Development of New Anti-CD52 Monoclonal Antibodies

Immunization Hybridomas Cloned & Converted IgGs Expression Purified IgGs

Fig. 1A

Fig. 1B

mAb	Original Isotype
4G7	mIgG$_2$
9D9	mIgG$_2$
7F11	mIgG$_1$
4B10	mIgG$_{2A}$
8G3	mIgG$_3$
11C11	mIgG$_3$
3G7	mIgG$_{2B}$
12G8	mIgG$_3$
5F7	mIgG$_1$
23E6	mIgG$_1$
2C3	mIgG$_3$

Anti-CD52 Binders

FIG. 1A - 1B

Light Chain Sequences of Mouse Anti-Human CD52 Antibodies

Light Chain (Kappa) sequence

1) Campath 1G Kappa (rat)
2) CF1D12 Kappa
3) Mouse 8G3.25.3.5 Kappa
4) Mouse GMA 4G7.F3 kappa
5) Mouse GMA 9D9.A2 kappa
6) Mouse GMA 11C11.C5 kappa
7) Mouse GMA 3G7.E9 kappa
8) Mouse 5F7.1.1.4 kappa
9) Mouse 12G6.15.1.2 kappa
10) Mouse 23E6.2.2.1 kappa
11) Mouse 2C3.3.8.1 kappa
12) Mouse 7F11.1.9.7 kappa
13) Mouse 4B10I.2.4 kappa

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    [----------FR1----------][----CDR1-----][-----FR2-----][CDR2-][--------------FR3----------------][--CDR3--][JREGION-]
1)  DIKMTQSPSFLSASVGDRVTLNCKASQNIDK.....YLNWYQQKLGESPKLLIYNTNNLQTGIPSRFSGSGSGTDFTLTISSLQPEDVATYFCLQHISRP.RTFGTGTKLELK (SEQ ID NO:1)

2)  DVVMTQTPLALSVTIGHPASISCKSSQSLLESDGKTYLNWLFQRPGQSPKRLIYLVSNLDSGVPDRFSGSGSGTDFTLKISRVEAEDLGVYYCWQGTHFP.WTFGGGTKLEIK (SEQ ID NO:2)

3)  DIVLTQSTSLSVTIGQPASISCKSSQSLLDSDGKTYLNWMLQRPGQSPERLIYLVSKLDSGVPDRFTGSGSGTDFTLKISRVEAEDLGVYYCWQGTHFP.WTFGGGTKLEIK (SEQ ID NO:3)

4)  DIVITQSTILSVTIGQPASISCKSSQSLLDSDGKTYLNWLQRPGQSPKRLMYLVSNLGSGVPDRFTGSGSGTDFTLKVSRVEAEDLGVYYCWQGTHFP.WTFGGGTKLEII (SEQ ID NO:4)

5)  DIVMTQTPLTLSVTIGQPASIFCKSSQSLLDSDGKTYLNWLLQRPGQSPKRLLYLVSALDSGVPDRFTGSGSGTDFTLKISRVEADDLGIYYCWQGFHFP.WTFGGGTKLEIK (SEQ ID NO:5)

6)  DIVMTQTPLTLSVTIGQPASISCKSSQSLLDSDGKTYLNWLSQRPGQSPERLIYLVSKLDSGVPDRFTGSGSGTDFTLKISRVEAED.GVYYCWQGTHFP.WTFGGGTKLEIK (SEQ ID NO:6)

7)  DIVMTQSPLTLSVTIGQPASISCKSSQSLLDSDGKTYLNWLLQRPGQSPKRLIYLVSNLNSGLPDRFIGSGSGTDFTLKISRVEADDLGVYYCWQGTHFP.WTFGGGTKLEIK (SEQ ID NO:7)

8)  DIVLTQTTLSVTIGQPASISCKSSQSLLDSDGRTYLNWLFQRPGQSPKRLIFLVSHLDSGVPDRFTGSGSGTDFTLKISRVEADDLGIYYCWQGTHFP.WTFGGGTKLEIK (SEQ ID NO:8)

9)  DIVMTQTPLTLSVTIGQPASISCKSSQSLLYSNGKTYLNWVLQRPGQSPKRLIYLVSKLDSGVPDRFTGSGSGTDFTLK:SRVEAEDLGVYYCVQGSHFH..TFGAGTKLELK (SEQ ID NO:9)

10) DIVLTQFPKTLSVTIGQPASISCKSSQSLLYSNGKTYLNWLLQRPGQSPKRLIYLVSKLDSGVPDRFKGSGSGTDFTLKISRVEAEDLGIYYCVQGTRFH..TFGAGTKLELK (SEQ ID NO:10)

11) DIVTQTPLTLSVTIGQPVSISCKSSQSLLYSNGKTYLNWLLQRPGQSPKRLIYLVSKLDSGVPDRFTGSGSGTDFTLKISRVEADLGVYYCVQGTHLR..TFGAGTKLEIK (SEQ ID NO:11)

12) DIVMTQTPLSLPVSLGGQASISCRSSQSLVHTNGNSYLHWYLQKPGQSPKLLIYNVSNRFSGVPDRFSGSGSGTDFTLKISRVEADLGVYYCSQSTHVP.FTFGSGTKLEIK (SEQ ID NO:12)

13) DIVMTQSPLSLTVSLGDQASISCRSSQSLVHTNGNTYLHWYLQKPGQSPKLLIYMVSNRFSGVPDRFSGSGSGTDFTLKISRVEADLGIYFCSQSAHVPPLTFGAGTKLELK (SEQ ID NO:13)
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FIG 2

Heavy Chain Sequences of Mouse Anti-Human CD52 Antibodies

Heavy Chain Sequence

1) Campath 1G heavy (rat) (SEQ ID NO:14)
2) CF1D12 IgG3 heavy (SEQ ID NO:15)
3) Mouse 8G3.25.3.5 IgG3 heavy (SEQ ID NO:16)
4) Mouse 4G7.F3 IgG3 heavy (SEQ ID NO:17)
5) Mouse 9D9.A2 IgG3 heavy (SEQ ID NO:18)
6) Mouse 11C11.C5 IgG3 heavy (SEQ ID NO:19)
7) Mouse 3G7.E9 IgG2b heavy (SEQ ID NO:20)
8) Mouse 5F7.1.1.4 IgG3 heavy (SEQ ID NO:21)
9) Mouse 12G6.15.1.2 IgG3 heavy (SEQ ID NO:22)
10) Mouse 23E6.2.2.1 IgG3 heavy (SEQ ID NO:23)
11) Mouse 2C3.3.8.1 IgG3 heavy (SEQ ID NO:24)
12) Mouse 7F11.1.9.7 IgG1 heavy (SEQ ID NO:25)
13) Mouse 4B10.1.2.4 IgG2a heavy (SEQ ID NO:26)

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    [--------FR1-----------][--CDR1--][----FR2-----][------CDR2-------][---------------FR3----------][----CDR3--][--JREGION-]
1)  EVKLLESGGGLVQPGGSMRLSCAGSGFTFTDFYMNWIRQPAGKAPEWLGFIRDKAKGYTTEYNPSVKGRFTISRDNTQNMLYLQMNTLRAEDTATYYCAREGHTAAPFDYWGQGVMVTVSS

2)  EVKLEESGGGLVQPGGSMKLSCAASGFTFSDAWMDWVRQSPEKGLEWVAEIRNKAKNHVAYYAESVKGRFTISRDDSKSSVYLQMNNLRAEDTGIYYC..TTL.....DSWGQGTALTVSS

3)  EVKLEESGGGLVQPGGSMKLSCAVSRFTFSDAWMDWVRQSPEKGLEWIAEIRNKANNHATYYAESVKGRFTISRDDSKSRVFLQMNNLRPEDTGIYYC..TSL.....DYWGQGTTLTVSS

4)  EVKLEESGGGLVQPGGSMKLSCAVSGFTFSDAWMDWVRQSPEKGLEWVAEIRNKAKNHVKYYAESVKGRFTISRDDSKSSVYLQMNNLRTEDTGIYYC..TSL.....DYWGQGTALTVSS

5)  EVKLEESGGGLVQPGGSMKLSCAASGFTFSDAWMDWVRQSPEKGLELTAEIRNKAKNHATYYAESVKGRFTISRDDSKSRVYLQMNSLRTEDTGIYYC..TTL.....DSWGQGTSVTVSS

6)  EVKLEESGGGLVQPGGSMKLSCAVSGFTFSDAWMDWVRQSPEKGLEWVAEIRNKAKNHATYYAESVKGRFTISRDDSKSSVYLQMNRLRAEDTGIYYC..TSL.....DYWGQGSTLTVSS

7)  EVKLEESGGGLVQPGGSMKLSCTASGFTFSDAWMDWVRQSPEKGLEWVAEIRKKVNNHATYYAESVKGRFTISRDDSKSSVYLQMNSLRAEDTGIYYC..TSL.....DYWGQGTTLSVSS

8)  EVKLEESGGGLVQPGGSMKLSCAVSGLTFSDAWMDWVRQSPEKGLEWIAEIRNKAKNHATYYAESVKGRFTISRDDSKSGVYLQMNNLRAEDTGIYYC..TGL.....DYWGHGTSVTVSS

9)  EVQLEESGGGLVQPGGSMKLSCVASGFPFSNYWMNWVRQSPEKGLEWVAQIRLKSNNYATHYAESVKGRFTIARDDSKSSVYLQMNNLRAEDTGIYYC..TPI.....DYWGQGTTLTVSS

10) EVKLEESGGGLVQPGGSMKLSCVASGFTFNKYWMNWVRQSPDKGLECIAQIRLKSDNYATHYAESVKGRFTISRDDSKSSVYLQMNNLRAEDTGIYYC..TPI.....DYWGQGTTLTVSS

11) EVKLEESGGGLVQPGGSMKLSCVASGFTFNTYWMNWVRQSPEKGLEWVAQIRLKSNNYATHYAESVKGRFTISRDDSKNSVYLQMNNLRAEDTGIYYC..TPV.....DFWGQGTTLTVSS

12) EVKLEESGGGLVQPGGSLSLSCVASGFTFTDYYMSWVRQPPGKALEWLGFIRNKANGYTTEYNASVKGRFTISRDYSQSILYLQMNALRAEDSATYYC..TRYIFF..DYWGQGTTLTVSS

13) EVQLEESGGGLVQPGGALSLSCAGSGFTFTDYYMSWVRQPPGKALEWLGFIRNKANGYTTEYSASVKGRFTISRDDSQSILYLQMNALRAEDSATYYC..TRYIWF..DYWGQGTTLTVSS
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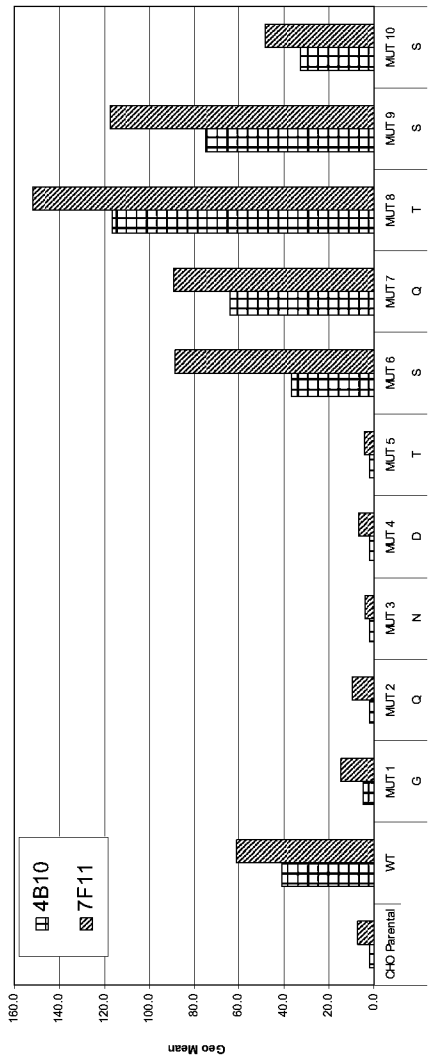
FIG 3

Point Mutations within the CD52 Protein

WT	GQNDTSQTSSPS
MUT 1	AQNDTSQTSSPS
MUT 2	GANDTSQTSSPS
MUT 3	GQADTSQTSSPS
MUT 4	GQNATSQTSSPS
MUT 5	GQNDASQTSSPS
MUT 6	GQNDTAQTSSPS
MUT 7	GQNDTSATSSPS
MUT 8	GQNDTSQASSPS
MUT 9	GQNDTSQTASPS
MUT 10	GQNDTSQTSAPS

FIG. 4

FIG. 5A


Geo Mean
160.0
140.0
120.0
100.0
80.0
60.0
40.0
20.0
0.0
4B10
7F11
CHO Parental
WT
MUT 1
G
MUT 2
Q
MUT 3
N
MUT 4
D
MUT 5
T
MUT 6
S
MUT 7
Q
MUT 8
T
MUT 9
S
MUT 10
S
N terminal binding

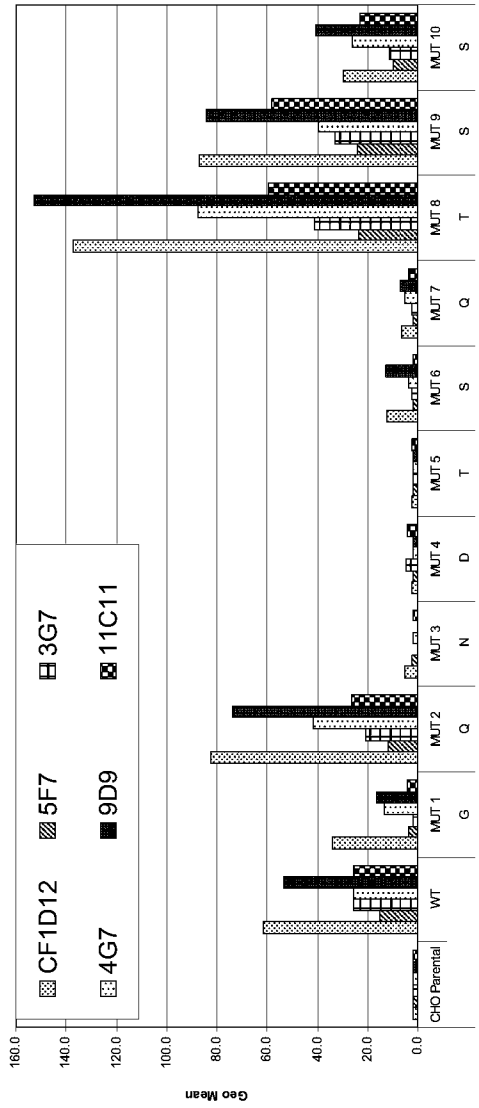

CF1D12
5F7
3G7
4G7
9D9
11C11
Geo Mean
160.0
140.0
120.0
100.0
80.0
60.0
40.0
20.0
0.0
CHO Parental
WT
MUT 1
G
MUT 2
Q
MUT 3
N
MUT 4
D
MUT 5
T
MUT 6
S
MUT 7
Q
MUT 8
T
MUT 9
S
MUT 10
S
Middle region binding

FIG. 5B

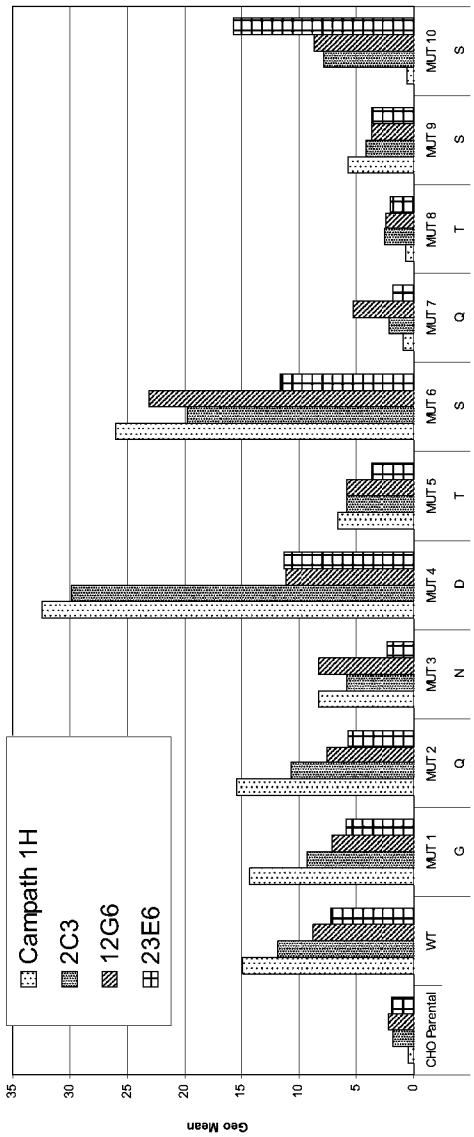

Geo Mean
0
5
10
15
20
25
30
35
Campath 1H
2C3
12G6
23E6
CHO Parental
WT
MUT 1
G
MUT 2
Q
MUT 3
N
MUT 4
D
MUT 5
T
MUT 6
S
MUT 7
Q
MUT 8
T
MUT 9
S
MUT 10
S

FIG. 5C

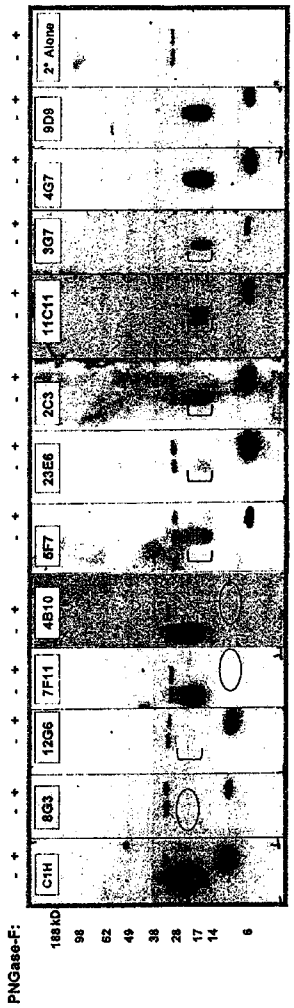

Immunoblots of CD52 +/- N-linked Glycosylation
PNGase-F:
C1H
8G3
12G6
7F11
4B10
6F7
23E6
2C3
11C11
3G7
4G7
9D8
2° Alone
188 kD
98
62
49
38
28
17
14
6

FIG. 5D

FIG. 6

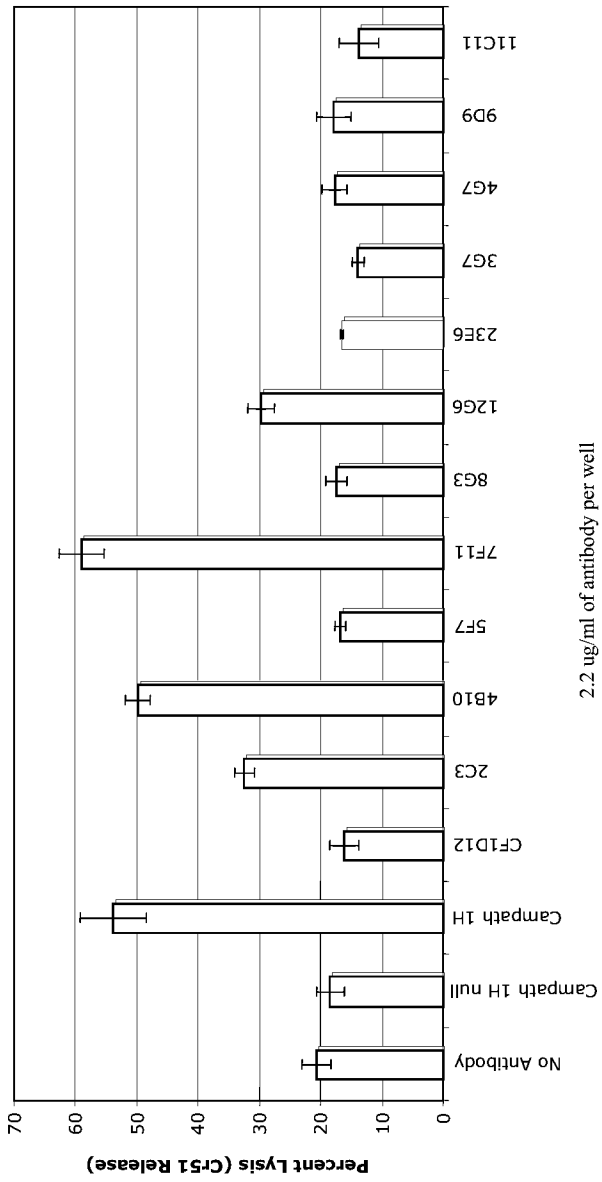

Percent Lysis (Cr51 Release)
0
10
20
30
40
50
60
70
No Antibody
Campath 1H null
Campath 1H
CF1D12
2C3
4B10
5F7
7F11
8G3
12G6
23E6
3G7
4G7
9D9
11C11
2.2 ug/ml of antibody per well

FIG. 7

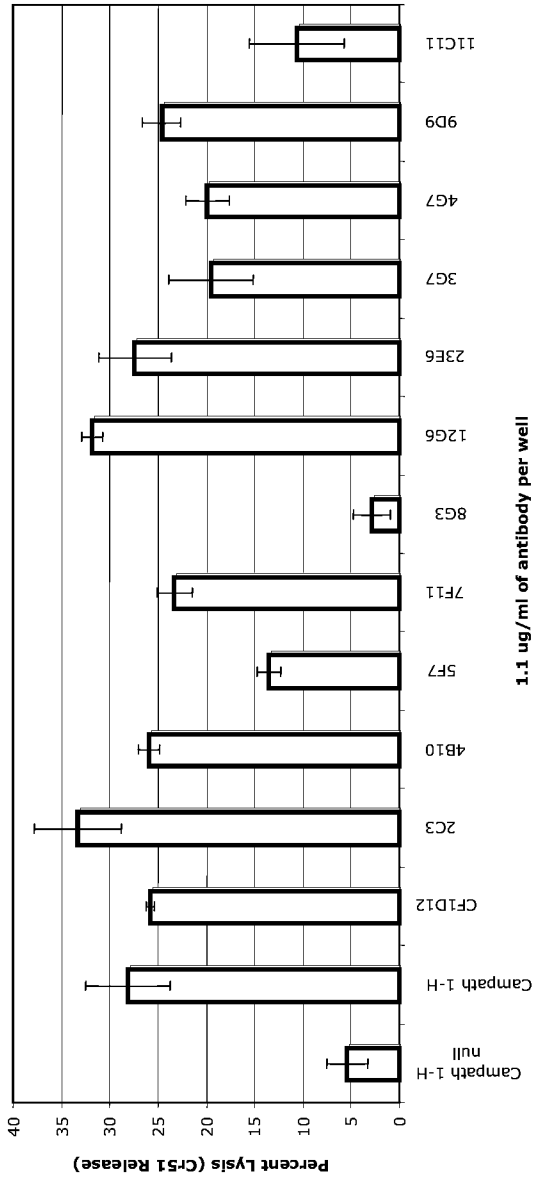

Percent Lysis (Cr51 Release)
0
5
10
15
20
25
30
35
40
Campath 1-H null
Campath 1-H
CF1D12
2C3
4B10
5F7
7F11
8G3
12G6
23E6
3G7
4G7
9D9
11C11
1.1 ug/ml of antibody per well

FIG. 8A

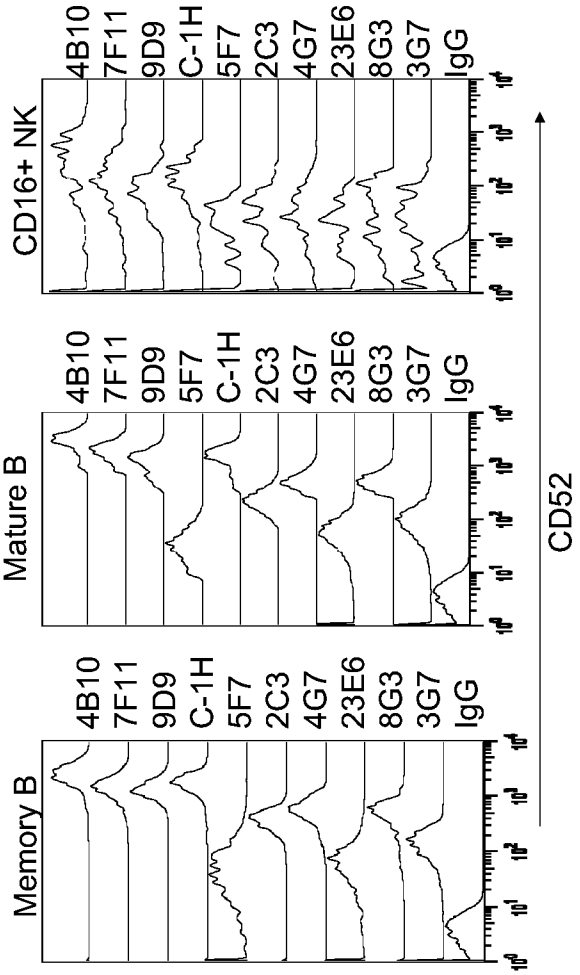
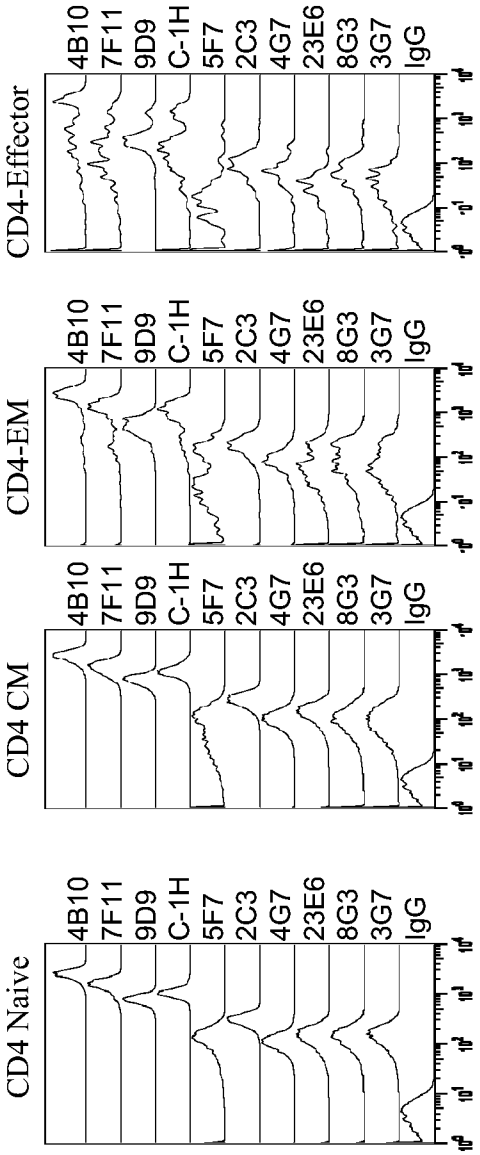

Memory B
Mature B
CD16+ NK
4B10
7F11
9D9
C-1H
5F7
2C3
4G7
23E6
8G3
3G7
IgG
CD52

FIG. 8B


CD4 Naive
CD4 CM
CD4-EM
CD4-Effector
4B10
7F11
9D9
C-1H
5F7
2C3
4G7
23E6
8G3
3G7
IgG

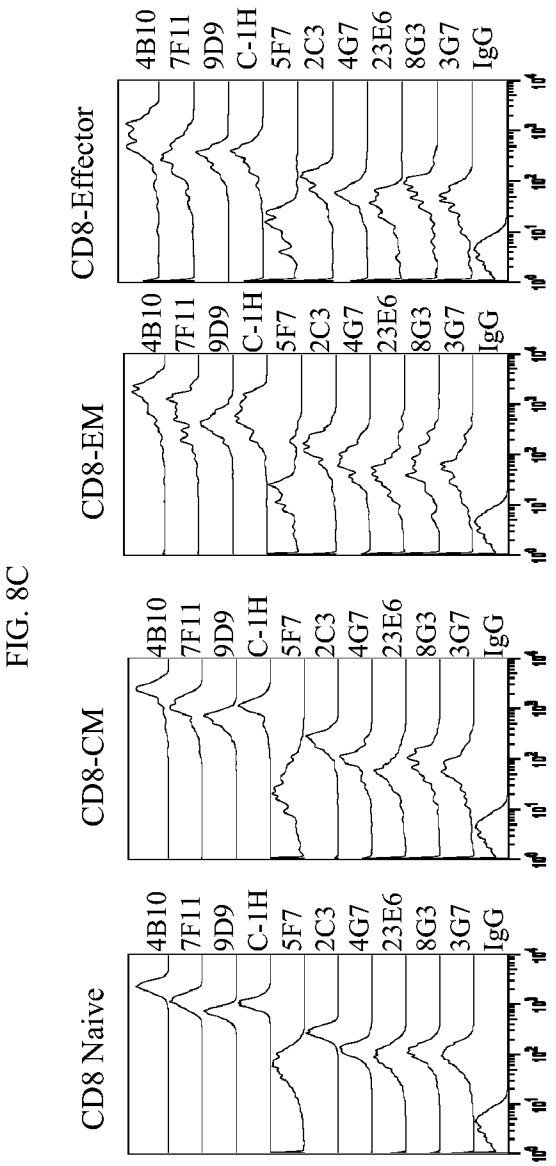

CD8 Naive
CD8-CM
CD8-EM
CD8-Effector
4B10
7F11
9D9
C-1H
5F7
2C3
4G7
23E6
8G3
3G7
IgG

FIG. 8C

Fig. 9A

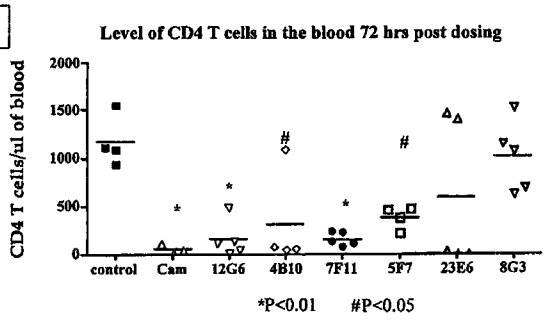


Fig. 9B

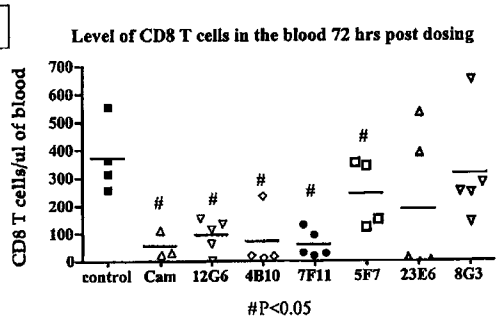


Fig. 9C

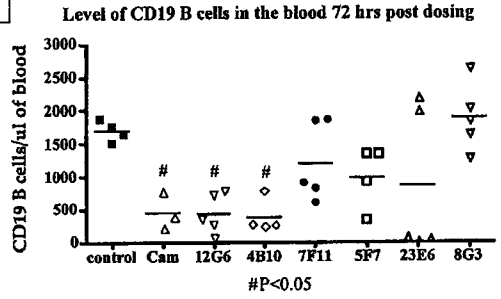
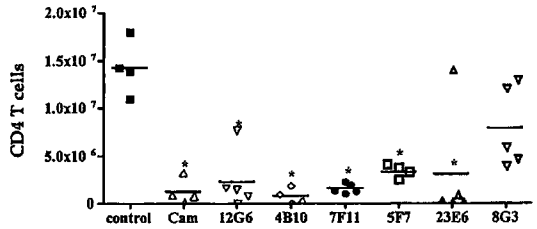


