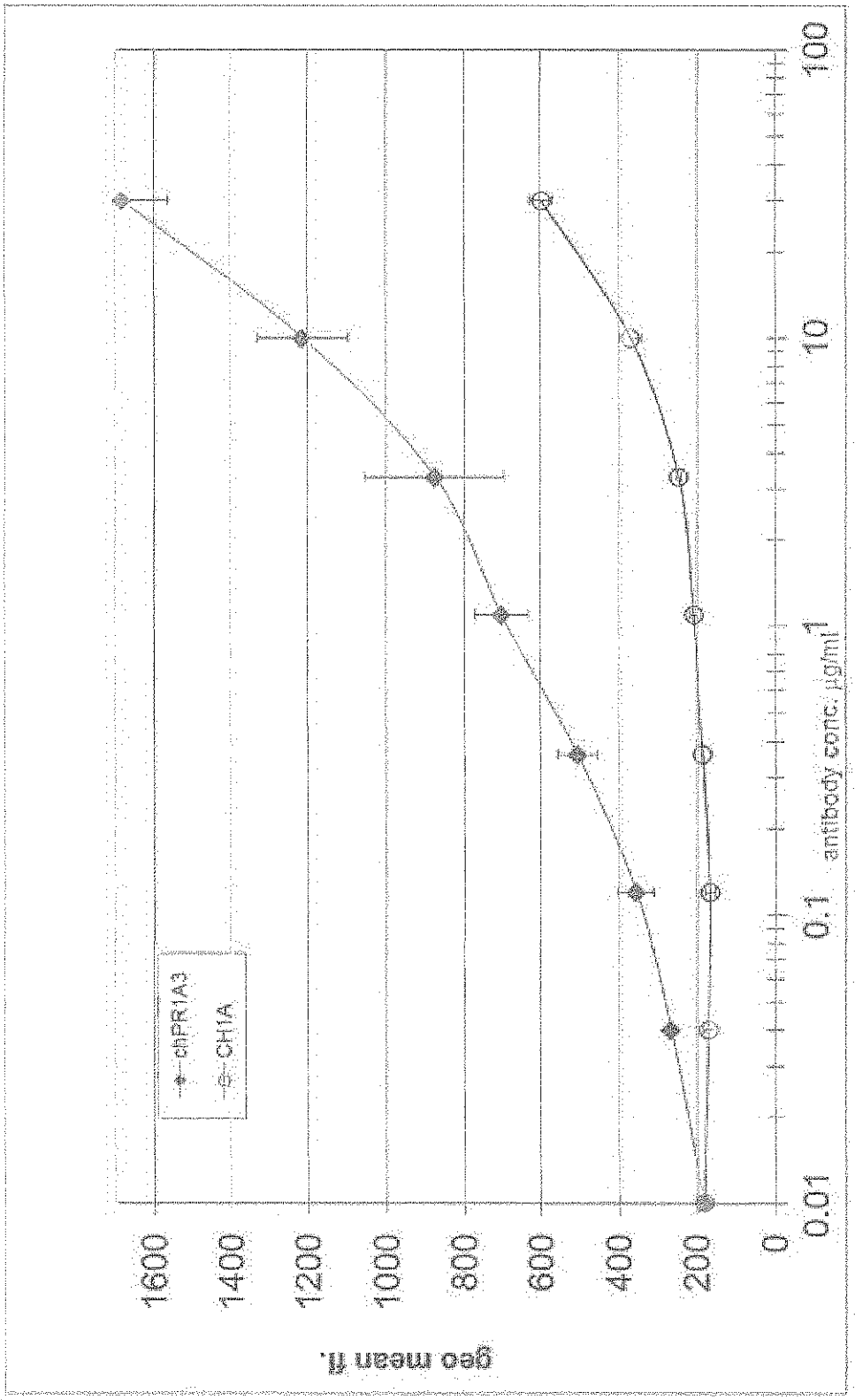

geo mean fl.
1600
1400
1200
1000
800
600
400
200
0
0.01
0.1
1
10
100
antibody conc. µg/ml
chPR1A3
CH1A

Fig. 17

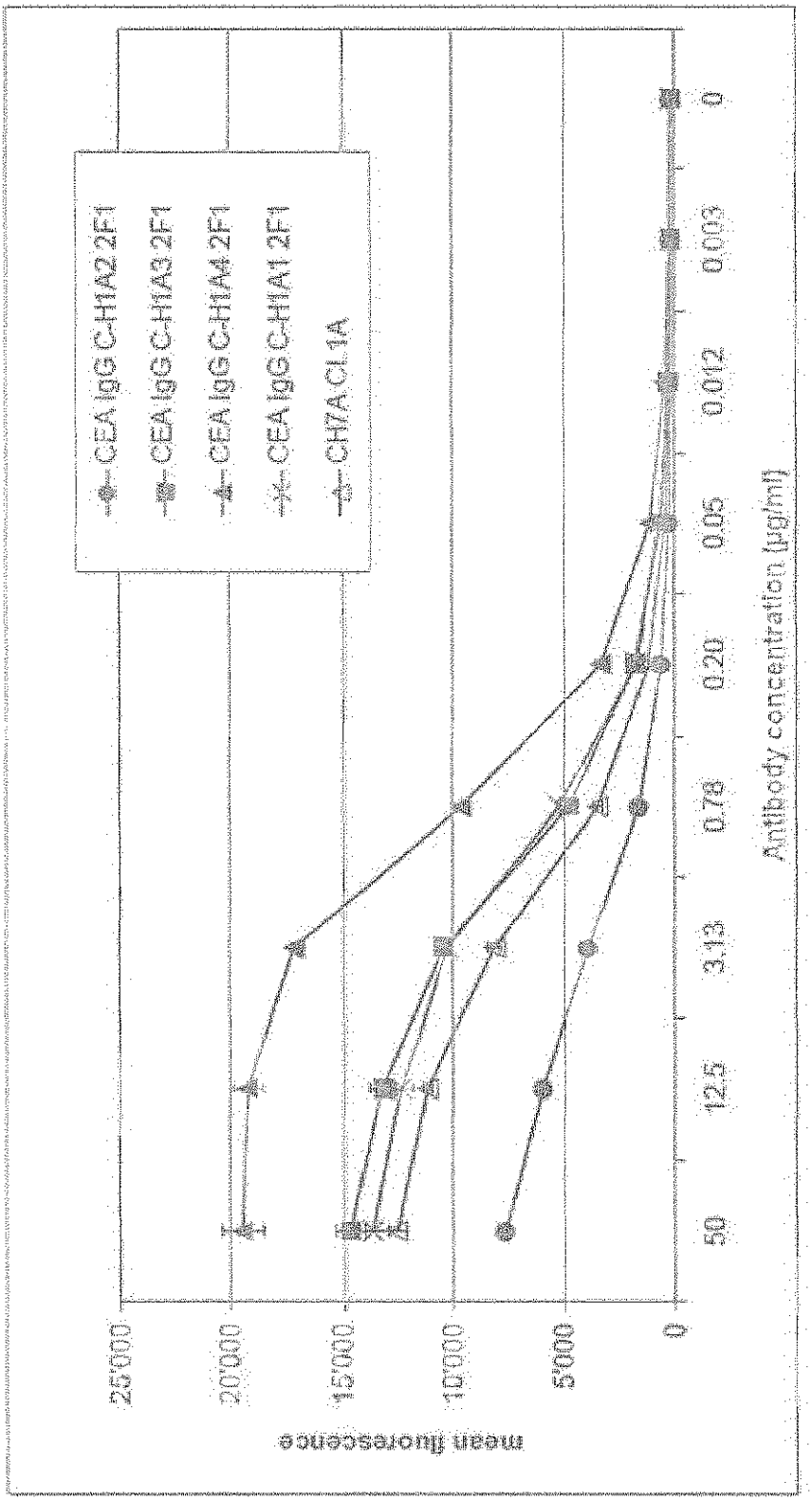

CEA IgG C-H1A2 2F1
CEA IgG C-H1A3 2F1
CEA IgG C-H1A4 2F1
CEA IgG C-H1A1 2F1
CH7A.CL1A
mean fluorescence
25000
20000
15000
10000
5000
0
50
12.5
3.13
0.78
0.20
0.05
0.012
0.003
0
Antibody concentration (µg/ml)

