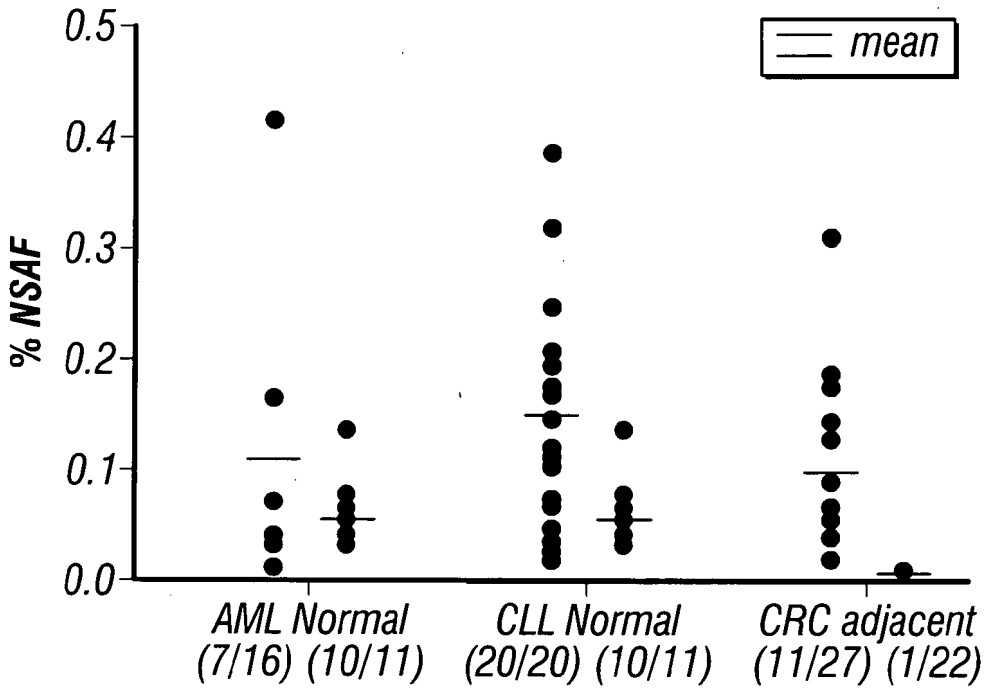

0.5
0.4
0.3
0.2
0.1
0.0
% NSAF
mean
AML Normal
(7/16) (10/11)
CLL Normal
(20/20) (10/11)
CRC adjacent
(11/27) (1/22)

FIG. 1

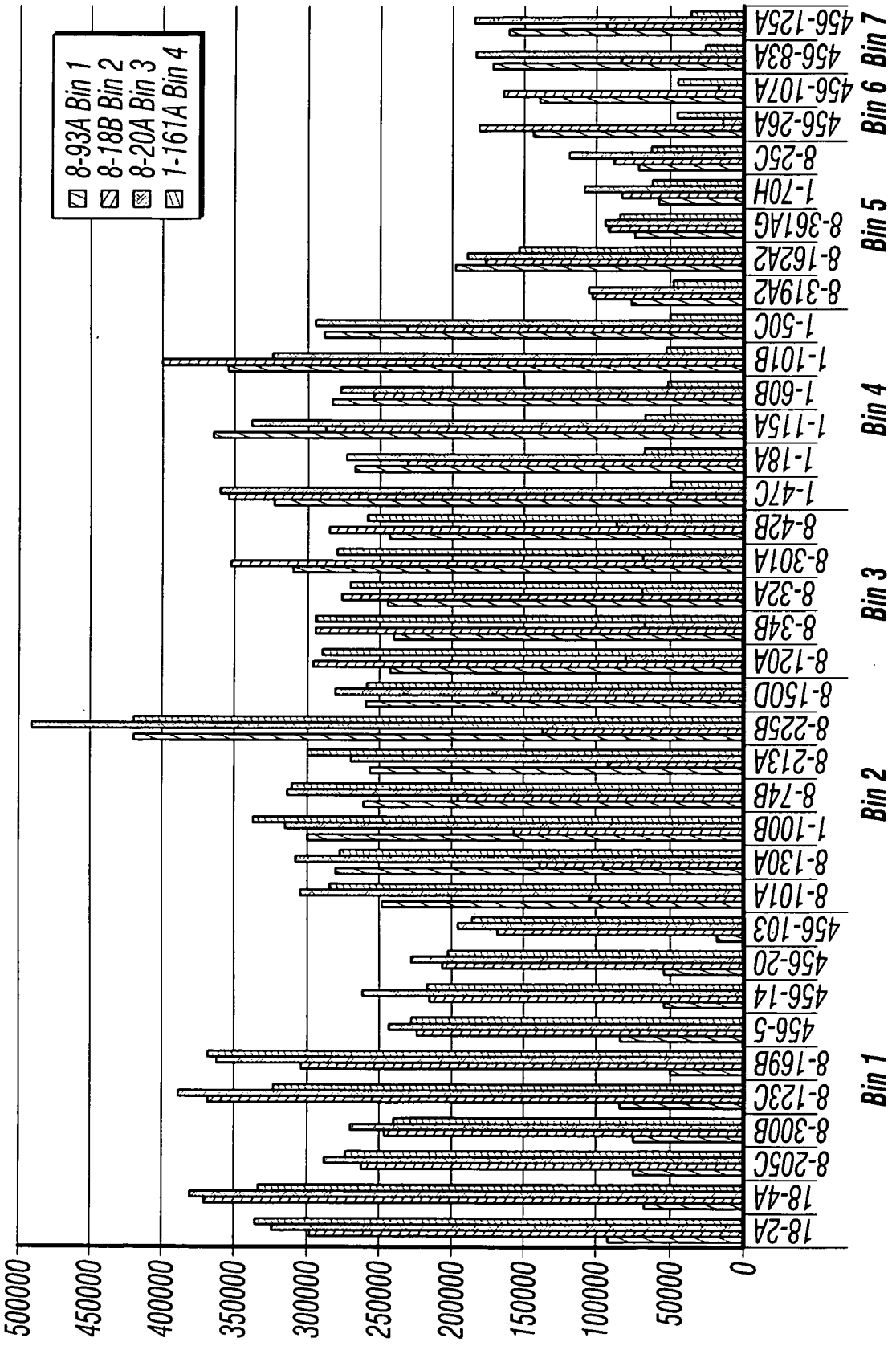

8-93A Bin 1
8-18B Bin 2
8-20A Bin 3
1-161A Bin 4
500000
450000
400000
350000
300000
250000
200000
150000
100000
50000
0
18-2A
18-4A
8-205C
8-300B
8-123C
8-169B
456-5
456-14
456-20
456-103
8-101A
8-130A
1-100B
8-74B
8-213A
8-225B
8-150D
8-120A
8-34B
8-32A
8-301A
8-42B
1-47C
1-18A
1-115A
1-60B
1-101B
1-50C
8-319A2
8-162A2
8-361AG
1-70H
8-25C
456-26A
456-107A
456-83A
456-125A
Bin 1
Bin 2
Bin 3
Bin 4
Bin 5
Bin 6
Bin 7

FIG. 2

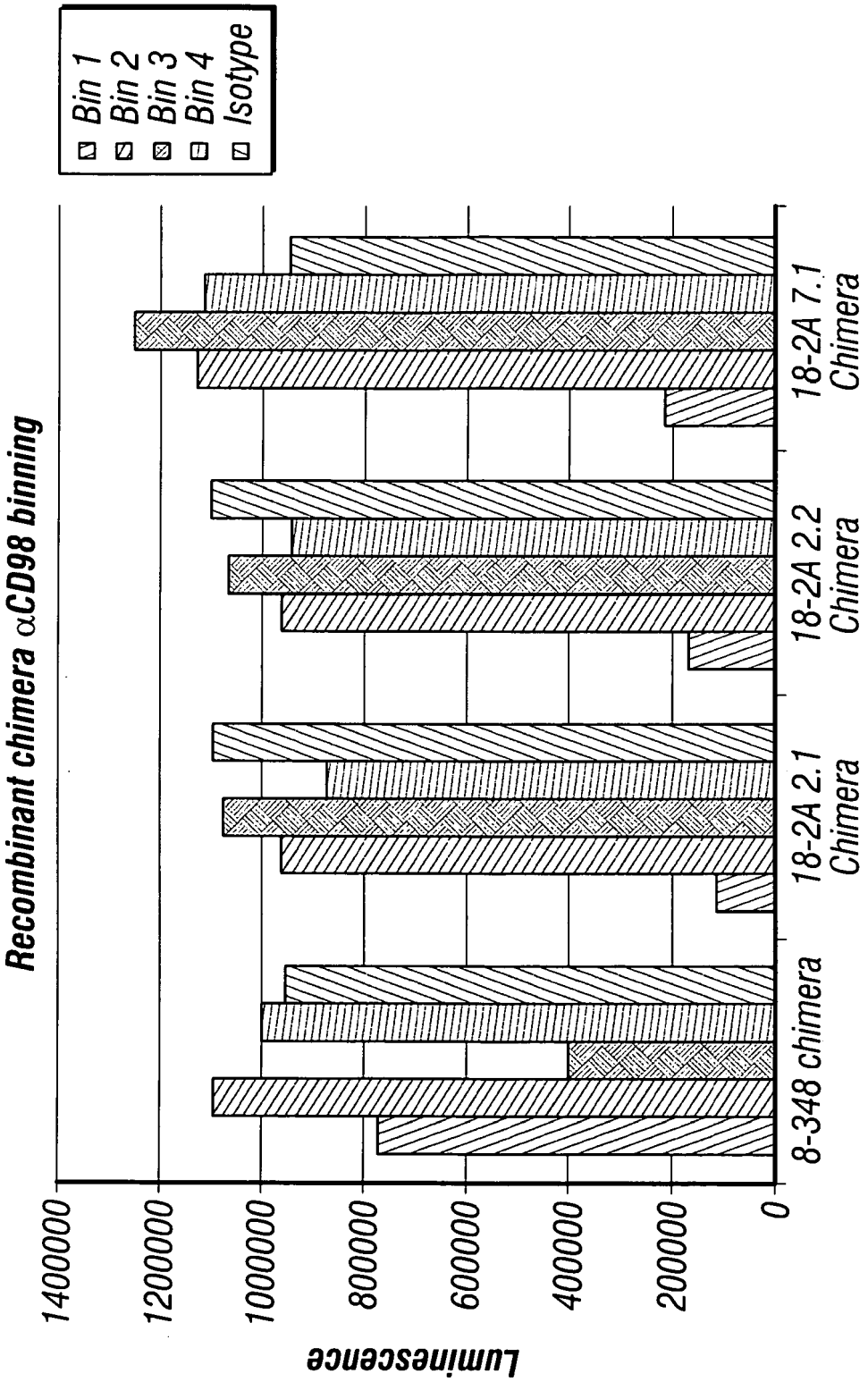

Recombinant chimera αCD98 binning
Luminescence
0
200000
400000
600000
800000
1000000
1200000
1400000
Bin 1
Bin 2
Bin 3
Bin 4
Isotype
8-348 chimera
18-2A 2.1 Chimera
18-2A 2.2 Chimera
18-2A 7.1 Chimera

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

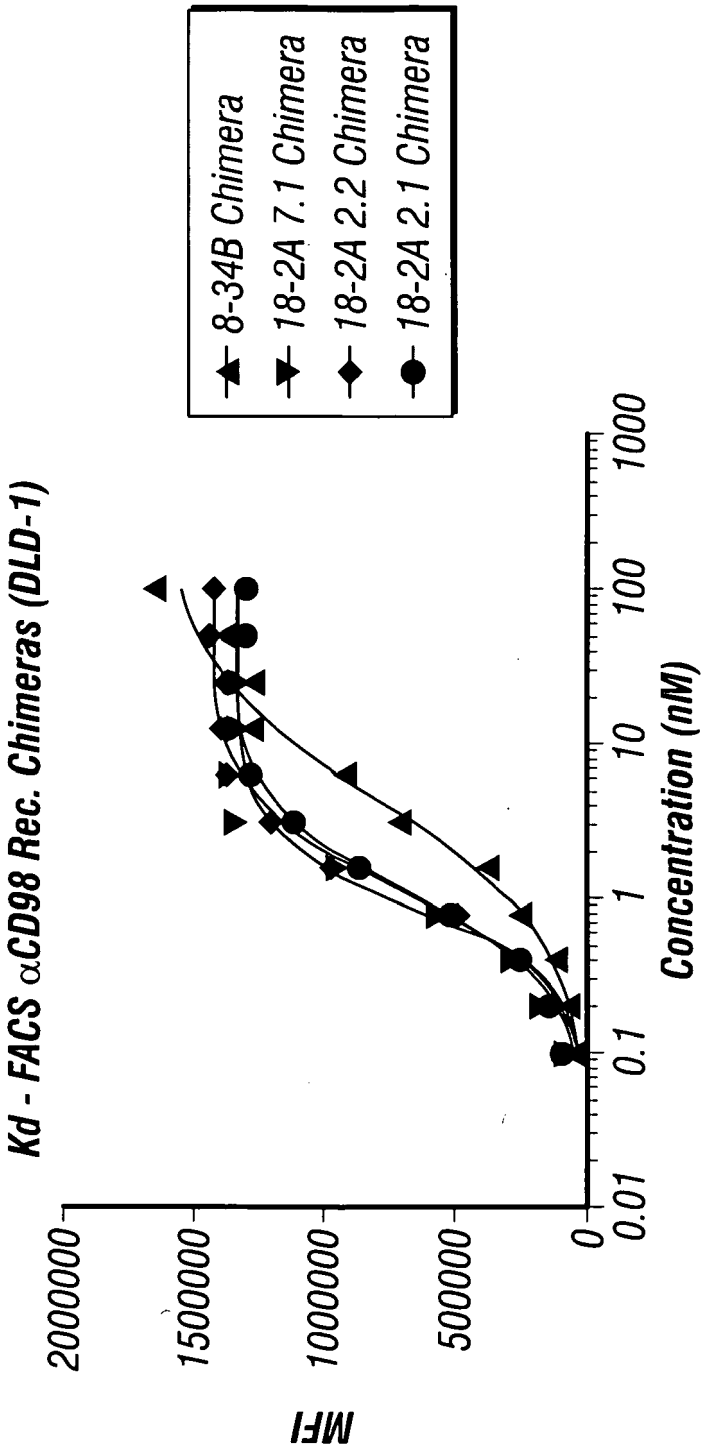


FIG. 3B

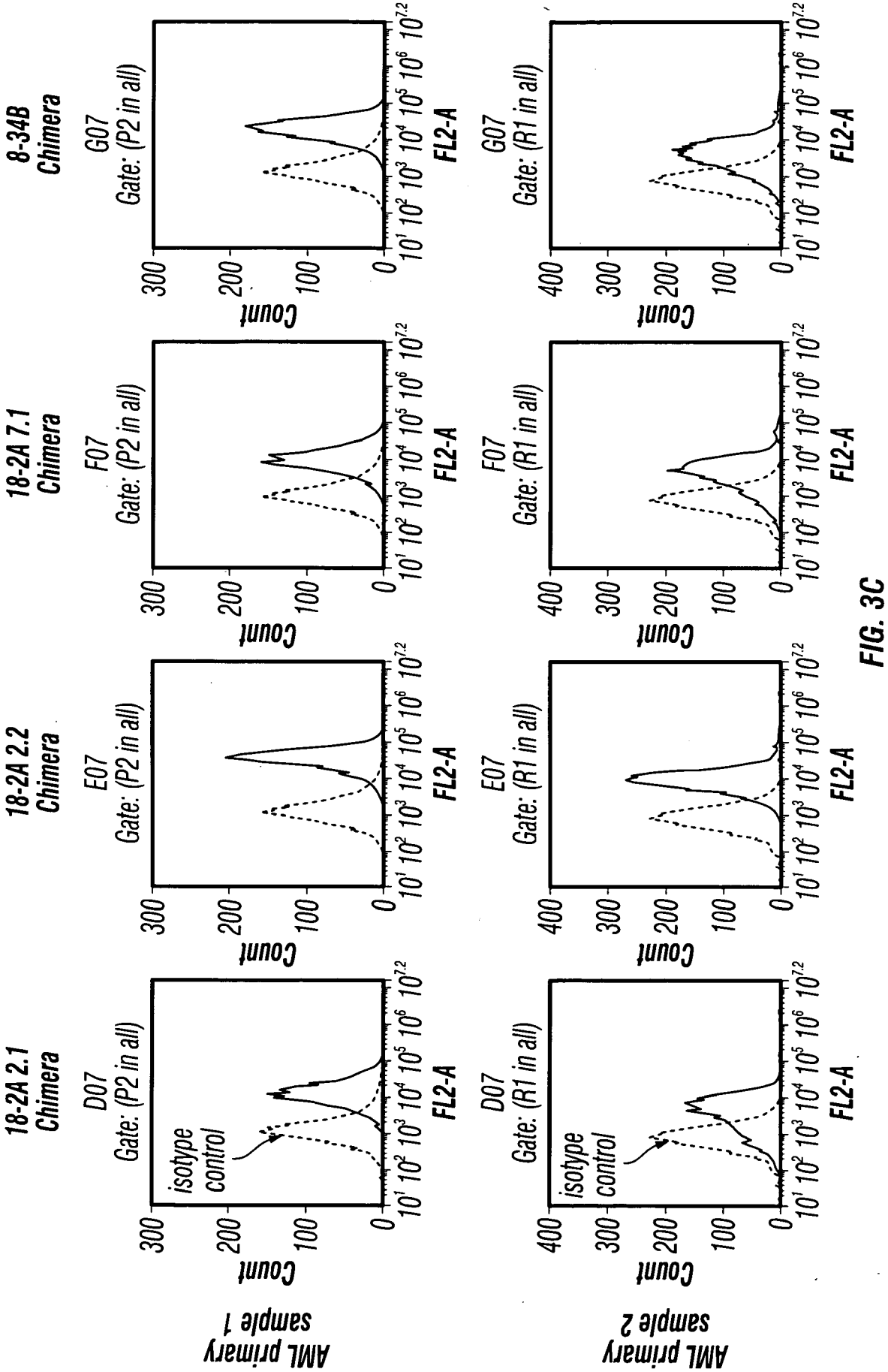

AML primary sample 1
AML primary sample 2
18-2A 2.1 Chimera
18-2A 2.2 Chimera
18-2A 7.1 Chimera
8-34B Chimera
D07 Gate: (P2 in all)
E07 Gate: (P2 in all)
F07 Gate: (P2 in all)
G07 Gate: (P2 in all)
D07 Gate: (R1 in all)
E07 Gate: (R1 in all)
F07 Gate: (R1 in all)
G07 Gate: (R1 in all)
isotype control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

FIG. 3C

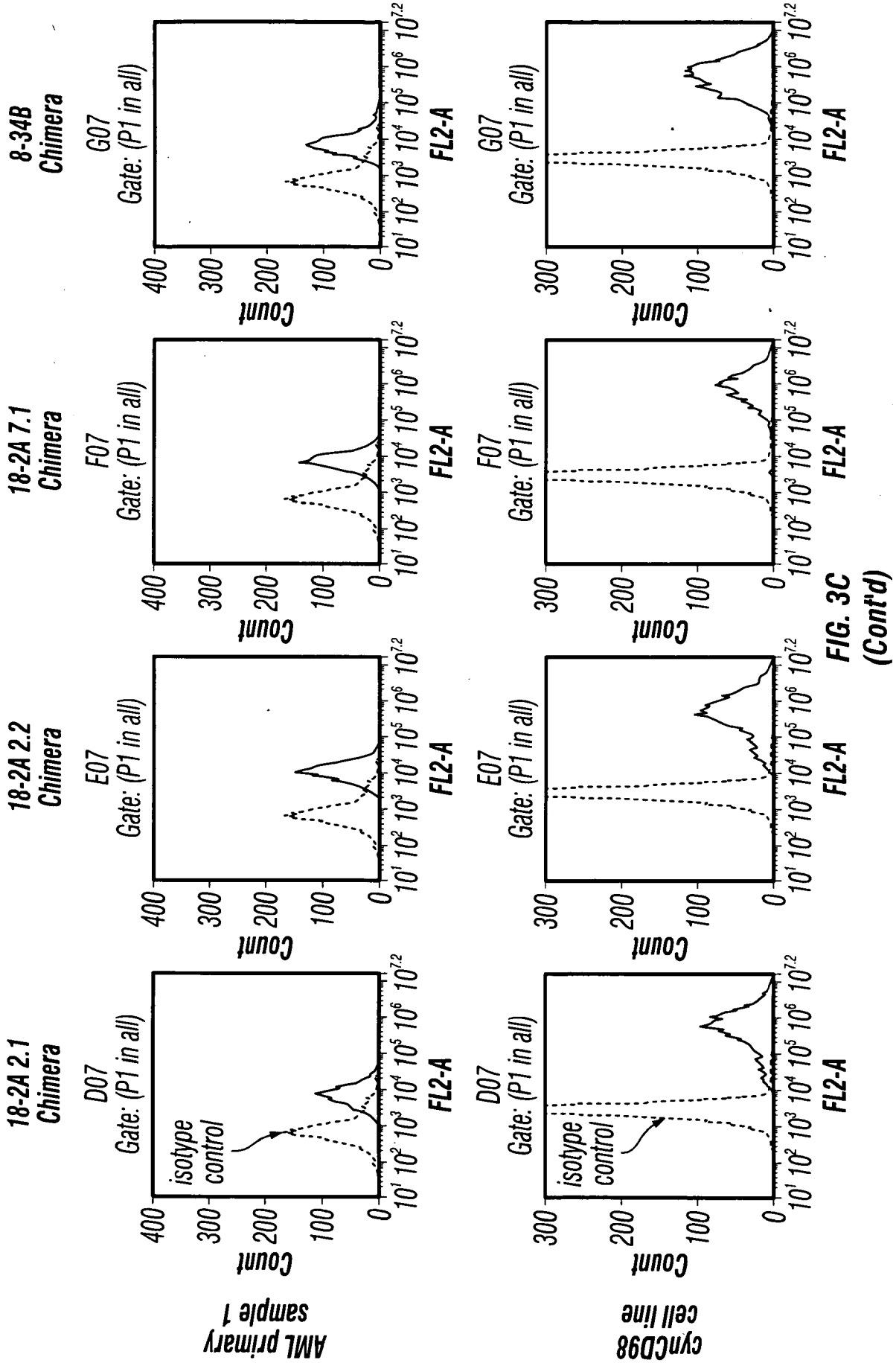

AML primary sample 1
cynCD98 cell line
18-2A 2.1 Chimera
18-2A 2.2 Chimera
18-2A 7.1 Chimera
8-34B Chimera
D07
E07
F07
G07
Gate: (P1 in all)
isotype control
Count
FL2-A

