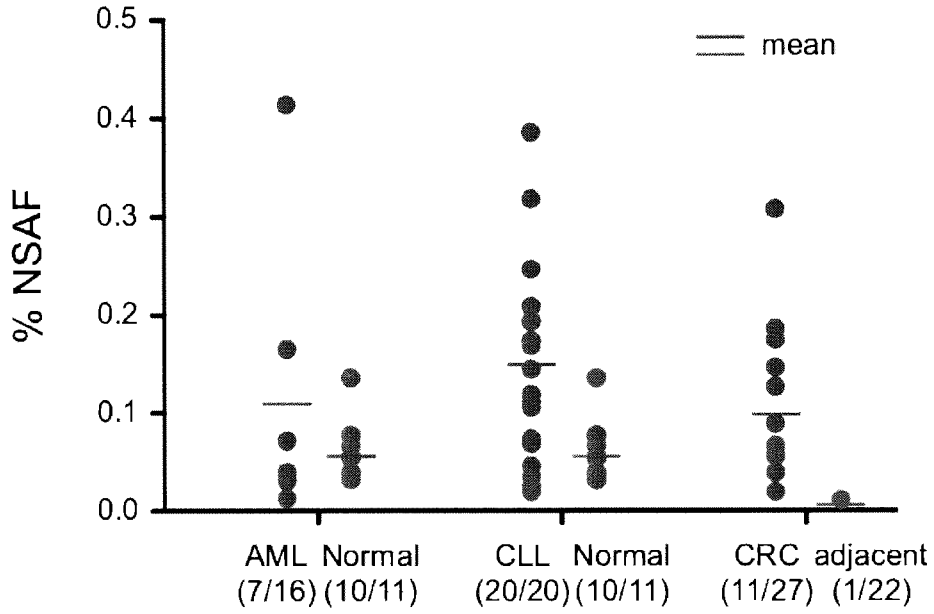

0.5
0.4
0.3
0.2
0.1
0.0
% NSAF
mean
AML Normal
(7/16) (10/11)
CLL Normal
(20/20) (10/11)
CRC adjacent
(11/27) (1/22)

FIG. 1

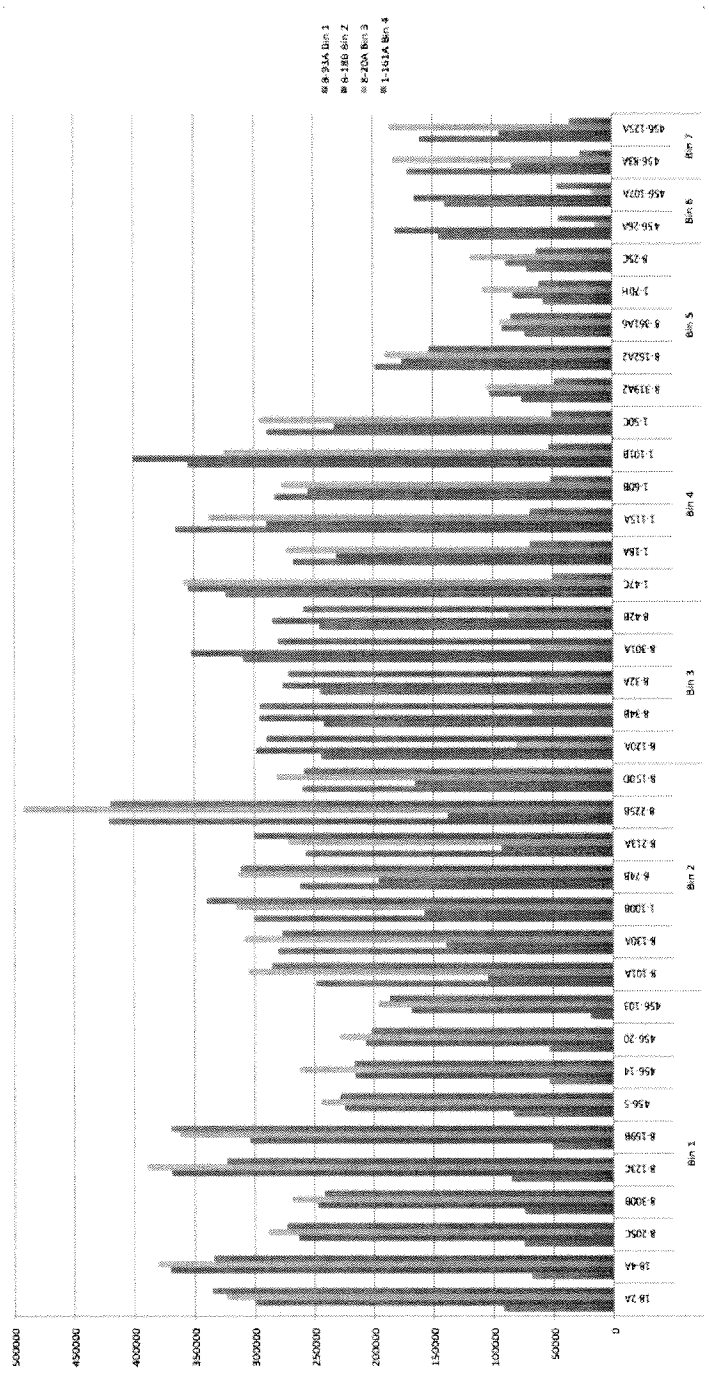

Bin 1
Bin 2
Bin 3
Bin 4
Bin 5
Bin 6
Bin 7
500000
450000
400000
350000
300000
250000
200000
150000
100000
50000
0

FIG. 2

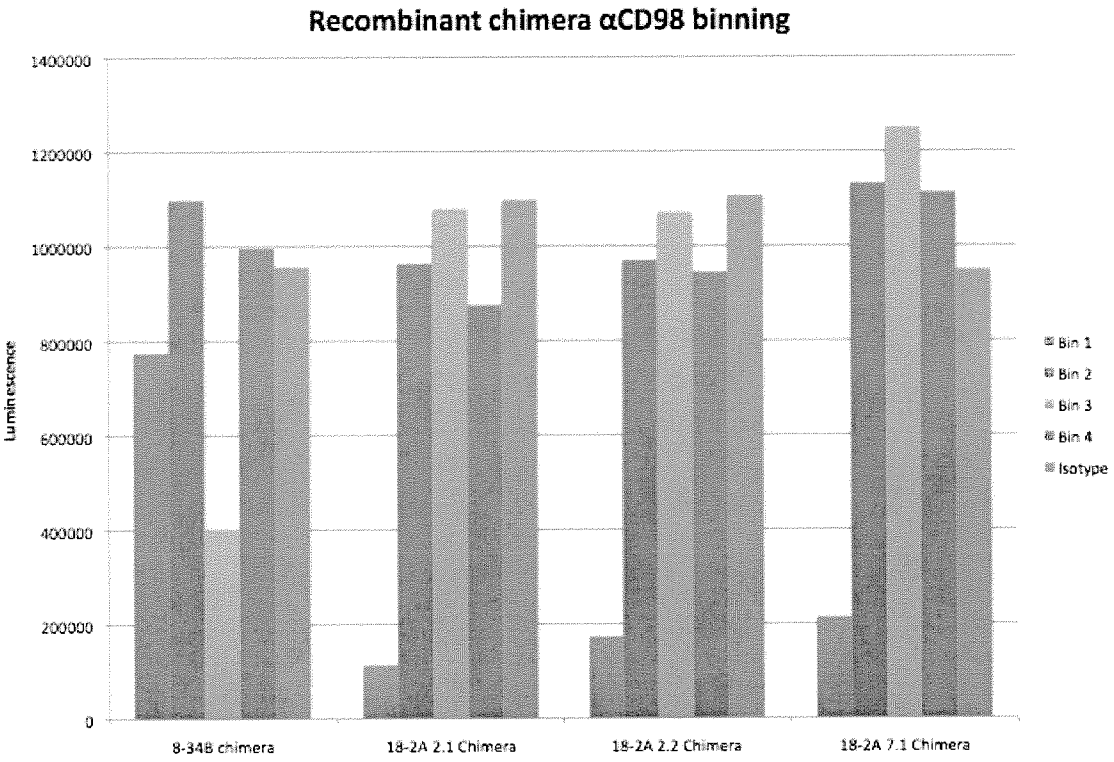

Recombinant chimera αCD98 binning
Luminescence
1400000
1200000
1000000
800000
600000
400000
200000
0
8-34B chimera
18-2A 2.1 Chimera
18-2A 2.2 Chimera
18-2A 7.1 Chimera
Bin 1
Bin 2
Bin 3
Bin 4
Isotype

FIG. 3A

	18-2A mouse	8-34B mouse	8-34B Chimera	18-2A 7.1 Chimera	18-2A 2.2 Chimera	18-2A 2.1 Chimera
Kd	1.272	2.22	4.548	0.8642	1.142	1.037
R square	0.9946	0.9921	0.9887	0.99	0.9973	0.9963

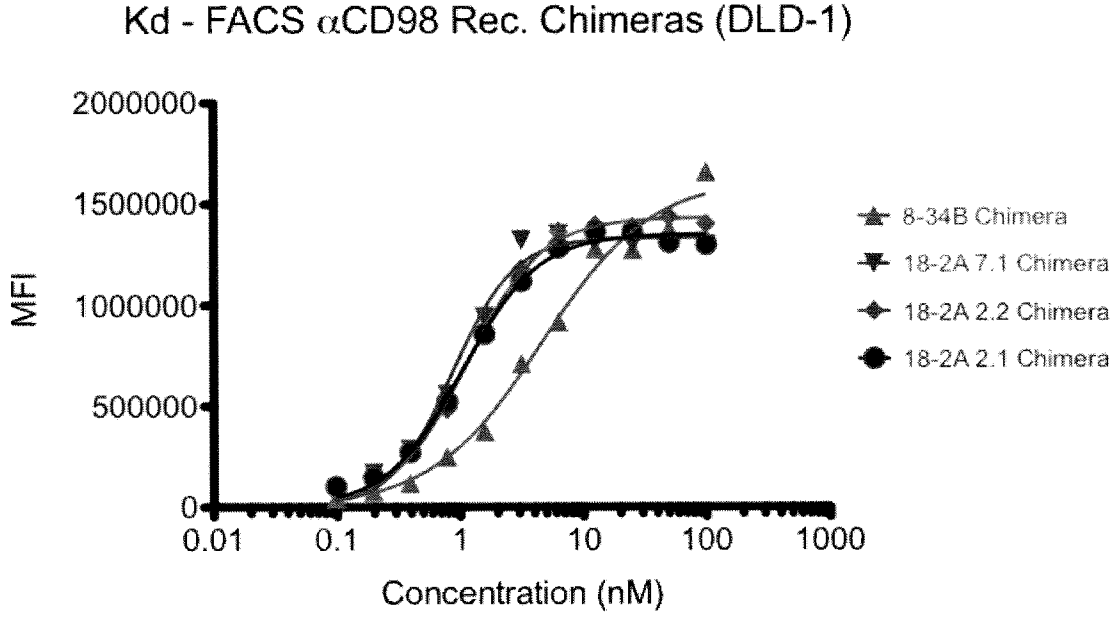


FIG. 3B

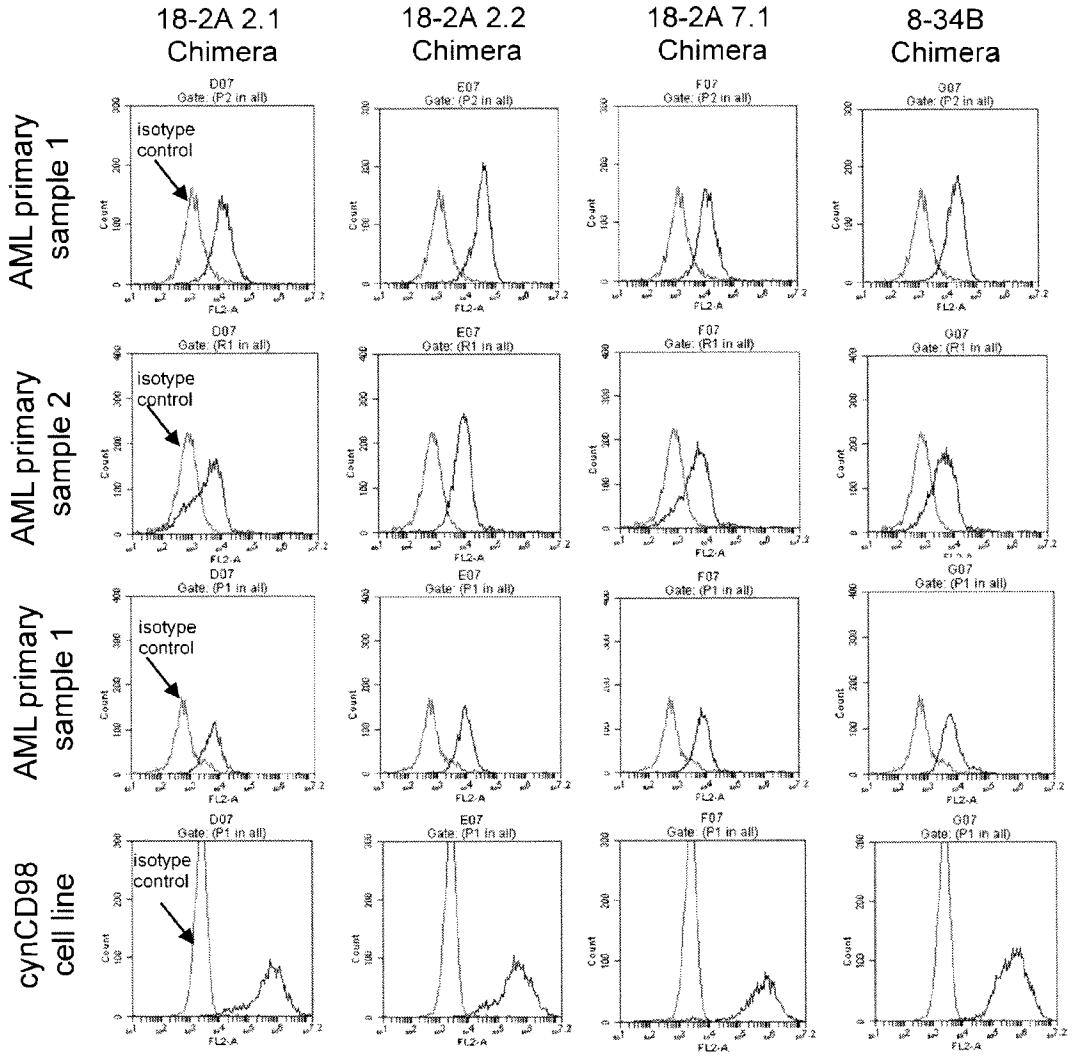

18-2A 2.1 Chimera
18-2A 2.2 Chimera
18-2A 7.1 Chimera
8-34B Chimera
AML primary sample 1
AML primary sample 2
AML primary sample 1
cynCD98 cell line
isotype control
D07
E07
F07
G07
Gate: (P2 in all)
Gate: (R1 in all)
Gate: (P1 in all)
Count
FL2-A