Fig. 18

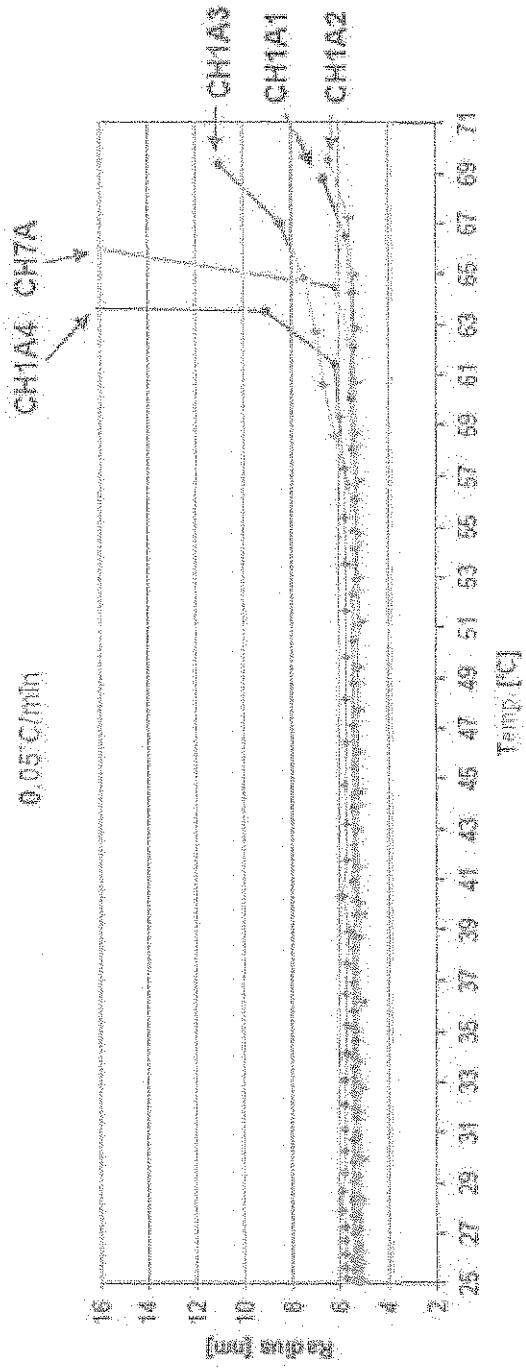
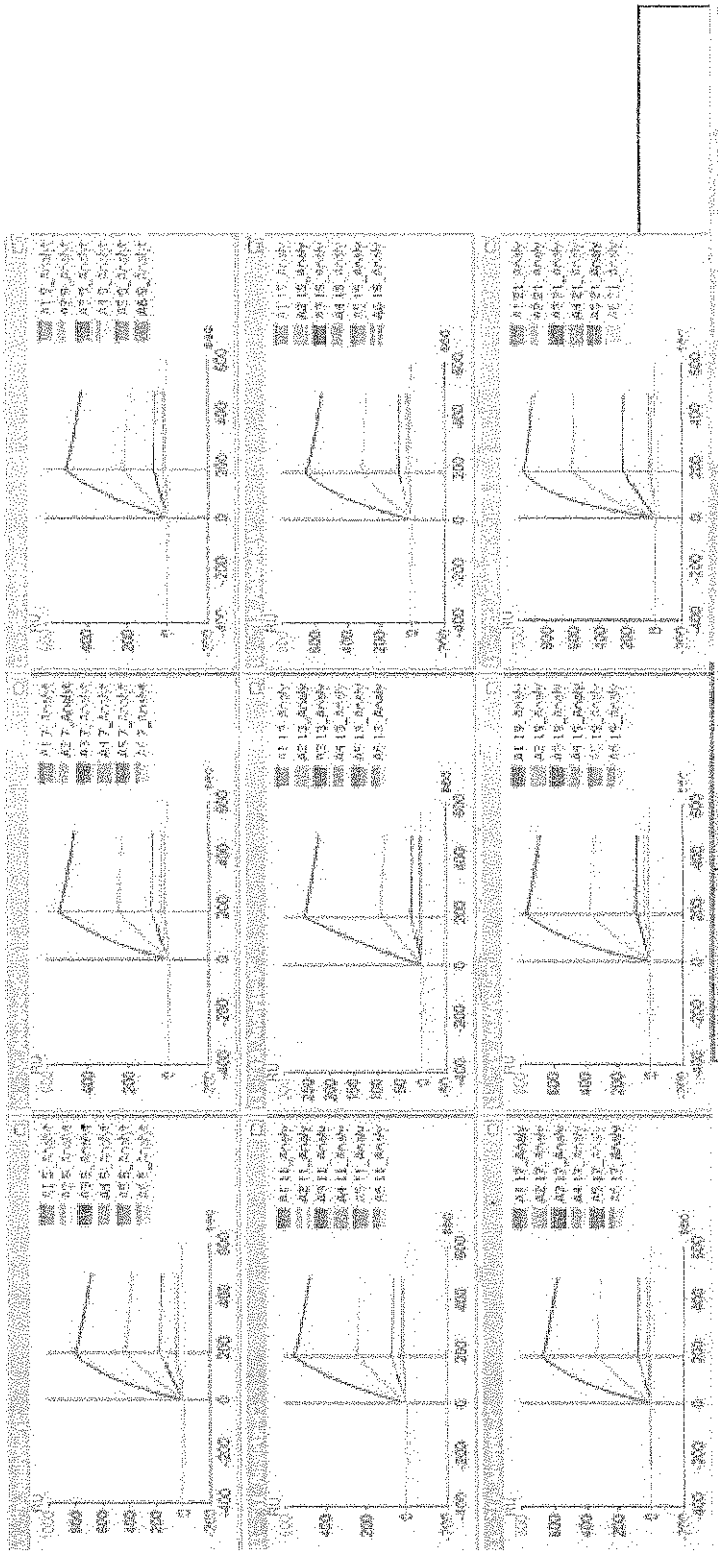


Fig. 9



Construct	Assay ID	Ka (M)	Kd (M)	KD (M)
CH1A1D	11 Analyte 4	$5.31x10^{4}$	$4.93x10^{-4}$	$9.28x10^{-9}$
CH1A1E	13 Analyte 5	$2.11x10^{4}$	$4.23x10^{-4}$	$2.00x10^{-8}$
CH1A1F	15 Analyte 6	$7.08x10^{4}$	$5.36x10^{-4}$	$7.58x10^{-9}$
CH1A1G	17 Analyte 7	$7.30x10^{4}$	$4.45x10^{-4}$	$6.10x10^{-9}$
CH1A1	19 Analyte 8	$8.19x10^{4}$	$3.47x10^{-4}$	$4.24x10^{-9}$
CH7A	21 Analyte 9	$1.22x10^{5}$	$2.24x10^{-4}$	$1.84x10^{-9}$
CH1A1A	5 Analyte 1	$8.18x10^{4}$	$4.83x10^{-4}$	$5.91x10^{-9}$
CH1A1B	7 Analyte 2	$5.37x10^{4}$	$4.78x10^{-4}$	$8.90x10^{-9}$
CH1A1C	9 Analyte 3	$4.49x10^{4}$	$5.84x10^{-4}$	$1.30x10^{-8}$

Fig. 20

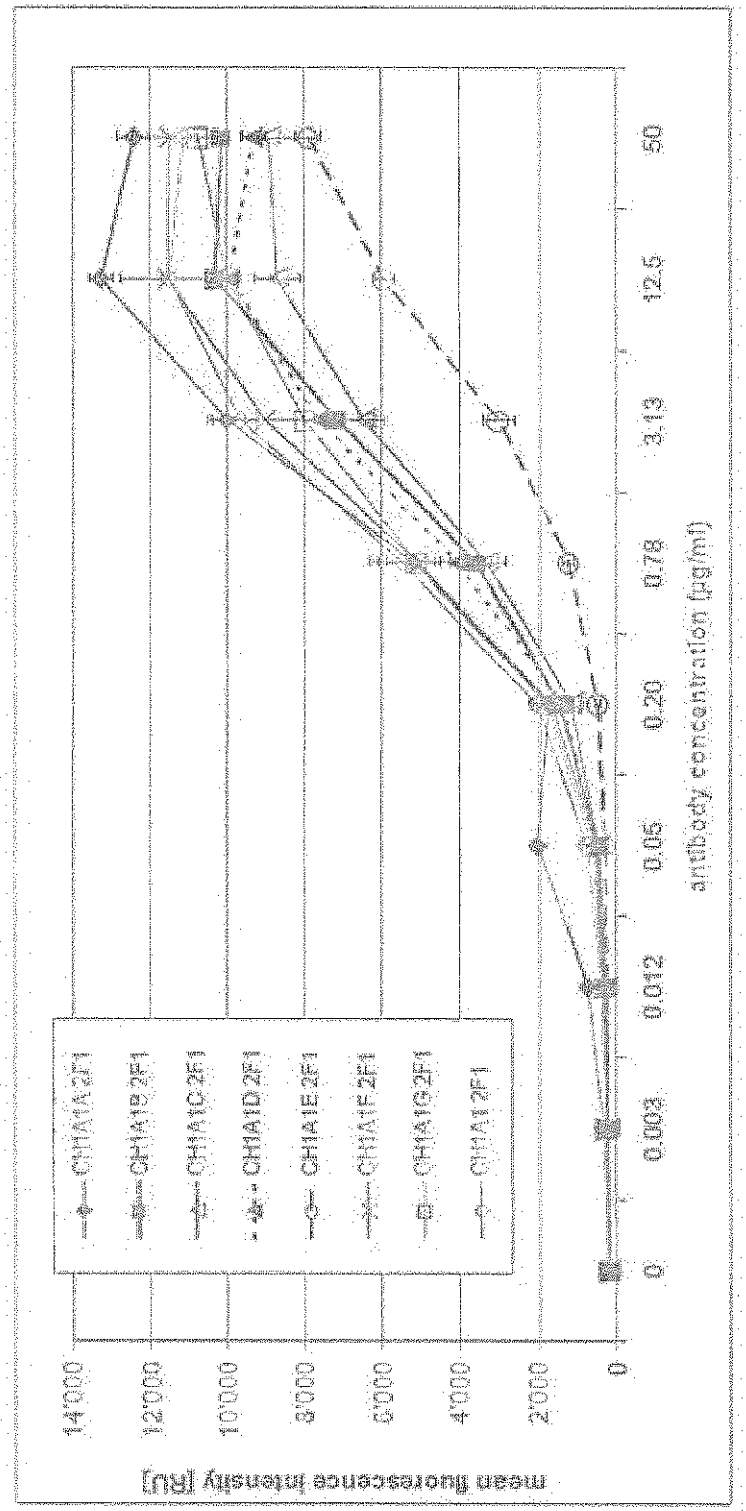
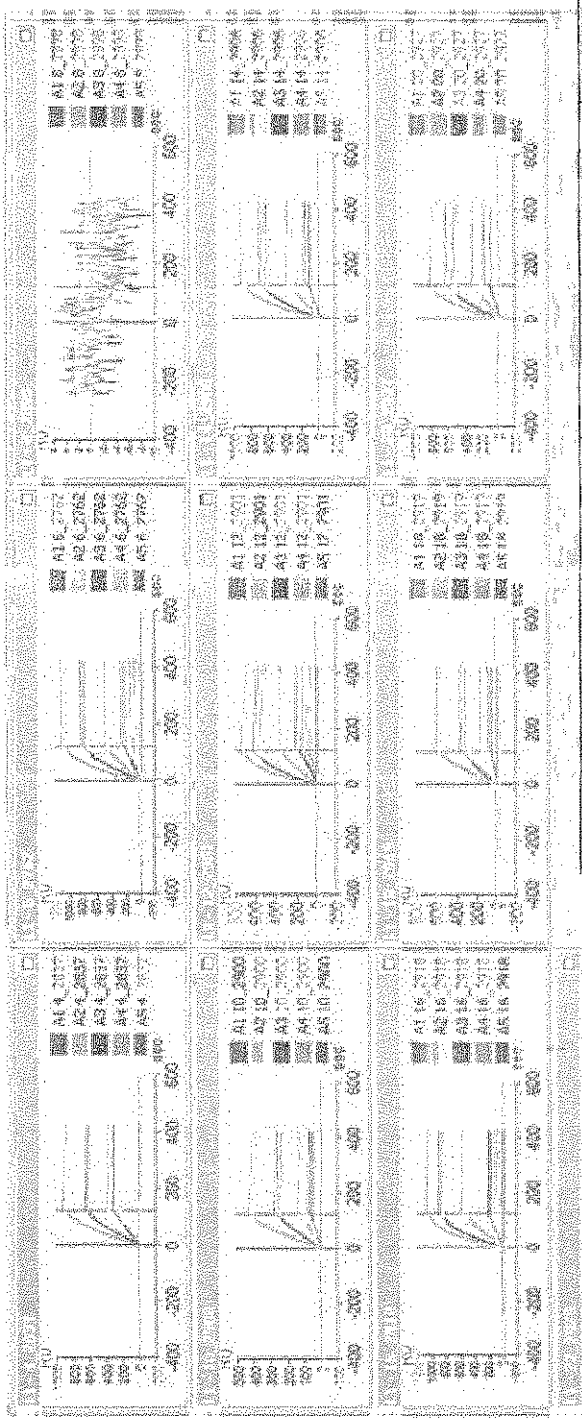

mean fluorescence intensity [RU]
14'000
12'000
10'000
8'000
6'000
4'000
2'000
0
0
0.002
0.012
0.05
0.20
0.78
3.13
12.5
50
antibody concentration (µg/ml)
CH1A1A 2F1
CH1A1B 2F1
CH1A1C 2F1
CH1A1D 2F1
CH1A1E 2F1
CH1A1F 2F1
CH1A1G 2F1
CH1A1I 2F1

