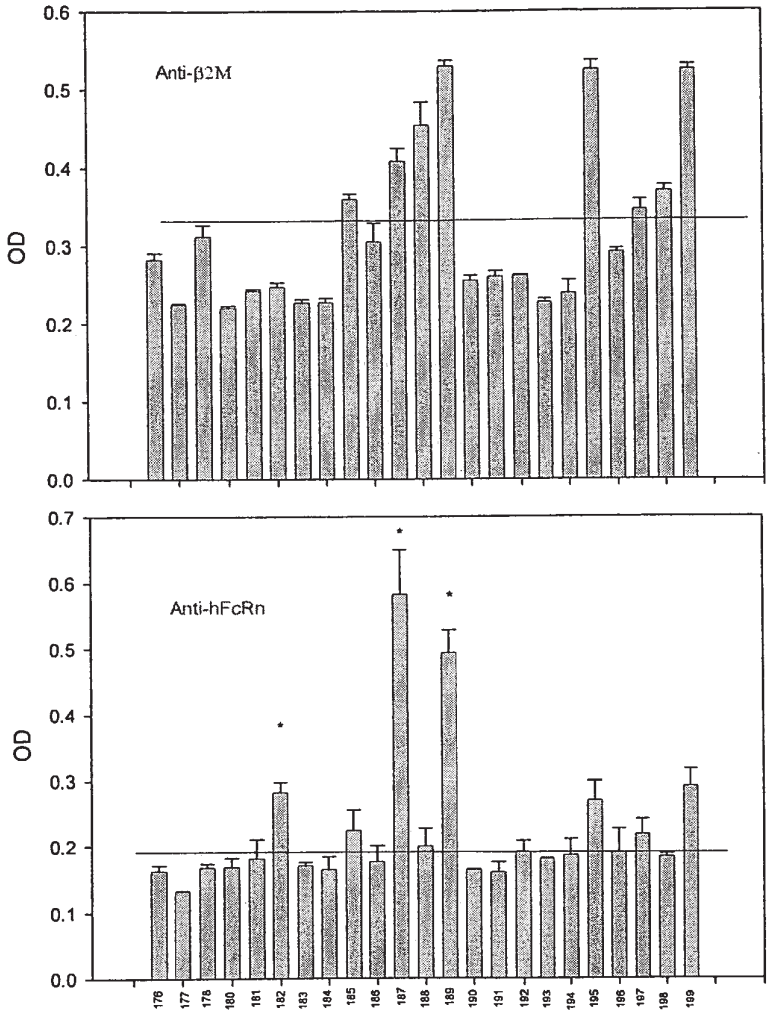

Anti-β2M
OD
0.0
0.1
0.2
0.3
0.4
0.5
0.6
Anti-hFcRn
OD
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
176
177
178
180
181
182
183
184
185
186
187
188
189
190
191
192
193
194
195
196
197
198
199

Figure 1

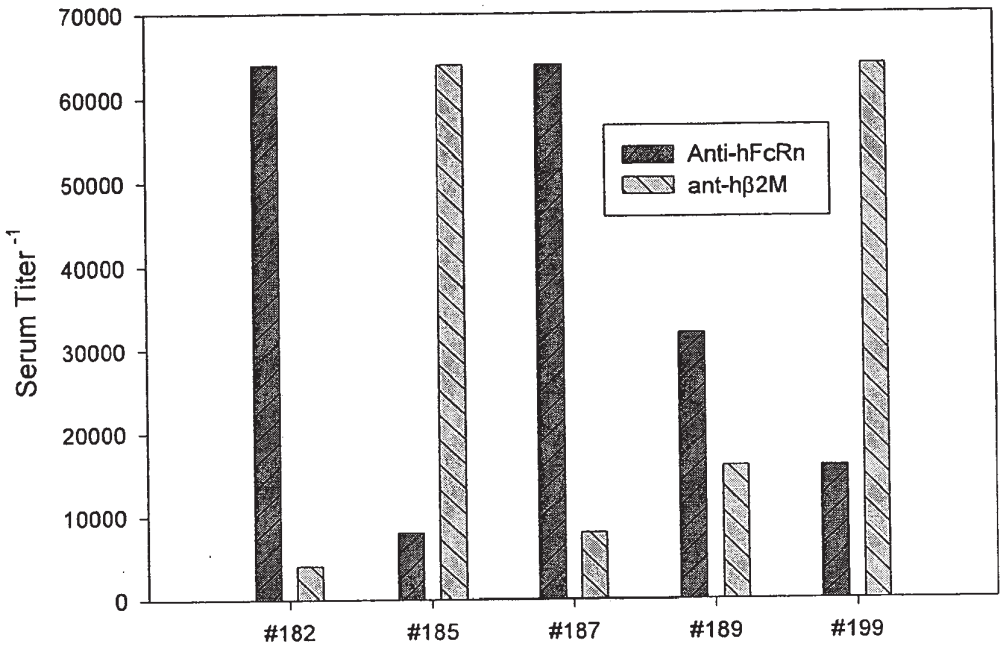

70000
60000
50000
40000
30000
20000
10000
0
Serum Titer-1
Anti-hFcRn
ant-hβ2M
#182
#185
#187
#189
#199

Figure 2

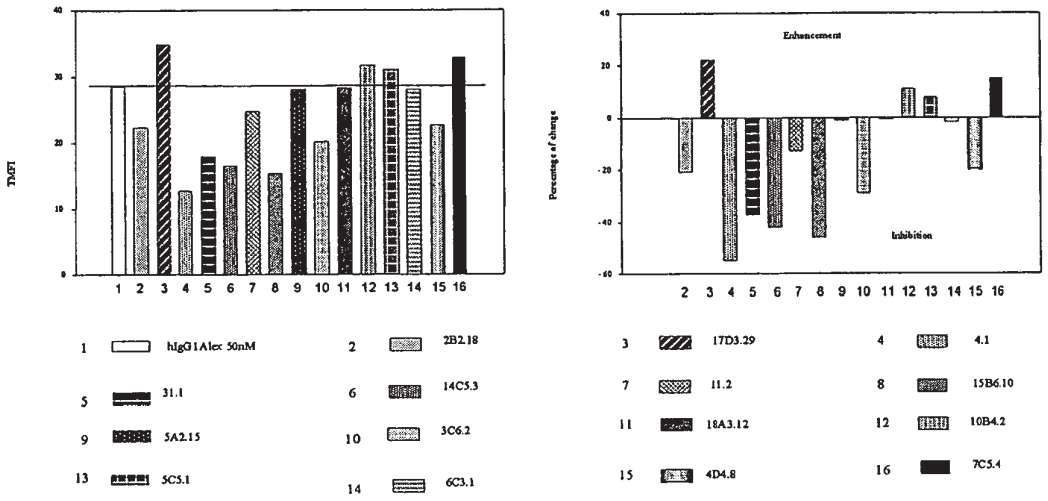

MFI
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
1 hIgG1Alex 50nM
2 2B2.18
3 17D3.29
4 4.1
5 31.1
6 14C5.3
7 11.2
8 15B6.10
9 5A2.15
10 3C6.2
11 18A3.12
12 10B4.2
13 5C5.1
14 6C3.1
15 4D4.8
16 7C5.4
Percentage of change
Enhancement
Inhibition
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16

Figure 3A

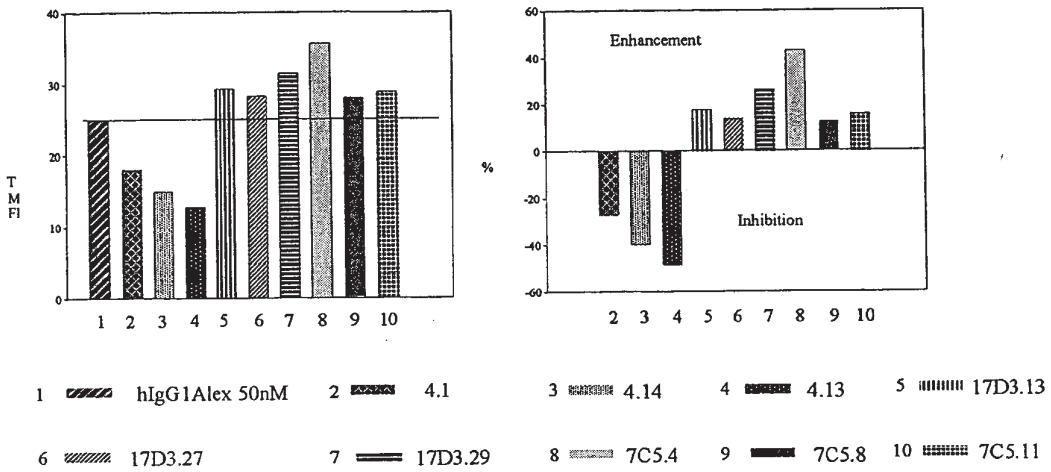
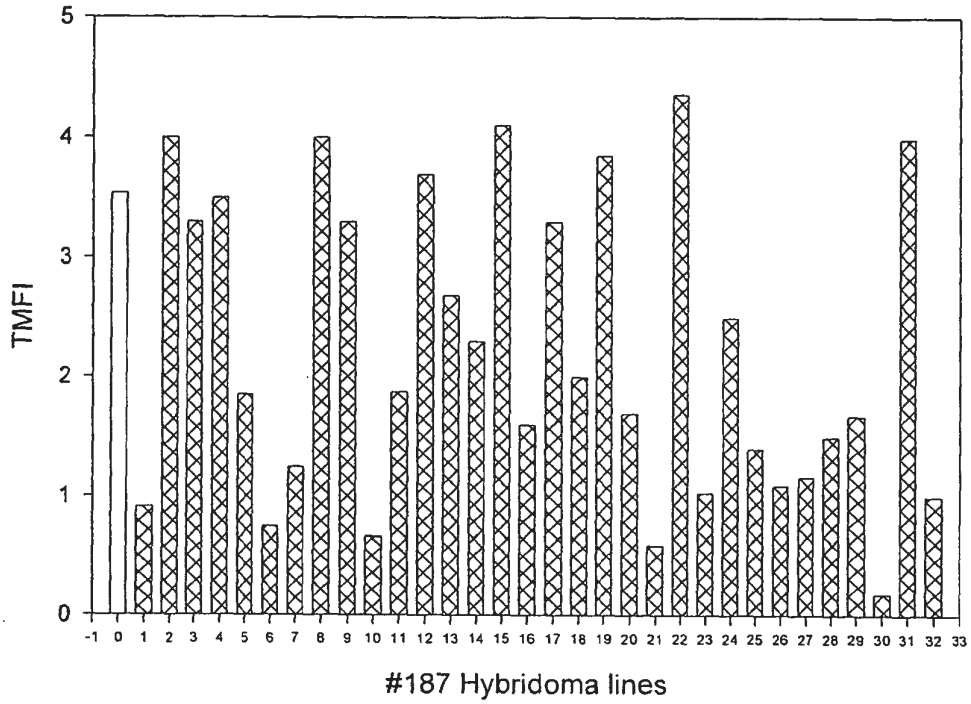

MFI
%
Enhancement
Inhibition
1 hIgG1Alex 50nM
2 4.1
3 4.14
4 4.13
5 17D3.13
6 17D3.27
7 17D3.29
8 7C5.4
9 7C5.8
10 7C5.11

Figure 3B



0: TMFI of the tube containing Alexa fluor 488 labeled hIgG1 alone.

1: TMFI of positive control 15B6.1 (anti-hFcRn blocking mAB from #182 fusion

2-4, 6-7, 9, 12-13, 15-17, 19-20, 22-28, 31-32: anti-hFcRn mAB sups.

5, 8, 10, 11, 14, 18, 21, 29 and 30: anti-human β-2M mAB sups.

Figure 4A

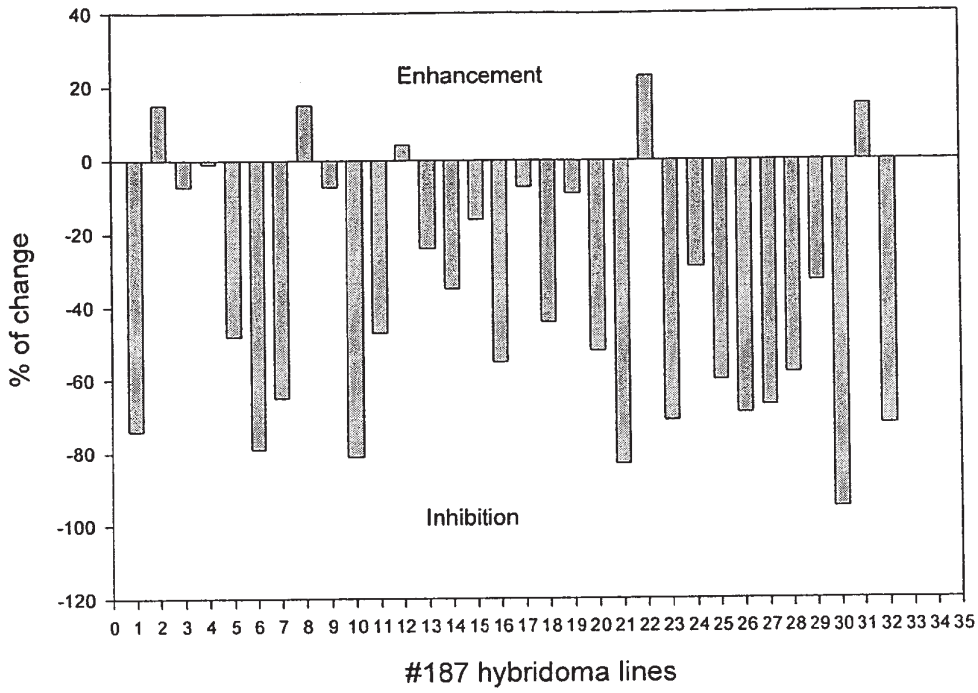

Enhancement
Inhibition
% of change
#187 hybridoma lines
40
20
0
-20
-40
-60
-80
-100
-120
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35