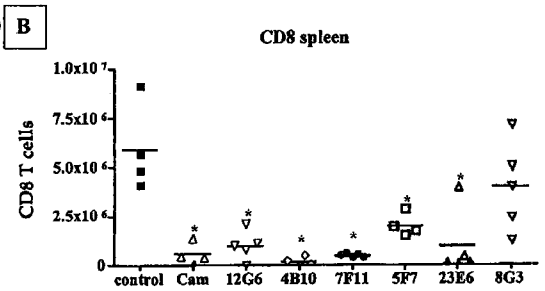
FIG. 9A - 9C

Fig. 10 A



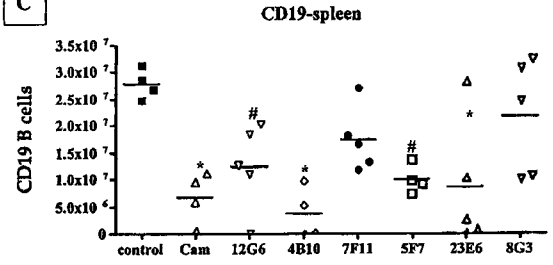
*P<0.01

Fig. 10 B



*P<0.01

Fig. 10 C



*P<0.01 #P<0.05

FIG. 10A - 10C

Fig. 11 A

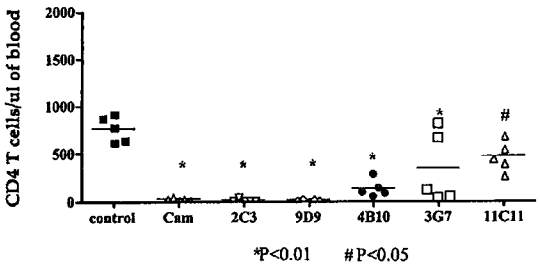


Fig. 11 B

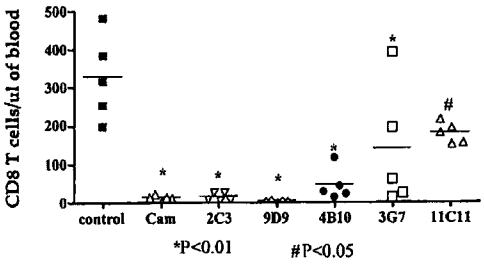


Fig. 11 C

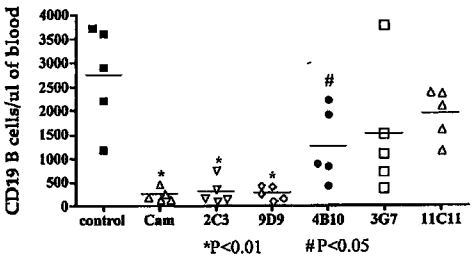


FIG. 11A - 11C

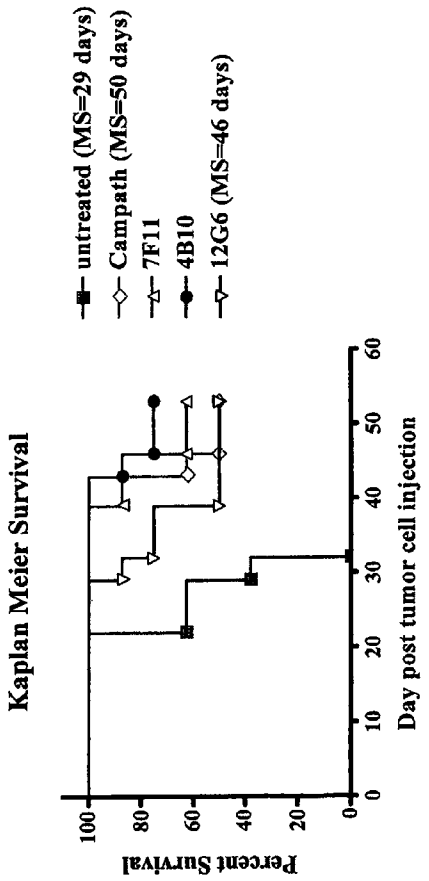

Kaplan Meier Survival
untreated (MS=29 days)
Campath (MS=50 days)
7F11
4B10
12G6 (MS=46 days)
Percent Survival
100
80
60
40
20
0
0
10
20
30
40
50
60
Day post tumor cell injection

FIG. 12

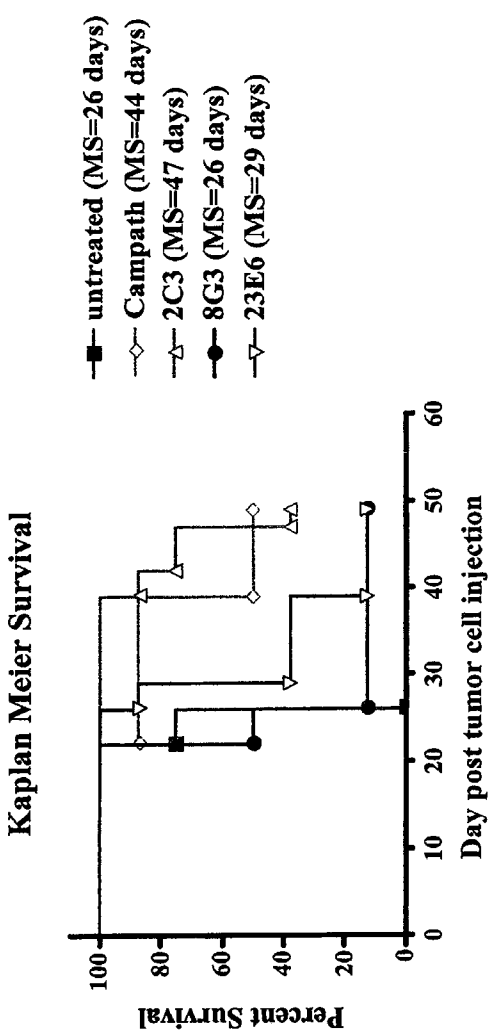

Kaplan Meier Survival
untreated (MS=26 days)
Campath (MS=44 days)
2C3 (MS=47 days)
8G3 (MS=26 days)
23E6 (MS=29 days)
Percent Survival
100
80
60
40
20
0
0
10
20
30
40
50
60
Day post tumor cell injection

FIG. 13

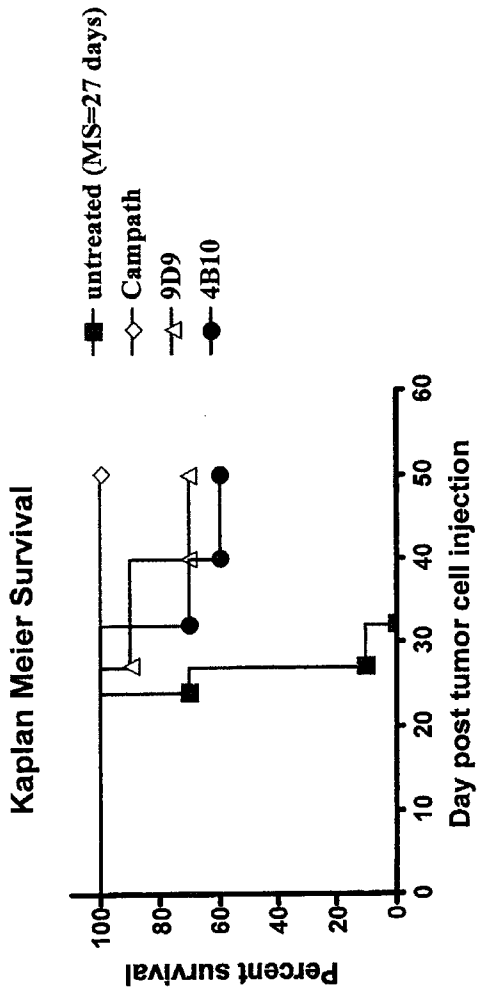

Kaplan Meier Survival
untreated (MS=27 days)
Campath
9D9
4B10
Percent survival
100
80
60
40
20
0
0
10
20
30
40
50
60
Day post tumor cell injection

FIG. 14

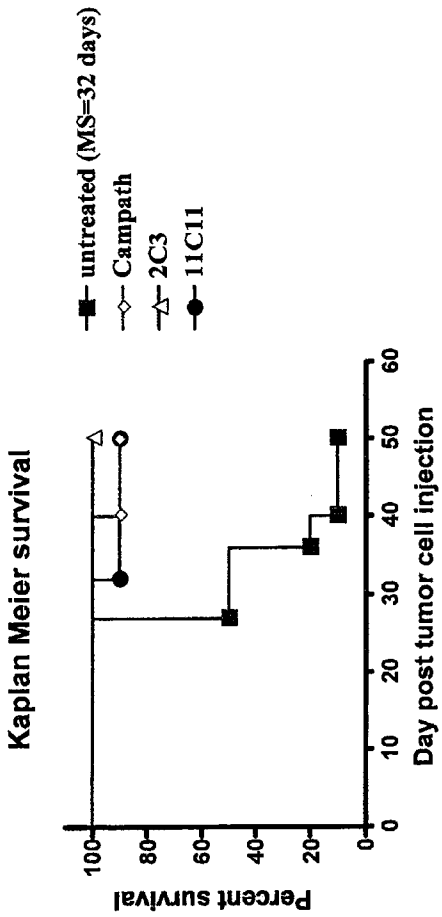

Kaplan Meier survival
untreated (MS=32 days)
Campath
2C3
11C11
Percent survival
100
80
60
40
20
0
0
10
20
30
40
50
60
Day post tumor cell injection

FIG. 15

Alignment of anti human CD52 mouse(m) antibody V region with human germline(h) and humanized anti-CD52 V region sequences

4B10 Heavy Chain V region

```
4B10 Heavy chain(m)   1 EVQLESGGGLVQPGGALSLSCAGSGFTFTDYYMSWVRQPPGKALEWLGF  50  (SEQ ID NO:96)
VH3-72 germline(h)    1 EVQLVESGGGLVQPGGSLRLSCAASGFTFSDHYMDWVRQAPGKGLEWVGR  50  (SEQ ID NO:97)
4B10 humanized HC     1 EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYYMSWVRQAPGKGLEWVGF  50  (SEQ ID NO:98)
                        ***** ************.* **** *****.* ** **** *** ***.*

4B10 Heavy chain(m)  51 IRNKANGYTTEYSASVKGRFTISRDDSQSILYLQMNALRAEDSATYYCTR 100
VH3-72 germline(h)   51 TRNKANSYTTEYAASVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCAR 100
4B10 humanized HC    51 IRNKANGYTTEYSASVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCAR 100
                        ***** *****.**************.  ******.*..**.* ***.*

4B10 Light chain V region

4B10 Light chain(m)   1 DIVMTQSPLSLTVSLGDQASISCRSSQSLVHTNGNTYLHWYLQKPGQSPK  50  (SEQ ID NO:99)
VK2-A18b germline(h)  1 DIVMTQTPLSLSVTPGQPASISCKSSQSLLHSDGKTYLYWYLQKPGQSPQ  50  (SEQ ID NO:100)
4B10 Humanized LC     1 DIVMTQTPLSLSVTPGQPASISCRSSQSLVHTNGNTYLHWYLQKPGQSPQ  50  (SEQ ID NO:101)
                        *******.****.*. *  *****.*****.*. * *** **********.

4B10 light chain(m)  51 LLIYMVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDLGIYFCSQSAHVP 100
VK2-A18b germline(h) 51 LLIYEVSSRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQGIHLP 100
4B10 Humanized LC    51 LLIYMVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSAHVP 100
                        **** ** ********************************.*.*.* *  *.*
```

FIG 16

Humanized 4B10 kappa (light chain) variable region

DIVMTQTPLSLSVTPGQPASISCRSSQSLVHTNGNTYLHWYLQKPGQSPQLLIYMVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC
SQSAHVPPLTFGQGTRLEIK
(SEQ ID NO:102)

Humanized 4B10 heavy chain variable region

EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYYMSWVRQAPGKGLEWVGFIRNKANGYTTEYSASVKGRFTISRDDSKNSLYLQMNSLKTEDT
AVYYCARYIWFDYWGQGTTVTVSS
(SEQ ID NO:103)

FIG 17

FIG. 18

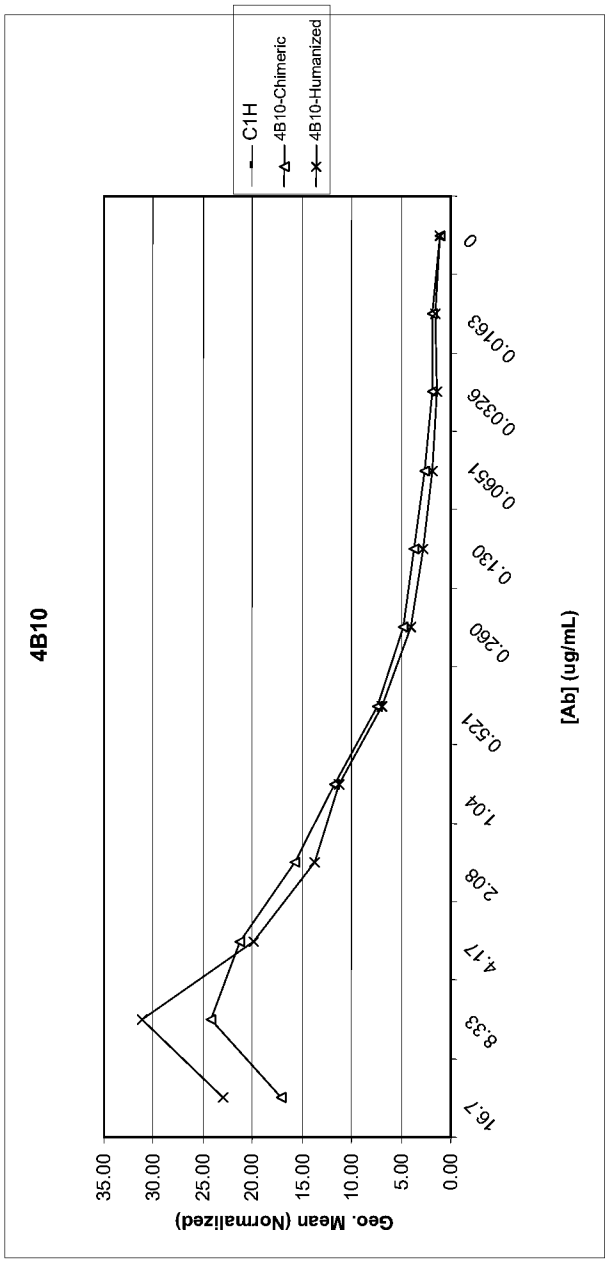
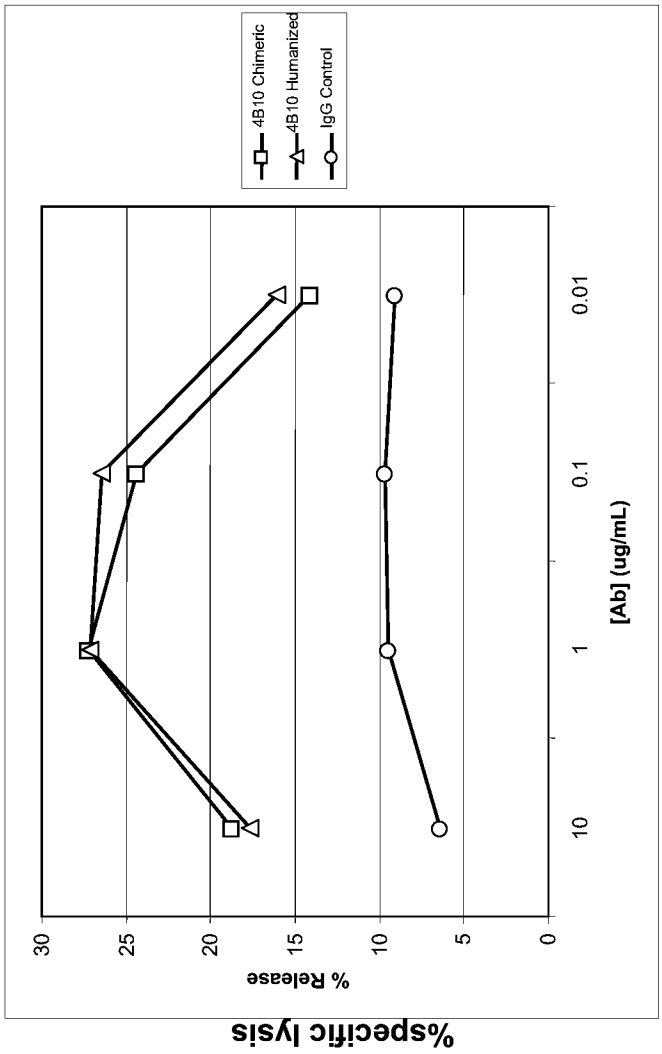

4B10
C1H
4B10-Chimeric
4B10-Humanized
Geo. Mean (Normalized)
35.00
30.00
25.00
20.00
15.00
10.00
5.00
0.00
[Ab] (ug/mL)
16.7
8.33
4.17
2.08
1.04
0.521
0.260
0.130
0.0651
0.0326
0.0163
0

FIG. 19


4B10 Chimeric
4B10 Humanized
IgG Control
% Release
%specific lysis
[Ab] (ug/mL)
0
5
10
15
20
25
30
0.01
0.1
1
10

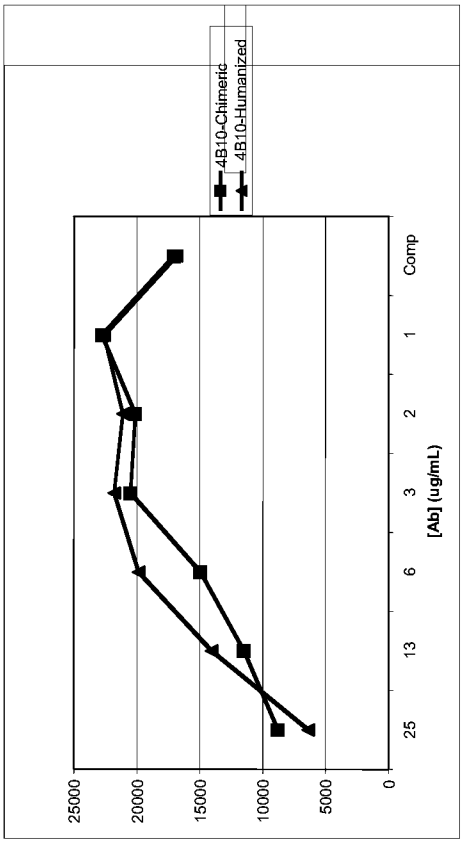

4B10-Chimeric
4B10-Humanized
25000
20000
15000
10000
5000
0
25
13
6
3
2
1
Comp
[Ab] (ug/mL)

FIG.20

FIG. 21

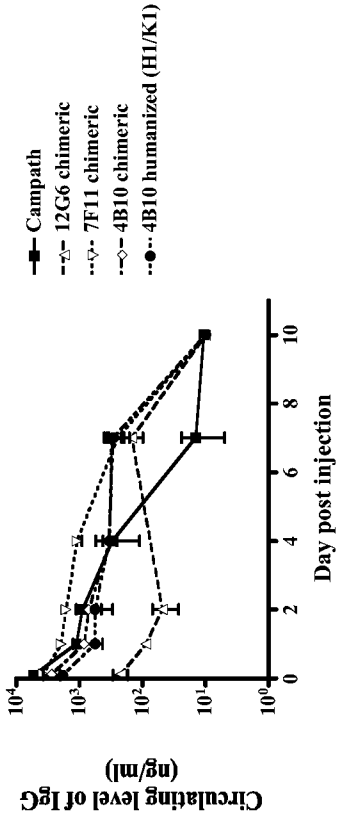

Campath
12G6 chimeric
7F11 chimeric
4B10 chimeric
4B10 humanized (H1/K1)
Circulating level of IgG (ng/ml)
Day post injection
10^4
10^3
10^2
10^1
10^0
0
2
4
6
8
10

Fig. 22 A

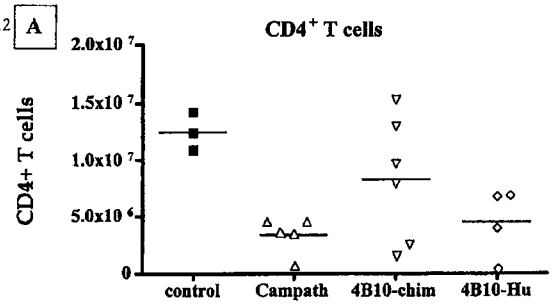


Fig. 22 B

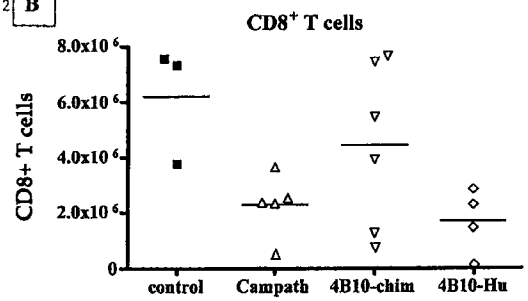


Fig. 22 C

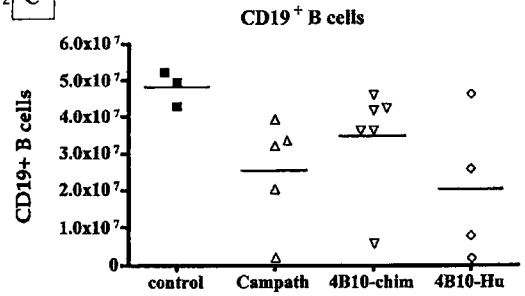


FIG. 22A - 22C

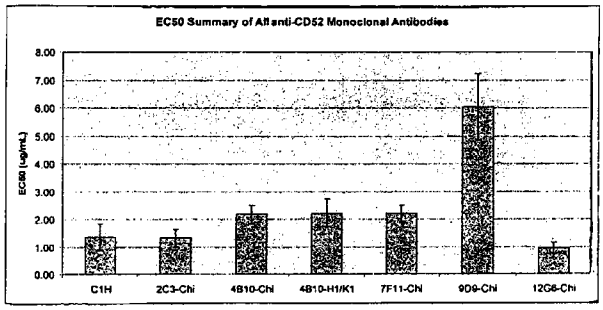

EC50 Summary of All anti-CD52 Monoclonal Antibodies
EC50 (ug/mL)
8.00
7.00
6.00
5.00
4.00
3.00
2.00
1.00
0.00
C1H
2C3-Chi
4B10-Chi
4B10-H1/K1
7F11-Chi
9D9-Chi
12G8-Chi

FIG. 23

Humanized 7F11 clone heavy chain variable region sequences

7F11-SFD1
EVQLVESGGGLVQPGGSLRLSCAAS**GFTFTDYYMS**WVRQAPGKGLEWVG**FIRNK**
ANGYTTEYNASVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYC**TRYIFFDY**WG
QGTTVTVSS (SEQ ID NO: 136)

7F11-SFD2
EVQLVESGGGLVQPGGSLRLSCAAS**GFTFTDYYMS**WVRQAPGKGLEWVG**FIRNK**
ANGYTTEYNASVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYC**ARYIFFDY**WG
QGTTVTVSS (SEQ ID NO: 137)

Humanized 7F11 clone light (kappa) chain variable region sequence

7F11-VK2
DIVMTQTPLSLSVTPGQPASISC**RSSQSLVHTNGNSYLH**WYLQKPGQSPQLLIY**MV**
SNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC**SQSTHVPFT**FGQGTKLEIK
(SEQ ID NO: 138)

FIG. 24

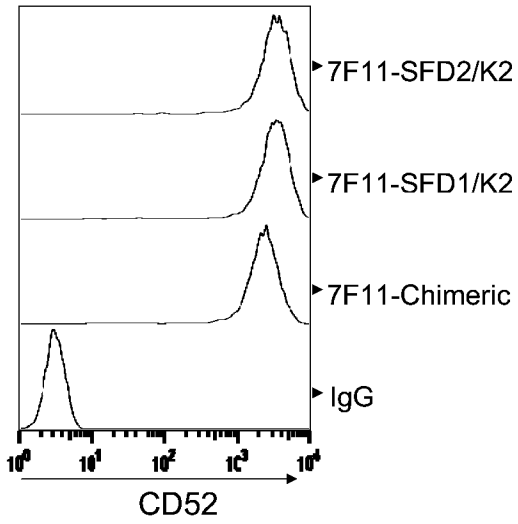

7F11-SFD2/K2
7F11-SFD1/K2
7F11-Chimeric
IgG
10^0
10^1
10^2
10^3
10^4
CD52

FIG. 25

Humanized 2C3 clone heavy chain variable region sequences

2C3-SFD1
EVQLVESGGGLVQPGGSLRLSCAAS**GFTFNTYWMN**WVRQAPGKGLEWVG**QIRLKSNNYATHYAESVKG**RFTISRDDSKNSLYLQM
NSLKTEDTAVYYC**TPVDF**WGQGTTVTVSS (SEQ ID NO: 139)

2C3-VH 12
EVQLVESGGGLVQPGGSLRLSCAAS**GFTFNTYWMN**WVRQAPGKGLEWVG**QIRLKSNNYATHYAESVKG**RFTISRDDSKNS<u>V</u>YLQ
MNSLKTEDTAVYYC**TPVDF**WGQGTTVTVSS (SEQ ID NO: 140)

2C3-VH 15
EVQLVESGGGLVQPGGSLRLSCAAS**GFTFNTYWMN**WVRQAPGKGLEWV<u>A</u>**QIRLKSNNYATHYAESVKG**RFTISRDDSKNSLYLQM
NSLKTEDTAVYYC**TPVDF**WGQGTTVTVSS (SEQ ID NO: 141)

2C3-VH16
EVQLVESGGGLVQPGGSLRLSCAAS**GFTFNTYWMN**WVRQAPGKGLEWV<u>A</u>**QIRLKSNNYATHYAESVKG**RFTISRDDSKNS<u>V</u>YLQ
MNSLKTEDTAVYYC**TPVDF**WGQGTTVTVSS (SEQ ID NO: 142)

2C3-VH17
EVQLVESGGGLVQPGGS<u>M</u>RLSCAAS**GFTFNTYWMN**WVRQAPGKGLEWV<u>A</u>**QIRLKSNNYATHYAESVKG**RFTISRDDSKNS<u>V</u>YLQ
MNSLKTEDTAVYYC**TPVDF**WGQGTTVTVSS (SEQ ID NO: 143)

2C3-VH19
EVQLVESGGGLVQPGGS<u>M</u>RLSCAAS**GFTFNTYWMN**WVRQAP<u>E</u>KGLEWV<u>A</u>**QIRLKSNNYATHYAESVKG**RFTISRDDSKNS<u>V</u>YLQ
MNSLKTEDTAVYYC**TPVDF**WGQGTTVTVSS (SEQ ID NO: 144)

FIG. 26A

Humanized 2C3 clone light (kappa) chain variable region sequences

2C3-VK1
DIVMTQTPLSLSVTPGQPASISC**KSSQSLLYSNGKTYLN**WYLQKPGQSPQLLIY**LVSKLDS**GVPDRFSGSGSGTDFTLKISRVEAE
DVGVYYC**VQGTHLHT**FGQGTRLEIK (SEQ ID NO: 145)

2C3-VK11
DIVMTQTPLSLSVTPGQPASISC**KSSQSLLYSNGKTYLN**WYLQKPGQSPQRLIY**LVSKLDS**GVPDRFSGSGSGTDFTLKISRVEAE
DVGVYYC**VQGTHLHT**FGQGTRLEIK (SEQ ID NO: 146)

2C3-VK12
DIVMTQTPLSLSVTPGQPASISC**KSSQSLLYSNGKTYLN**WLLQKPGQSPQRLIY**LVSKLDS**GVPDRFSGSGSGTDFTLKISRVEAE
DVGVYYC**VQGTHLHT**FGQGTRLEIK (SEQ ID NO: 147)

2C3-VK13
DIVITQTPLSLSVTPGQPVSISC**KSSQSLLYSNGKTYLN**WLLQKPGQSPKRLIY**LVSKLDS**GVPDRFSGSGSGTDFTLKISRVEAE
DVGVYYC**VQGTHLHT**FGQGTRLEIK (SEQ ID NO: 148)

FIG. 26B

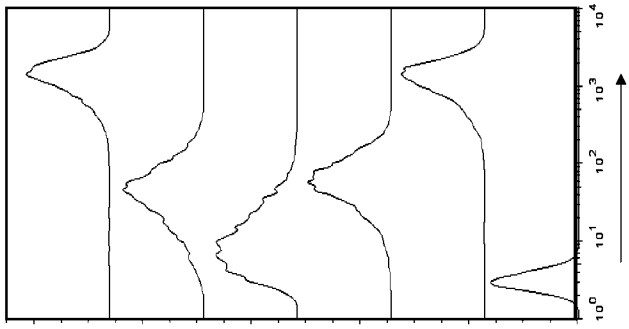


FIG. 27A

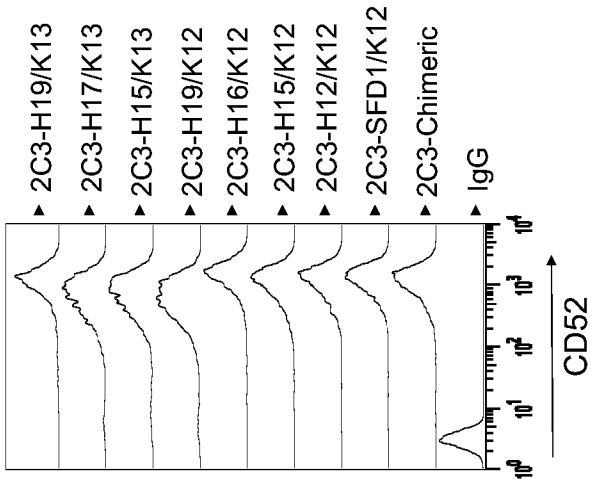


FIG. 27B

Humanized 12G6 clone heavy chain variable region sequences

12G6-SFD1
EVQLVESGGGLVQPGGSLRLSCAAS**GFPFSNYWMN**WVRQAPGKGLEWVG**QIRLK**
SNNYATHYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYC**TPIDY**WGQGTT
VTVSS (SEQ ID NO: 149)

12G6-VH 10
EVQLVESGGGLVQPGGSLRLSCAAS**GFPFSNYWMN**WVRQAPGKGLEWVG**QIRLK**
SNNYATHYAESVKGRFTISRDDSKNS<u>V</u>YLQMNSLKTEDTAVYYC**TPIDY**WGQGTT
VTVSS (SEQ ID NO: 150)

12G6-VH 11
EVQLVESGGGLVQPGGSLRLSCAAS**GFPFSNYWMN**WVRQAPGKGLEWV<u>A</u>**QIRLK**
SNNYATHYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYC**TPIDY**WGQGTT
VTVSS (SEQ ID NO: 151)

12G6-VH12
EVQLVESGGGLVQPGGSLRLSCAAS**GFPFSNYWMN**WVRQAPGKGLEWV<u>A</u>**QIRLK**
SNNYATHYAESVKGRFTISRDDSKNS<u>V</u>YLQMNSLKTEDTAVYYC**TPIDY**WGQGTT
VTVSS (SEQ ID NO: 152)

FIG. 28A

Humanized 12G6 clone light (kappa) chain variable region sequence

12G6-VK1
DIVMTQTPLSLSVTPGQPASISC**KSSQSLLYSNGKTYLN**WYLQKPGQSPQLLIY
LVSKLDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC**VQGSHFHT**FGQGTK
LEIK (SEQ ID NO: 153)

12G6-VK10
DIVMTQTPLSLSVTPGQPASISC**KSSQSLLYSNGKTYLN**WVLQKPGQSPQLLIY
LVSKLDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC**VQGSHFHT**FGQGTK
LEIK (SEQ ID NO: 154)

12G6-VK11
DIVMTQTPLSLSVTPGQPASISC**KSSQSLLYSNGKTYLN**WVLQKPGQSPKRLIY
LVSKLDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC**VQGSHFHT**FGQGTK
LEIK (SEQ ID NO: 155)

12G6-VK12
DIVMTQTPLSLSVTPGQPASISC**KSSQSLLYSNGKTYLN**WVLQKPGQSPQRLIY
LVSKLDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC**VQGSHFHT**FGQGTK
LEIK (SEQ ID NO: 156)

12G6-VK13
DIVMTQTPLSLSVTPGQPASISC**KSSQSLLYSNGKTYLN**WYLQKPGQSPQRLIY
LVSKLDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC**VQGSHFHT**FGQGTK
LEIK (SEQ ID NO: 157)

FIG. 28B

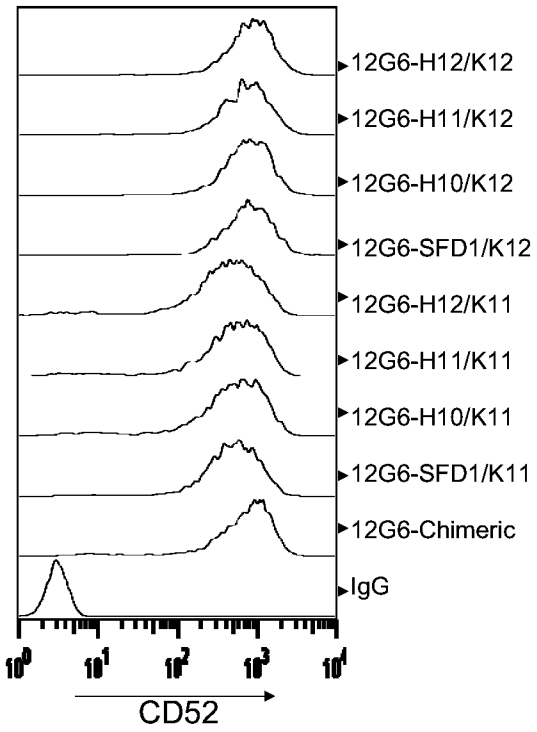

12G6-H12/K12
12G6-H11/K12
12G6-H10/K12
12G6-SFD1/K12
12G6-H12/K11
12G6-H11/K11
12G6-H10/K11
12G6-SFD1/K11
12G6-Chimeric
IgG
10^0
10^1
10^2
10^3
10^4
CD52

