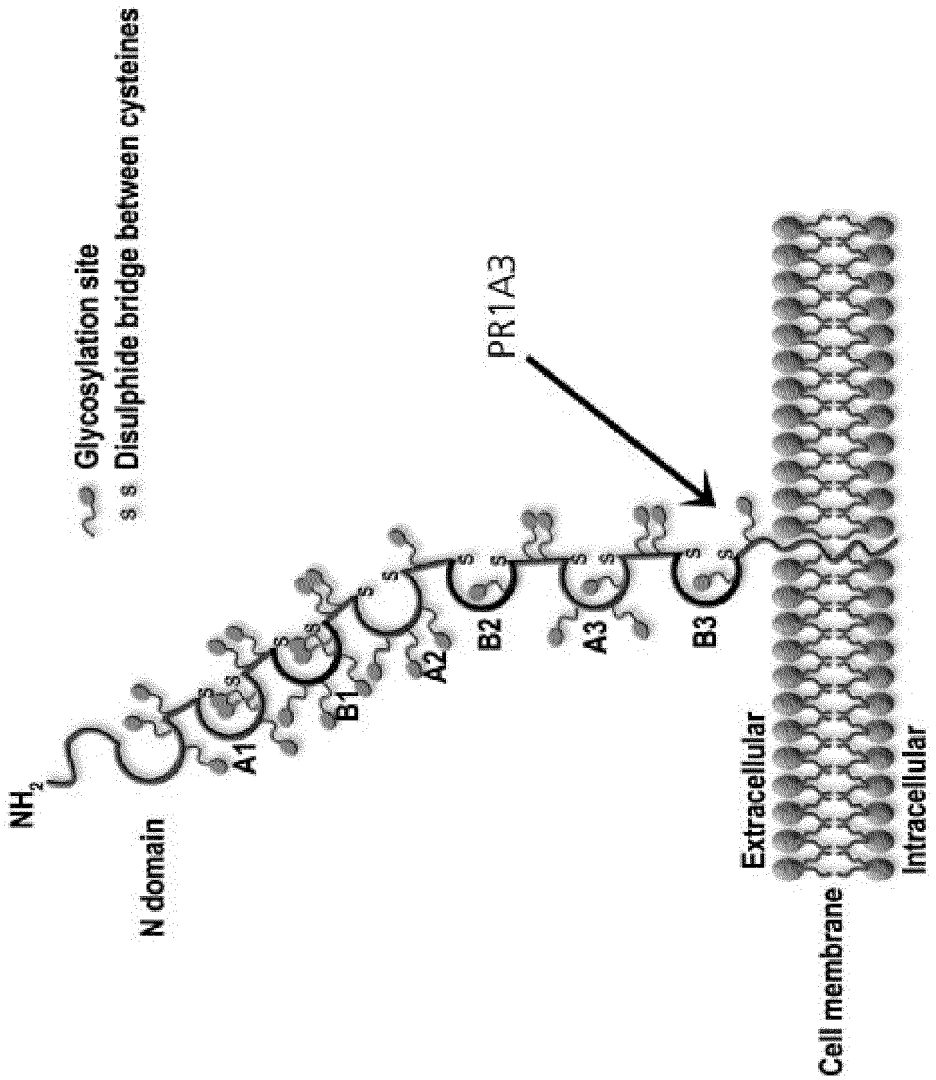

Glycosylation site
s s Disulphide bridge between cysteines
PR1A3
NH2
N domain
A1
B1
A2
B2
A3
B3
Extracellular
Cell membrane
Intracellular

Fig. 1

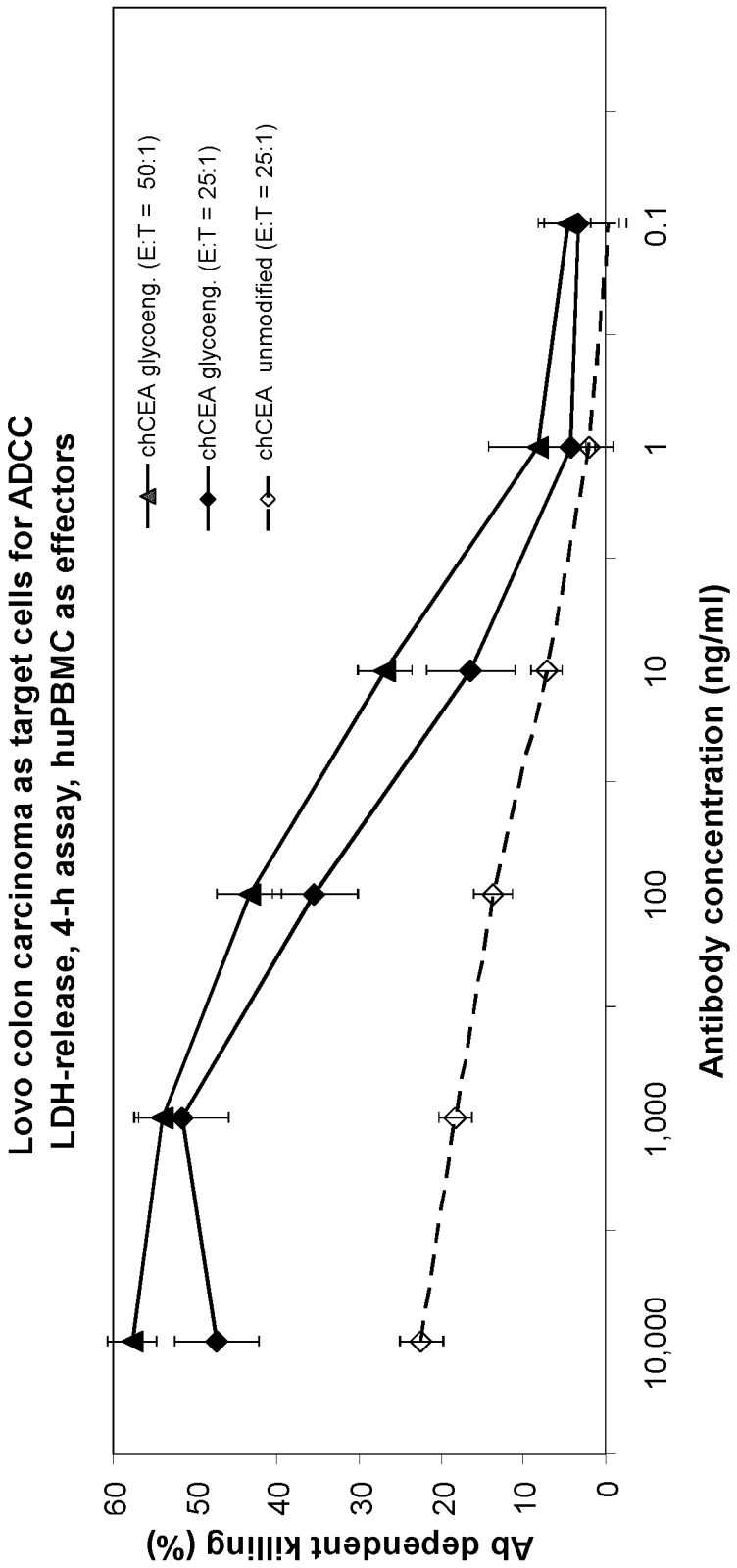

Lovo colon carcinoma as target cells for ADCC
LDH-release, 4-h assay, huPBMC as effectors
chCEA glycoeng. (E:T = 50:1)
chCEA glycoeng. (E:T = 25:1)
chCEA unmodified (E:T = 25:1)
Ab dependent killing (%)
0
10
20
30
40
50
60
Antibody concentration (ng/ml)
10,000
1,000
100
10
1
0.1

Fig. 2

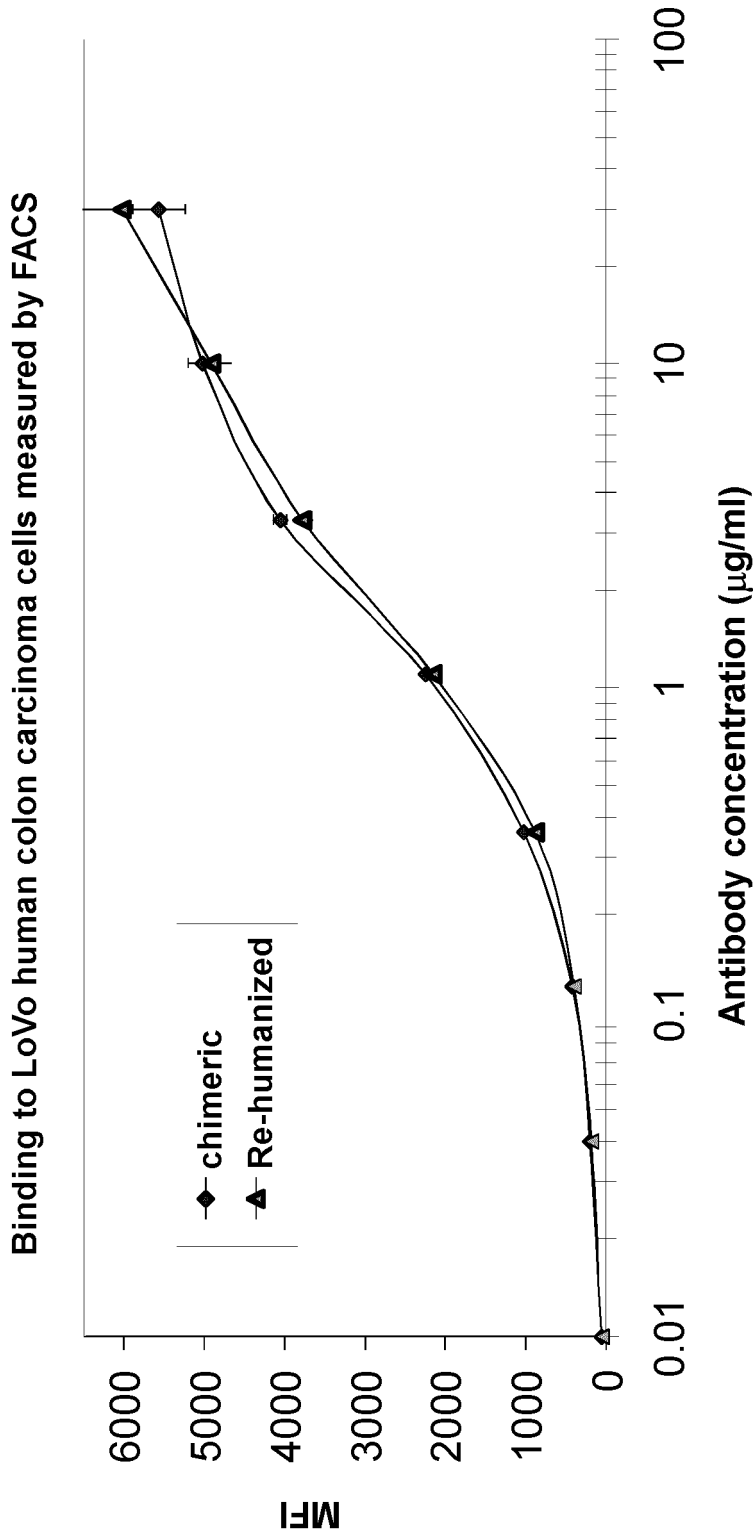

Binding to LoVo human colon carcinoma cells measured by FACS
chimeric
Re-humanized
MFI
6000
5000
4000
3000
2000
1000
0
0.01
0.1
1
10
100
Antibody concentration (µg/ml)