Figure 4B

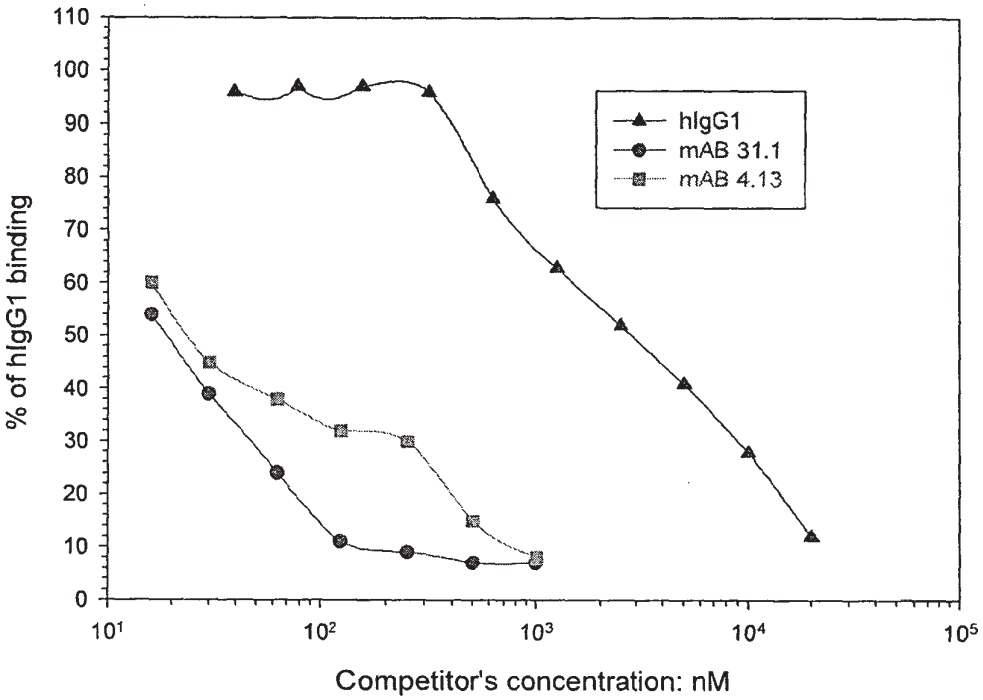

110
100
90
80
70
60
50
40
30
20
10
0
% of hIgG1 binding
10¹
10²
10³
10⁴
10⁵
Competitor's concentration: nM
hIgG1
mAB 31.1
mAB 4.13

Figure 5A

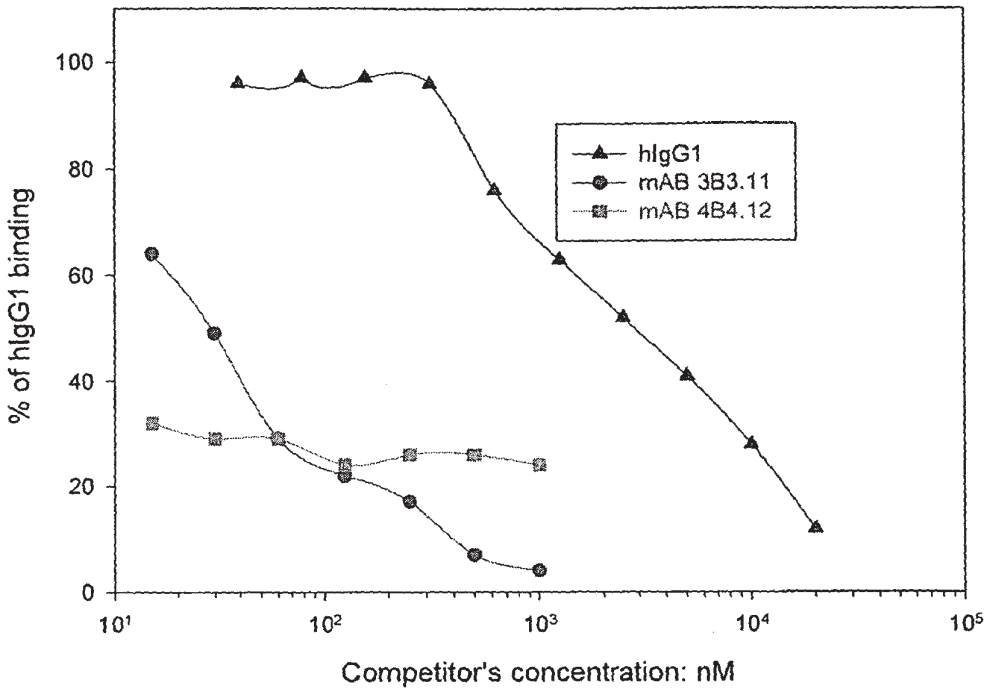
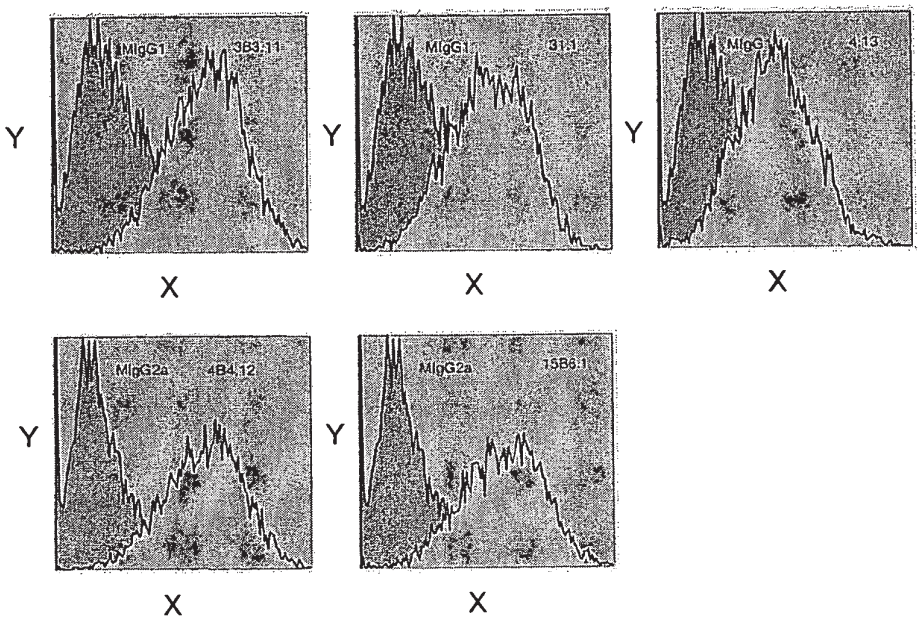

100
80
60
40
20
0
% of hIgG1 binding
10¹
10²
10³
10⁴
10⁵
Competitor's concentration: nM
hIgG1
mAB 3B3.11
mAB 4B4.12