FIG. 3C

```
IGN 34   DIVMTQSPSSLTVTAGEKVTMSC KSSQSLLNSGNQKTYLT WYQQKPGQPPKLLIY WASTRES
AC       DIVMTQSPDSLAVSLGERATINC KSSQSVLYSSNNKNYLA WYQQKPGQPPKLLIY WASTRES
L1       DIVMTQSPDSLAVSLGERATINC KSSQSLLNSGNQKTYLT WYQQKPGQPPKLLIY WASTRES
L2       DIVMTQSPDSLAVSLGERATINC KSSQSLLNSGNQKTYLT WYQQKPGQPPKLLIY WASTRES

IGN 34   GVPDRFTGSGSGTEFTLTISSVQAEDLAVYYC QNDYSYPPWT FGGGTKLEIK
AC       GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYC QQYYSTP-LT FGQGTKVEIK
L1       GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYC QNDYSYPPWT FGQGTKVEIK
L2       GVPDRFTGSGSGTEFTLTISSLQAEDVAVYYC QNDYSYPPWT FGQGTKVEIK
```

Red: Kabat CDRs Blue: Substitutions

Human Acceptor Sequence (AC)
>gi|215982738|gb|ACJ71709.1|
DIVMTQSPDSLAVSLGERATINCKSSQSVLYSSNNKNYLAWYQQ
KPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVA
VYYCQQYYSTPLTFGQGTKVEIK (SEQ ID NO:38)

FIG. 4A

```
IGN 34   QVQLKESGPGLVAPSQSLSITCTVSGFSLT SYGVH WIRQPPGKGLEWLG LIWAGGSINYNSALMS
AC       QVQLQESGPGLVKPSETLSLTCTVSGGSIS SYYWS WIRQPPGKGLEWIG YIYYSGSTNYNPSLKS
H1       QVQLQESGPGLVKPSETLSLTCTVSGFSLT SYGVH WIRQPPGKGLEWIG LIWAGGSINYNSALMS
H2       QVQLQESGPGLVKPSETLSLTCTVSGFSLT SYGVH WIRQPPGKGLEWLG LIWAGGSINYNSALMS
H3       QVQLQESGPGLVKPSETLSLTCTVSGFSLT SYGVH WIRQPPGKGLEWLG LIWAGGSINYNSALMS
```

Kabat + Chothia

```
IGN 34   RLSISKDNSKSQVFLKMNSLETEDTAMYYCAR KGHMYS---YAMDY WGQGTSVTVSS
AC       RVTISVDTSKNQFSLKLSSVTAADTAVYYCAR RHNSSSWYGRYFDY WGQGTLVTVSS
H1       RVTISVDTSKNQFSLKLSSVTAADTAVYYCAR KGHMYS---YAMDY WGQGTLVTVSS
H2       RVTISKDTSKNQVSLKLSSVTAADTAVYYCAR KGHMYS---YAMDY WGQGTLVTVSS
H3       RLTISKDNSKNQVSLKLSSVTAADTAVYYCAR KGHMYS---YAMDY WGQGTLVTVSS
```

Human Acceptor Sequence (AC)
>gi|2135460|pir||I37782
QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPPGKGLE
WIGYIYYSGSTNYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYY
CARHNSSSWYGRYFDYWGQGTLVTVSS (SEQ ID NO:40)

FIG. 4B

FIG. 5A

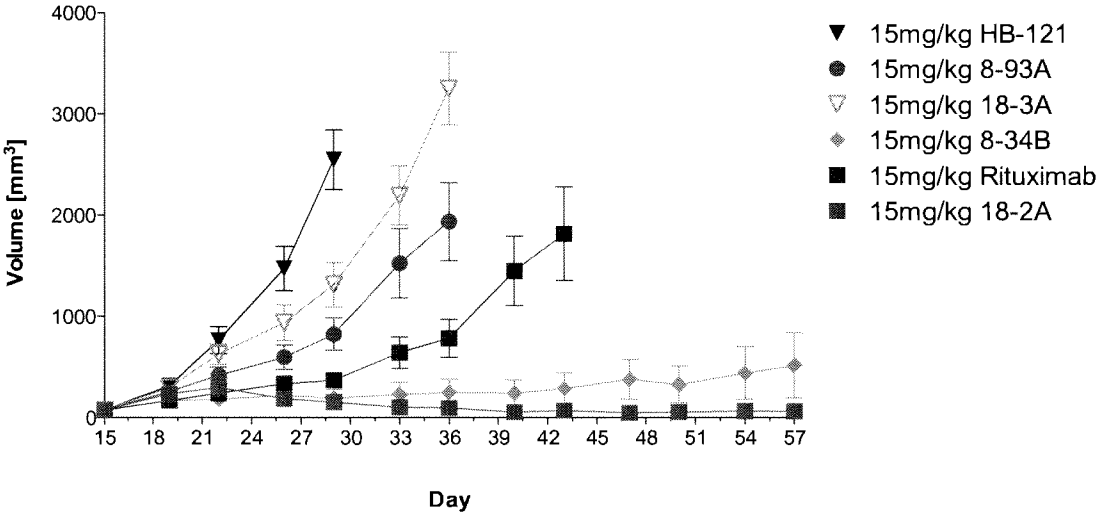

Volume [mm3]
4000
3000
2000
1000
0
15 18 21 24 27 30 33 36 39 42 45 48 51 54 57
Day
15mg/kg HB-121
15mg/kg 8-93A
15mg/kg 18-3A
15mg/kg 8-34B
15mg/kg Rituximab
15mg/kg 18-2A

FIG. 5B

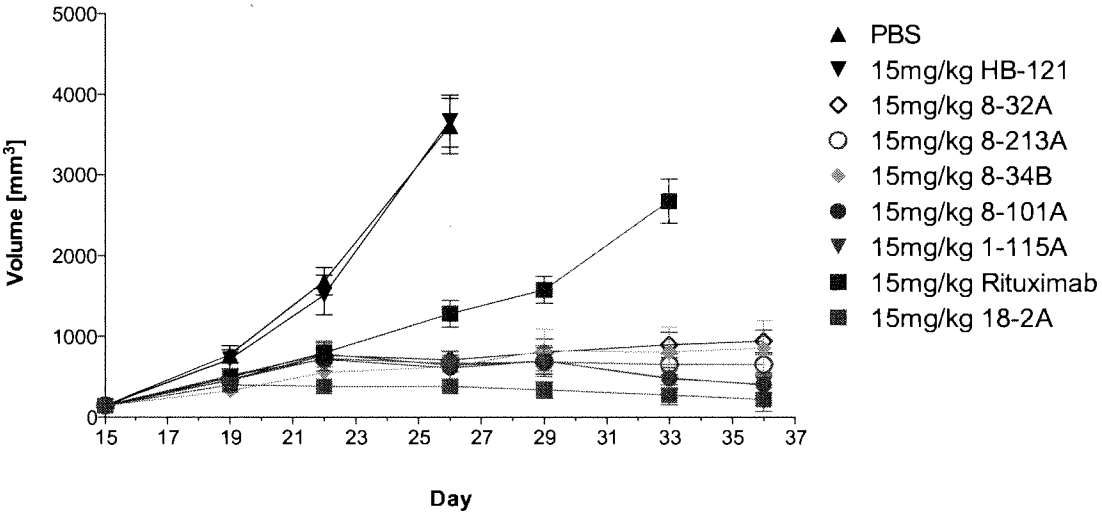

Volume [mm3]
5000
4000
3000
2000
1000
0
15 17 19 21 23 25 27 29 31 33 35 37
Day
PBS
15mg/kg HB-121
15mg/kg 8-32A
15mg/kg 8-213A
15mg/kg 8-34B
15mg/kg 8-101A
15mg/kg 1-115A
15mg/kg Rituximab
15mg/kg 18-2A

FIG. 5C

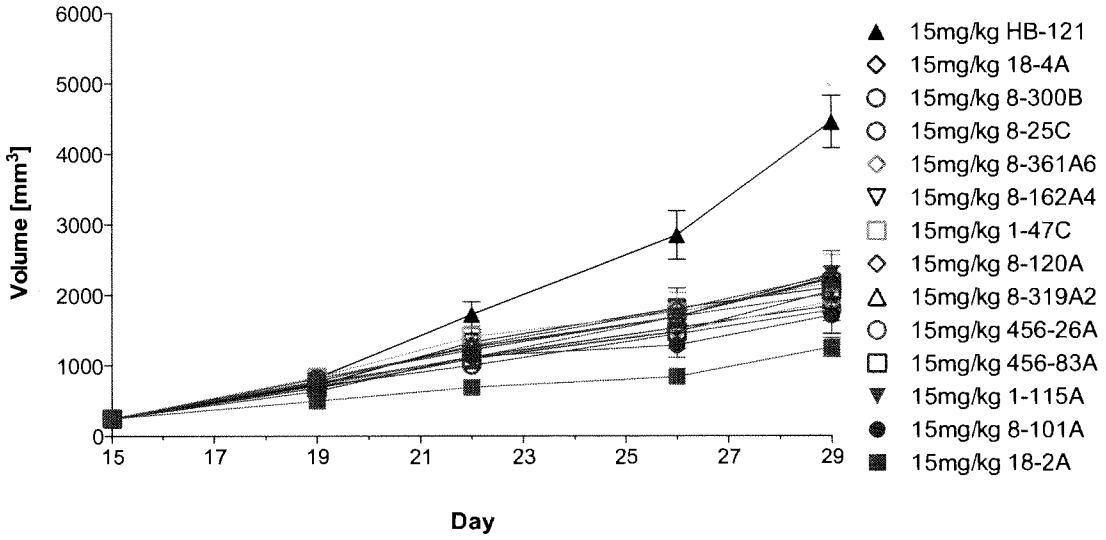

6000
5000
4000
3000
2000
1000
0
Volume [mm3]
15
17
19
21
23
25
27
29
Day
15mg/kg HB-121
15mg/kg 18-4A
15mg/kg 8-300B
15mg/kg 8-25C
15mg/kg 8-361A6
15mg/kg 8-162A4
15mg/kg 1-47C
15mg/kg 8-120A
15mg/kg 8-319A2
15mg/kg 456-26A
15mg/kg 456-83A
15mg/kg 1-115A
15mg/kg 8-101A
15mg/kg 18-2A

FIG. 6A

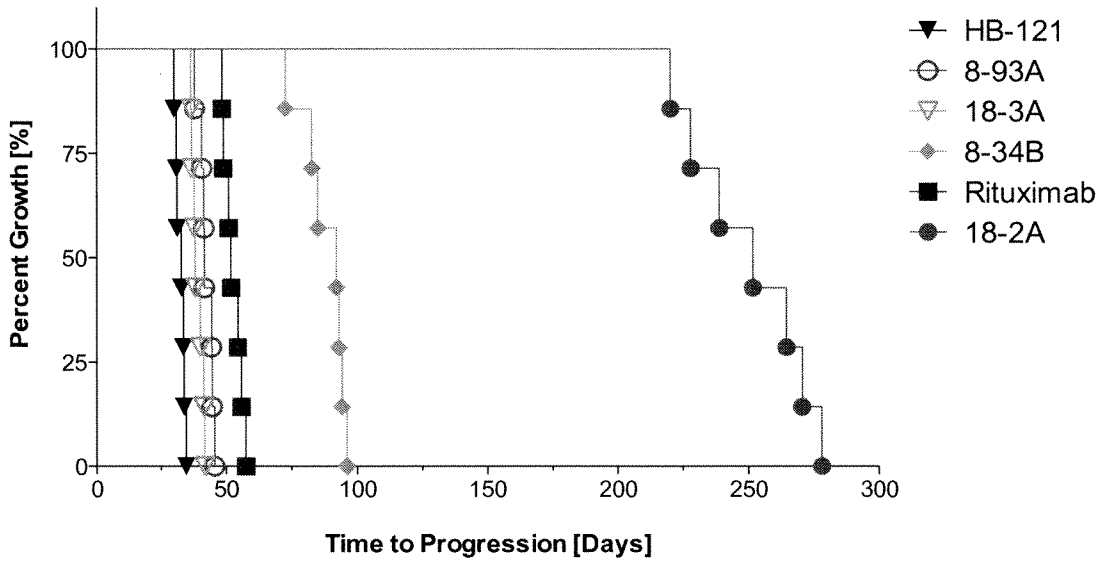

Percent Growth [%]
100
75
50
25
0
0
50
100
150
200
250
300
Time to Progression [Days]
HB-121
8-93A
18-3A
8-34B
Rituximab
18-2A