FIG. 3C (Cont'd)

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
VYYCQQYYSTPLITFGQGTKVEIK (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

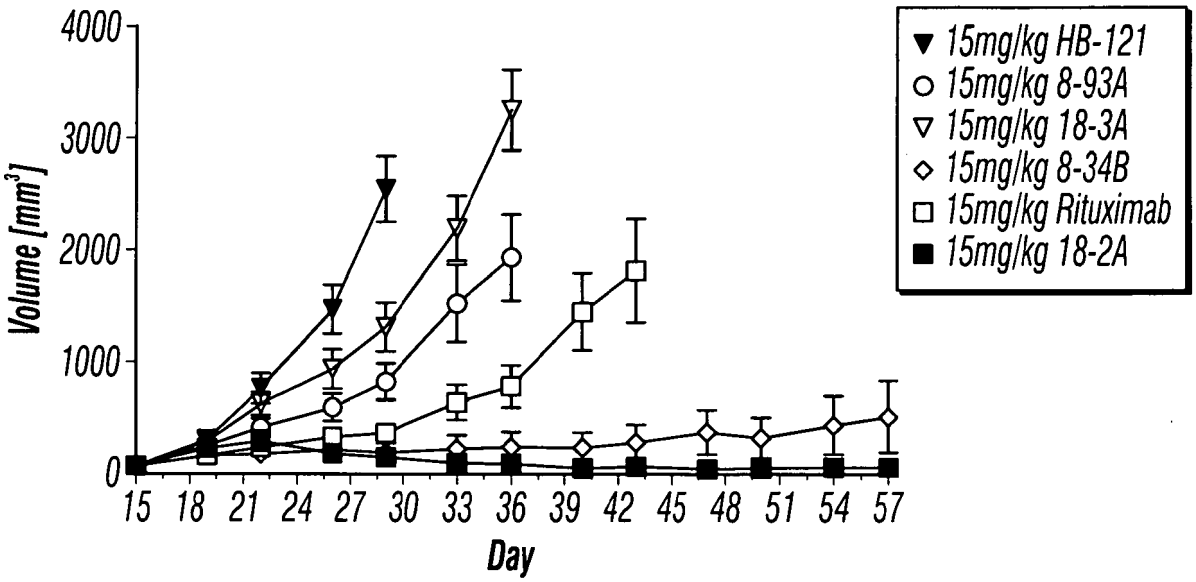

4000
3000
2000
1000
0
Volume [mm³]
15 18 21 24 27 30 33 36 39 42 45 48 51 54 57
Day
15mg/kg HB-121
15mg/kg 8-93A
15mg/kg 18-3A
15mg/kg 8-34B
15mg/kg Rituximab
15mg/kg 18-2A

FIG. 5A

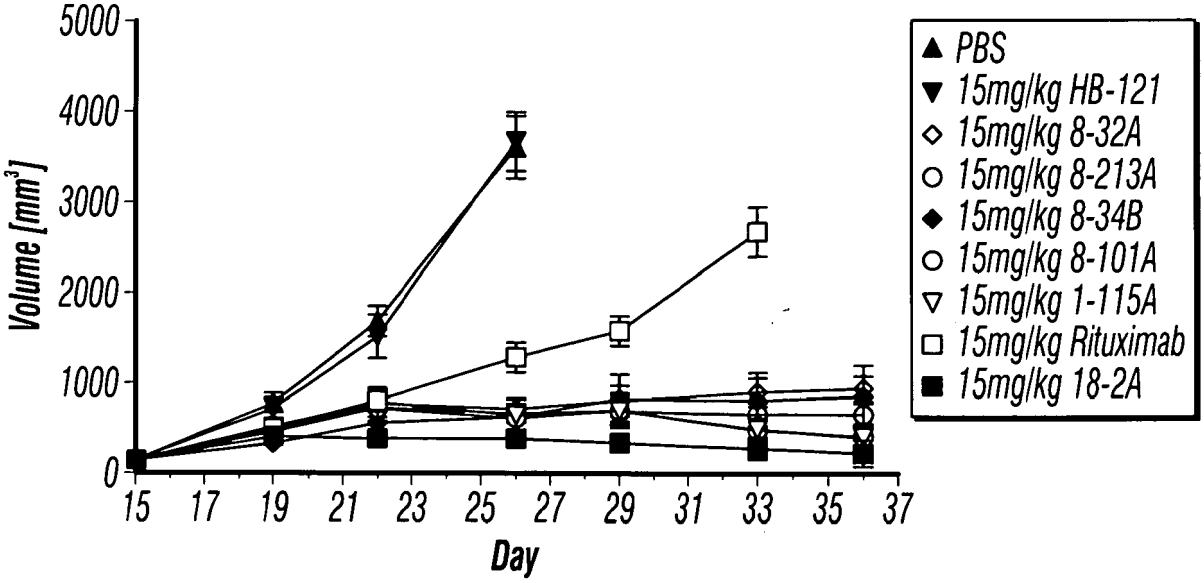

5000
4000
3000
2000
1000
0
Volume [mm³]
15 17 19 21 23 25 27 29 31 33 35 37
Day
PBS
15mg/kg HB-121
15mg/kg 8-32A
15mg/kg 8-213A
15mg/kg 8-34B
15mg/kg 8-101A
15mg/kg 1-115A
15mg/kg Rituximab
15mg/kg 18-2A

FIG. 5B

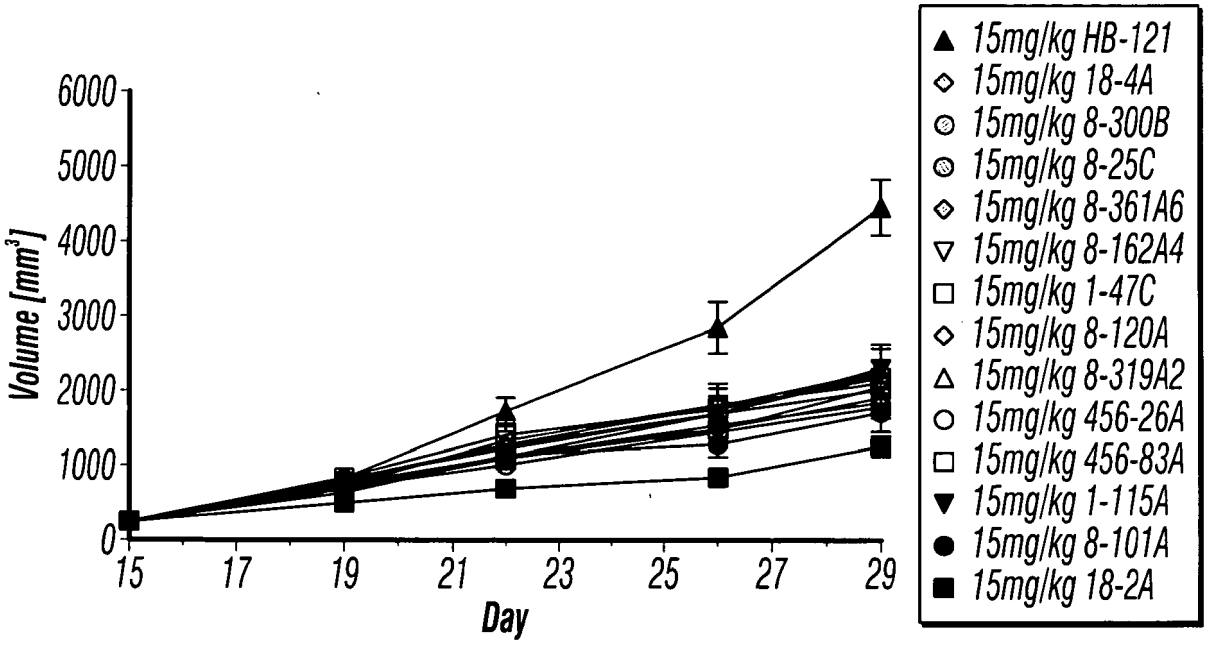

Volume [mm³]
6000
5000
4000
3000
2000
1000
0
15
17
19
21
23
25
27
29
Day
15mg/kg HB-121
15mg/kg 18-4A
15mg/kg 8-300B
15mg/kg 8-25C
15mg/kg 8-361A6
15mg/kg 8-162A4
15mg/kg 1-47C
15mg/kg 8-120A
15mg/kg 8-319A2
15mg/kg 456-26A
15mg/kg 456-83A
15mg/kg 1-115A
15mg/kg 8-101A
15mg/kg 18-2A

FIG. 5C

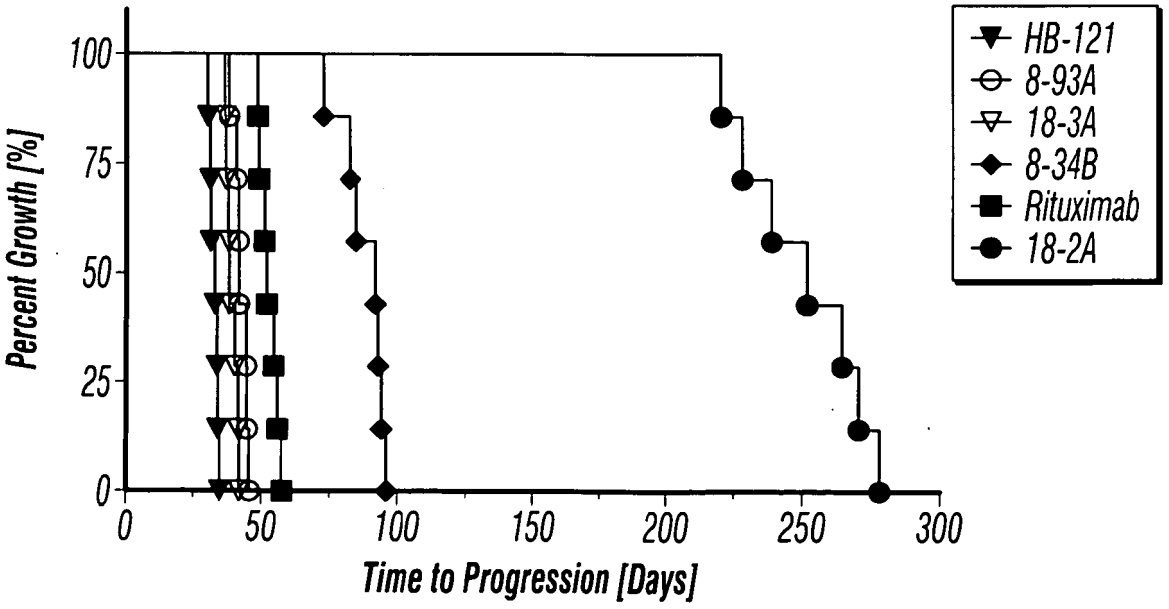

Percent Growth [%]
100
75
50
25
0
0
50
100
150
200
250
300
Time to Progression [Days]
HB-121
8-93A
18-3A
8-34B
Rituximab
18-2A

FIG. 6A

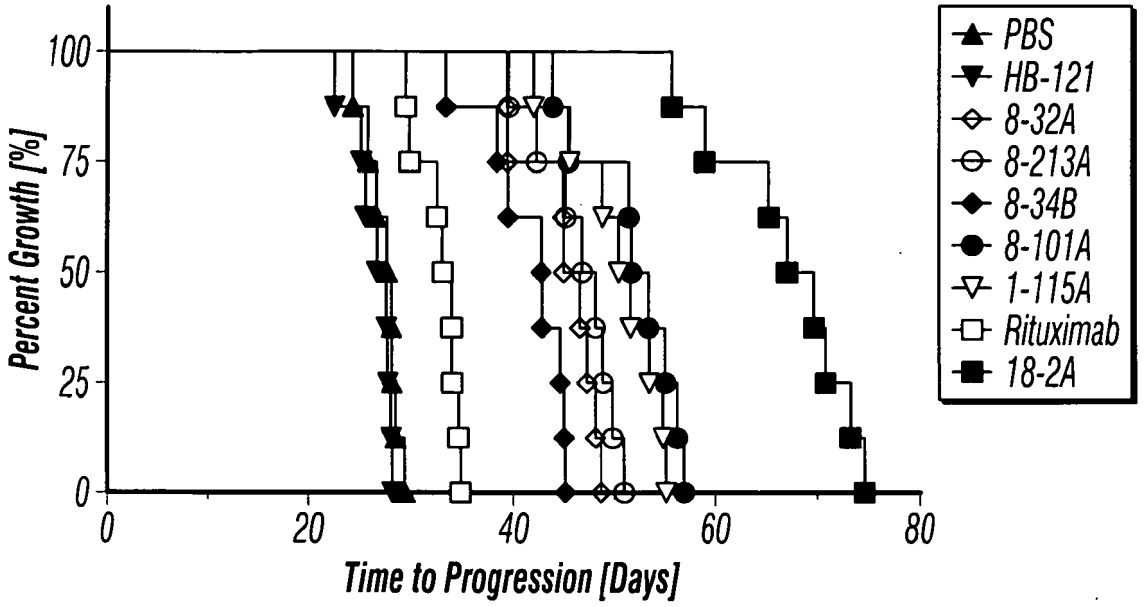

Percent Growth [%]
100
75
50
25
0
0
20
40
60
80
Time to Progression [Days]
PBS
HB-121
8-32A
8-213A
8-34B
8-101A
1-115A
Rituximab
18-2A

FIG. 6B

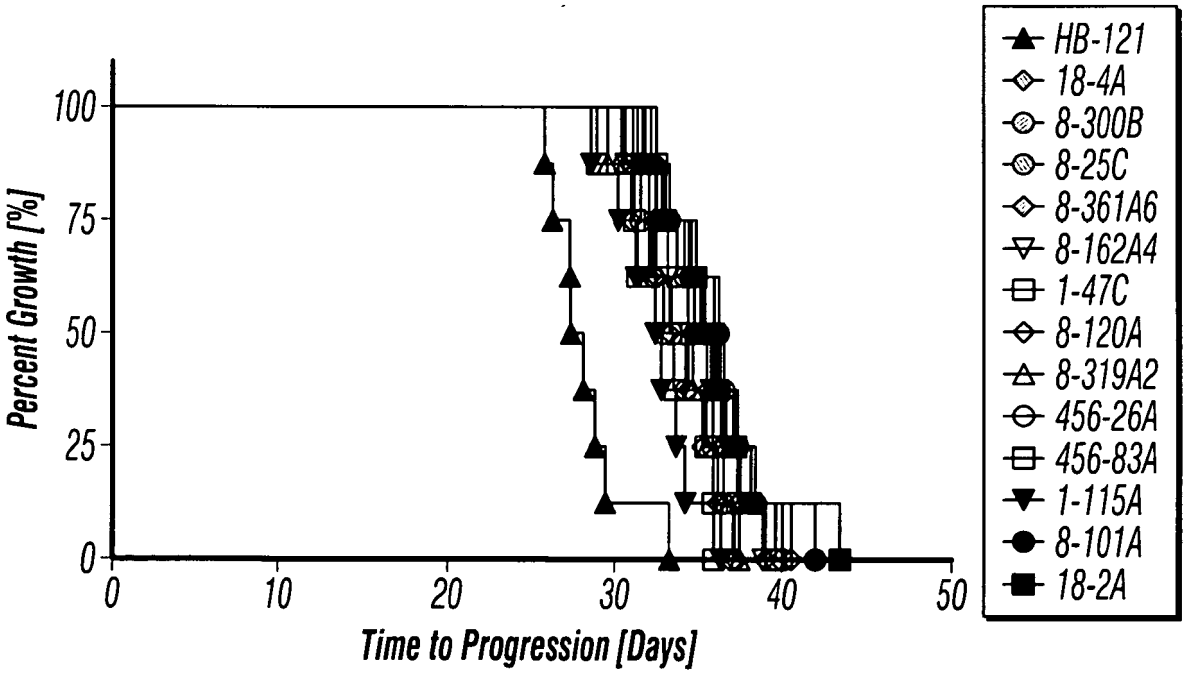
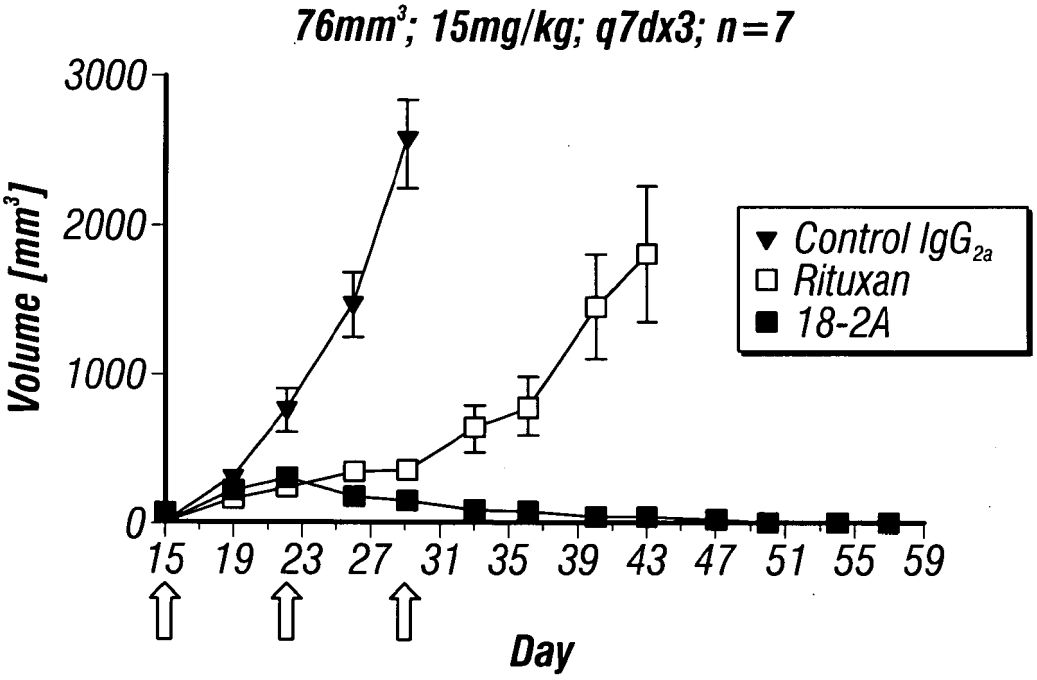
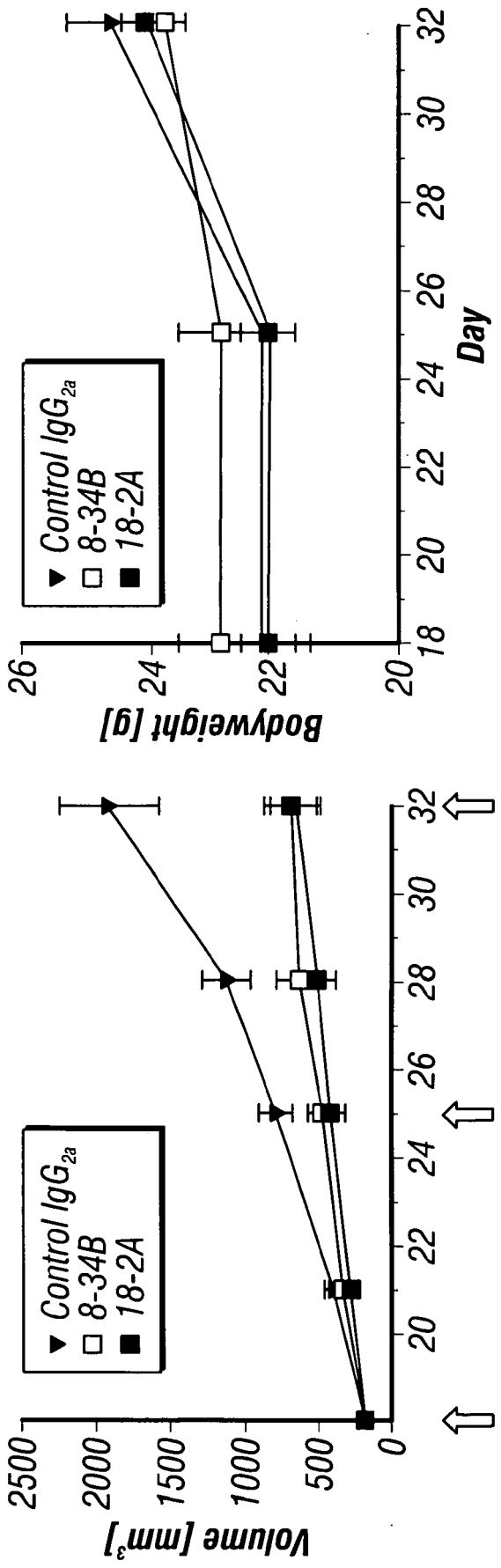

Percent Growth [%]
100
75
50
25
0
0
10
20
30
40
50
Time to Progression [Days]
HB-121
18-4A
8-300B
8-25C
8-361A6
8-162A4
1-47C
8-120A
8-319A2
456-26A
456-83A
1-115A
8-101A
18-2A

FIG. 6C



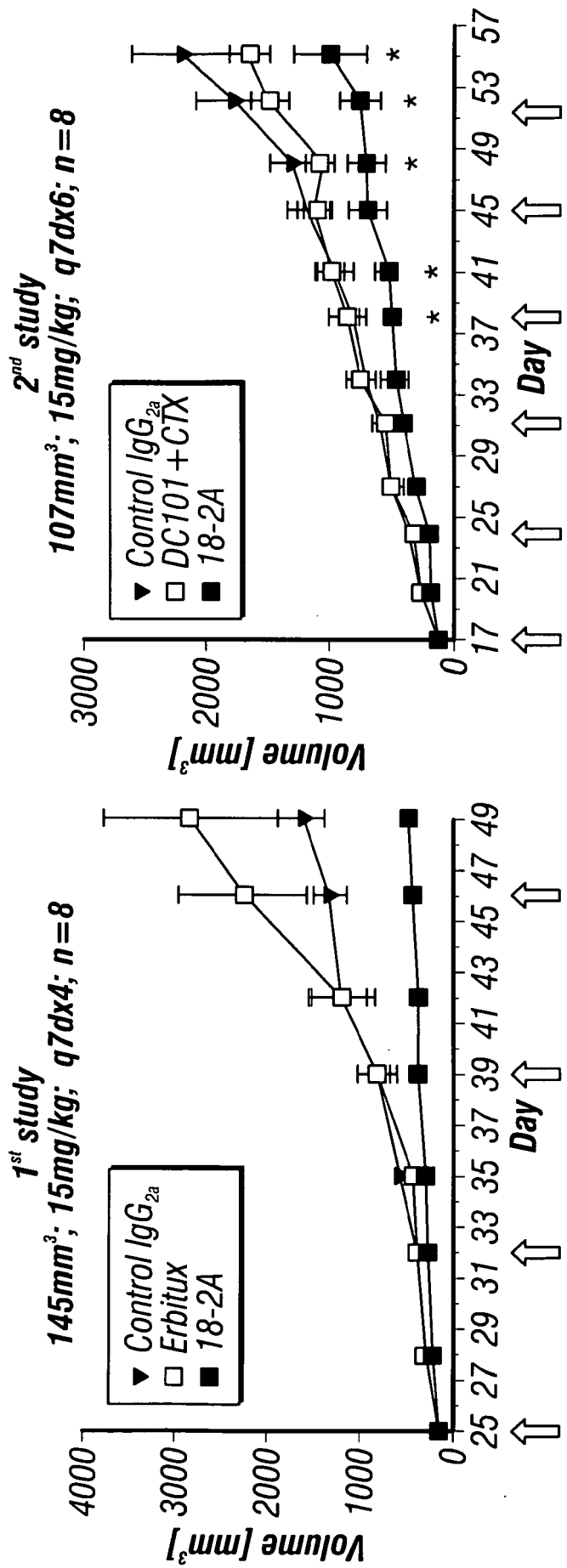
RAMOS/SCID	Control IgG_{2a}	Rituxan	18-2A
Volume ±SD [mm³]	2667 ±816	387 ±204	160 ±191
TGI [%]	-	-88	-96.7
p-Value	-	0.0002	0.0001