FIG. 29

Humanized 9D9 clone heavy chain variable region sequences

9D9-VH10
EVQLLESGGGLVQPGGSLRLSCAAS**GFTFSDAWMD**WVRQAPGKGLEWVS**EIRNKA**
KNHATYYAESVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYC**TTLDS**WGQGTTV
TVSS (SEQ ID NO: 158)

9D9-VH11
EVQLLESGGGLVQPGGSLRLSCAAS**GFTFSDAWMD**WVRQAPGKGLELTA**EIRNK**
AKNHATYYAESVKGRFTISRDNSKSTVYLQMNSLRAEDTAVYYC**TTLDS**WGQGT
TVTVSS (SEQ ID NO: 159)

9D9-VH15
EVQLLESGGGLVQPGGSLRLSCAAS**GFTFSDAWMD**WVRQAPGKGLELTA**EIRNK**
AKNHATYYAESVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYC**TTLDS**WGQGT
TVTVSS (SEQ ID NO: 160)

9D9-VH 16
EVQLLESGGGLVQPGGSLRLSCAAS**GFTFSDAWMD**WVRQAPGKGLELVS**EIRNK**
AKNHATYYAESVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYC**TTLDS**WGQGT
TVTVSS (SEQ ID NO: 161)

9D9-VH 17
EVQLLESGGGLVQPGGSLRLSCAAS**GFTFSDAWMD**WVRQAPGKGLELTS**EIRNK**
AKNHATYYAESVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYC**TTLDS**WGQGT
TVTVSS (SEQ ID NO: 162)

9D9-VH 18
EVQLLESGGGLVQPGGSLRLSCAAS**GFTFSDAWMD**WVRQAPGKGLELVA**EIRNK**
AKNHATYYAESVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYC**TTLDS**WGQGT
TVTVSS (SEQ ID NO: 163)

FIG. 30A

Humanized 9D9 clone light (kappa) chain variable region sequences

9D9-VK2
DIVMTQTPLSLSVTPGQPASISC**KSSQSLLDSDGKTYLN**WYLQKPGQSPQLLIY**L**
VSALDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC**WQGTHFPWT**FGQGTK
LEIK (SEQ ID NO: 164)

9D9-VK12
DIVMTQTPLSLSVTPGQPASISC**KSSQSLLDSDGKTYLN**WLLQKPGQSPKRLIY**L**
VSALDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC**WQGTHFPWT**FGQGTK
LEIK (SEQ ID NO: 165)

9D9-VK13
DIVMTQTPLSLSVTPGQPASISC**KSSQSLLDSDGKTYLN**WLLQKPGQSPQRLIY**L**
VSALDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC**WQGTHFPWT**FGQGTK
LEIK (SEQ ID NO: 166)

9D9-VK14
DIVMTQTPLSLSVTPGQPASISC**KSSQSLLDSDGKTYLN**WYLQKPGQSPQRLIY**L**
VSALDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC**WQGTHFPWT**FGQGTK
LEIK (SEQ ID NO: 167)

9D9-VK15
DIVMTQTPLSLSVTPGQPASISC**KSSQSLLDSDGKTYLN**WYLQKPGQSPKRLIY**L**
VSALDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC**WQGTHFPWT**FGQGTK
LEIK (SEQ ID NO: 168)

FIG. 30B

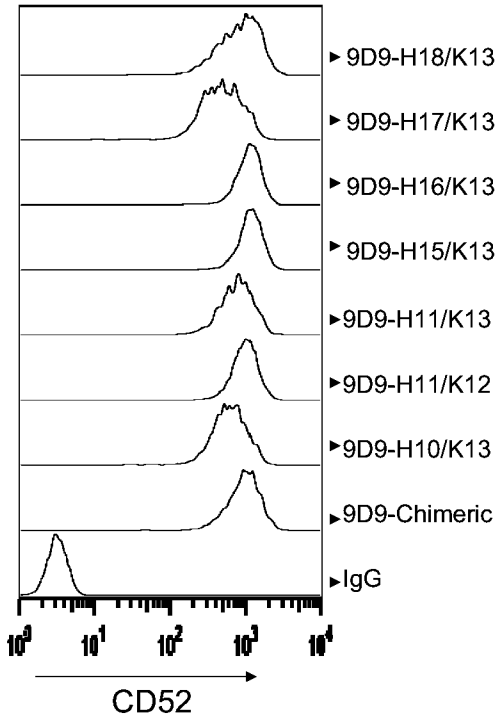

9D9-H18/K13
9D9-H17/K13
9D9-H16/K13
9D9-H15/K13
9D9-H11/K13
9D9-H11/K12
9D9-H10/K13
9D9-Chimeric
IgG
10^0
10^1
10^2
10^3
10^4
CD52

FIG. 31

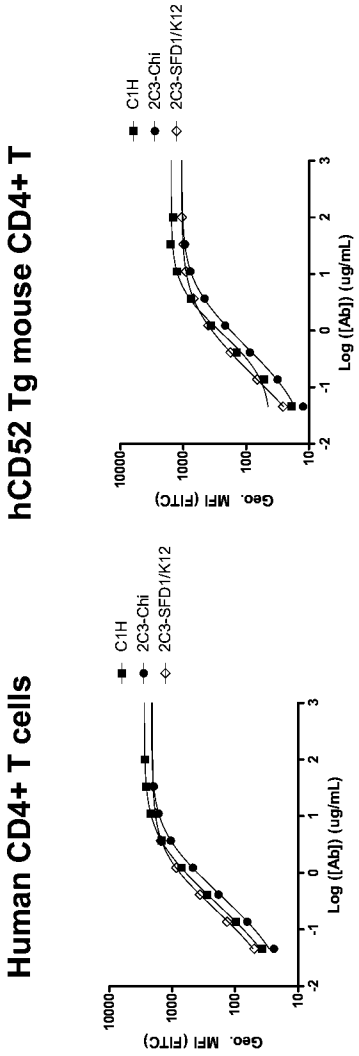

Human CD4+ T cells
hCD52 Tg mouse CD4+ T
C1H
2C3-Chi
2C3-SFD1/K12
Geo. MFI (FITC)
Log ([Ab]) (ug/mL)
10000
1000
100
10
-2
-1
0
1
2
3

FIG. 32A

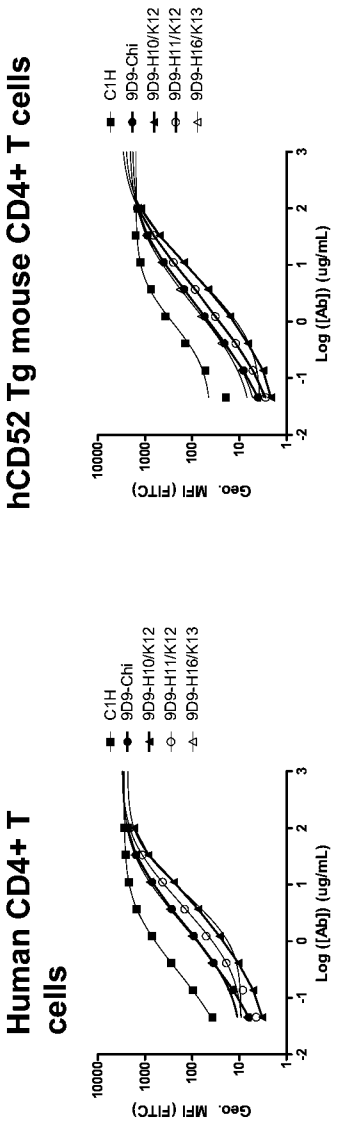

Human CD4+ T cells
hCD52 Tg mouse CD4+ T cells
C1H
9D9-Chi
9D9-H10/K12
9D9-H11/K12
9D9-H16/K13
Geo. MFI (FITC)
Log ([Ab]) (ug/mL)

FIG. 32B

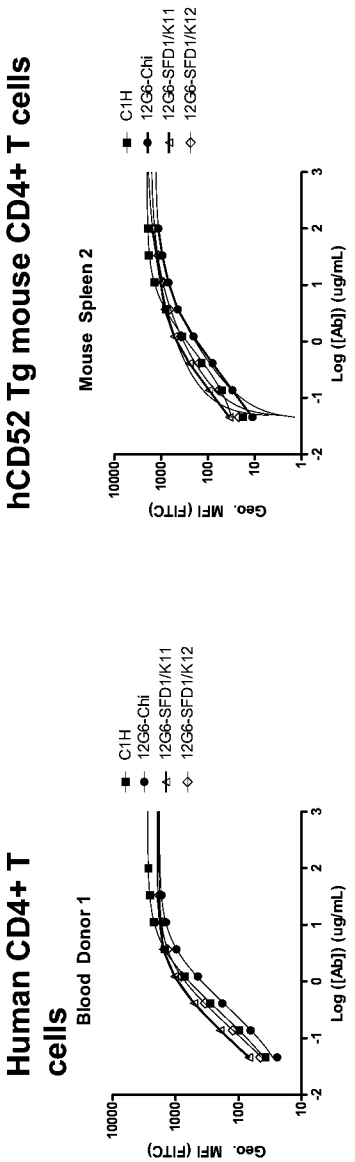

hCD52 Tg mouse CD4+ T cells
Mouse Spleen 2
C1H
12G6-Chi
12G6-SFD1/K11
12G6-SFD1/K12
Geo. MFI (FITC)
Log ([Ab]) (ug/mL)
Human CD4+ T cells
Blood Donor 1
C1H
12G6-Chi
12G6-SFD1/K11
12G6-SFD1/K12
Geo. MFI (FITC)
Log ([Ab]) (ug/mL)

FIG. 32C

	EC_{50} (nM)	
	Human CD4+ T cells	huCD52 transgenic mouse CD4+ T cells
Campath-1H®	21.91	25.08
2C3-Chimeric	25.93	30.81
2C3-SFD1/K12	11.00	13.61
12G6-Chimeric	22.41	34.42
12G6-SFD1/K11	7.30	13.17
12G6-SFD1/K12	10.58	

FIG. 33

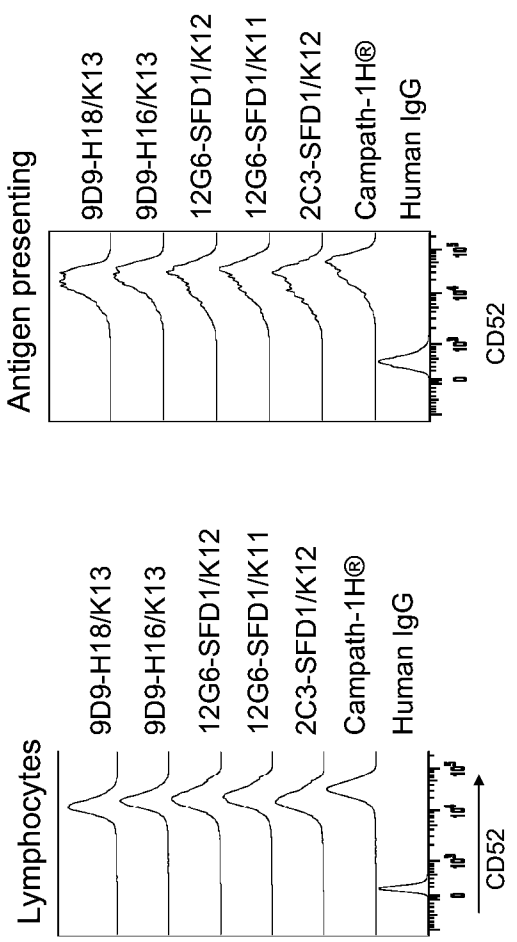

Antigen presenting
9D9-H18/K13
9D9-H16/K13
12G6-SFD1/K12
12G6-SFD1/K11
2C3-SFD1/K12
Campath-1H®
Human IgG
CD52
Lymphocytes
9D9-H18/K13
9D9-H16/K13
12G6-SFD1/K12
12G6-SFD1/K11
2C3-SFD1/K12
Campath-1H®
Human IgG
CD52

FIG. 34

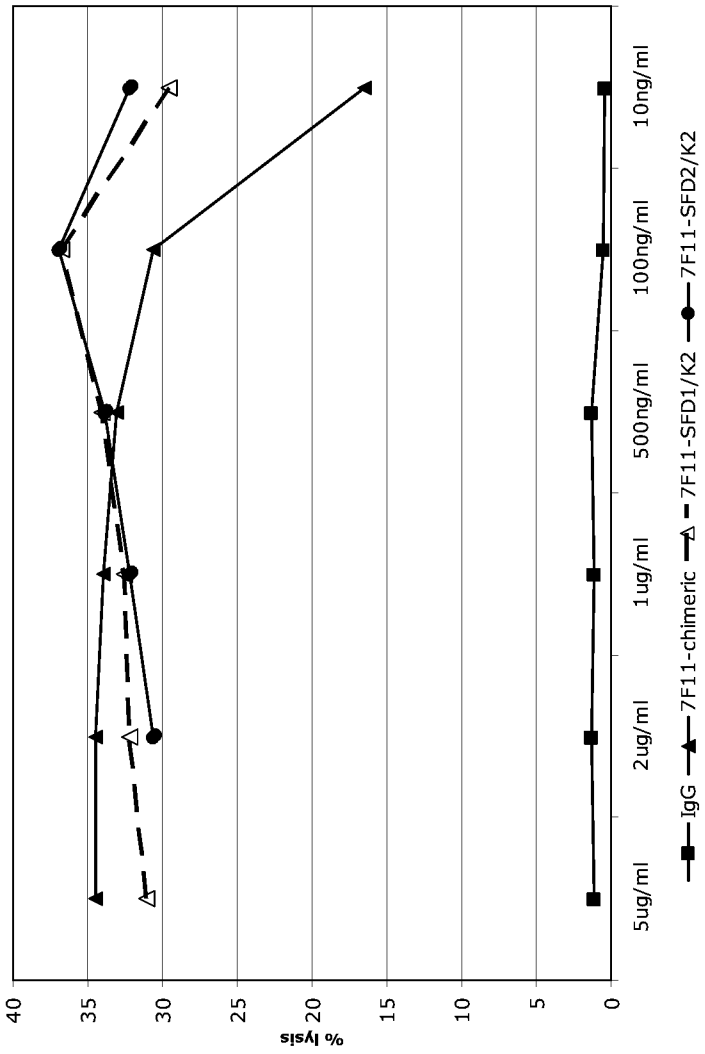

% lysis
40
35
30
25
20
15
10
5
0
5ug/ml
2ug/ml
1ug/ml
500ng/ml
100ng/ml
10ng/ml
IgG
7F11-chimeric
7F11-SFD1/K2
7F11-SFD2/K2

FIG. 35

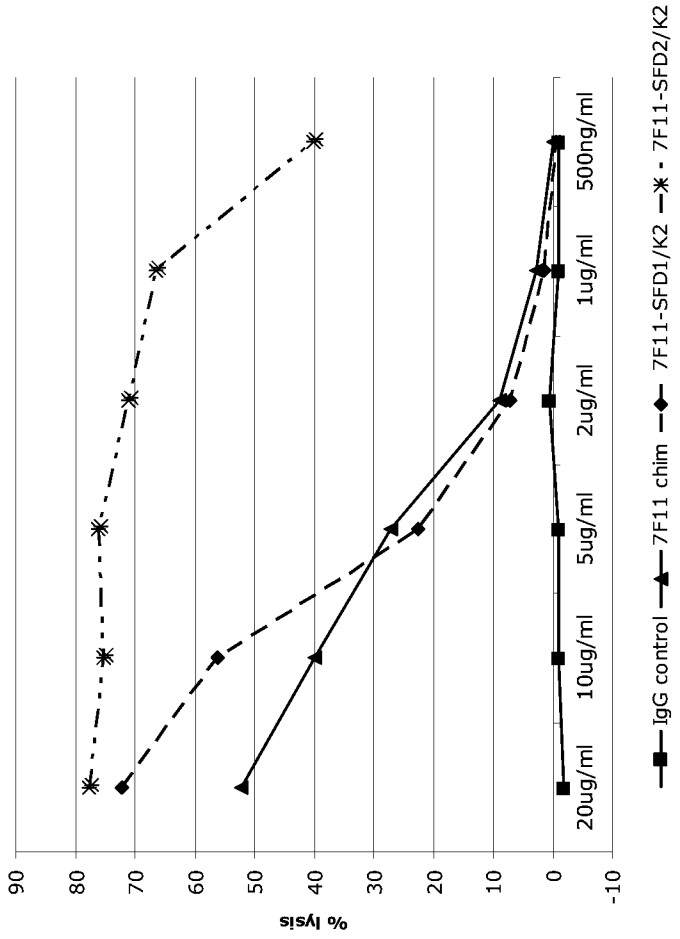

% lysis
90
80
70
60
50
40
30
20
10
0
-10
20ug/ml
10ug/ml
5ug/ml
2ug/ml
1ug/ml
500ng/ml
IgG control
7F11 chim
7F11-SFD1/K2
7F11-SFD2/K2

FIG. 36

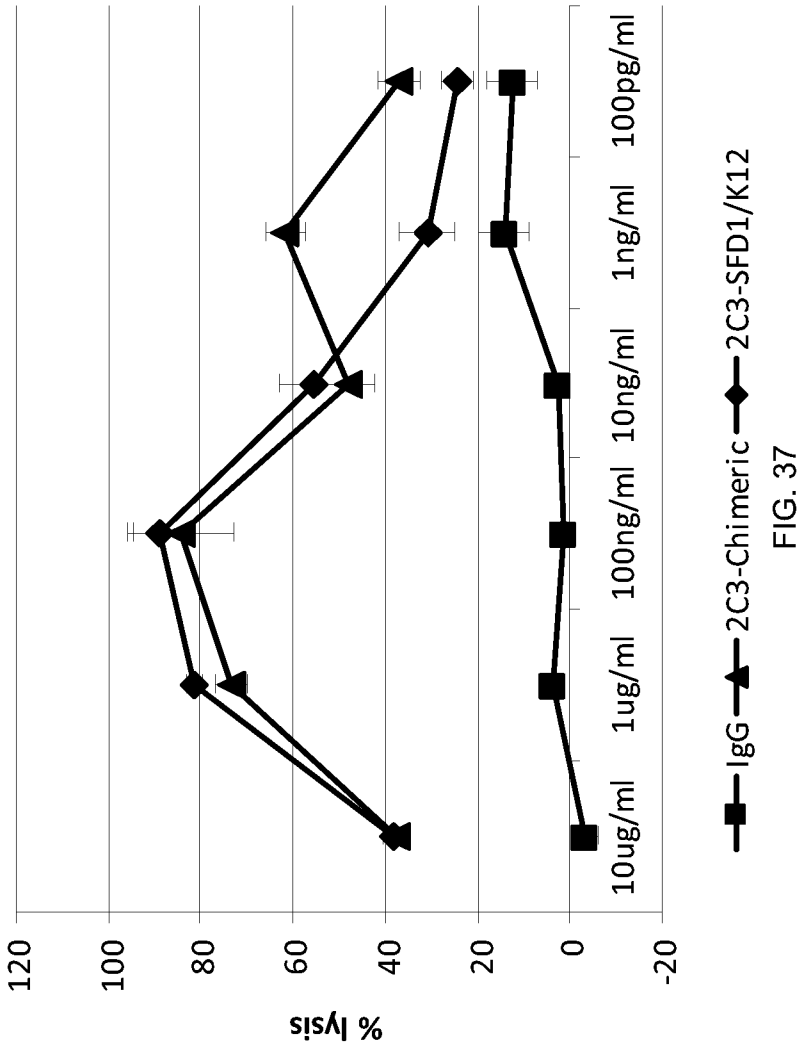

% lysis
120
100
80
60
40
20
0
-20
10ug/ml
1ug/ml
100ng/ml
10ng/ml
1ng/ml
100pg/ml
IgG
2C3-Chimeric
2C3-SFD1/K12

FIG. 37

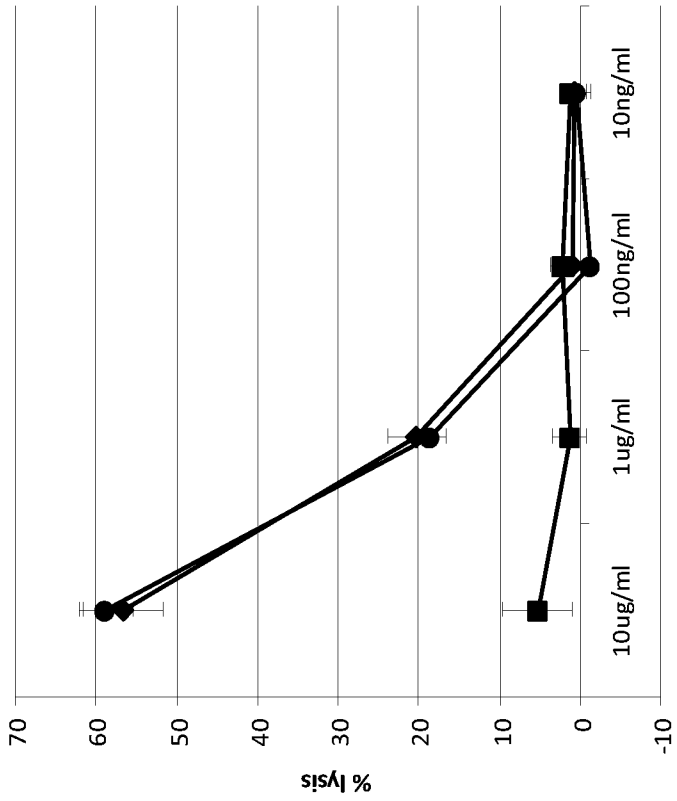

% lysis
70
60
50
40
30
20
10
0
-10
10ug/ml
1ug/ml
100ng/ml
10ng/ml
IgG
2C3-Chimeric
2C3-SFD1/K12

FIG. 38

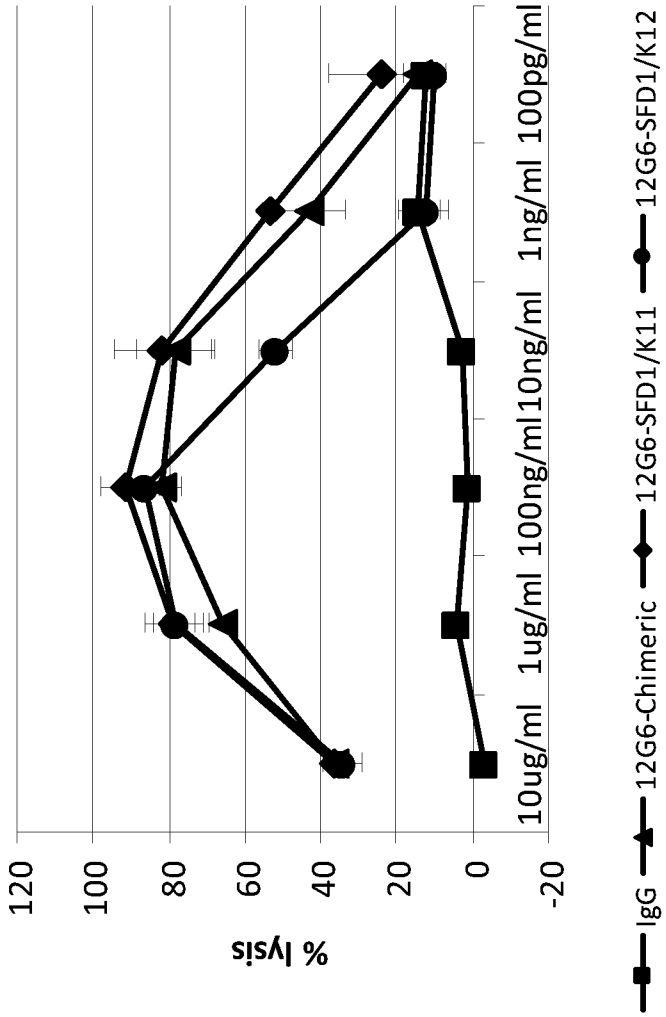

% lysis
120
100
80
60
40
20
0
-20
10ug/ml
1ug/ml
100ng/ml
10ng/ml
1ng/ml
100pg/ml
IgG
12G6-Chimeric
12G6-SFD1/K11
12G6-SFD1/K12

FIG. 39

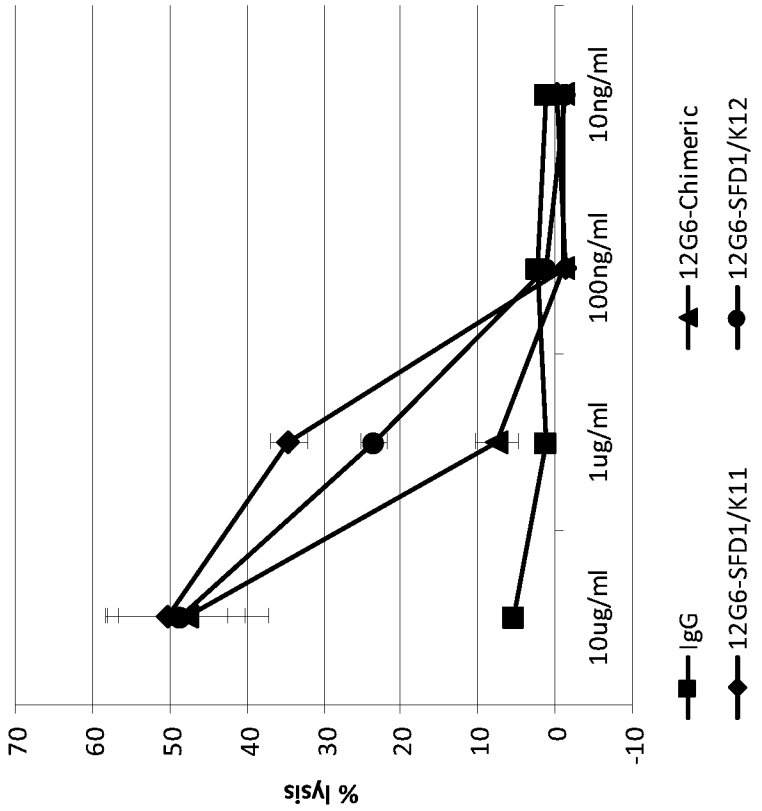

% lysis
70
60
50
40
30
20
10
0
-10
10ug/ml
1ug/ml
100ng/ml
10ng/ml
IgG
12G6-Chimeric
12G6-SFD1/K11
12G6-SFD1/K12

FIG. 40

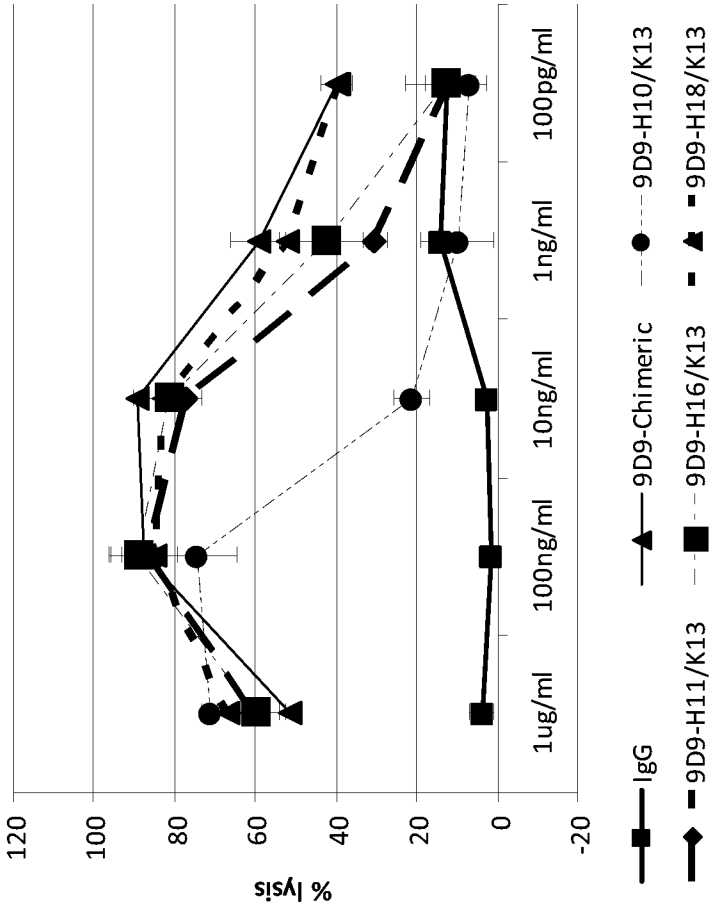

% lysis
120
100
80
60
40
20
0
-20
1ug/ml
100ng/ml
10ng/ml
1ng/ml
100pg/ml
IgG
9D9-Chimeric
9D9-H10/K13
9D9-H11/K13
9D9-H16/K13
9D9-H18/K13

FIG. 41

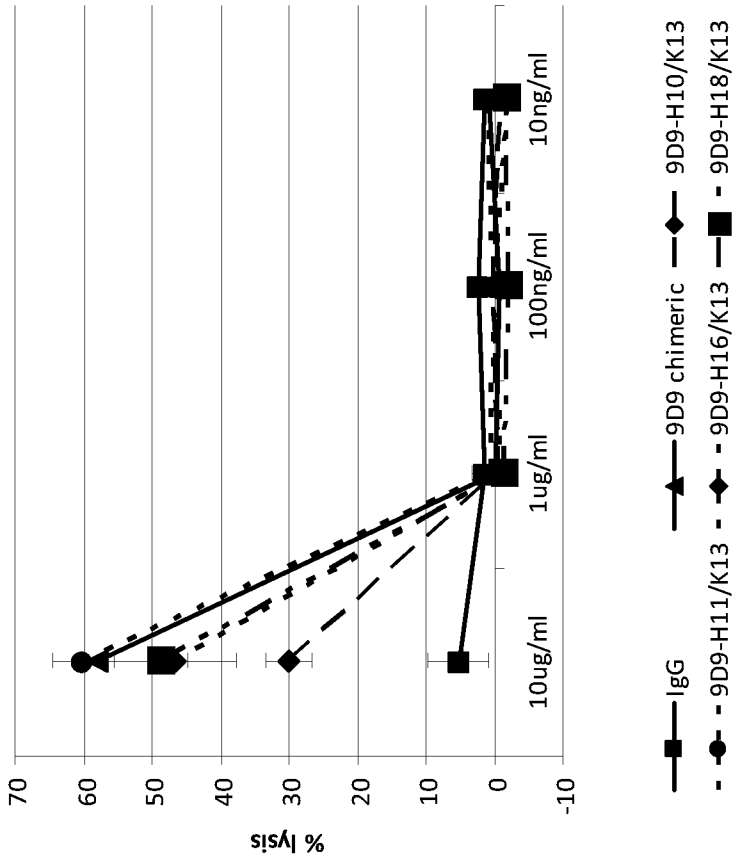

% lysis
70
60
50
40
30
20
10
0
-10
10ug/ml
1ug/ml
100ng/ml
10ng/ml
IgG
9D9 chimeric
9D9-H10/K13
9D9-H11/K13
9D9-H16/K13
9D9-H18/K13