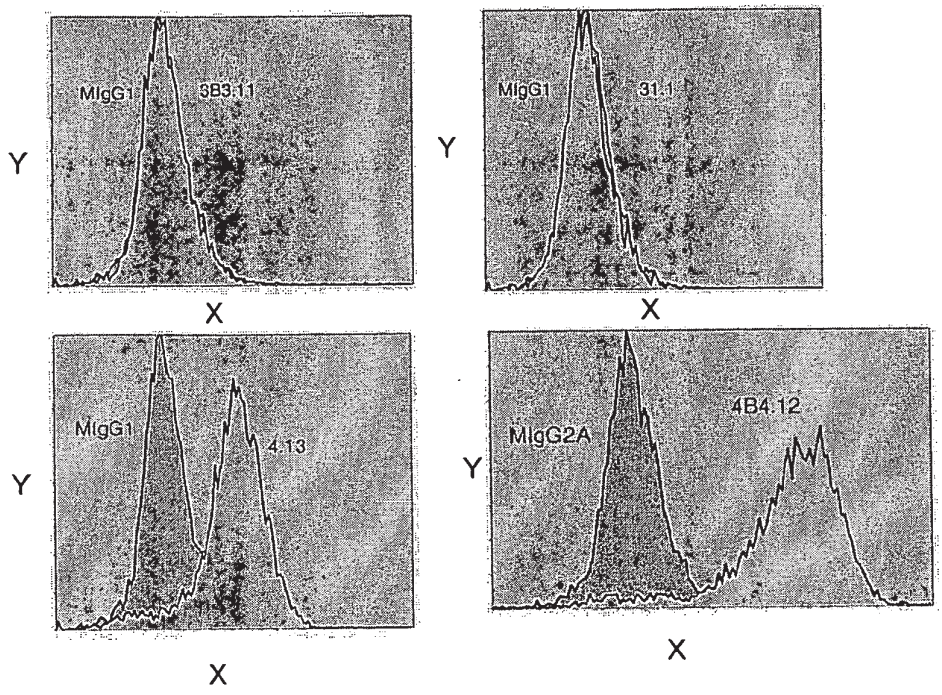
Figure 5B



X is fluorescent intensity

Y is cell number

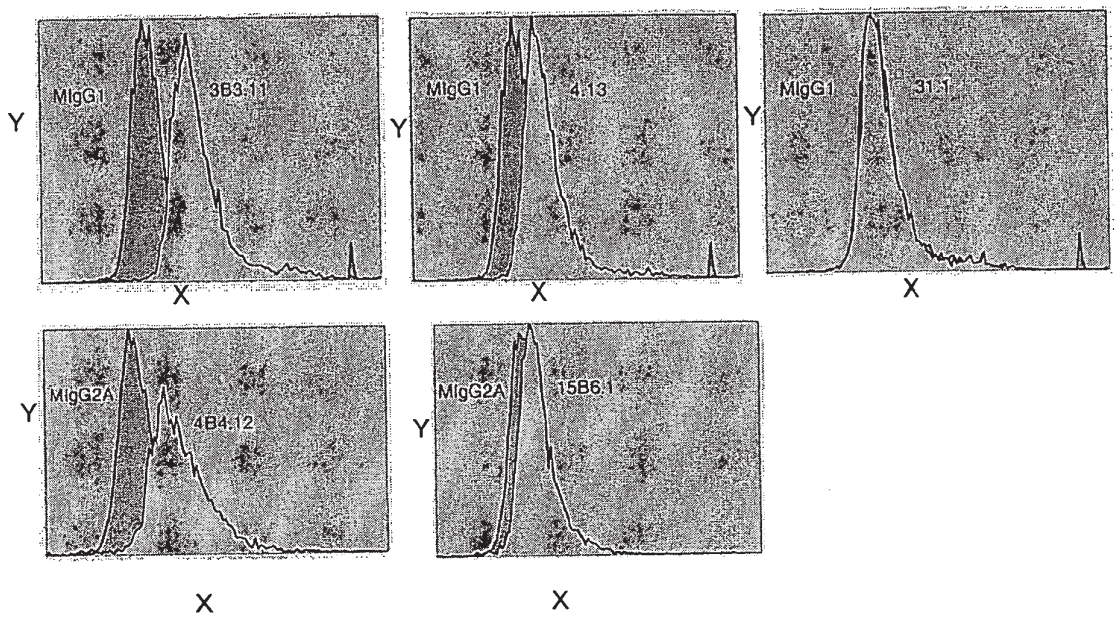
Figure 6



X is fluorescent intensity

Y is cell number

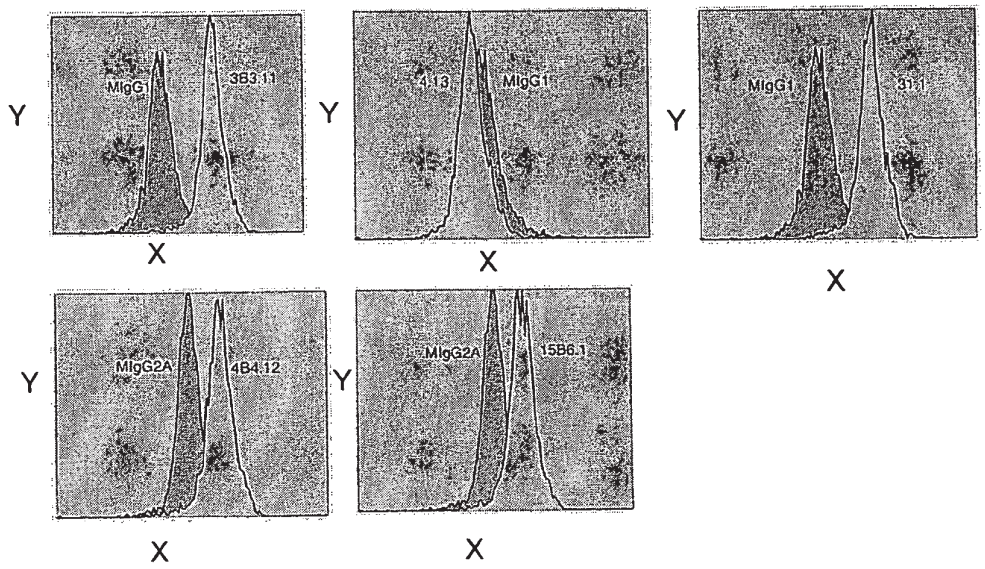
Figure 7



X is fluorescent intensity

Y is cell number

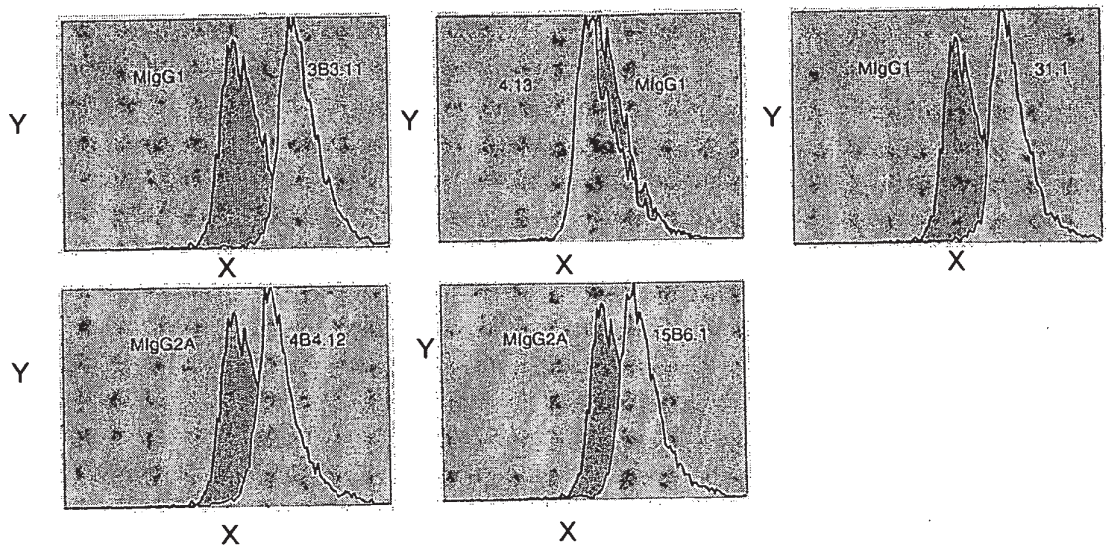
Figure 8



X is fluorescent intensity

Y is cell number

Figure 9



X is fluorescent intensity

Y is cell number

Figure 10

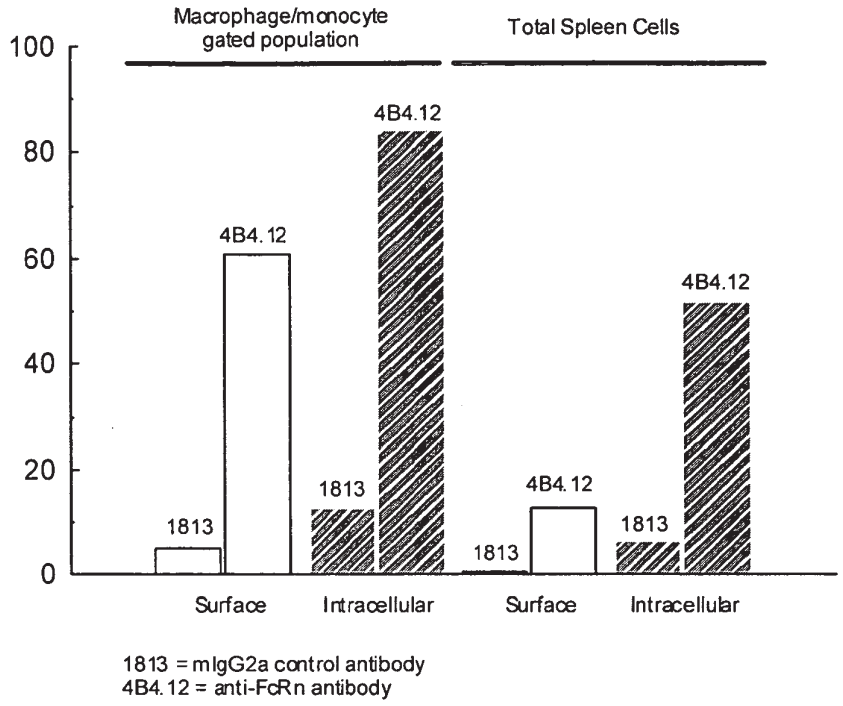


Figure 11A

Figure 11B

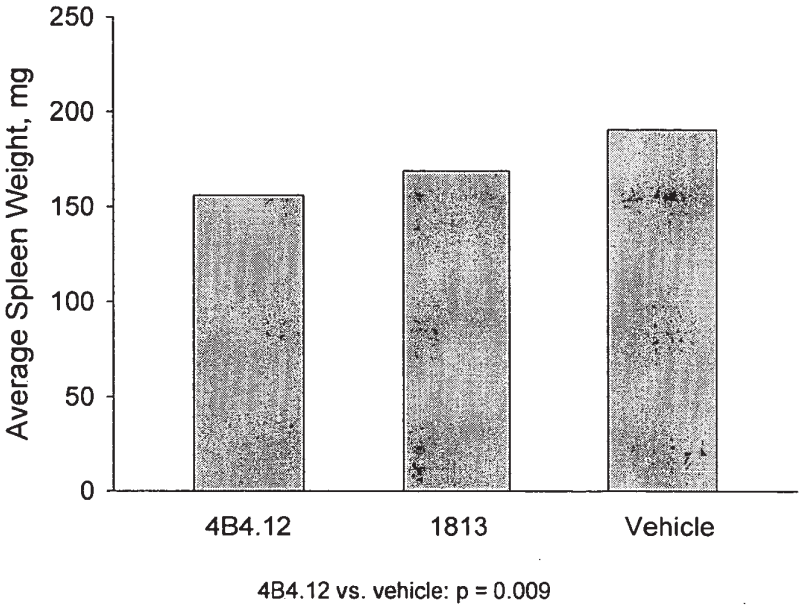


Figure 12A

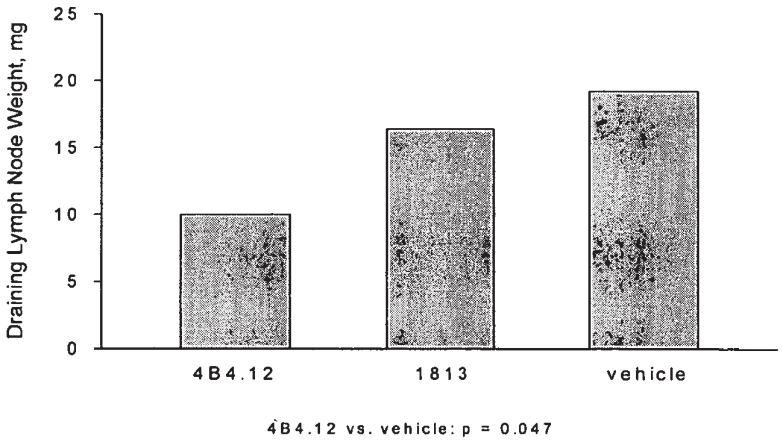
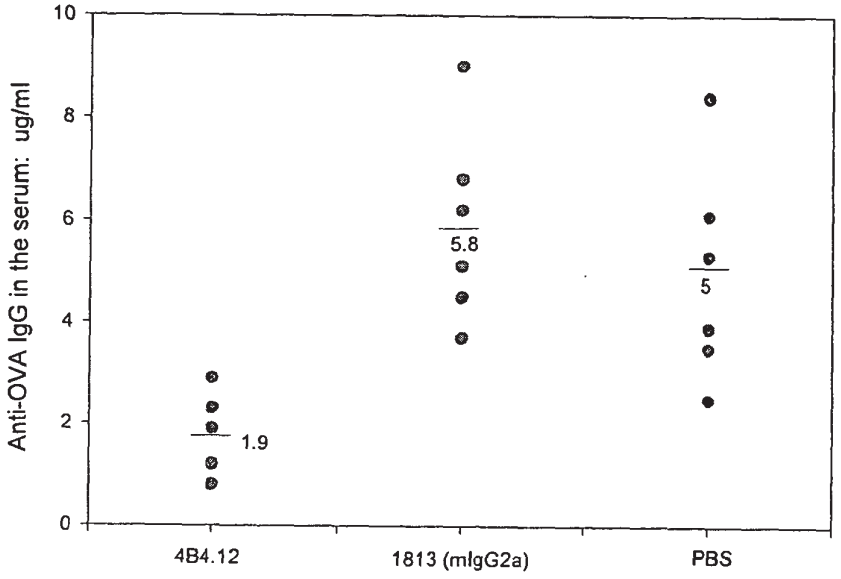


Figure 12B



4B4.12 V 1813: p= 0.0008
4B4.12 V PBS: p= 0.008
1813 V PBS: p= 0.4

Figure 13

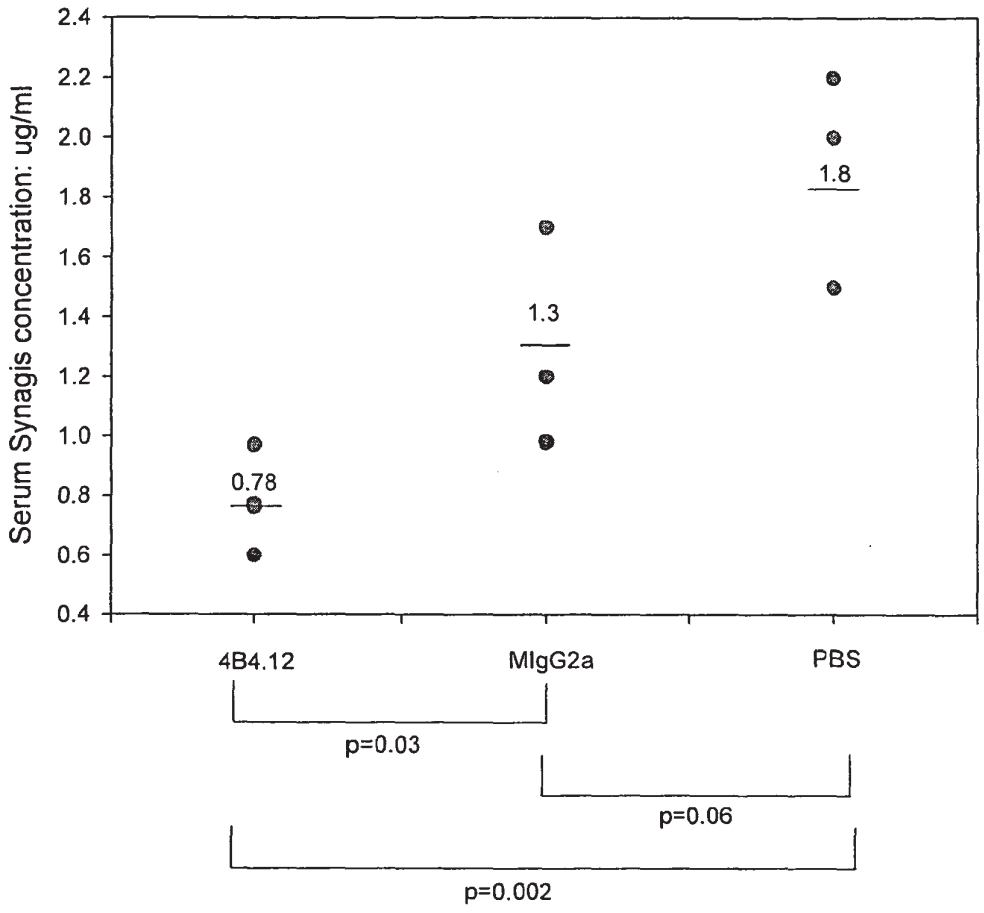

Serum Synagis concentration: ug/ml
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.78
1.3
1.8
4B4.12
MIgG2a
PBS
p=0.03
p=0.06
p=0.002

Figure 14

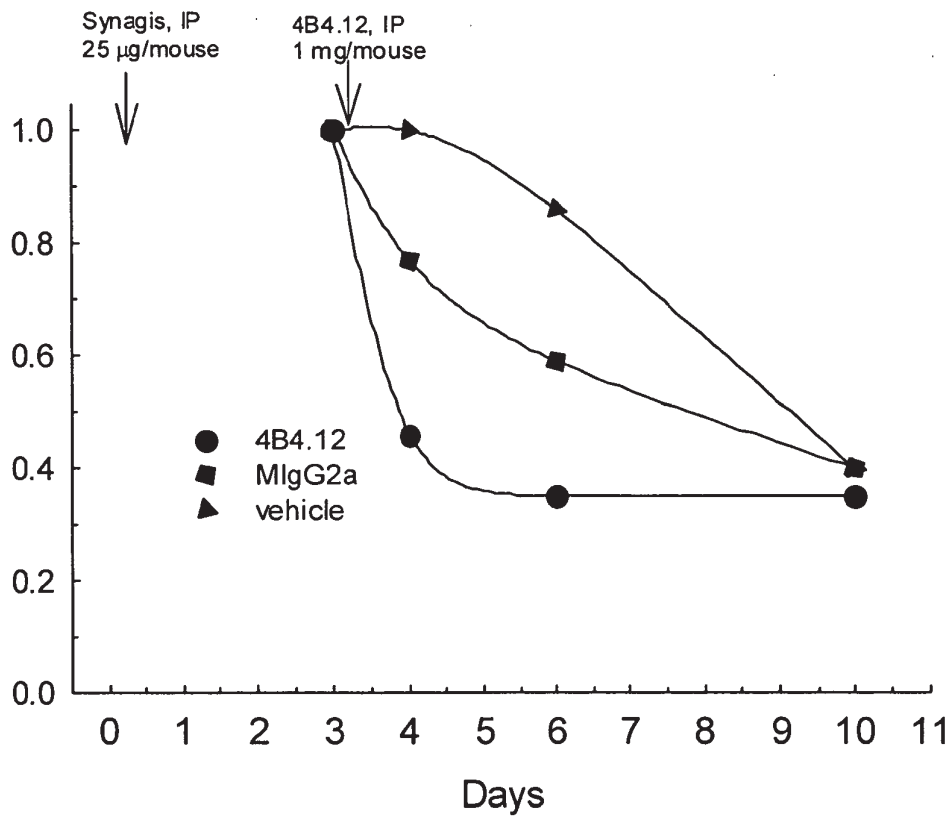
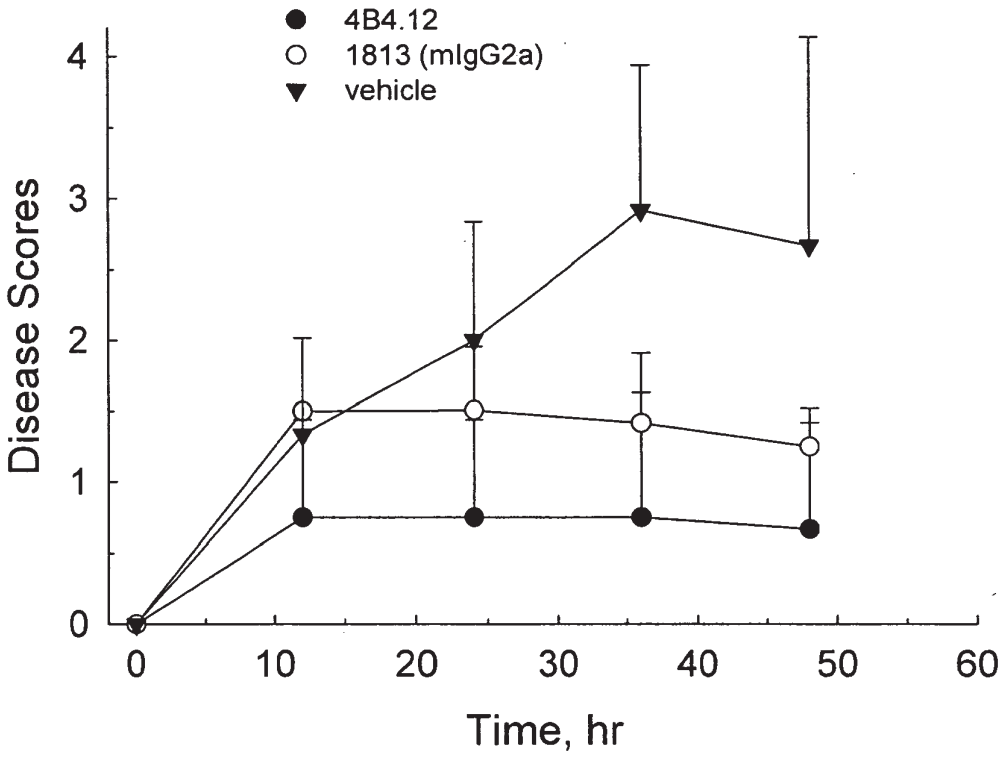

Synagis, IP
25 µg/mouse
4B4.12, IP
1 mg/mouse
1.0
0.8
0.6
0.4
0.2
0.0
4B4.12
MIgG2a
vehicle
0 1 2 3 4 5 6 7 8 9 10 11
Days

Figure 15



Student's T test:
4B4.12 vs. 1813: p = 0.00001
4B4.12 vs. vehicle: p = 0.006
1813 vs. vehicle: p = 0.07