Fig. 3

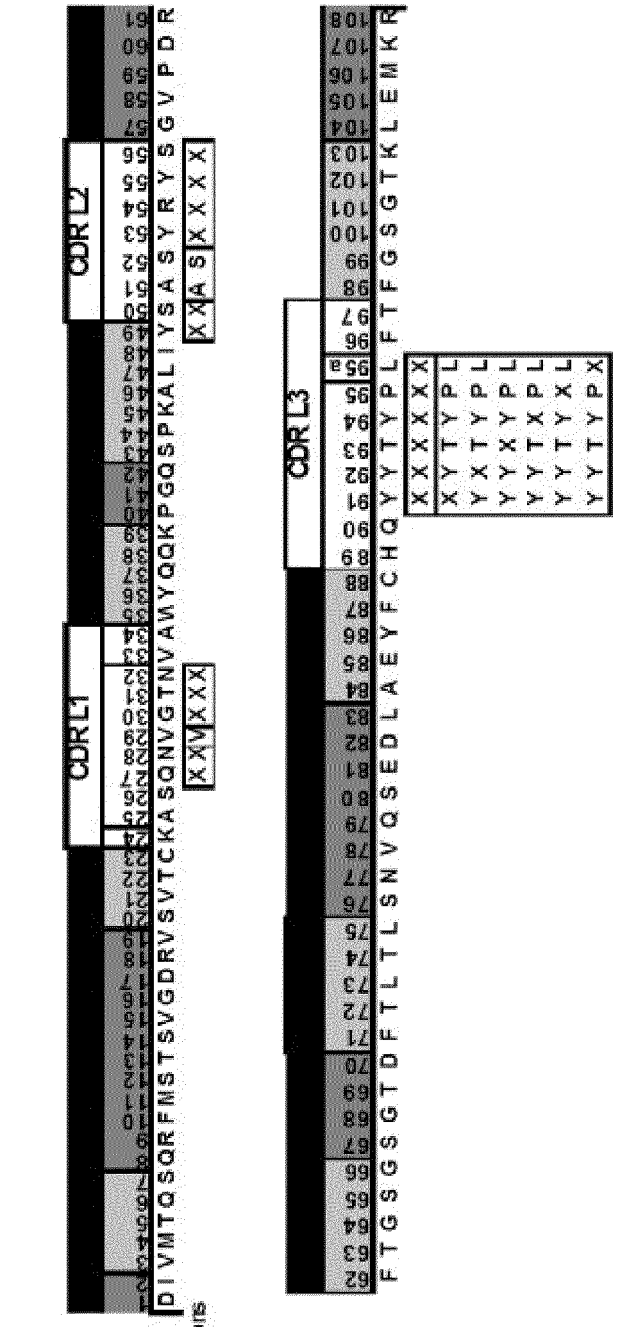

VL's
Kabat V
PR1A3-VL
Randomized Positions
CDR L1
CDR L2
CDR L3

Fig. 4

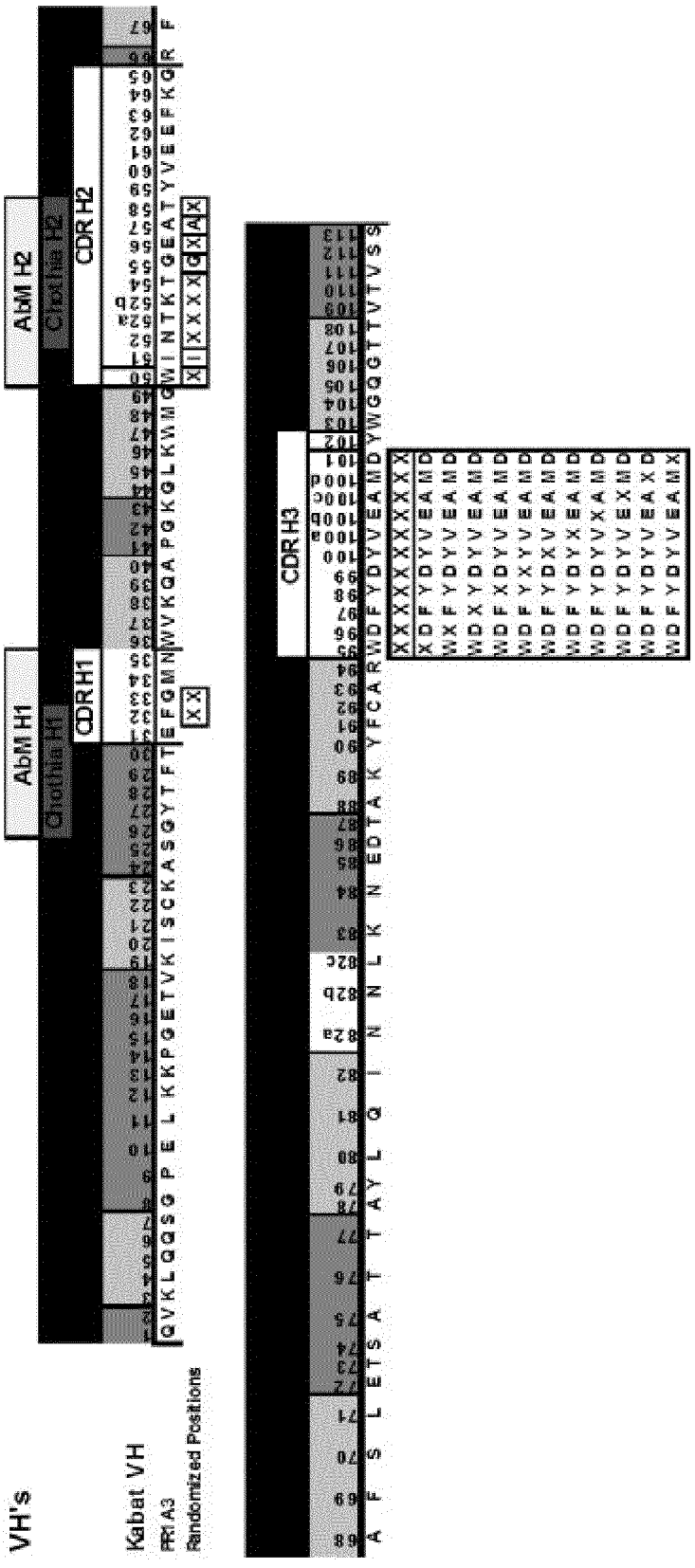

VH's
Kabat VH
FR1 A3
Randomized Positions
AbM H1
Chothia H1
CDR H1
AbM H2
Chothia H2
CDR H2
CDR H3

Fig. 5

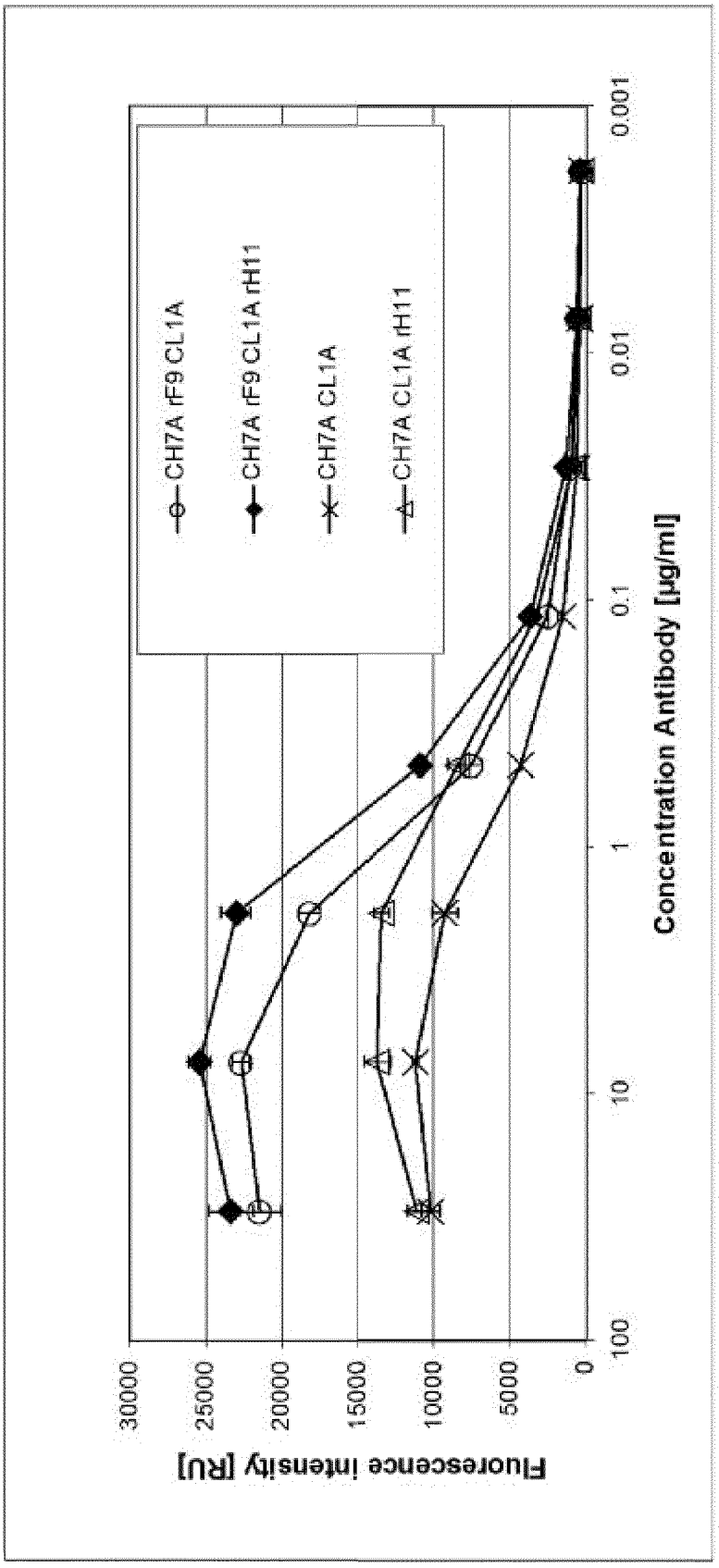

CH7A rF9 CL1A
CH7A rF9 CL1A rH11
CH7A CL1A
CH7A CL1A rH11
Fluorescence intensity [RU]
30000
25000
20000
15000
10000
5000
0
100
10
1
0.1
0.01
0.001
Concentration Antibody [µg/ml]

Fig. 6

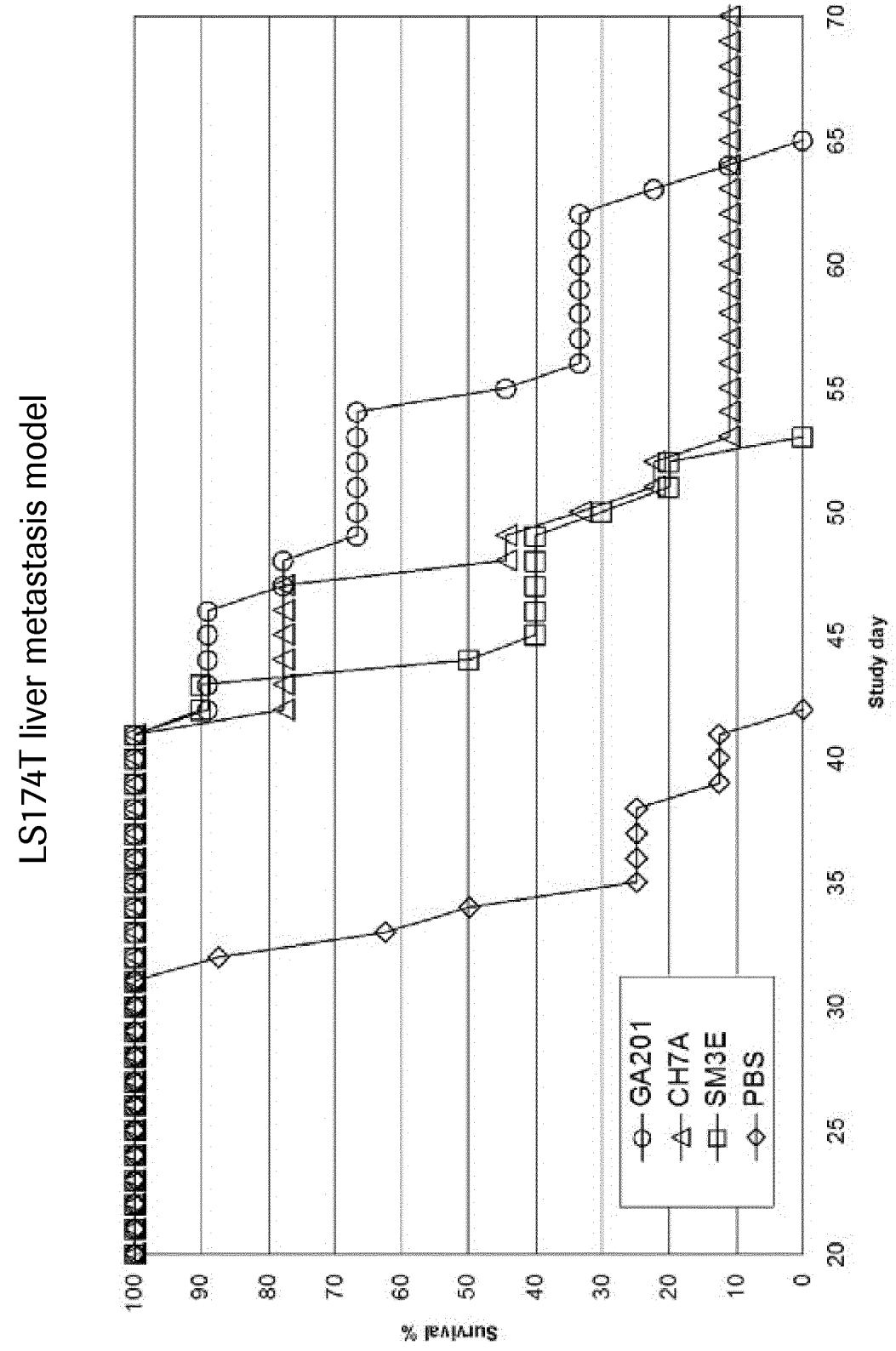

LS174T liver metastasis model
Survival %
Study day
GA201
CH7A
SM3E
PBS

Fig. 7

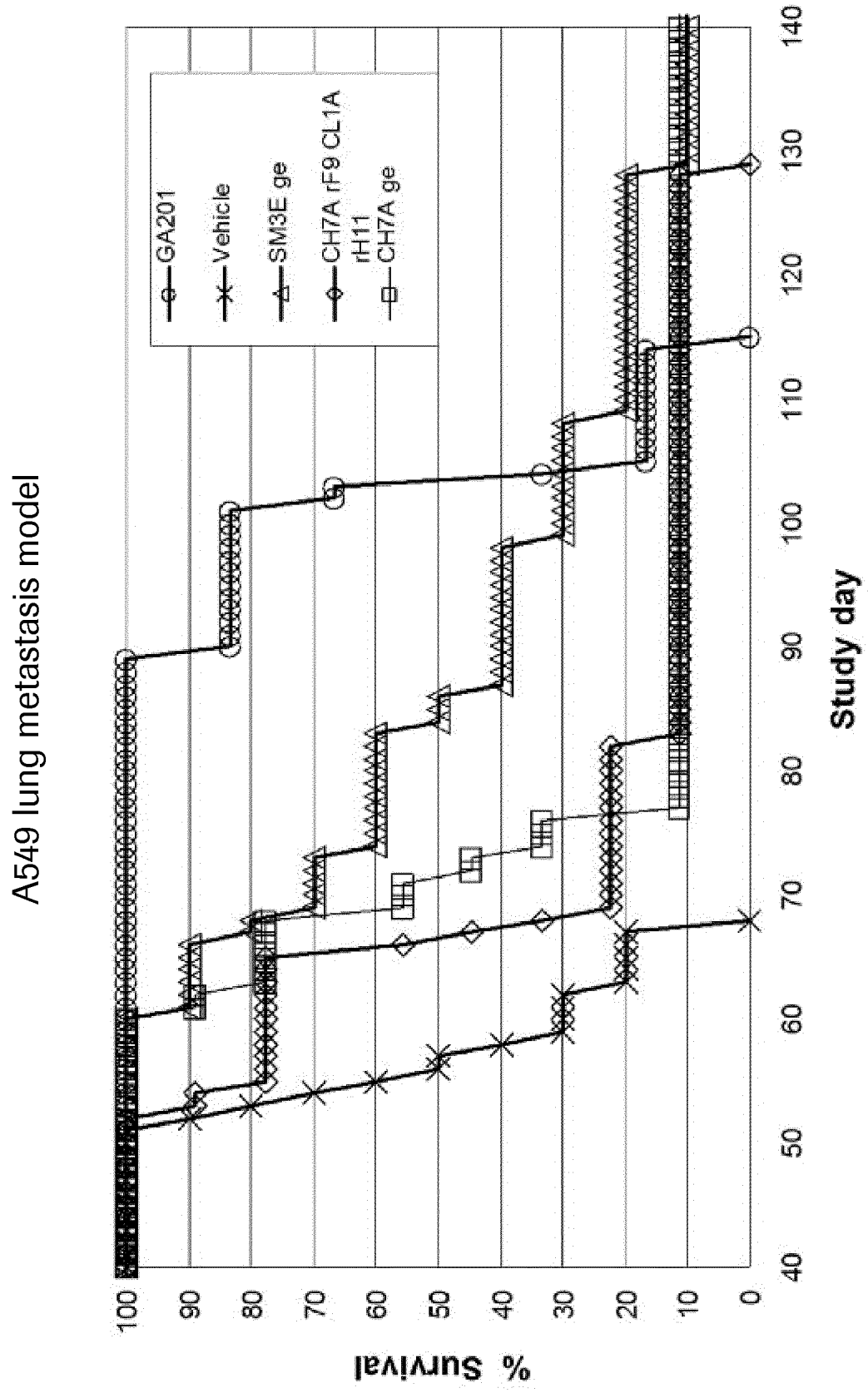

A549 lung metastasis model
% Survival
Study day
GA201
Vehicle
SM3E ge
CH7A rF9 CL1A rH11
CH7A ge
100
90
80
70
60
50
40
30
20
10
0
40
50
60
70
80
90
100
110
120
130
140