FIG. 42

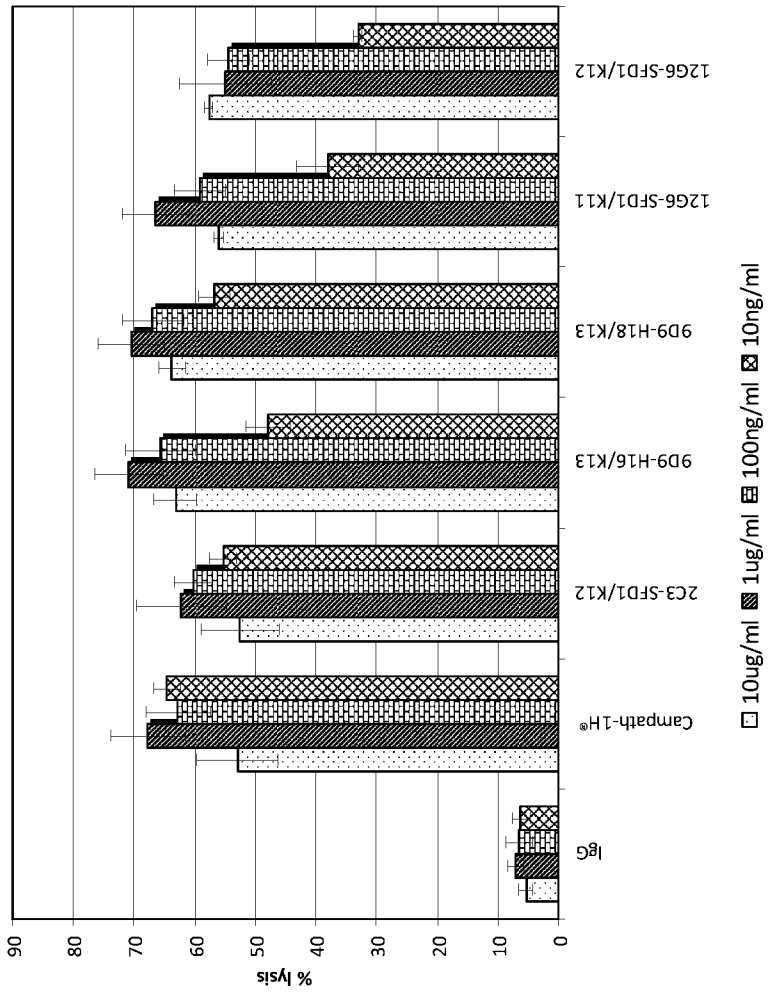

% lysis
0
10
20
30
40
50
60
70
80
90
IgG
Campath-1H®
2C3-SFD1/K12
9D9-H16/K13
9D9-H18/K13
12G6-SFD1/K11
12G6-SFD1/K12
10ug/ml
1ug/ml
100ng/ml
10ng/ml

FIG. 43

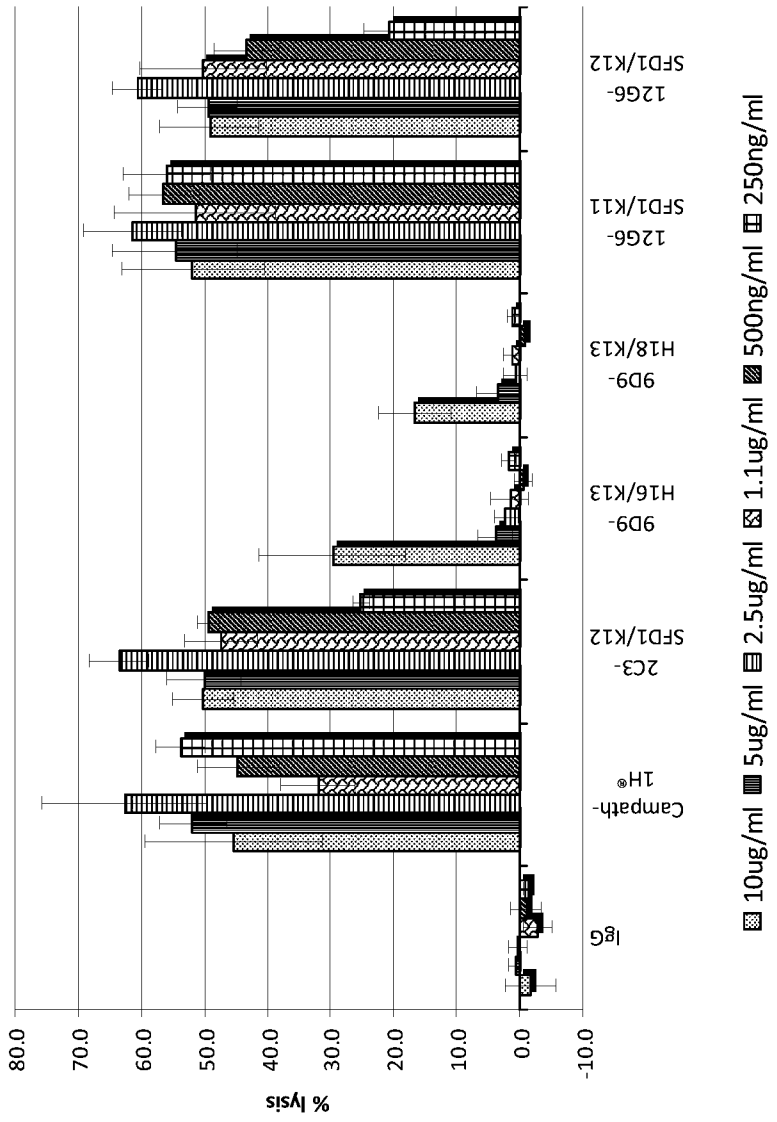

% lysis
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
IgG
Campath-1H®
2C3-SFD1/K12
9D9-H16/K13
9D9-H18/K13
12G6-SFD1/K11
12G6-SFD1/K12
10ug/ml
5ug/ml
2.5ug/ml
1.1ug/ml
500ng/ml
250ng/ml

FIG. 44

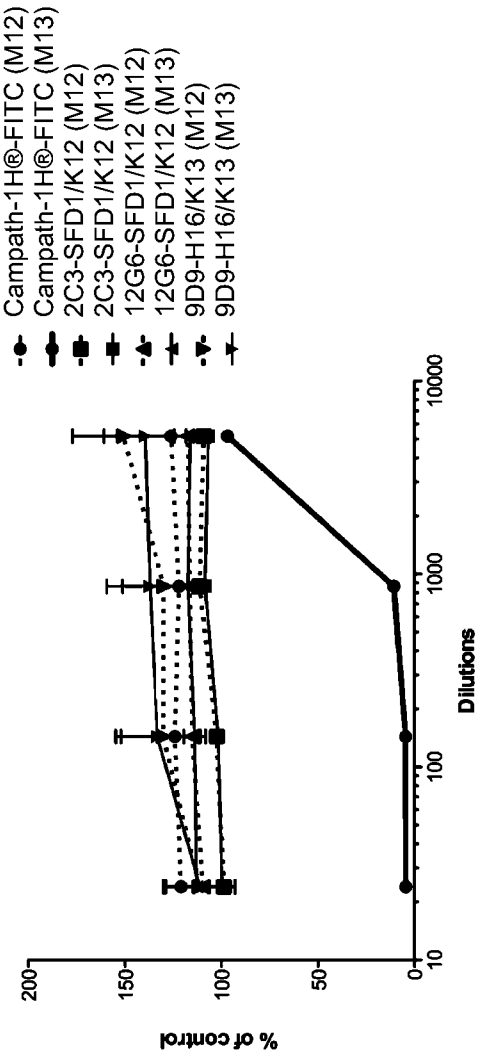

Campath-1H®-FITC (M12)
Campath-1H®-FITC (M13)
2C3-SFD1/K12 (M12)
2C3-SFD1/K12 (M13)
12G6-SFD1/K12 (M12)
12G6-SFD1/K12 (M13)
9D9-H16/K13 (M12)
9D9-H16/K13 (M13)
% of control
0
50
100
150
200
10
100
1000
10000
Dilutions

FIG. 45

FIG. 46A

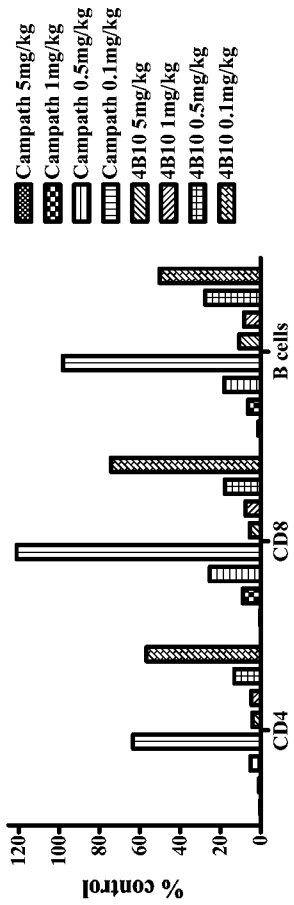
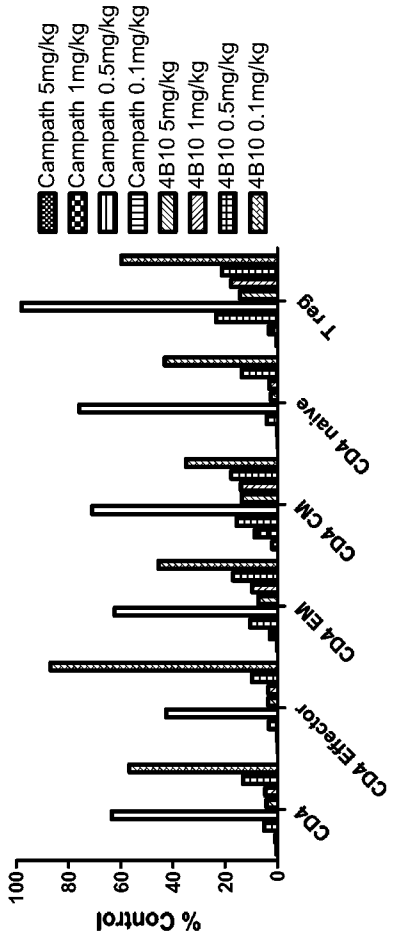

Campath 5mg/kg
Campath 1mg/kg
Campath 0.5mg/kg
Campath 0.1mg/kg
4B10 5mg/kg
4B10 1mg/kg
4B10 0.5mg/kg
4B10 0.1mg/kg
% control
120
100
80
60
40
20
0
CD4
CD8
B cells

FIG. 46B


Campath 5mg/kg
Campath 1mg/kg
Campath 0.5mg/kg
Campath 0.1mg/kg
4B10 5mg/kg
4B10 1mg/kg
4B10 0.5mg/kg
4B10 0.1mg/kg
% Control
0
20
40
60
80
100
CD4
CD4 Effector
CD4 EM
CD4 CM
CD4 naive
T reg

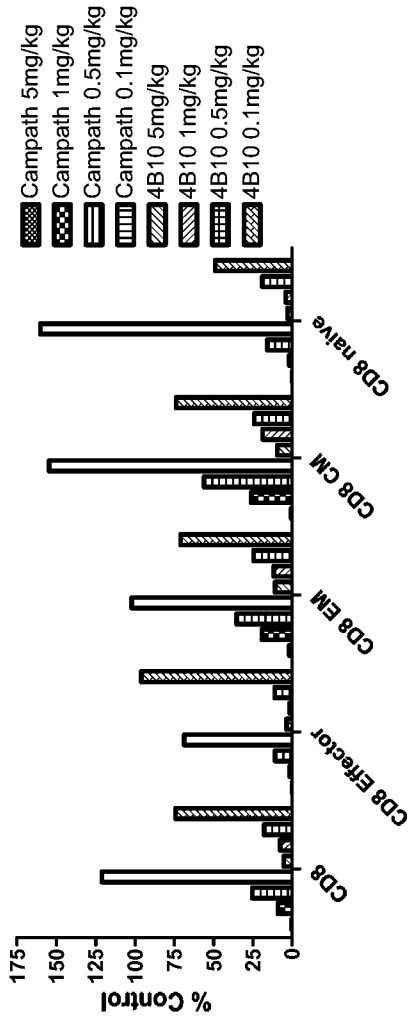

Campath 5mg/kg
Campath 1mg/kg
Campath 0.5mg/kg
Campath 0.1mg/kg
4B10 5mg/kg
4B10 1mg/kg
4B10 0.5mg/kg
4B10 0.1mg/kg
% Control
0
25
50
75
100
125
150
175
CD8
CD8 Effector
CD8 EM
CD8 CM
CD8 naive

FIG. 46C

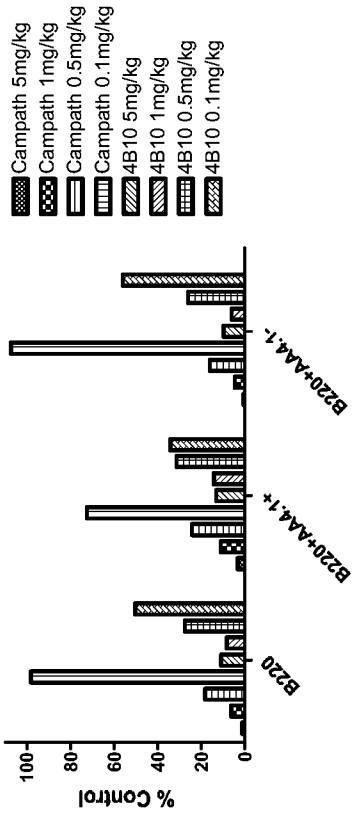


FIG. 46D

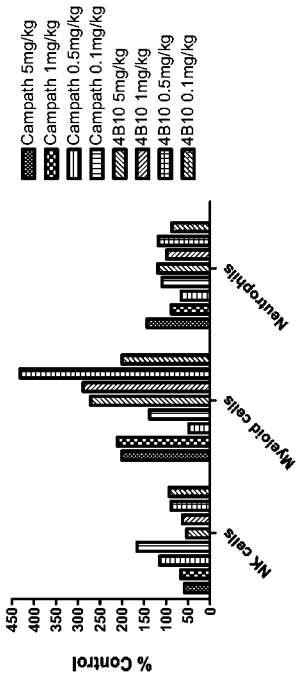


FIG. 46E

FIG. 47A

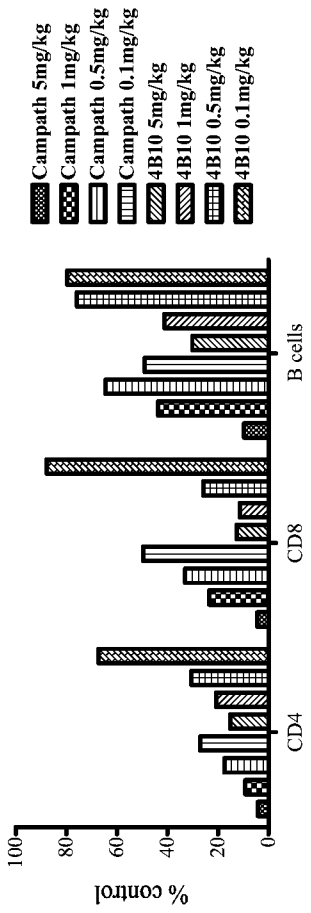
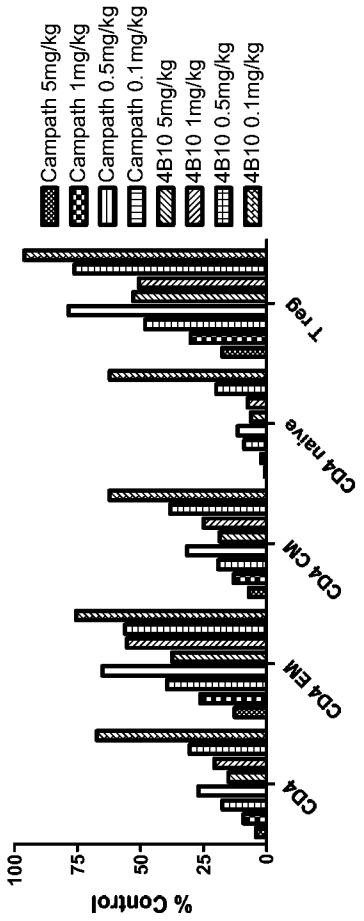

Campath 5mg/kg
Campath 1mg/kg
Campath 0.5mg/kg
Campath 0.1mg/kg
4B10 5mg/kg
4B10 1mg/kg
4B10 0.5mg/kg
4B10 0.1mg/kg
% control
100
80
60
40
20
0
CD4
CD8
B cells

FIG. 47B


Campath 5mg/kg
Campath 1mg/kg
Campath 0.5mg/kg
Campath 0.1mg/kg
4B10 5mg/kg
4B10 1mg/kg
4B10 0.5mg/kg
4B10 0.1mg/kg
% Control
100
75
50
25
0
CD4
CD4 EM
CD4 CM
CD4 naive
T reg

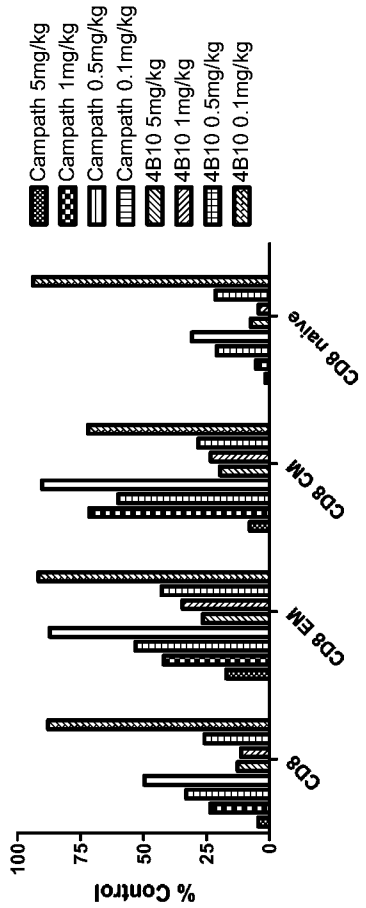

Campath 5mg/kg
Campath 1mg/kg
Campath 0.5mg/kg
Campath 0.1mg/kg
4B10 5mg/kg
4B10 1mg/kg
4B10 0.5mg/kg
4B10 0.1mg/kg
% Control
100
75
50
25
0
CD8
CD8 EM
CD8 CM
CD8 naive

FIG. 47C

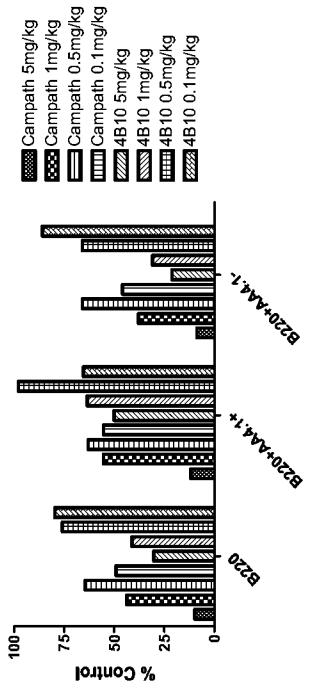


FIG. 47D

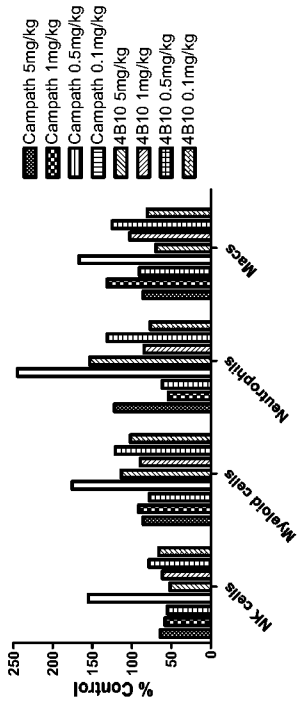


FIG. 47E

FIG. 48

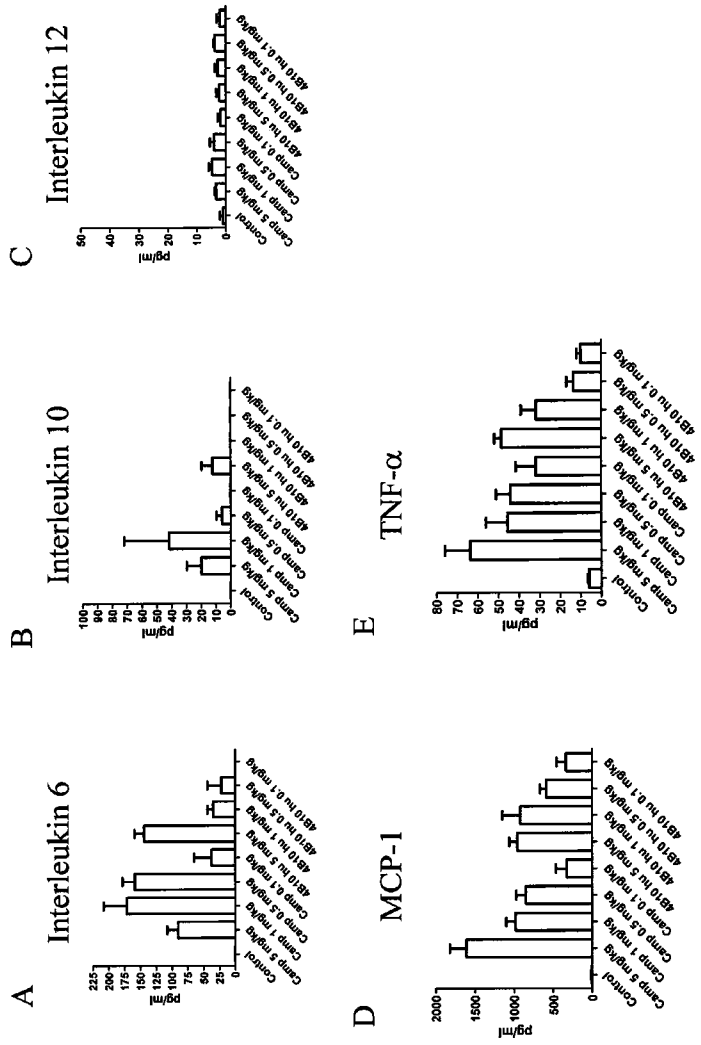

A
Interleukin 6
pg/ml
B
Interleukin 10
pg/ml
C
Interleukin 12
pg/ml
D
MCP-1
pg/ml
E
TNF-α
pg/ml
Control
Camp 5 mg/kg
Camp 1 mg/kg
Camp 0.5 mg/kg
Camp 0.1 mg/kg
4B10 hu 5 mg/kg
4B10 hu 1 mg/kg
4B10 hu 0.5 mg/kg
4B10 hu 0.1 mg/kg

FIG. 49

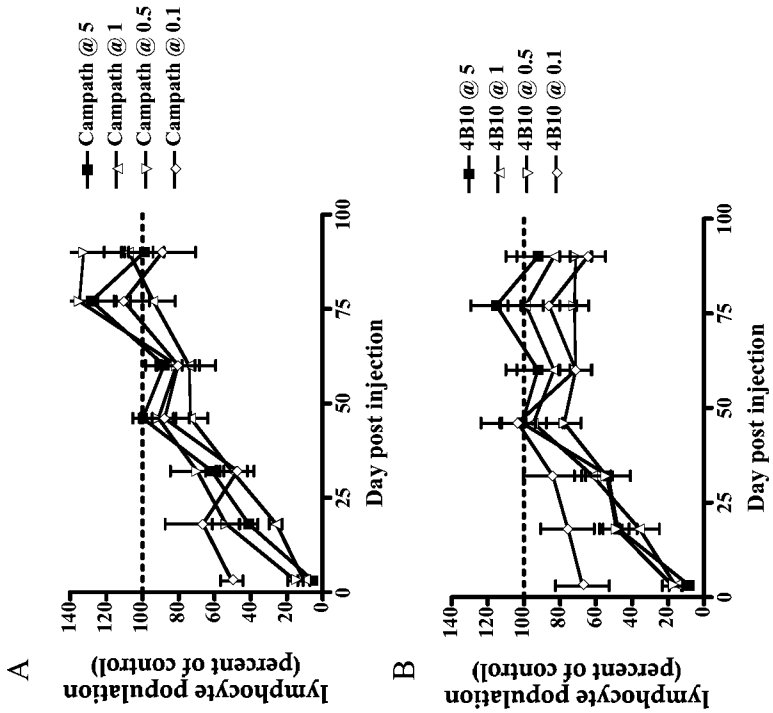

A
Campath @ 5
Campath @ 1
Campath @ 0.5
Campath @ 0.1
Lymphocyte population (percent of control)
Day post injection
B
4B10 @ 5
4B10 @ 1
4B10 @ 0.5
4B10 @ 0.1
Lymphocyte population (percent of control)
Day post injection

FIG. 50A

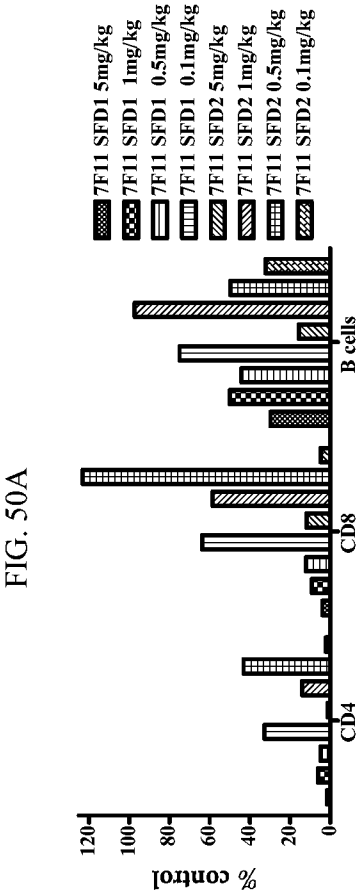

7F11 SFD1 5mg/kg
7F11 SFD1 1mg/kg
7F11 SFD1 0.5mg/kg
7F11 SFD1 0.1mg/kg
7F11 SFD2 5mg/kg
7F11 SFD2 1mg/kg
7F11 SFD2 0.5mg/kg
7F11 SFD2 0.1mg/kg
% control
120
100
80
60
40
20
0
CD4
CD8
B cells

FIG. 50B

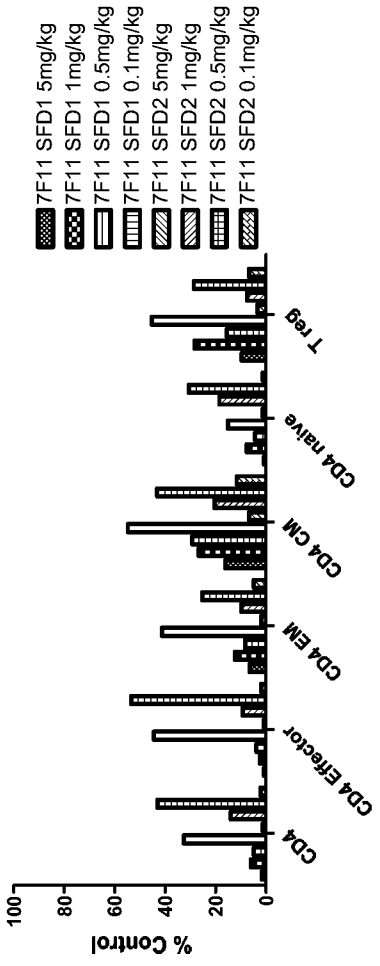
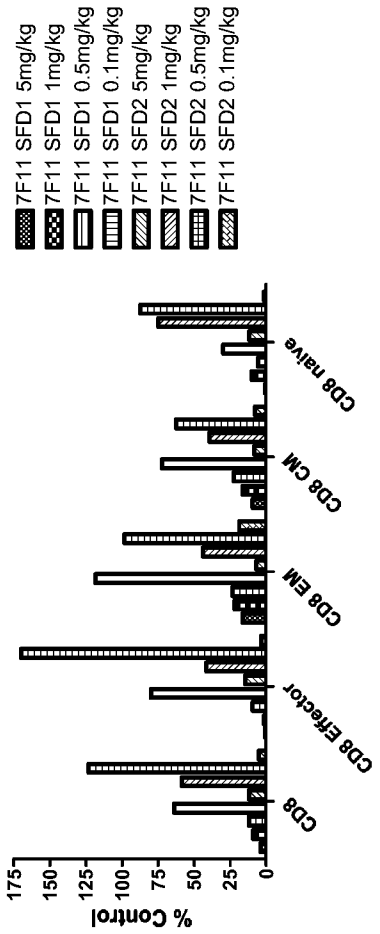

7F11 SFD1 5mg/kg
7F11 SFD1 1mg/kg
7F11 SFD1 0.5mg/kg
7F11 SFD1 0.1mg/kg
7F11 SFD2 5mg/kg
7F11 SFD2 1mg/kg
7F11 SFD2 0.5mg/kg
7F11 SFD2 0.1mg/kg
% Control
0
20
40
60
80
100
CD4
CD4 Effector
CD4 EM
CD4 CM
CD4 naive
T reg

FIG. 50C


7F11 SFD1 5mg/kg
7F11 SFD1 1mg/kg
7F11 SFD1 0.5mg/kg
7F11 SFD1 0.1mg/kg
7F11 SFD2 5mg/kg
7F11 SFD2 1mg/kg
7F11 SFD2 0.5mg/kg
7F11 SFD2 0.1mg/kg
% Control
0
25
50
75
100
125
150
175
CD8
CD8 Effector
CD8 EM
CD8 CM
CD8 naive

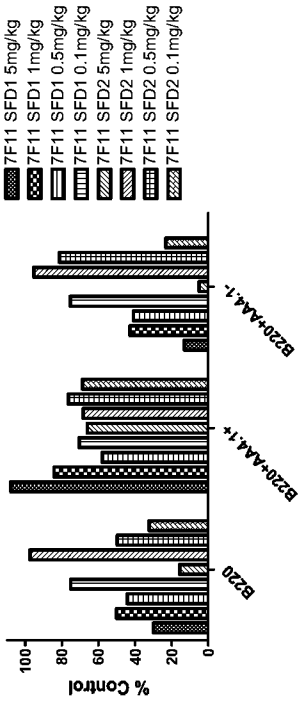


FIG. 50D

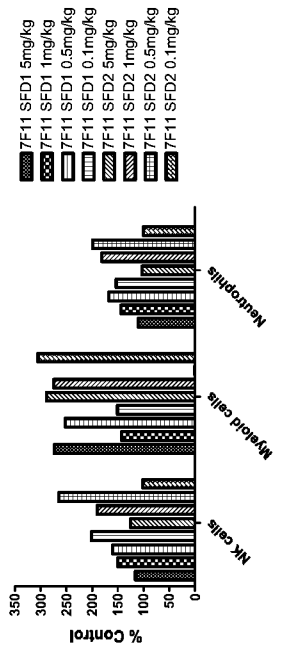


FIG. 50E

FIG. 51A

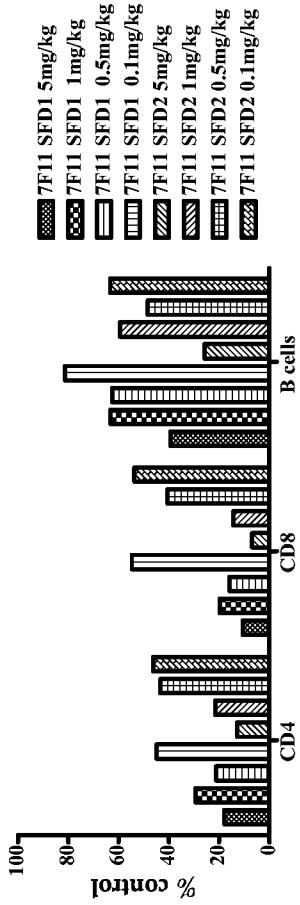
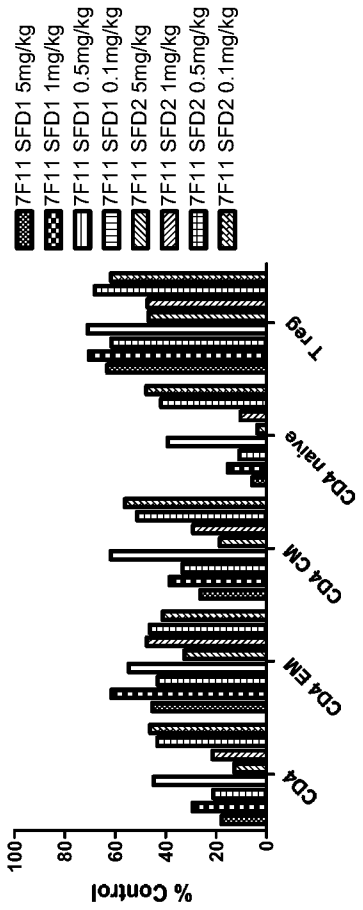

7F11 SFD1 5mg/kg
7F11 SFD1 1mg/kg
7F11 SFD1 0.5mg/kg
7F11 SFD1 0.1mg/kg
7F11 SFD2 5mg/kg
7F11 SFD2 1mg/kg
7F11 SFD2 0.5mg/kg
7F11 SFD2 0.1mg/kg
% control
100
80
60
40
20
0
CD4
CD8
B cells

FIG. 51B


7F11 SFD1 5mg/kg
7F11 SFD1 1mg/kg
7F11 SFD1 0.5mg/kg
7F11 SFD1 0.1mg/kg
7F11 SFD2 5mg/kg
7F11 SFD2 1mg/kg
7F11 SFD2 0.5mg/kg
7F11 SFD2 0.1mg/kg
% Control
100
80
60
40
20
0
CD4
CD4 EM
CD4 CM
CD4 naive
T reg