Figure 16

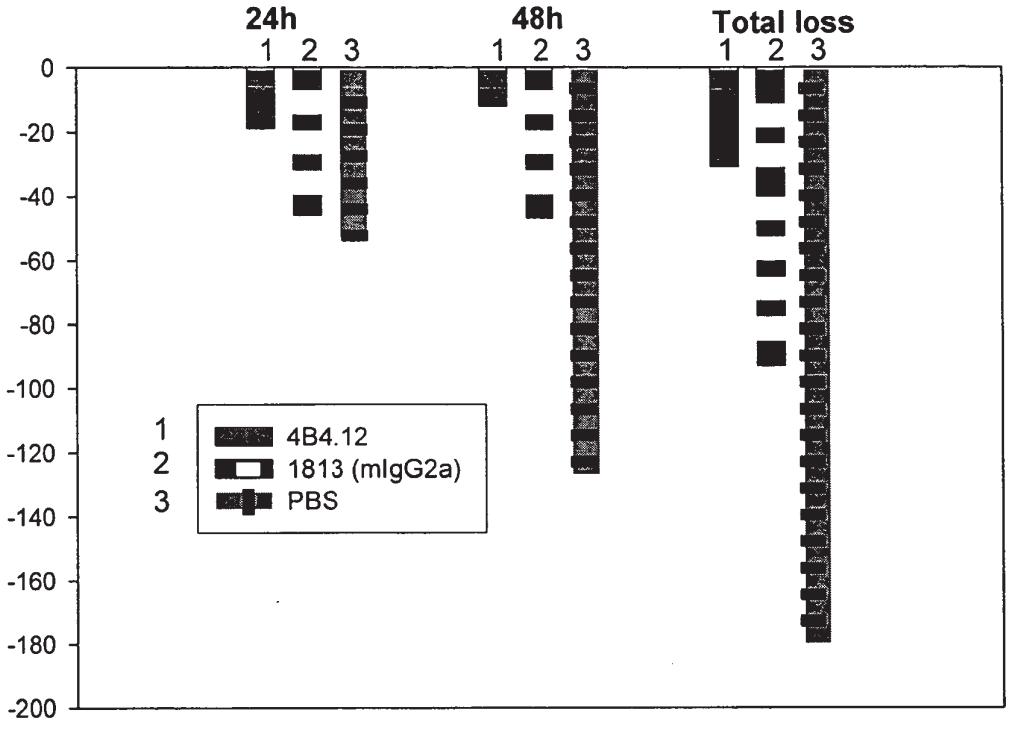
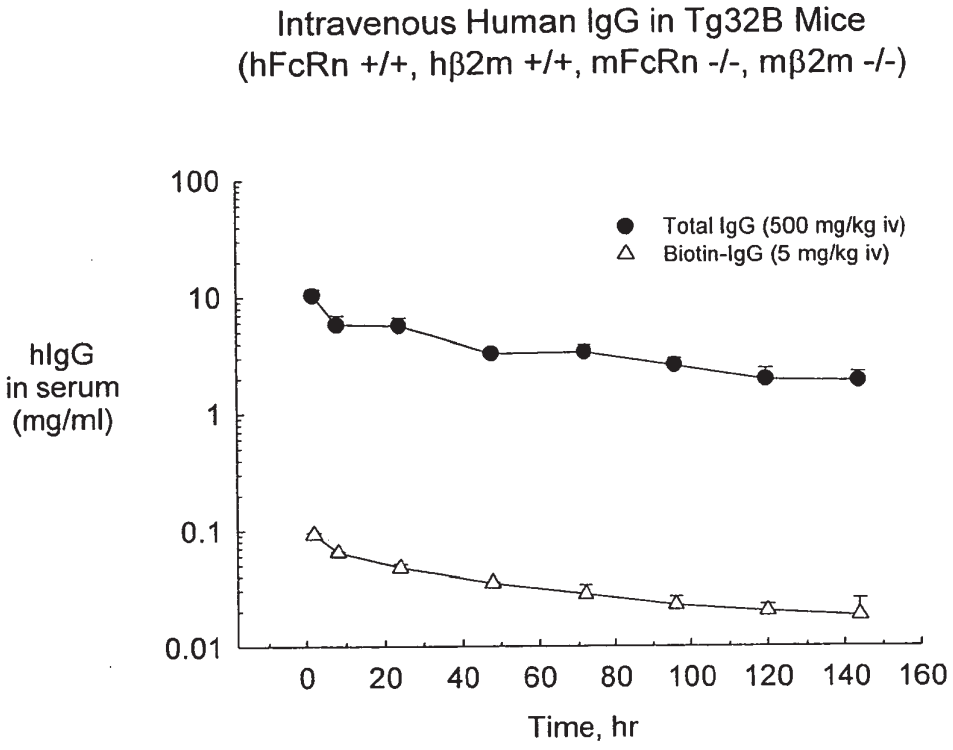

24h
48h
Total loss
1 2 3
1 2 3
1 2 3
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
1
2
3
4B4.12
1813 (mIgG2a)
PBS

Figure 17



	$t_{1/2}$ (hr)	Cmax (mg/ml)	AUC (hr*mg/ml)
Total IgG	78	10.41	739
Biotin IgG	87	0.093	7.19

Figure 18

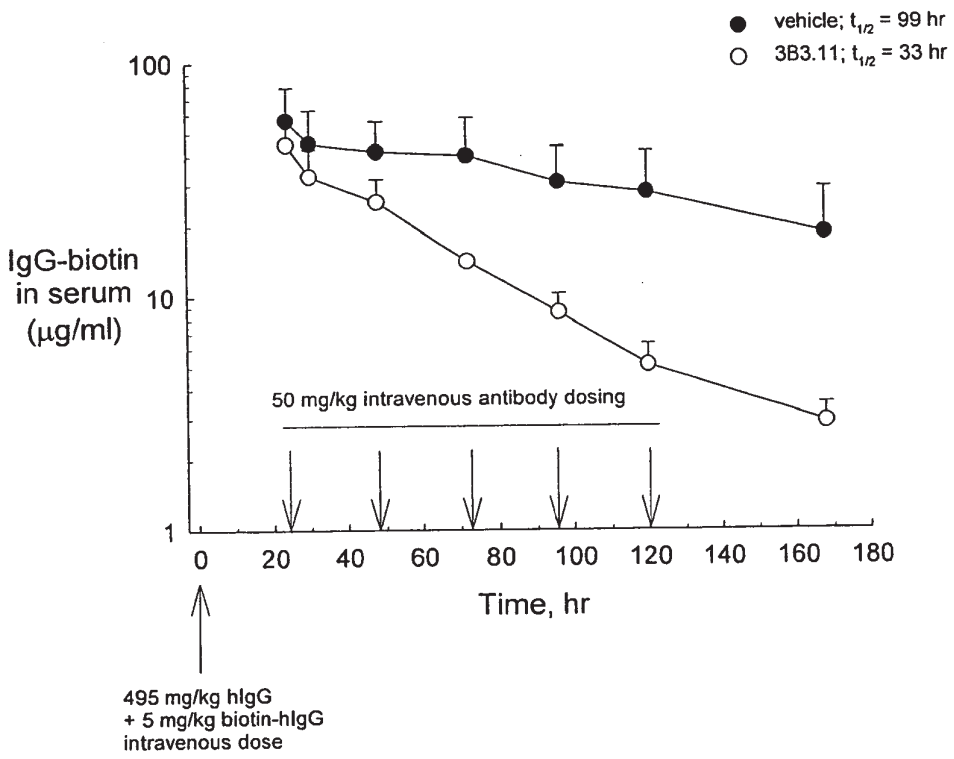

vehicle; $t_{1/2}$ = 99 hr
3B3.11; $t_{1/2}$ = 33 hr
100
10
1
IgG-biotin in serum (μg/ml)
50 mg/kg intravenous antibody dosing
0
20
40
60
80
100
120
140
160
180
Time, hr
495 mg/kg hIgG
+ 5 mg/kg biotin-hIgG
intravenous dose

Figure 19

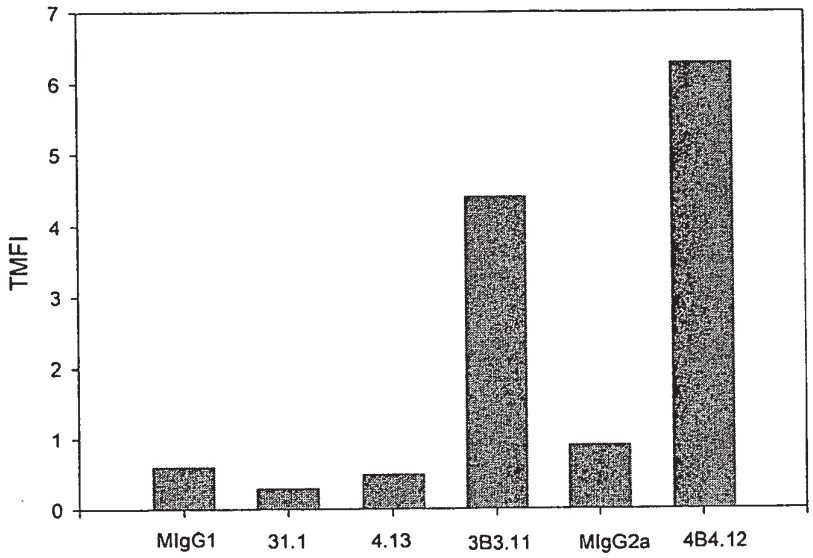


Figure 20

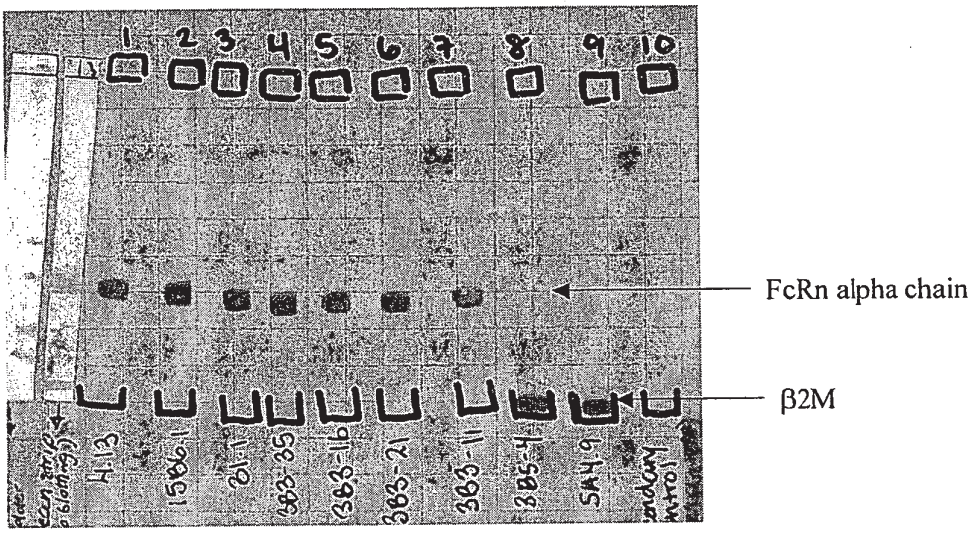

1 2 3 4 5 6 7 8 9 10
FcRn alpha chain
β2M
4.13
1566-1
01-1
383-35
383-16
383-21
383-11
385-4
SA4-9

Figure 21

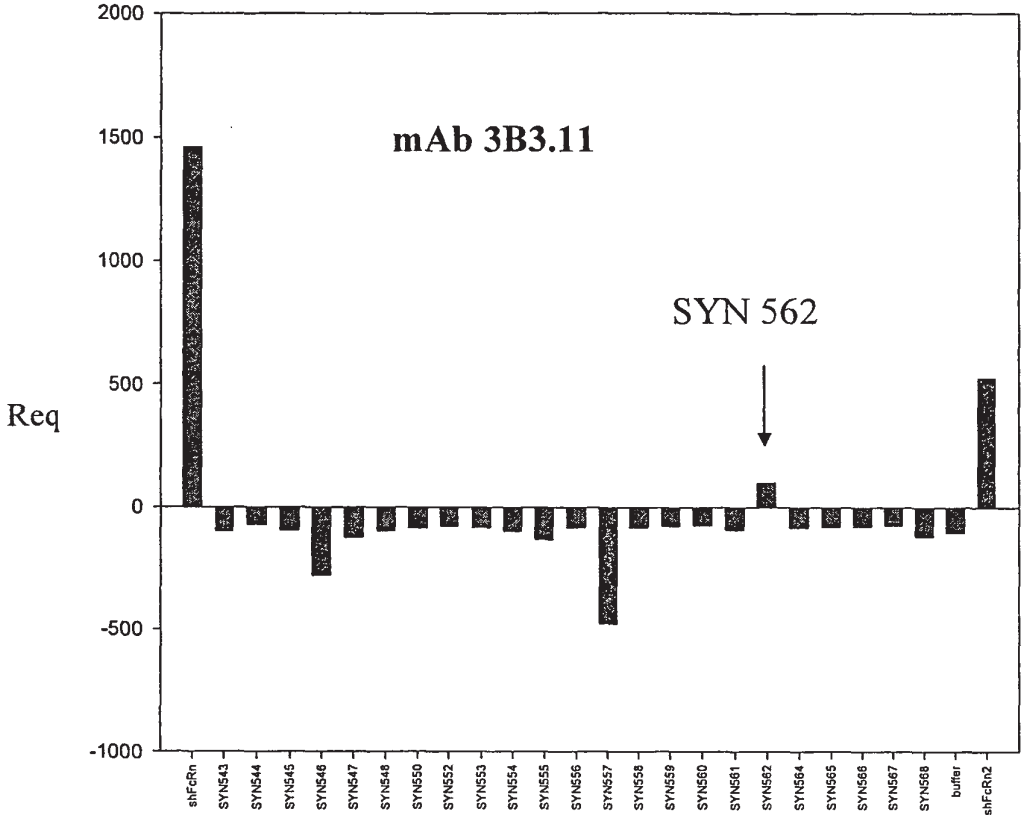

mAb 3B3.11
SYN 562
Req
2000
1500
1000
500
0
-500
-1000
shFcRn
SYN543
SYN544
SYN545
SYN546
SYN547
SYN548
SYN550
SYN552
SYN553
SYN554
SYN555
SYN556
SYN557
SYN558
SYN559
SYN560
SYN561
SYN562
SYN564
SYN565
SYN566
SYN567
SYN568
buffer
shFcRn2