FIG. 6B

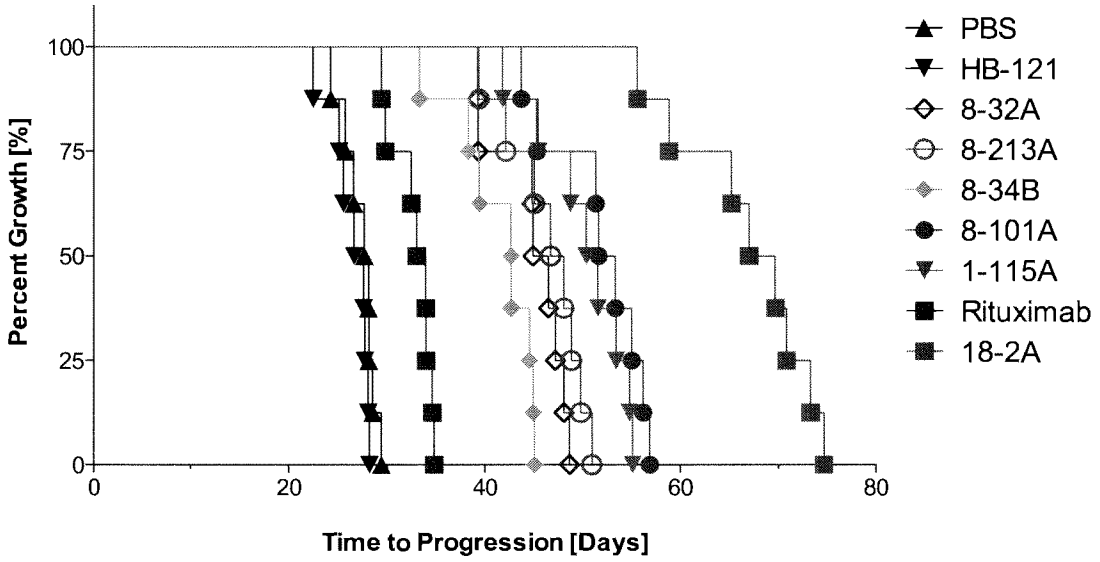
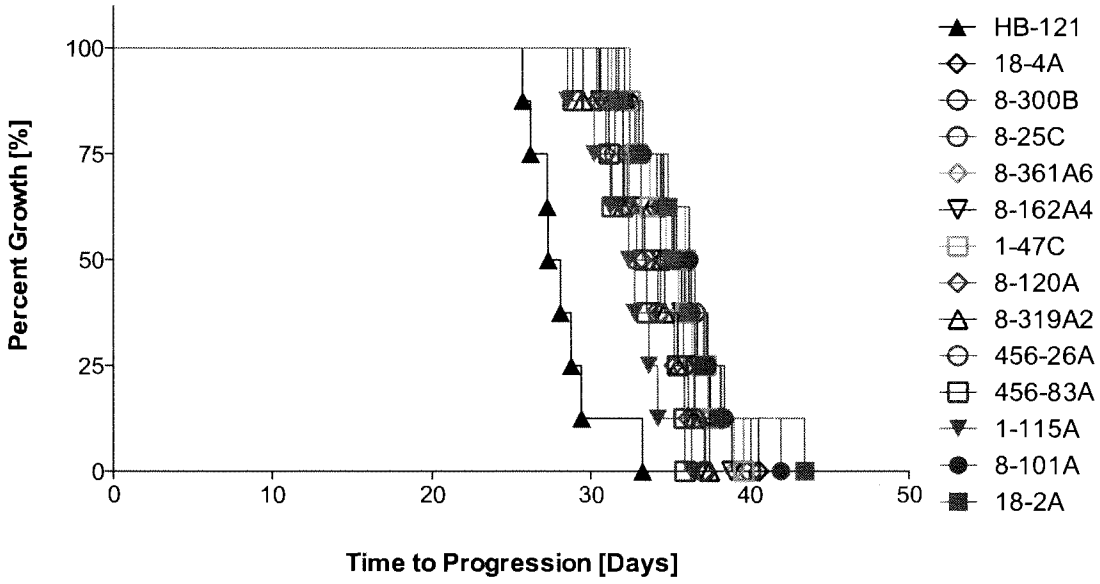
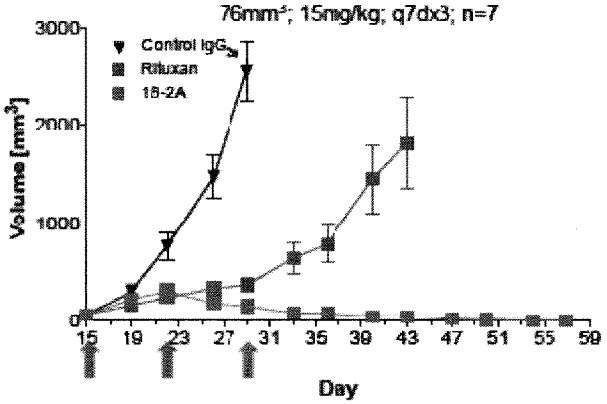

Percent Growth [%]
100
75
50
25
0
0
20
40
60
80
Time to Progression [Days]
PBS
HB-121
8-32A
8-213A
8-34B
8-101A
1-115A
Rituximab
18-2A

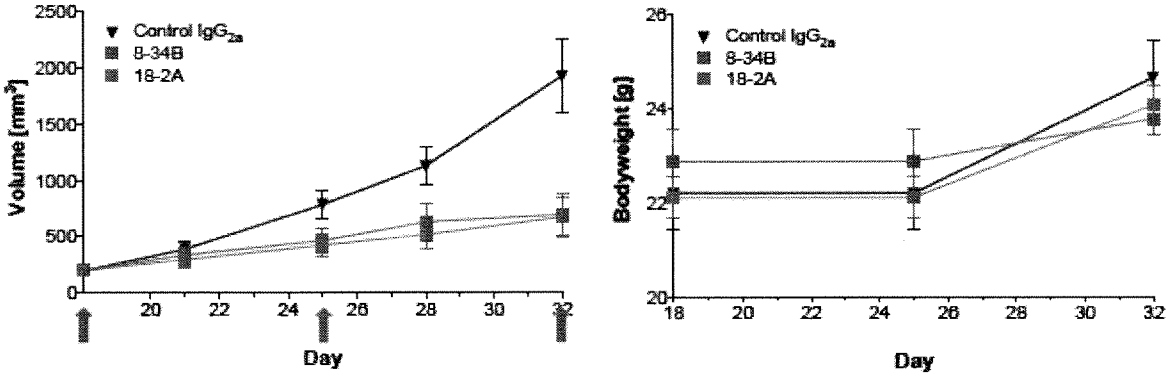
FIG. 6C


Percent Growth [%]
100
75
50
25
0
0
10
20
30
40
50
Time to Progression [Days]
HB-121
18-4A
8-300B
8-25C
8-361A6
8-162A4
1-47C
8-120A
8-319A2
456-26A
456-83A
1-115A
8-101A
18-2A



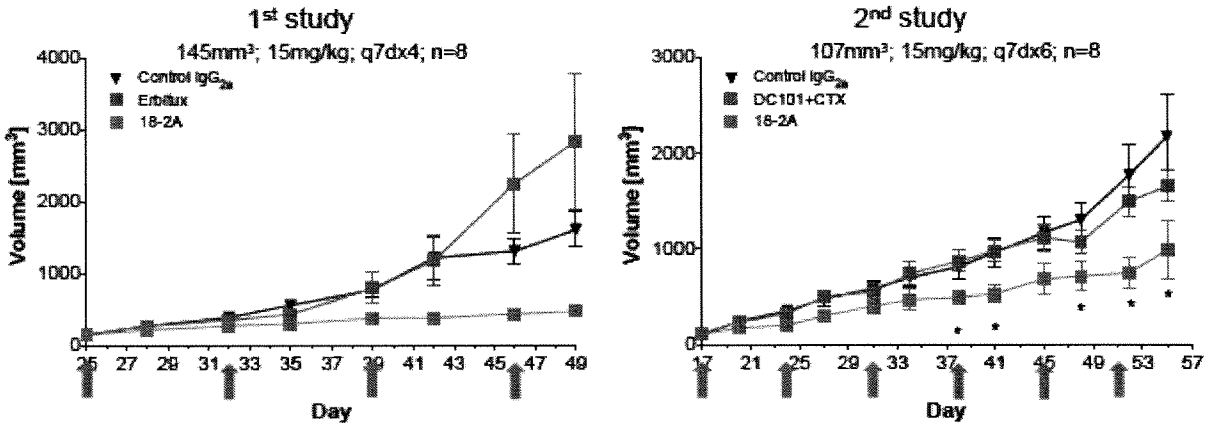
RAMOS/SCID	Control IgG_{2a}	Rituxan	18-2A
Volume ±SD [mm³]	2667 ±816	387 ±204	160 ±191
TGI [%]	-	-88	-96.7
p-Value	-	0.0002	0.0001

FIG. 7



mAb	Control IgG_{2a}	18-2A	8-34B
Volume ±SD, [mm³]	1921 ±863	671 ±468	694 ±492
p-Value	-	0.0080	0.0091

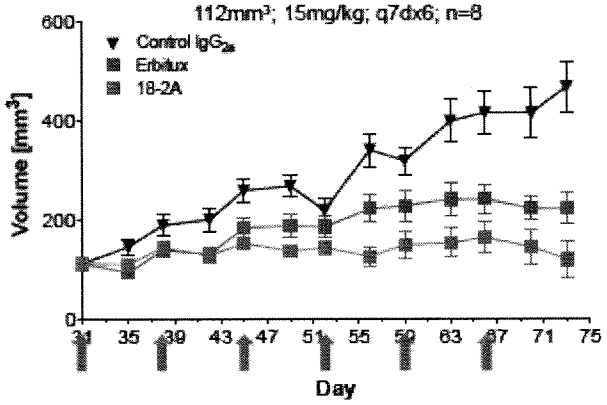
FIG. 8



= administration of treatment

mAb	Control IgG_{2a}	Erbitux	18-2A	Control IgG_{2a}	DC101+ CTX	18-2A
Vol ±SD [mm³]	1600 ±644	2824 ±2477	463 ±195	2165 ±1249	1647 ±459	985 ±854
TGI [%]	-	+84.1	-78.1	-	-25.2	-57.3
p-Value	-	0.1936	0.0029	-	0.3001	0.0471

FIG. 9



A549/NU	Control IgG_{2a}	Erbitux	18-2A
Volume ±SD [mm³]	467 ±144	222 ±87	119 ±102
TGI [%]	-	-68.8	-97.9
p-Value	-	0.0015	0.0001

FIG. 10

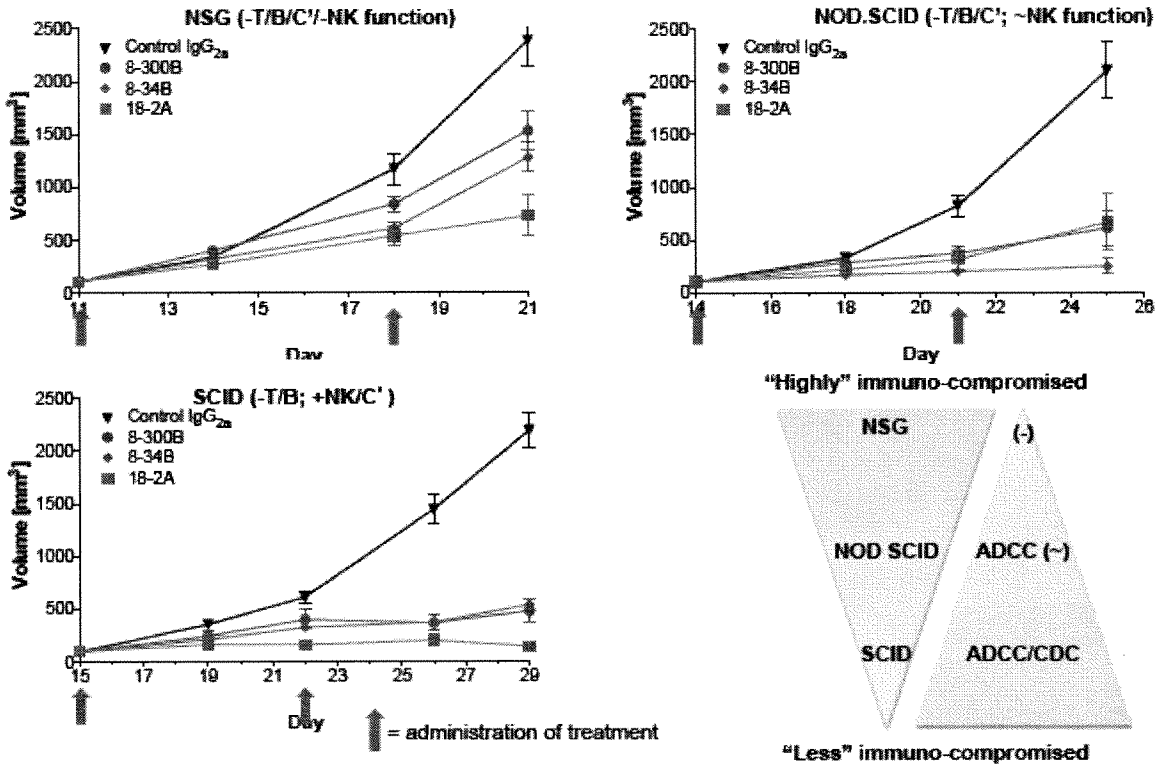
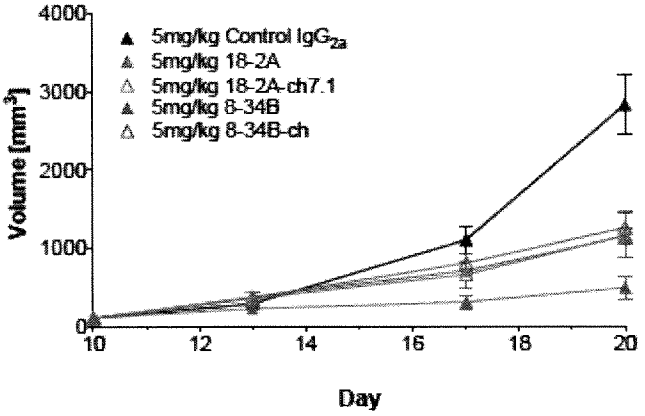