Fig. 21



Construct	Assay ID	Ka (M)	Kd (M)	KD (M)
CH7A (V101F)	2900	$5.94x10^{4}$	$1.89x10^{-4}$	$3.18x10^{-9}$
CH7A (E102Q)	2901	$1.98x10^{5}$	$3.24x10^{-4}$	$1.63x10^{-9}$
CH7A (Y98A)	2906	$1.32x10^{5}$	$6.86x10^{-5}$	$5.20x10^{-10}$
CH7A (Y98A/D99Y)	2918	$2.36x10^{5}$	$4.40x10^{-5}$	$1.86x10^{-10}$
CH7A (A103T)	2919	$2.51x10^{4}$	$7.20x10^{-5}$	$2.87x10^{-9}$
CH7A (D99Y)	2927	$1.14x10^{5}$	$1.97x10^{-4}$	$1.73x10^{-9}$
CH7A (D99H)	2928	$8.65x10^{4}$	$1.95x10^{-4}$	$2.25x10^{-9}$
CH7A CL1A 2F1	2837	$1.32x10^{5}$	$1.41x10^{-4}$	$1.07x10^{-9}$
5HF12 2F1	2762	$1.52x10^{5}$	$1.94x10^{-5}$	$1.28x10^{-10}$
CH7A (W95Y)	2898	$5.61x10^{-4}$	109.73	$1.95 x10^{5}$

Fig. 22

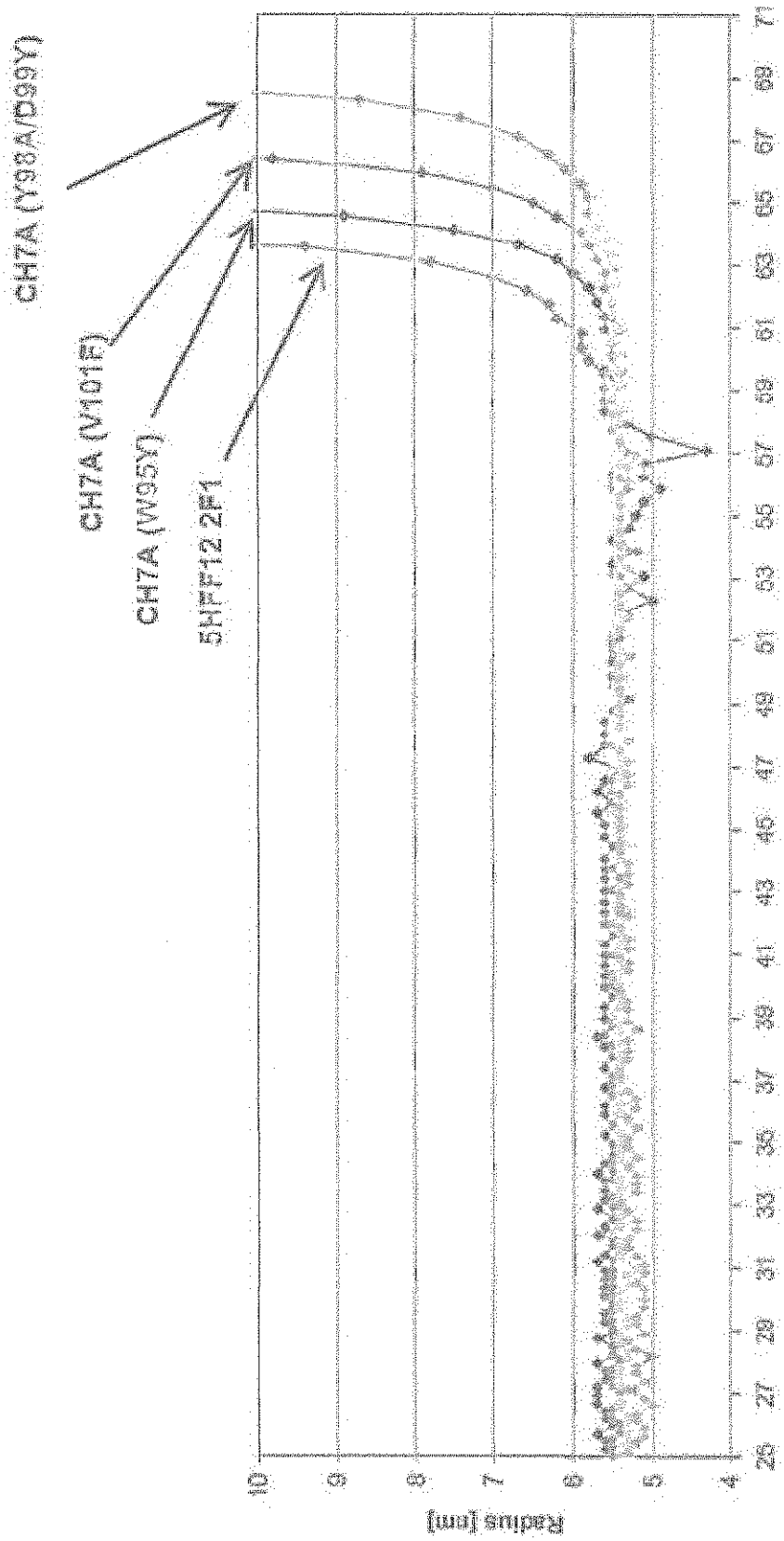


Fig. 23

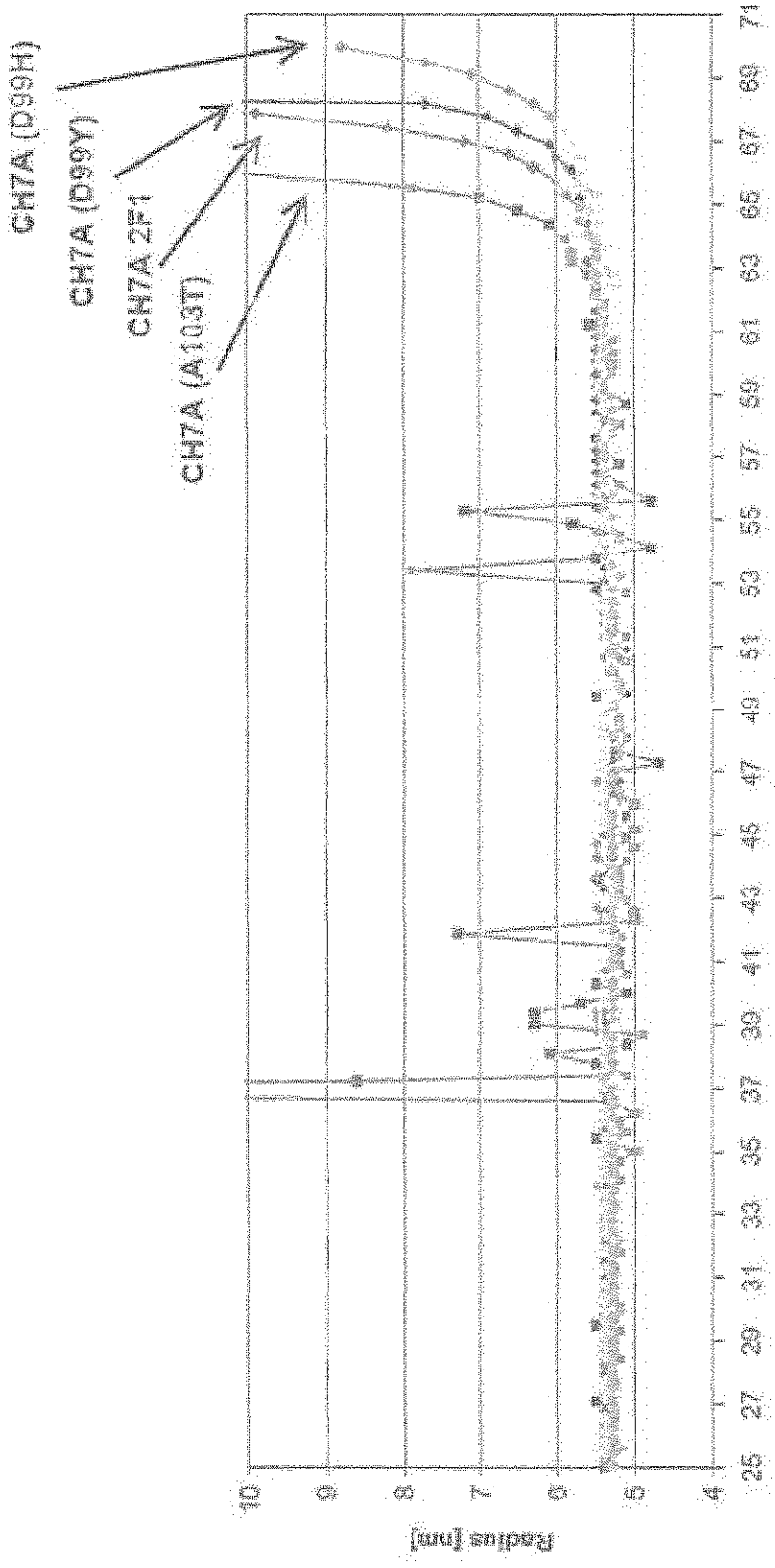
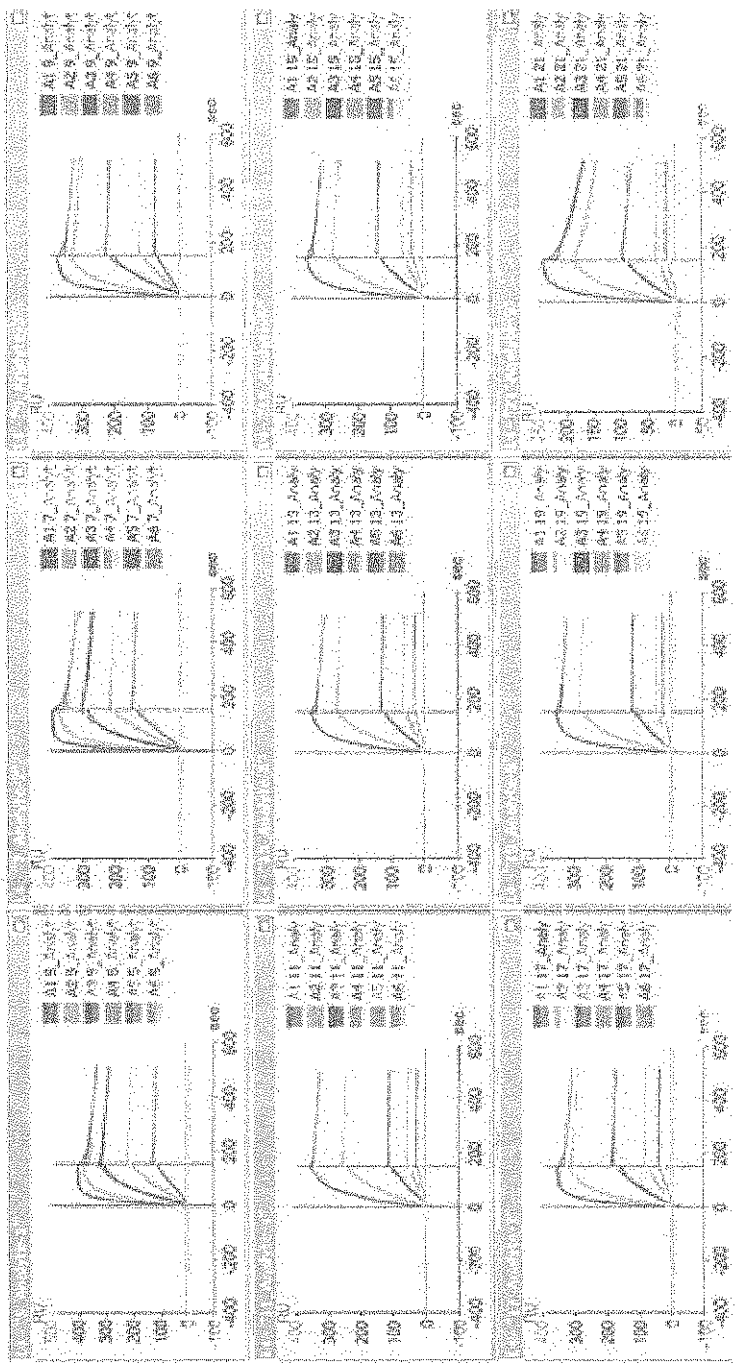