Fig. 8

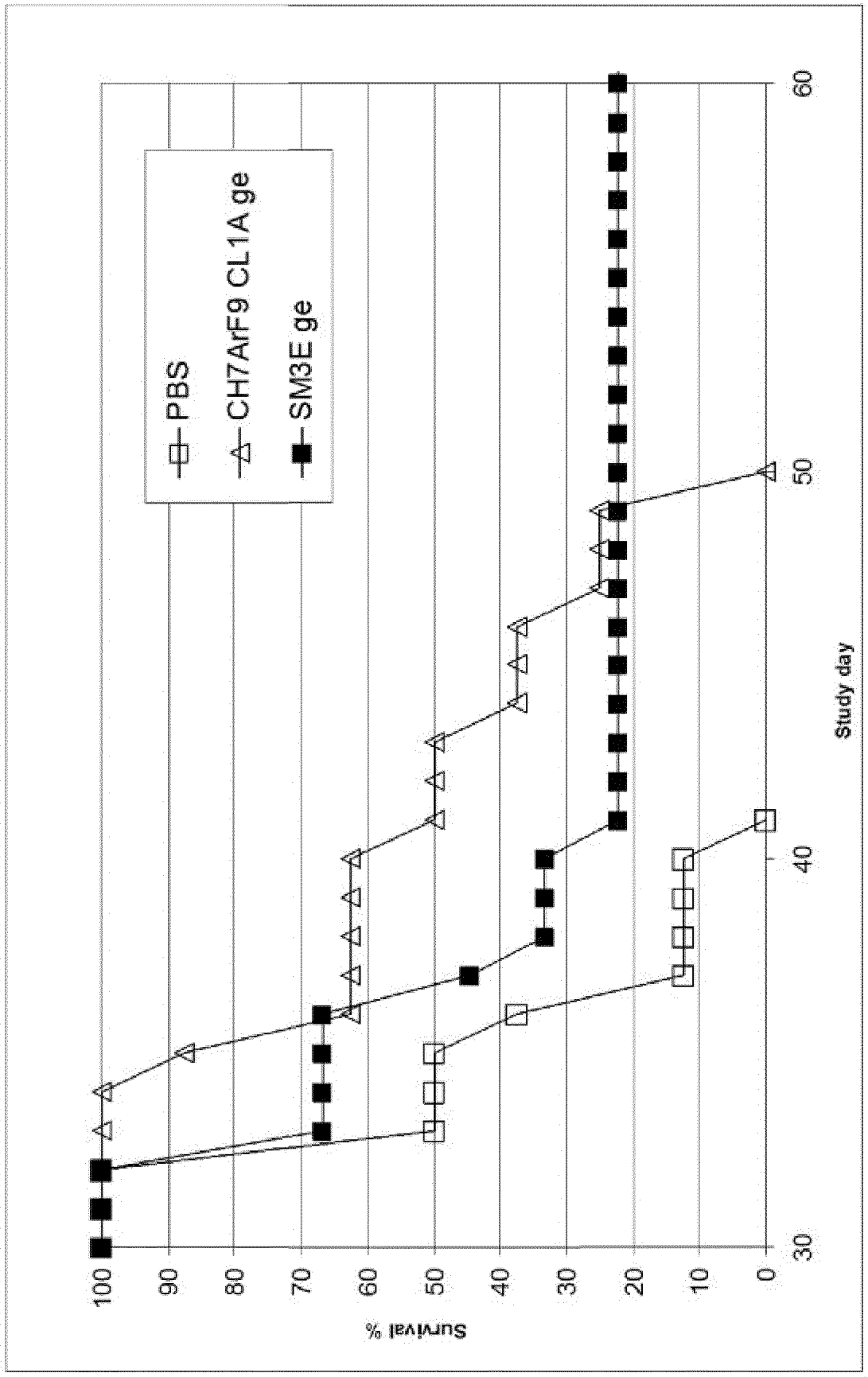
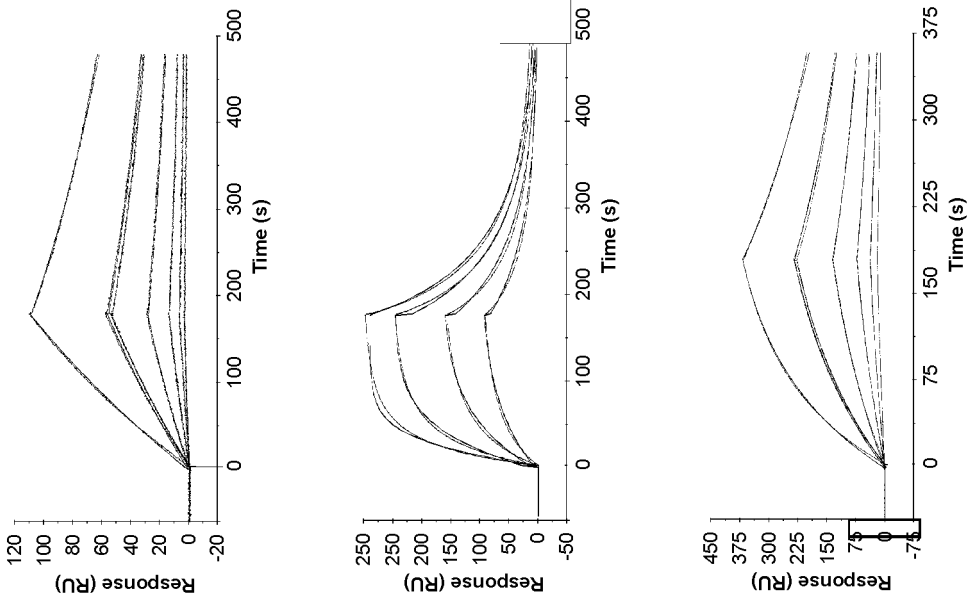

MKN45 liver metastasis model
PBS
CH7ArF9 CL1A ge
SM3E ge
Survival %
100
90
80
70
60
50
40
30
20
10
0
30
40
50
60
Study day

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

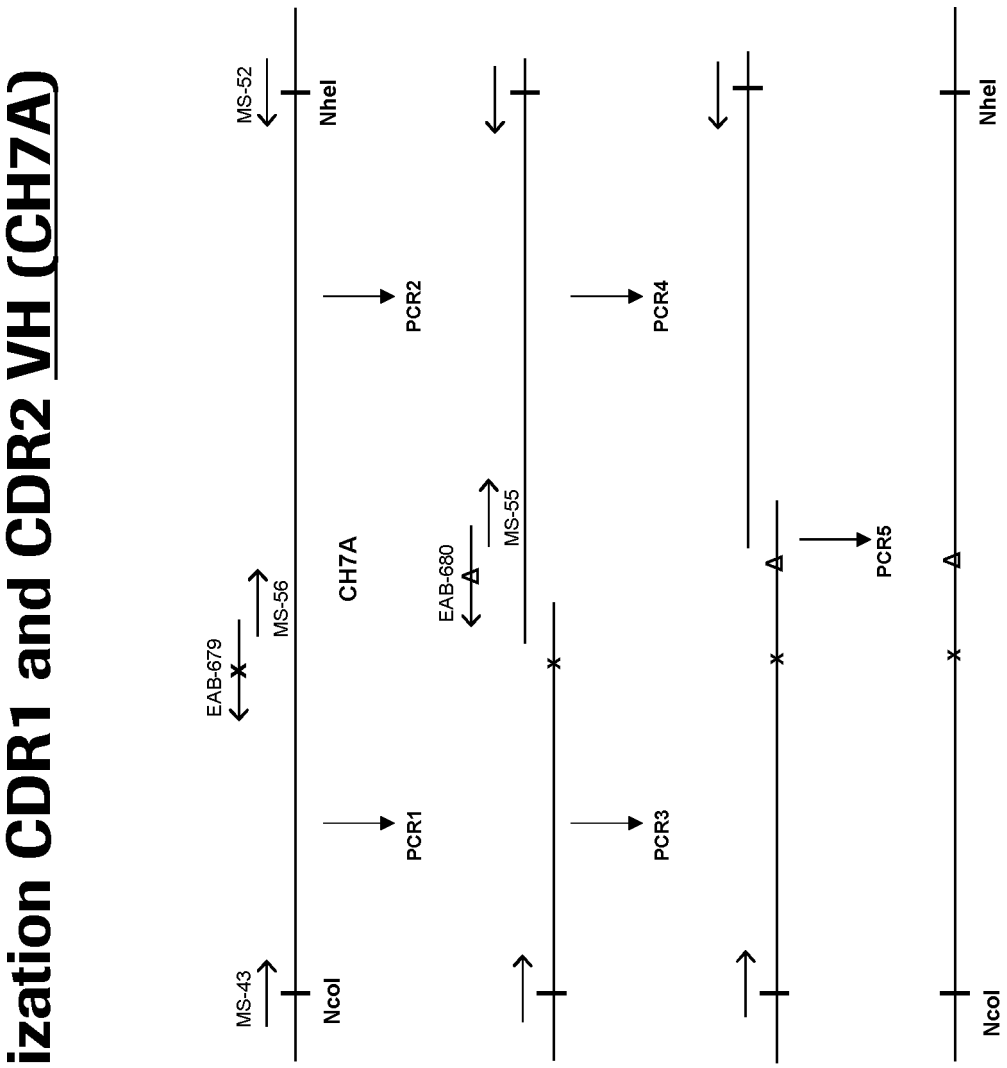

randomization CDR1 and CDR2 VH (CH7A)
MS-43
NcoI
EAB-679
MS-56
CH7A
PCR1
MS-52
NheI
PCR2
EAB-680
MS-55
PCR3
PCR4
PCR5

Fig. 11

randomization CDR1 and CDR2 VL(CL1A)

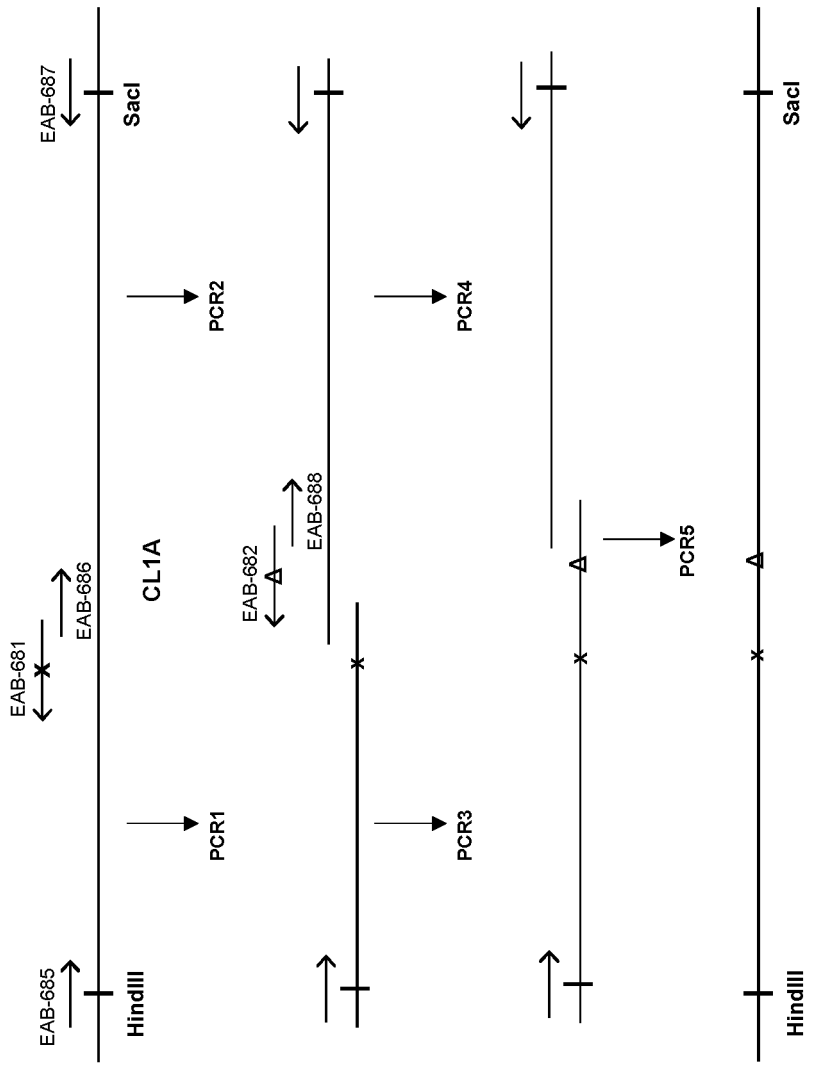


Fig. 12

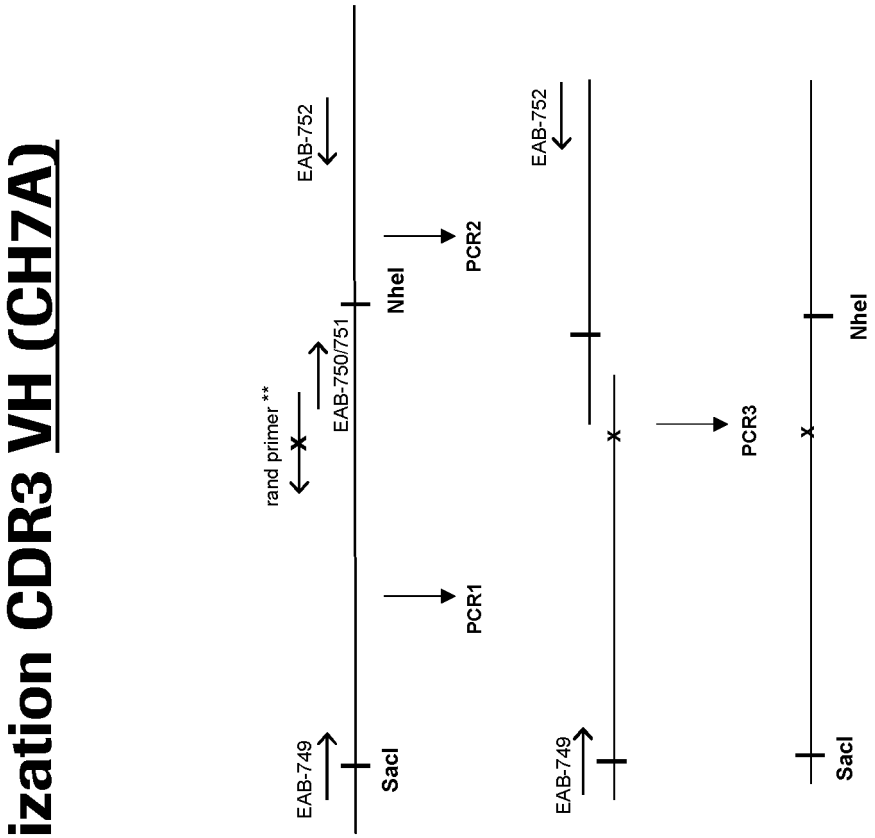

randomization CDR3 VH (CH7A)
EAB-749
SacI
PCR1
rand primer **
EAB-750/751
EAB-752
NheI
PCR2
EAB-749
EAB-752
PCR3
NheI
SacI