NSG (-T/B/C'/-NK function)
Control IgG2a
8-300B
8-34B
18-2A
Volume [mm3]
Day
NOD.SCID (-T/B/C'; ~NK function)
SCID (-T/B; +NK/C')
= administration of treatment
"Highly" immuno-compromised
NSG
(-)
NOD SCID
ADCC (~)
SCID
ADCC/CDC
"Less" immuno-compromised

FIG. 11



RAMOS, (n=8)	Control IgG_{2a}	18-2A	18-2A-ch7.1	8-34B	8-34B-ch
Volume±SD, [mm³]	2831±1089	490±415	1162±805	1149±296	1259±602
TGI, [%]	-	-86	-61	-62	-58
p-Value	-	0.00030	0.00407	0.00291	0.00443

FIG. 12

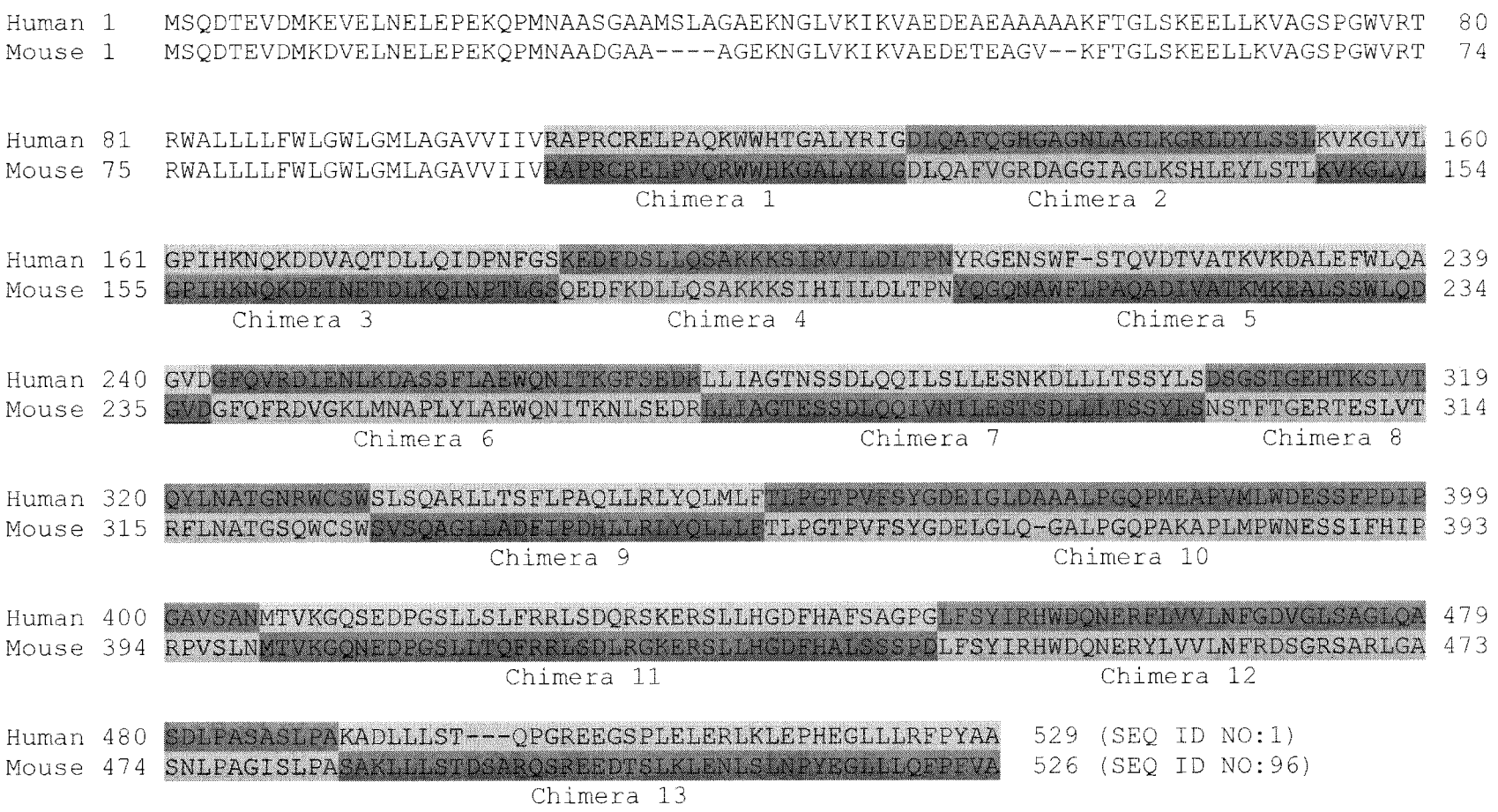

Human 1 MSQDTEVDMKEVELNELEPEKQPMNAASGAAMSLAGAEKNGLVKIKVAEDEAEAAAAAKFTGLSKEELLKVAGSPGWVRT 80
Mouse 1 MSQDTEVDMKDVELNELEPEKQPMNAADGAA----AGEKNGLVKIKVAEDETEAGV--KFTGLSKEELLKVAGSPGWVRT 74
Human 81 RWALLLLFWLGWLGMLAGAVVIIVRAPRCRELPAQKWWHTGALYRIGDLQAFQGHGAGNLAGLKGRLDYLSSLKVKGLVL 160
Mouse 75 RWALLLLFWLGWLGMLAGAVVIIVRAPRCRELPVQRWWHKGALYRIGDLQAFVGRDAGGIAGLKSHLEYLSTLKVKGLVL 154
Chimera 1
Chimera 2
Human 161 GPIHKNQKDDVAQTDLLQIDPNFGSKEDFDSLLQSAKKKSIRVILDLTPNYRGENSWF-STQVDTVATKVKDALEFWLQA 239
Mouse 155 GPIHKNQKDEINETDLKQINPTLGSQEDFKDLLQSAKKKSIHIILDLTPNYQGQNAWFLPAQADIVALKMKEALSSWLQD 234
Chimera 3
Chimera 4
Chimera 5
Human 240 GVDGFQVRDIENLKDASSFLAEWQNITKGFSEDRLLIAGTNSSDLQQILSLLESNKDLLLTSSYLSDSGSIGEHTKSLVT 319
Mouse 235 GVDGFQFRDVGKLMNAPLYLAEWQNITKNLSEDRLLIAGTESSDLQQIVNILESISDLLLTSSYLSNSTFTGERTESLVT 314
Chimera 6
Chimera 7
Chimera 8
Human 320 QYLNATGNRWCSWSLSQARLLTSFLPAQLLRLYQLMLFTLPGTPVFSYGDEIGLDAAALPGQPMEAFVMLWDESSFPDIP 399
Mouse 315 RFLNATGSQWCSWSVSQAGLLADFIPDHLLRLYQLLLFTLPGTPVFSYGDELGLQ-GALPGQPAKAPLMPWNESSIFHIP 393
Chimera 9
Chimera 10
Human 400 GAVSANMTVKGQSEDPGSLLSLFRRLSDQRSKERSLLHGDFHAFSAGPGLFSYIRHWDQNERFLVVLNFGDVGLSAGLQA 479
Mouse 394 RPVSLNMTVKGQNEDPGSLLTQFRRLSDLRGKERSLLHGDFHALSSSPDLFSYIRHWDQNERYLVVLNFRDSGRSARLGA 473
Chimera 11
Chimera 12
Human 480 SDLPASASLPAKADLLLST---QPGREEGSPLELERLKLEPHEGLLLRFPYAA 529 (SEQ ID NO:1)
Mouse 474 SNLPAGISLPASAKLLLSTDSARQSREEDTSLKLENLSLNPYEGLLLQFPFVA 526 (SEQ ID NO:96)
Chimera 13