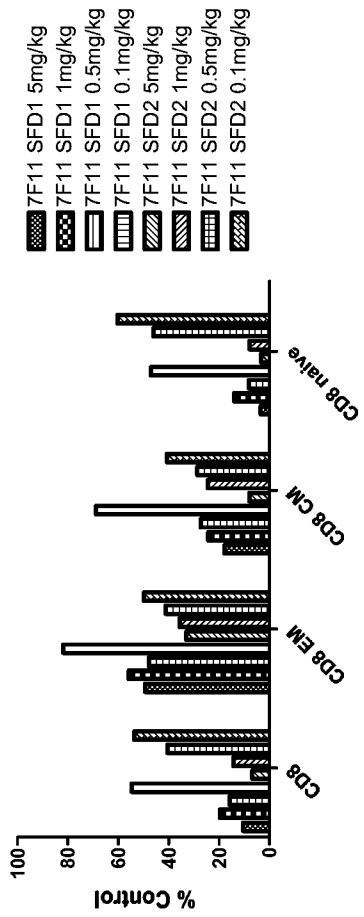

7F11 SFD1 5mg/kg
7F11 SFD1 1mg/kg
7F11 SFD1 0.5mg/kg
7F11 SFD1 0.1mg/kg
7F11 SFD2 5mg/kg
7F11 SFD2 1mg/kg
7F11 SFD2 0.5mg/kg
7F11 SFD2 0.1mg/kg
% Control
0
20
40
60
80
100
CD8
CD8 EM
CD8 CM
CD8 naive

FIG. 51C

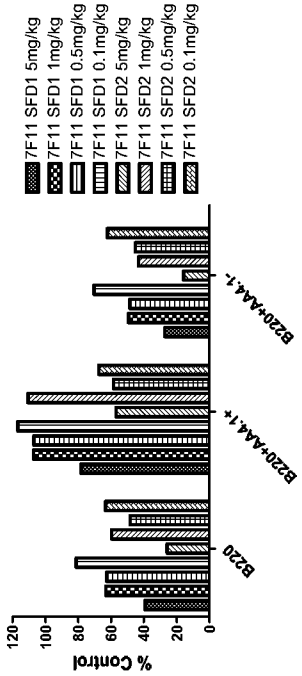


FIG. 51D

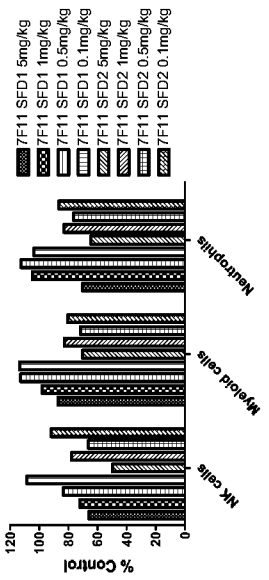


FIG. 51E

FIG. 52

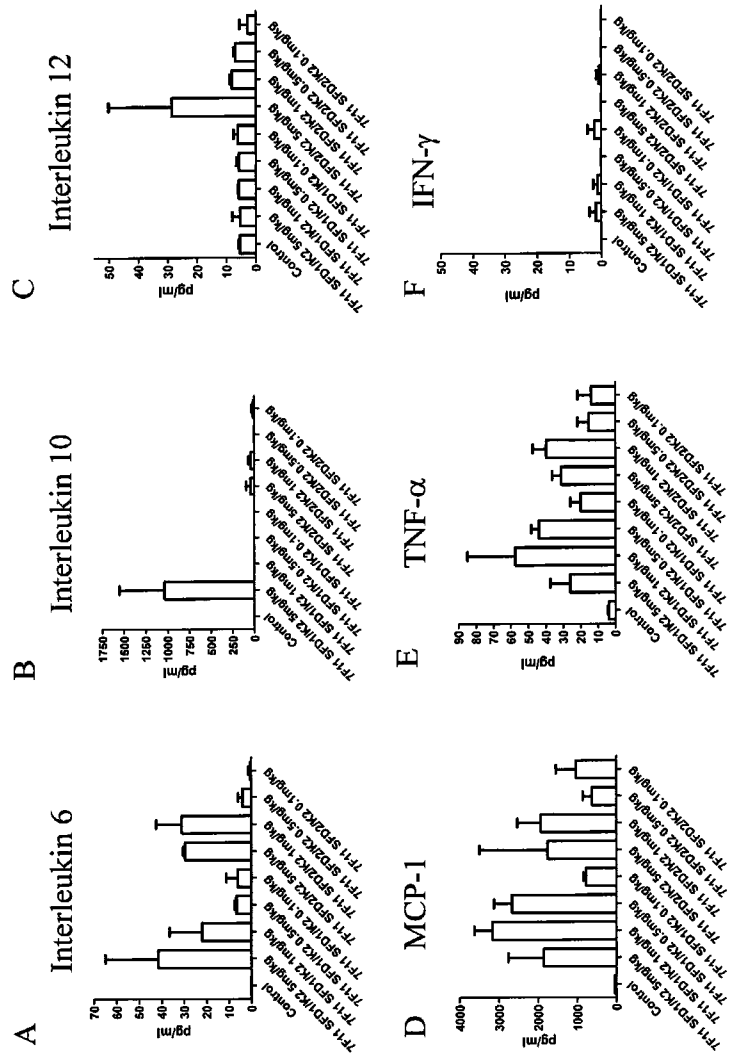

A
Interleukin 6
B
Interleukin 10
C
Interleukin 12
D
MCP-1
E
TNF-α
F
IFN-γ
pg/ml
Control
TF11 SFD1/K2 5mg/kg
TF11 SFD1/K2 1mg/kg
TF11 SFD1/K2 0.5mg/kg
TF11 SFD1/K2 0.1mg/kg
TF11 SFD2/K2 5mg/kg
TF11 SFD2/K2 1mg/kg
TF11 SFD2/K2 0.5mg/kg
TF11 SFD2/K2 0.1mg/kg

FIG. 53

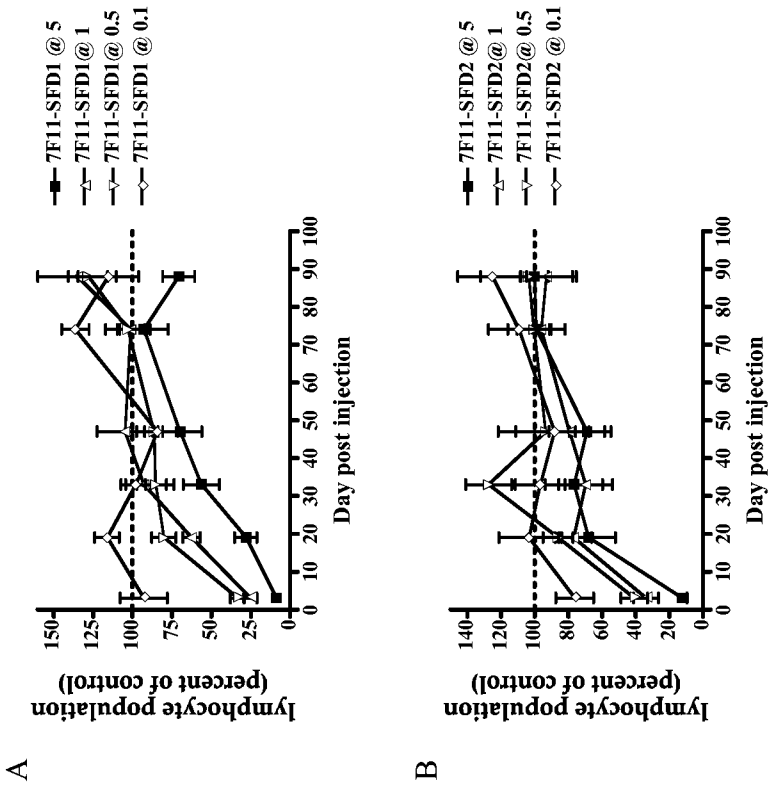

A
Lymphocyte population (percent of control)
Day post injection
7F11-SFD1 @ 5
7F11-SFD1@ 1
7F11-SFD1@ 0.5
7F11-SFD1 @ 0.1
B
Lymphocyte population (percent of control)
Day post injection
7F11-SFD2 @ 5
7F11-SFD2@ 1
7F11-SFD2@ 0.5
7F11-SFD2 @ 0.1

FIG. 54

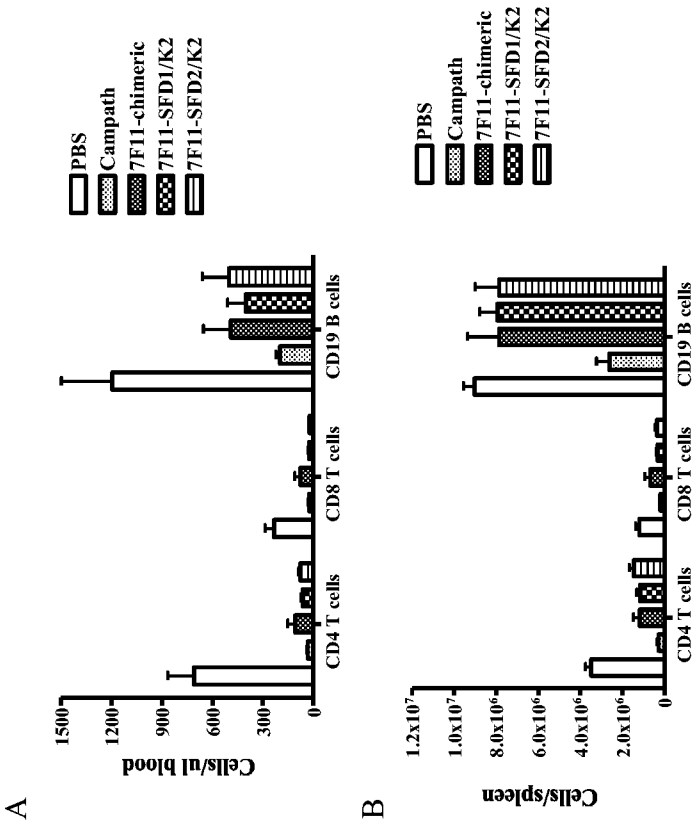

A
PBS
Campath
7F11-chimeric
7F11-SFD1/K2
7F11-SFD2/K2
Cells/ul blood
1500
1200
900
600
300
0
CD4 T cells
CD8 T cells
CD19 B cells
B
PBS
Campath
7F11-chimeric
7F11-SFD1/K2
7F11-SFD2/K2
Cells/spleen
1.2x10^7
1.0x10^7
8.0x10^6
6.0x10^6
4.0x10^6
2.0x10^6
0
CD4 T cells
CD8 T cells
CD19 B cells

FIG. 55

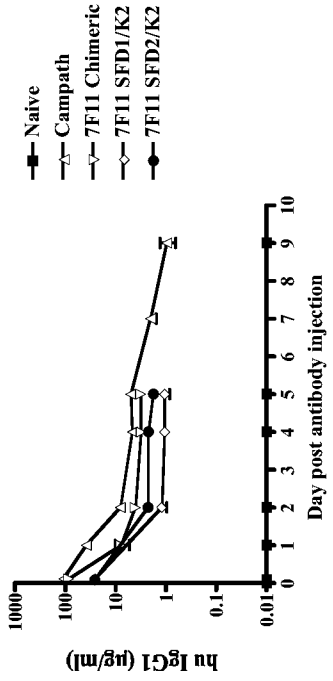
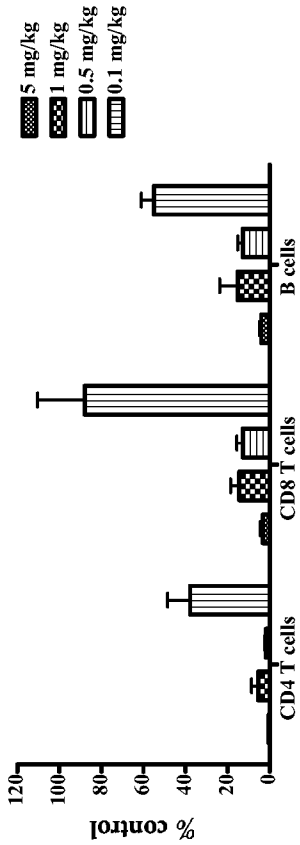

Naive
Campath
7F11 Chimeric
7F11 SFD1/K2
7F11 SFD2/K2
hu IgG1 (μg/ml)
1000
100
10
1
0.1
0.01
0
1
2
3
4
5
6
7
8
9
10
Day post antibody injection

FIG. 56A


5 mg/kg
1 mg/kg
0.5 mg/kg
0.1 mg/kg
% control
120
100
80
60
40
20
0
CD4 T cells
CD8 T cells
B cells

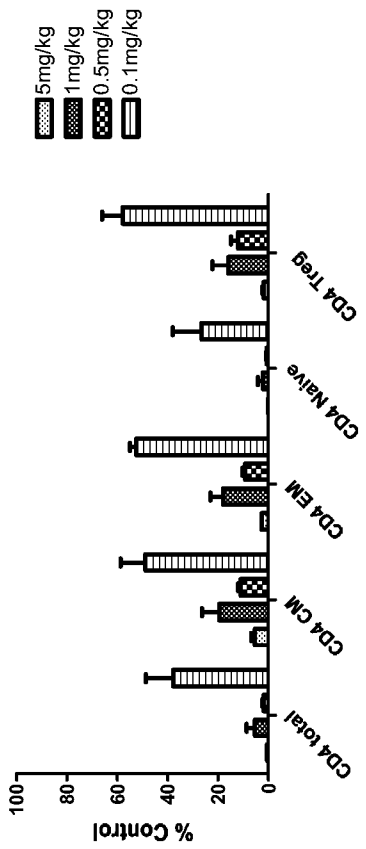

5mg/kg
1mg/kg
0.5mg/kg
0.1mg/kg
% Control
100
80
60
40
20
0
CD4 total
CD4 CM
CD4 EM
CD4 Naive
CD4 Treg

FIG. 56B

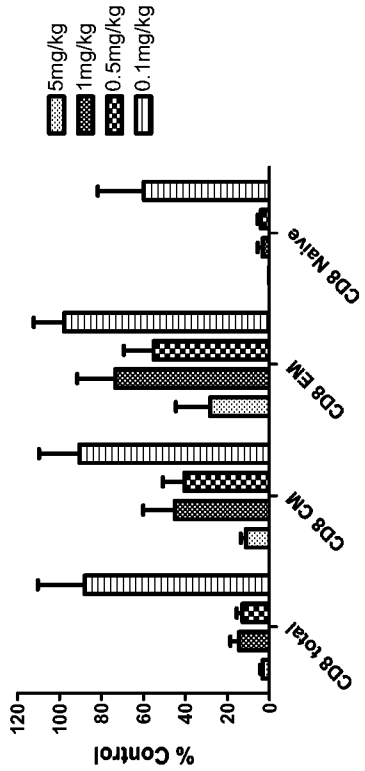

5mg/kg
1mg/kg
0.5mg/kg
0.1mg/kg
% Control
120
100
80
60
40
20
0
CD8 total
CD8 CM
CD8 EM
CD8 Naive

FIG. 56C

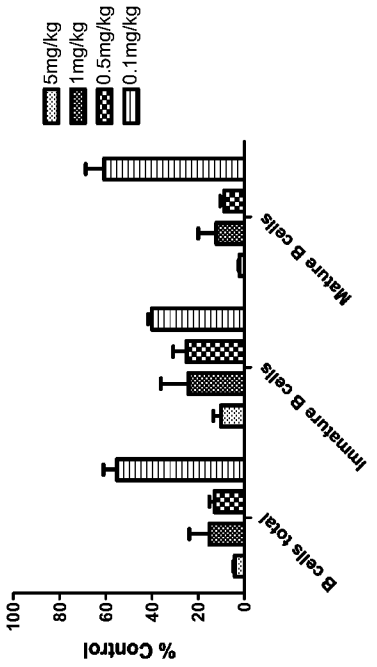


FIG. 56D

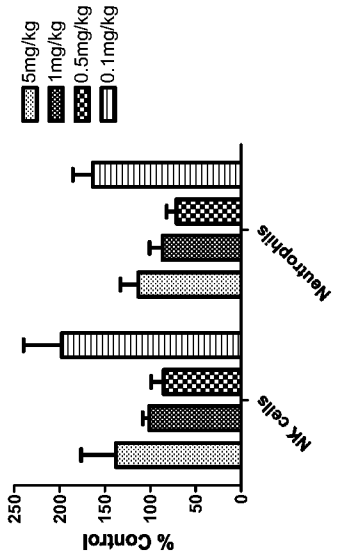


FIG. 56E

FIG. 57A

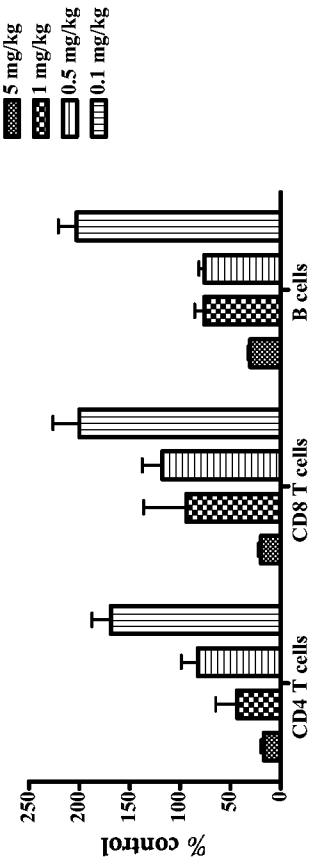
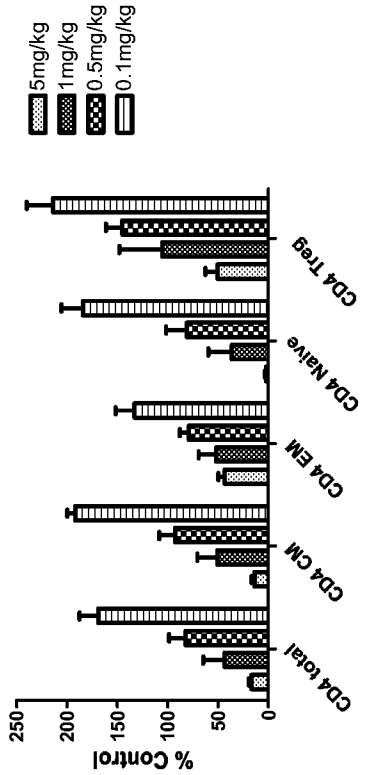

5 mg/kg
1 mg/kg
0.5 mg/kg
0.1 mg/kg
% control
250
200
150
100
50
0
CD4 T cells
CD8 T cells
B cells

FIG. 57B


5mg/kg
1mg/kg
0.5mg/kg
0.1mg/kg
% Control
250
200
150
100
50
0
CD4 total
CD4 CM
CD4 EM
CD4 Naive
CD4 Treg

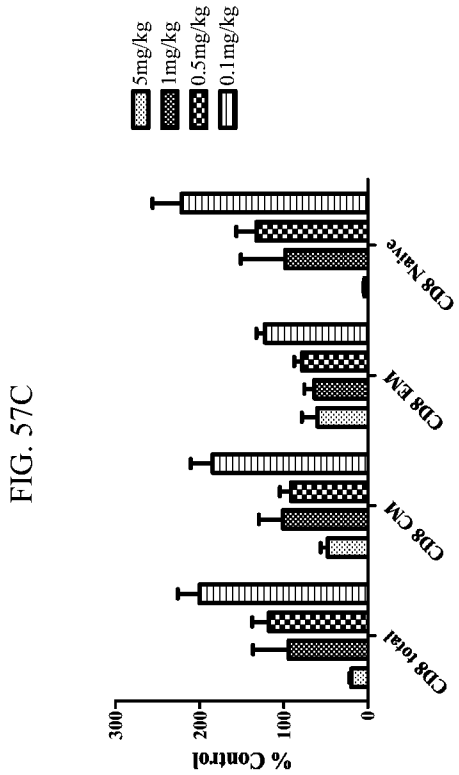

5mg/kg
1mg/kg
0.5mg/kg
0.1mg/kg
% Control
300
200
100
0
CD8 total
CD8 CM
CD8 EM
CD8 Naive

FIG. 57C

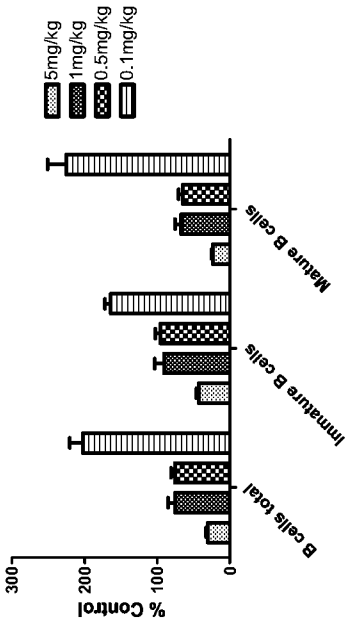


FIG. 57D

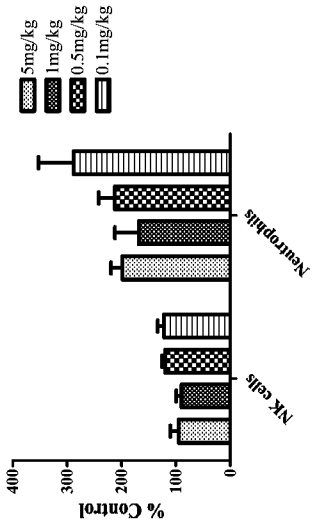


FIG. 57E

FIG. 58

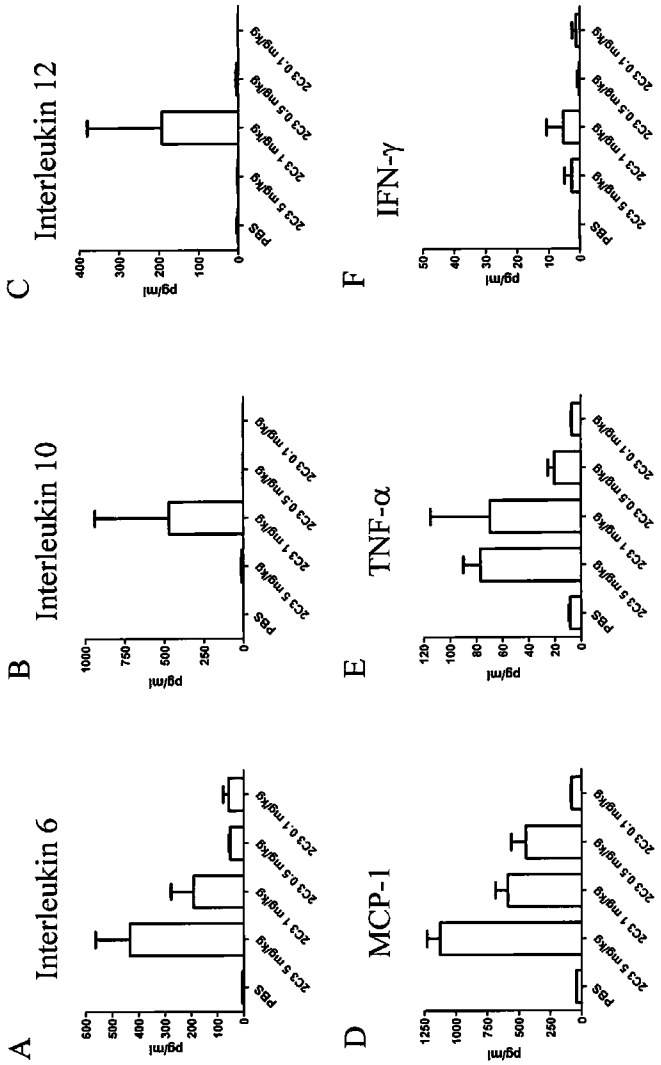

A
Interleukin 6
B
Interleukin 10
C
Interleukin 12
D
MCP-1
E
TNF-α
F
IFN-γ
pg/ml
PBS
2C3 5 mg/kg
2C3 1 mg/kg
2C3 0.5 mg/kg
2C3 0.1 mg/kg

FIG. 59

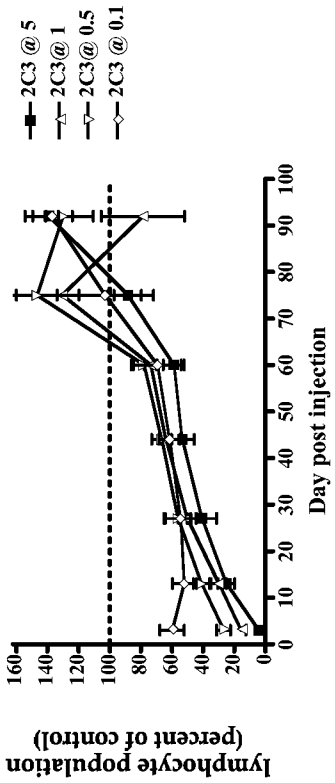

2C3 @ 5
2C3@ 1
2C3@ 0.5
2C3 @ 0.1
Lymphocyte population
(percent of control)
Day post injection
0
20
40
60
80
100
120
140
160
0
10
20
30
40
50
60
70
80
90
100

FIG. 60A

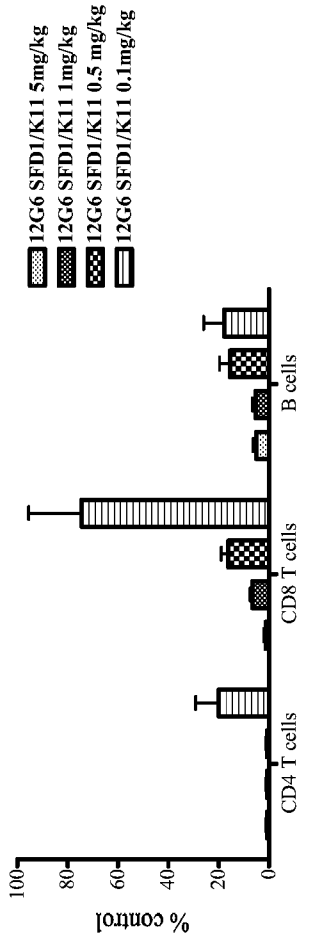

12G6 SFD1/K11 5mg/kg
12G6 SFD1/K11 1mg/kg
12G6 SFD1/K11 0.5 mg/kg
12G6 SFD1/K11 0.1mg/kg
% control
100
80
60
40
20
0
CD4 T cells
CD8 T cells
B cells

FIG 60B

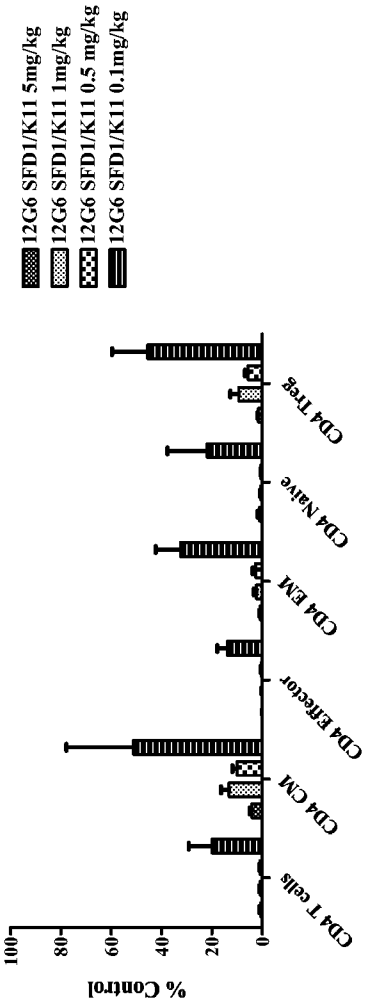
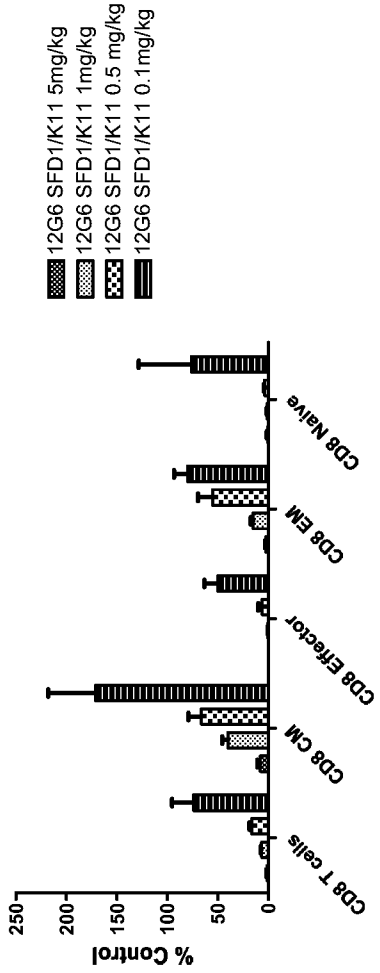

12G6 SFD1/K11 5mg/kg
12G6 SFD1/K11 1mg/kg
12G6 SFD1/K11 0.5 mg/kg
12G6 SFD1/K11 0.1mg/kg
% Control
100
80
60
40
20
0
CD4 T cells
CD4 CM
CD4 Effector
CD4 EM
CD4 Naive
CD4 Tregs

FIG. 60C


12G6 SFD1/K11 5mg/kg
12G6 SFD1/K11 1mg/kg
12G6 SFD1/K11 0.5 mg/kg
12G6 SFD1/K11 0.1mg/kg
% Control
250
200
150
100
50
0
CD8 T cells
CD8 CM
CD8 Effector
CD8 EM
CD8 Naïve

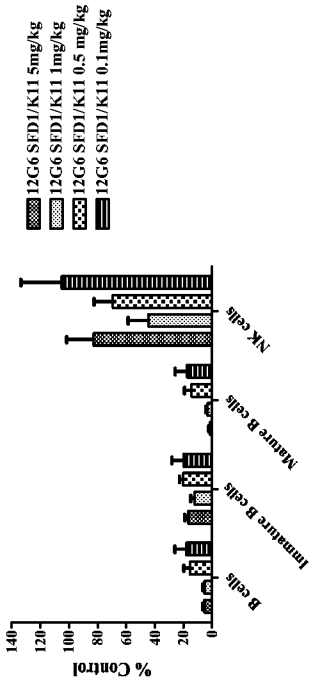


FIG. 60D

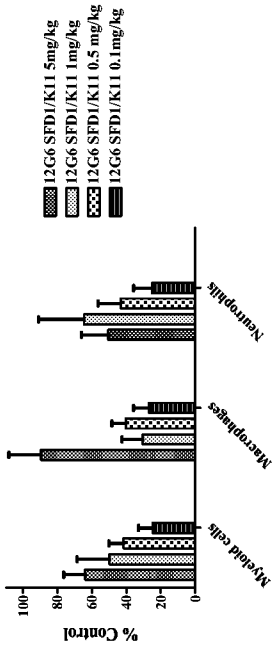
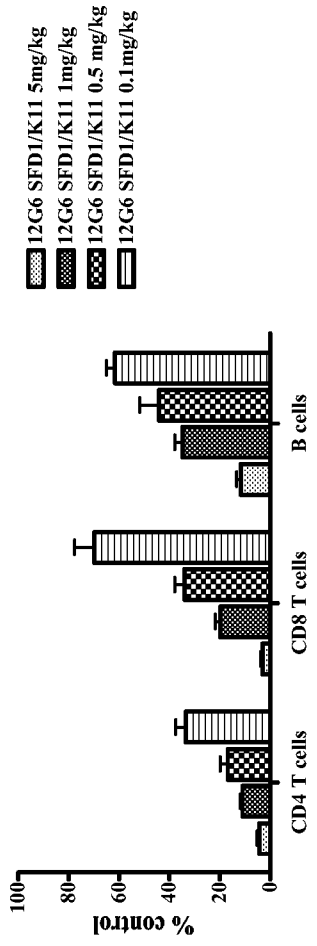


FIG. 60E

FIG. 61A


12G6 SFD1/K11 5mg/kg
12G6 SFD1/K11 1mg/kg
12G6 SFD1/K11 0.5 mg/kg
12G6 SFD1/K11 0.1mg/kg
% control
100
80
60
40
20
0
CD4 T cells
CD8 T cells
B cells