Fig. 13

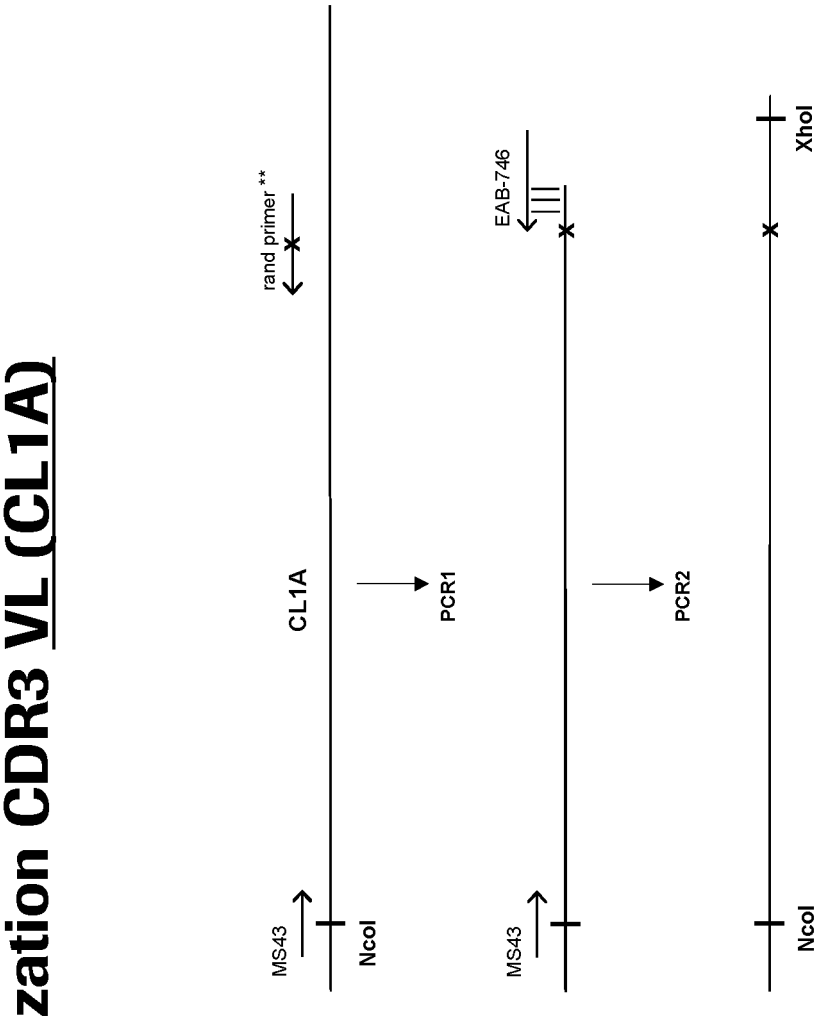
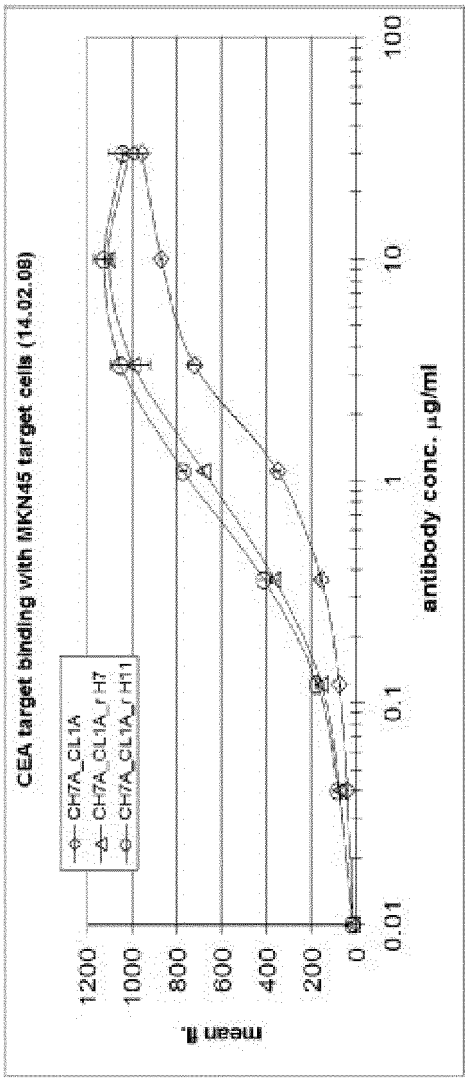

randomization CDR3 VL (CL1A)
rand primer **
CL1A
PCR1
MS43
NcoI
EAB-746
PCR2
MS43
NcoI
XhoI

Fig. 14


CEA target binding with MKN45 target cells (14.02.08)
CH7A_CL1A
CH7A_CL1A_r H7
CH7A_CL1A_r H11
mean fl.
1200
1000
800
600
400
200
0
0.01
0.1
1
10
100
antibody conc. µg/ml

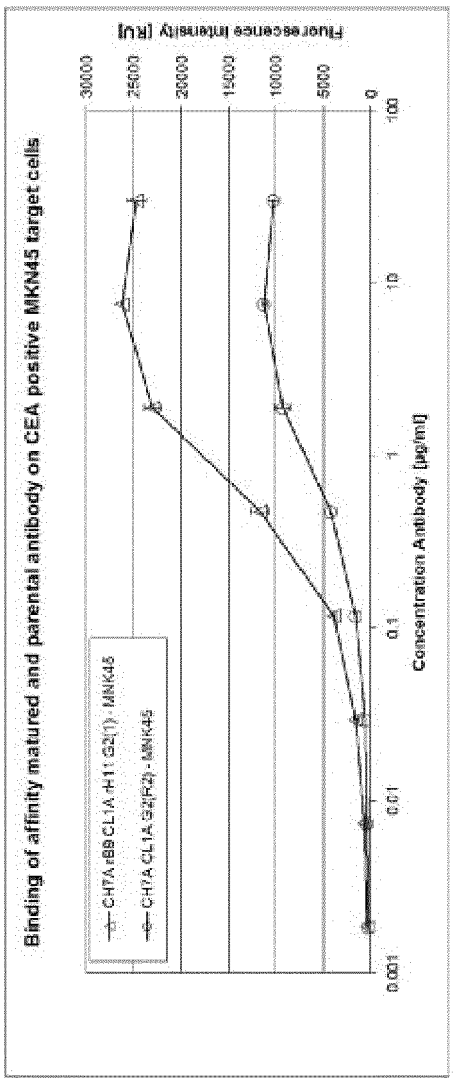

Binding of affinity matured and parental antibody on CEA positive MKN45 target cells
CH7A rBB CL1A rH11 S2(1) - MKN45
CH7A CL1A S2(R2) - MKN45
Fluorescence Intensity [RU]
30000
25000
20000
15000
10000
5000
0
0.001
0.01
0.1
1
10
100
Concentration Antibody [µg/ml]

Fig. 15

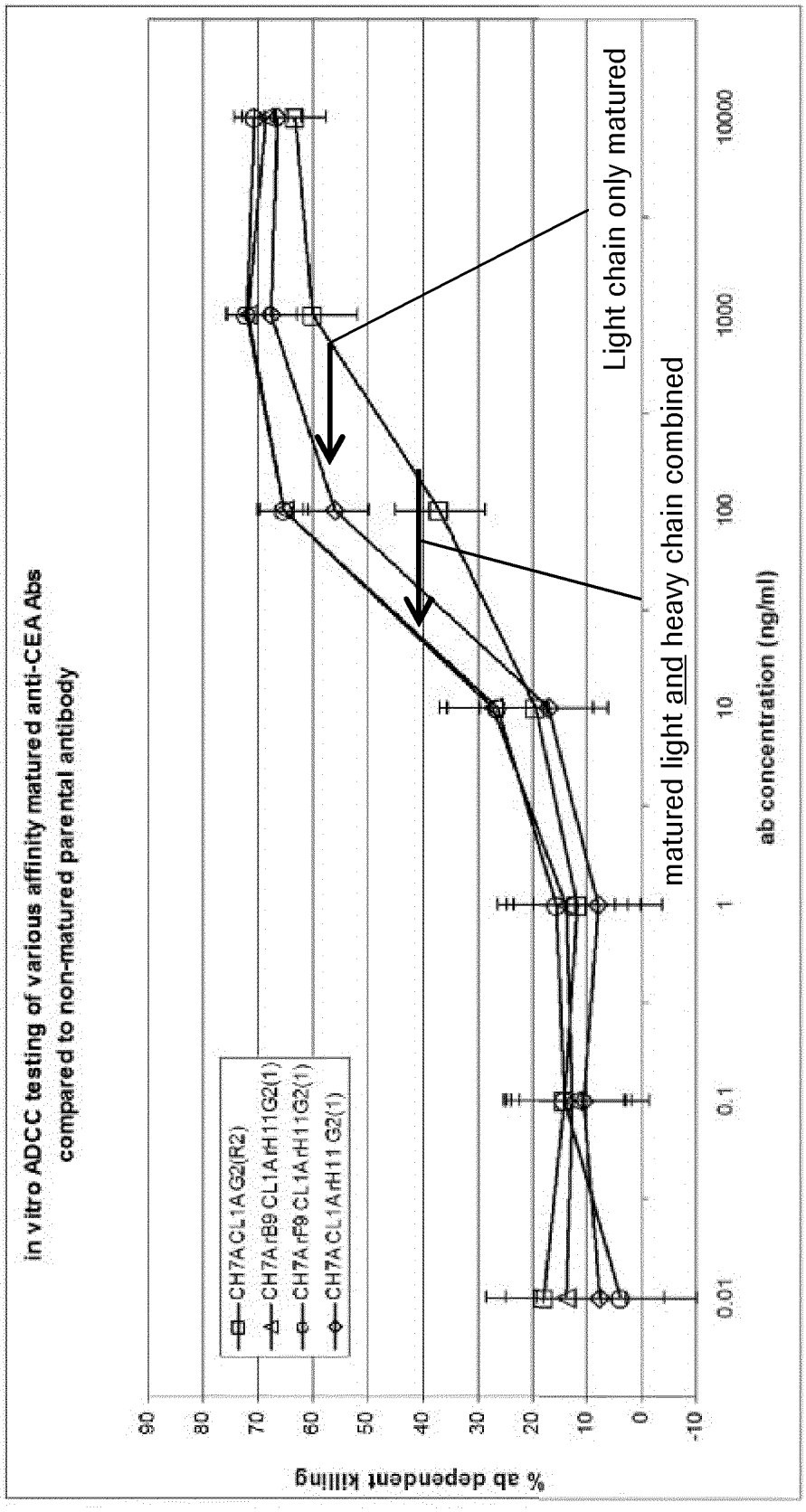

in vitro ADCC testing of various affinity matured anti-CEA Abs
compared to non-matured parental antibody
% ab dependent killing
ab concentration (ng/ml)
CH7A CL1A G2(R2)
CH7A rB9 CL1A rH11G2(1)
CH7A rF9 CL1A rH11G2(1)
CH7A CL1A rH11 G2(1)
Light chain only matured
matured light and heavy chain combined

Fig. 16

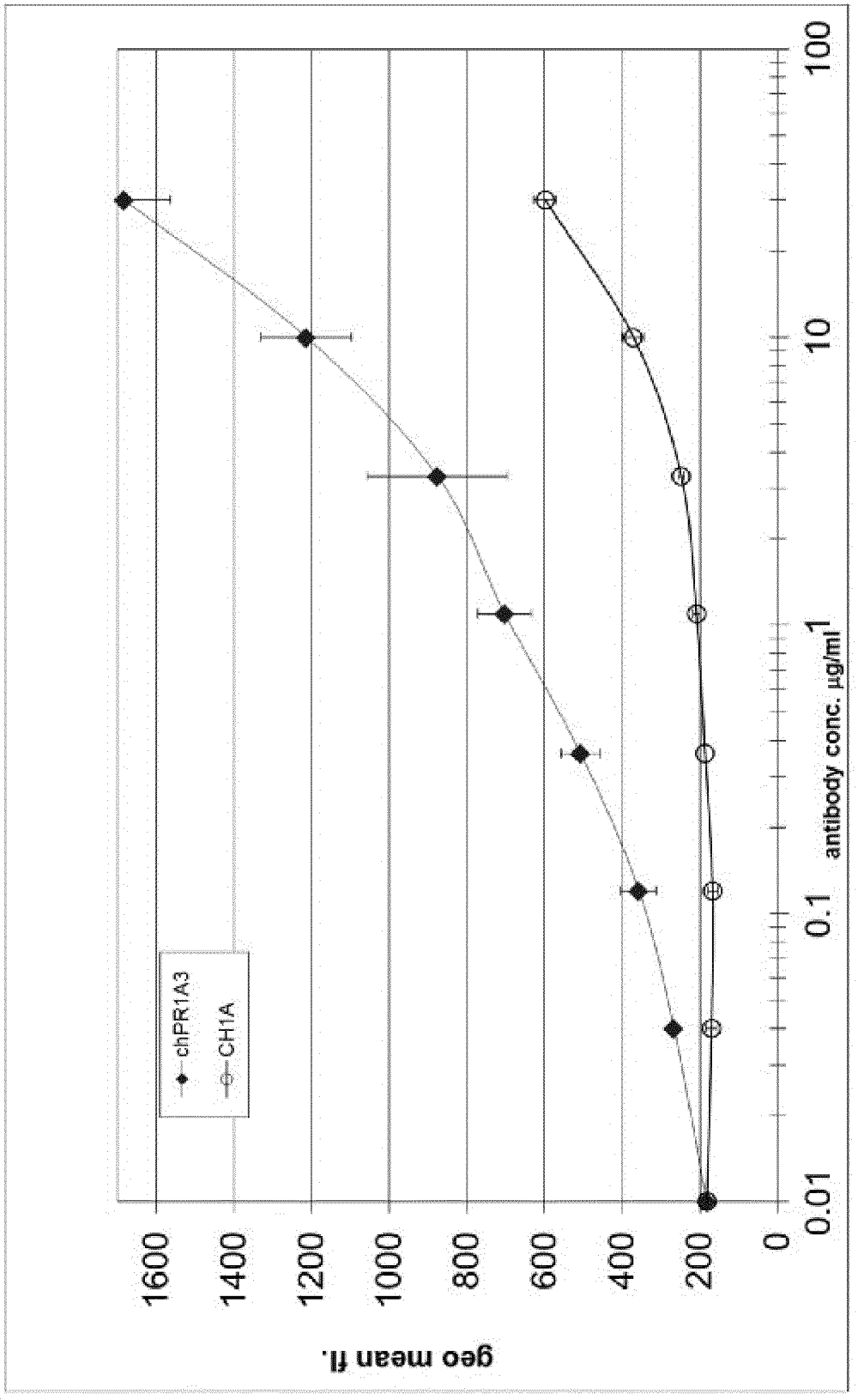

geo mean fl.
1600
1400
1200
1000
800
600
400
200
0
0.01
0.1
1
10
100
antibody conc. µg/ml
chPR1A3
CH1A