Fig. 24



Construct	Assay ID	Ka (M)	Kd (M)	KD (M)
CH1B 5L1A10 2F1	11 Analyte 4	$2.21x10^{5}$	$1.54x10^{-4}$	$6.98x10^{-10}$
CH1A1A 5L1A10 2F1	13 Analyte 5	$2.80x10^{5}$	$2.18x10^{-4}$	$7.80x10^{-10}$
CH1A1B 5L1A10 2F1	15 Analyte 6	$3.30x10^{5}$	$2.47x10^{-4}$	$7.47x10^{-10}$
CH7A (Y98A/D99Y) 2F1	17 Analyte 7	$4.81x10^{5}$	$2.24x10^{-4}$	$4.65x10^{-10}$
5L1A10 2F1	19 Analyte 8	$3.36x10^{5}$	$1.78x10^{-4}$	$5.29x10^{-10}$
CH7A 2F1	21 Analyte 9	$3.69x10^{5}$	$7.27x10^{-4}$	$1.97x10^{-9}$
CH1A1A (Y98A/D99Y) 2F1	5 Analyte 1	$6.28x10^{5}$	$3.37x10^{-4}$	$5.37x10^{-10}$
CH1A1B (Y98A/D99Y) 2F1	7 Analyte 2	$7.11x10^{5}$	$3.61x10^{-4}$	$5.07x10^{-10}$
CH1B (Y98A/D99Y) 2F1	9 Analyte 3	$4.19x10^{5}$	$2.45x10^{-4}$	$5.85x10^{-10}$

Fig. 25

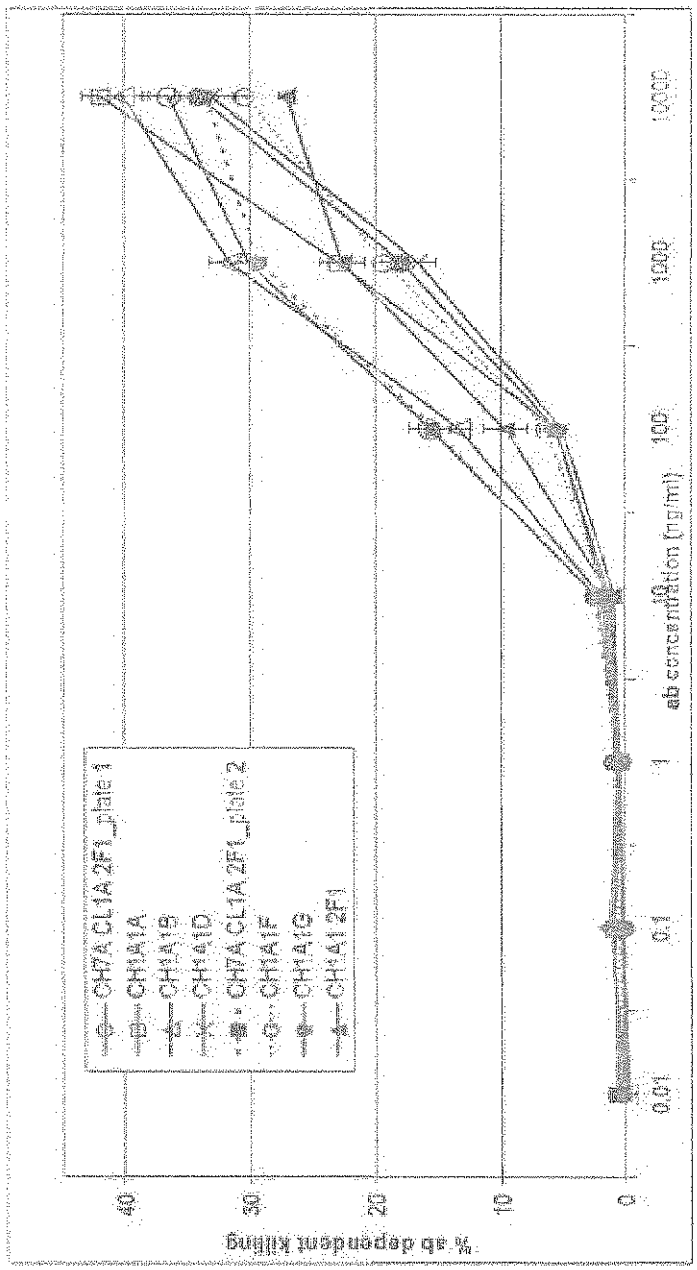

% ab dependent killing
40
30
20
10
0
0.01
0.1
1
10
100
1000
10000
ab concentration (ng/ml)
CH7A CL1A 2F1_plate 1
CH1A1A
CH1A1B
CH1A1D
CH7A CL1A 2F1_plate 2
CH1A1F
CH1A1G
CH1A1 2F1