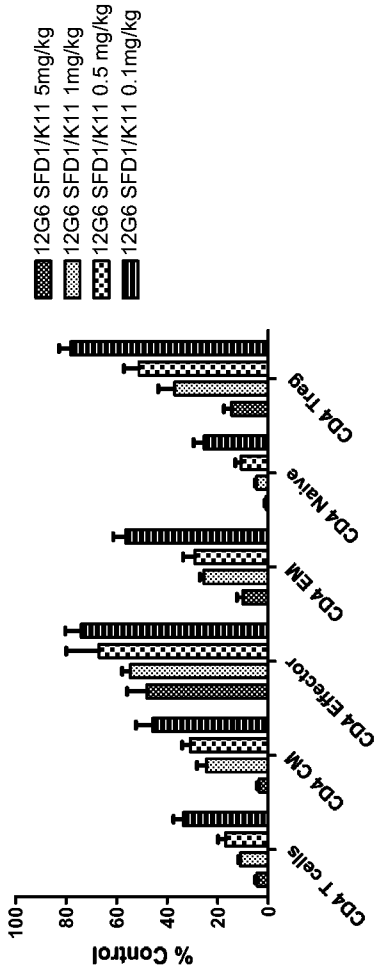
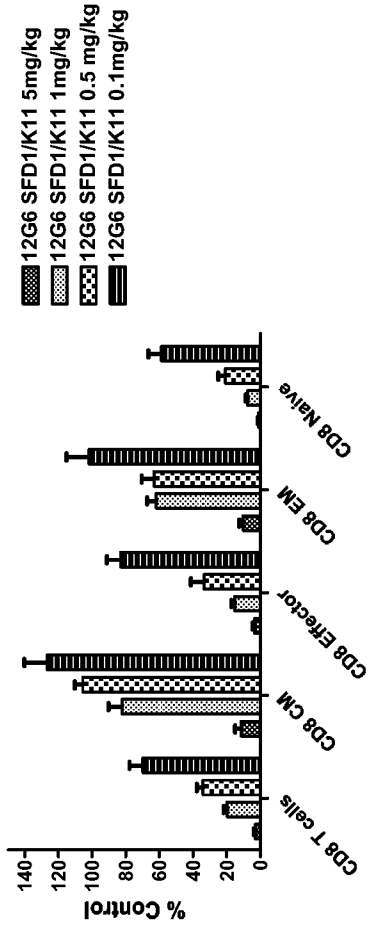

12G6 SFD1/K11 5mg/kg
12G6 SFD1/K11 1mg/kg
12G6 SFD1/K11 0.5 mg/kg
12G6 SFD1/K11 0.1mg/kg
% Control
0
20
40
60
80
100
CD4 T cells
CD4 CM
CD4 Effector
CD4 EM
CD4 Naive
CD4 Treg

FIG. 61B

FIG. 61C


12G6 SFD1/K11 5mg/kg
12G6 SFD1/K11 1mg/kg
12G6 SFD1/K11 0.5 mg/kg
12G6 SFD1/K11 0.1mg/kg
% Control
0
20
40
60
80
100
120
140
CD8 T cells
CD8 CM
CD8 Effector
CD8 EM
CD8 Naive

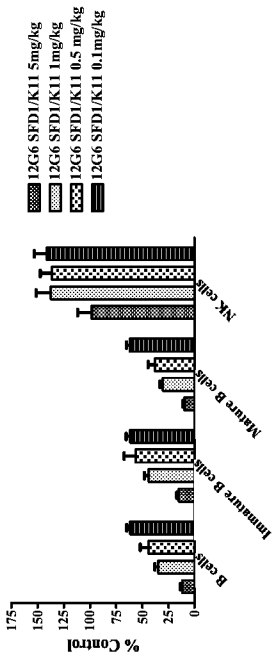


FIG. 61D

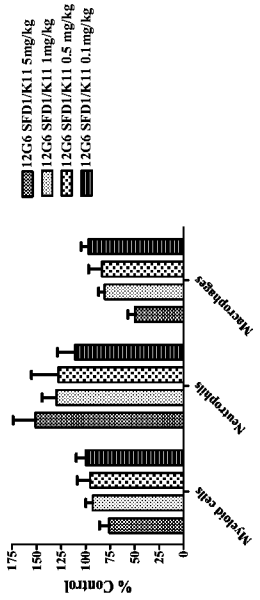


FIG. 61E

FIG. 62

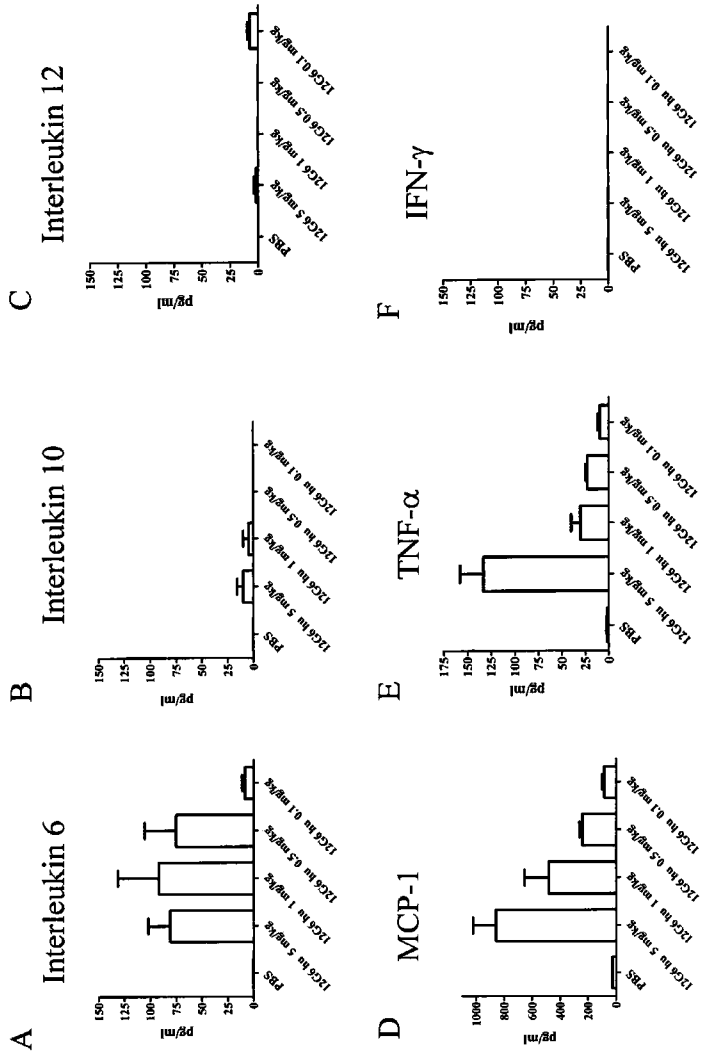

A
Interleukin 6
B
Interleukin 10
C
Interleukin 12
D
MCP-1
E
TNF-α
F
IFN-γ
pg/ml
PBS
12G6 5 mg/kg
12G6 1 mg/kg
12G6 0.5 mg/kg
12G6 0.1 mg/kg
12G6 hu 5 mg/kg
12G6 hu 1 mg/kg
12G6 hu 0.5 mg/kg
12G6 hu 0.1 mg/kg

FIG. 63

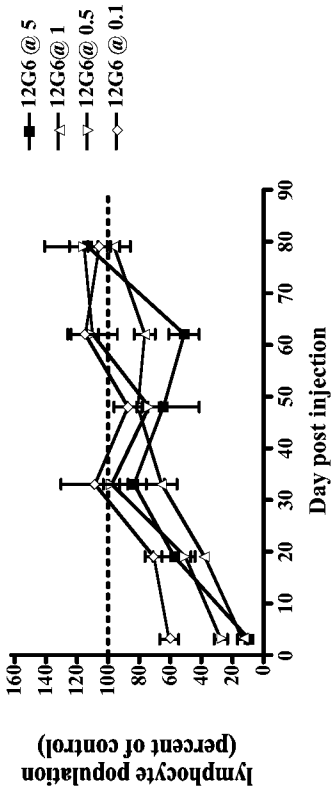

12G6 @ 5
12G6@ 1
12G6@ 0.5
12G6 @ 0.1
lymphocyte population
(percent of control)
160
140
120
100
80
60
40
20
0
0
10
20
30
40
50
60
70
80
90
Day post injection

FIG. 64

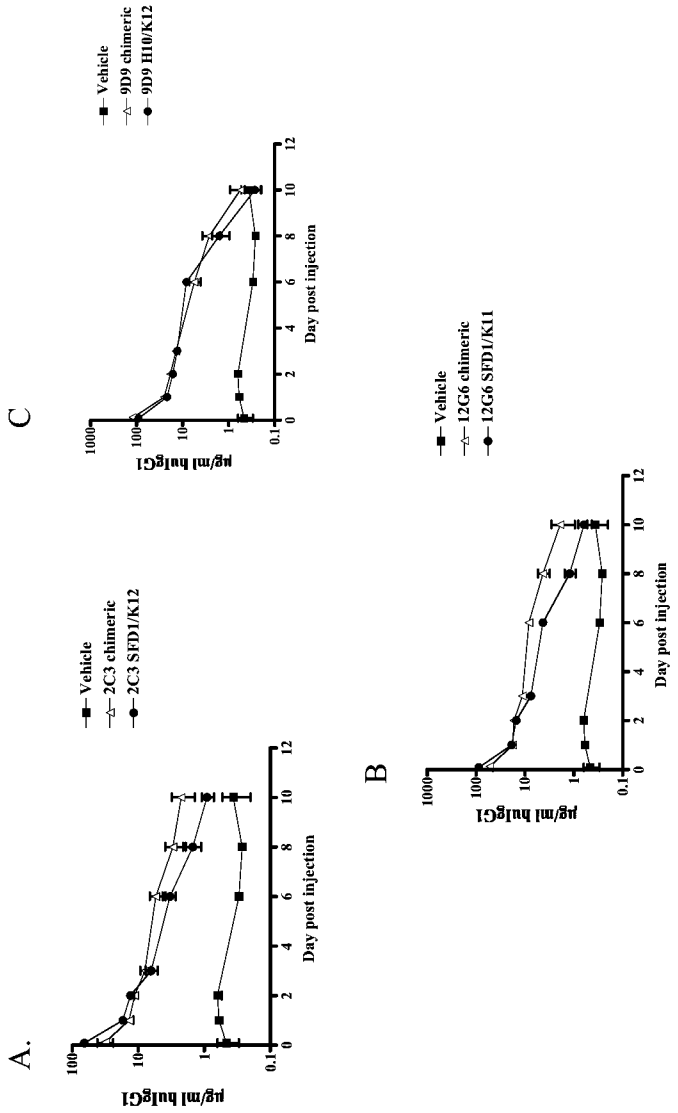
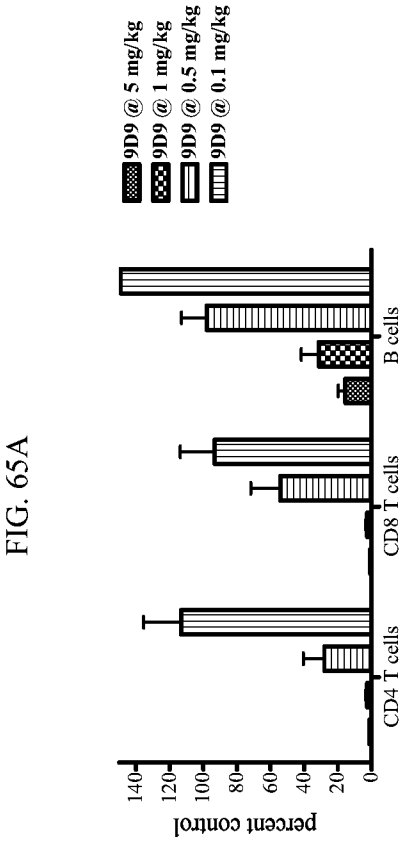

A.
Vehicle
2C3 chimeric
2C3 SFD1/K12
μg/ml huIgG1
Day post injection
B
Vehicle
12G6 chimeric
12G6 SFD1/K11
μg/ml huIgG1
Day post injection
C
Vehicle
9D9 chimeric
9D9 H10/K12
μg/ml huIgG1
Day post injection

FIG. 65A


9D9 @ 5 mg/kg
9D9 @ 1 mg/kg
9D9 @ 0.5 mg/kg
9D9 @ 0.1 mg/kg
percent control
0
20
40
60
80
100
120
140
CD4 T cells
CD8 T cells
B cells

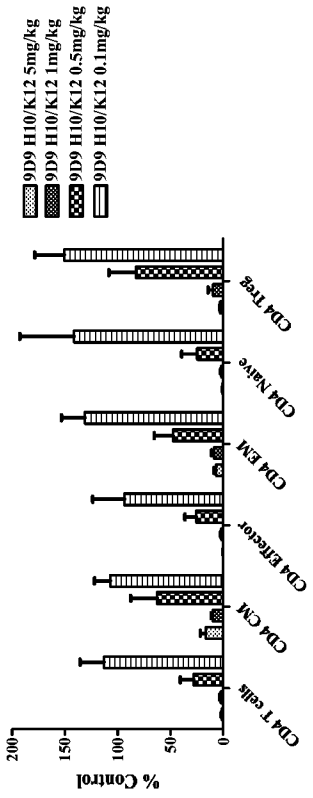


FIG. 65B

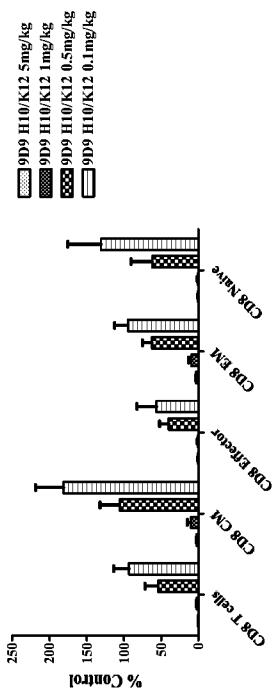


FIG. 65C

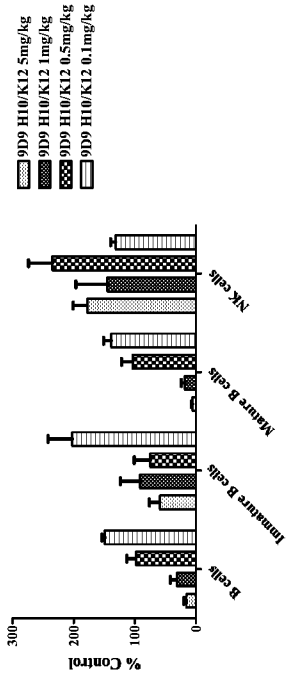


FIG. 65D

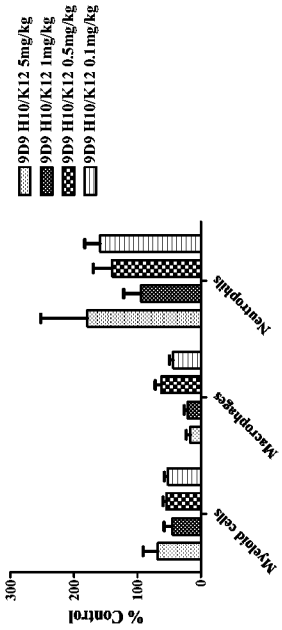
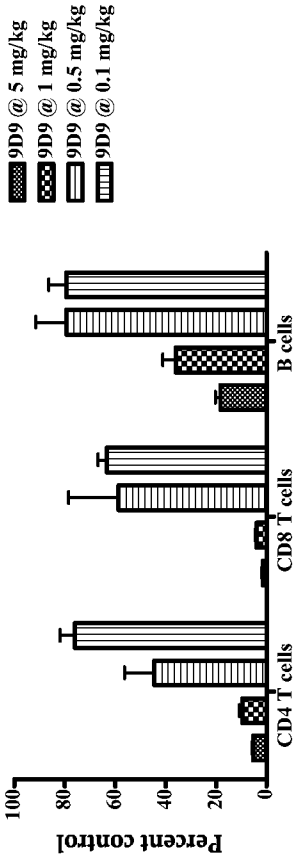


FIG. 65E

FIG. 66A


9D9 @ 5 mg/kg
9D9 @ 1 mg/kg
9D9 @ 0.5 mg/kg
9D9 @ 0.1 mg/kg
Percent control
100
80
60
40
20
0
CD4 T cells
CD8 T cells
B cells

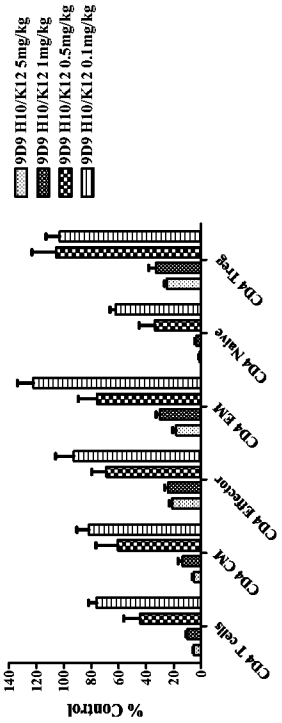


FIG. 66B

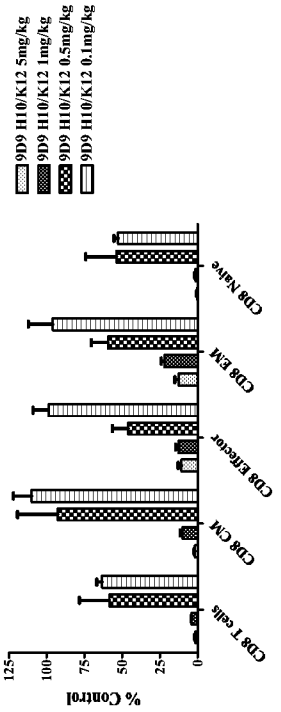


FIG. 66C

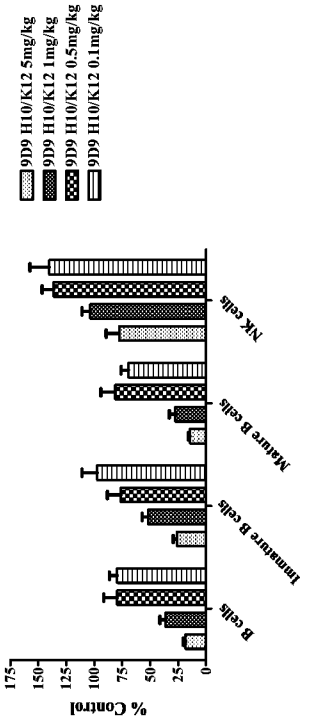


FIG. 66D

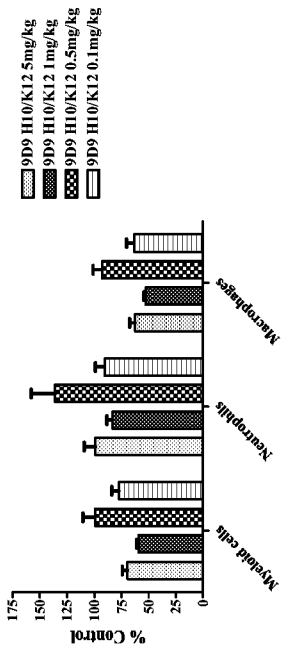


FIG. 66E

FIG. 67

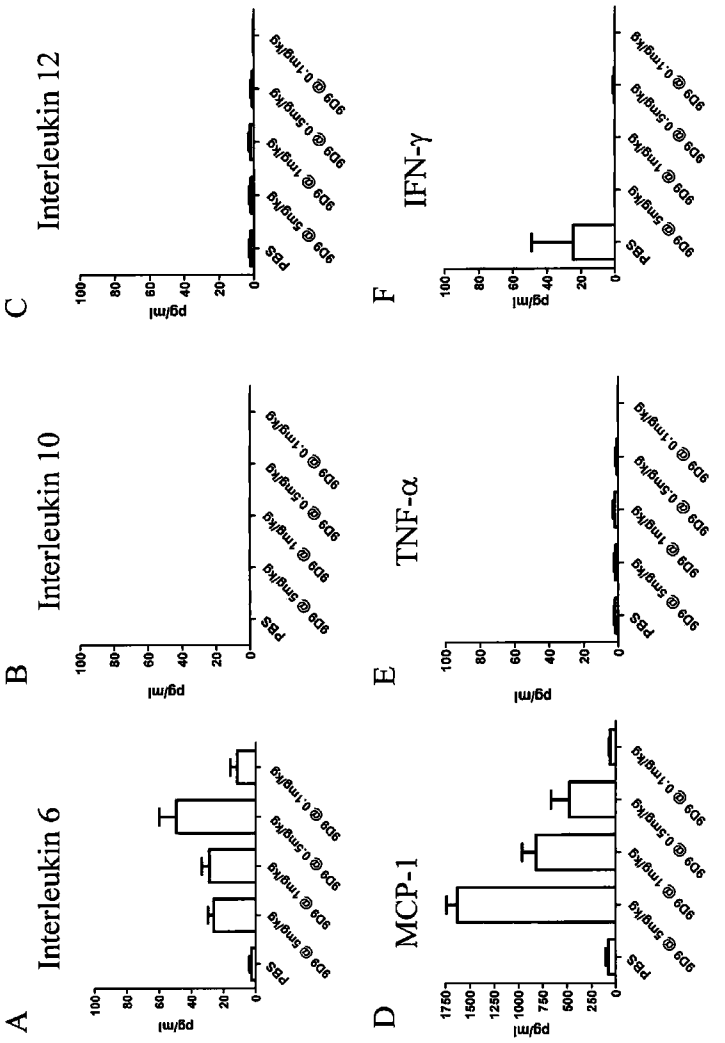

A
Interleukin 6
B
Interleukin 10
C
Interleukin 12
D
MCP-1
E
TNF-α
F
IFN-γ
pg/ml
PBS
9D9 @ 5mg/kg
9D9 @ 1mg/kg
9D9 @ 0.5mg/kg
9D9 @ 0.1mg/kg

FIG. 68

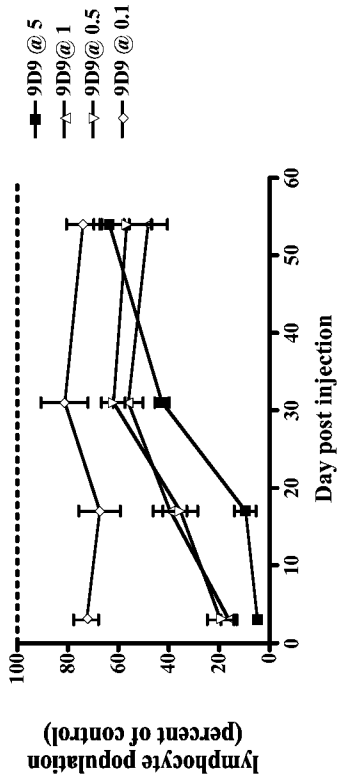
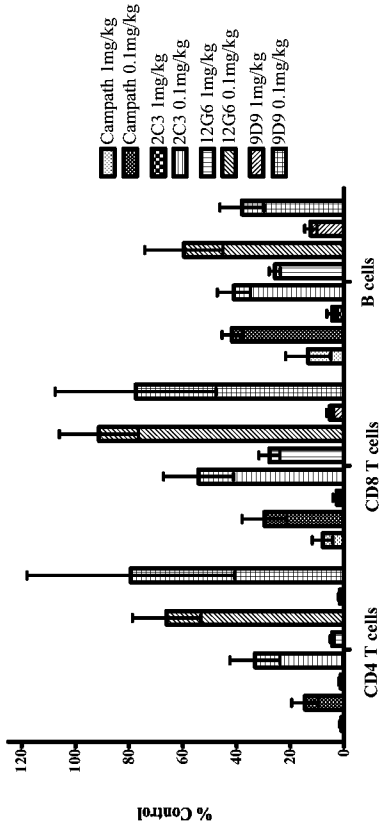

9D9 @ 5
9D9@ 1
9D9@ 0.5
9D9 @ 0.1
lymphocyte population
(percent of control)
100
80
60
40
20
0
0
10
20
30
40
50
60
Day post injection

FIG. 69A


Campath 1mg/kg
Campath 0.1mg/kg
2C3 1mg/kg
2C3 0.1mg/kg
12G6 1mg/kg
12G6 0.1mg/kg
9D9 1mg/kg
9D9 0.1mg/kg
% Control
0
20
40
60
80
100
120
CD4 T cells
CD8 T cells
B cells

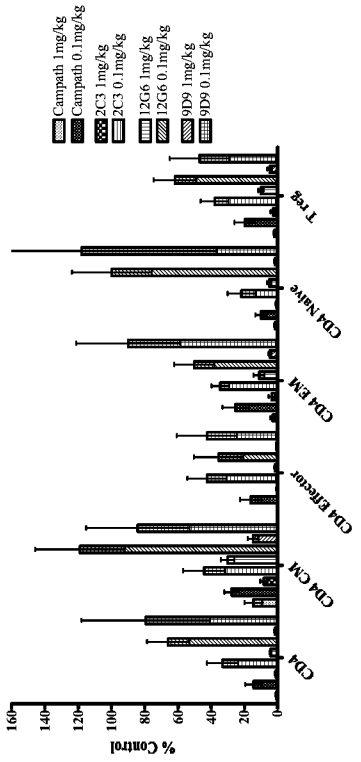


FIG. 69B

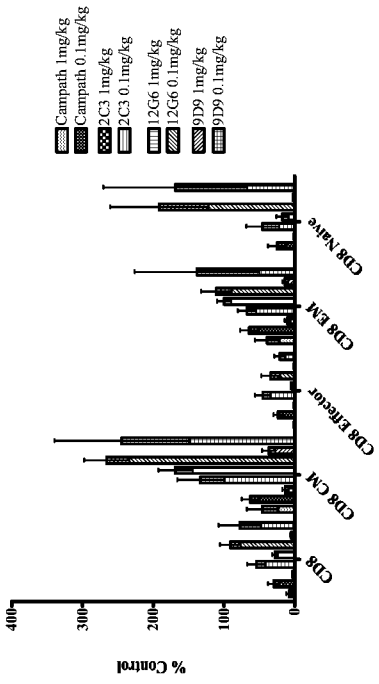


FIG. 69C

FIG. 69D

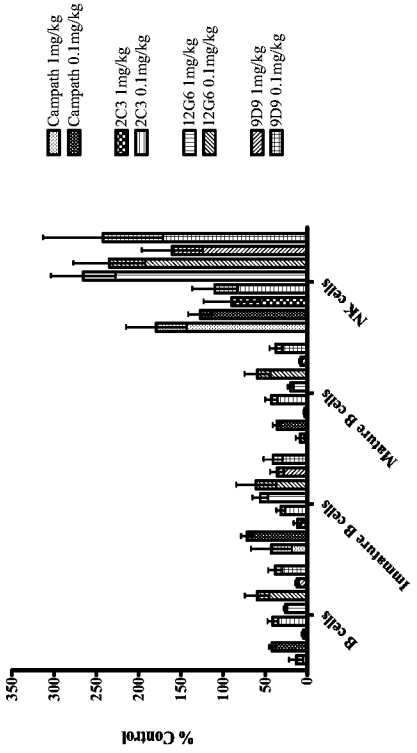
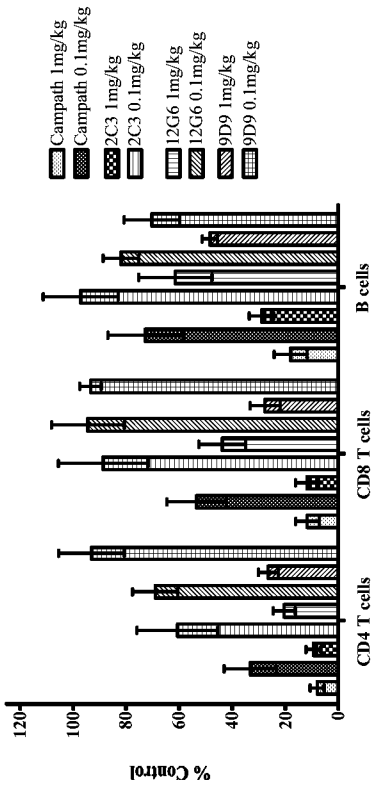

Campath 1mg/kg
Campath 0.1mg/kg
2C3 1mg/kg
2C3 0.1mg/kg
12G6 1mg/kg
12G6 0.1mg/kg
9D9 1mg/kg
9D9 0.1mg/kg
% Control
0
50
100
150
200
250
300
350
B cells
Immature B cells
Mature B cells
NK cells

FIG. 70A


Campath 1mg/kg
Campath 0.1mg/kg
2C3 1mg/kg
2C3 0.1mg/kg
12G6 1mg/kg
12G6 0.1mg/kg
9D9 1mg/kg
9D9 0.1mg/kg
% Control
0
20
40
60
80
100
120
CD4 T cells
CD8 T cells
B cells

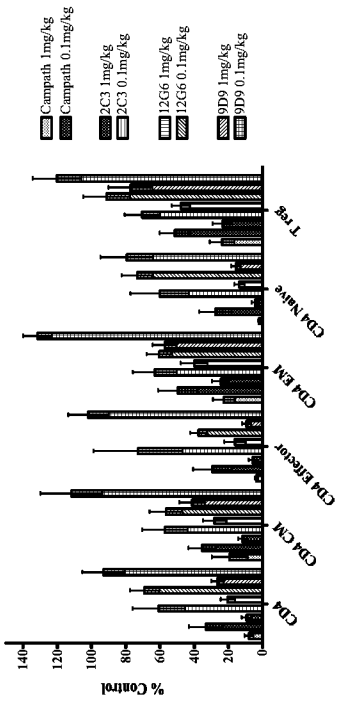


FIG. 70B

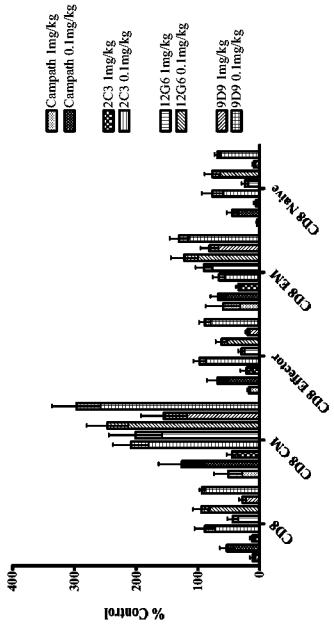


FIG. 70C

FIG. 70D

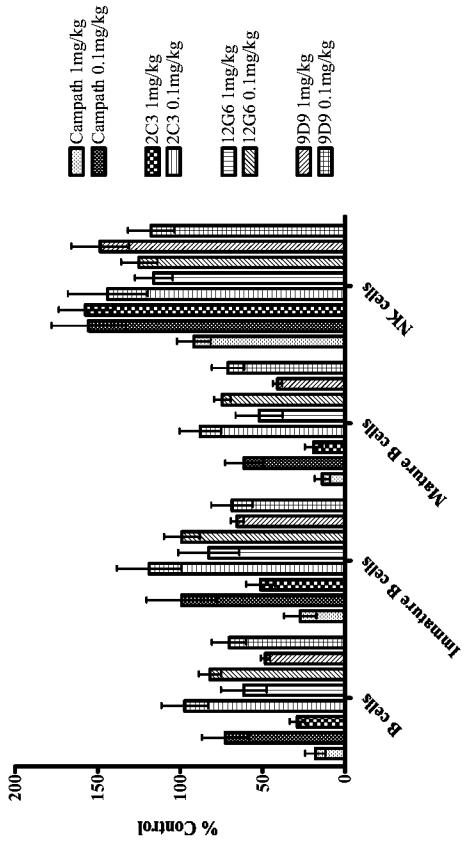
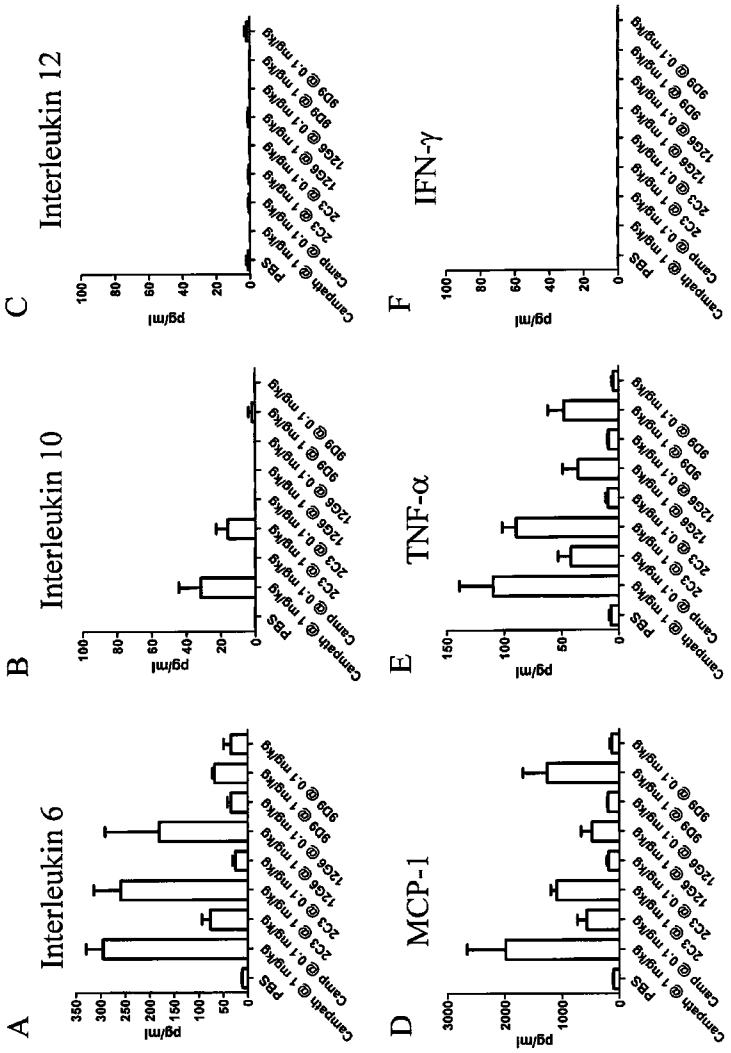