FIG. 7



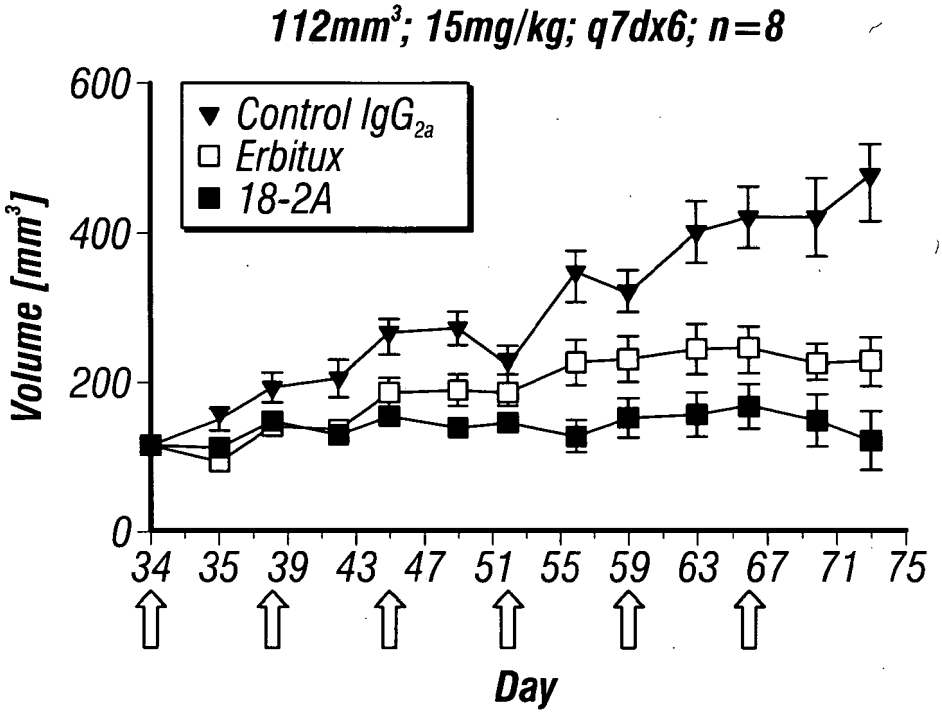
mAb	Control IgG_{2a}	18-2A	8-34B
Volume ±SD, [mm^3]	1921 ±863	671 ±468	694 ±492
p-Value	-	0.0080	0.0091

FIG. 8



mAb	Control IgG_{2a}	Erbitux	18-2A	Control IgG_{2a}	DC101+ CTX	18-2A
Vol ±SD [mm^3]	**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

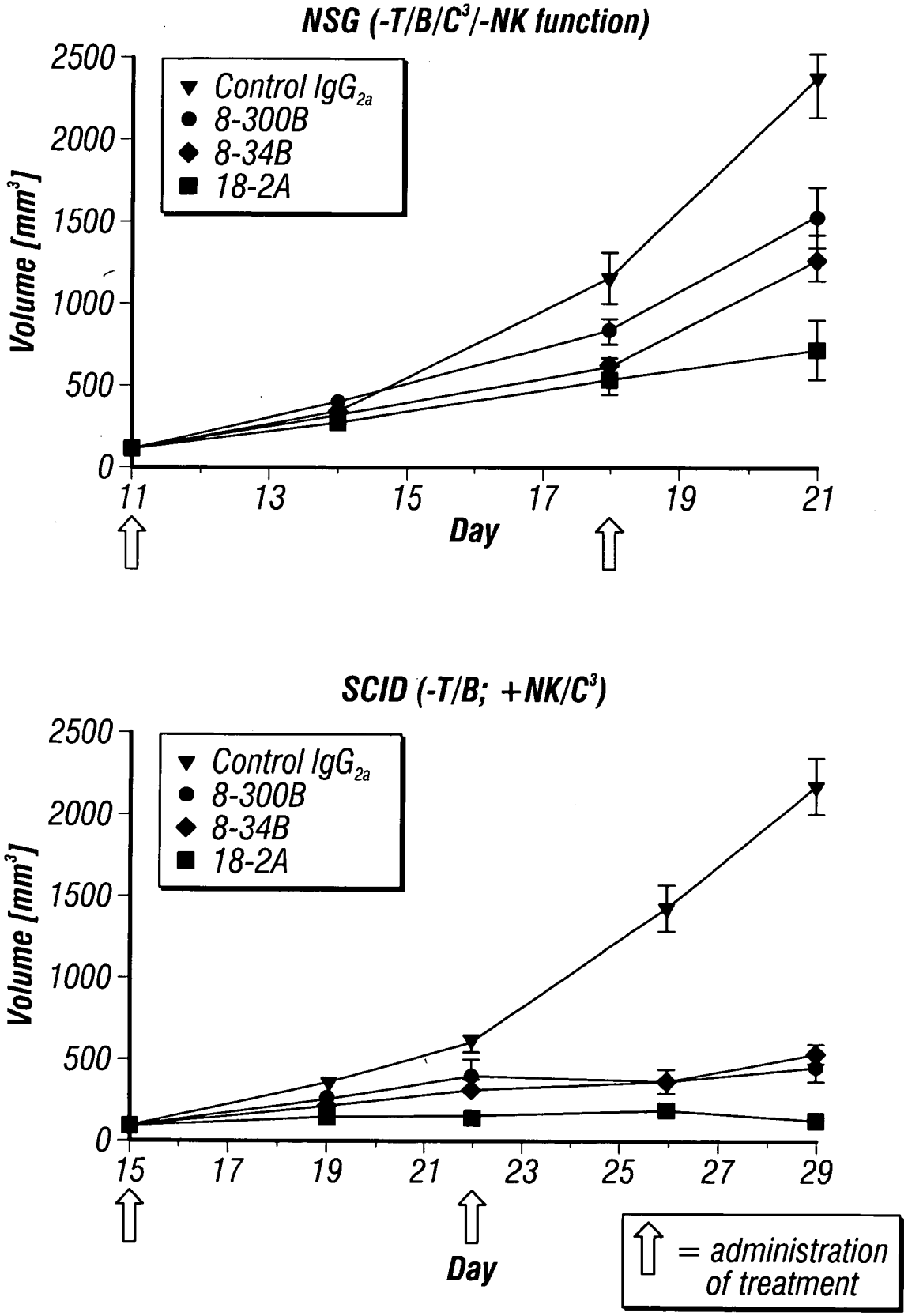
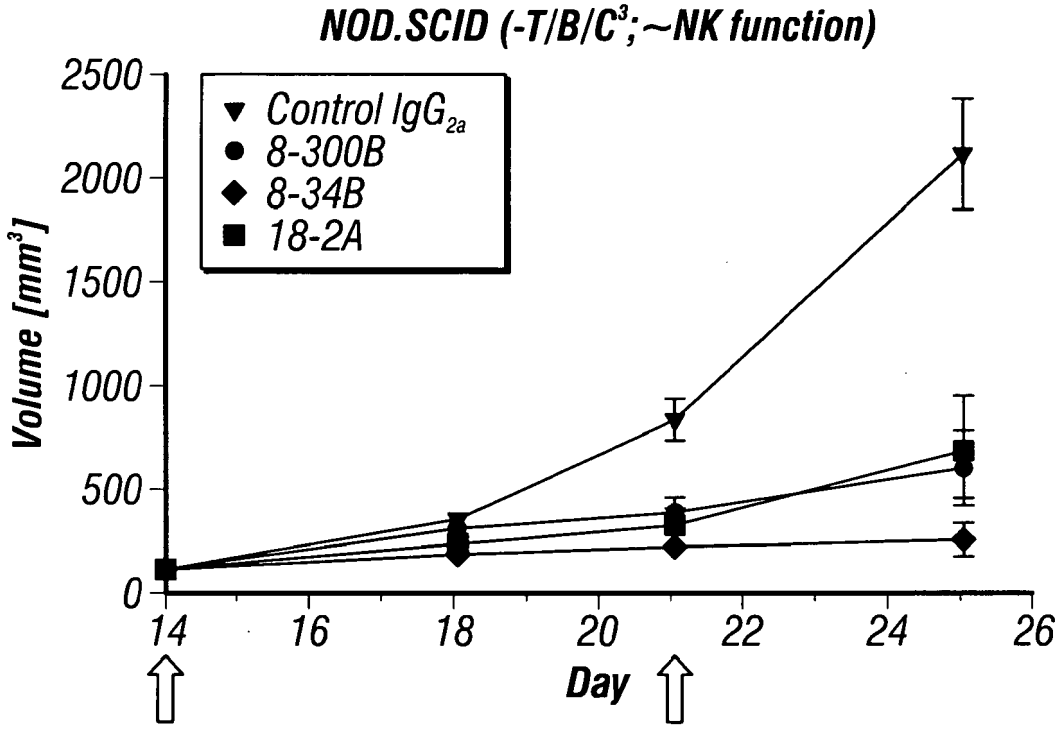

NSG (-T/B/C3/-NK function)
Control IgG2a
8-300B
8-34B
18-2A
Volume [mm3]
2500
2000
1500
1000
500
0
11
13
15
17
19
21
Day
SCID (-T/B; +NK/C3)
Control IgG2a
8-300B
8-34B
18-2A
Volume [mm3]
2500
2000
1500
1000
500
0
15
17
19
21
23
25
27
29
Day
= administration of treatment

FIG. 11


NOD.SCID (-T/B/C3;~NK function)
Control IgG2a
8-300B
8-34B
18-2A
Volume [mm3]
2500
2000
1500
1000
500
0
14
16
18
20
22
24
26
Day

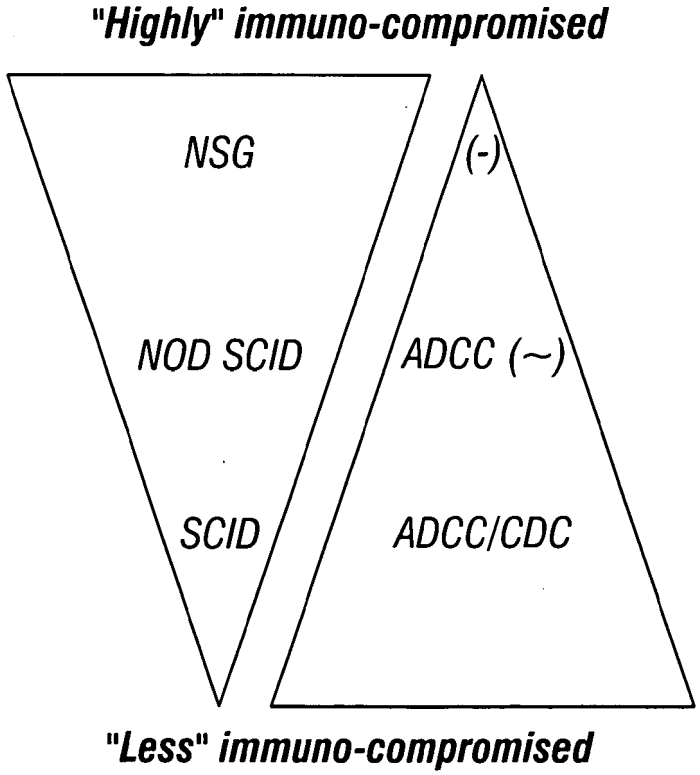
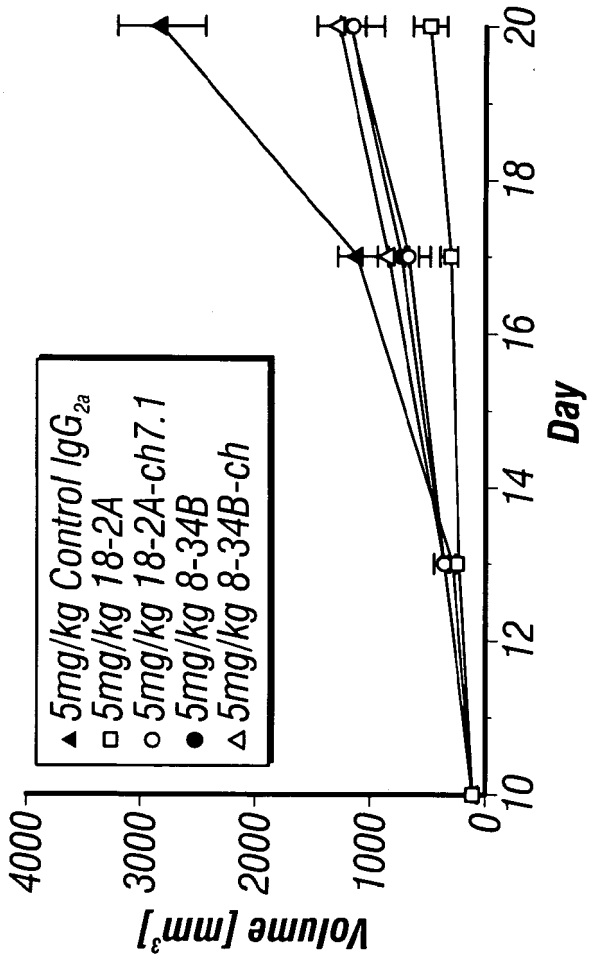

"Highly" immuno-compromised
NSG
NOD SCID
SCID
(-)
ADCC (~)
ADCC/CDC
"Less" immuno-compromised

FIG. 11
(Cont'd)



RAMOS, (n=8)	Control IgG2a	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	0.0043

FIG. 12

SUBSTITUTE SHEET (RULE 26)



FIG. 13

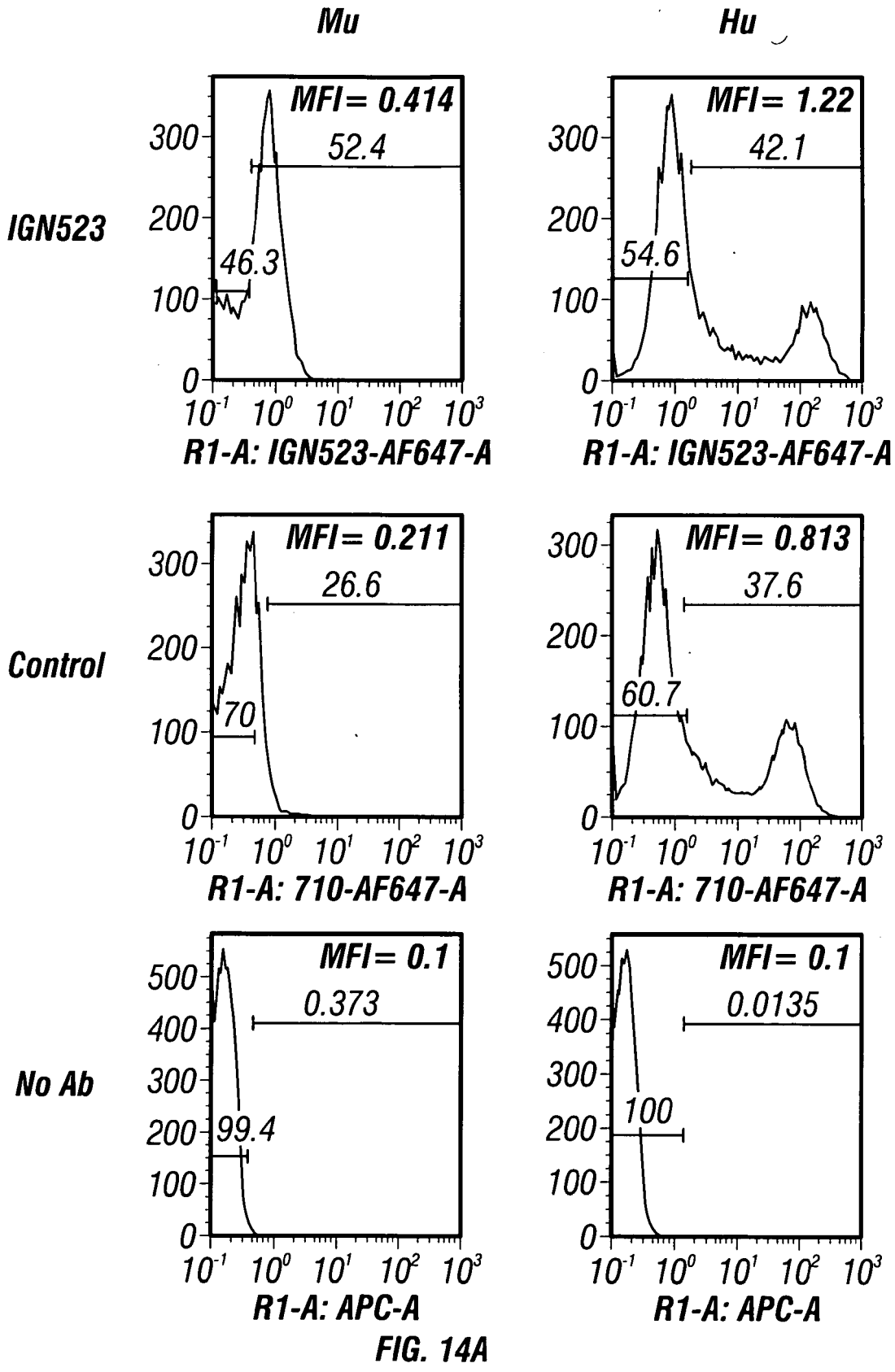

Mu
Hu
IGN523
Control
No Ab
MFI= 0.414
52.4
46.3
MFI= 1.22
42.1
54.6
MFI= 0.211
26.6
70
MFI= 0.813
37.6
60.7
MFI= 0.1
0.373
99.4
MFI= 0.1
0.0135
100
R1-A: IGN523-AF647-A
R1-A: IGN523-AF647-A
R1-A: 710-AF647-A
R1-A: 710-AF647-A
R1-A: APC-A
R1-A: APC-A

FIG. 14A

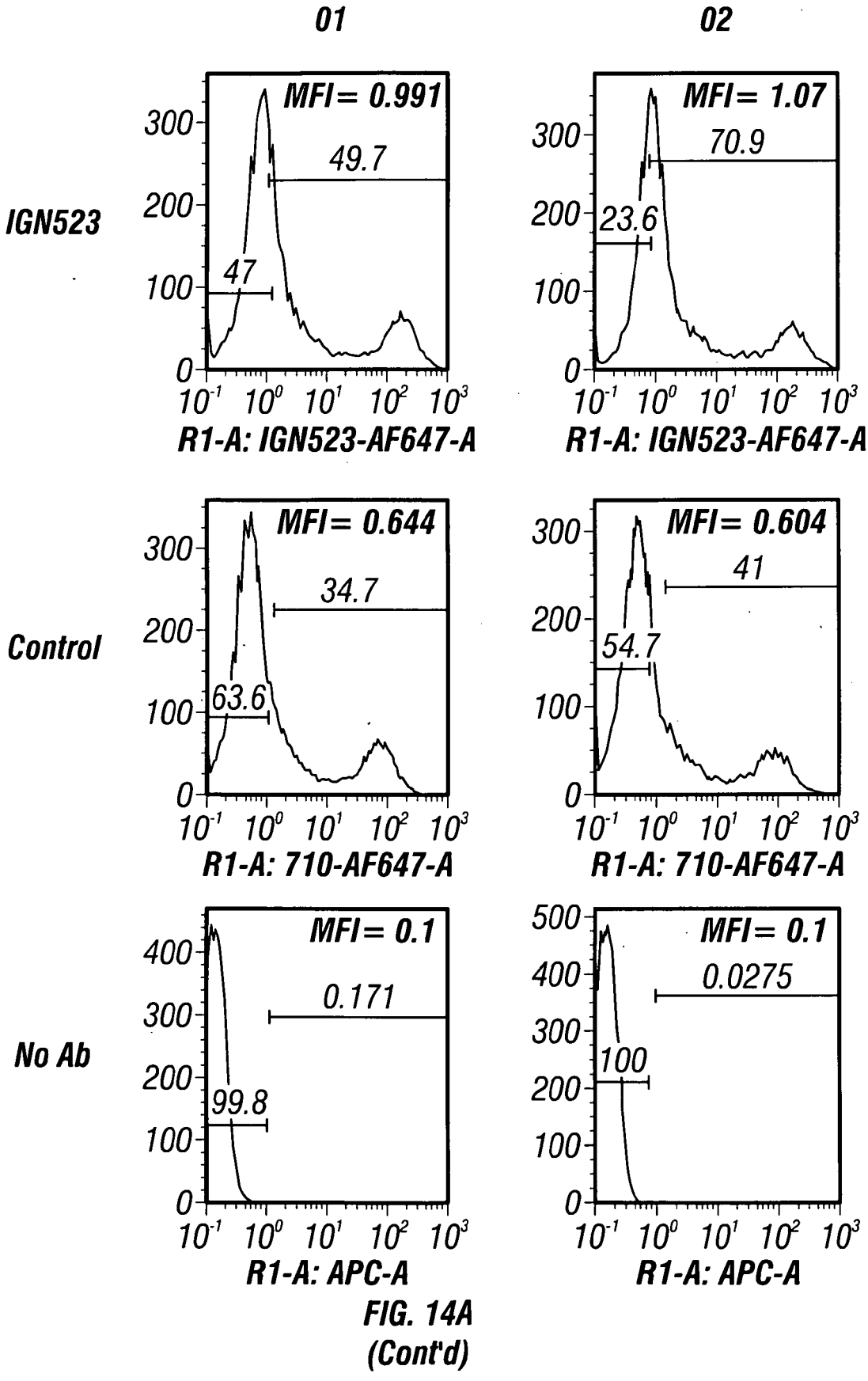


FIG. 14A
(Cont'd)