Fig. 17

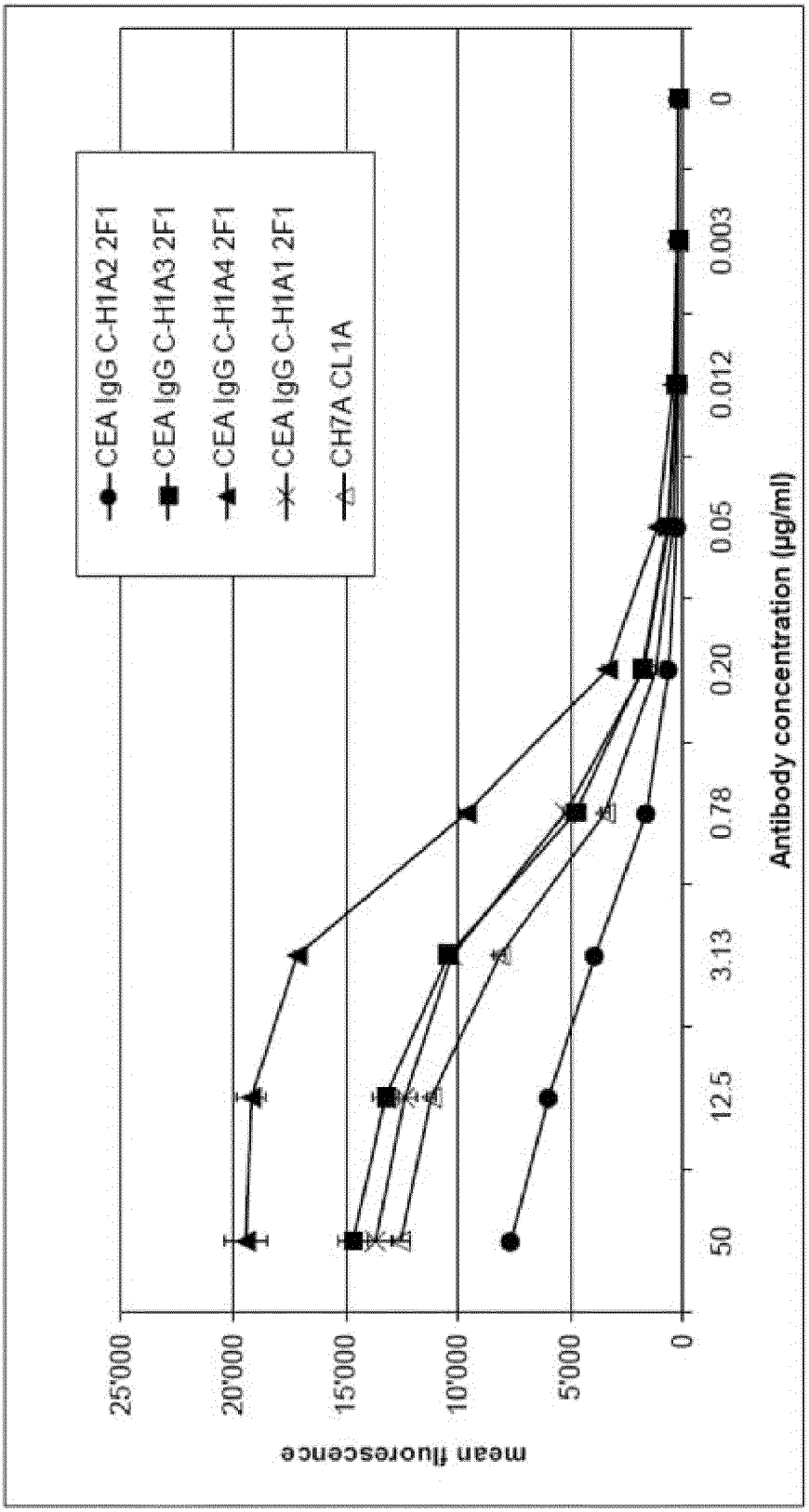

CEA IgG C-H1A2 2F1
CEA IgG C-H1A3 2F1
CEA IgG C-H1A4 2F1
CEA IgG C-H1A1 2F1
CH7A CL1A
mean fluorescence
25'000
20'000
15'000
10'000
5'000
0
Antibody concentration (µg/ml)
50
12.5
3.13
0.78
0.20
0.05
0.012
0.003
0

Fig. 18

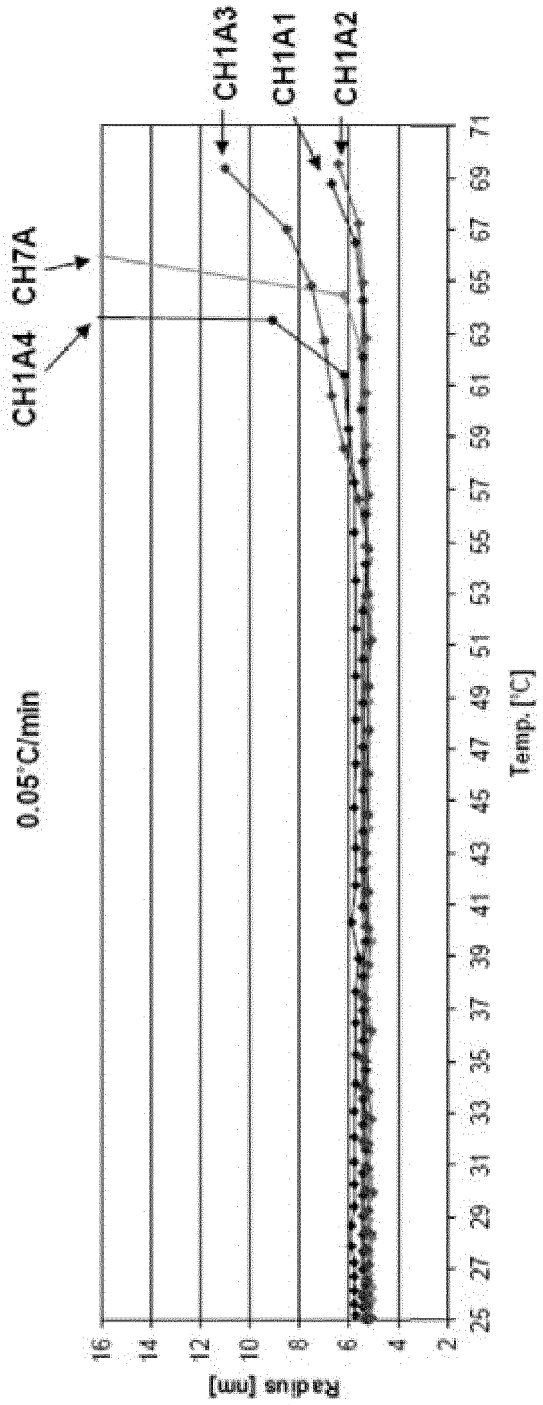
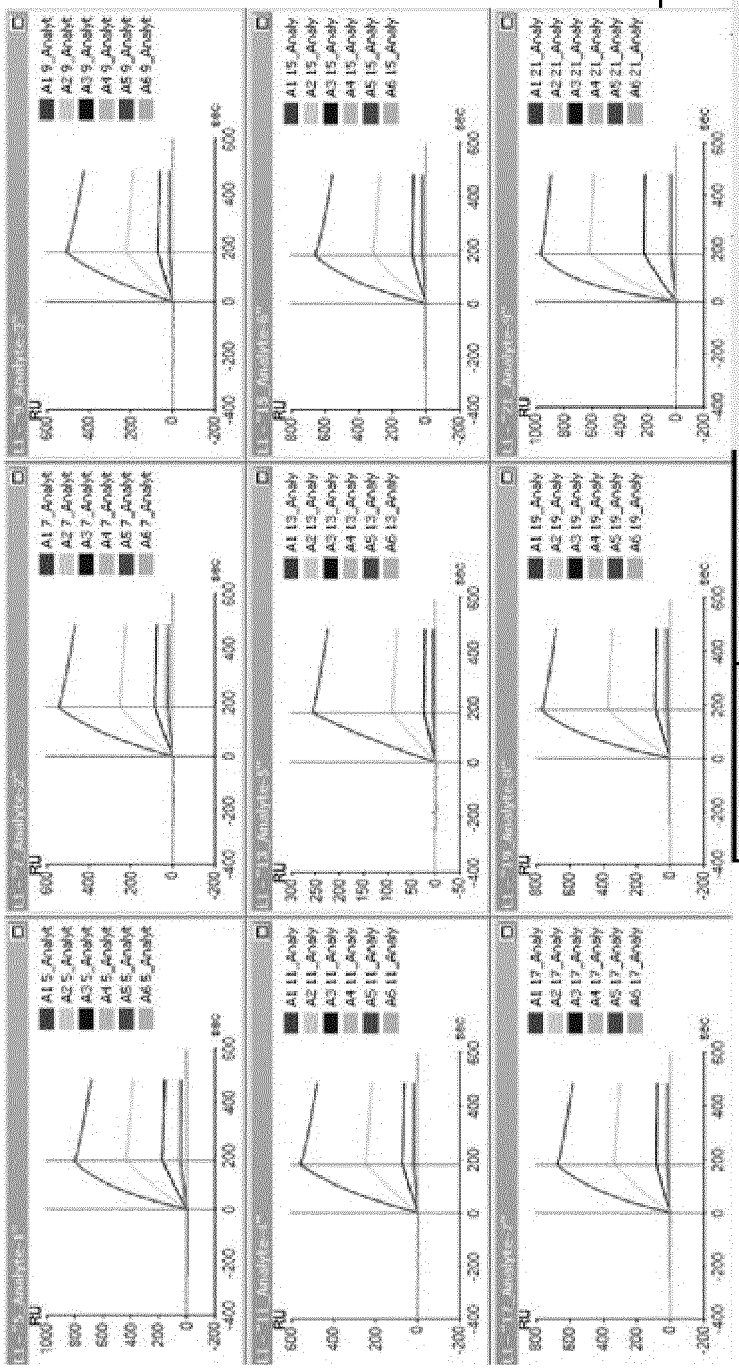


Fig. 19



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

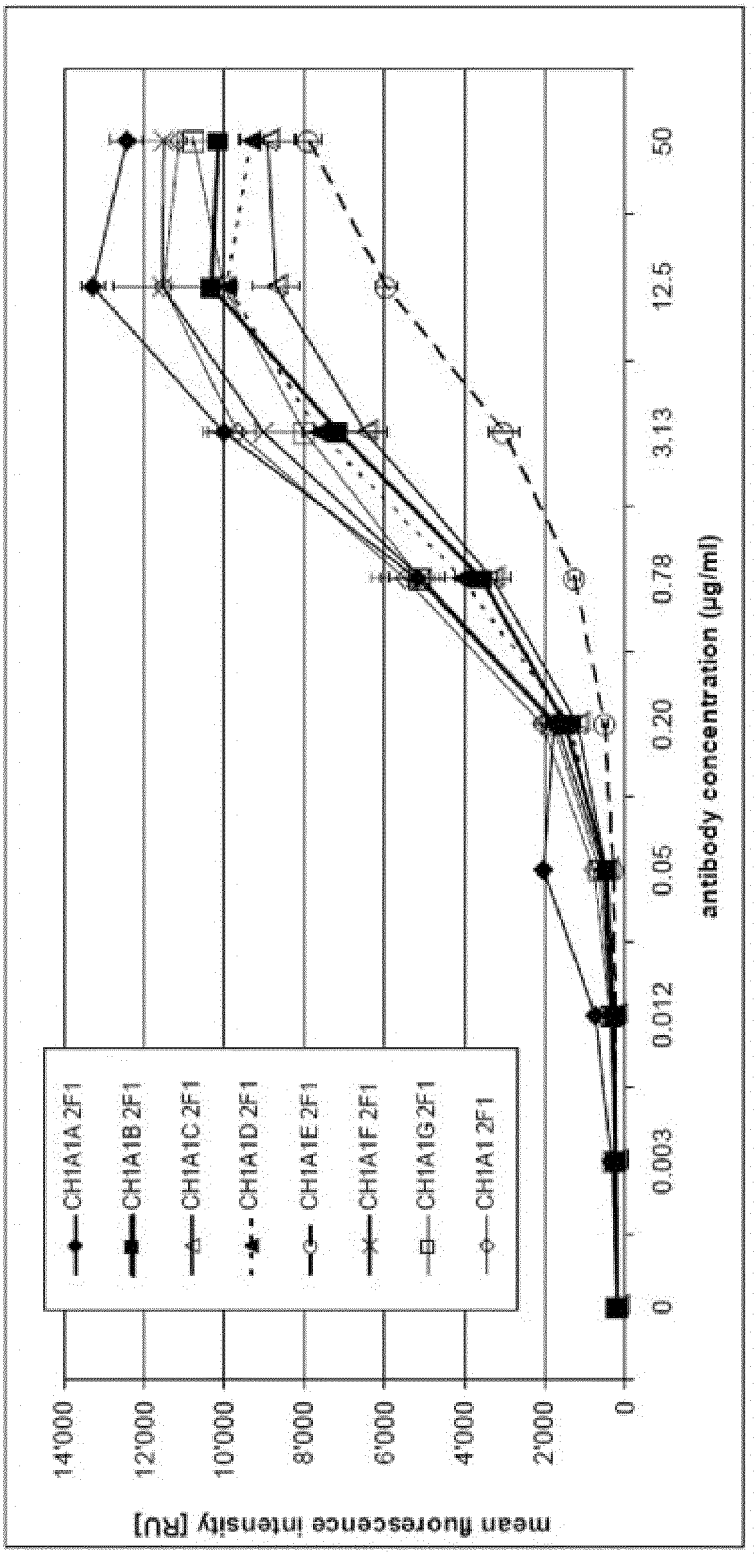
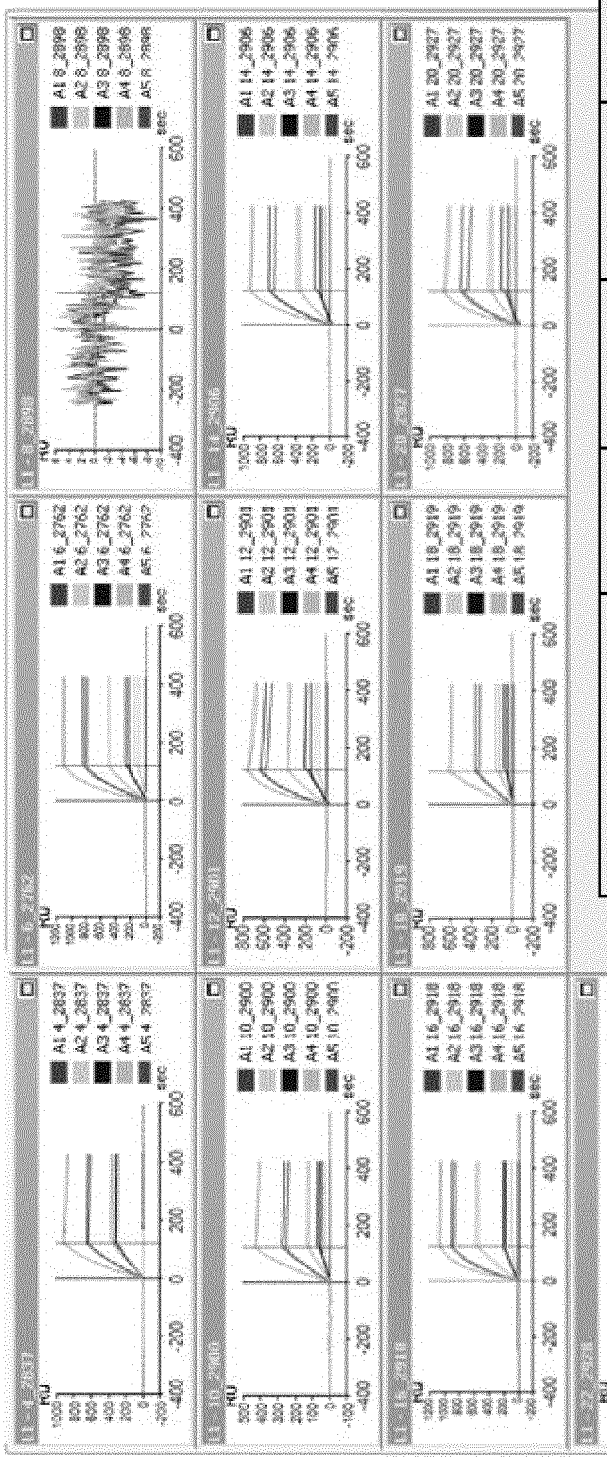

mean fluorescence intensity [RU]
14'000
12'000
10'000
8'000
6'000
4'000
2'000
0
antibody concentration (µg/ml)
0
0.003
0.012
0.05
0.20
0.78
3.13
12.5
50
CH1A1A 2F1
CH1A1B 2F1
CH1A1C 2F1
CH1A1D 2F1
CH1A1E 2F1
CH1A1F 2F1
CH1A1G 2F1
CH1A1 2F1