Fig. 13

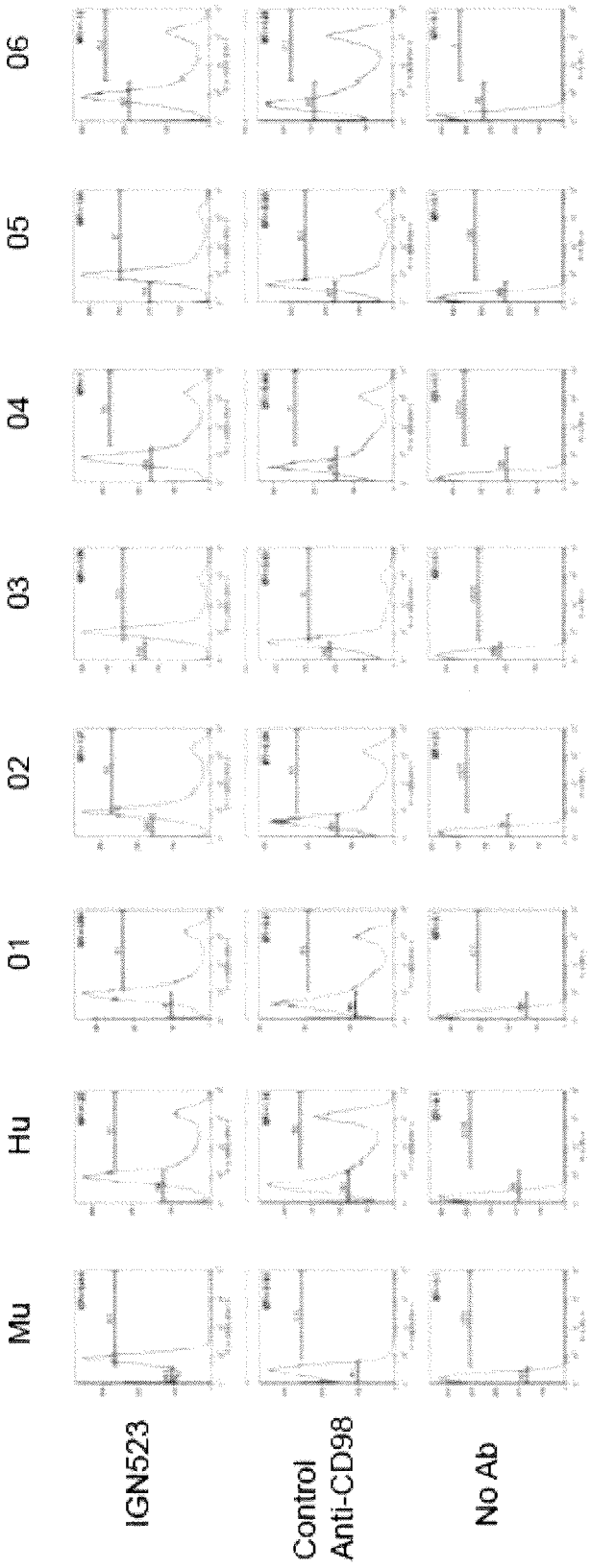


Fig. 14A

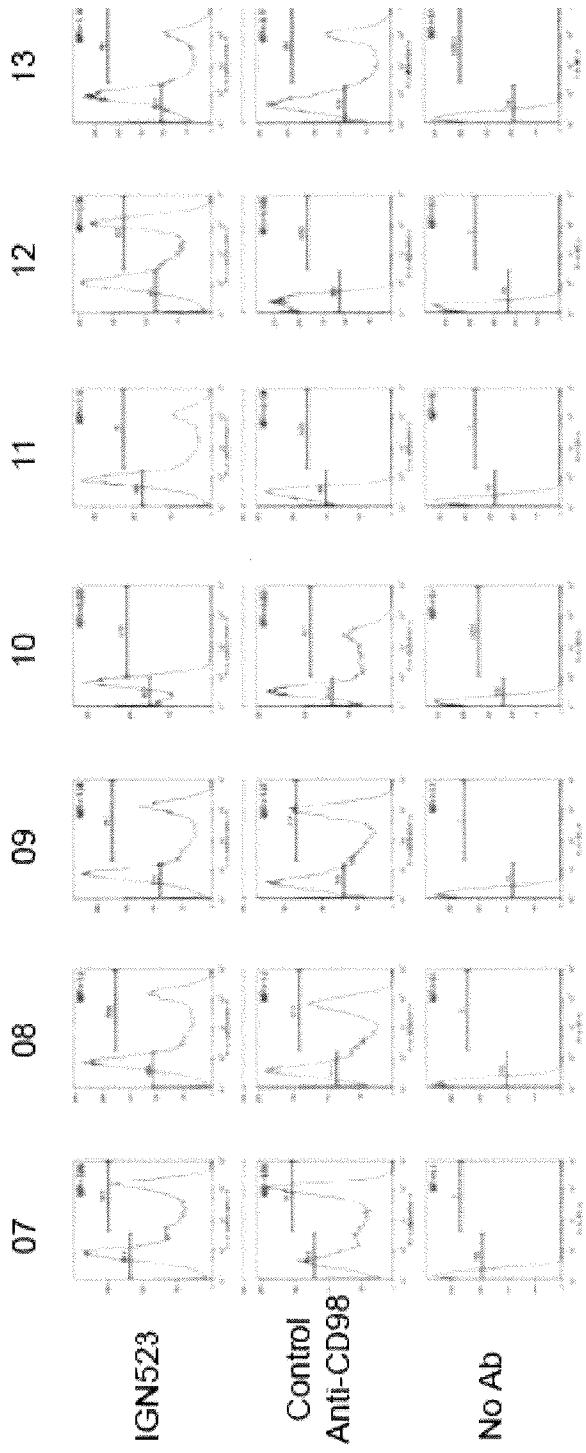
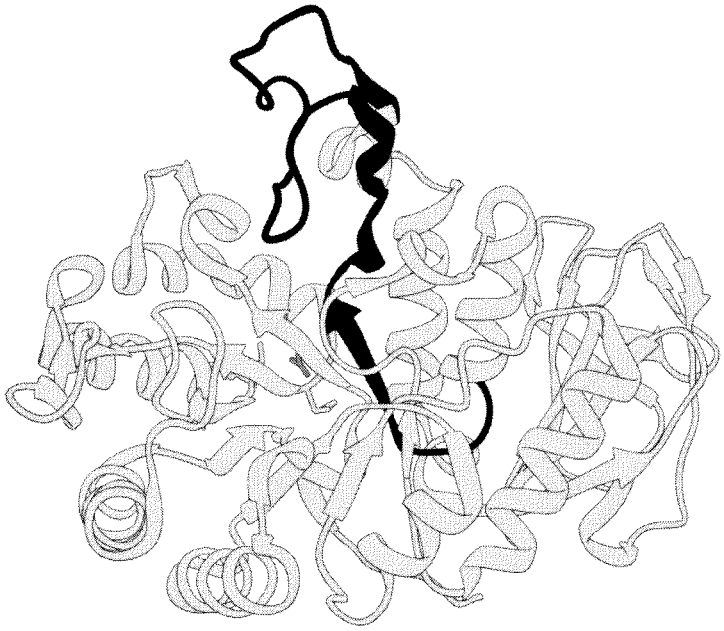


Fig. 14B



T358 I371 N405

Human TLPGTPVFSYGDE**I**GL**DAA**ALPGQP**ME**AP**V**M**L**W**D**ESS**FPD**IP**GA**VS**A**N (SEQ ID NO:97)

Mouse TLPGTPVFSYGDELGLQG-ALPGQPAKAPLMPWNESSIFHIPRPVSLN (SEQ ID NO:98)

FIG. 15

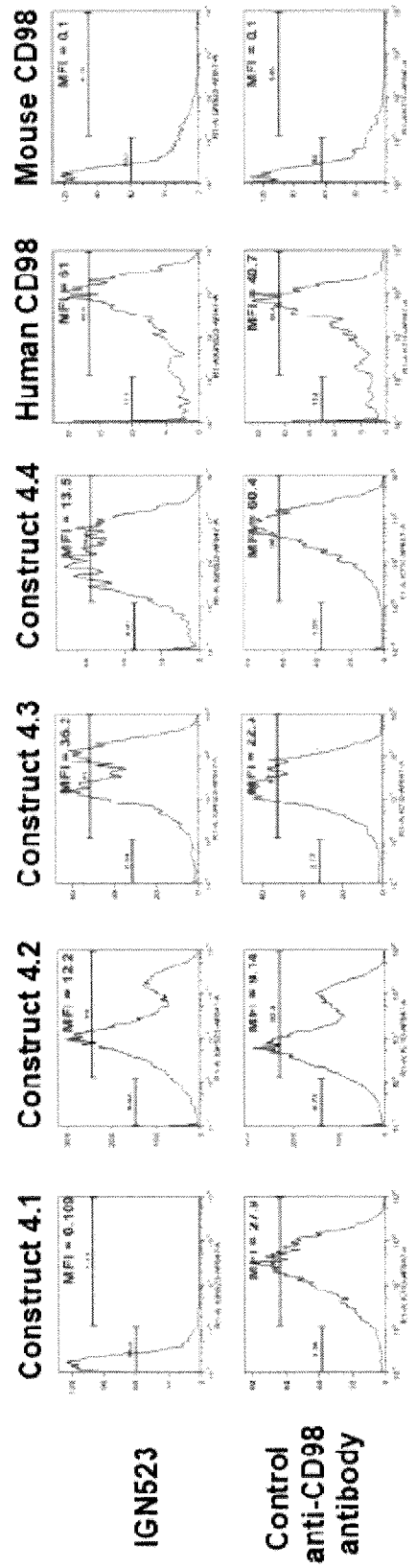

Construct 4.1
Construct 4.2
Construct 4.3
Construct 4.4
Human CD98
Mouse CD98
IGN523
Control anti-CD98 antibody

Fig. 16

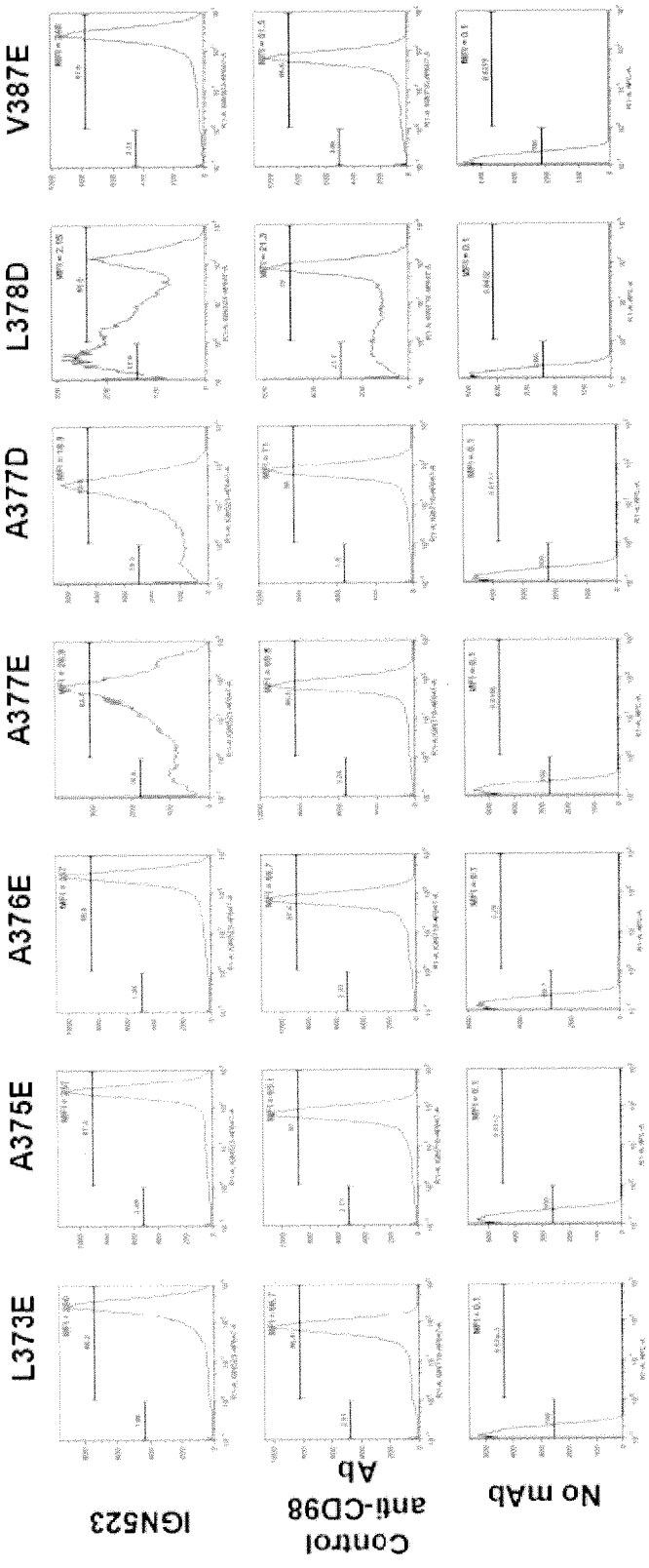

L373E
A375E
A376E
A377E
A377D
L378D
V387E
IGN523
Control anti-CD98 Ab
No mAb

Fig. 17A

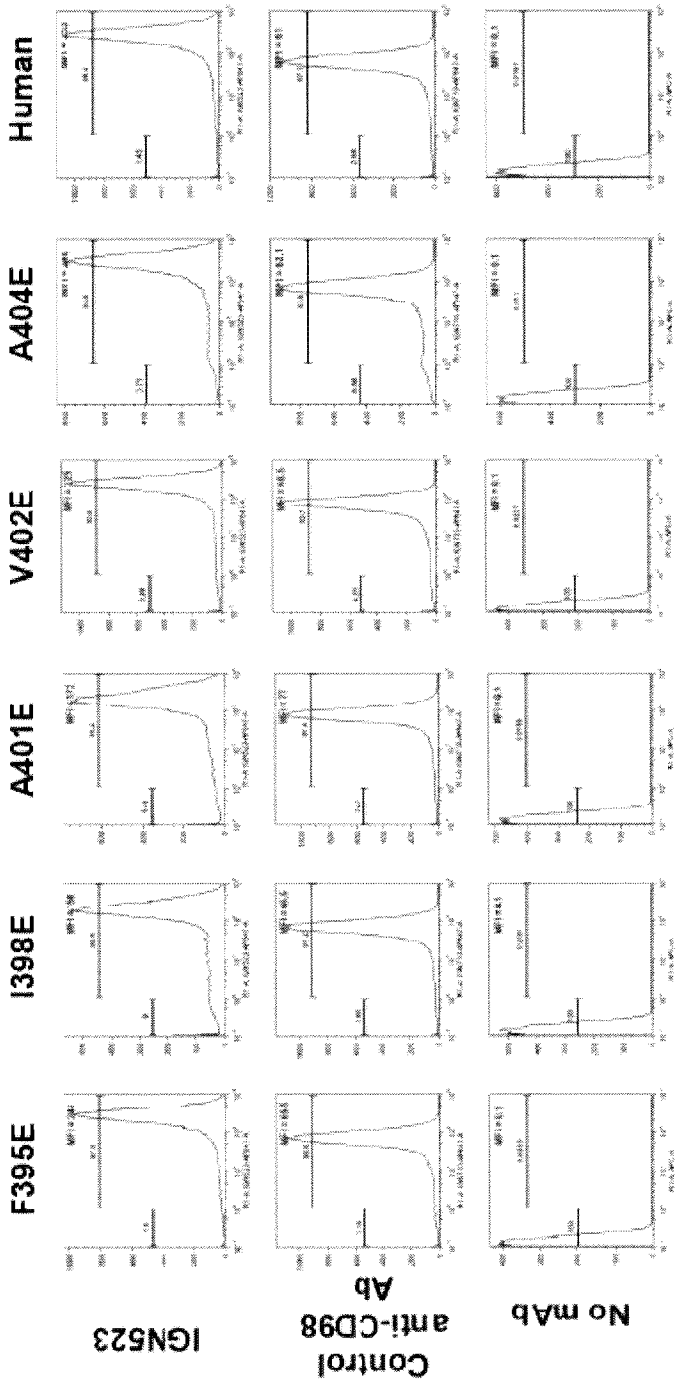
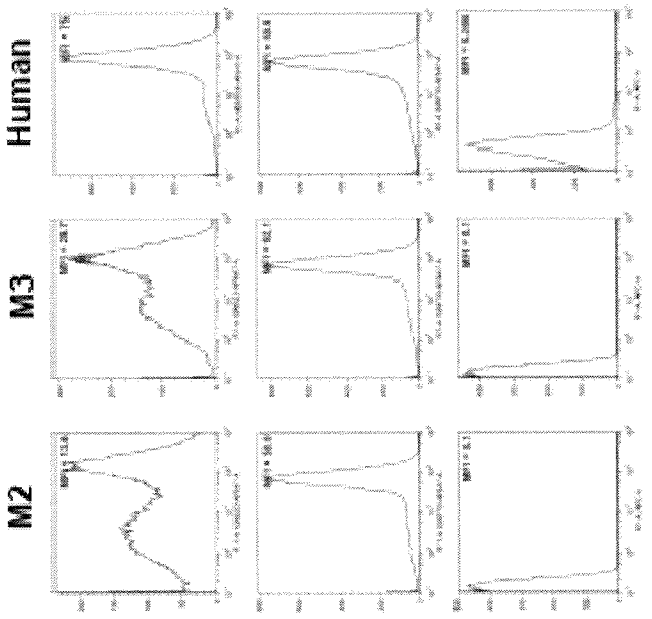