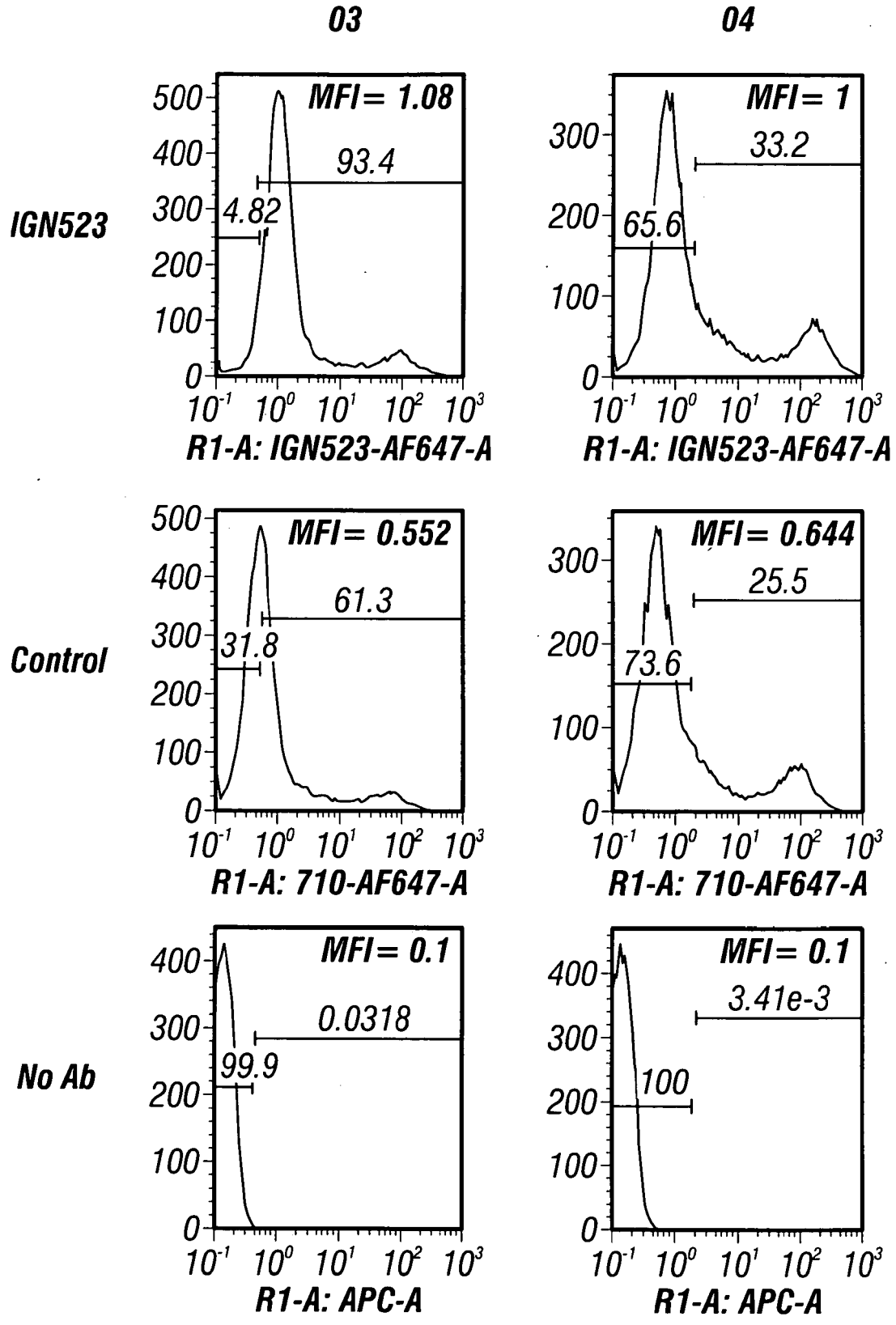


FIG. 14A
(Cont'd)

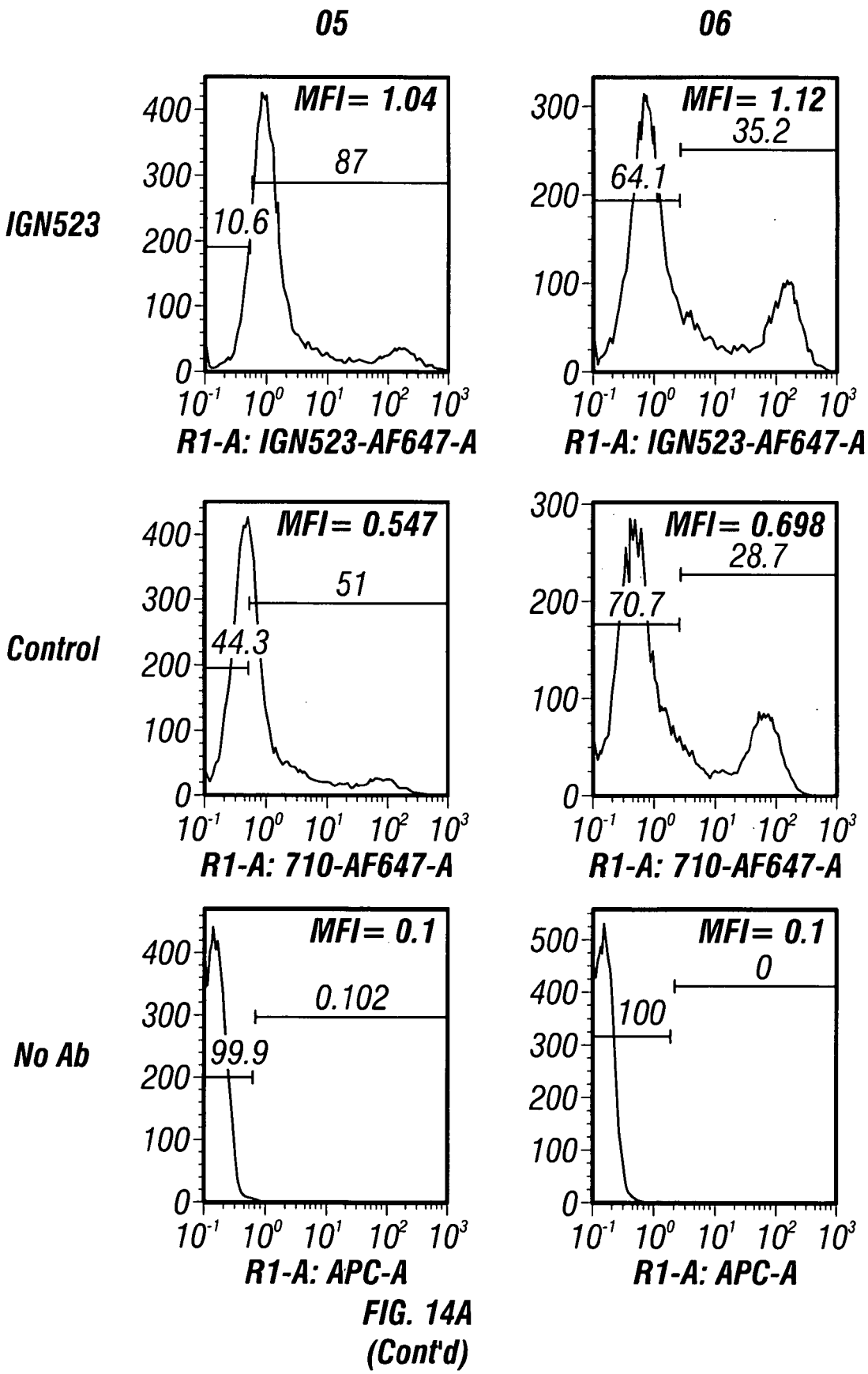


FIG. 14A
(Cont'd)

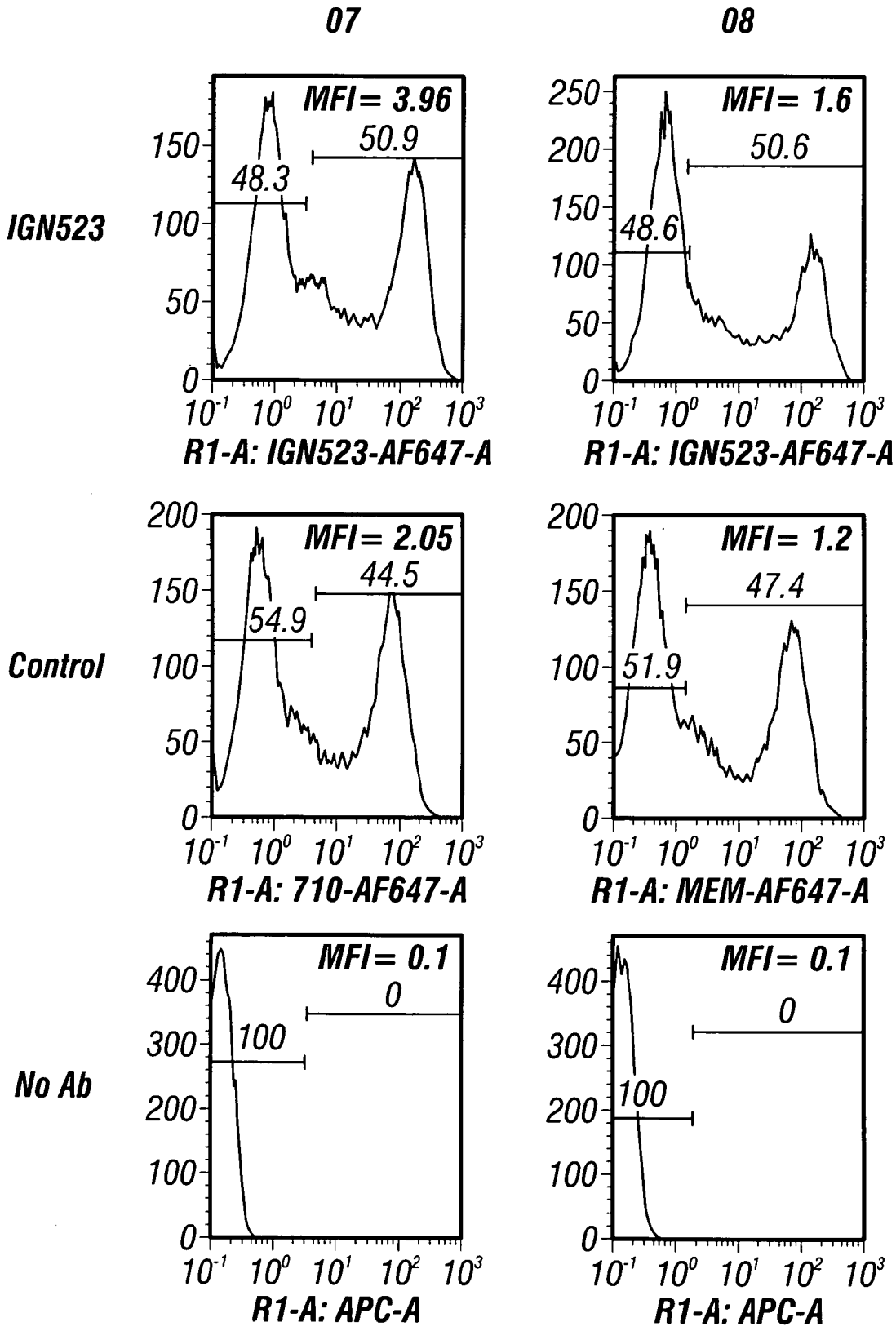

07
08
IGN523
MFI= 3.96
50.9
48.3
MFI= 1.6
50.6
48.6
R1-A: IGN523-AF647-A
R1-A: IGN523-AF647-A
Control
MFI= 2.05
44.5
54.9
MFI= 1.2
47.4
51.9
R1-A: 710-AF647-A
R1-A: MEM-AF647-A
No Ab
MFI= 0.1
0
100
MFI= 0.1
0
100
R1-A: APC-A
R1-A: APC-A

FIG. 14B

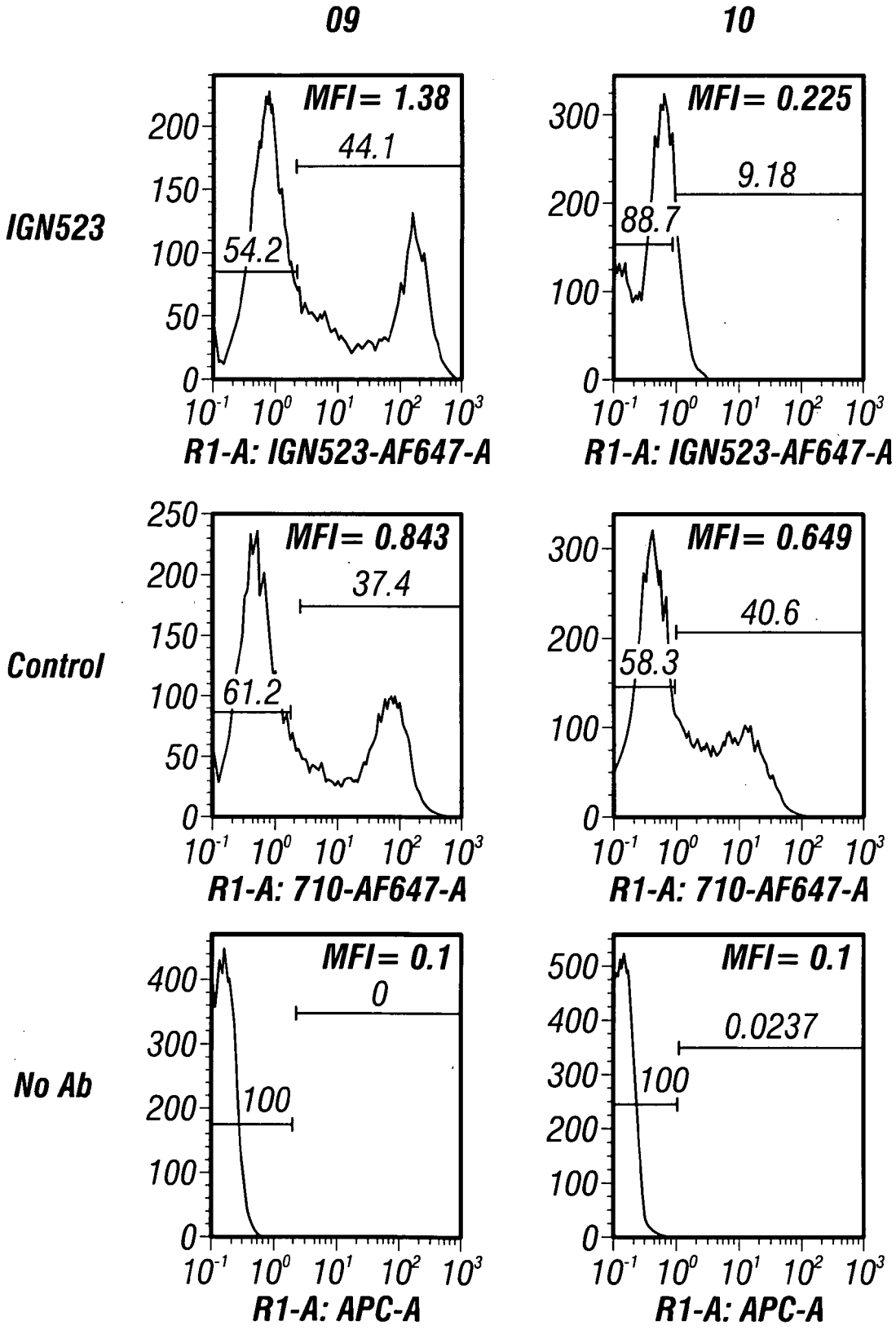


FIG. 14B
(Cont'd)

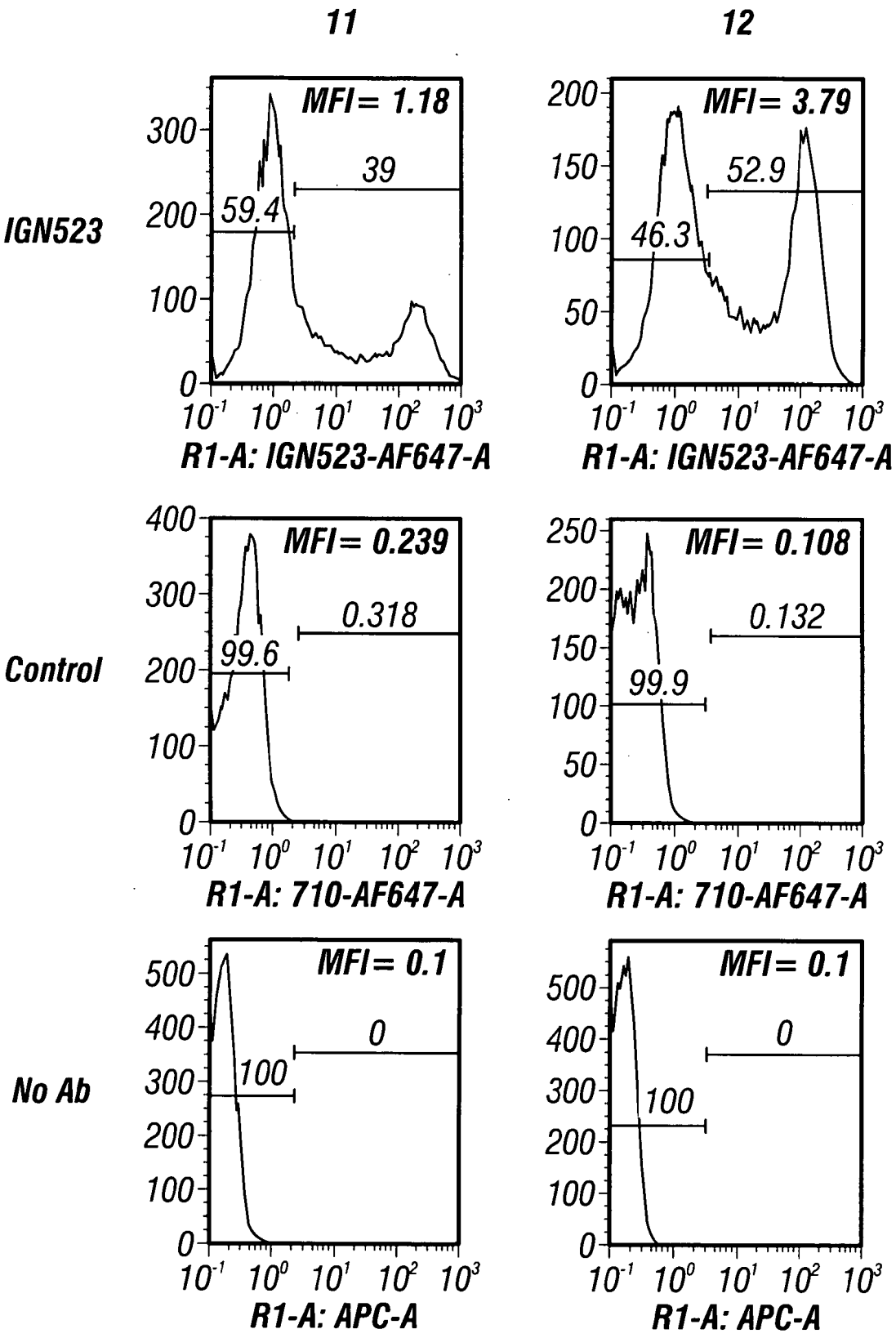
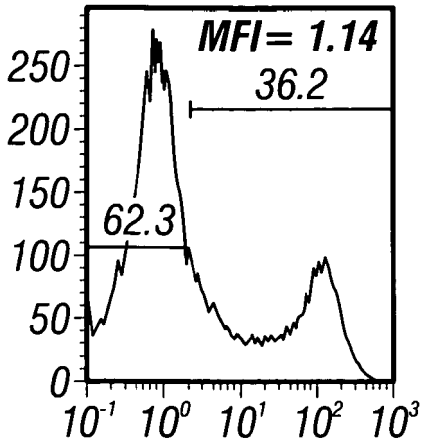


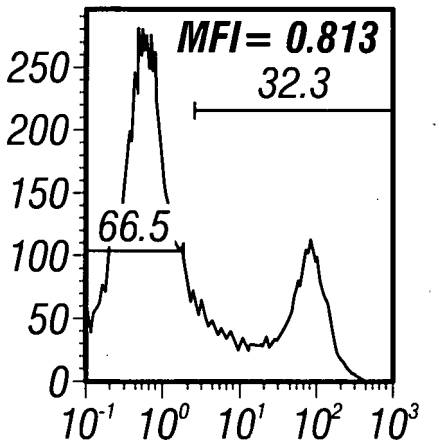
FIG. 14B
(Cont'd)

13

IGN523



Control



No Ab

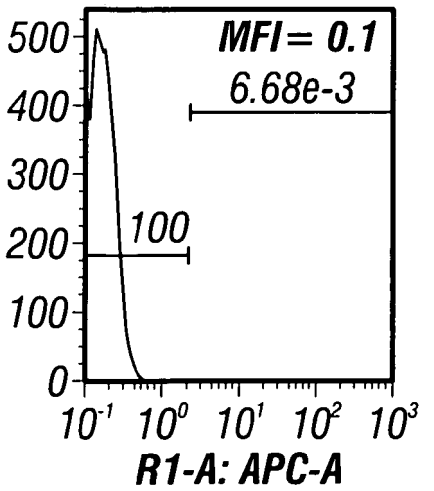
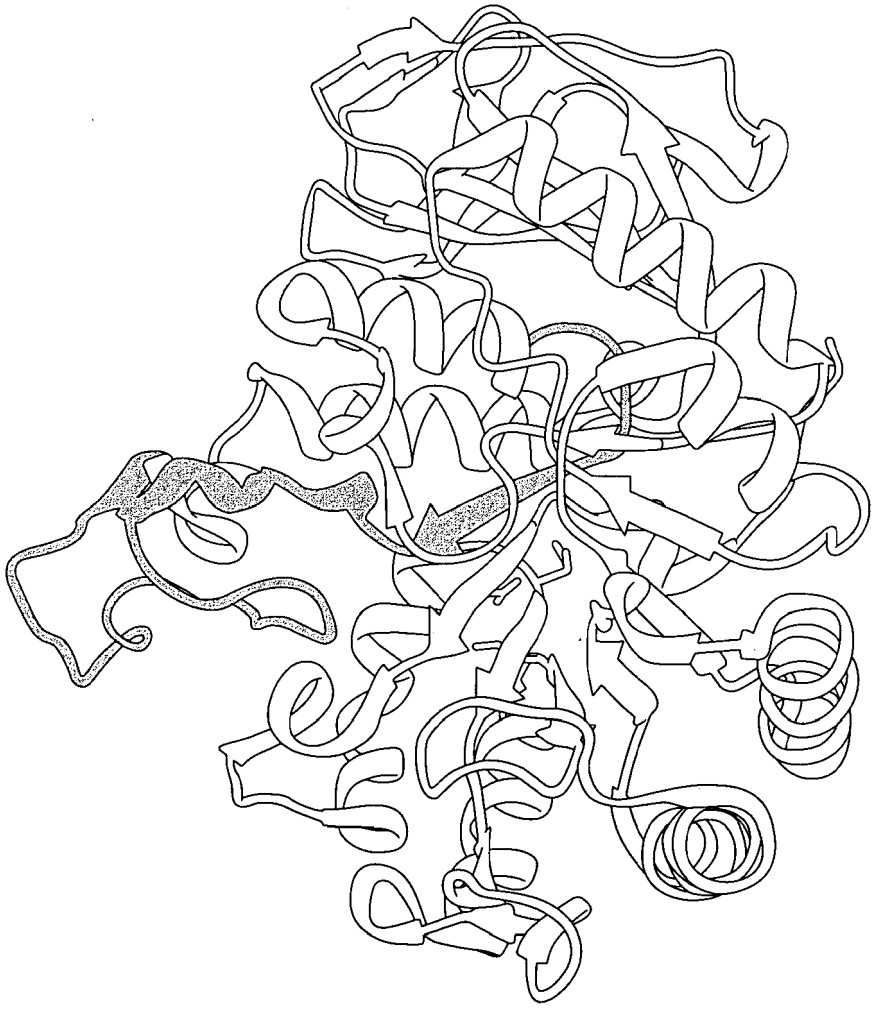