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	$1.32x10^{5}$	$1.41x10^{-4}$	$1.07x10^{-9}$
5HFF12 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

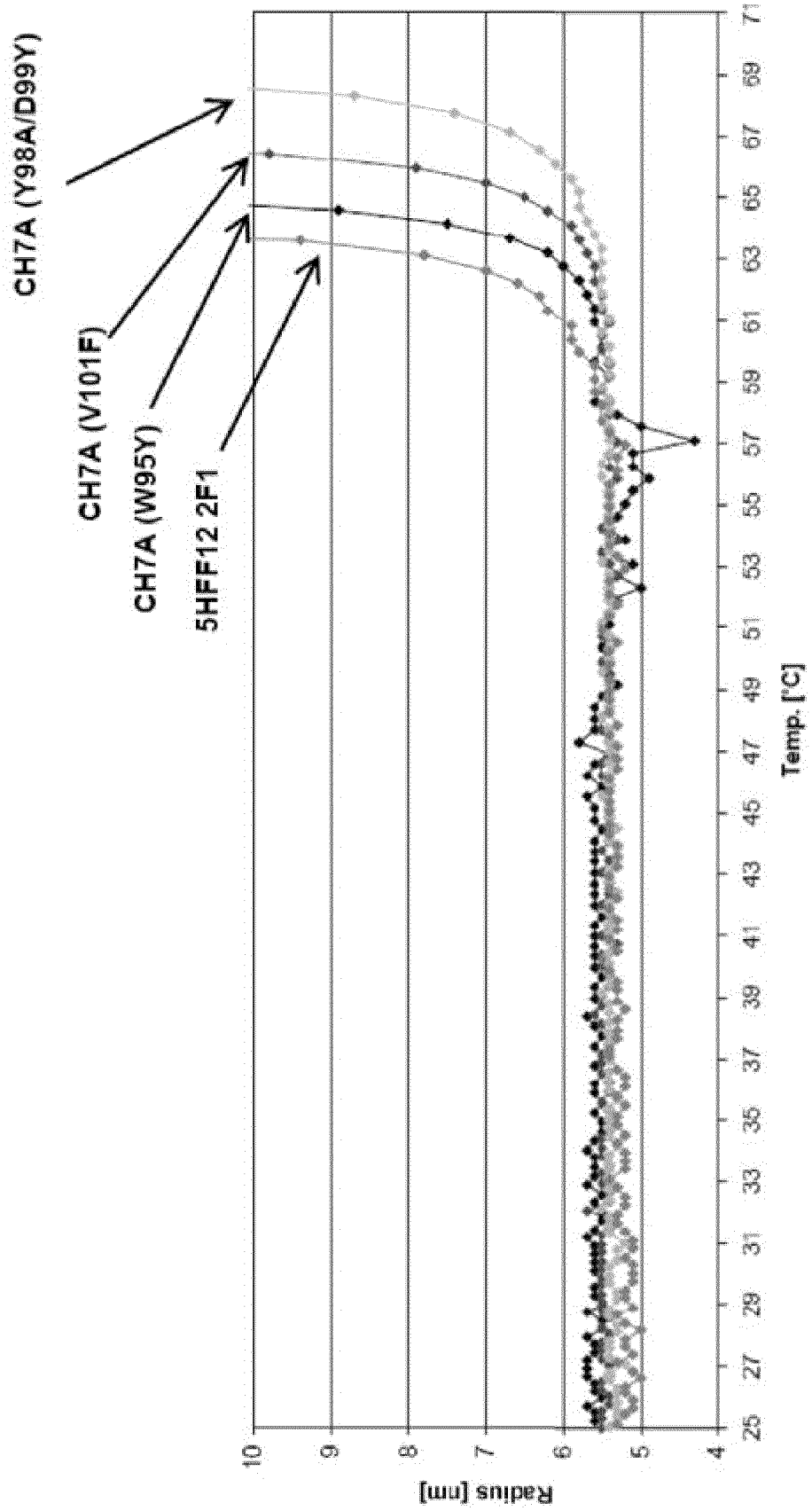

CH7A (Y98A/D99Y)
CH7A (V101F)
CH7A (W95Y)
5HFF12 2F1
Radius [nm]
Temp. [°C]

Fig. 23

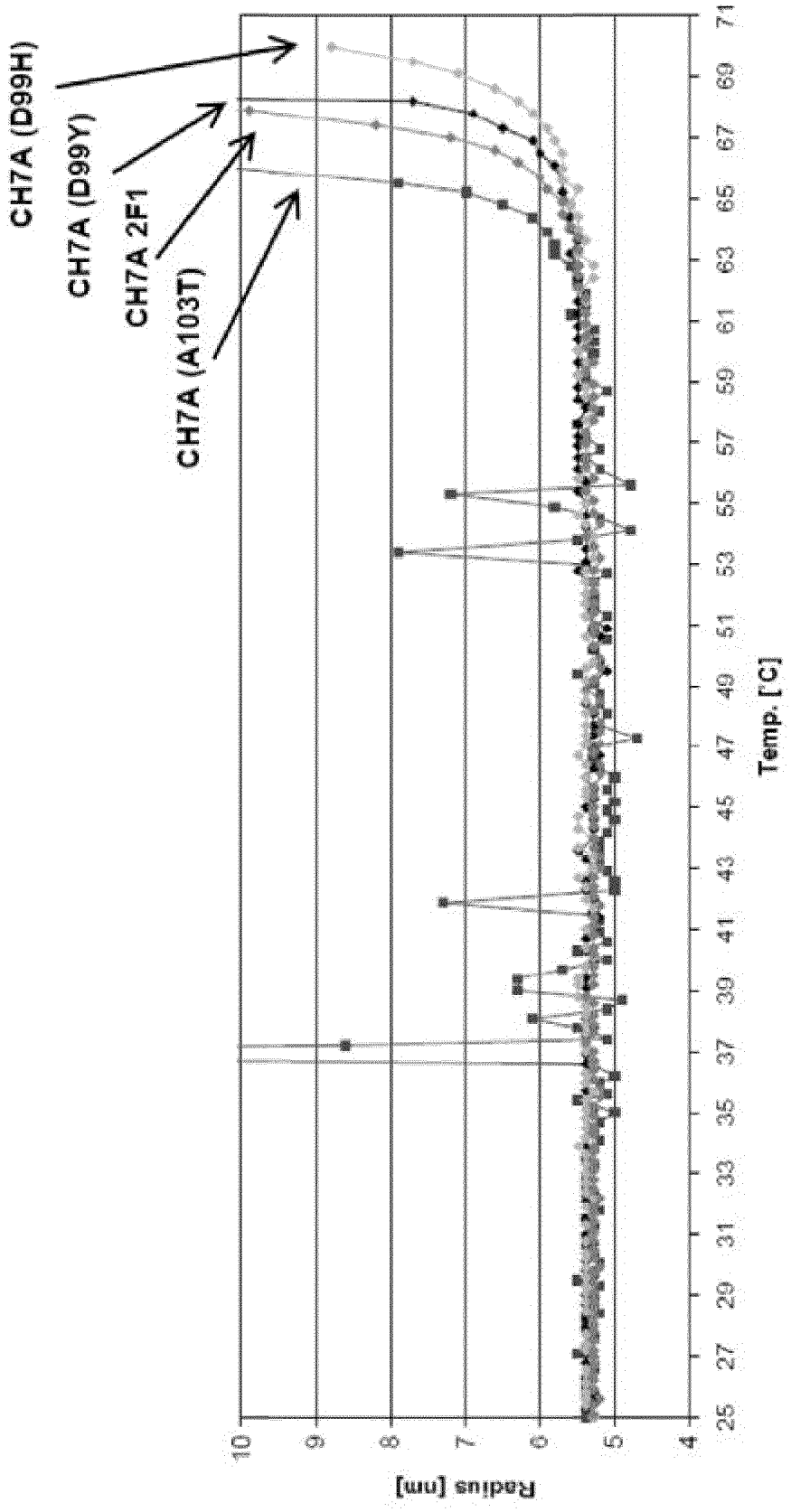
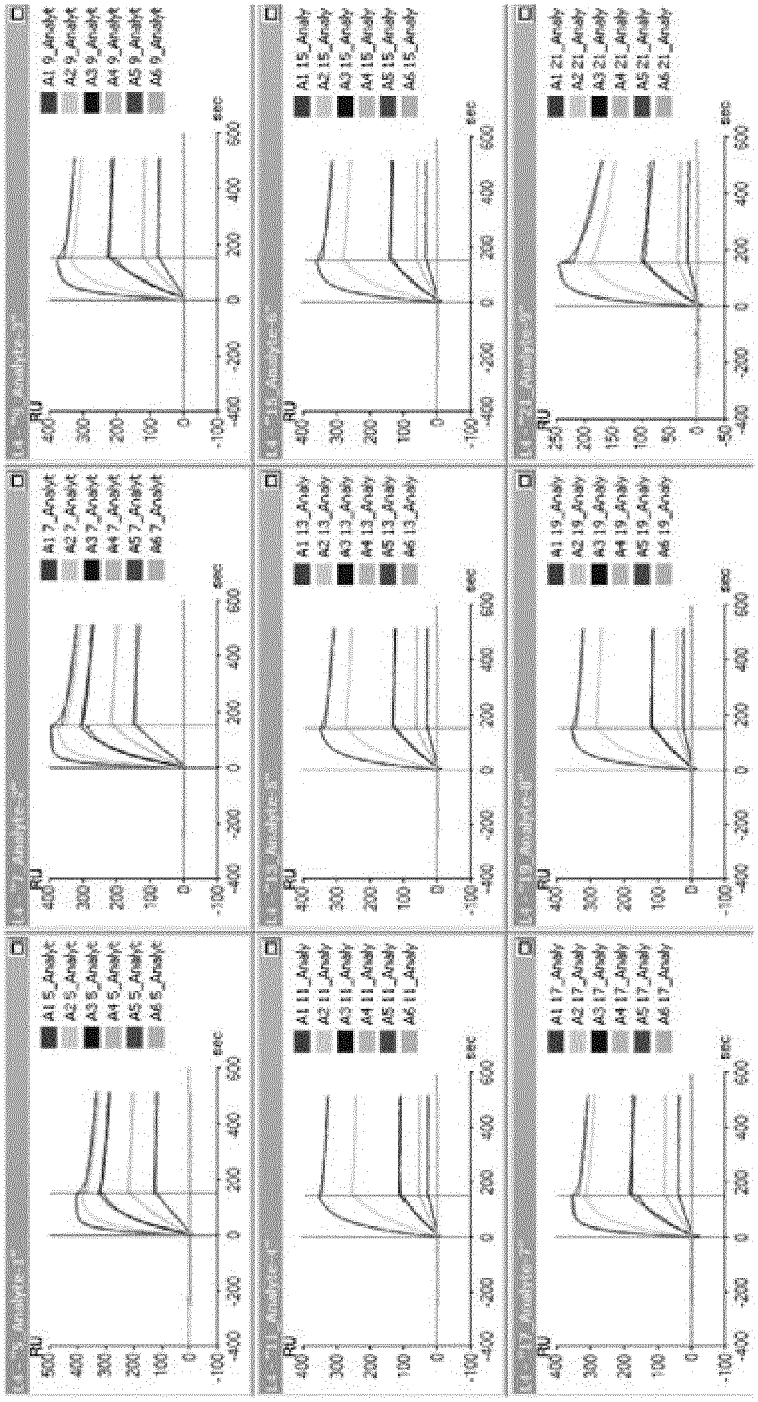


Fig. 24



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

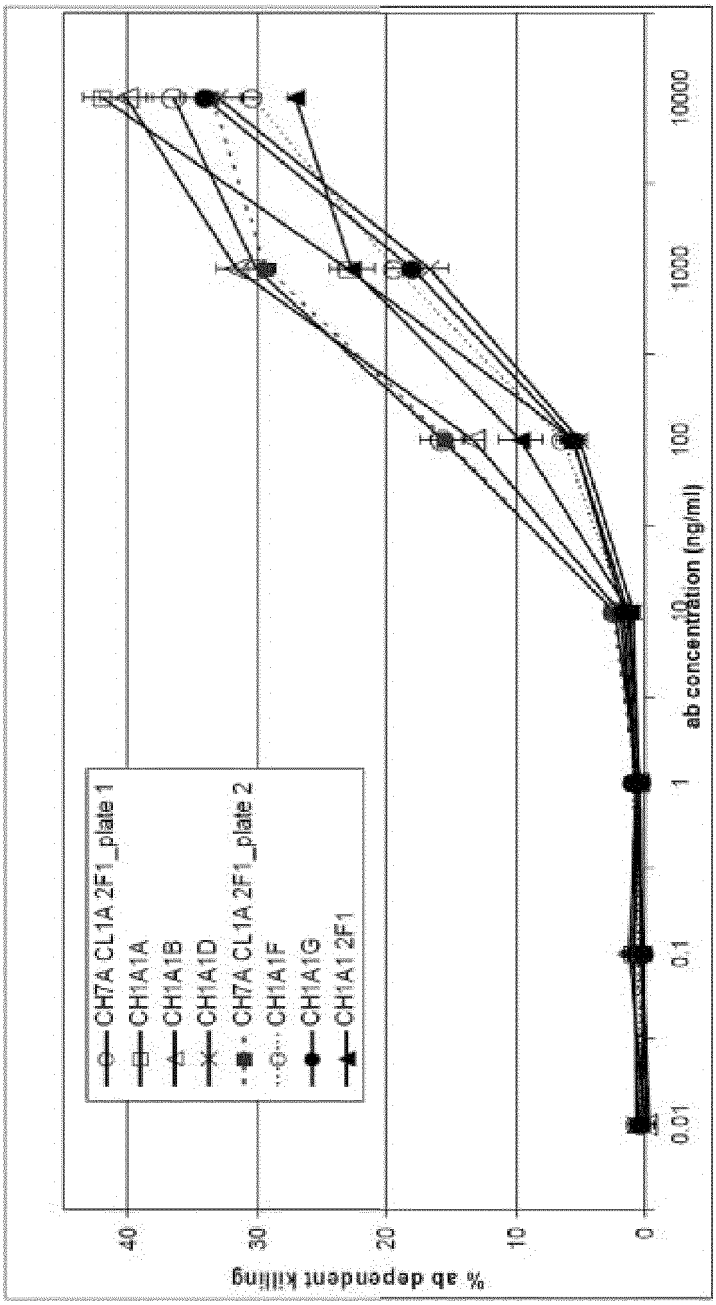

% ab dependent killing
0
10
20
30
40
0.01
0.1
1
10
100
1000
10000
ab concentration (ng/ml)
CH7A CL1A 2F1_plate 1
CH1A1A
CH1A1B
CH1A1D
CH7A CL1A 2F1_plate 2
CH1A1F
CH1A1G
CH1A1 2F1