Figure 22A

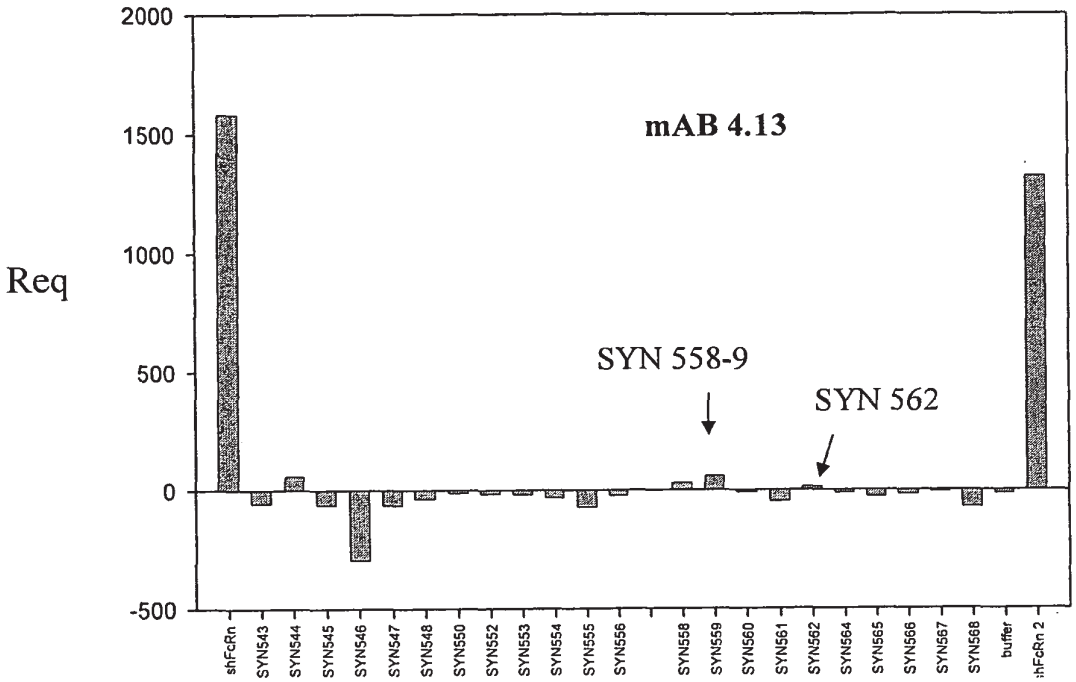

Req
2000
1500
1000
500
0
-500
mAB 4.13
SYN 558-9
SYN 562
shFcRn
SYN543
SYN544
SYN545
SYN546
SYN547
SYN548
SYN550
SYN552
SYN553
SYN554
SYN555
SYN556
SYN558
SYN559
SYN560
SYN561
SYN562
SYN564
SYN565
SYN566
SYN567
SYN568
buffer
shFcRn 2

Figure 22B

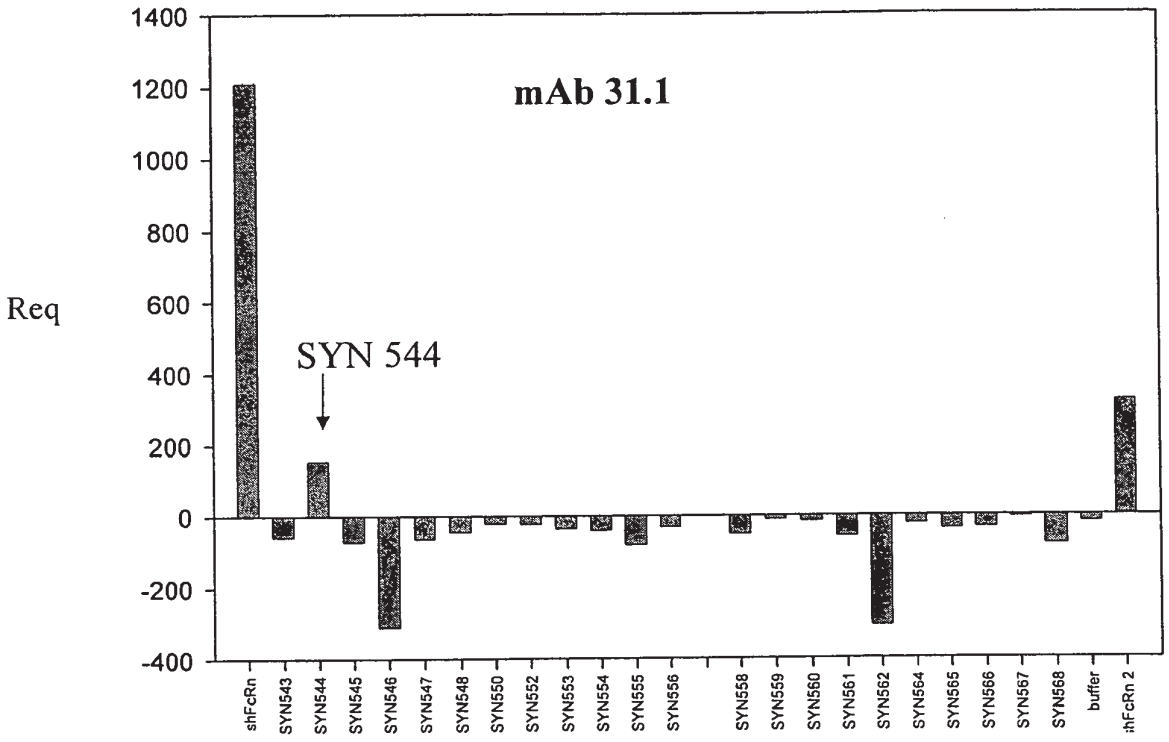

Req
1400
1200
1000
800
600
400
200
0
-200
-400
mAb 31.1
SYN 544
shFcRn
SYN543
SYN544
SYN545
SYN546
SYN547
SYN548
SYN550
SYN552
SYN553
SYN554
SYN555
SYN556
SYN558
SYN559
SYN560
SYN561
SYN562
SYN564
SYN565
SYN566
SYN567
SYN568
buffer
shFcRn 2

Figure 22C

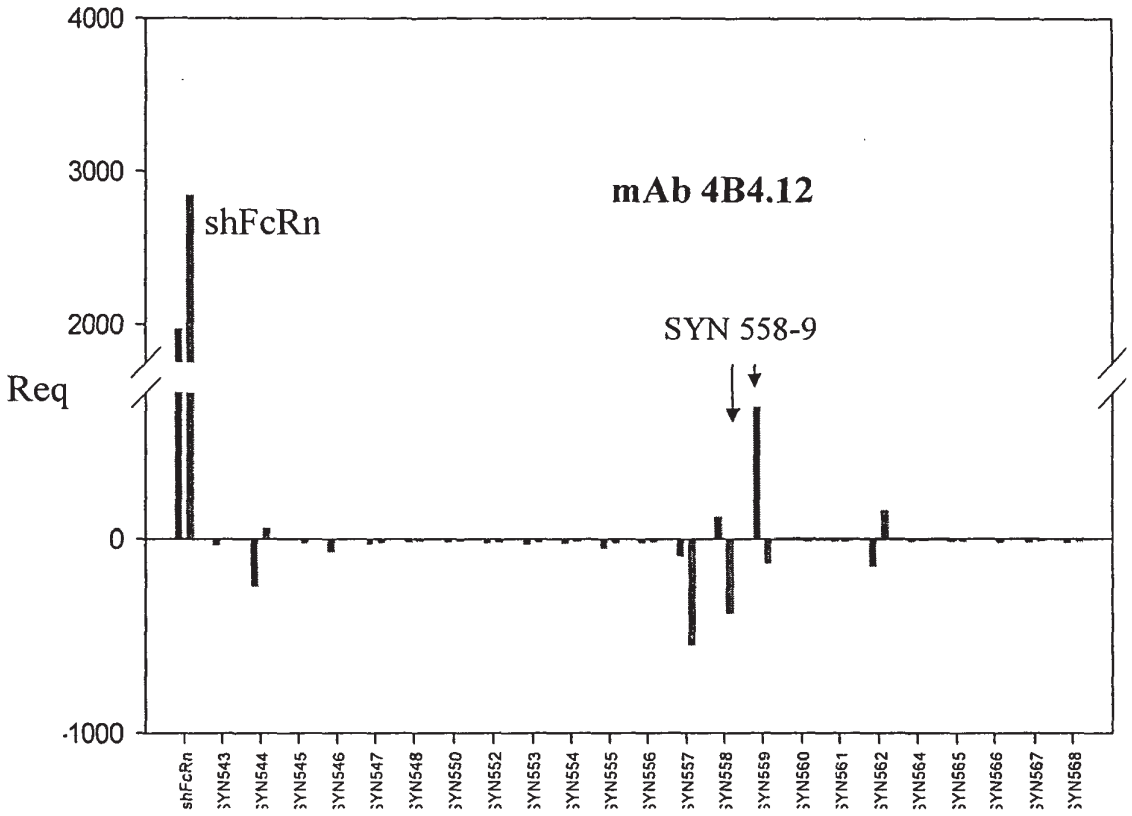

4000
3000
2000
Req
0
-1000
shFcRn
mAb 4B4.12
SYN 558-9
shFcRn
SYN543
SYN544
SYN545
SYN546
SYN547
SYN548
SYN550
SYN552
SYN553
SYN554
SYN555
SYN556
SYN557
SYN558
SYN559
SYN560
SYN561
SYN562
SYN564
SYN565
SYN566
SYN567
SYN568

Figure 22D

FIGURE 23

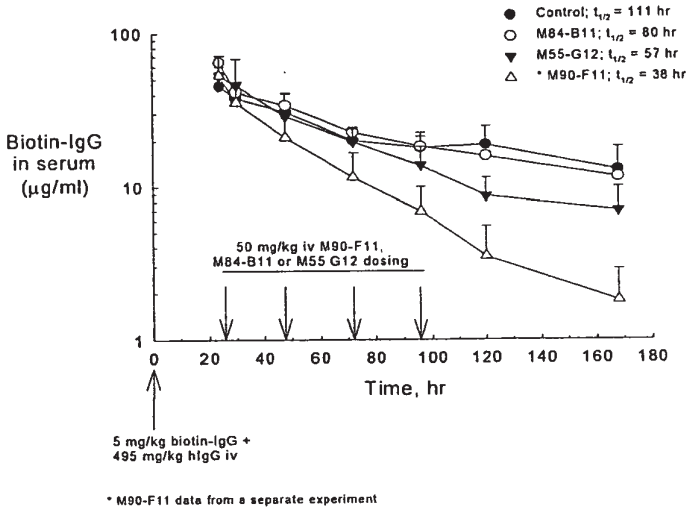

Control; $t_{1/2}$ = 111 hr
M84-B11; $t_{1/2}$ = 80 hr
M55-G12; $t_{1/2}$ = 57 hr
* M90-F11; $t_{1/2}$ = 38 hr
Biotin-IgG in serum (µg/ml)
100
10
1
50 mg/kg iv M90-F11, M84-B11 or M55 G12 dosing
0
20
40
60
80
100
120
140
160
180
Time, hr
5 mg/kg biotin-IgG + 495 mg/kg hIgG iv
* M90-F11 data from a separate experiment

FIGURE 24

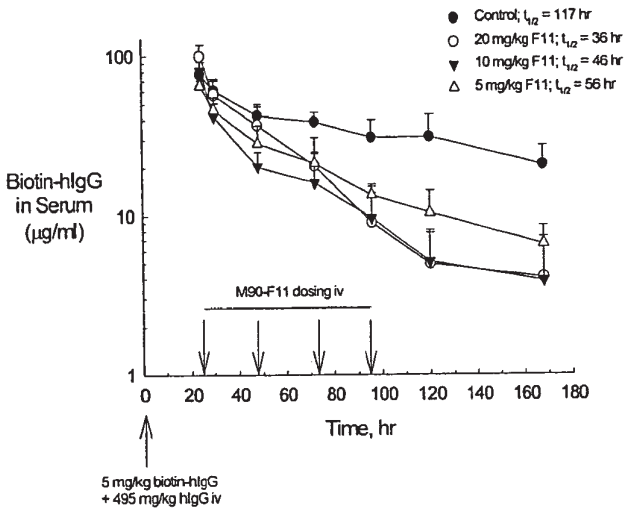

Control; $t_{1/2}$ = 117 hr
20 mg/kg F11; $t_{1/2}$ = 36 hr
10 mg/kg F11; $t_{1/2}$ = 46 hr
5 mg/kg F11; $t_{1/2}$ = 56 hr
Biotin-hIgG in Serum (µg/ml)
100
10
1
M90-F11 dosing iv
0
20
40
60
80
100
120
140
160
180
Time, hr
5 mg/kg biotin-hIgG + 495 mg/kg hIgG iv

FIGURE 25

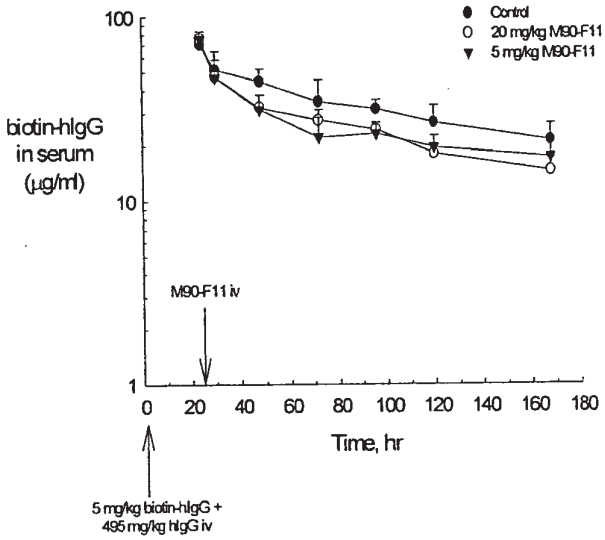
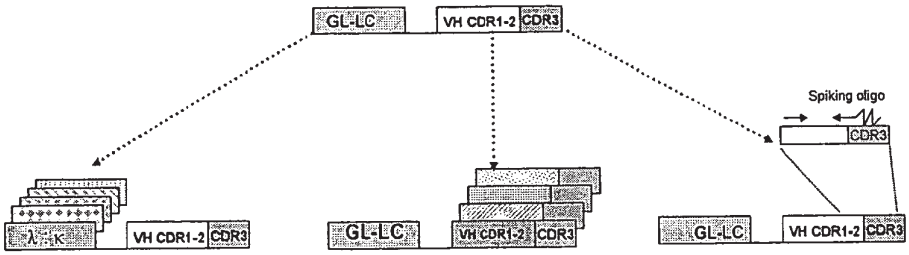

Control
20 mg/kg M90-F11
5 mg/kg M90-F11
biotin-hIgG in serum (µg/ml)
100
10
1
M90-F11 iv
0
20
40
60
80
100
120
140
160
180
Time, hr
5 mg/kg biotin-hIgG + 495 mg/kg hIgG iv

FIGURE 26



Library 1
Expected size: 10^9

Outcome:
Kappa LC shuffled secondary library: 5E+08
Lambda LC shuffled secondary library: 6E+08

Library 2
Expected size: 5x10e8

Out come:
VH CDR1-2 secondary library: 2E+09

Library 3
Wobbling HC-CDR3
Expected size: 5x10e6.