FIG. 14B
(Cont'd)



T358 I371 N405
Human TLPGTPVFSYGDEIGLDAAALPGQPMEAPVMLWDESSFPDIPGAVSAN (SEQ ID NO:97)
Mouse TLPGTPVFSYGDELGLQG-ALPGQPAKAPLMPWNESSIFHIPRPVSLN (SEQ ID NO:98)

FIG. 15

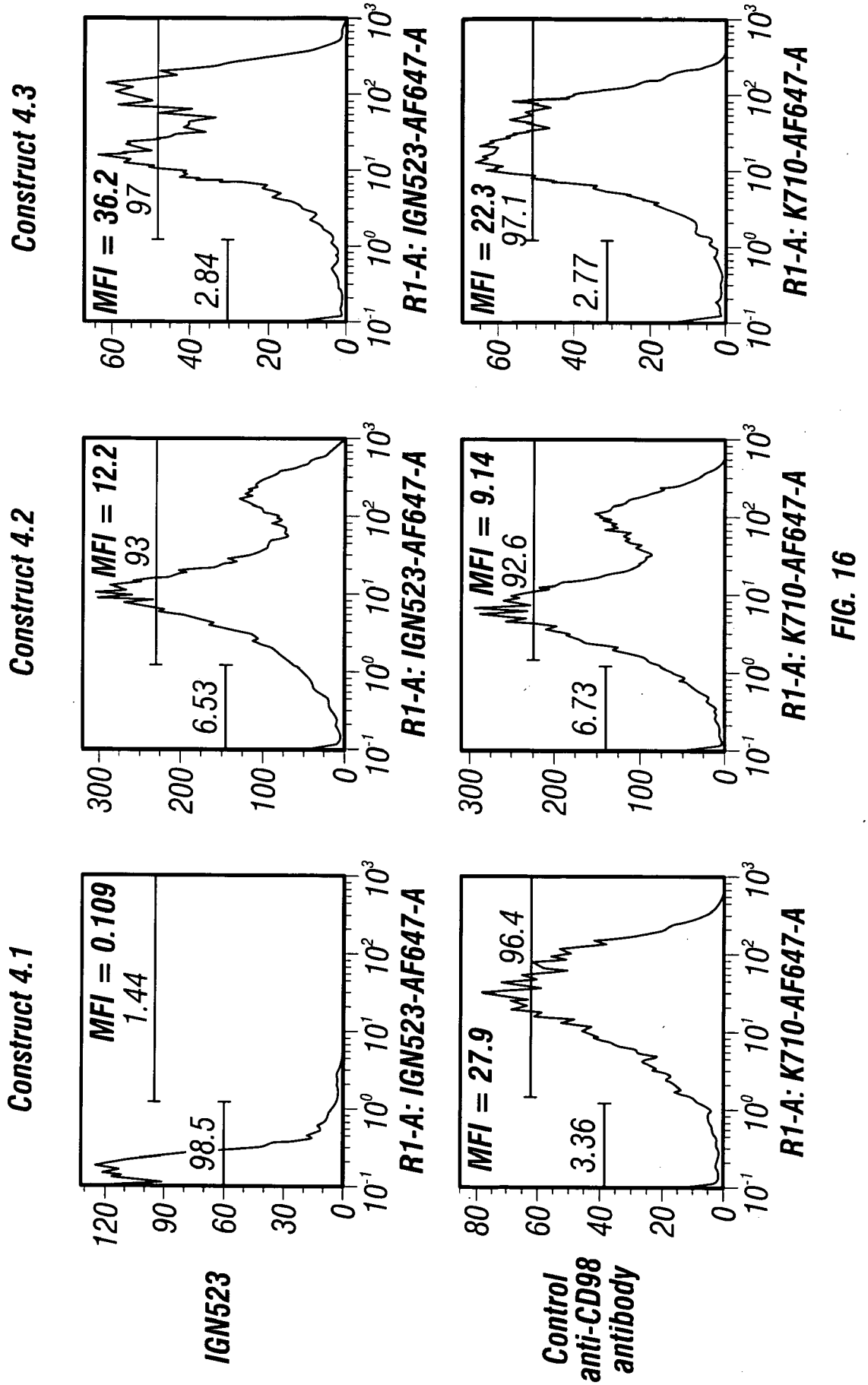

Construct 4.1
Construct 4.2
Construct 4.3
IGN523
Control anti-CD98 antibody
MFI = 0.109
1.44
98.5
MFI = 12.2
93
6.53
MFI = 36.2
97
2.84
MFI = 27.9
96.4
3.36
MFI = 9.14
92.6
6.73
MFI = 22.3
97.1
2.77
R1-A: IGN523-AF647-A
R1-A: K710-AF647-A

FIG. 16

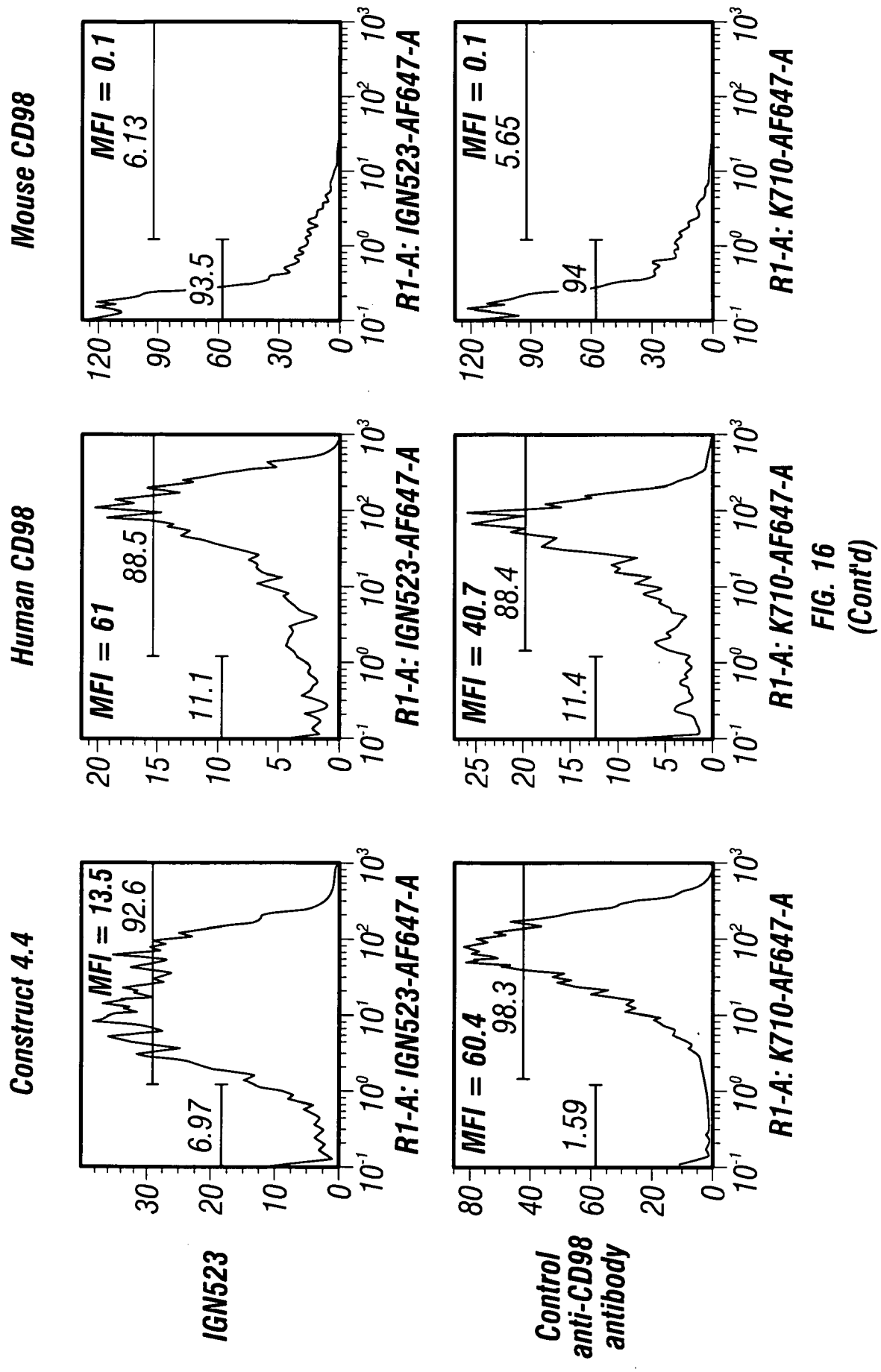

Construct 4.4
Human CD98
Mouse CD98
IGN523
Control anti-CD98 antibody
MFI = 13.5
92.6
6.97
MFI = 61
88.5
11.1
MFI = 0.1
6.13
93.5
MFI = 60.4
98.3
1.59
MFI = 40.7
88.4
11.4
MFI = 0.1
5.65
94
R1-A: IGN523-AF647-A
R1-A: K710-AF647-A

FIG. 16
(Cont'd)

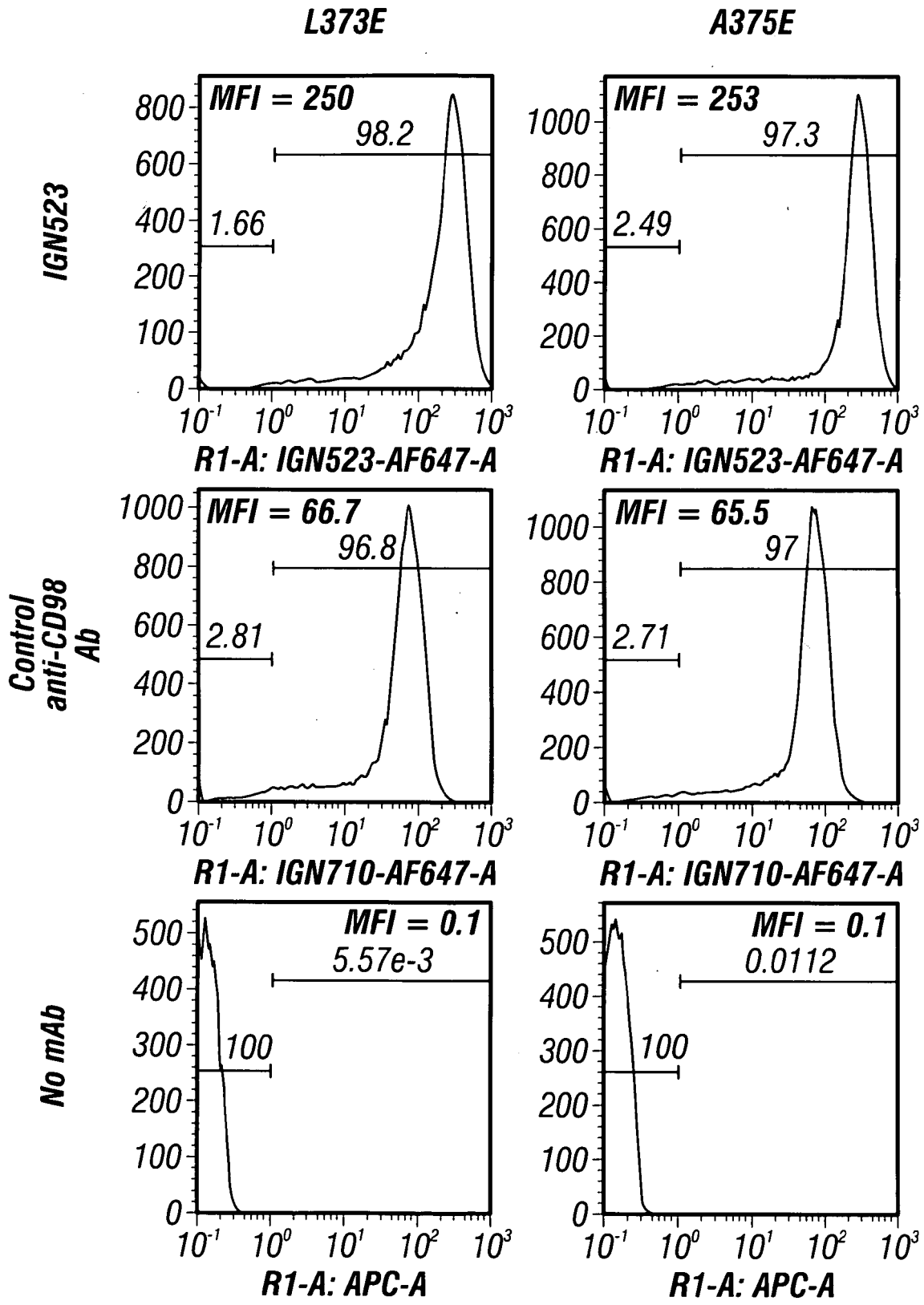

L373E
A375E
IGN523
Control anti-CD98 Ab
No mAb
MFI = 250
98.2
1.66
MFI = 253
97.3
2.49
MFI = 66.7
96.8
2.81
MFI = 65.5
97
2.71
MFI = 0.1
5.57e-3
100
MFI = 0.1
0.0112
100
R1-A: IGN523-AF647-A
R1-A: IGN710-AF647-A
R1-A: APC-A

FIG. 17A

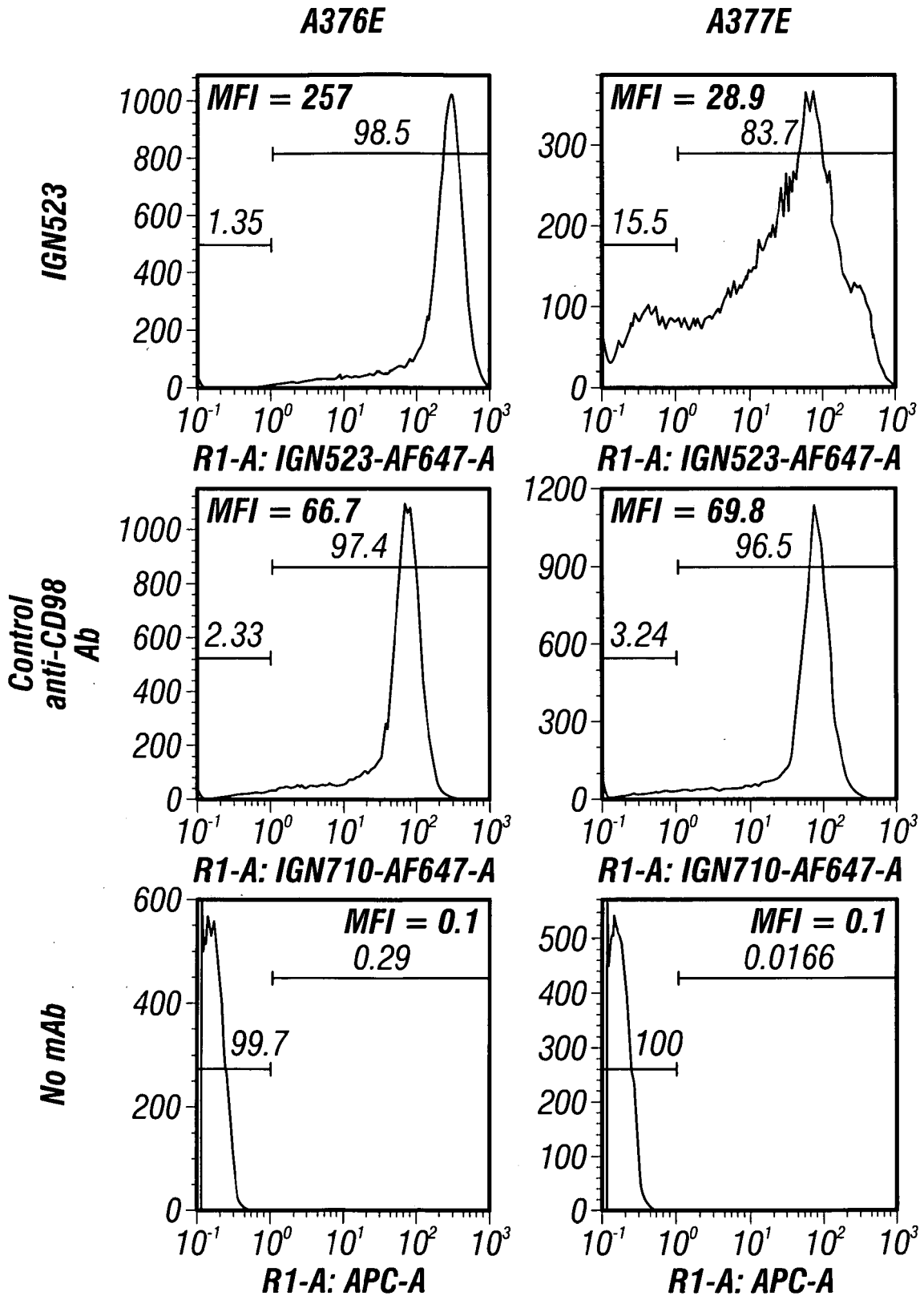


FIG. 17A
(Cont'd)

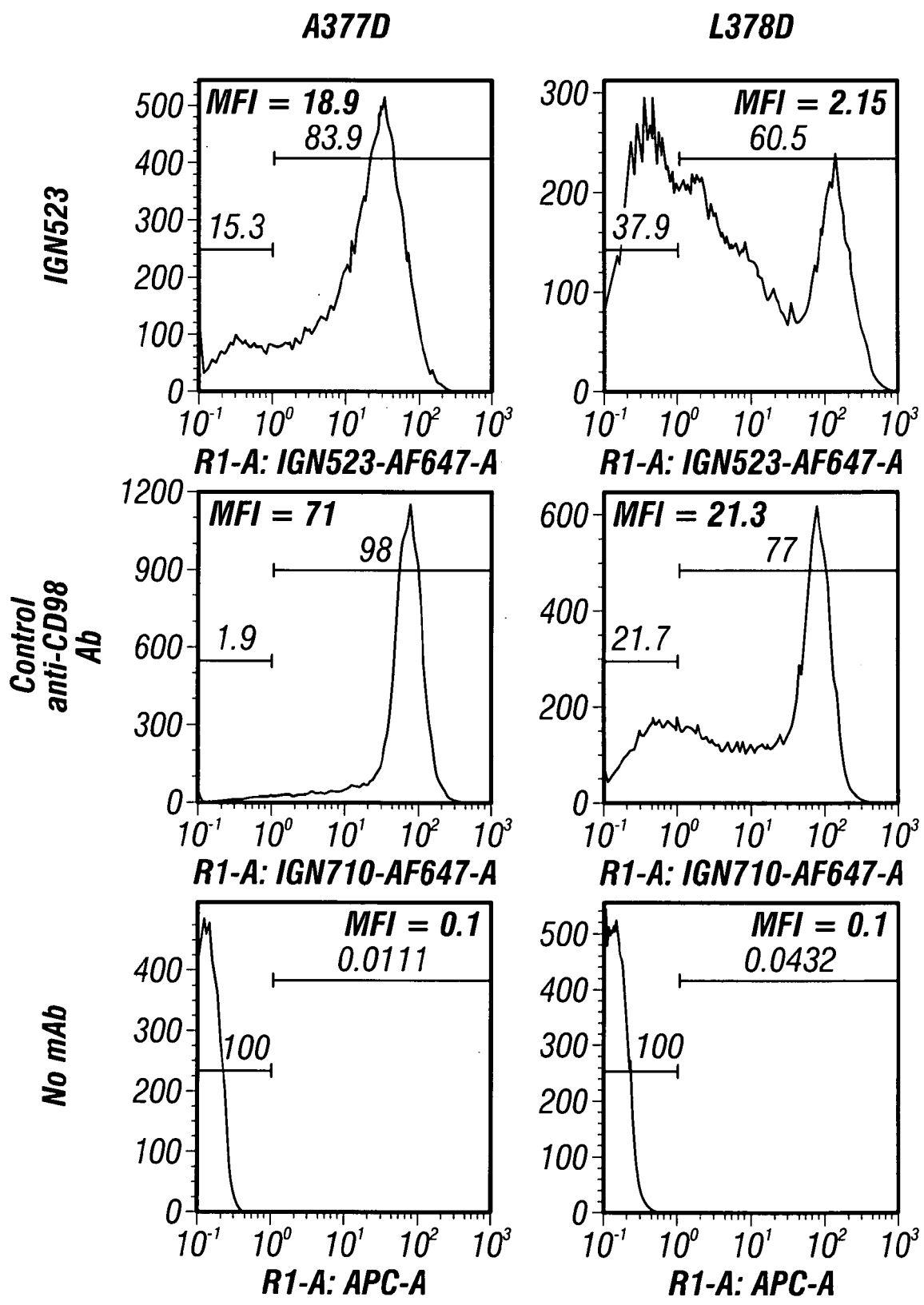


FIG. 17A
(Cont'd)