F395E
I398E
A401E
V402E
A404E
Human
IGN523
Control anti-CD98 Ab
No mAb

Fig. 17B



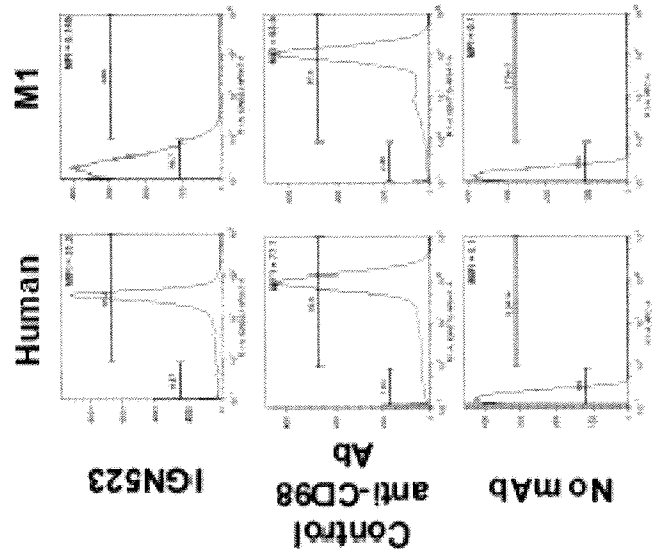


Fig. 18

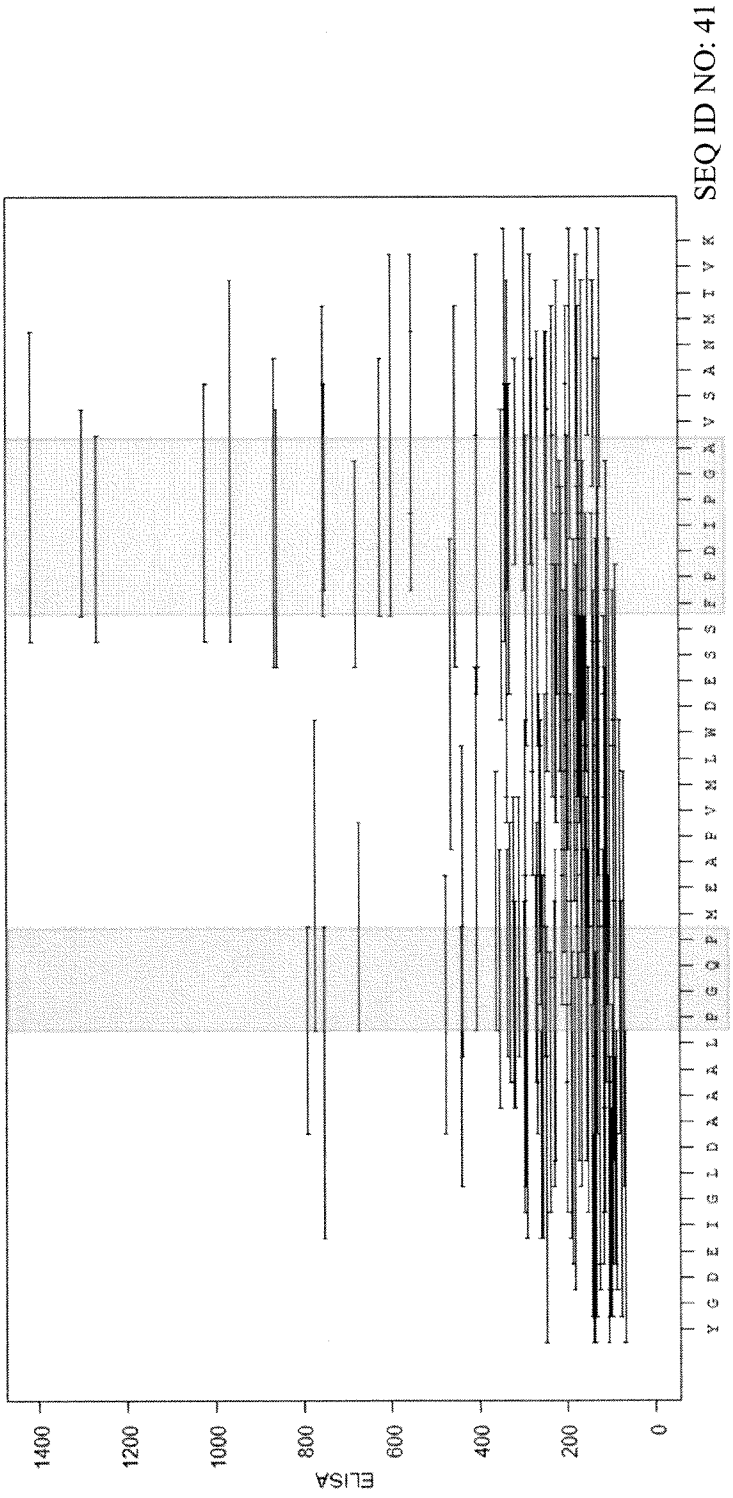

SEQ ID NO: 41
Y G D E I G I L D A A A L P G Q P M E A P V M L W D E S S F P D I P G A V S A N M I V K
position
ELISA
0
200
400
600
800
1000
1200
1400