Fig. 2G

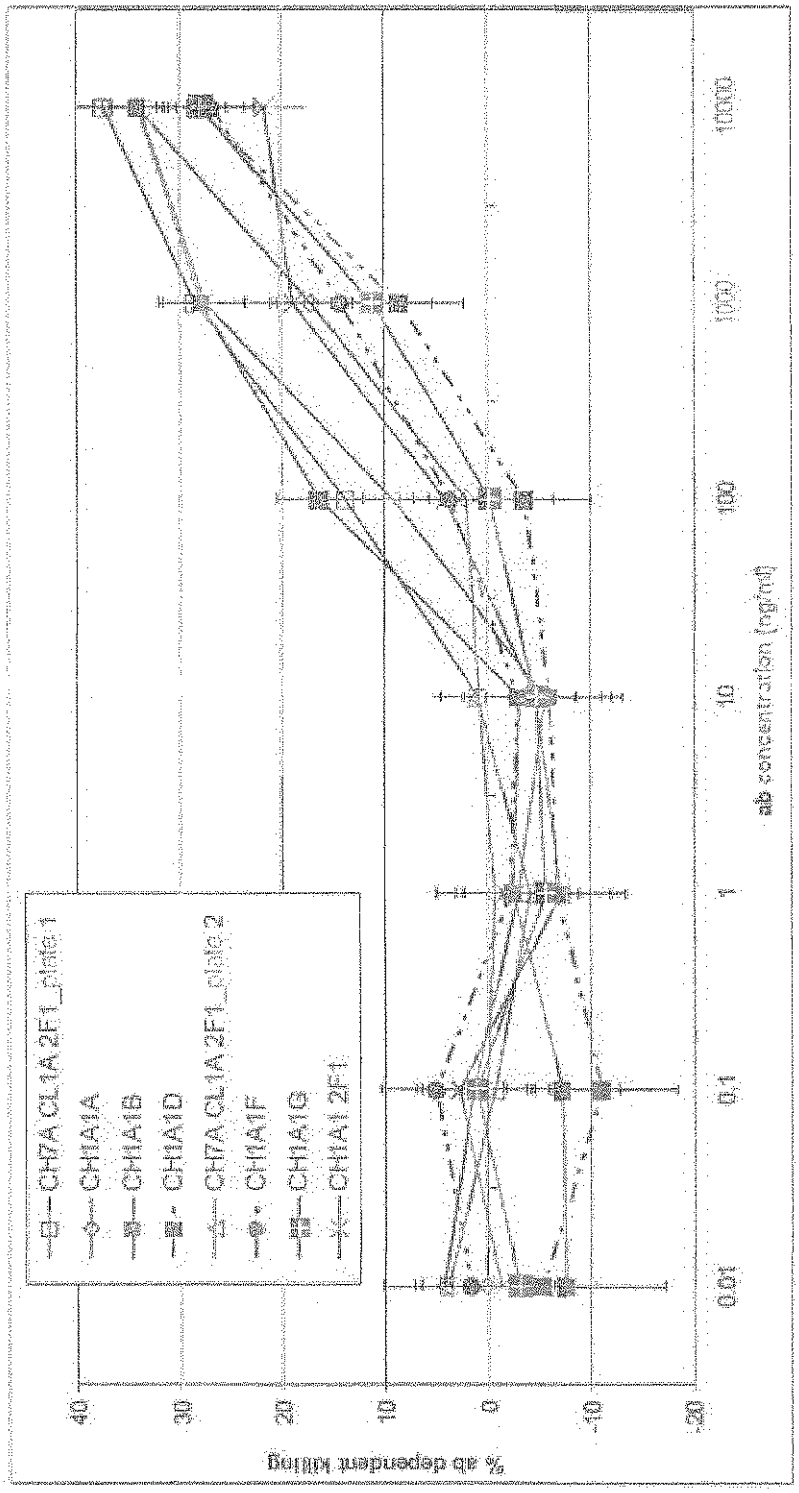

CH7A CL1A 2F1_plate 1
CH1A1A
CH1A1B
CH1A1D
CH7A CL1A 2F1_plate 2
CH1A1F
CH1A1G
CH1A1 2F1
% ab dependent killing
40
30
20
10
0
-10
-20
0.01
0.1
1
10
100
1000
ab concentration (ng/ml)

Fig. 27

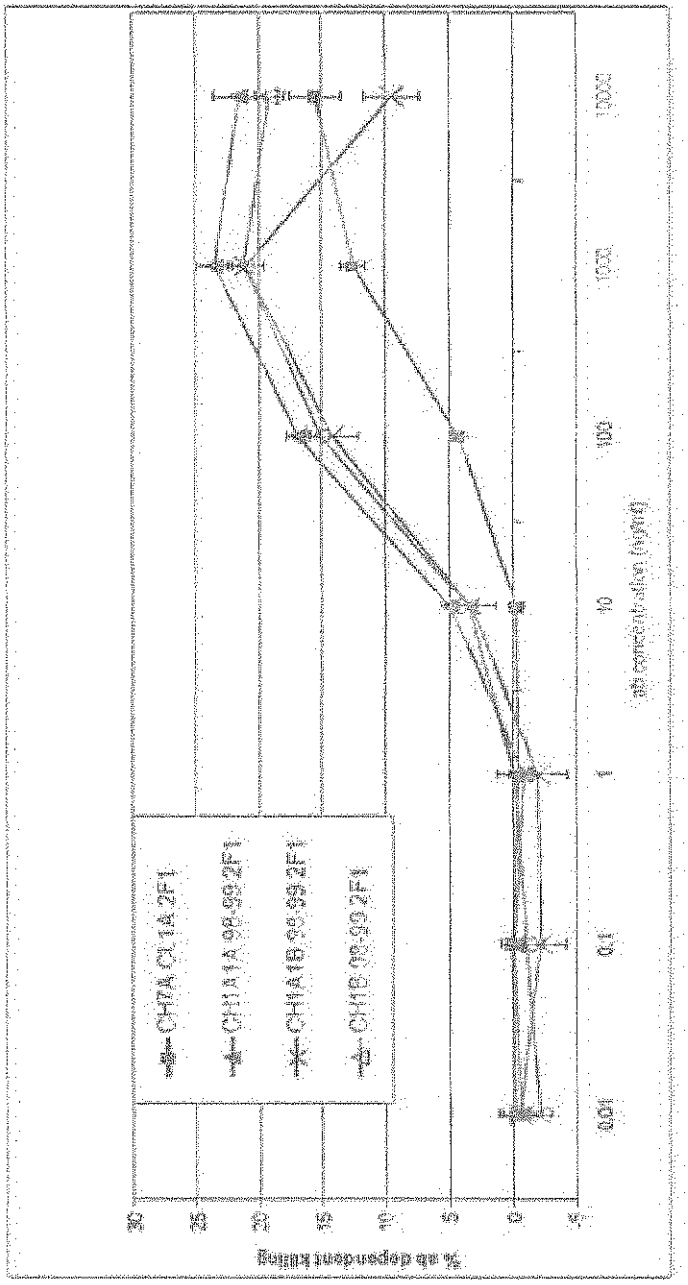

% ab dependent killing
CHTA C11A 2F1
CHTA C11A 99-2F1
CHTA D-99-2F1
CHTB 99-2F1
Ab concentration (nM)

Fig. 2B

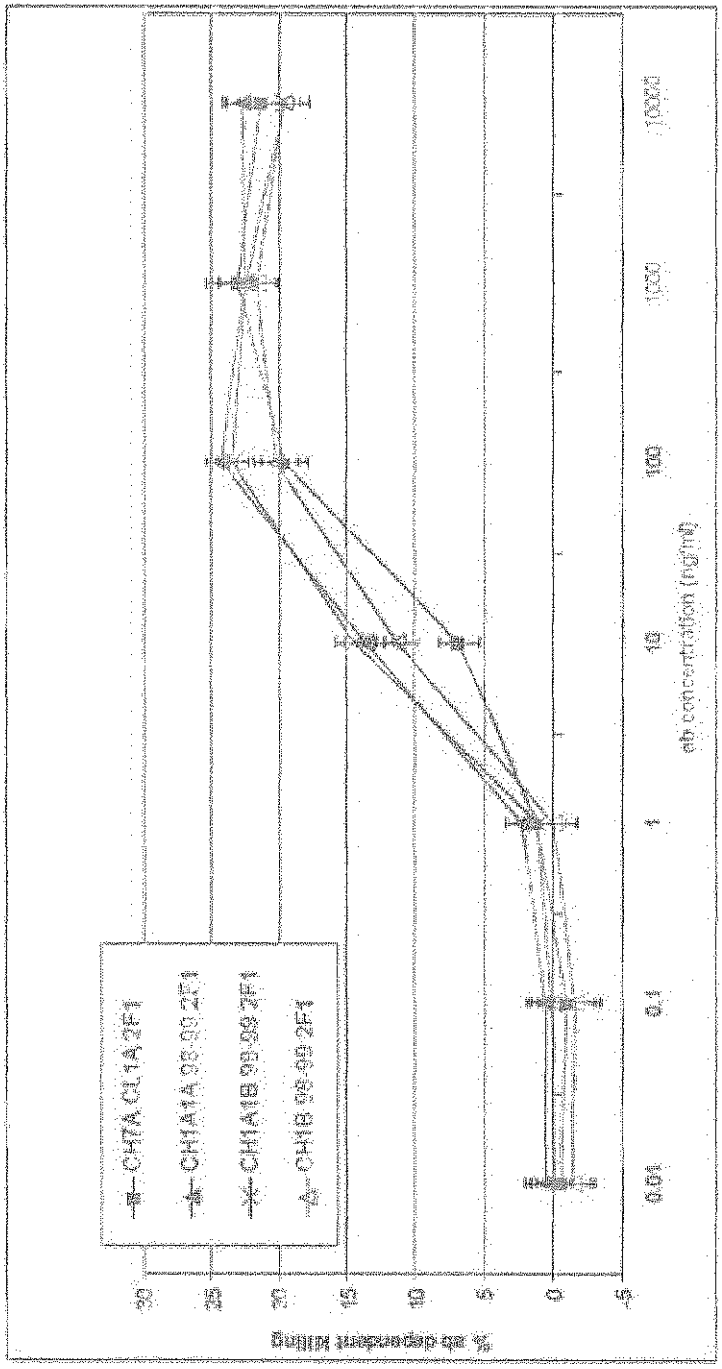

CH7A.C1.1.2FT
CH1A1A 05.00.2F1
CH1A1B 05.08.2F1
CH1B 05.09.2FT
% ab dependent killing
ab concentration (ng/ml)
0.01
0.1
1
10
100
1000
10000