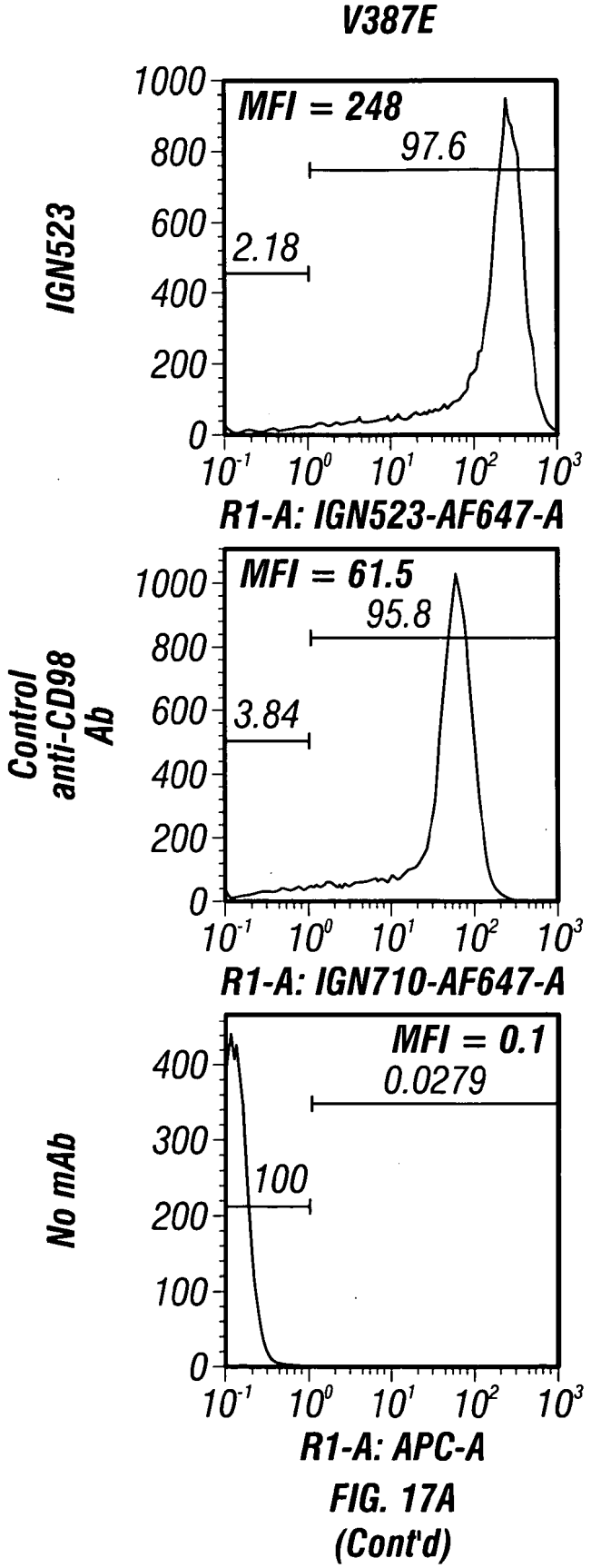


FIG. 17A
(Cont'd)

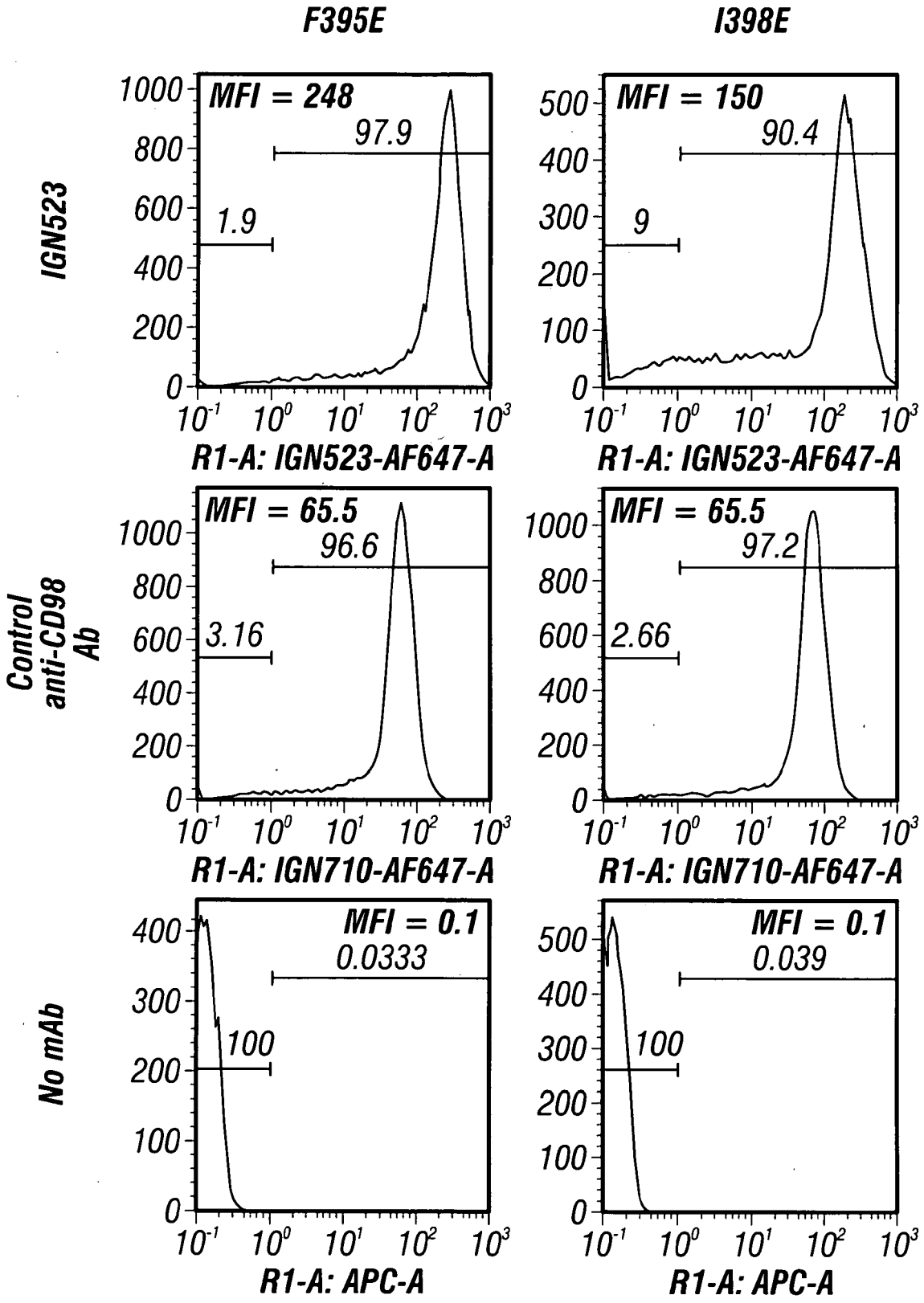

F395E
I398E
IGN523
Control anti-CD98 Ab
No mAb
MFI = 248
97.9
1.9
MFI = 150
90.4
9
MFI = 65.5
96.6
3.16
MFI = 65.5
97.2
2.66
MFI = 0.1
0.0333
100
MFI = 0.1
0.039
100
R1-A: IGN523-AF647-A
R1-A: IGN523-AF647-A
R1-A: IGN710-AF647-A
R1-A: IGN710-AF647-A
R1-A: APC-A
R1-A: APC-A

FIG. 17B

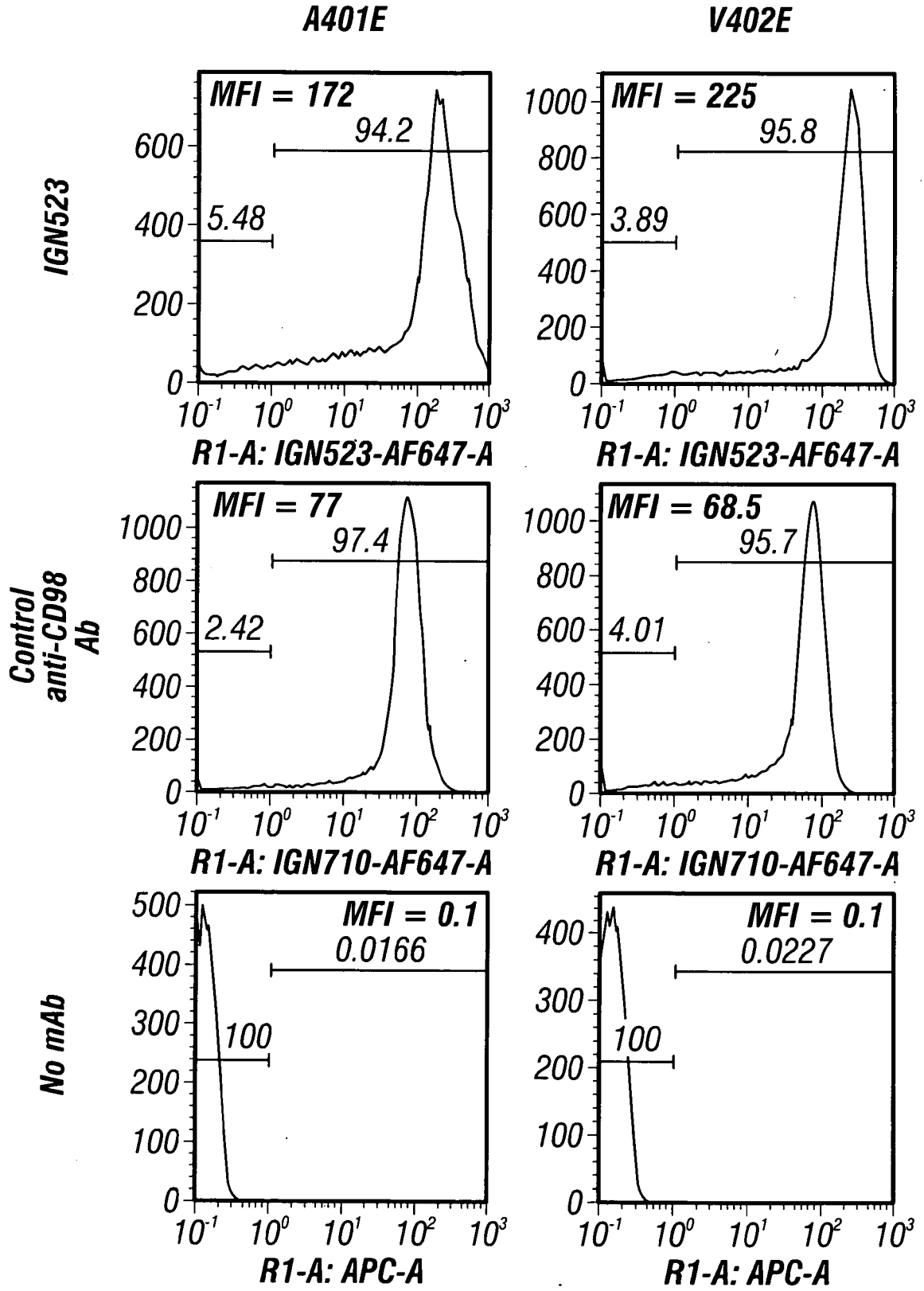


FIG. 17B
(Cont'd)

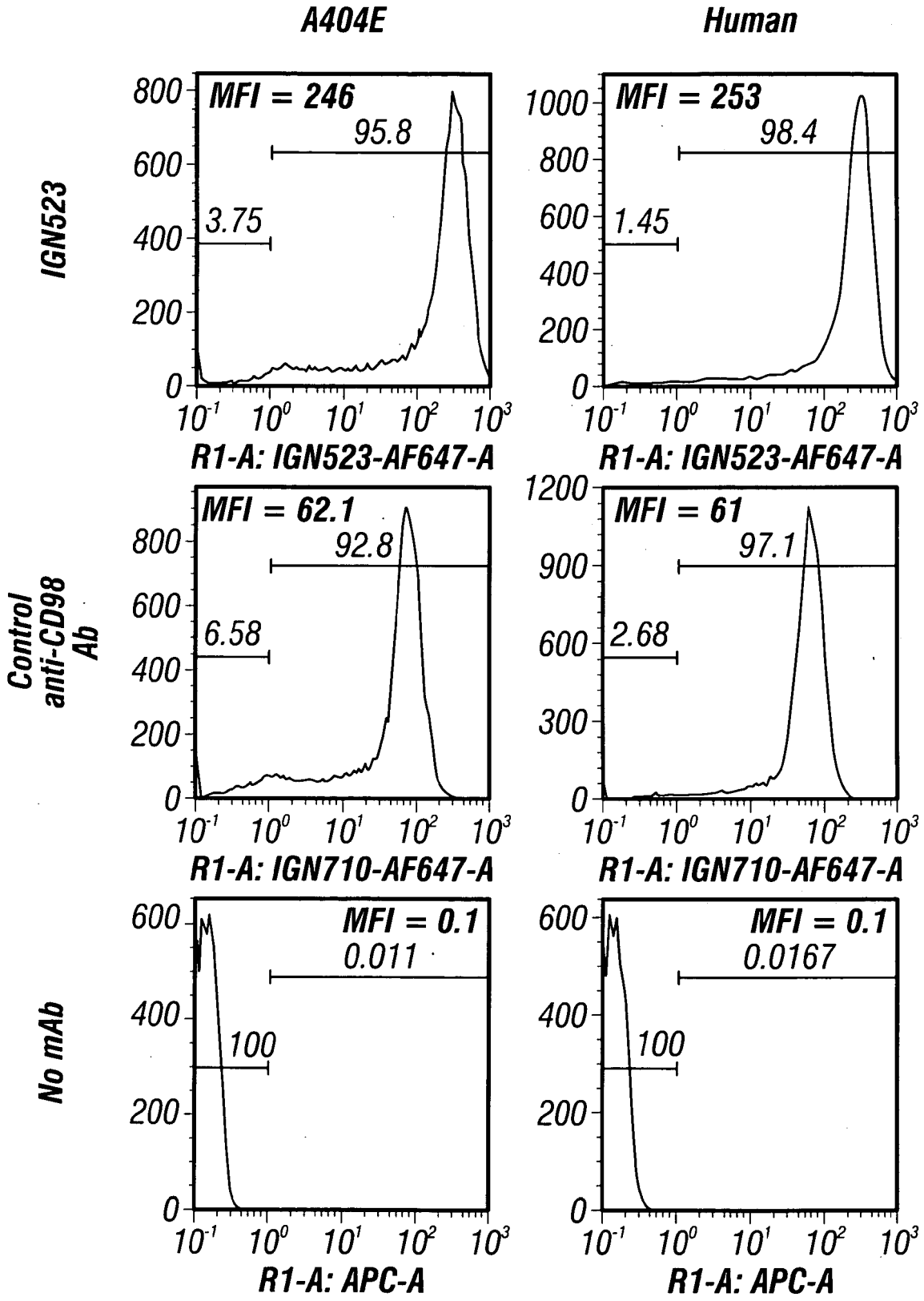


FIG. 17B
(Cont'd)

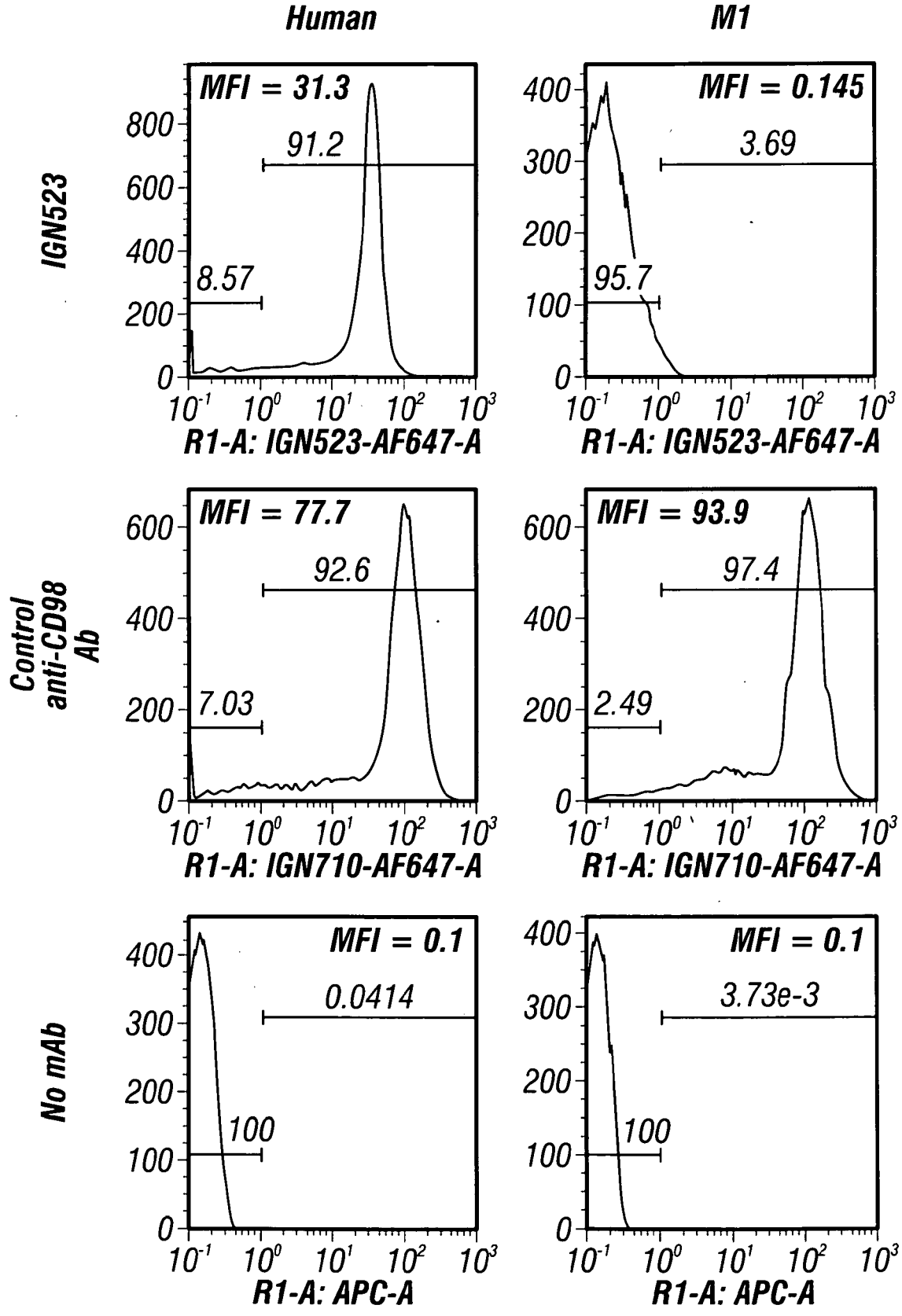

Human
M1
IGN523
Control anti-CD98 Ab
No mAb
MFI = 31.3
91.2
8.57
MFI = 0.145
3.69
95.7
MFI = 77.7
92.6
7.03
MFI = 93.9
97.4
2.49
MFI = 0.1
0.0414
100
MFI = 0.1
3.73e-3
100
R1-A: IGN523-AF647-A
R1-A: IGN710-AF647-A
R1-A: APC-A

FIG. 18

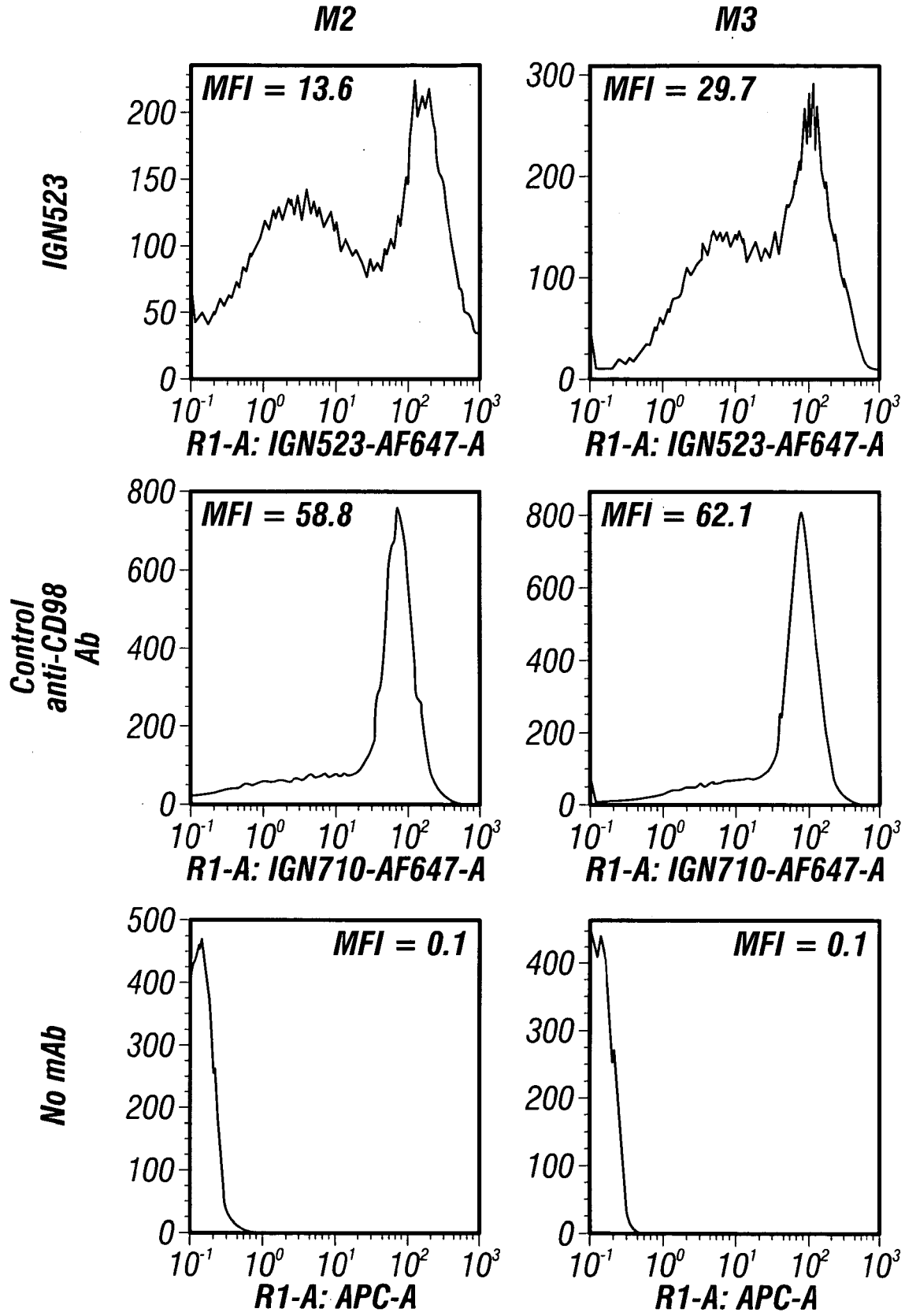

M2
M3
IGN523
MFI = 13.6
MFI = 29.7
R1-A: IGN523-AF647-A
Control anti-CD98 Ab
MFI = 58.8
MFI = 62.1
R1-A: IGN710-AF647-A
No mAb
MFI = 0.1
MFI = 0.1
R1-A: APC-A

FIG. 18
(Cont'd)