Fig. 19

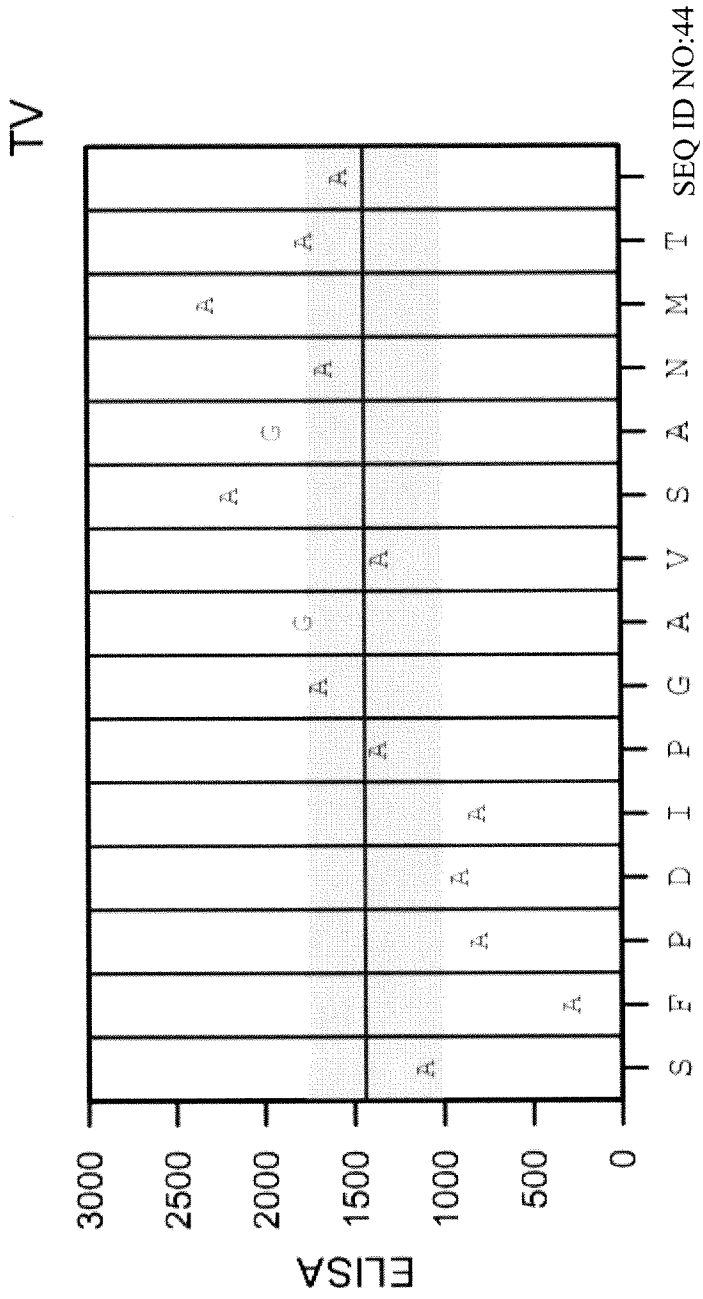

TV
ELISA
3000
2500
2000
1500
1000
500
0
S E P D I P G A V S A N M T
SEQ ID NO:44

Fig. 20

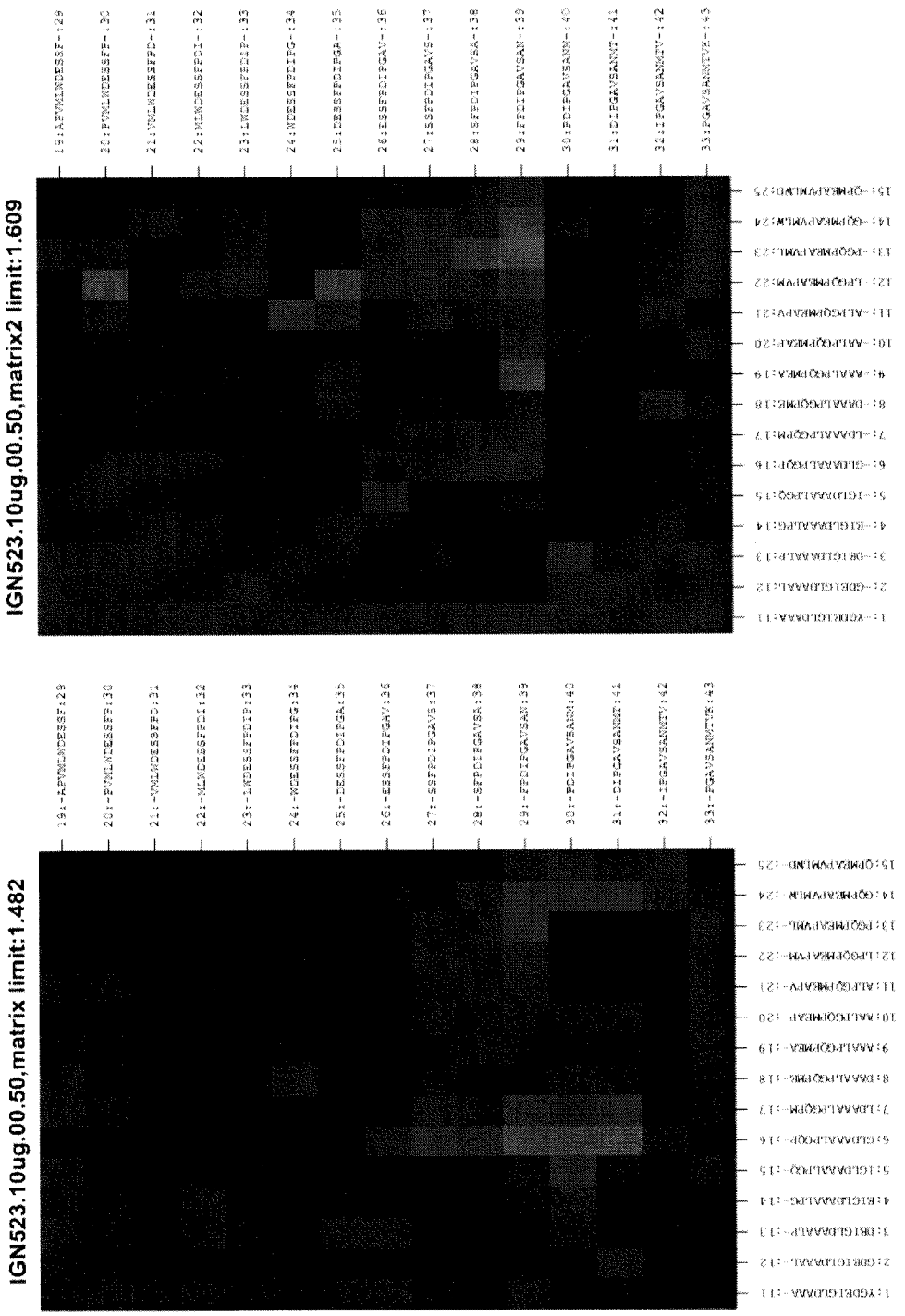

IGN523.10ug.00.50,matrix2 limit:1.609
IGN523.10ug.00.50,matrix limit:1.482

Fig. 21

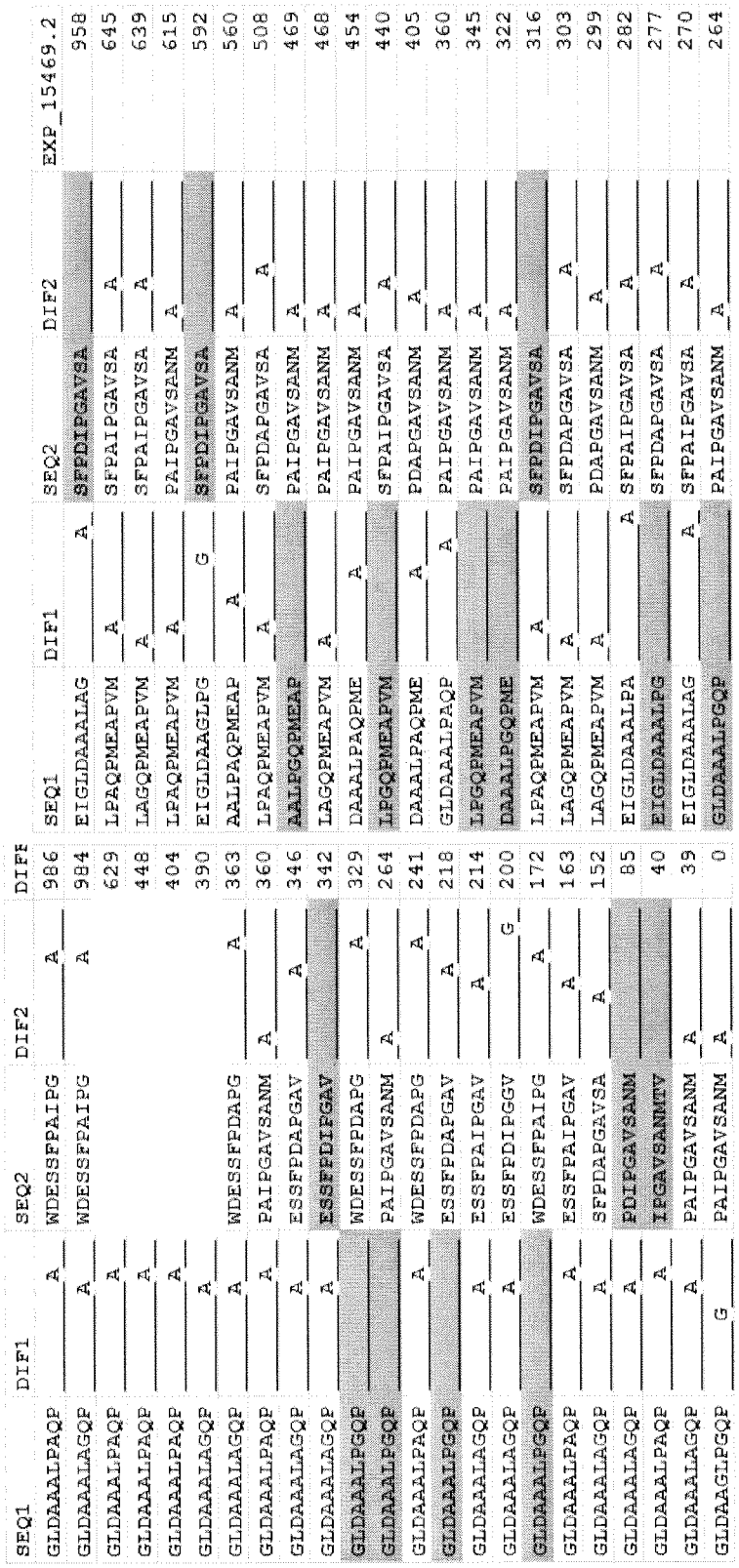

SEQ1 DIF1 SEQ2 DIF2 DIFF SEQ1 DIF1 SEQ2 DIF2 EXP_15469.2
GLDAAAALPAQP A WDESSFPAIPG A 986 EIGLDAAALAG A SFPDIPGAVSA 958
GLDAAAALAGQP A WDESSFPAIPG A 984 LPAQPMEAPVM A SFPAIPGAVSA A 645
GLDAAALPAQP A 629 LAGQPMEAPVM A SFPAIPGAVSA A 639
GLDAAALPAQP A 448 LPAQPMEAPVM A PAIPGAVSANM A 615
GLDAAALPAQP A 404 EIGLDAAGLPG G SFPDIPGAVSA 592
GLDAAALAGQP A WDESSFPDAPG A 363 AALPAQPMEAP A PAIPGAVSANM A 560
GLDAAALAGQP A PAIPGAVSANM A 360 LPAQPMEAPVM A SFPDAPGAVSA A 508
GLDAAALPAQP A ESSFPDAPGAV A 346 AALPGQPMEAP PAIPGAVSANM A 469
GLDAAALAGQP A ESSFPDIPGAV 342 LAGQPMEAPVM A PAIPGAVSANM A 468
GLDAAALPGQP WDESSFPDAPG A 329 DAAALPAQPME A PAIPGAVSANM A 454
GLDAAALPGQP PAIPGAVSANM A 264 LPGQPMEAPVM SFPAIPGAVSA A 440
GLDAAALPAQP A WDESSFPDAPG A 241 DAAALPAQPME A PDAPGAVSANM A 405
GLDAAALPGQP ESSFPDAPGAV A 218 GLDAAALPAQP A PAIPGAVSANM A 360
GLDAAALAGQP A ESSFPAIPGAV A 214 LPGQPMEAPVM PAIPGAVSANM A 345
GLDAAALAGQP A ESSFPDIPGGV G 200 DAAALPGQPME PAIPGAVSANM A 322
GLDAAALPGQP A WDESSFPAIPG A 172 LPAQPMEAPVM A SFPDIPGAVSA 316
GLDAAALPAQP A ESSFPAIPGAV A 163 LAGQPMEAPVM A SFPDAPGAVSA A 303
GLDAAALAGQP A SFPDAPGAVSA A 152 LAGQPMEAPVM A PDAPGAVSANM A 299
GLDAAALAGQP A FDIPGAVSANM 85 EIGLDAAALPA A SFPAIPGAVSA A 282
GLDAAALPAQP A IPGAVSANMTV 40 EIGLDAAALPG SFPDAPGAVSA A 277
GLDAAALAGQP A PAIPGAVSANM A 39 EIGLDAAALAG A SFPAIPGAVSA A 270
GLDAAGLPGQP G PAIPGAVSANM A 0 GLDAAALPGQP A PAIPGAVSANM A 264

Fig. 22

Fig. 23A TLPGTPVFSYGDEIGLDAAALPGQPMEAPVMLWDESSFPDIGAVSAN

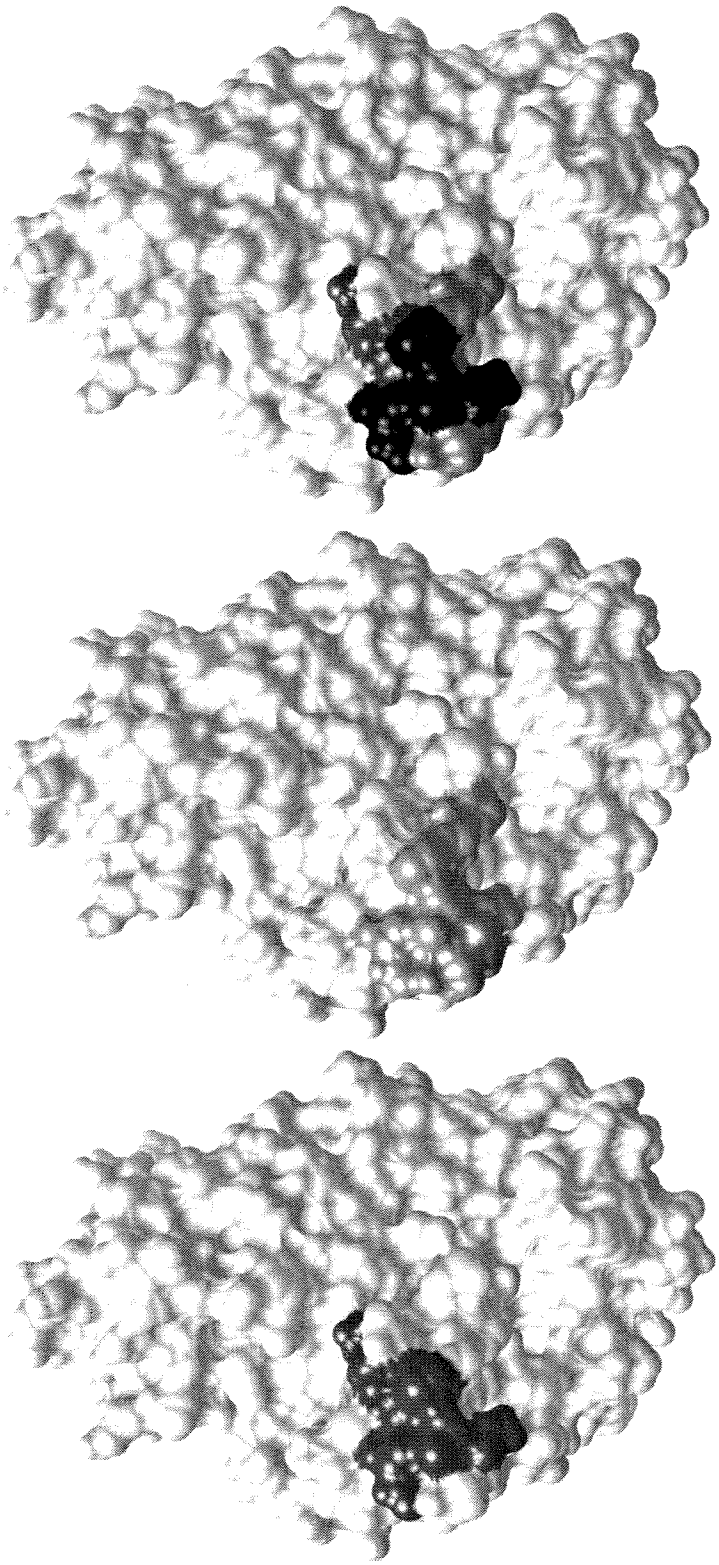


Fig. 23B

Fig. 23C

Fig. 23D

Fig. 24

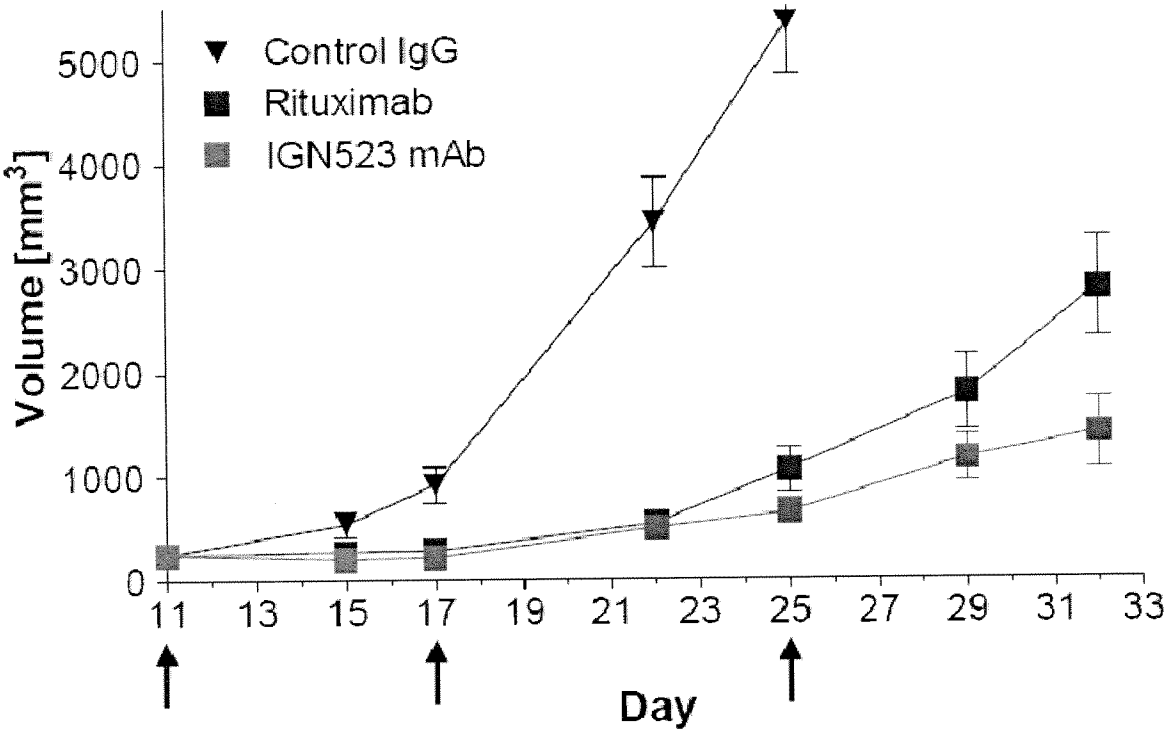

Control IgG
Rituximab
IGN523 mAb
Volume [mm3]
5000
4000
3000
2000
1000
0
11
13
15
17
19
21
23
25
27
29
31
33
Day

Fig. 25

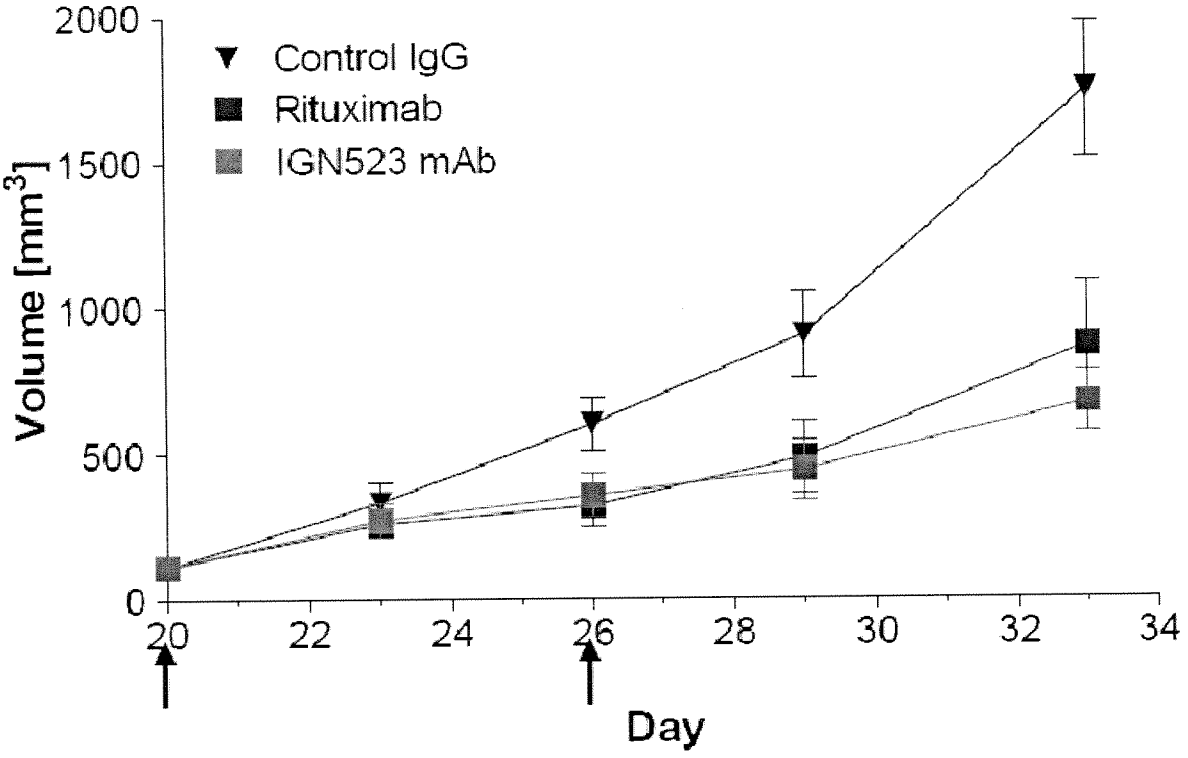

Control IgG
Rituximab
IGN523 mAb
Volume [mm3]
2000
1500
1000
500
0
20
22
24
26
28
30
32
34
Day