Campath 1mg/kg
Campath 0.1mg/kg
2C3 1mg/kg
2C3 0.1mg/kg
12G6 1mg/kg
12G6 0.1mg/kg
9D9 1mg/kg
9D9 0.1mg/kg
% Control
200
150
100
50
0
B cells
Immature B cells
Mature B cells
NK cells

FIG. 71


A
Interleukin 6
B
Interleukin 10
C
Interleukin 12
D
MCP-1
E
TNF-α
F
IFN-γ
pg/ml
PBS
Camp @ 1 mg/kg
2C3 @ 1 mg/kg
12G6 @ 1 mg/kg
9D9 @ 1 mg/kg
Campath @ 1 mg/kg
PBS
Camp @ 0.1 mg/kg
2C3 @ 0.1 mg/kg
12G6 @ 0.1 mg/kg
9D9 @ 0.1 mg/kg
Campath @ 0.1 mg/kg

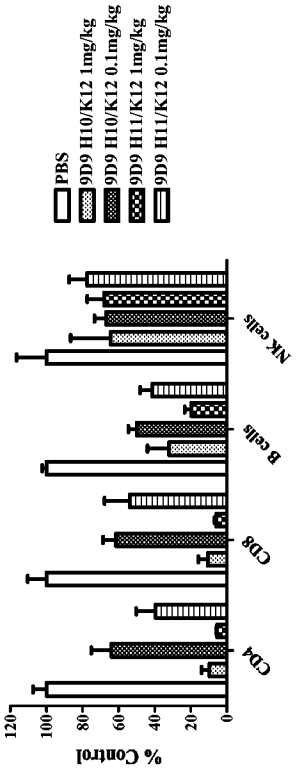

PBS
9D9 H10/K12 1mg/kg
9D9 H10/K12 0.1mg/kg
9D9 H11/K12 1mg/kg
9D9 H11/K12 0.1mg/kg
% Control
0
20
40
60
80
100
120
CD4
CD8
B cells
NK cells

FIG. 72

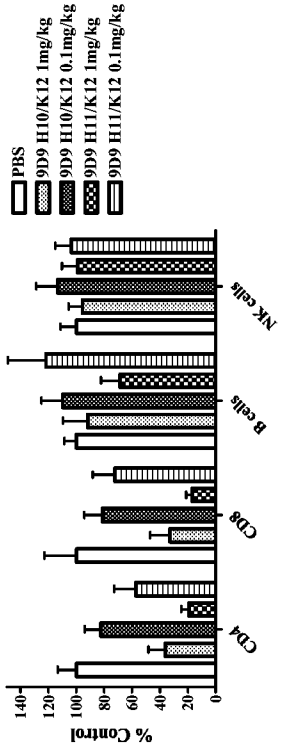

PBS
9D9 H10/K12 1mg/kg
9D9 H10/K12 0.1mg/kg
9D9 H11/K12 1mg/kg
9D9 H11/K12 0.1mg/kg
% Control
0
20
40
60
80
100
120
140
CD4
CD8
B cells
NK cells

FIG. 73

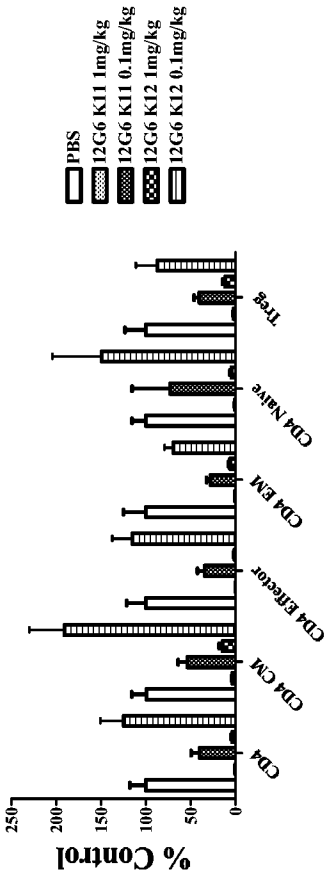


FIG. 74A

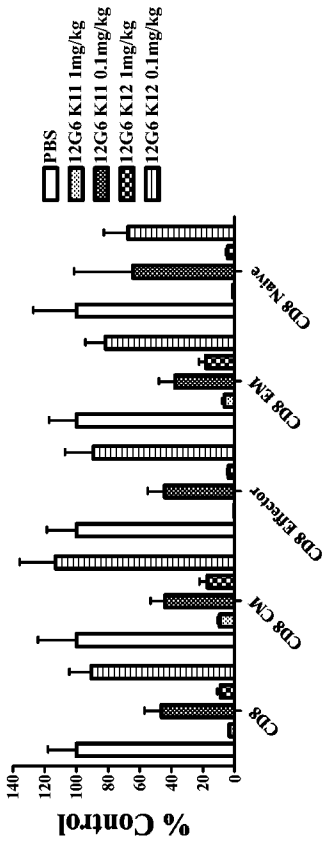


FIG. 74B

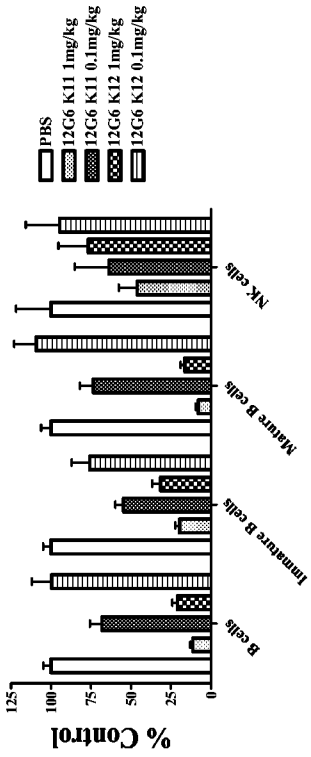


FIG. 74C

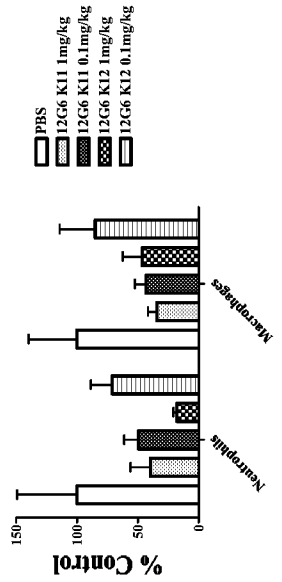


FIG. 74D

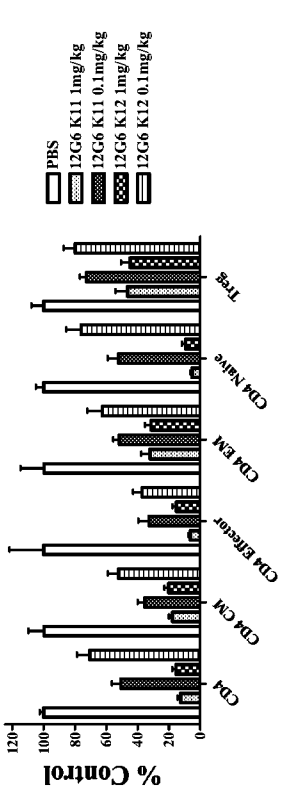


FIG. 75A

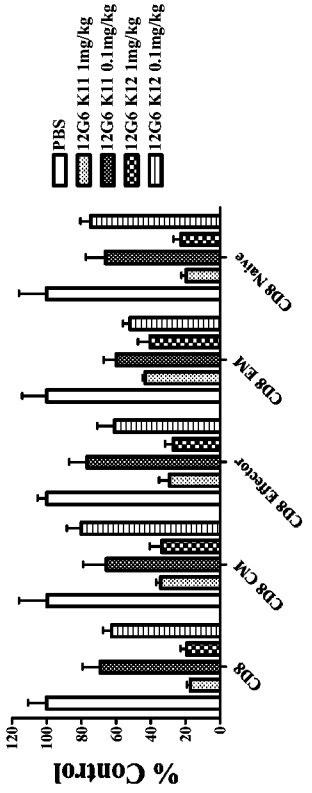


FIG. 75B

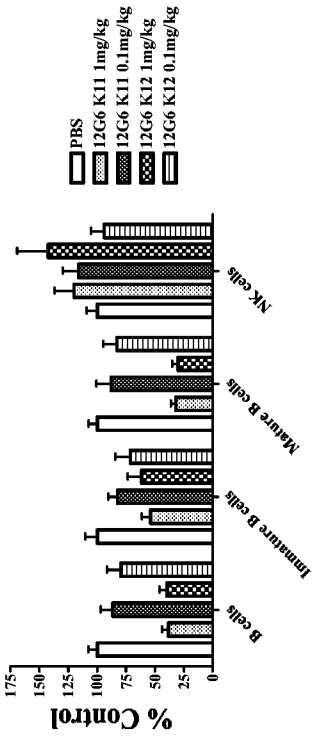


FIG. 75C

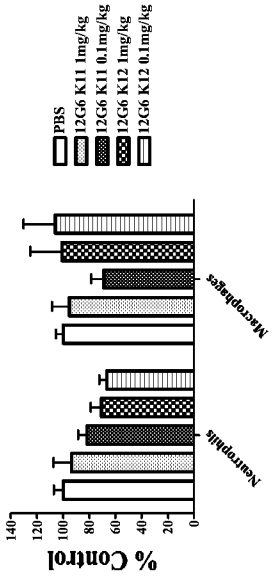
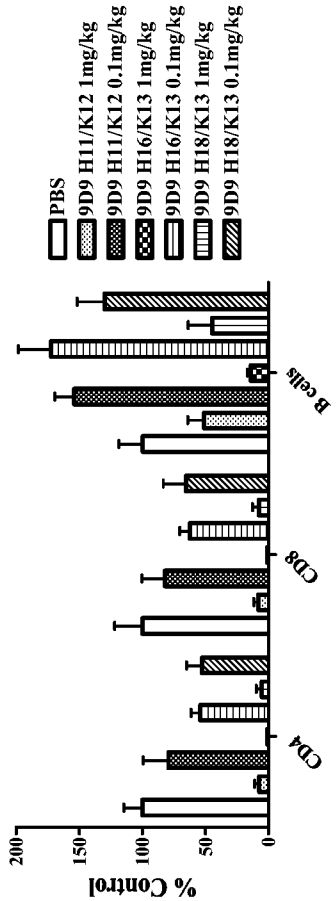


FIG. 75D

FIG. 76


PBS
9D9 H11/K12 1mg/kg
9D9 H11/K12 0.1mg/kg
9D9 H16/K13 1mg/kg
9D9 H16/K13 0.1mg/kg
9D9 H18/K13 1mg/kg
9D9 H18/K13 0.1mg/kg
% Control
200
150
100
50
0
CD4
CD8
B cells

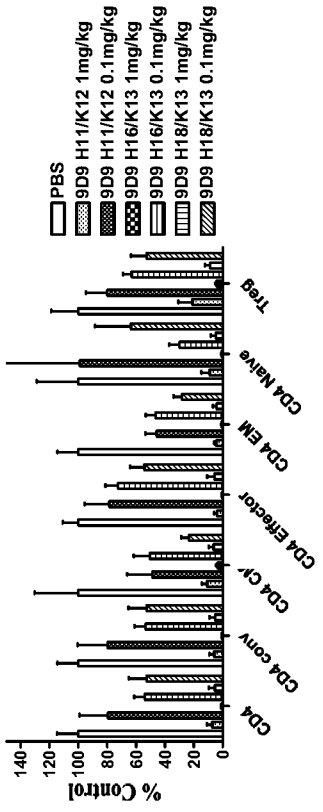


FIG. 77A

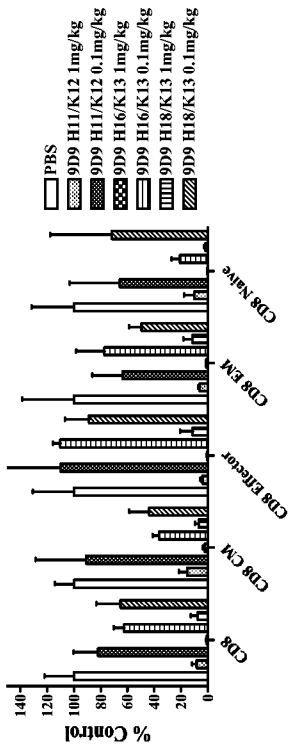


FIG. 77B

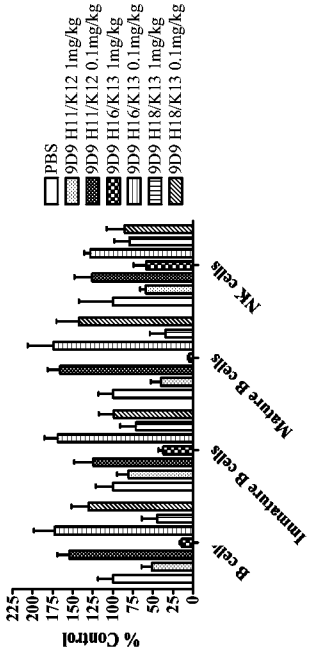


FIG. 77C

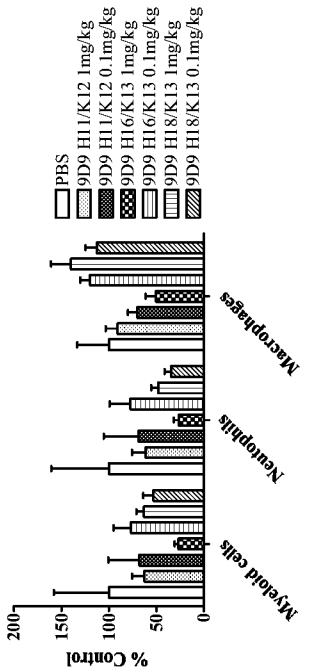
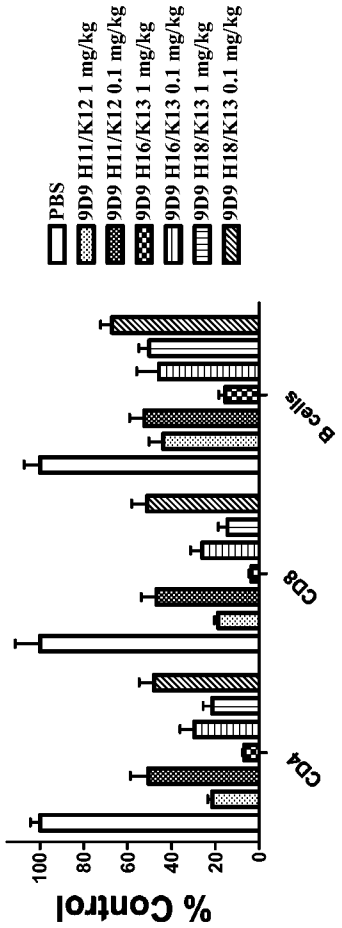


FIG. 77D

FIG. 78


PBS
9D9 H11/K12 1 mg/kg
9D9 H11/K12 0.1 mg/kg
9D9 H16/K13 1 mg/kg
9D9 H16/K13 0.1 mg/kg
9D9 H18/K13 1 mg/kg
9D9 H18/K13 0.1 mg/kg
% Control
0
20
40
60
80
100
CD4
CD8
B cells

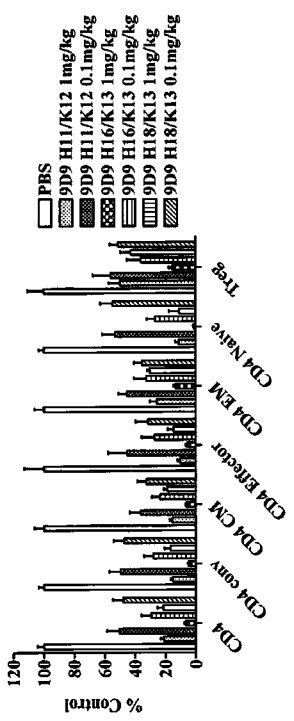


FIG. 79A

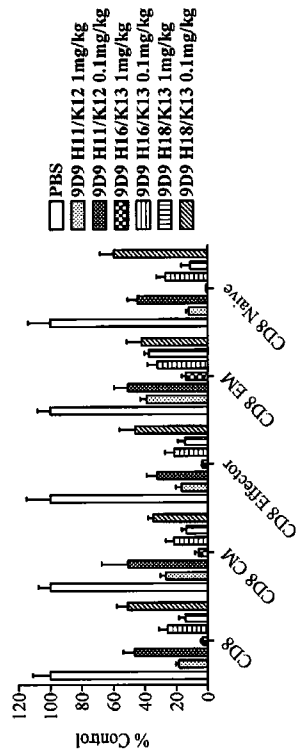


FIG. 79B

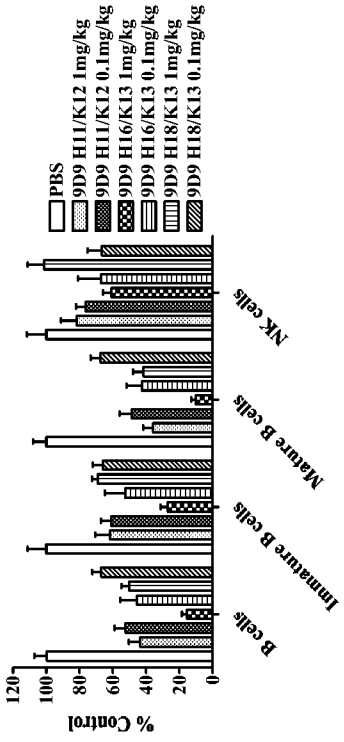


FIG. 79C

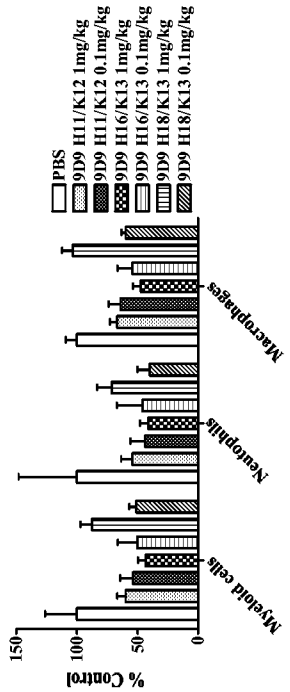


FIG. 79D

FIG. 80

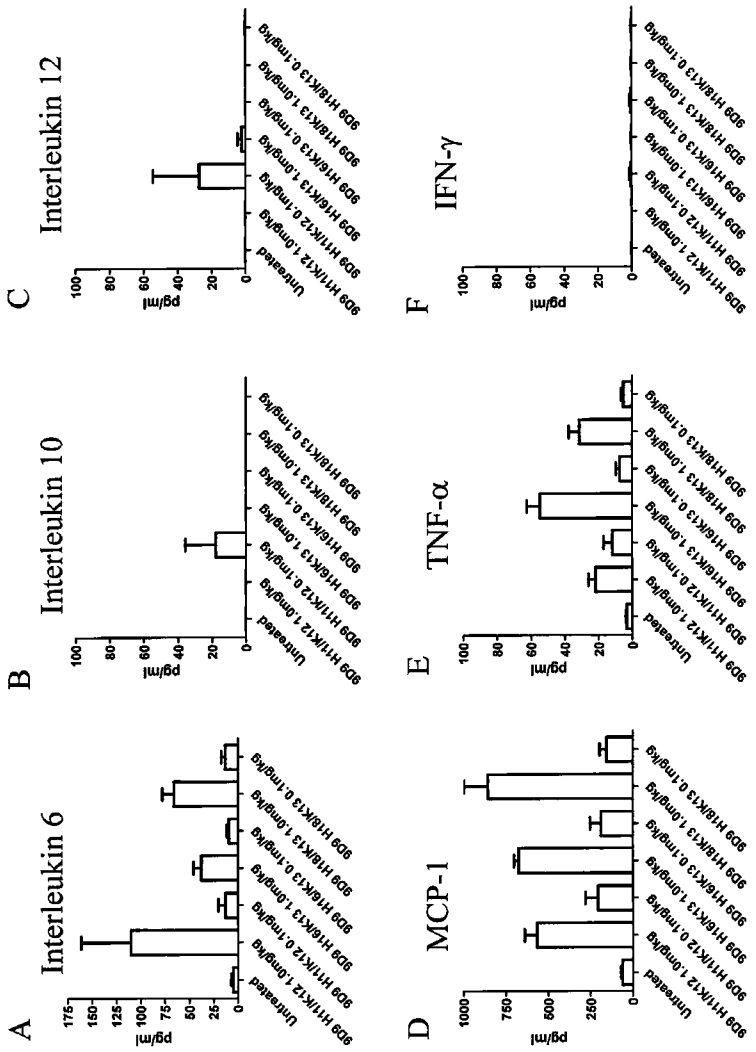
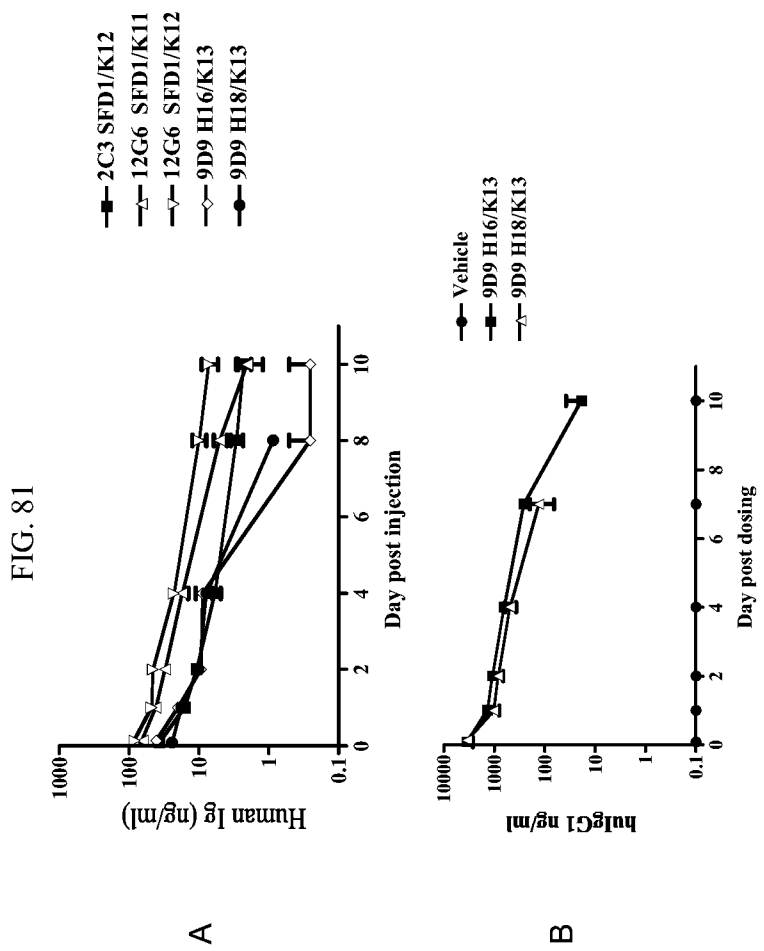

A
Interleukin 6
pg/ml
B
Interleukin 10
pg/ml
C
Interleukin 12
pg/ml
D
MCP-1
pg/ml
E
TNF-α
pg/ml
F
IFN-γ
pg/ml
Untreated
9D9 H11/K12 1.0mg/kg
9D9 H11/K12 0.1mg/kg
9D9 H16/K13 1.0mg/kg
9D9 H16/K13 0.1mg/kg
9D9 H18/K13 1.0mg/kg
9D9 H18/K13 0.1mg/kg

FIG. 81


2C3 SFD1/K12
12G6 SFD1/K11
12G6 SFD1/K12
9D9 H16/K13
9D9 H18/K13
Human Ig (ng/ml)
1000
100
10
1
0.1
0
2
4
6
8
10
Day post injection
A
Vehicle
9D9 H16/K13
9D9 H18/K13
huIgG1 ng/ml
10000
1000
100
10
1
0.1
0
2
4
6
8
10
Day post dosing
B

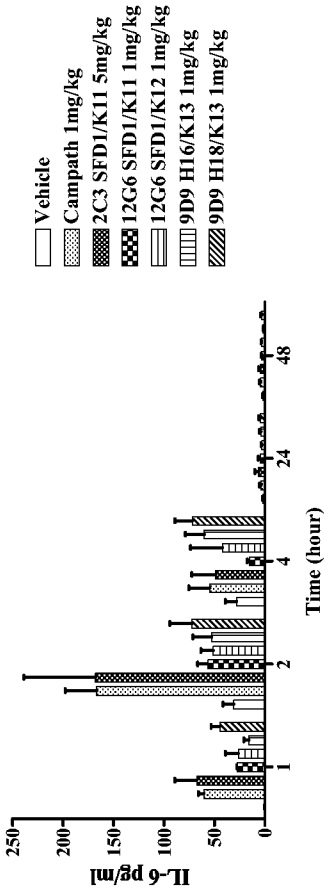


FIG. 82A

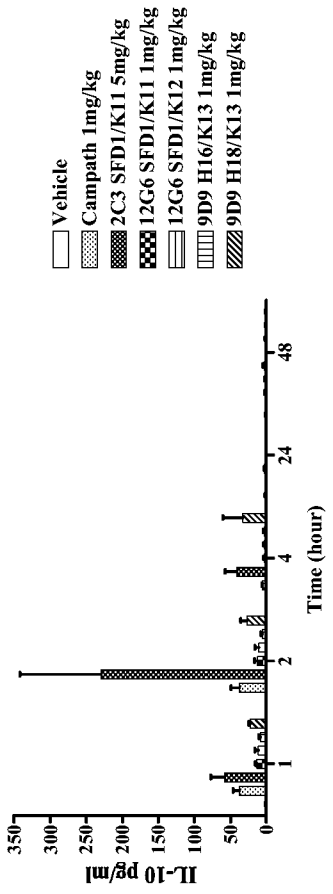


FIG. 82B

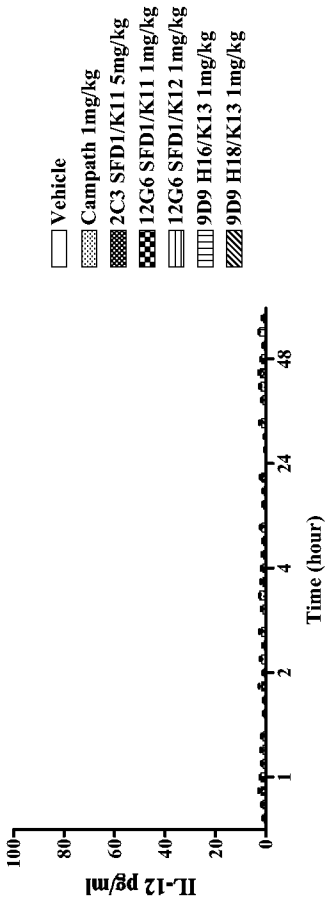


FIG. 82C

FIG. 82D

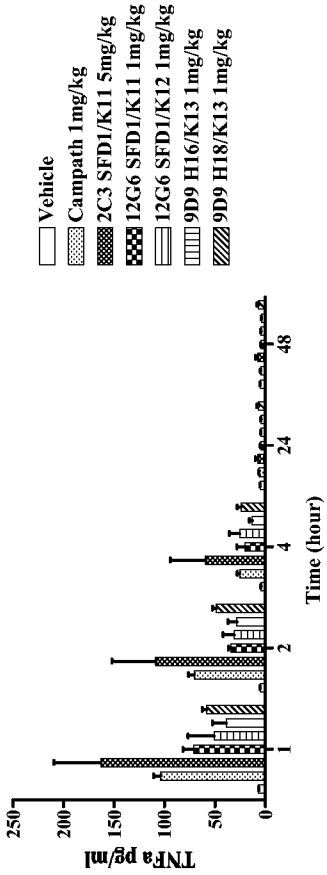


FIG. 82E

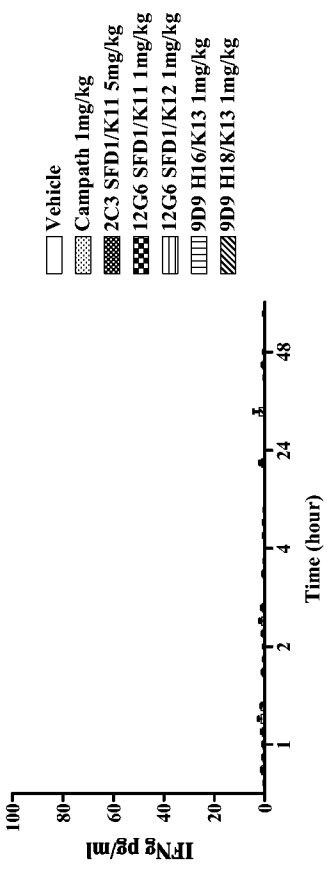


FIG. 82F

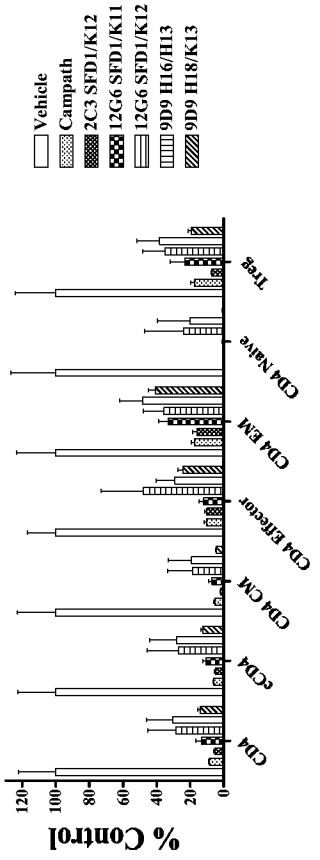


FIG. 83A

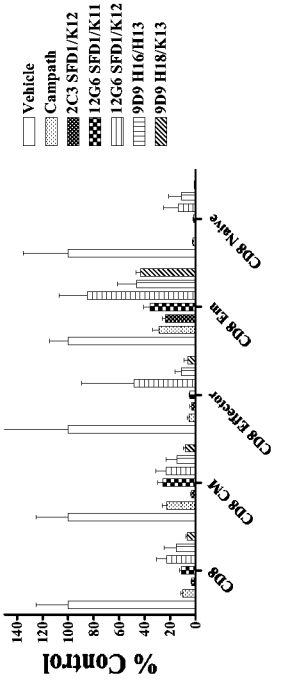


FIG. 83B

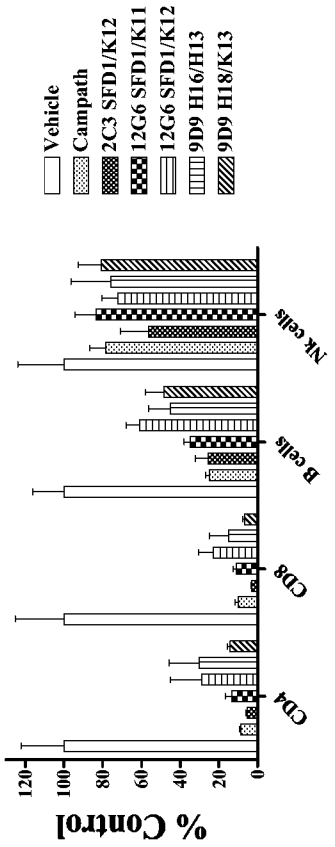

Vehicle
Campath
2C3 SFD1/K12
12G6 SFD1/K11
12G6 SFD1/K12
9D9 H16/H13
9D9 H18/K13
% Control
120
100
80
60
40
20
0
CD4
CD8
B cells
Nk cells