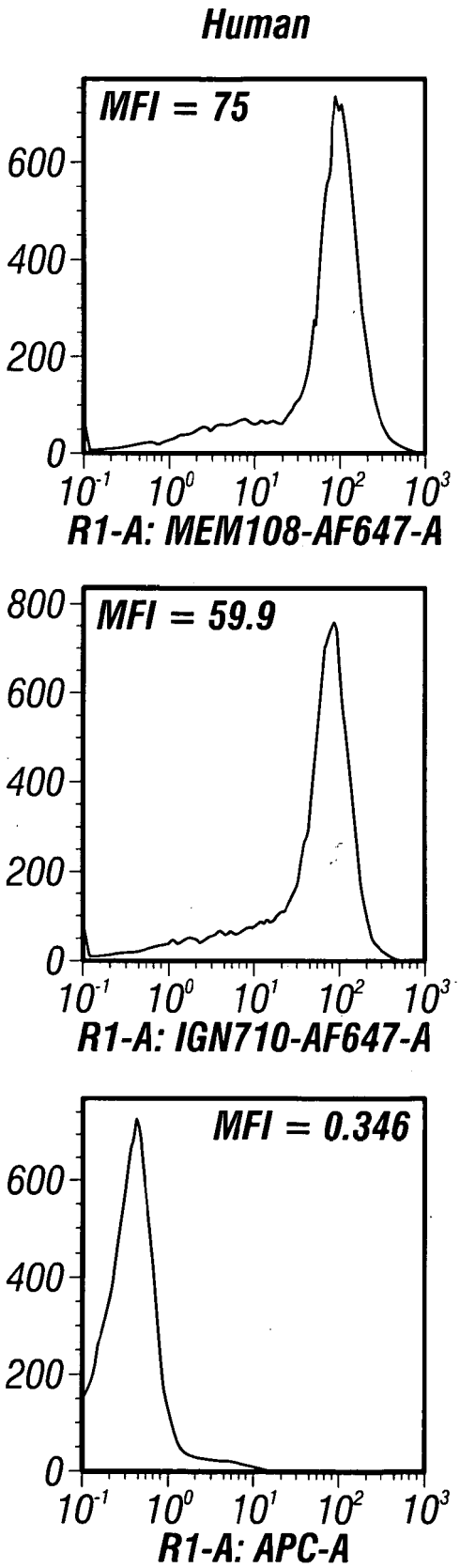

Human
MFI = 75
600
400
200
0
10-1 10^0 10^1 10^2 10^3
R1-A: MEM108-AF647-A
MFI = 59.9
800
600
400
200
0
10-1 10^0 10^1 10^2 10^3
R1-A: IGN710-AF647-A
MFI = 0.346
600
400
200
0
10-1 10^0 10^1 10^2 10^3
R1-A: APC-A

FIG. 18
(Cont'd)

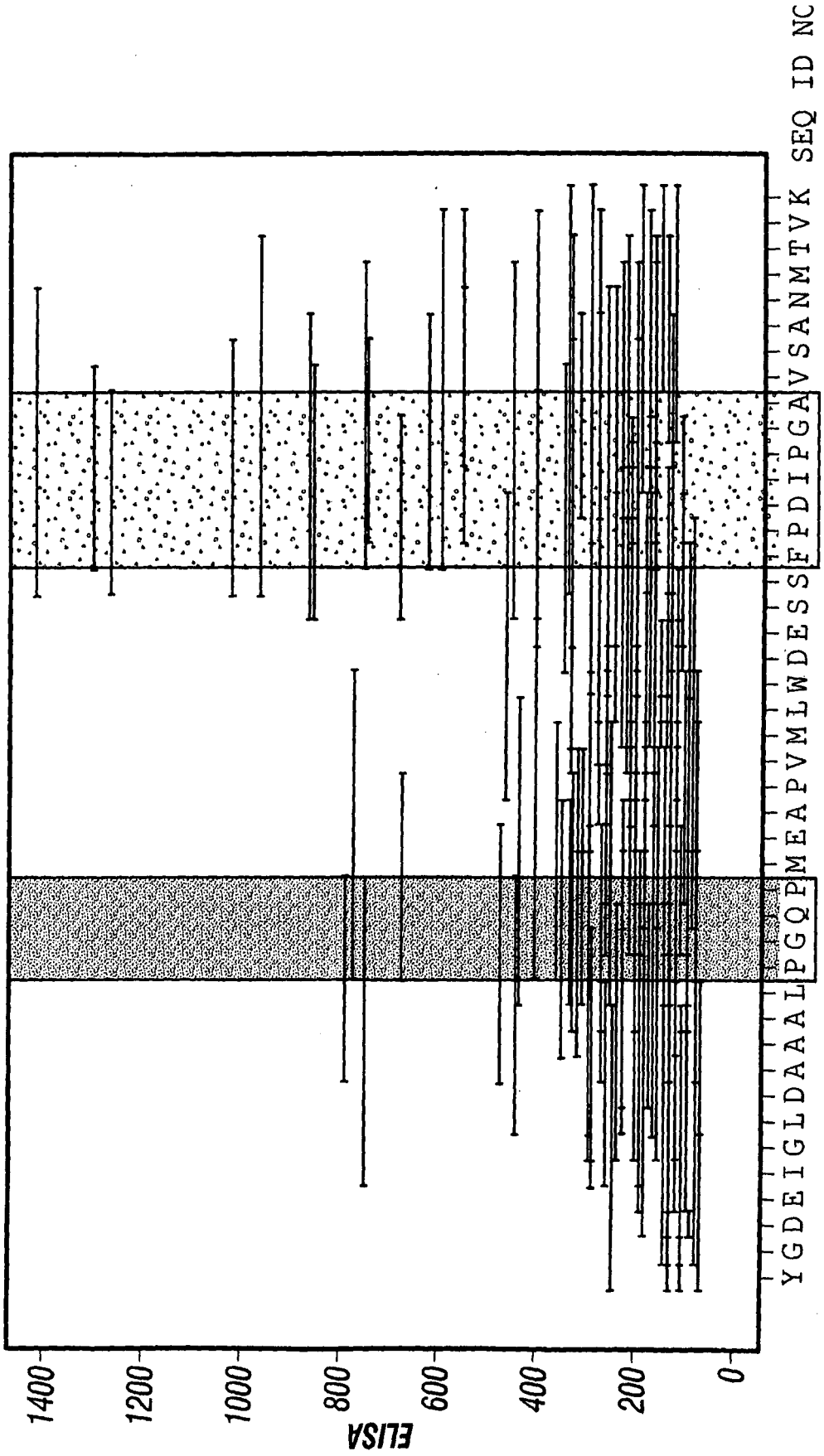

ELISA
1400
1200
1000
800
600
400
200
0
Y G D E I G L D A A A L P G Q P M E A P V M L W D E S S F P D I P G A V S A N M T V K
SEQ ID NC
position

FIG. 19

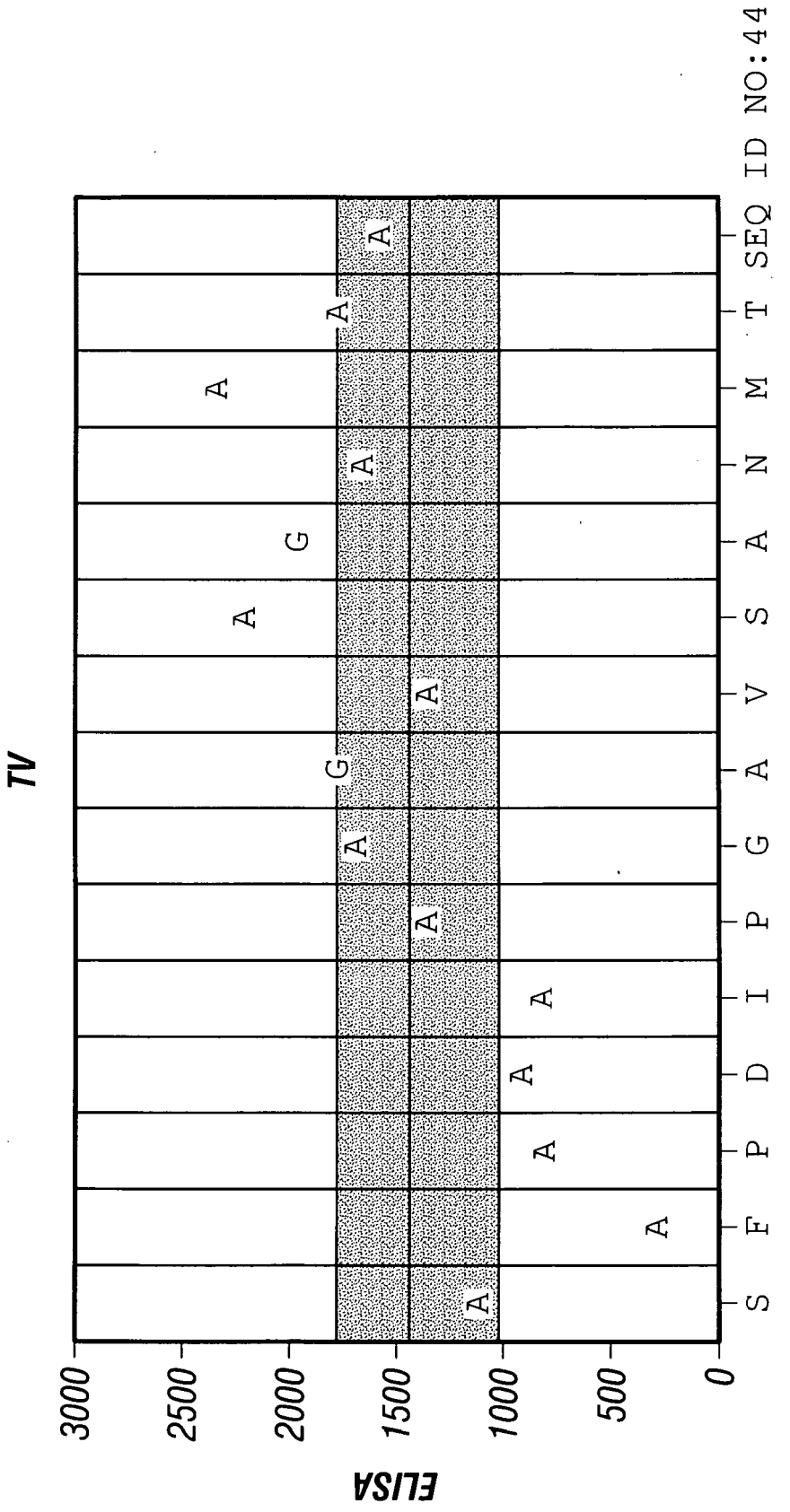

ELISA
3000
2500
2000
1500
1000
500
0
TV
S F P P D I P G A V S A N M T SEQ ID NO:44

FIG. 20

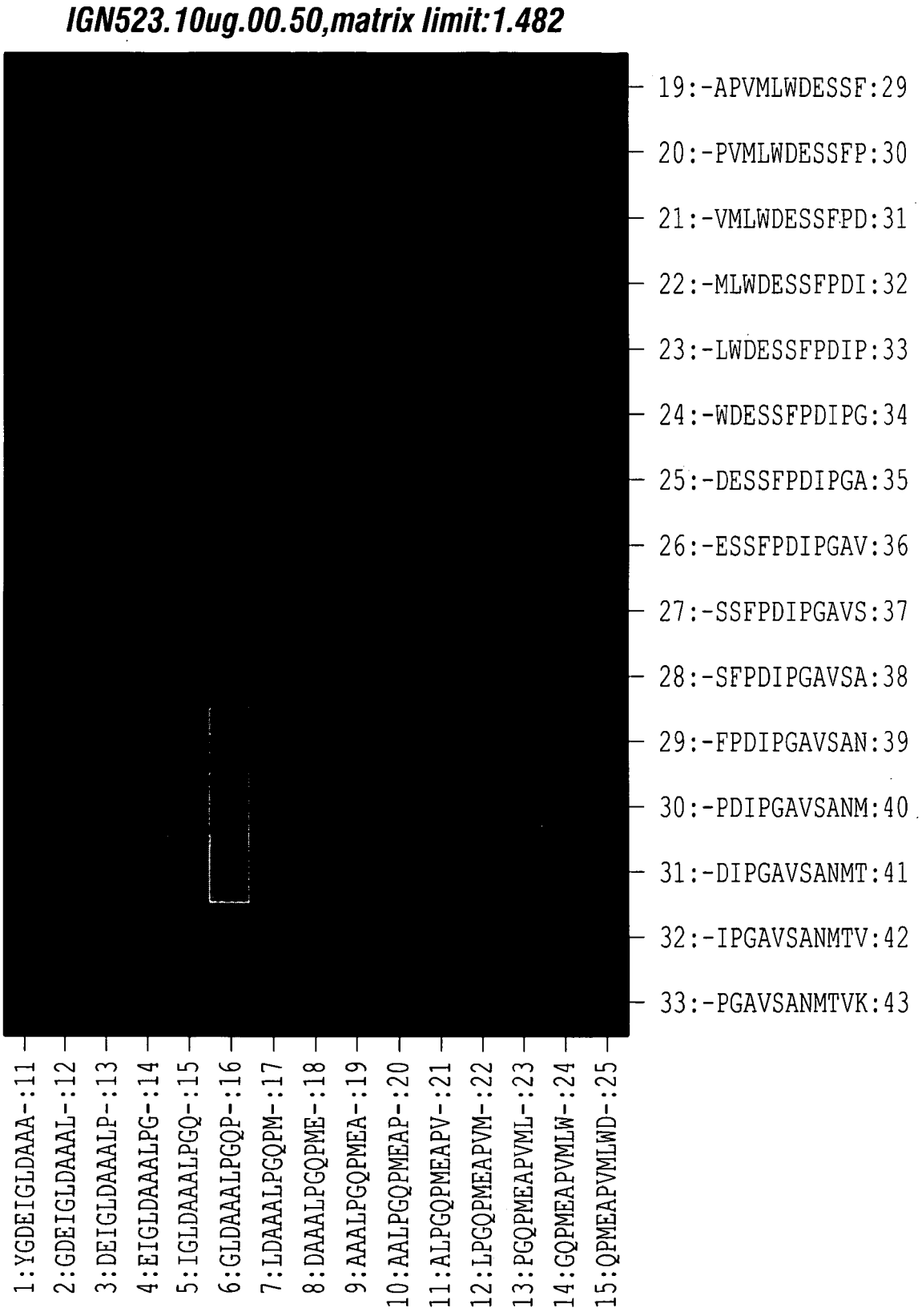

IGN523.10ug.00.50,matrix limit:1.482
19:-APVMLWDESSF:29
20:-PVMLWDESSFP:30
21:-VMLWDESSFPD:31
22:-MLWDESSFPDI:32
23:-LWDESSFPDIP:33
24:-WDESSFPDIPG:34
25:-DESSFPDIPGA:35
26:-ESSFPDIPGAV:36
27:-SSFPDIPGAVS:37
28:-SFPDIPGAVSA:38
29:-FPDIPGAVSAN:39
30:-PDIPGAVSANM:40
31:-DIPGAVSANMT:41
32:-IPGAVSANMTV:42
33:-PGAVSANMTVK:43
1:YGDEIGLDAAA-:11
2:GDEIGLDAAAL-:12
3:DEIGLDAAALP-:13
4:EIGLDAAALPG-:14
5:IGLDAAALPGQ-:15
6:GLDAAALPGQP-:16
7:LDAAALPGQPM-:17
8:DAAALPGQPME-:18
9:AAALPGQPMEA-:19
10:AALPGQPMEAP-:20
11:ALPGQPMEAPV-:21
12:LPGQPMEAPVM-:22
13:PGQPMEAPVML-:23
14:GQPMEAPVMLW-:24
15:QPMEAPVMLWD-:25

FIG. 21

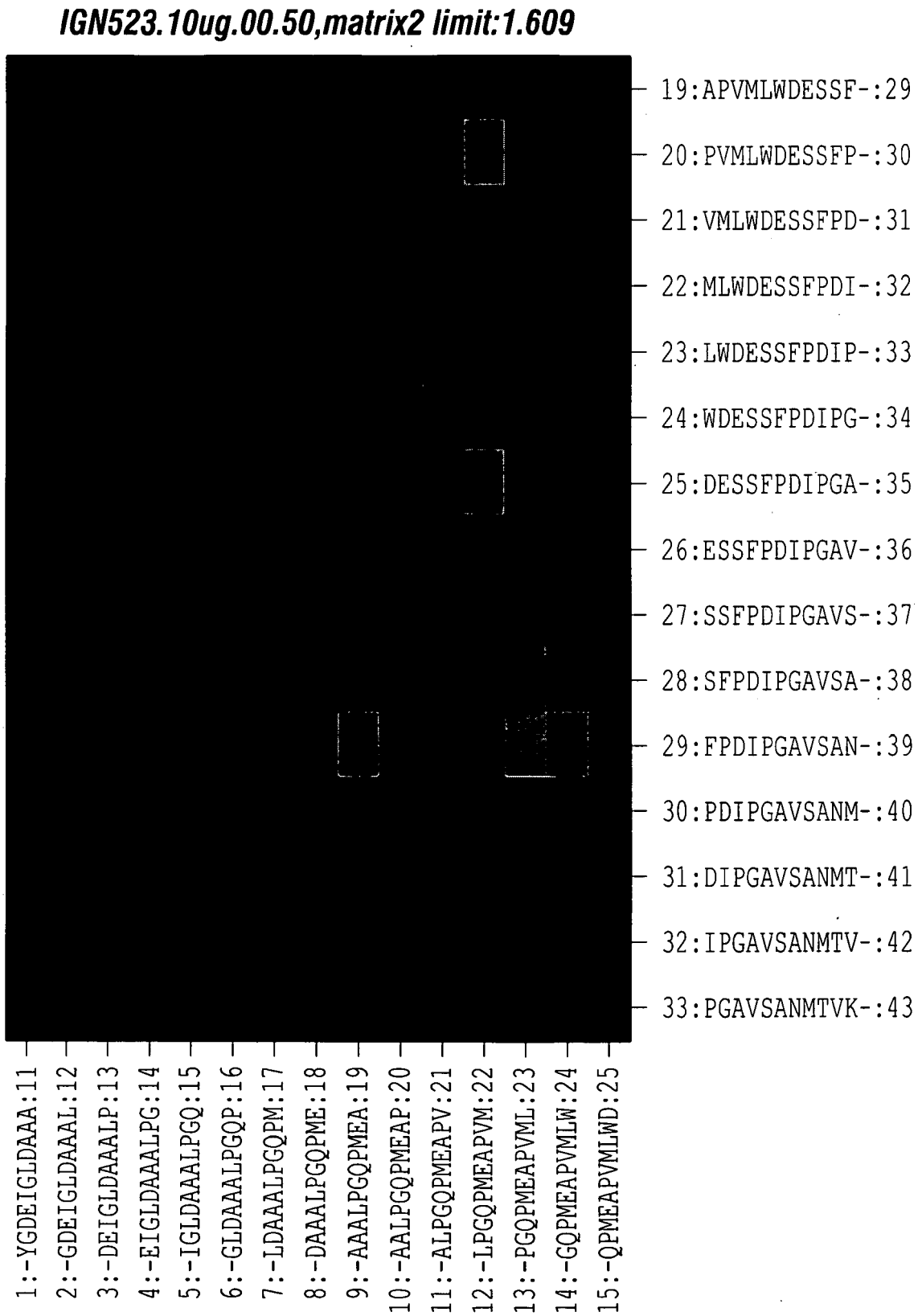

IGN523.10ug.00.50,matrix2 limit:1.609
19:APVMLWDESSF-:29
20:PVMLWDESSFP-:30
21:VMLWDESSFPD-:31
22:MLWDESSFPDI-:32
23:LWDESSFPDIP-:33
24:WDESSFPDIPG-:34
25:DESSFPDIPGA-:35
26:ESSFPDIPGAV-:36
27:SSFPDIPGAVS-:37
28:SFPDIPGAVSA-:38
29:FPDIPGAVSAN-:39
30:PDIPGAVSANM-:40
31:DIPGAVSANMT-:41
32:IPGAVSANMTV-:42
33:PGAVSANMTVK-:43
1:-YGDEIGLDAAA:11
2:-GDEIGLDAAAL:12
3:-DEIGLDAAALP:13
4:-EIGLDAAALPG:14
5:-IGLDAAALPGQ:15
6:-GLDAAALPGQP:16
7:-LDAAALPGQPM:17
8:-DAAALPGQPME:18
9:-AAALPGQPMEA:19
10:-AALPGQPMEAP:20
11:-ALPGQPMEAPV:21
12:-LPGQPMEAPVM:22
13:-PGQPMEAPVML:23
14:-GQPMEAPVMLW:24
15:-QPMEAPVMLWD:25

FIG. 21
(Cont'd)

SEQ1	DIF1	SEQ2	DIF2	DIFF
GLDAAALPAQP	A	WDESSFPAIPG	A	986
GLDAAALAGQP	A	WDESSFPAIPG	A	984
GLDAAALPAQP	A	WDESSFPDIPG		629
GLDAAALPAQP	A	ESSFPDAPGAV	A	448
GLDAAALPAQP	A	ESSFPDIPGAV		404
GLDAAALPGQP	A	WDESSFPDIPG		390
GLDAAALAGQP	A	WDESSFPDAPG	A	363
GLDAAALAAQP	A	PAIPGAVSANM	A	360
GLDAAALAGQP	A	ESSFPDAPGAV	A	346
GLDAAALAGQP	A	ESSFPDIPGAV		342
GLDAAALPGQP		WDESSFPDAPG	A	329
GLDAAALPAQP		PAIPGAVSANM	A	264
GLDAAALPGQP	A	WDESSFPDAPG	A	241
GLDAAALAGQP		ESSFPDAPGAV	A	218
GLDAAALPGQP	A	ESSFPAIPGAV	A	214
GLDAAALPAQP	A	ESSFPDIPGAV	G	200
GLDAAALPGQP		WDESSFPAIPG	A	172
GLDAAALPAQP	A	ESSFPAIPGAV	A	163
GLDAAALAGQP	A	SFPDAPGAVSA	A	152
GLDAAALAGQP	A	PDIPGAVSANM		85
GLDAAALPAQP	A	IPGAVSANMTV		40
GLDAAALAGQP	A	PAIPGAVSANM	A	39
GLDAAGLPGQP	G	PAIPGAVSANM	A	0