Outcome:
VH CDR3 wobbled sec library: E+07 to E+08

FIGURE 27

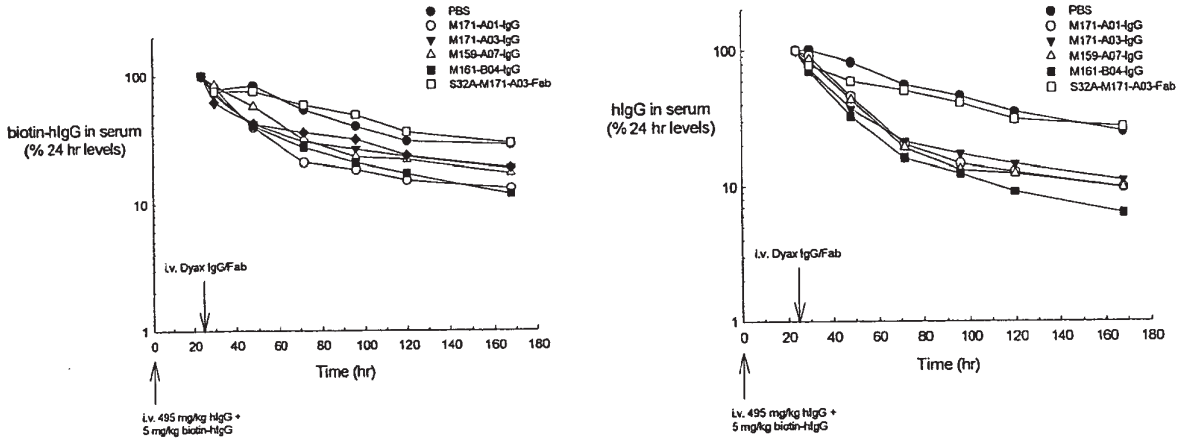

PBS
M171-A01-IgG
M171-A03-IgG
M159-A07-IgG
M161-B04-IgG
S32A-M171-A03-Fab
biotin-hIgG in serum
(% 24 hr levels)
100
10
1
i.v. Dyax IgG/Fab
0
20
40
60
80
100
120
140
160
180
Time (hr)
i.v. 495 mg/kg hIgG +
5 mg/kg biotin-hIgG
hIgG in serum
(% 24 hr levels)

FIGURE 28

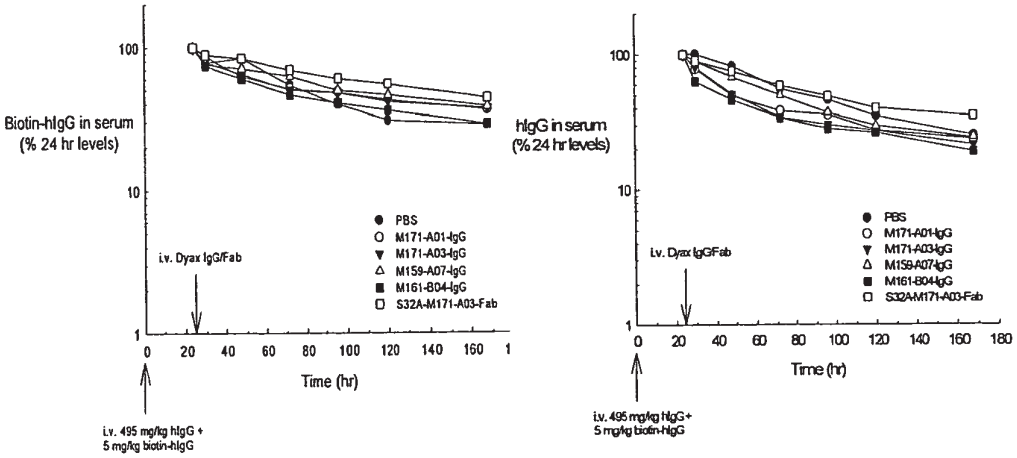

Biotin-hIgG in serum
(% 24 hr levels)
100
10
1
0
20
40
60
80
100
120
140
160
Time (hr)
i.v. Dyax IgG/Fab
i.v. 495 mg/kg hIgG +
5 mg/kg biotin-hIgG
PBS
M171-A01-IgG
M171-A03-IgG
M159-A07-IgG
M161-B04-IgG
S32A-M171-A03-Fab
hIgG in serum
(% 24 hr levels)
100
10
1
0
20
40
60
80
100
120
140
160
180
Time (hr)
i.v. Dyax IgGFab
i.v. 495 mg/kg hIgG+
5 mg/kg biotin-hIgG
PBS
M171-A01-IgG
M171-A03-IgG
M159-A07-IgG
M161-B04-IgG
S32A-M171-A03-Fab

FIGURE 29

532A-M0090-F11 (532A-R0004-E04)

LIGHT: V:VL2_2b2; J:JL1

```
                          FR1-L            CDR1-L           FR2-L       CDR2-L
532A-M0090-F11: QSVLTQPASVSGSPGQSITISC TGTGSDVGSYNLVS WYQKYPGKAPKLIIY GDSQRPS
GERMLINE:       QSALTQPASVSGSPGQSITISC TGTSSDVGSYNLVS WYQQHPGKAPKLMIY EVSKRPS

                          FR3-L                       CDR3-L     FR4-L
532A-M0090-F11: GLSSRFSGSKSGNSASLTISGLQAEDEADYYCC SYAGSGIYYV FGSGTKVTVL
GERMLINE:       GVSNRFSGSKSGNTASLTISGLQAEDEADYYCC SYAGSSTFYV FGTGTKVTVL

532A-M0090-F11 (SEQ ID NO: 177);
GERMLINE (SEQ ID NO: 178)
--------------------------------------------------------------------------------
--------
LC-lambda1

532A-M0090-F11-C
SPKANPTVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADGSPVKAGVETTKPSKQSNNKYAASSYL

GERMLINE-C:
GPKANPTVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADGSPVKAGVETTKPSKQSNNKYAASSYL

532A-M0090-F11-C   SLTPEQWKSHRSYSCQVTHEGSTVEKTVAPAECS (SEQ ID NO: 179)
GERMLINE-C:        SLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS (SEQ ID NO: 180)

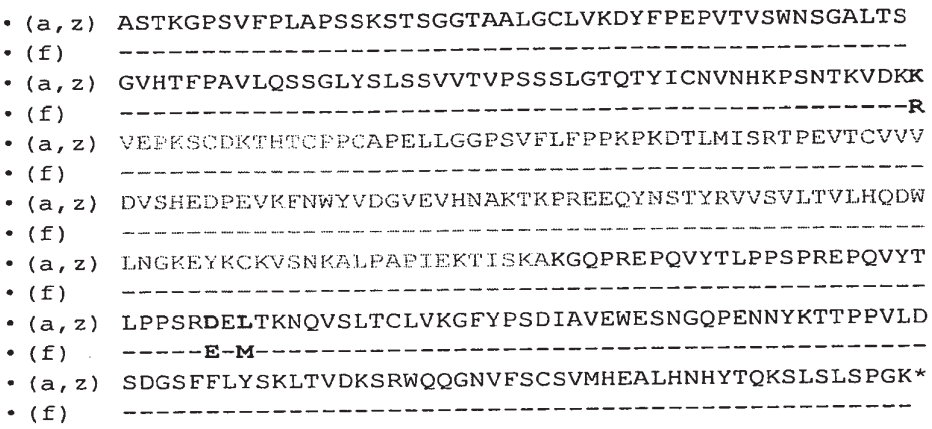
------------------------------------------
HEAVY: V:VH3-23; J:JH4

                           FR1-H                CDR1-H    FR2-H         CDR2-H
532A-M0090-F11: EVQLLESGGGLVQPGGSLRLSCAASGFTFS EYAMG WVRQAPGKGLEWVS
SIGSSGGQTKY
GERMLINE:       EVQLLESGGGLVQPGGSLRLSCAASGFTFS SYAMS WVRQAPGKGLEWVS
AISGSGGSTYY

                                FR3-H                      CDR3-H    FR4-H
532A-M0090-F11: ADSVKG RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR LSTGELY WGQGTLVTVSS
GERMLINE:       ADSVKG RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK       Y WGQGTLVTVSS

532A-M0090-F11 (SEQ ID NO: 111);
GERMLINE (SEQ ID NO: 113)
```

FIGURE 30

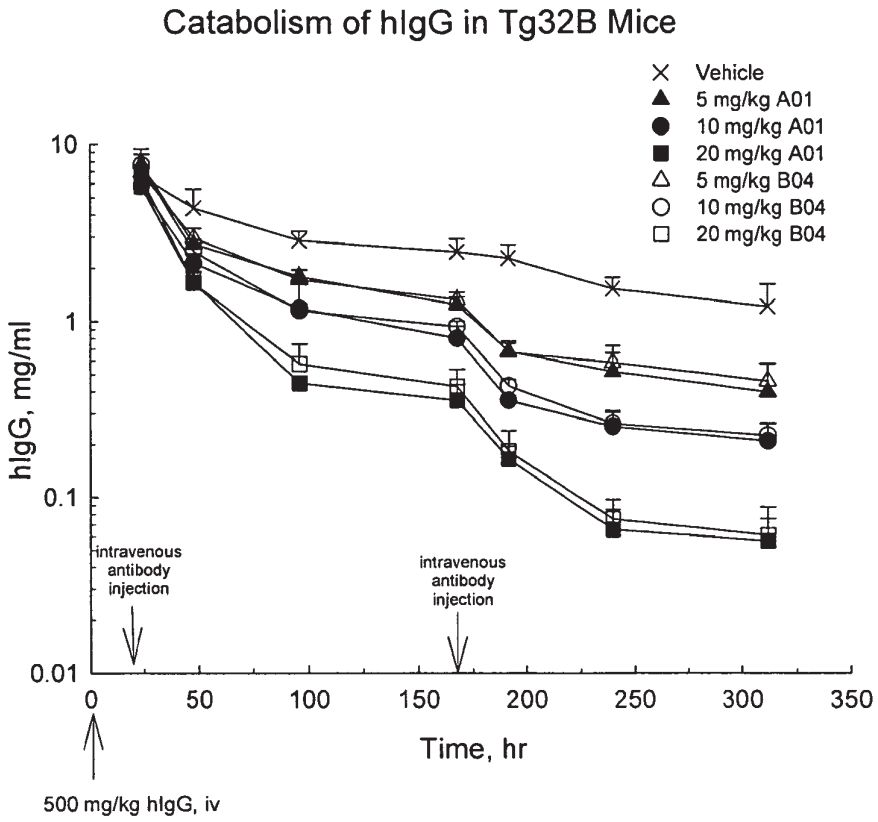


(a, z) (SEQ ID NO: 115)

(f) (SEQ ID NO: 116)

FIGURE 31

A


Catabolism of hIgG in Tg32B Mice
Vehicle
5 mg/kg A01
10 mg/kg A01
20 mg/kg A01
5 mg/kg B04
10 mg/kg B04
20 mg/kg B04
hIgG, mg/ml
10
1
0.1
0.01
intravenous antibody injection
intravenous antibody injection
0
50
100
150
200
250
300
350
Time, hr
500 mg/kg hIgG, iv

B

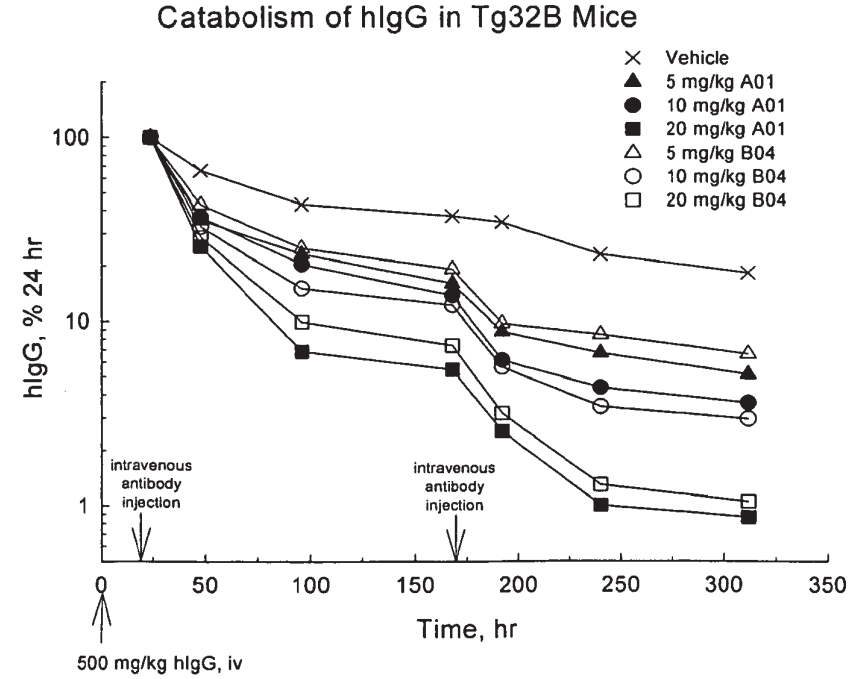

Catabolism of hIgG in Tg32B Mice
Vehicle
5 mg/kg A01
10 mg/kg A01
20 mg/kg A01
5 mg/kg B04
10 mg/kg B04
20 mg/kg B04
hIgG, % 24 hr
100
10
1
intravenous antibody injection
intravenous antibody injection
0
50
100
150
200
250
300
350
Time, hr
500 mg/kg hIgG, iv

FIGURE 32

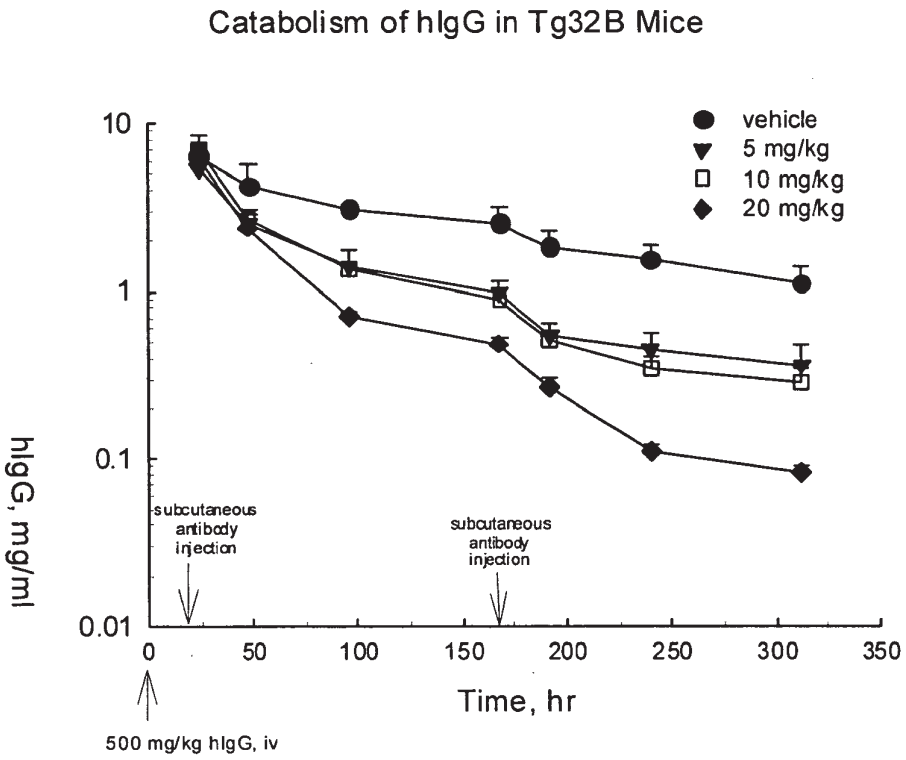
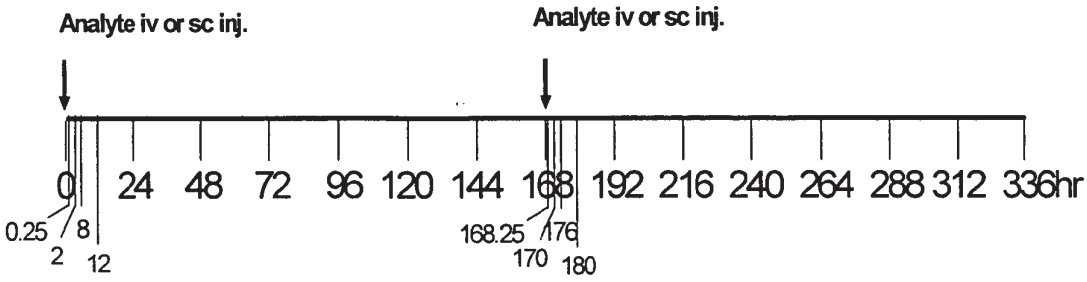