Fig. 2g

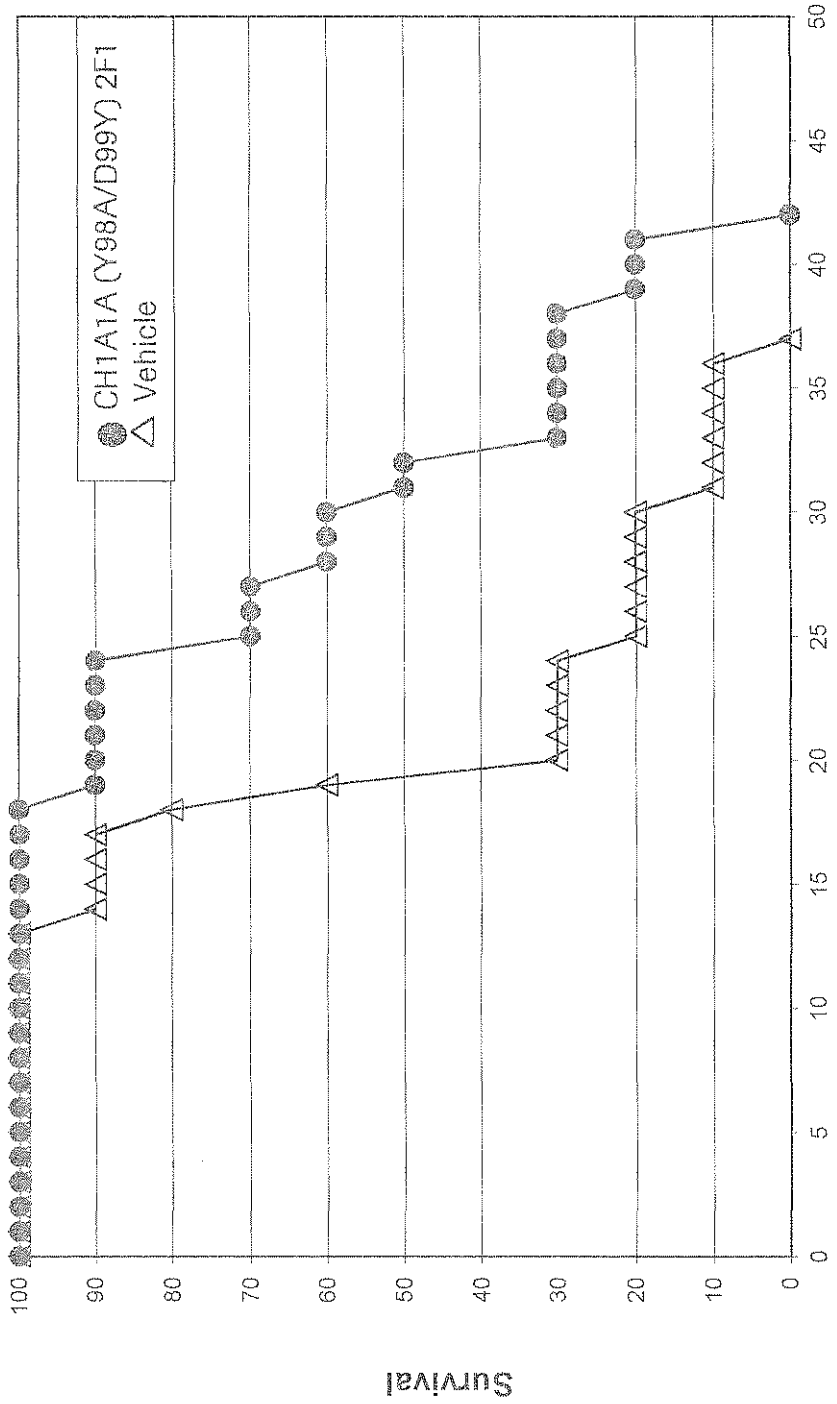

CH1A1A (Y98A/D99Y) 2F1
Vehicle
Survival
Study day
0
10
20
30
40
50
60
70
80
90
100
0
5
10
15
20
25
30
35
40
45
50

Fig. 30

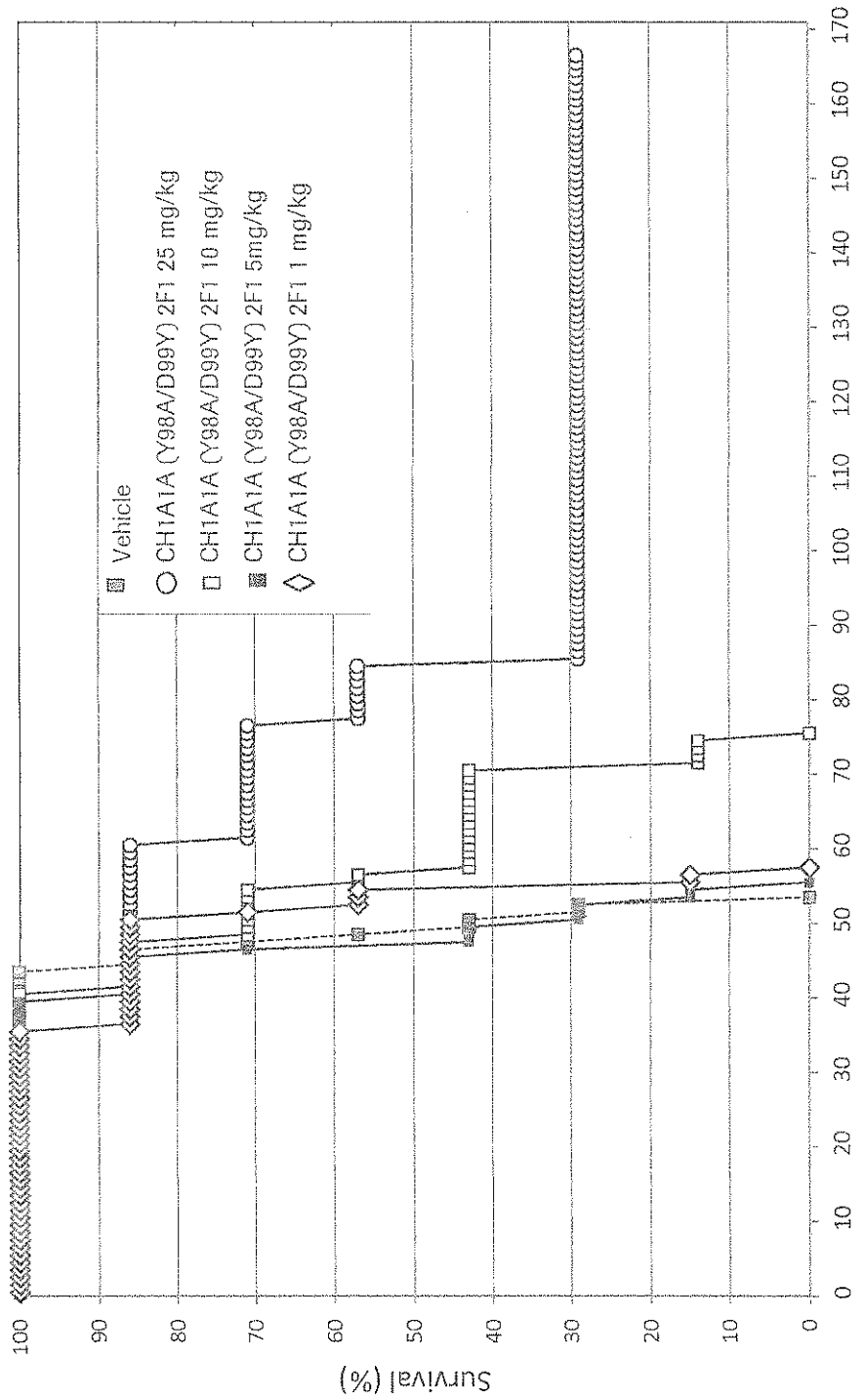

Survival (%)
100
90
80
70
60
50
40
30
20
10
0
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170
Study day
Vehicle
CH1A1A (Y98A/D99Y) 2F1 25 mg/kg
CH1A1A (Y98A/D99Y) 2F1 10 mg/kg
CH1A1A (Y98A/D99Y) 2F1 5mg/kg
CH1A1A (Y98A/D99Y) 2F1 1 mg/kg

Fig 31

CDR		Amino Acid Sequence	SEQ ID NO
Heavy Chain CDR1	Kabat	EFGMN	1
		EYGMN	2
		EYSMN	3
		EFGMS	5
	Chothia	GYTFTEF	6
		GYTFTEY	7
	AbM	GYTFTEFGMN	8
		GYTFTEYGMN	9
		GYTFTEYSMN	10
		GYTFTEFGMS	12
Heavy Chain CDR2	Kabat	WINTKTGEATYVEEFKG	13
		WINTKTGEATYIEEFKG	14
		WINTKSGEATYVEEFKG	15
		YINTKNGEANYVEEFKG	16
		WINTKNGEATYIEEFKG	17
	Chothia	NTKTGEAT	18
		NTKSGEAT	19
		NTKNGEAN	20
	AbM	WINTKTGEAT	21
		WINTKSGEAT	22
		YINTKNGEAN	23
		WINTKNGEAT	24
Heavy Chain CDR3	Kabat Chothia and AbM	WDFYDYVEAMDY	25
		WDFYHYVEAMDY	26
		WDFVDYVEAMDY	27
		WDFYWYVEAMDY	28
		WDAFEYVKALDY	29
		WDFFEYFKTMDY	30
		WDFFYYVQTMDY	31
		WDFSYYVEAMDY	32
		WDFAHYFQTMDY	33
		WDFAYYFQTMDY	34
		WDFAYYLEAMDY	35

CDR	Amino Acid Sequence	SEQ ID NO
Light Chain CDR1	KASQNVGTNVA	36
	KASANVGNNVA	37
	KASKNVGTNVA	38
	KASAAVGTYVA	39
	KASQYASTNVA	40
	KASHNVGTNVA	41
	KASQIMGPNVA	42
	KASQIVGTNVA	43
	KASQKVLTNVA	44
	KASQTVSANVA	45
Light Chain CDR2	SASYRYS	46
	YLASNLSG	47
	YLASYPQI	48
	YSASYRKR	49
	YWASYRYS	50
	YSASHRYS	51
	YLASYHES	52
	YSASHRPS	53
	YLASYRYS	54
	YLASYRYR	55
Light Chain CDR3	HQYYTYPLFT	56

Fig. 32

SEQ ID NO:	LIGHT CHAIN CONSTRUCT	AMINO ACID SEQUENCE
207	pAC21 (3A1)	DIQMTQSPSSLSASVGDRVTITCKASANVGNNVAWYQQKPGKAPKLLIYLASNRSGGVPSRFSG SGSGTDFTLTISSLQPEDFATYYCHQYYTYPLFTFGQGTKLEIKRT
208	pAC19 (2C6)	DIQMTQSPSSLSASVGDRVTITCKASKNVGTNVAWYQQKPGKAPKPLIYLASYPQIGVPSRFSGS GSGTDFTLTISSLQPEDFATYYCHQYYTYPLFTFGQGTKLEIKRT
209	pAC18 (2F1)	DIQMTQSPSSLSASVGDRVTITCKASAAVGTYVAWYQQKPGKAPKLLIYSASYRKRGVPSRFSGS GSGTDFTLTISSLQPEDFATYYCHQYYTYPLFTFGQGTKLEIKRT
210	pAC23 (2F11)	DIQMTQSPSSLSASVGDRVTITCKASQIASTNVAWYQQKPGKAPKLLIYWASYRYSGVPSRFSGS GSGTDFTLTISSLQPEDFATYYCHQYYTYPLFTFGQGTKLEIKRT
211	H4E9 light chain	DIQMTQSPSSLSASVGDRVTITCKASQNVGTNVAWYQQKPGKAPKPLIYSASYRYSGVPSRFSG SGSGTDFTLTISSLQPEDFATYYCHQYYTYPLFTFGQGTKLEIKRT
212	L2D2	DIQMTQSPSSLSASVGDRVTITCKASHNVGTNVAWYQQKPGKAPKLLIYSASHRYSGVPSRFSG SGSGTDFTLTISSLQPEDFATYYCHQYYTYPLFTFGQGTKLEIKRT
213	pAC6 (C1)	DIQMTQSPSSLSASVGDRVTITCKASQIMGPNVAWYQQKPGKAPKLLIYLASYHESGVPSRFSGS GSGTDFTLTISSLQPEDFATYYCHQYYTYPLFTFGQGTKLEIKRT
214	pAC7 (E10)	DIQMTQSPSSLSASVGDRVTITCKASQIVGTNVAWYQQKPGKAPKLLIYSASHRPSGVPSRFSGS GSGTDFTLTISSLQPEDFATYYCHQYYTYPLFTFGQGTKLEIKRT
215	pAC12 (H7)	DIQMTQSPSSLSASVGDRVTITCKASQKVLTNVAWYQQKPGKAPKLLIYLASYRYSGVPSRFSGS GSGTDFTLTISSLQPEDFATYYCHQYYTYPLFTFGQGTKLEIKRT
216	pAC13 (H11)	DIQMTQSPSSLSASVGDRVTITCKASQTVSANVAWYQQKPGKAPKLLIYLASYRYRGVPSRFSGS GSGTDFTLTISSLQPEDFATYYCHQYYTYPLFTFGQGTKLEIKRT