Fig. 26A

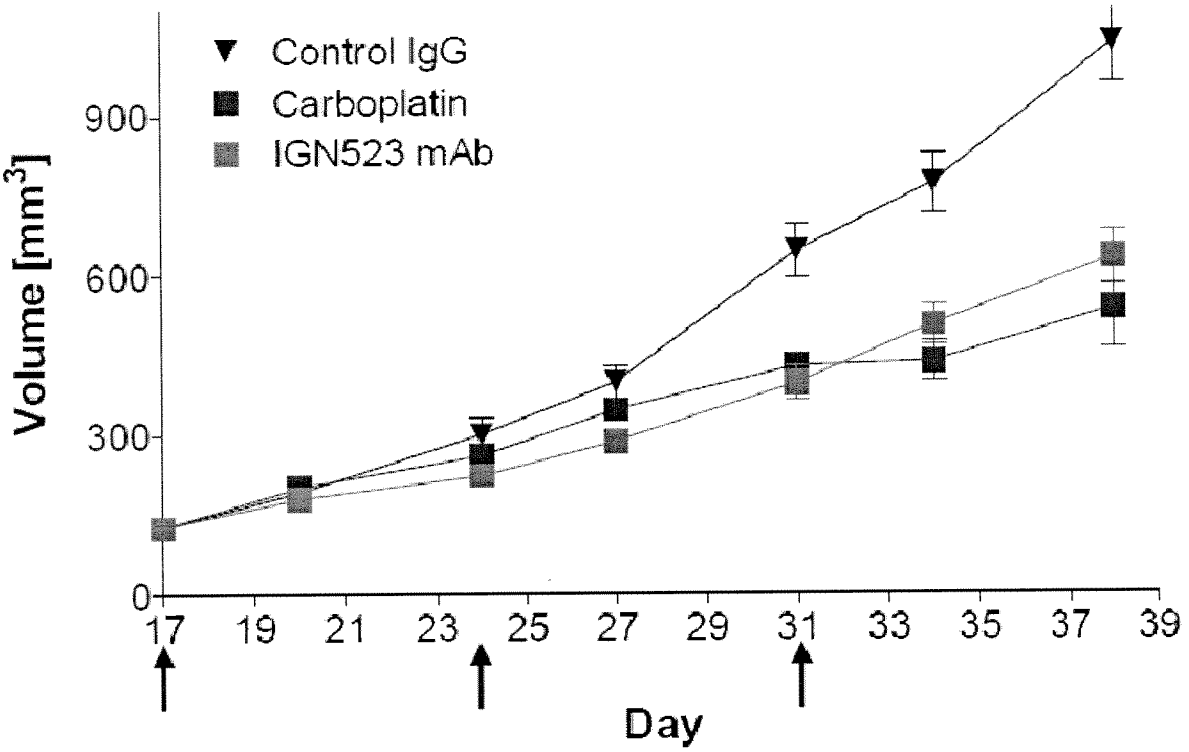


Fig. 26B

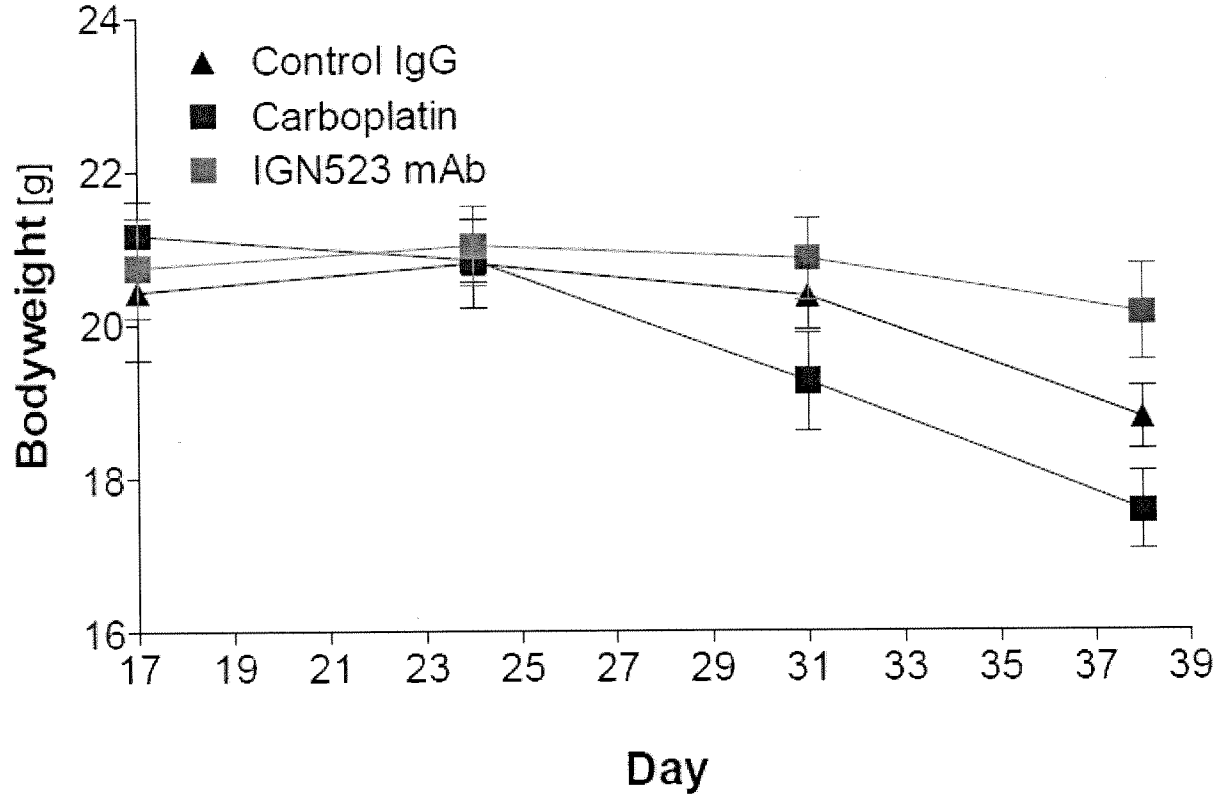


Fig. 27

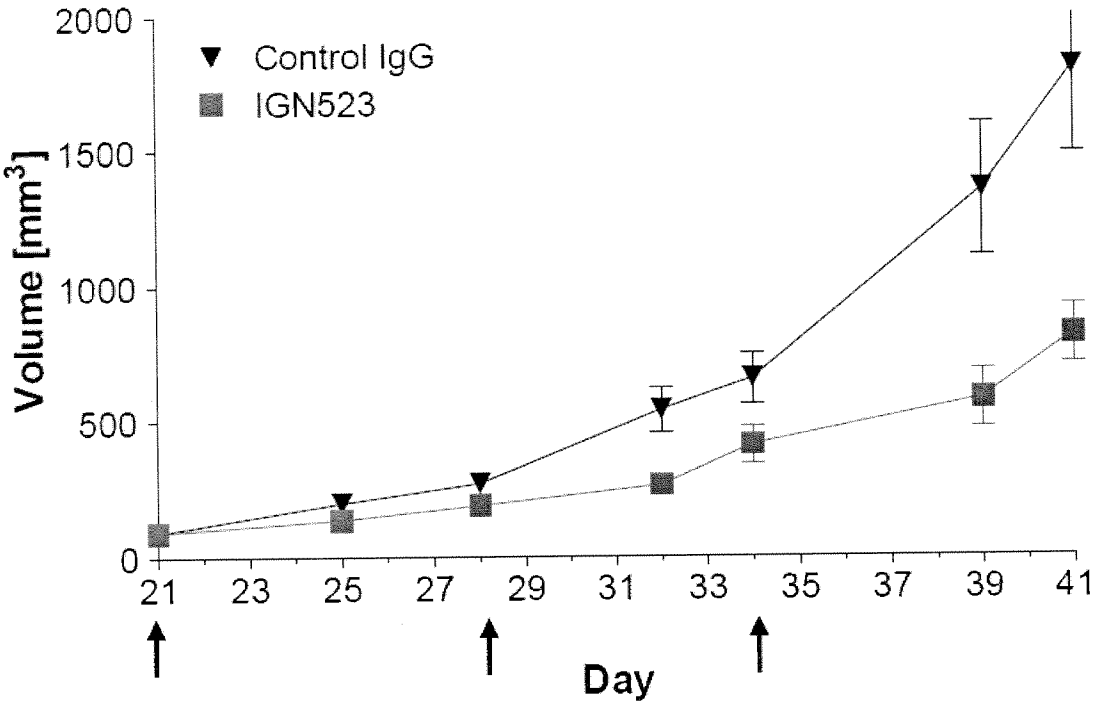
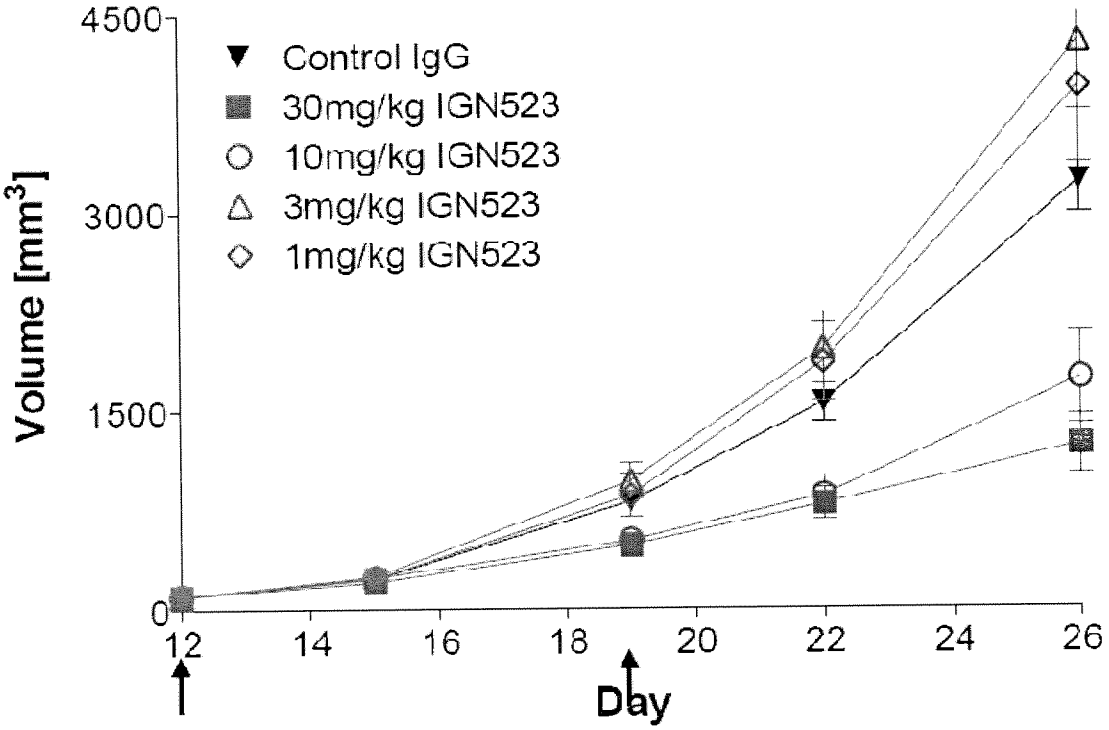

Control IgG
IGN523
Volume [mm3]
2000
1500
1000
500
0
21
23
25
27
29
31
33
35
37
39
41
Day

Fig. 28


Control IgG
30mg/kg IGN523
10mg/kg IGN523
3mg/kg IGN523
1mg/kg IGN523
Volume [mm3]
4500
3000
1500
0
12
14
16
18
20
22
24
26
Day

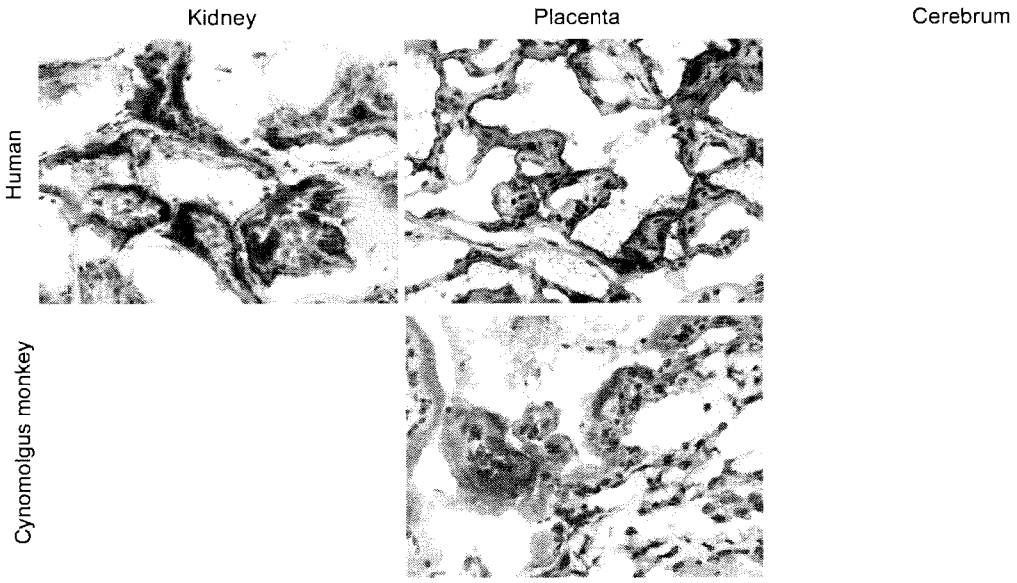


Fig. 29