SEQ1	DIF1	SEQ2	DIF2	EXP_15469.2
EIGLDAAALAG	A	SFPDIPGAVSA		958
LPAQPMEAPVM	A	SFPAIPGAVSA	A	645
LAGQPMEAPVM	A	SFPAIPGAVSA	A	639
LPAQPMEAPVM	A	PAIPGAVSANM	A	615
EIGLDAAGLPG	G	SFPDIPGAVSA		592
AALPAQPMEAP	A	PAIPGAVSANM	A	560
LPAQPMEAPVM	A	SFPDAPGAVSA	A	508
AALPGQPMEAP		PAIPGAVSANM	A	469
LAGQPMEAPVM	A	PAIPGAVSANM	A	468
DAAALPAQPME	A	PAIPGAVSANM	A	454
LPGQPMEAPVM		SFPAIPGAVSA	A	440
DAAALPAQPME	A	PDAPGAVSANM	A	405
GLDAAALPAQP	A	PAIPGAVSANM	A	360
LPGQPMEAPVM		PAIPGAVSANM	A	345
DAAALPGQPME		PAIPGAVSANM	A	322
LPAQPMEAPVM	A	SFPDIPGAVSA		316
LAGQPMEAPVM	A	SFPDAPGAVSA	A	303
LAGQPMEAPVM	A	PDAPGAVSANM	A	299
EIGLDAAALPA	A	SFPAIPGAVSA	A	282
EIGLDAAALPG		SFPDAPGAVSA	A	277
EIGLDAAALAG	A	SFPAIPGAVSA	A	270
GLDAAALPGQP		PAIPGAVSANM	A	264

FIG. 22

TLPGTPVFSYGDEIGLDAAALPGQPMEAPVMLWDESSFPDIPGAVSAN

FIG. 23A

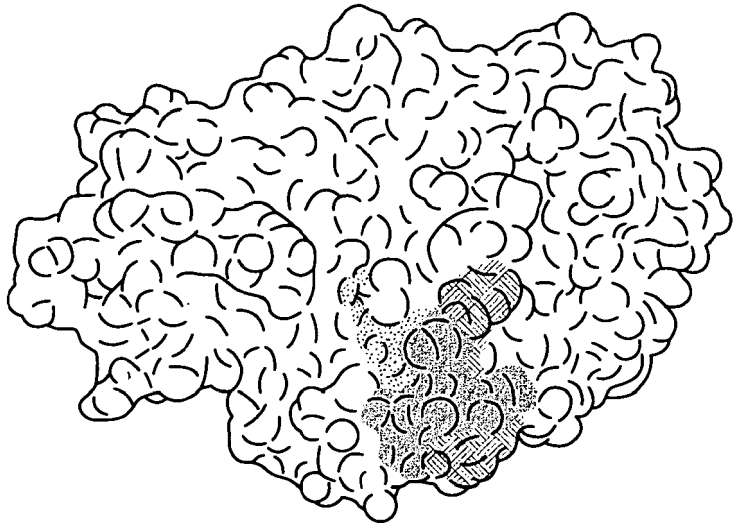


FIG. 23D

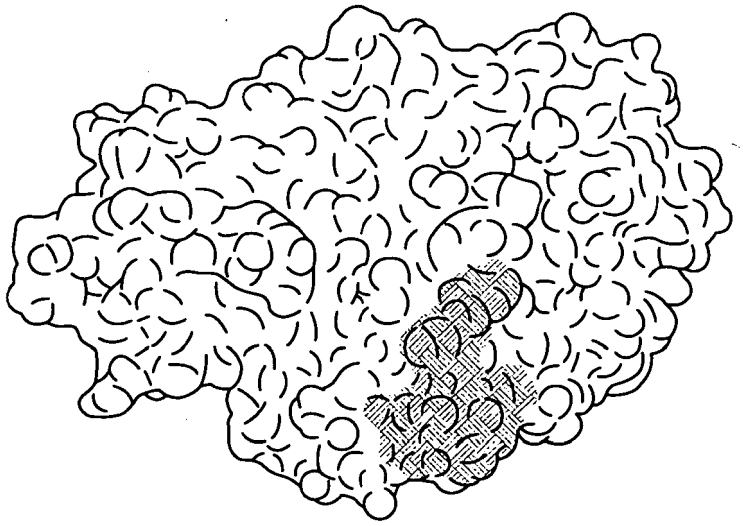


FIG. 23C

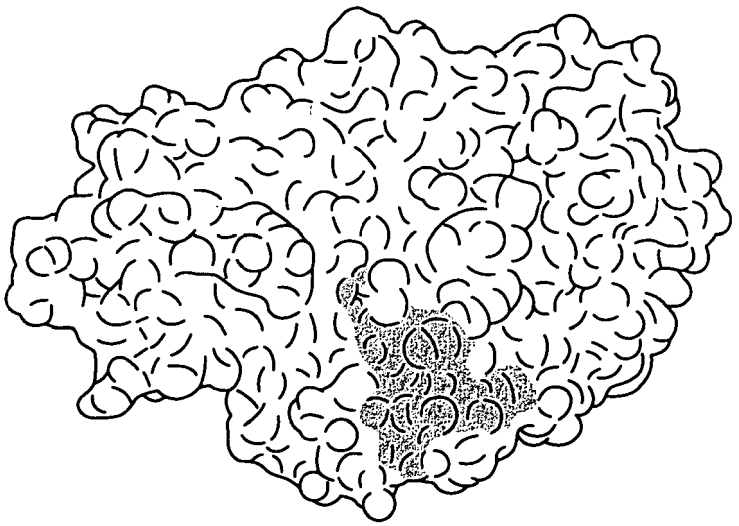


FIG. 23B

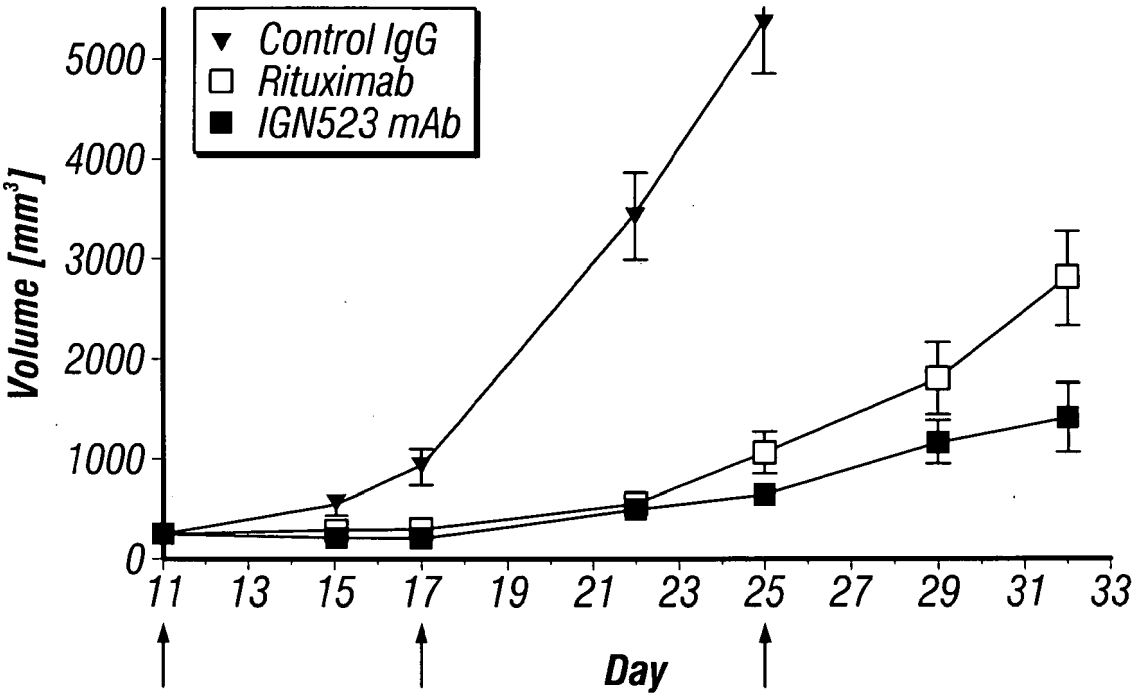

Control IgG
Rituximab
IGN523 mAb
Volume [mm³]
5000
4000
3000
2000
1000
0
11
13
15
17
19
21
23
25
27
29
31
33
Day

FIG. 24

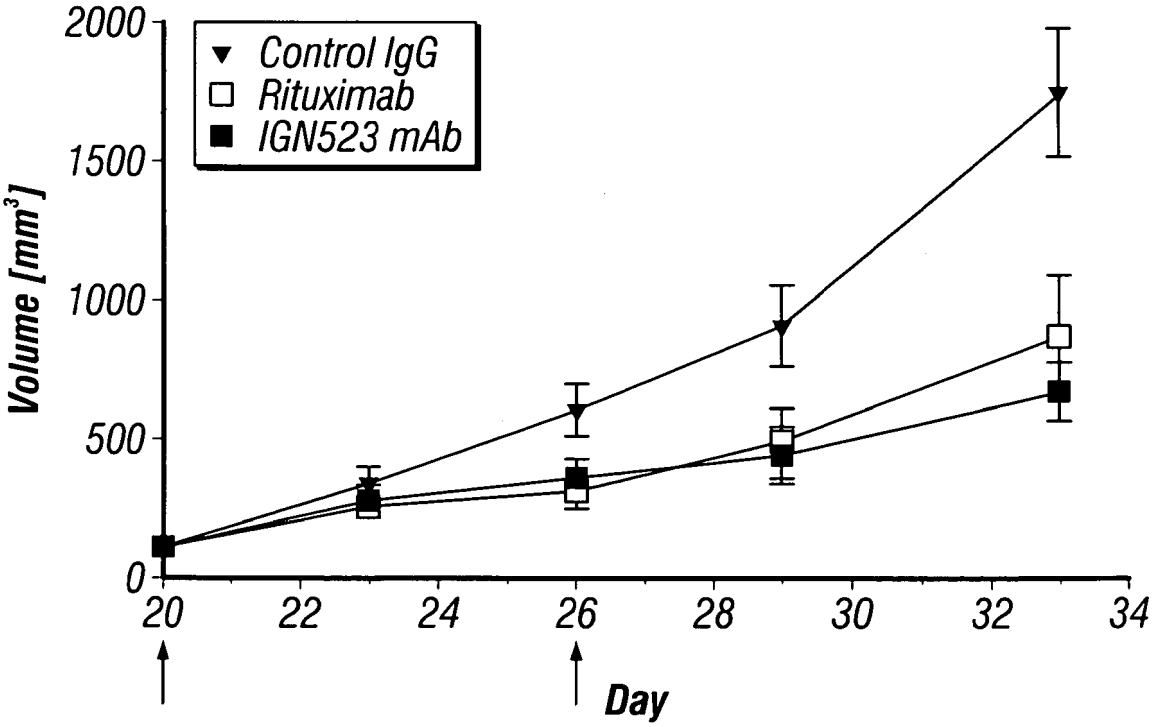

Control IgG
Rituximab
IGN523 mAb
Volume [mm³]
2000
1500
1000
500
0
20
22
24
26
28
30
32
34
Day

FIG. 25

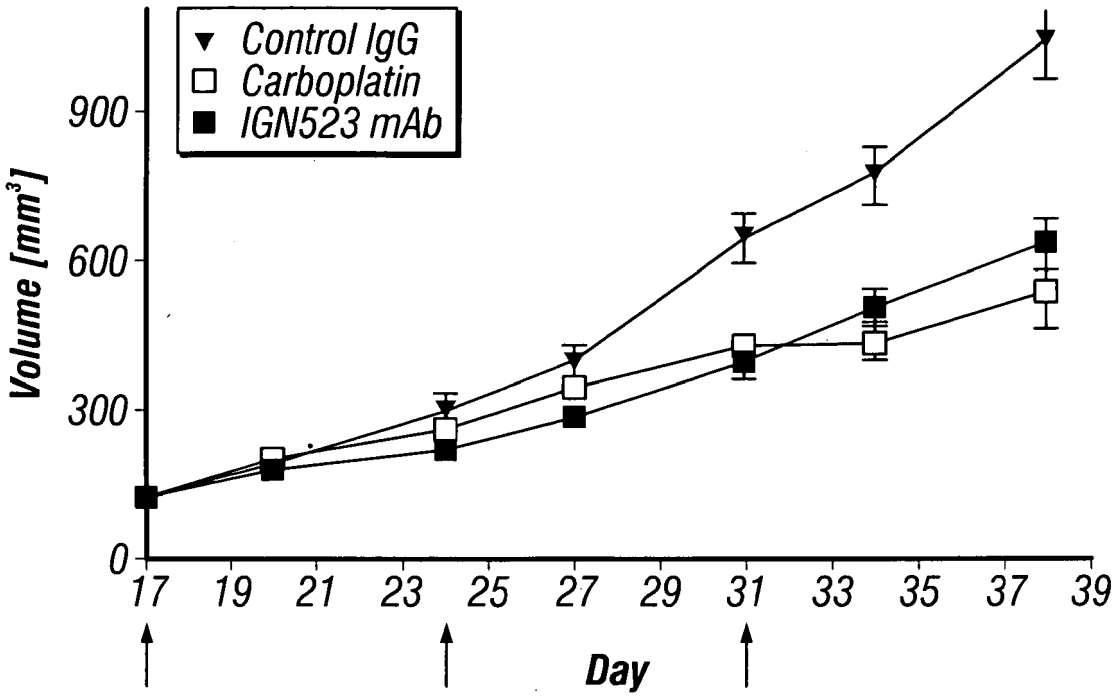


FIG. 26A

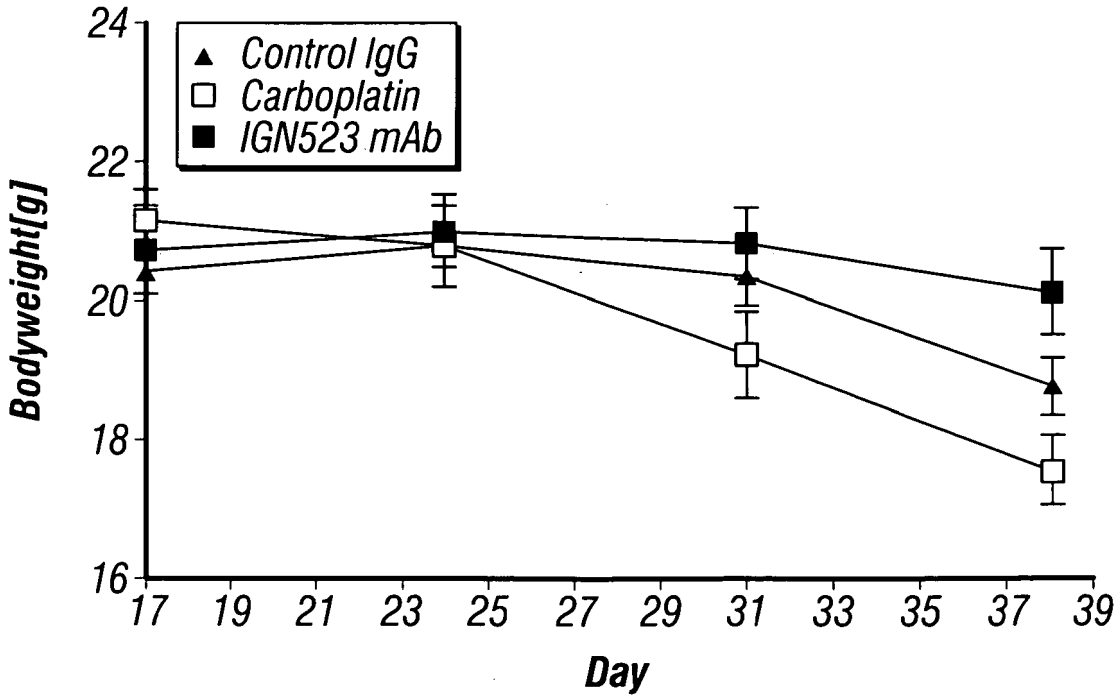


FIG. 26B

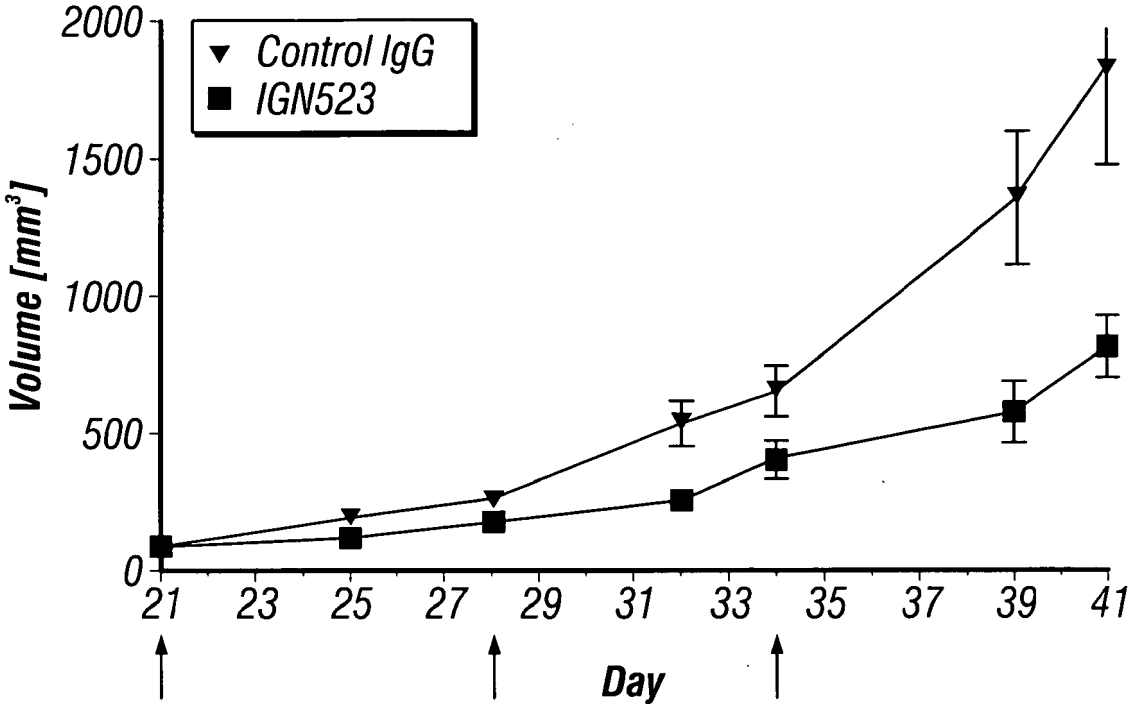

2000
1500
1000
500
0
Volume [mm³]
Control IgG
IGN523
21
23
25
27
29
31
33
35
37
39
41
Day

FIG. 27

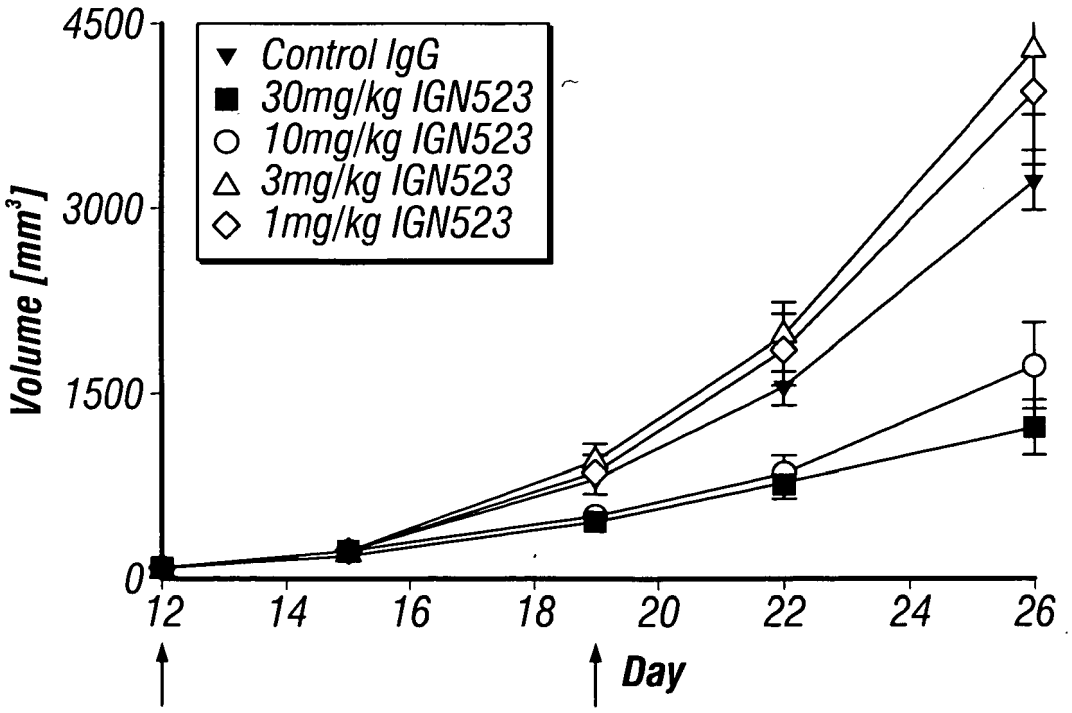

4500
3000
1500
0
Volume [mm³]
Control IgG
30mg/kg IGN523
10mg/kg IGN523
3mg/kg IGN523
1mg/kg IGN523
12
14
16
18
20
22
24
26
Day

FIG. 28

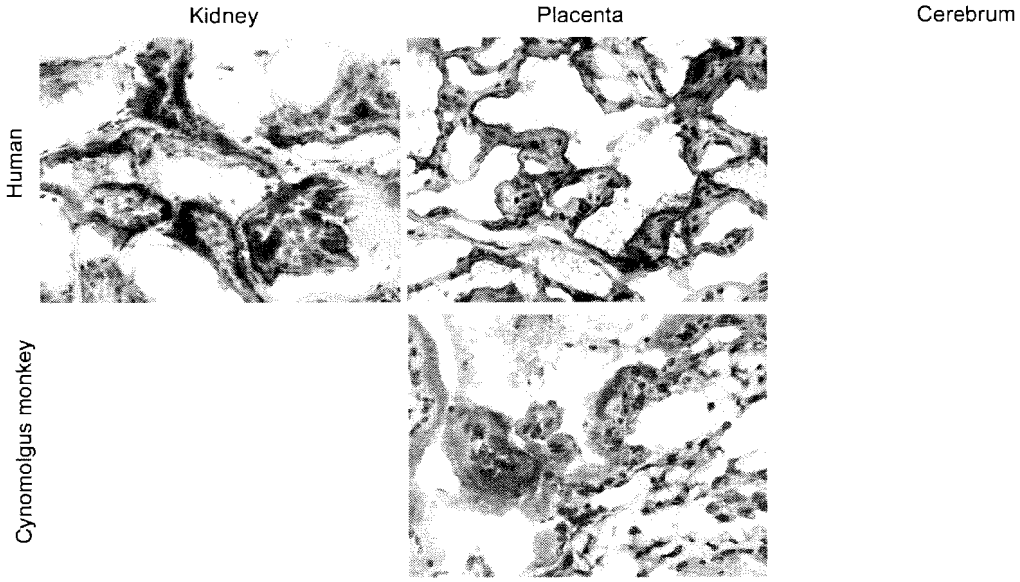


Fig. 29