Fig. 33

SEQ ID NO:	CDR-H3 (randomized residues are underlined selected residues in bold)	Affinity (determined by Biacore)	Construct
25	WDFYDYVEAMDY	3681 nM	PMS22
26	WDFYHYVEAMDY	586 nM	1C8
27	WDFVDYVEAMDY	1893 nM	3E1
28	WDFYWYVEAMDY	746 nM	2D7
33	WDFAHYFQTMDY	59 nM	Affinity Matured CDRH-3
34	WDFAYYFQTMD	44 nM	Affinity Matured CDRH-3
35	WDFAYYLEAMD	69 nM	Affinity Matured CDRH-3
29	WDAFEYVKALDY	26 nM	H3 Full (5) 19
30	WDFFEYFKTMDY	51 nM	H3 Full (5) 8
31	WDFFYYVQTMDY	81 nM	H3 Full (5) 28
33	WDFSYYVEAMDY	132 nM	H3 Full (5) 27
	CDR-H1 and CDR-H2		
1 and 13	EFGMN and WINTKTGEATYVEEFKG	3681 nM	pMS22
1 and 14	EFGMN and WINTKTGEATYIEEFKG	402 nM	H4E9
1 and 15	EFGMN and WINTKSGEATYVEEFKG		pAC14 (B9)
2 and 15	EYGMN and WINTKSGEATYVEEFKG		pAC15 (F9)
3 and 16	EYSMN and YINTKNGEANYVEEFKG		H1/H2 (5) 2

Fig. 34A

SEQ ID NO:	CDR-H3 (randomized residues are underlined selected residues in bold)	Affinity (determined by Biacore)	Construct
2 and 17	EYGMN and WINTKNGEATYIEEFKG		H1/H2 (5) 11
1 and 16	EFGMN and YINTKNGEANYVEEFKG		H1/H2 (5) 13
2 and 16	EYGMN and YINTKNGEANYVEEFKG		H1/H2 (5) 14
5 and 13	EFGMS and WINTKTGEATYVEEFKG	26 nM	H3 Full (5) 19
	CDR-L1 and CDR-L2		
36 and 46	QNVGTN and YSASYRYS	3681 nM	pMS22
37 and 47	ANVGNN and YLASNLSG	250 nM	pAC21 (3A1)
38 and 48	KNVGTN and YLASYPQI	700 nM	pAC19 (2C6)
39 and 49	AAVGTY and YSASYRKR	220 nM	pAC18 (2F1)
40 and 50	QYASTN and YWASYRYS	290 nM	pAC23 (2F11)
36 and __	QNVGTN and PLI-YSASYRYS	402 nM	H4E9
41 and 51	HNVGTN and YSASHRYS	2255 nM	L2D2
42 and 52	QIMGPN and YLASYHES		pAC6 (C1)
43 and 53	QIVGTN and YSASHRPS		pAC7 (E10)
44 and 54	QKVLTN and YLASYRYS		pAC12 (H7)
45 and 55	QTVSAN and YLASYRYR		pAC13 (H11)
	CDR-L3		
56	HQYYTYPLFT		pMS22

Fig. 34B

Clone Name	Chain	Monovalent Affinity	Bivalent Affinity
PR1A3	wt/wt	k_{on}: 6.74x10^{3} 1/Ms; k_{off}: 2.48x10^{-2} 1/s; KD 3681x10^{-9}M	k_{on}: 2.82x10^{5} 1/Ms; k_{off}: 5.52x10^{-4} 1/s; KD: 2x10^{-9}M
1C8	hc/wt	k_{on}: 12.9x10^{3} 1/Ms; k_{off}: 0.76x10^{-2} 1/s; KD 586x10^{-9}M	k_{on}: 4.67x10^{5} 1/Ms; k_{off}: 3.24x10^{-4} 1/s; KD: 0.693x10^{-9}M
H4E9	hc/wt	k_{on}: 5.22x10^{3} 1/Ms; k_{off}: 0.21x10^{-2} 1/s; KD 402x10^{-9}M	k_{on}: 2.92x10^{5} 1/Ms; k_{off}: 2.04x10^{-3} 1/s; KD: 0.7x10^{-9}M
H3 Full (5) 19	hc/wt	k_{on}: 54.2x10^{3} 1/Ms; k_{off}: 0.13x10^{-2} 1/s; KD 24x10^{-9}M	k_{on}: 9.02x10^{5} 1/Ms; k_{off}: 1.75x10^{-4} 1/s; KD: 0.19x10^{-9}M
H3 Full (5) 8	hc/wt	k_{on}: 27.3x10^{3} 1/Ms; k_{off}: 0.14x10^{-2} 1/s; KD 51x10^{-9}M	N/D
3A1	wt/ lc	k_{on}: 46.8x10^{3} 1/Ms; k_{off}: 1.17x10^{-2} 1/s; KD 250x10^{-9}M	k_{on}: 2.42x10^{5} 1/Ms; k_{off}: 3.64x10^{-4} 1/s; KD: 1.5x10^{-9}M
2F1	wt/ lc	k_{on}: 95.7x10^{3} 1/Ms; k_{off}: 2.07x10^{-2} 1/s; KD 220x10^{-9}M	k_{on}: 4.23x10^{5} 1/Ms; k_{off}: 4.10x10^{-4} 1/s; KD: 0.952x10^{-9}M
5L1A10	hc/wt	k_{on}: 15.6x10^{3} 1/Ms; k_{off}: 0.09x10^{-2} 1/s; KD 59x10^{-9}M	N/D
5HFF12	hc/wt	k_{on}: 20.8x10^{3} 1/Ms; k_{off}: 0.09x10^{-2} 1/s; KD 44x10^{-9}M	N/D
M4F1	hc/wt	k_{on}: 25.7x10^{3} 1/Ms; k_{off}: 0.17x10^{-2} 1/s; KD 69x10-9M	N/D
H4E9 x 2F1	hc/lc	k_{on}: 36.4x10^{3} 1/Ms; k_{off}: 0.35x10^{-2} 1/s; KD 96x10^{-9}M	k_{on}: 4.23x10^{5} 1/Ms; k_{off}: 1.91x10^{-4} 1/s; KD: 0.452x10^{-9}M
H4E9 x 3A1	hc/lc	N/D	k_{on}: 2.46x10^{5} 1/Ms; k_{off}: 1.36x10^{-4} 1/s; KD: 0.55x10^{-9}M
1C8 x 2F1	hc/lc	k_{on}: 68.1x10^{3} 1/Ms; k_{off}: 0.87x10^{-2} 1/s; KD 128x10^{-9}M	k_{on}: 9.68x10^{5} 1/Ms; k_{off}: 6.36x10^{-4} 1/s; KD: 0.66x10^{-9}M
1C8 x 3A1	hc/lc	N/D	k_{on}: 2.89x10^{5} 1/Ms; k_{off}: 2.57x10^{-4} 1/s; KD: 0.888x10^{-9}M
H3 Full (5) 19 x 2F1	hc/lc	k_{on}: 206x10^{3} 1/Ms; k_{off}: 0.25x10-2 1/s; KD: 12.2x10^{-9}M	k_{on}: 1.76x10^{6} 1/Ms; k_{off}: 2.84x10^{-4} 1/s; KD: 0.16x10^{-9}M
H3 Full (5) 8 x 2F1	hc/lc	N/D	k_{on}: 9.93x10^{5}; 1/Ms; k_{off}: 2.71x10^{-4} 1/s; KD: 0.28x10^{-9}M

Fig. 35

SEQ ID NO:	CDR-H3 CONSTRUCTS	AMINO ACID SEQUENCE
25	PR1A3 CDR-H3	WDFYDYVEAMDY
33	5HFF12 CDR-H3	WDFAHYFQTMDY
34	5L1A10 CDR-H3	WDFAYYFQTMDY
217	PR1A3 (Y98A)	WDFADYVEAMDY
218	PR1A3 (D99Y)	WDFYYYVEAMDY
219	PR1A3 (D99H)	WDFYHYVEAMDY
220	PR1A3 (V101F)	WDFYDYFEAMDY
221	PR1A3 (E101aQ)	WDFYDYVQAMDY
222	PR1A3 (A103T)	WDFYDYVETMDY
223	PR1A3 (Y98A / D99Y)	WDFAYYVEAMDY
224	PR1A3 (W95Y)	YDFYDYVEAMDY