Fig. 26

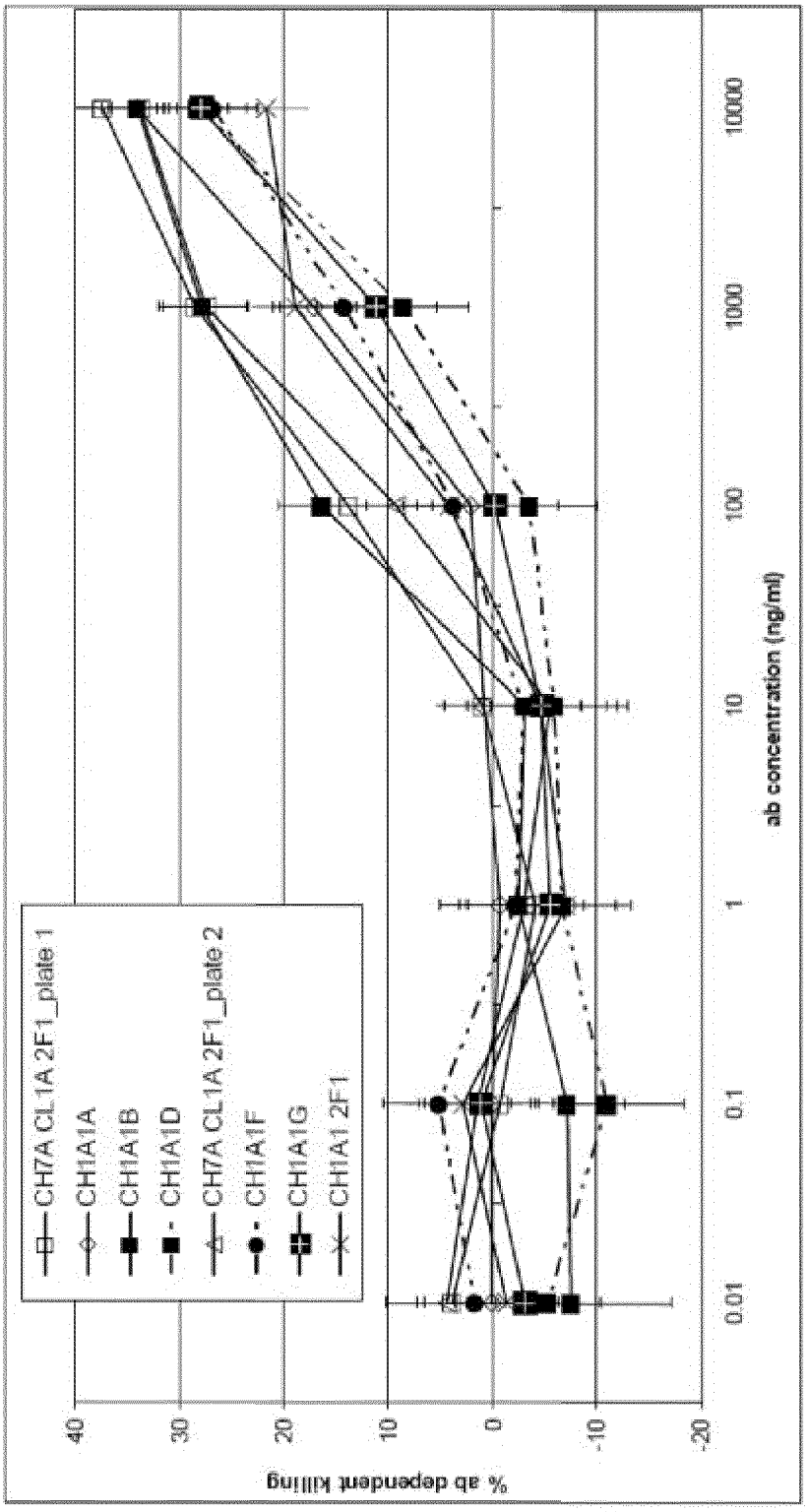

% ab dependent killing
40
30
20
10
0
-10
-20
0.01
0.1
1
10
100
1000
10000
ab concentration (ng/ml)
CH7A CL1A 2F1_plate 1
CH1A1A
CH1A1B
CH1A1D
CH7A CL1A 2F1_plate 2
CH1A1F
CH1A1G
CH1A1 2F1

Fig. 27

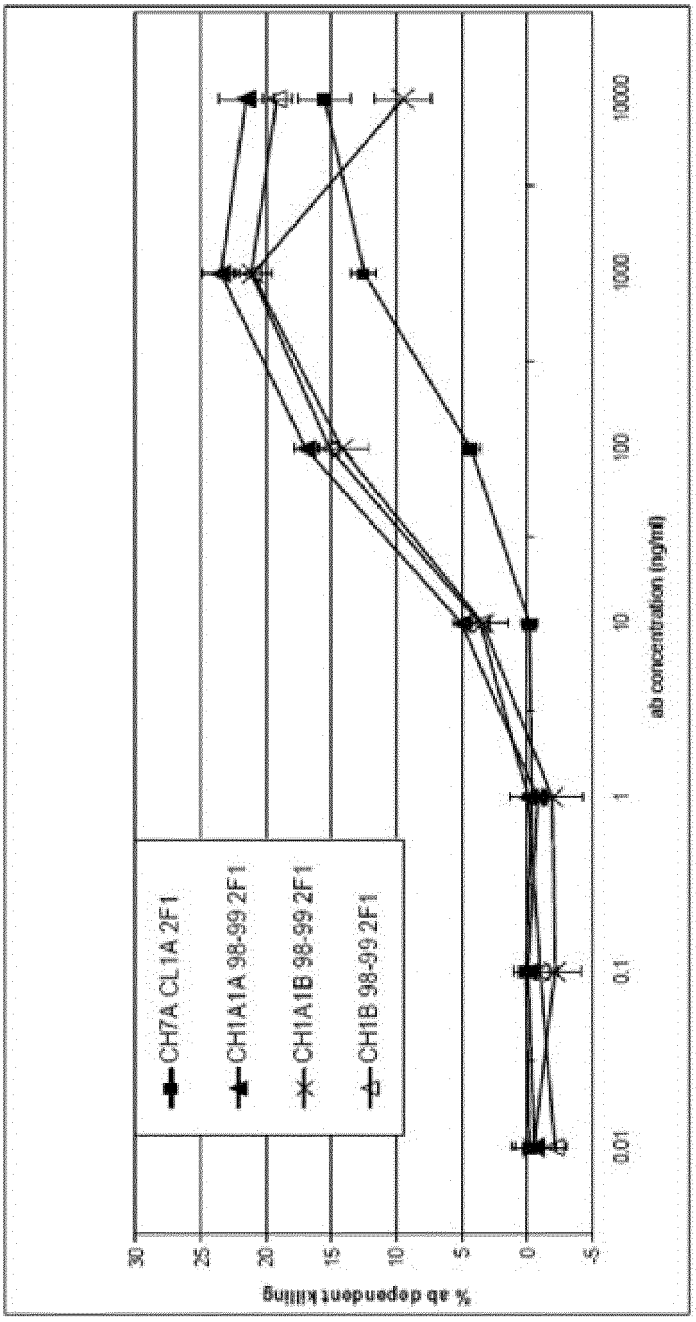

% ab dependent killing
30
25
20
15
10
5
0
-5
0.01
0.1
1
10
100
1000
10000
ab concentration (ng/ml)
CH7A CL1A 2F1
CH1A1A 98-99 2F1
CH1A1B 98-99 2F1
CH1B 98-99 2F1

Fig. 28

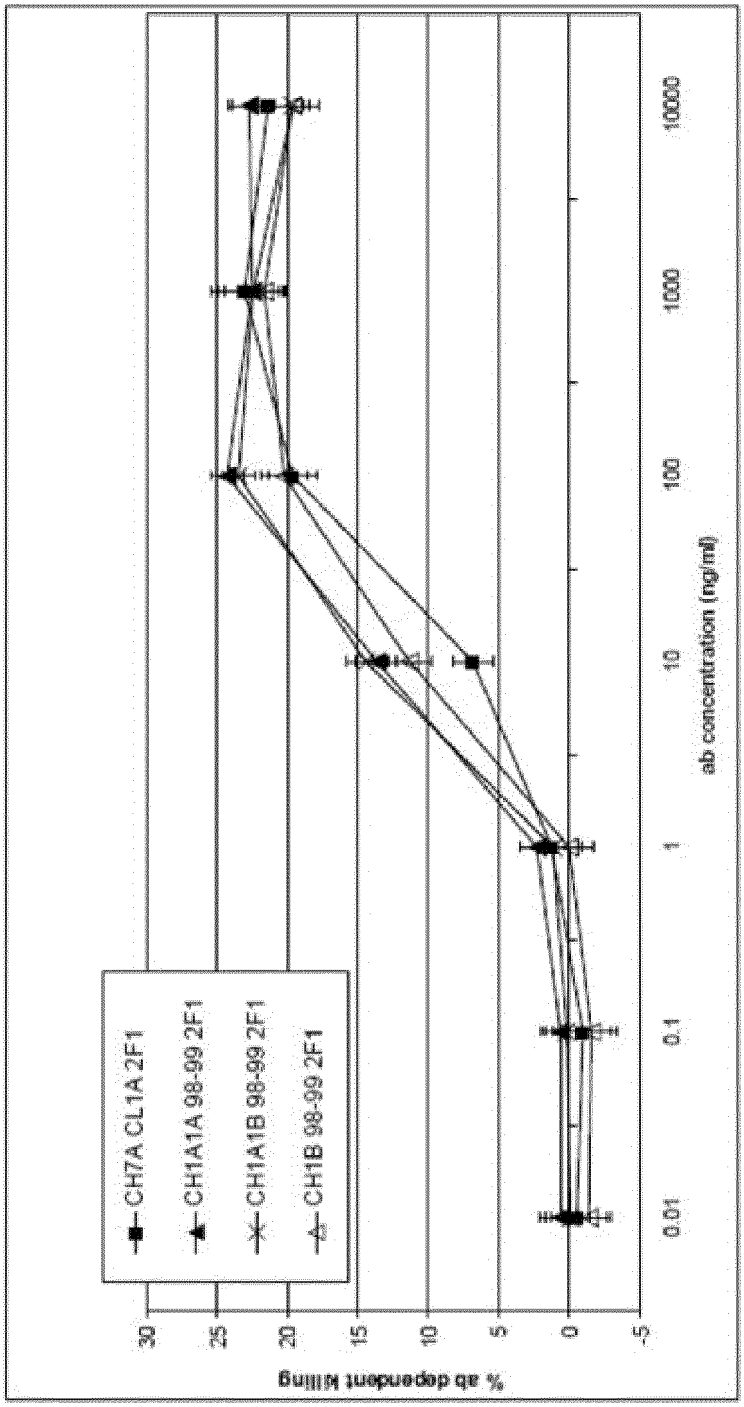

% ab dependent killing
30
25
20
15
10
5
0
-5
0.01
0.1
1
10
100
1000
10000
ab concentration (ng/ml)
CH7A CL1A 2F1
CH1A1A 98-99 2F1
CH1A1B 98-99 2F1
CH1B 98-99 2F1

Fig. 29

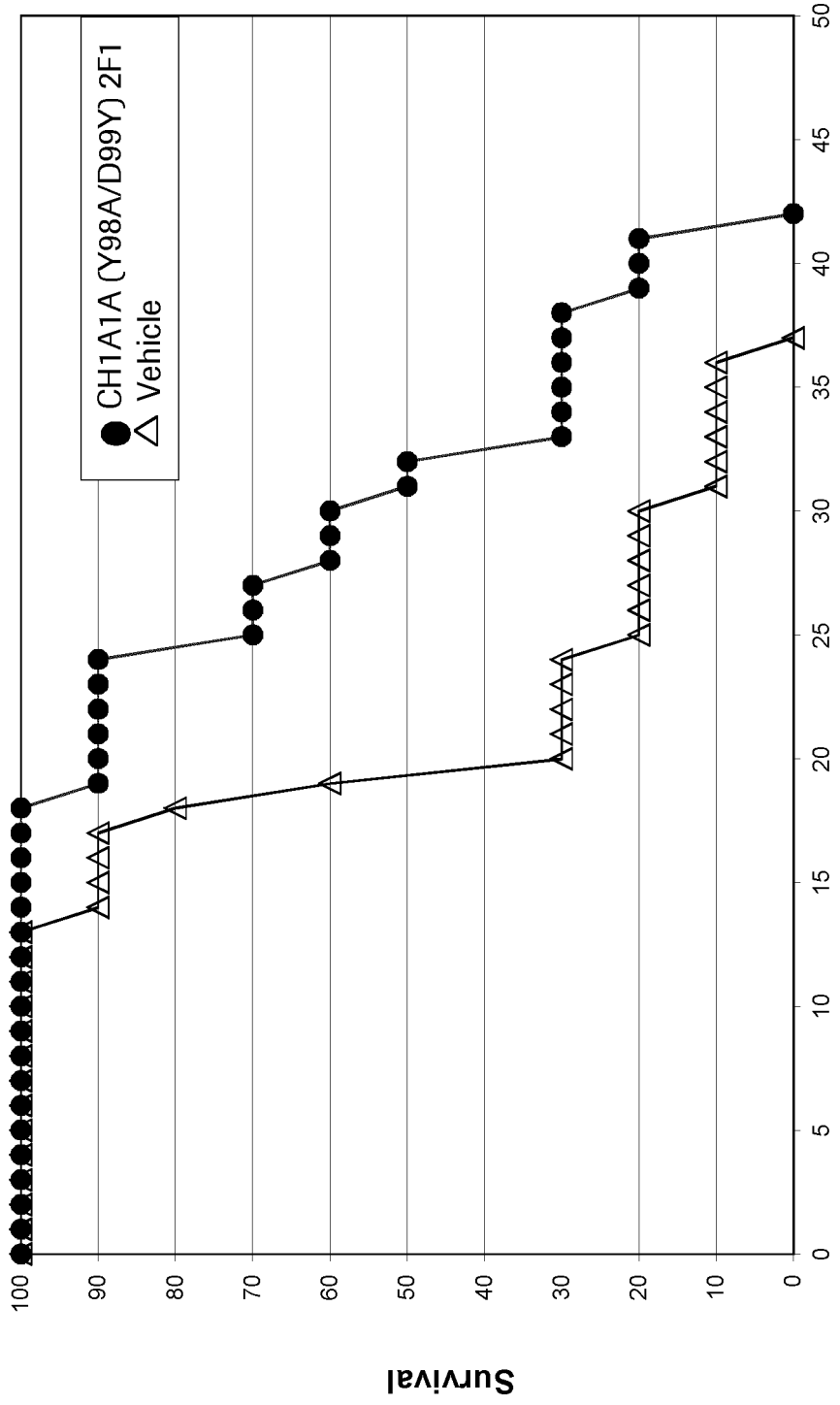

CH1A1A (Y98A/D99Y) 2F1
Vehicle
Survival
Study day
0
10
20
30
40
50
60
70
80
90
100
0
5
10
15
20
25
30
35
40
45
50