Catabolism of hIgG in Tg32B Mice
vehicle
5 mg/kg
10 mg/kg
20 mg/kg
10
1
0.1
0.01
hIgG, mg/ml
subcutaneous antibody injection
subcutaneous antibody injection
0
50
100
150
200
250
300
350
Time, hr
500 mg/kg hIgG, iv

FIGURE 33

A


Analyte iv or sc inj.
Analyte iv or sc inj.
0
24
48
72
96
120
144
168
192
216
240
264
288
312
336hr
0.25
2
8
12
168.25
170
176
180

B

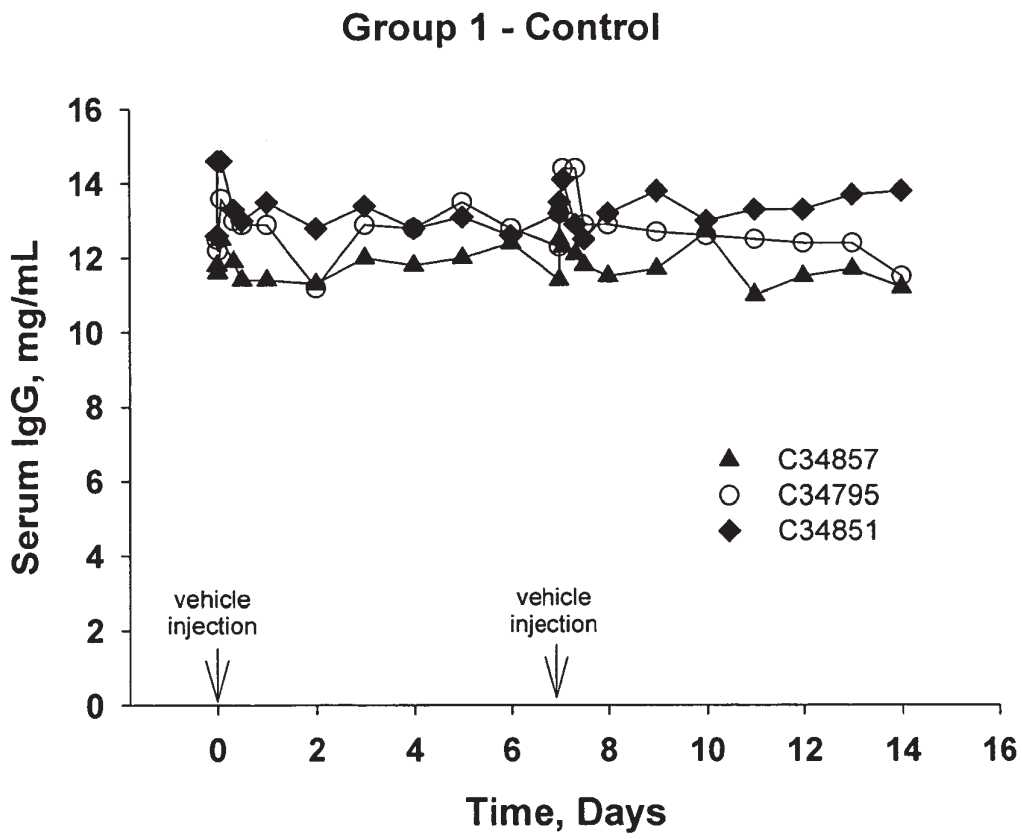
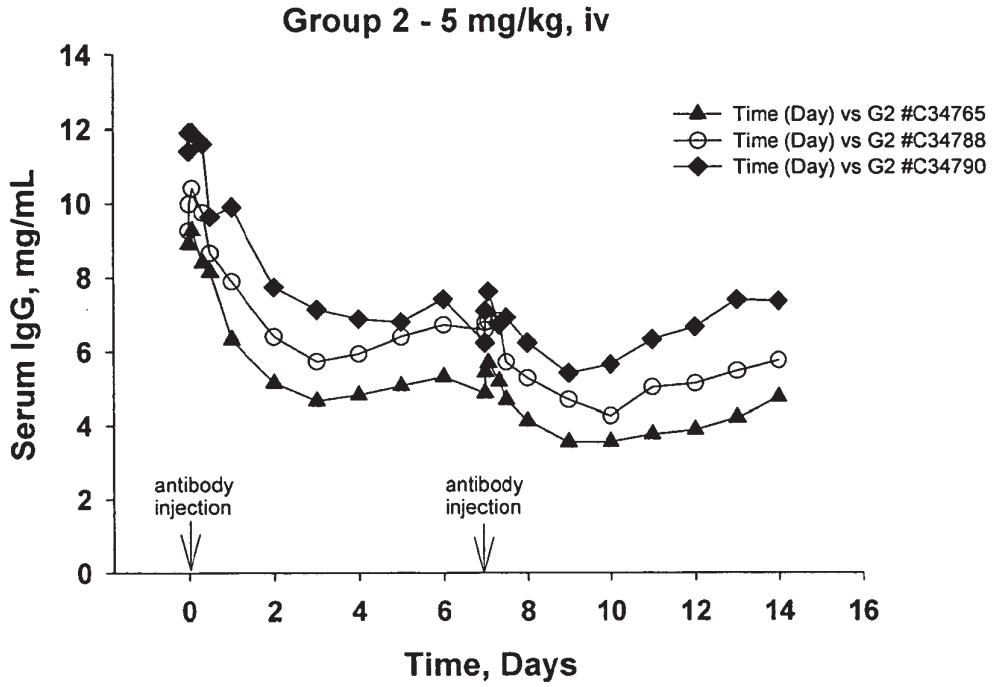

Group 1 - Control
Serum IgG, mg/mL
Time, Days
C34857
C34795
C34851
vehicle injection
vehicle injection
0
2
4
6
8
10
12
14
16

FIGURE 34

A


Group 2 - 5 mg/kg, iv
Time (Day) vs G2 #C34765
Time (Day) vs G2 #C34788
Time (Day) vs G2 #C34790
Serum IgG, mg/mL
antibody injection
antibody injection
Time, Days

B

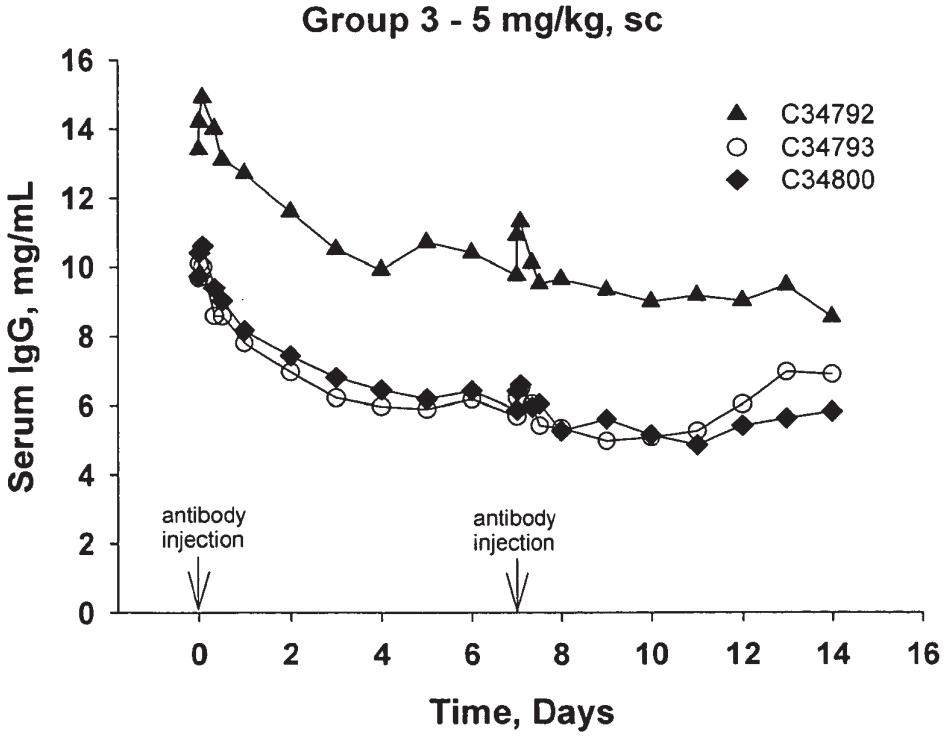
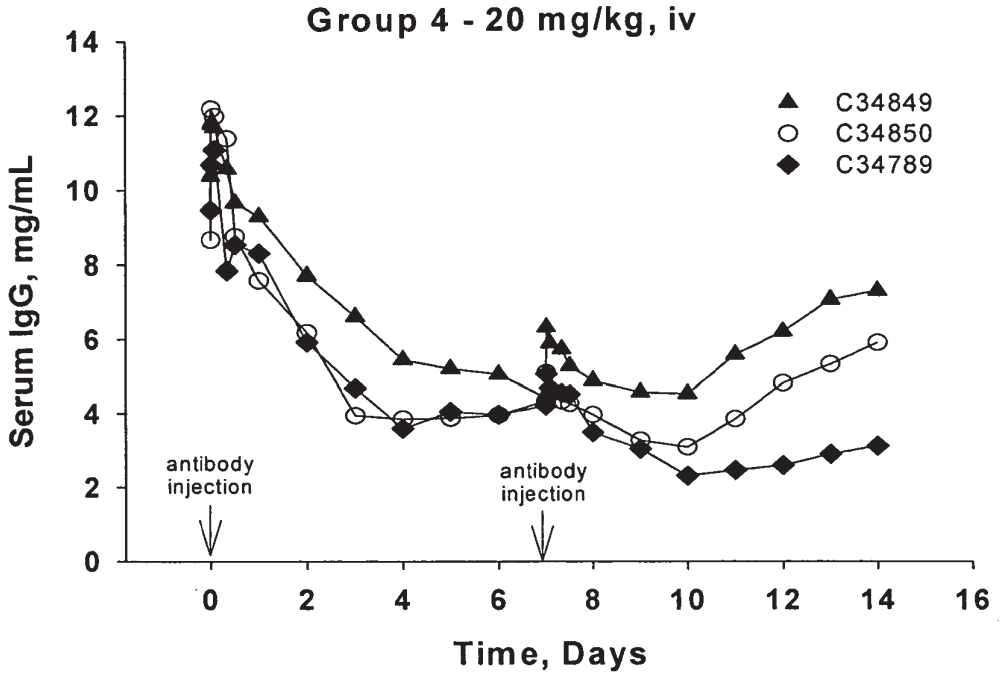

Group 3 - 5 mg/kg, sc
C34792
C34793
C34800
Serum IgG, mg/mL
antibody injection
antibody injection
Time, Days

FIGURE 35

A


Group 4 - 20 mg/kg, iv
C34849
C34850
C34789
Serum IgG, mg/mL
antibody injection
antibody injection
Time, Days
0
2
4
6
8
10
12
14
16

B

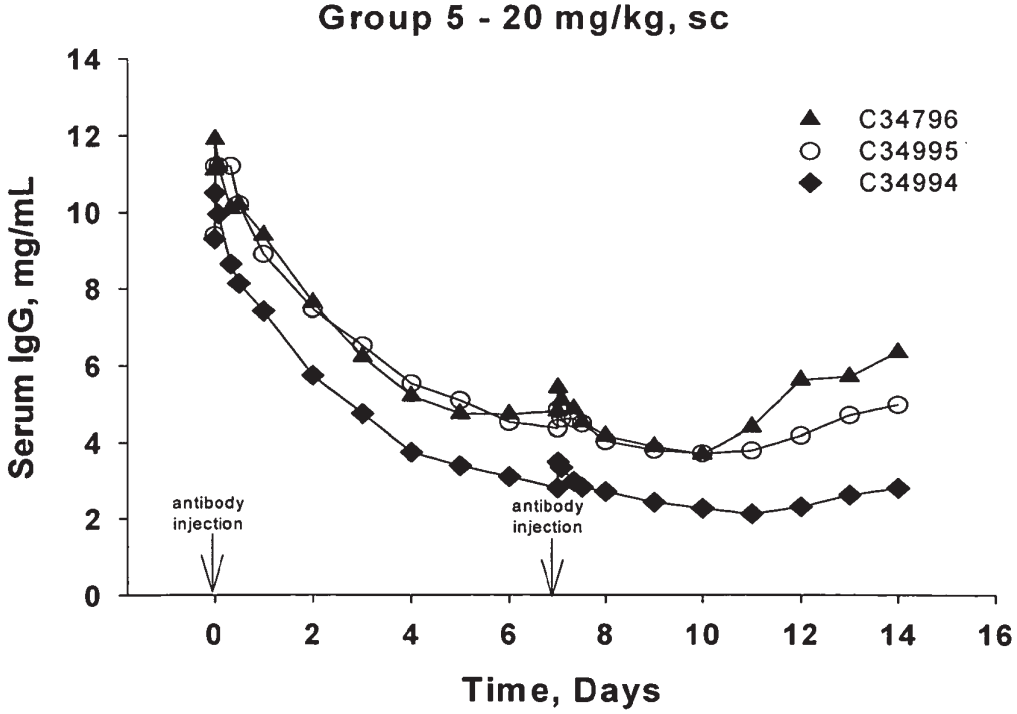

Group 5 - 20 mg/kg, sc
C34796
C34995
C34994
Serum IgG, mg/mL
antibody injection
antibody injection
Time, Days
0
2
4
6
8
10
12
14
16