Fig. 36

SEQ. ID NO:	HEAVY CHAIN CONSTRUCT	AMINO ACID SEQUENCE
225	CH7A (Y98A)	QVQLVQSGSELKKPGASVKVSCKASGYTFTEFGMNWVRQAPGQGLEWMGWINTKTGEATYVEE FKGRFVFSLDTSVSTAYLQISSLKAEDTAVYYCARWDFADYVEAMDYWGQGTTVTVSS
226	CH7A (D99Y)	QVQLVQSGSELKKPGASVKVSCKASGYTFTEFGMNWVRQAPGQGLEWMGWINTKTGEATYVEE FKGRFVFSLDTSVSTAYLQISSLKAEDTAVYYCARWDFYYYVEAMDYWGQGTTVTVSS
227	CH7A (D99H)	QVQLVQSGSELKKPGASVKVSCKASGYTFTEFGMNWVRQAPGQGLEWMGWINTKTGEATYVEE FKGRFVFSLDTSVSTAYLQISSLKAEDTAVYYCARWDFYHYVEAMDYWGQGTTVTVSS
228	CH7A (V101F)	QVQLVQSGSELKKPGASVKVSCKASGYTFTEFGMNWVRQAPGQGLEWMGWINTKTGEATYVEE FKGRFVFSLDTSVSTAYLQISSLKAEDTAVYYCARWDFYDYFEAMDYWGQGTTVTVSS
229	CH7A (E102Q)	QVQLVQSGSELKKPGASVKVSCKASGYTFTEFGMNWVRQAPGQGLEWMGWINTKTGEATYVEE FKGRFVFSLDTSVSTAYLQISSLKAEDTAVYYCARWDFYDYVQAMDYWGQGTTVTVSS
230	CH7A (A103T)	QVQLVQSGSELKKPGASVKVSCKASGYTFTEFGMNWVRQAPGQGLEWMGWINTKTGEATYVEE FKGRFVFSLDTSVSTAYLQISSLKAEDTAVYYCARWDFYDYVETMDYWGQGTTVTVSS
231	CH7A (Y98A / D99Y)	QVQLVQSGSELKKPGASVKVSCKASGYTFTEFGMNWVRQAPGQGLEWMGWINTKTGEATYVEE FKGRFVFSLDTSVSTAYLQISSLKAEDTAVYYCARWDFAYYVEAMDYWGQGTTVTVSS
232	CH7A (W95Y)	QVQLVQSGSELKKPGASVKVSCKASGYTFTEFGMNWVRQAPGQGLEWMGWINTKTGEATYVEE FKGRFVFSLDTSVSTAYLQISSLKAEDTAVYYCARYDFYDYVEAMDYWGQGTTVTVSS
233	CH1A1A (Y98A)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTEFGMNWVRQAPGQGLEWMGWINTKTGEATYVEE FKGRVTFTTDTSTSTAYMELRSLRSDDTAVYYCARWDFADYVEAMDYWGQGTTVTVSS
234	CH1A1A (D99Y)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTEFGMNWVRQAPGQGLEWMGWINTKTGEATYVEE FKGRVTFTTDTSTSTAYMELRSLRSDDTAVYYCARWDFYYYVEAMDYWGQGTTVTVSS

Fig. 37A

SEQ. ID NO:	HEAVY CHAIN CONSTRUCT	AMINO ACID SEQUENCE
235	CH1A1A (D99H)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTEFGMNWVRQAPGQGLEWMGWINTKTGEATY VEEFKGRVTFTTDTSTSTAYMELRSLRSDDTAVYY CARWDFYHYVEAMDYWGQGTTVTVSS
236	CH1A1A (V101F)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTEFGMNWVRQAPGQGLEWMGWINTKTGEATY VEEFKGRVTFTTDTSTSTAYMELRSLRSDDTAVYYCARWDFYDYFEAMDYWGQGTTVTVSS
237	CH1A1A (E102Q)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTEFGMNWVRQAPGQGLEWMGWINTKTGEATY VEEFKGRVTFTTDTSTSTAYMELRSLRSDDTAVYYCARWDFYDYVQAMDYWGQGTTVTVSS
238	CH1A1A (A103T)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTEFGMNWVRQAPGQGLEWMGWINTKTGEATY VEEFKGRVTFTTDTSTSTAYMELRSLRSDDTAVYYCARWDFYDYVETMDYWGQGTTVTVSS
239	CH1A1A (Y98A / D99Y)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTEFGMNWVRQAPGQGLEWMGWINTKTGEATY VEEFKGRVTFTTDTSTSTAYMELRSLRSDDTAVYYCARWDFAYYVEAMDYWGQGTTVTVSS
240	CH1A1B (W95Y)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTEFGMNWVRQAPGQGLEWMGWINTKTGEATY VEEFKGRVTFTTDTSTSTAYMELRSLRSDDTAVYYCARYDFYDYVEAMDYWGQGTTVTVSS
241	CH1A1B (Y98A)	QVKLQQSGAEVKKPGASVKVSCKASGYTFTEFGMNWVRQAPGQGLEWMGWINTKTGEATY VEEFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARWDFADYVEAMDYWGQGTTVTVSS
242	CH1A1B (D99Y)	QVKLQQSGAEVKKPGASVKVSCKASGYTFTEFGMNWVRQAPGQGLEWMGWINTKTGEATY VEEFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARWDFYYYVEAMDYWGQGTTVTVSS
243	CH1A1B (D99H)	QVKLQQSGAEVKKPGASVKVSCKASGYTFTEFGMNWVRQAPGQGLEWMGWINTKTGEATY VEEFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARWDFYHYVEAMDYWGQGTTVTVSS
244	CH1A1B (V101F)	QVKLQQSGAEVKKPGASVKVSCKASGYTFTEFGMNWVRQAPGQGLEWMGWINTKTGEATY VEEFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARWDFYDYFEAMDYWGQGTTVTVSS

Fig. 37B

SEQ. ID NO:	HEAVY CHAIN CONSTRUCT	AMINO ACID SEQUENCE
245	CH1A1B (E102Q)	QVKLQQSGAEVKKPGASVKVSCKASGYTFTEFGMNWVRQAPGQGLEWMGWINTKTGEATY VEEFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARWDFYDYVQAMDYWGQGTTVTVSS
246	CH1A1B (A103T)	QVKLQQSGAEVKKPGASVKVSCKASGYTFTEFGMNWVRQAPGQGLEWMGWINTKTGEATY VEEFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARWDFYDYVETMDYWGQGTTVTVSS
247	CH1A1B (Y98A / D99Y)	QVKLQQSGAEVKKPGASVKVSCKASGYTFTEFGMNWVRQAPGQGLEWMGWINTKTGEATY VEEFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARWDFAYYVEAMDYWGQGTTVTVSS
248	CH1A1B (W95Y)	QVKLQQSGAEVKKPGASVKVSCKASGYTFTEFGMNWVRQAPGQGLEWMGWINTKTGEATY VEEFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARYDFYDYVEAMDYWGQGTTVTVSS
261	CH1A1A	QVQLVQSGAEVKKPGASVKVSCKASGYTFTEFGMNWVRQAPGQGLEWMGWINTKTGEATY VEEFKGRVTFTTDTSTSTAYMELRSLRSDDTAVYYCARWDFYDYVEAMDYWGQGTTVTVSS
262	CH1A1B	QVKLQQSGAEVKKPGASVKVSCKASGYTFTEFGMNWVRQAPGQGLEWMGWINTKTGEATY VEEFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARWDFYDYVEAMDYWGQGTTVTVSS
263	CH1A1C	QVQLVQSGPELKKPGASVKVSCKASGYTFTEFGMNWVRQAPGQGLEWMGWINTKTGEATY VEEFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARWDFYDYVEAMDYWGQGTTVTVSS

Fig. 37C

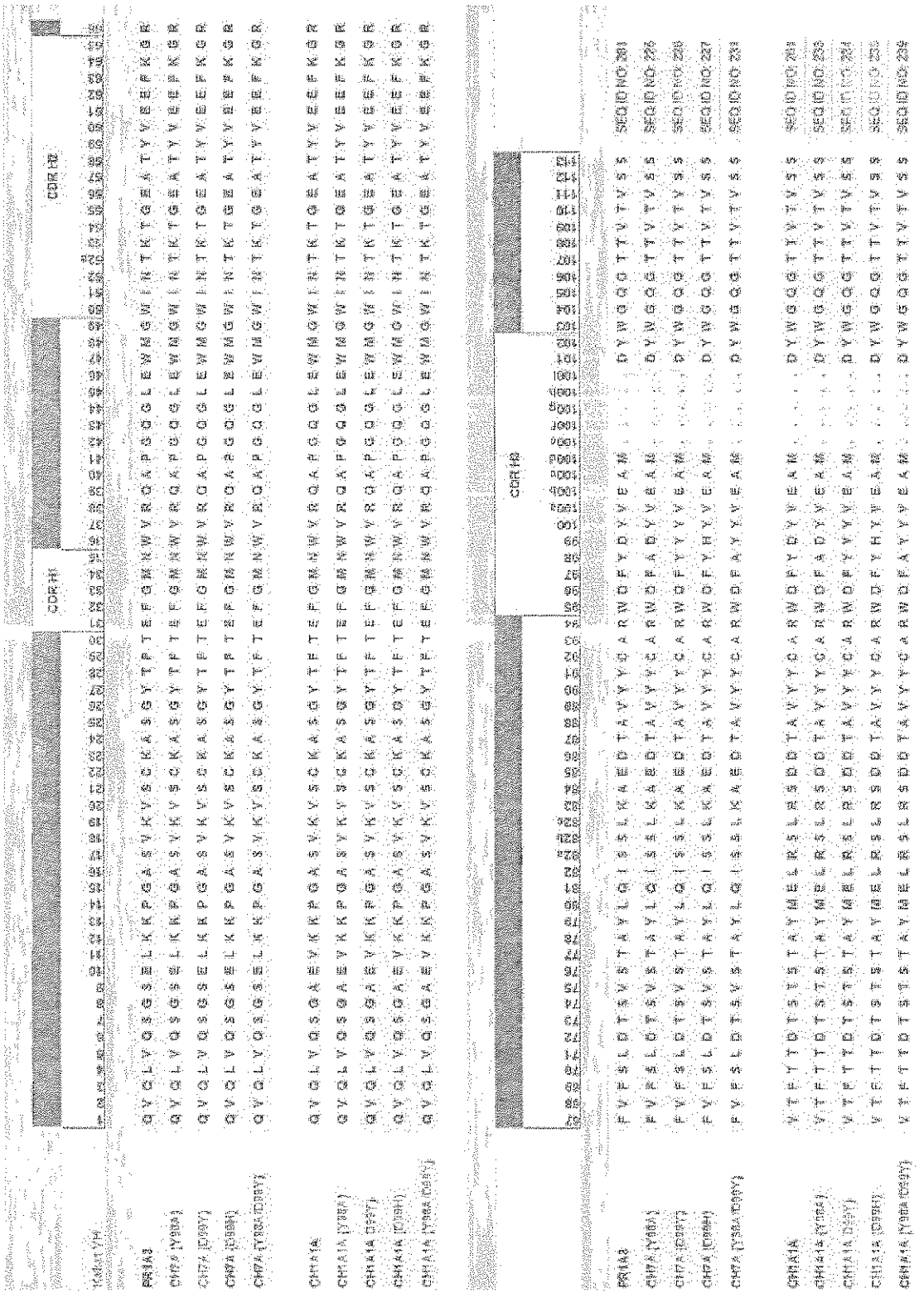


FIG. 38