Fig. 30

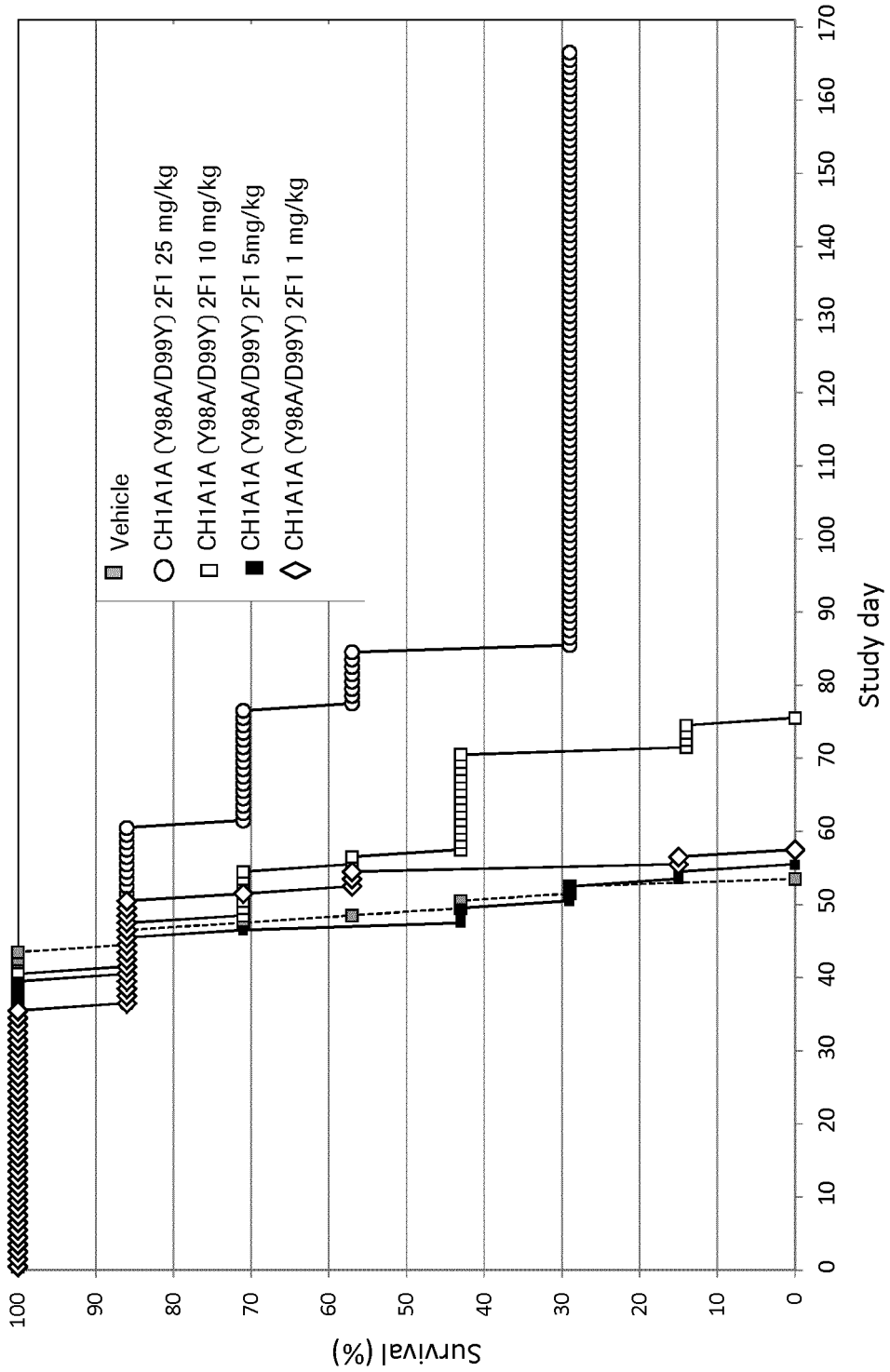

Survival (%)
100
90
80
70
60
50
40
30
20
10
0
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
Study day
Vehicle
CH1A1A (Y98A/D99Y) 2F1 25 mg/kg
CH1A1A (Y98A/D99Y) 2F1 10 mg/kg
CH1A1A (Y98A/D99Y) 2F1 5mg/kg
CH1A1A (Y98A/D99Y) 2F1 1 mg/kg

Fig. 31

CDR		Amino Acid Sequence	SEQ ID NO
Heavy Chain CDR1	Kabat	EFGMN	1
		E**Y**GMN	2
		E**YS**MN	3
		EFGM**S**	5
	Chothia	GYTFTEF	6
		GYTFTE**Y**	7
	AbM	GYTFTEFGMN	8
		GYTFTE**Y**GMN	9
		GYTFTE**YS**MN	10
		GYTFTEFGM**S**	12
Heavy Chain CDR2	Kabat	WINTKTGEATYVEEFKG	13
		WINTKTGEATY**I**EEFKG	14
		WINTK**S**GEATYVEEFKG	15
		YINTK**N**GEA**N**YVEEFKG	16
		WINTK**N**GEATY**I**EEFKG	17
	Chothia	NTKTGEAT	18
		NTK**S**GEAT	19
		NTK**N**GEA**N**	20
	AbM	WINTKTGEAT	21
		WINTK**S**GEAT	22
		YINTK**N**GEA**N**	23
		WINTK**N**GEAT	24
Heavy Chain CDR3	Kabat Chothia and AbM	WDFYDYVEAMDY	25
		WDFY**H**YVEAMDY	26
		WDF**V**DYVEAMDY	27
		WDFY**W**YVEAMDY	28
		WD**AFE**YV**K**A**L**DY	29
		WDF**FE**Y**FKT**MDY	30
		WDF**FY**YV**QT**MDY	31
		WDF**SY**YVEAMDY	32
		WDF**AH**Y**FQT**MDY	33
		WDF**AY**Y**FQT**MDY	34
		WDF**AY**YLEAMDY	35

CDR	Amino Acid Sequence	SEQ ID NO
Light Chain CDR1	KASQNVGTNVA	36
	KAS**A**NVG**N**NVA	37
	KAS**K**NVGTNVA	38
	KAS**AA**VGT**Y**VA	39
	KASQ**YAS**TNVA	40
	KAS**H**NVGTNVA	41
	KASQ**IMGP**NVA	42
	KASQ**I**VGTNVA	43
	KASQ**K**V**L**TNVA	44
	KASQ**T**V**SA**NVA	45
Light Chain CDR2	SASYRYS	46
	Y**L**ASNLSG	47
	YLASY**PQI**	48
	YSASYR**KR**	49
	Y**W**ASYRYS	50
	YSAS**H**RYS	51
	YLASY**HE**S	52
	YSAS**HRP**S	53
	Y**L**ASYRYS	54
	Y**L**ASYRY**R**	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	W D F Y D Y V E A M D Y	3681 nM	PMS22
26	W D F Y **H** Y V E A M D Y	586 nM	1C8
27	W D F **V** D Y V E A M D Y	1893 nM	3E1
28	W D F Y **W** Y V E A M D Y	746 nM	2D7
33	W D F **A H** Y **F Q T** M D Y	59 nM	Affinity Matured CDRH-3
34	W D F **A Y** Y **F Q T** M D	44 nM	Affinity Matured CDRH-3
35	W D F **A Y** Y **L** E A M D	69 nM	Affinity Matured CDRH-3
29	W D**A F E** Y V **K** A **L** D Y	26 nM	H3 Full (5) 19
30	W D F **F E** Y **F K T** M D Y	51 nM	H3 Full (5) 8
31	W D F **F Y** Y V **Q T** M D Y	81 nM	H3 Full (5) 28
33	W D F **S Y** Y V E A M D Y	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 WINTKTGEATY**I**EEFKG	402 nM	H4E9
1 and 15	EFGMN and WINTK**S**GEATYVEEFKG		pAC14 (B9)
2 and 15	E**Y**GMN and WINTK**S**GEATYVEEFKG		pAC15 (F9)
3 and 16	E**YS**MN and **Y**INTK**N**GEA**N**YVEEFKG		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	E**Y**GMN and WINTK**N**GEATY**I**EEFKG		H1/H2 (5) 11
1 and 16	E**F**GMN and **Y**INTK**N**GEA**N**YVEEFKG		H1/H2 (5) 13
2 and 16	E**Y**GMN and **Y**INTK**N**GEA**N**YVEEFKG		H1/H2 (5) 14
5 and 13	EFGM**S** 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	**A**NVG**N**N and Y**L**ASNLSG	250 nM	pAC21 (3A1)
38 and 48	**K**NVGTN and Y**L**ASY**PQI**	700 nM	pAC19 (2C6)
39 and 49	**AA**VGT**Y** and YSASYR**KR**	220 nM	pAC18 (2F1)
40 and 50	Q**YAS**TN and Y**W**ASYRYS	290 nM	pAC23 (2F11)
36 and __	QNVGTN and **P**LI-YSASYRYS	402 nM	H4E9
41 and 51	**H**NVGTN and YSAS**H**RYS	2255 nM	L2D2
42 and 52	Q**IM**G**P**N and YLASY**HE**S		pAC6 (C1)
43 and 53	Q**I**VGTN and YSAS**H**R**P**S		pAC7 (E10)
44 and 54	Q**K**V**L**TN and Y**L**ASYRYS		pAC12 (H7)
45 and 55	QT**VSA**N and Y**L**ASYRY**R**		pAC13 (H11)
	CDR-L3		
56	H Q Y Y T Y P L F T		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	WDF**AH**Y**FQT**MDY
34	5L1A10 CDR-H3	WDF**AY**Y**FQT**MDY
217	PR1A3 (Y98A)	WDF**A**DYVEAMDY
218	PR1A3 (D99Y)	WDFY**Y**YVEAMDY
219	PR1A3 (D99H)	WDFY**H**YVEAMDY
220	PR1A3 (V101F)	WDFYDY**F**EAMDY
221	PR1A3 (E101aQ)	WDFYDYV**Q**AMDY
222	PR1A3 (A103T)	WDFYDYVE**T**MDY
223	PR1A3 (Y98A / D99Y)	WDF**AY**YVEAMDY
224	PR1A3 (W95Y)	**Y**DFYDYVEAMDY

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

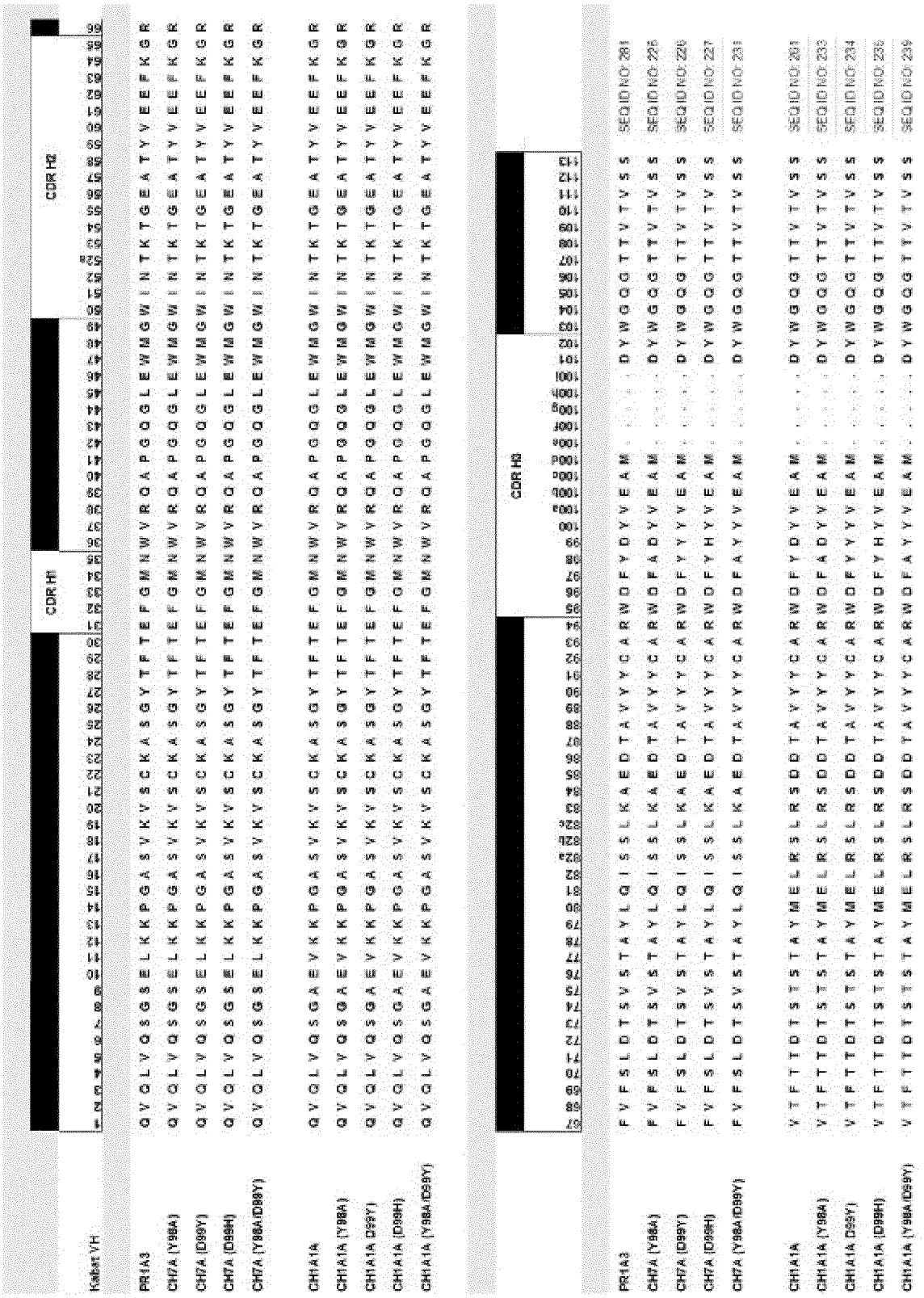

CDR H1
CDR H2
CDR H3
Kabat VH
PR1A3
CH7A (Y98A)
CH7A (D99Y)
CH7A (D99H)
CH7A (Y98A/D99Y)
CH1A1A
CH1A1A (Y98A)
CH1A1A D99Y)
CH1A1A (D99H)
CH1A1A (Y98A/D99Y)
SEQ ID NO: 231
SEQ ID NO: 232
SEQ ID NO: 233
SEQ ID NO: 234
SEQ ID NO: 235
SEQ ID NO: 236

Fig. 38