FIGURE 36

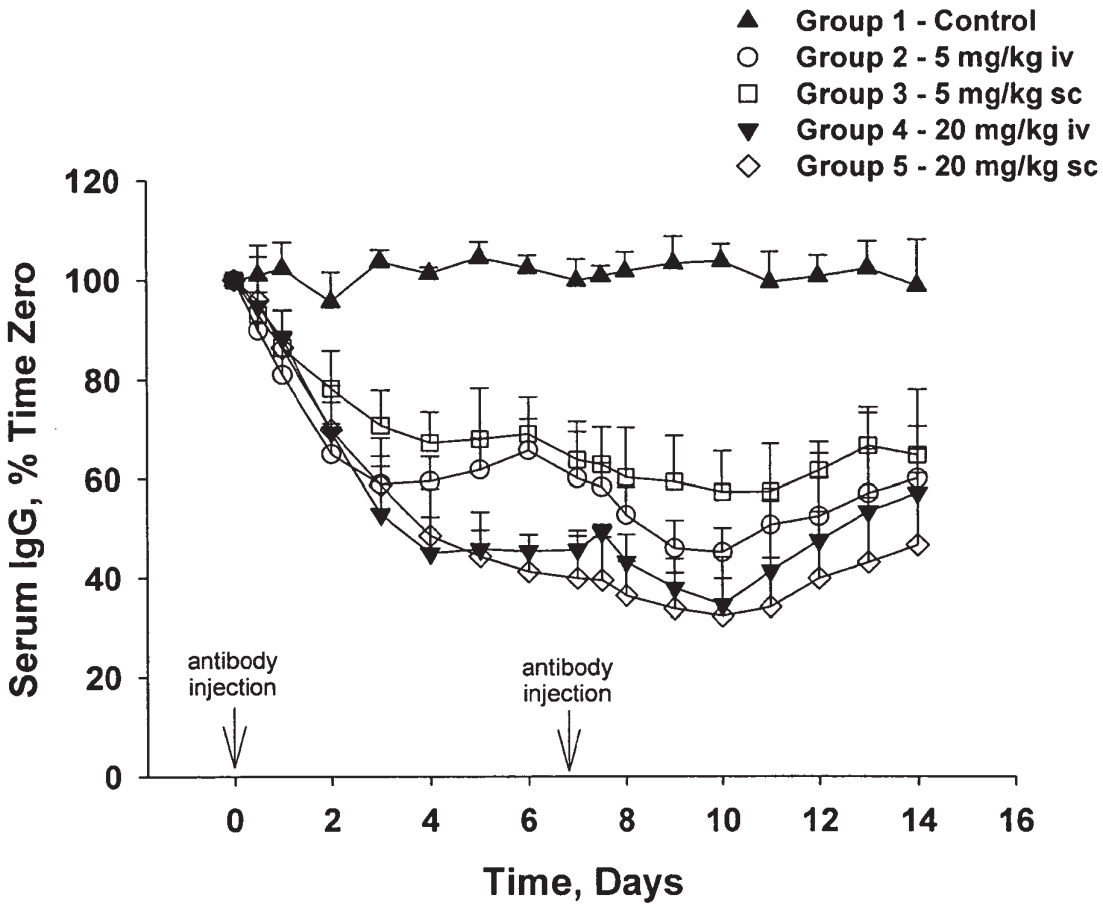

Group 1 - Control
Group 2 - 5 mg/kg iv
Group 3 - 5 mg/kg sc
Group 4 - 20 mg/kg iv
Group 5 - 20 mg/kg sc
Serum IgG, % Time Zero
120
100
80
60
40
20
0
antibody injection
antibody injection
0
2
4
6
8
10
12
14
16
Time, Days

FIGURE 37

A

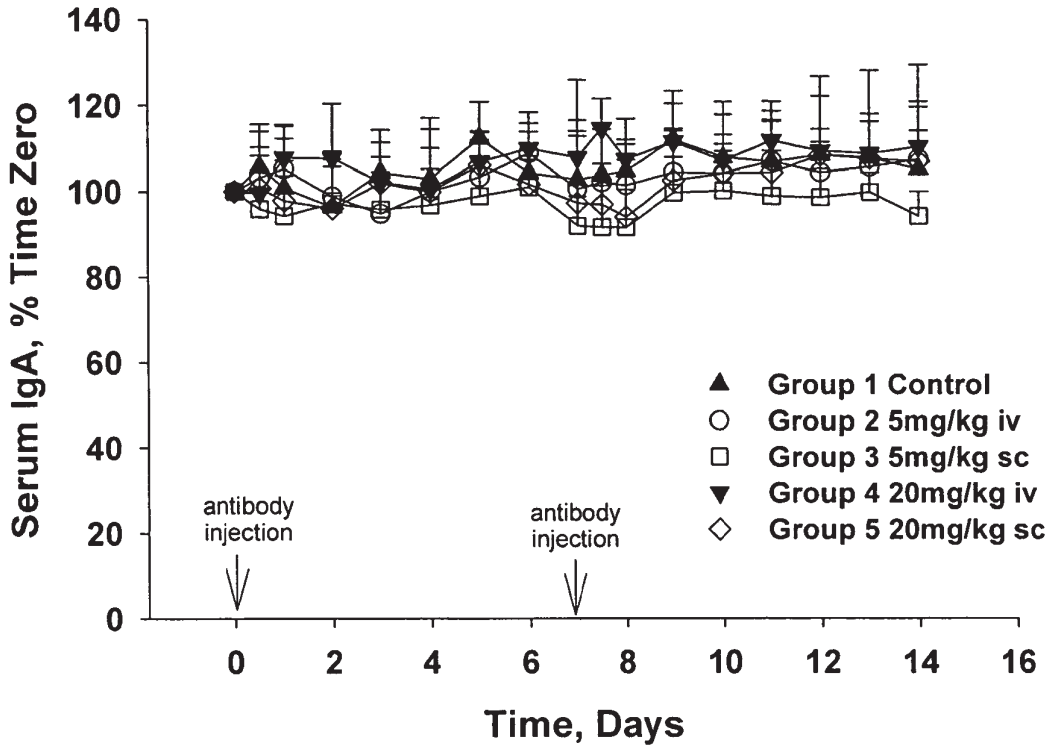

Serum IgA, % Time Zero
140
120
100
80
60
40
20
0
antibody injection
antibody injection
Group 1 Control
Group 2 5mg/kg iv
Group 3 5mg/kg sc
Group 4 20mg/kg iv
Group 5 20mg/kg sc
0
2
4
6
8
10
12
14
16
Time, Days

FIGURE 37

B

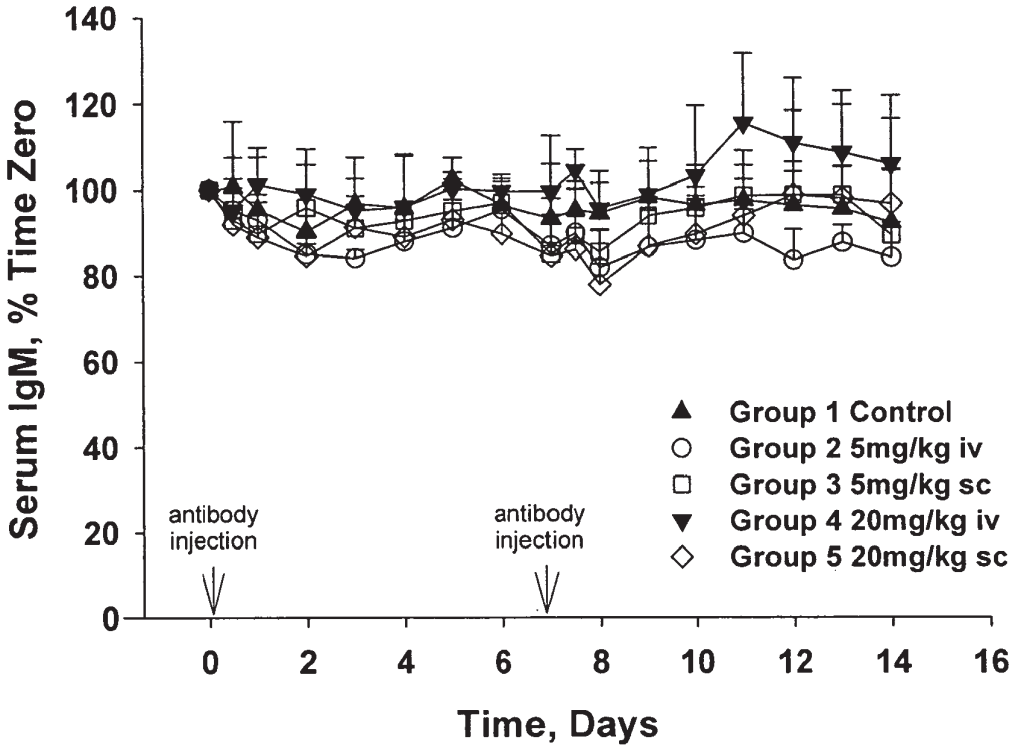

Serum IgM, % Time Zero
140
120
100
80
60
40
20
0
antibody injection
antibody injection
Group 1 Control
Group 2 5mg/kg iv
Group 3 5mg/kg sc
Group 4 20mg/kg iv
Group 5 20mg/kg sc
0
2
4
6
8
10
12
14
16
Time, Days

FIGURE 37

C

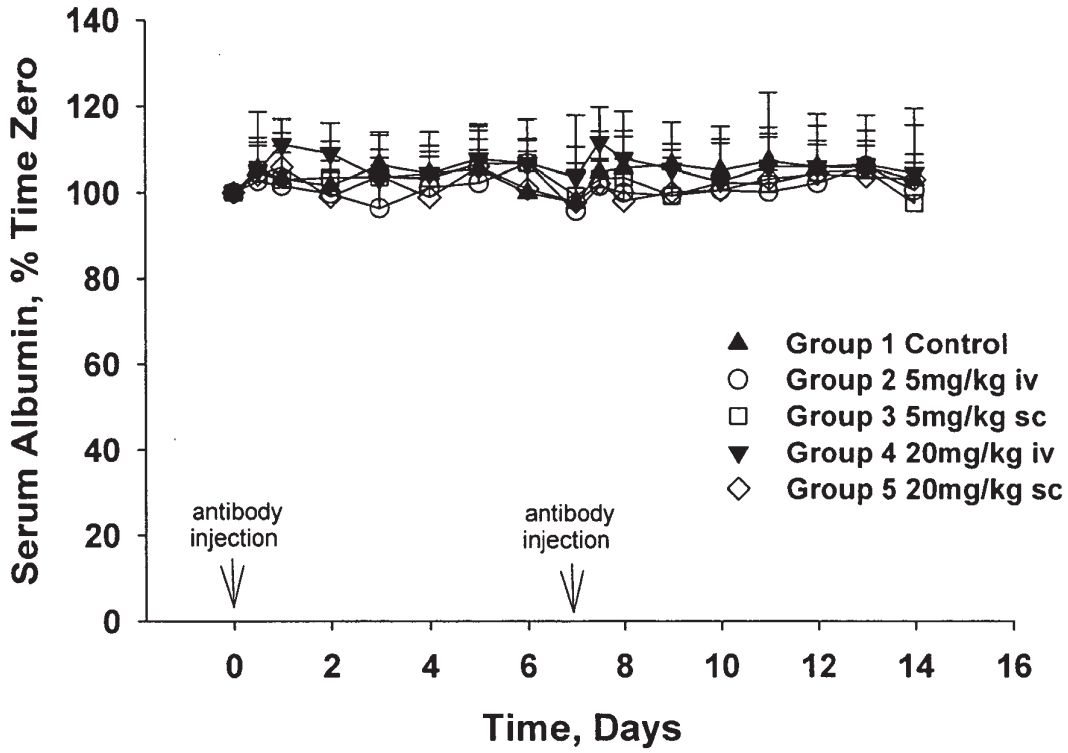

Serum Albumin, % Time Zero
140
120
100
80
60
40
20
0
0
2
4
6
8
10
12
14
16
Time, Days
antibody injection
antibody injection
Group 1 Control
Group 2 5mg/kg iv
Group 3 5mg/kg sc
Group 4 20mg/kg iv
Group 5 20mg/kg sc

FIGURE 38

DX-2504 (532A-M0161-B04)

Light V gene = VL2_2b2; J gene = JL1

```
                      FR1-L              CDR1-L          FR2-L         CDR2-L
GERMLINE:    QSALTQPASVSGSPGQSITISC TGTSSDVGSYNLVS WYQQHPGKAPKLMIY EVSKRPS
DX-2504:     QSALTQPASVSGSPGQSITISC TGTGSDVGSYNLVS WYQQHPGKAPKLMIY GDSQRPS

                        FR3-L                              CDR3-L      FR4-L
GERMLINE:    GVSNRFSGSKSGNTASLTISGLQAEDEADYYC CSYAGSSTYV FGTGTKVTVL
DX-2504:     GVSNRFSGSKSGNTASLTISGLQAEDEADYYC CSYAGSGIYV FGTGTKVTVL
```

GERMLINE (SEQ ID NO: 181); DX-2504 (SEQ ID NO: 182)

Heavy V gene = VH3-23; J gene = JH3

```
                      FR1-H                                CDR1-H      FR2-H
CDR2-H
GERMLINE:    EVQLLESGGGLVQPGGSLRLSCAASGFTFS SYAMS WVRQAPGKGLEWVS
AISGSGGSTYYADSVKG
DX-2504:     EVQLLESGGGLVQPGGSLRLSCAASGFTFS EYAMG WVRQAPGKGLEWVS
SIGSSGGQTKYADSVKG

                        FR3-H                          CDR3-H    FR4-H
GERMLINE:    RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK      AEDI WGQGTMVTVSS
DX-2504:     RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR LAIGDSY WGQGTMVTVSS
```

GERMLINE (SEQ ID NO: 183); DX-2504 (SEQ ID NO: 184)

Top Alignments against Germline sequences

```
DX-2504: QSALTQPASVSGSPGQSITISC TGTGSDVGSYNLVS WYQQHPGKAPKLMIY GDSQRPS
VL2_2b2: QSALTQPASVSGSPGQSITISC TGTSSDVGSYNLVS WYQQHPGKAPKLMIY EVSKRPS
VL2_2e2: QSALTQPRSVSGSPGQSVTISC TGTSSDVGGYNYVS WYQQHPGKAPKLMIY DVSKRPS
VL2_2a2: QSALTQPASVSGSPGQSITISC TGTSSDVGGYNYVS WYQQHPGKAPKLMIY EVSNRPS
VL2_2c:  QSALTQPPSASGSPGQSVTISC TGTSSDVGGYNYVS WYQQHPGKAPKLMIY EVSKRPS
VL2_2d:  QSALTQPPSVSGSPGQSVTISC TGTSSDVGSYNRVS WYQQPPGTAPKLMIY EVSNRPS

DX-2504: GVSNRFSGSKSGNTASLTISGLQAEDEADYYC CSYAGSGIYYV FGTGTKVTVL
VL2_2b2: GVSNRFSGSKSGNTASLTISGLQAEDEADYYC CSYAGSSTT
VL2_2e2: GVPDRFSGSKSGNTASLTISGLQAEDEADYYC CSYAGSYTF
VL2_2a2: GVSNRFSGSKSGNTASLTISGLQAEDEADYYC SSYTSSSTL
VL2_2c:  GVPDRFSGSKSGNTASLTVSGLQAEDEADYYC SSYAGSNNF
VL2_2d:  GVPDRFSGSKSGNTASLTISGLQAEDEADYYC SLYTSSSTF
```

DX-2504: SEQ ID NO: 185; VL2_2b2: SEQ ID NO: 186; VL2_2e2: SEQ ID NO: 187;
VL2_2a2: SEQ ID NO: 188; VL2_2c: SEQ ID NO: 189; VL2_d: SEQ ID NO: 190;