FIG. 83C

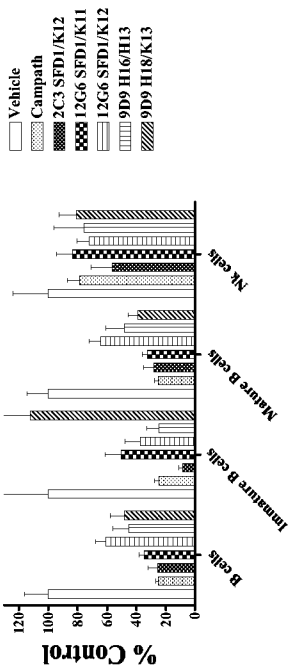


FIG. 83D

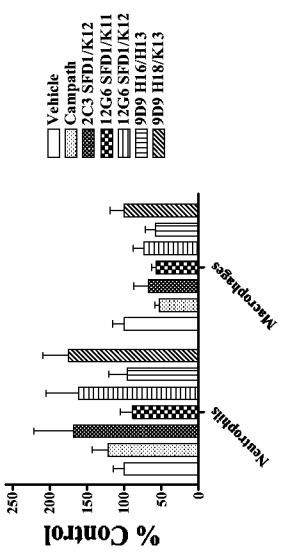


FIG. 83E

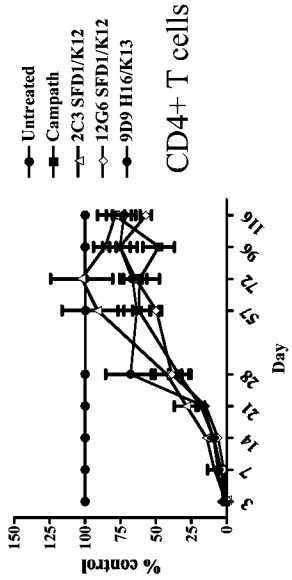


FIG. 84A

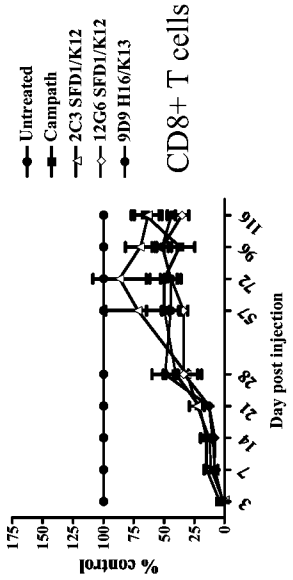


FIG. 84B

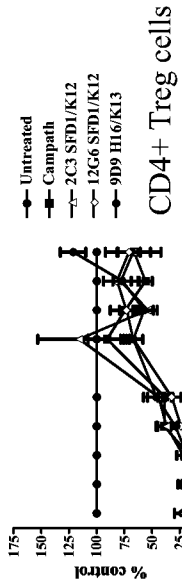


FIG. 84C

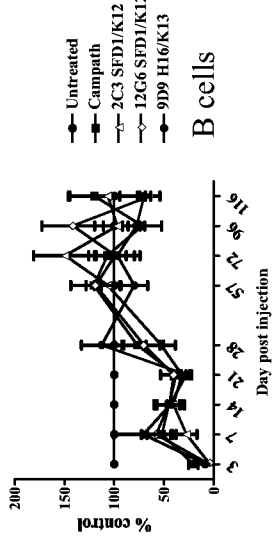


FIG. 84D

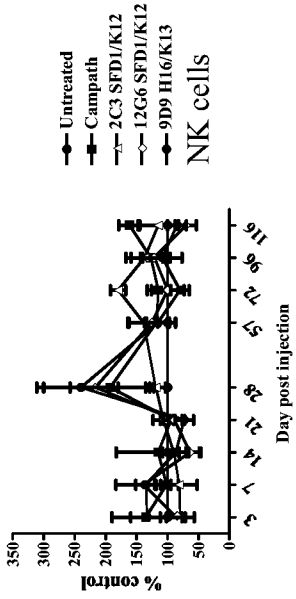


FIG. 84E

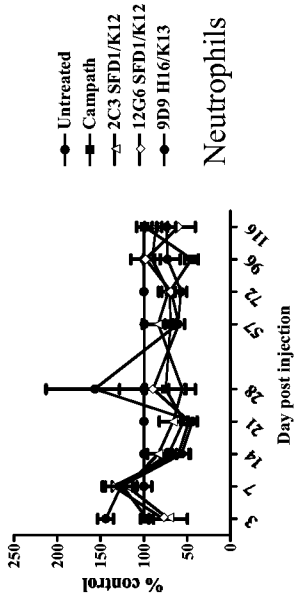


FIG. 84F

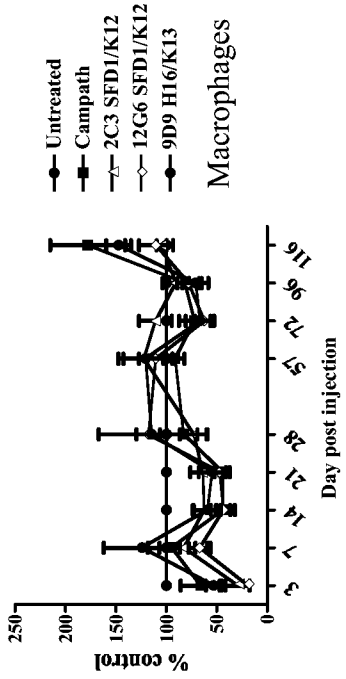

Untreated
Campath
2C3 SFD1/K12
12G6 SFD1/K12
9D9 H16/K13
Macrophages
% control
250
200
150
100
50
0
3
7
14
21
28
57
72
96
116
Day post injection

FIG. 84G

FIG. 85

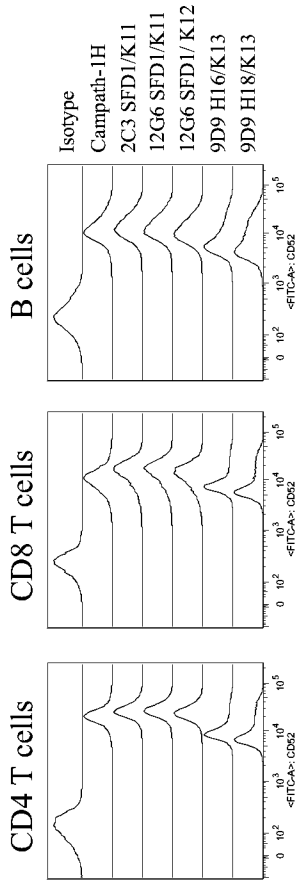
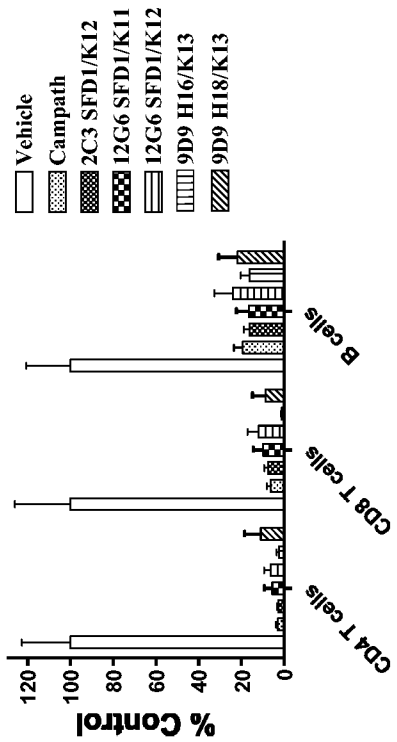

CD4 T cells
CD8 T cells
B cells
Isotype
Campath-1H
2C3 SFD1/K11
12G6 SFD1/K11
12G6 SFD1/ K12
9D9 H16/K13
9D9 H18/K13
<FITC-A>: CD52

FIG. 86A


Vehicle
Campath
2C3 SFD1/K12
12G6 SFD1/K11
12G6 SFD1/K12
9D9 H16/K13
9D9 H18/K13
% Control
120
100
80
60
40
20
0
CD4 T cells
CD8 T cells
B cells

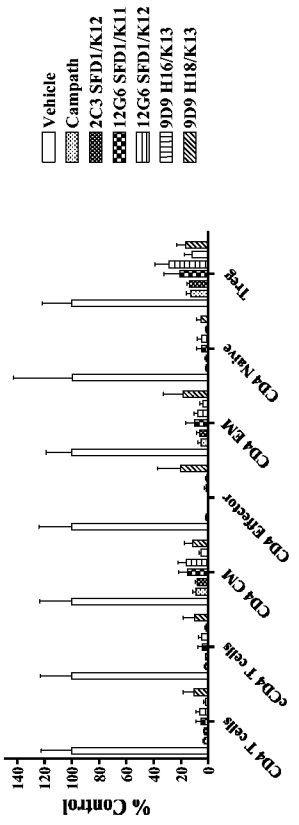


FIG. 86B

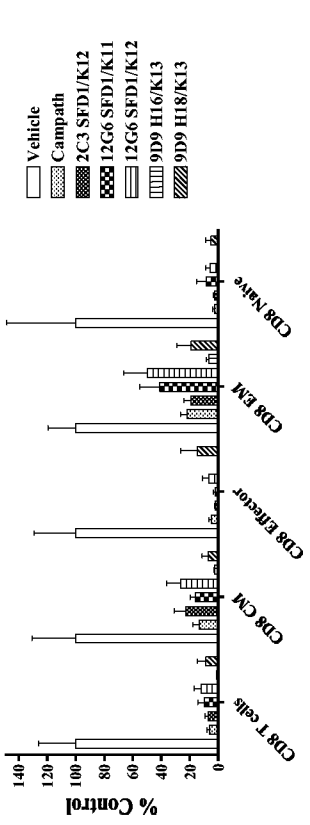


FIG. 86C

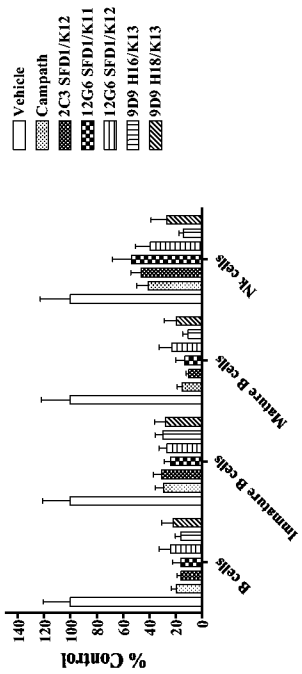


FIG. 86D

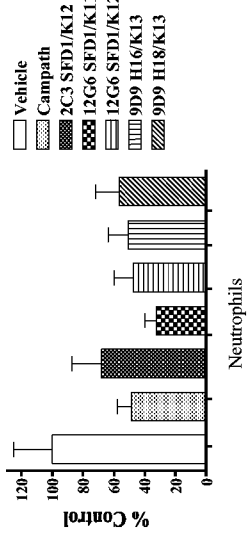
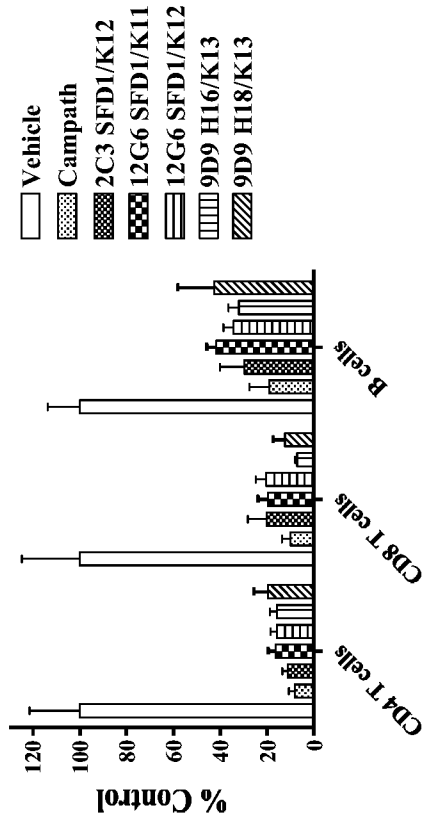


FIG. 86E

FIG. 87A


Vehicle
Campath
2C3 SFD1/K12
12G6 SFD1/K11
12G6 SFD1/K12
9D9 H16/K13
9D9 H18/K13
% Control
120
100
80
60
40
20
0
CD4 T cells
CD8 T cells
B cells

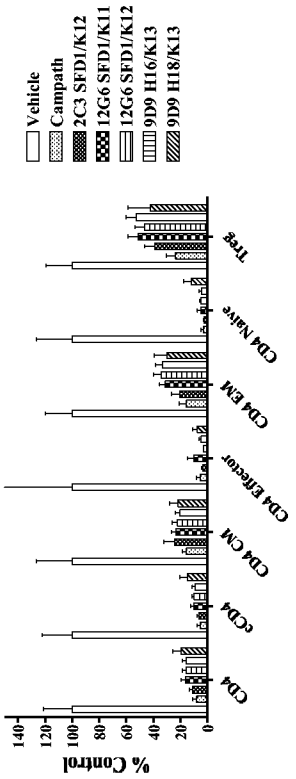


FIG. 87B

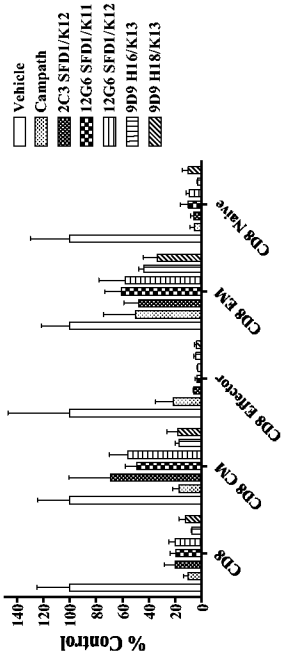


FIG. 87C

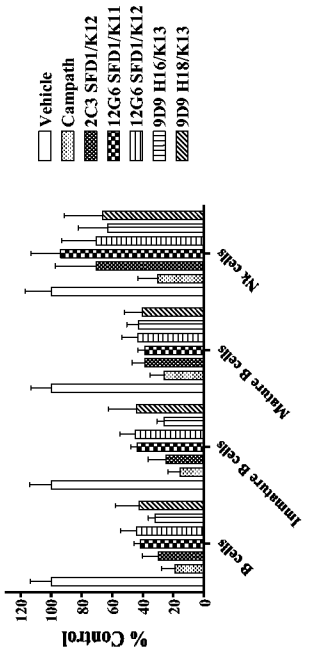


FIG. 87D

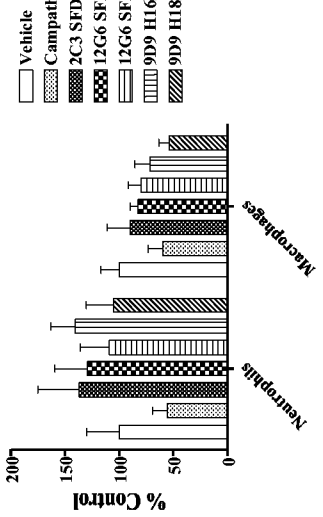
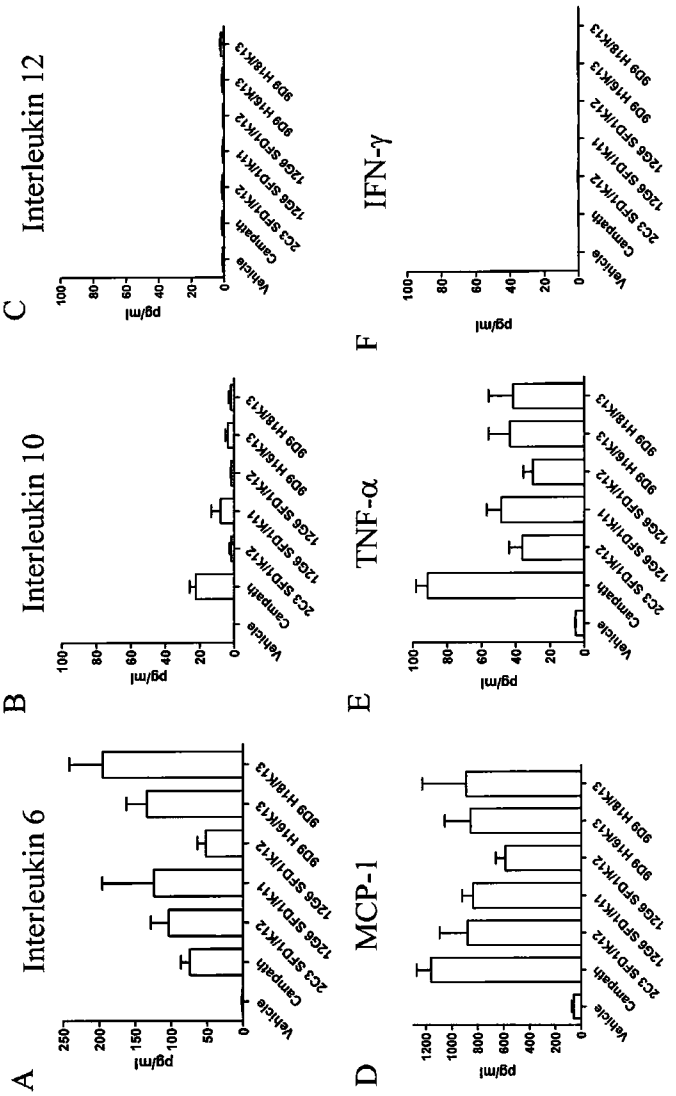


FIG. 87E

FIG. 88


A
Interleukin 6
B
Interleukin 10
C
Interleukin 12
D
MCP-1
E
TNF-α
F
IFN-γ
pg/ml
Vehicle
Campath
2C3 SFD1/K12
12G6 SFD1/K11
12G6 SFD1/K12
9D9 H16/K13
9D9 H18/K13

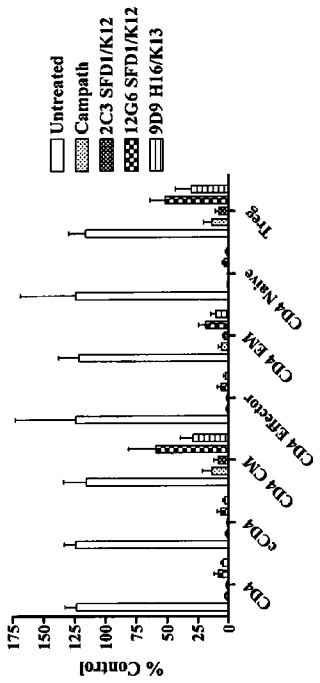


FIG. 89A

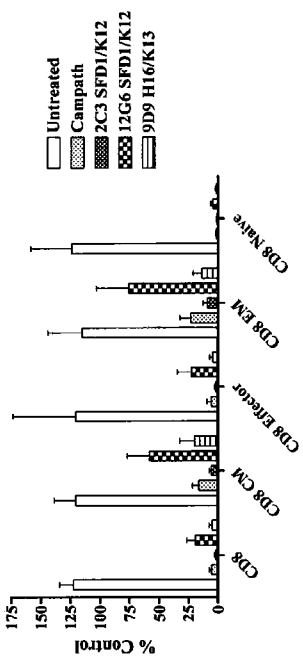


FIG. 89B

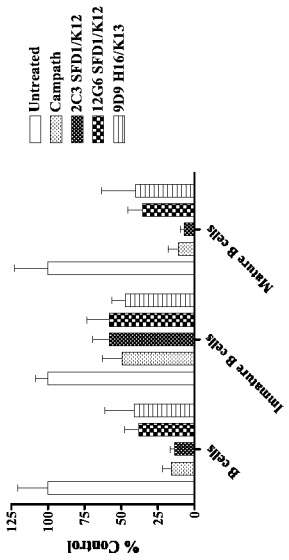


FIG. 89C

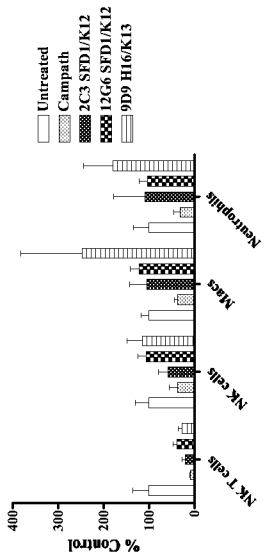


FIG. 89D

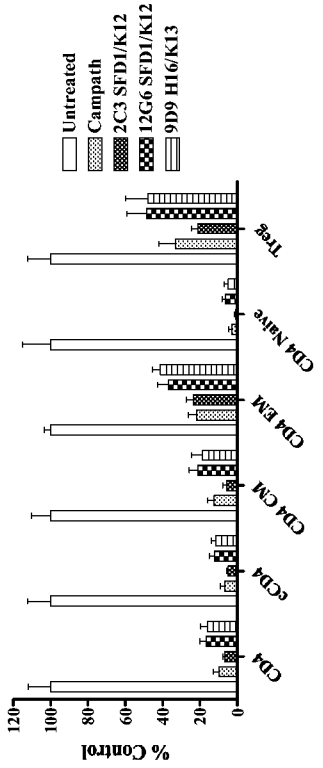


FIG. 90A

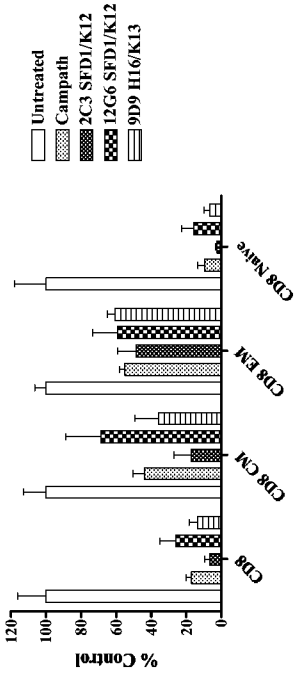


FIG. 90B

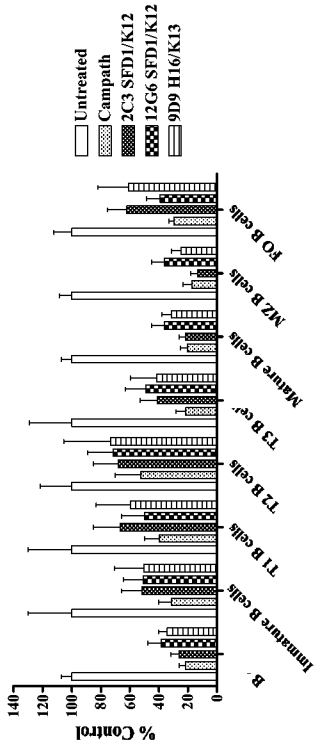


FIG. 90C

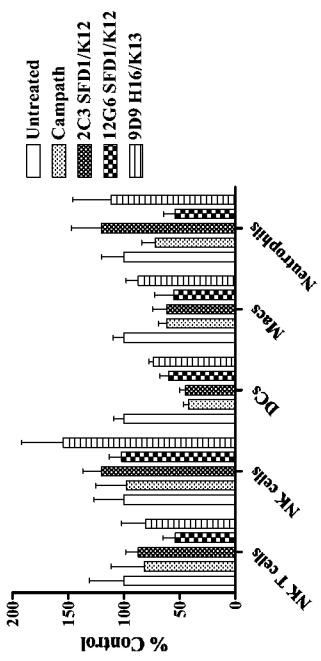


FIG. 90D

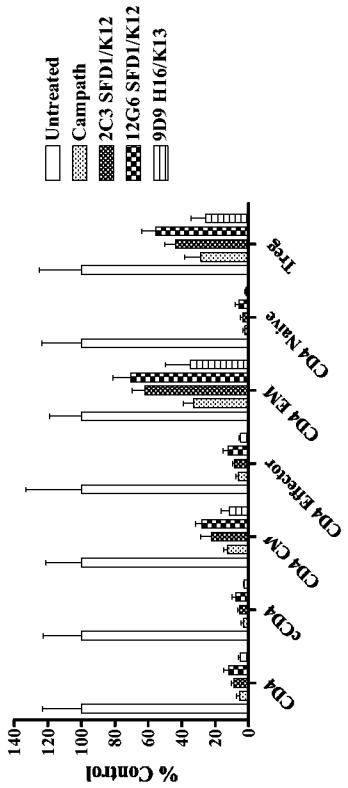


FIG. 91A

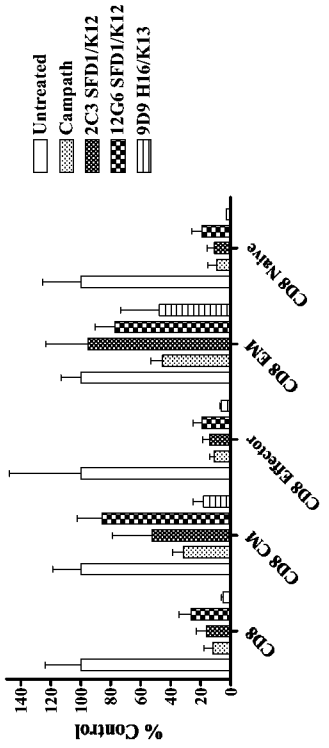


FIG. 91B

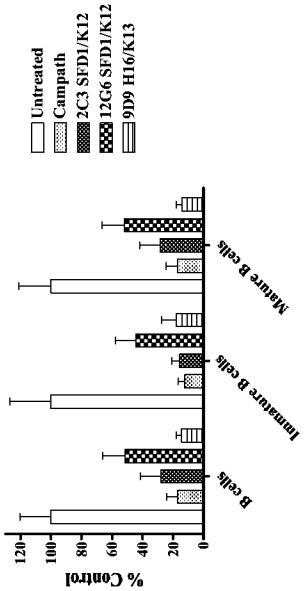


FIG. 91C

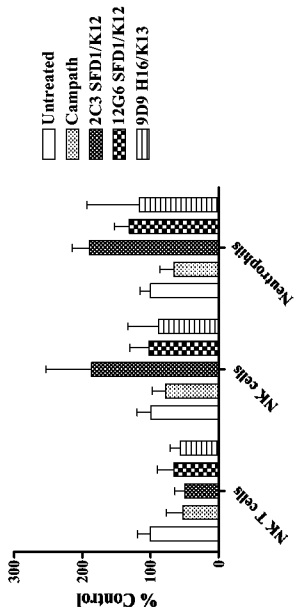


FIG. 91D

FIG. 92

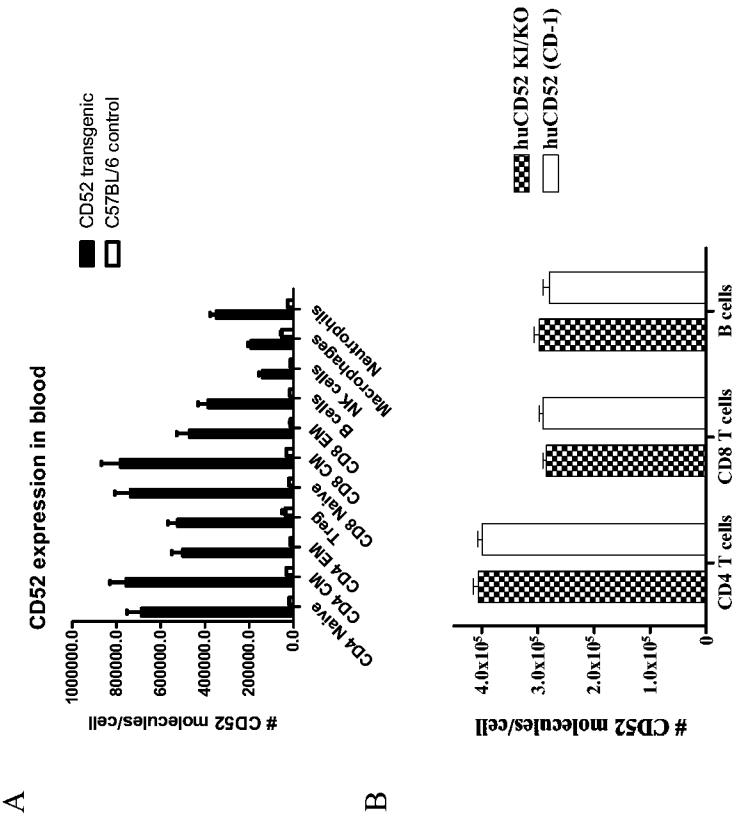
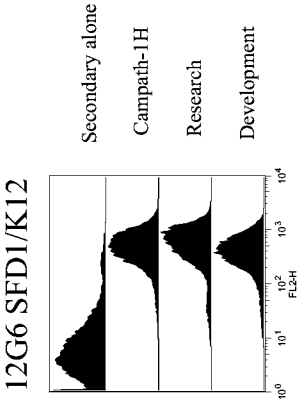

A
CD52 expression in blood
CD52 transgenic
C57BL/6 control
CD52 molecules/cell
1000000.0
800000.0
600000.0
400000.0
200000.0
0.0
CD4 Naive
CD4 CM
CD4 EM
Treg
CD8 Naive
CD8 CM
CD8 EM
B cells
NK cells
Macrophages
Neutrophils
B
huCD52 KI/KO
huCD52 (CD-1)
CD52 molecules/cell
4.0x10^5
3.0x10^5
2.0x10^5
1.0x10^5
0
CD4 T cells
CD8 T cells
B cells

FIG. 93


12G6 SFD1/K12
Secondary alone
Campath-1H
Research
Development
FL2-H

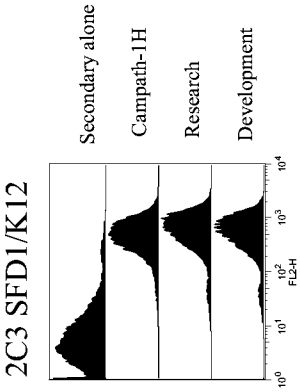

2C3 SFD1/K12
Secondary alone
Campath-1H
Research
Development
FL2-H

FIG. 94

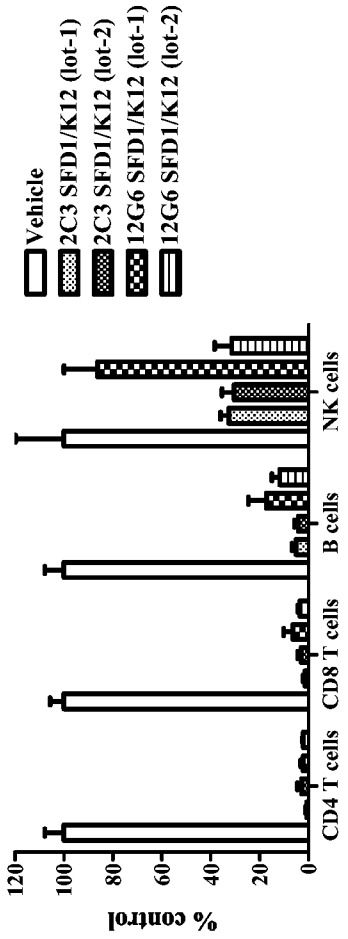

Vehicle
2C3 SFD1/K12 (lot-1)
2C3 SFD1/K12 (lot-2)
12G6 SFD1/K12 (lot-1)
12G6 SFD1/K12 (lot-2)
% control
120
100
80
60
40
20
0
CD4 T cells
CD8 T cells
B cells
NK cells

FIG. 95

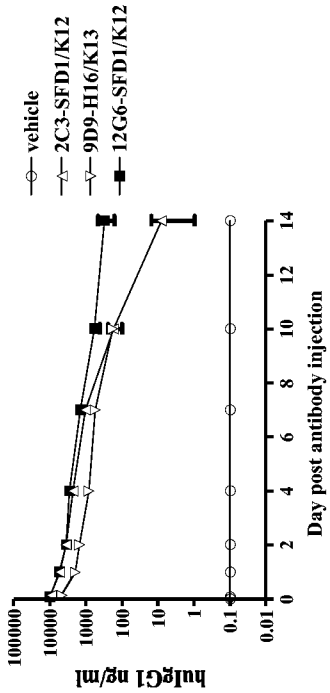

vehicle
2C3-SFD1/K12
9D9-H16/K13
12G6-SFD1/K12
huIgG1 ng/ml
100000
10000
1000
100
10
1
0.1
0.01
0
2
4
6
8
10
12
14
Day post antibody injection

FIG. 96

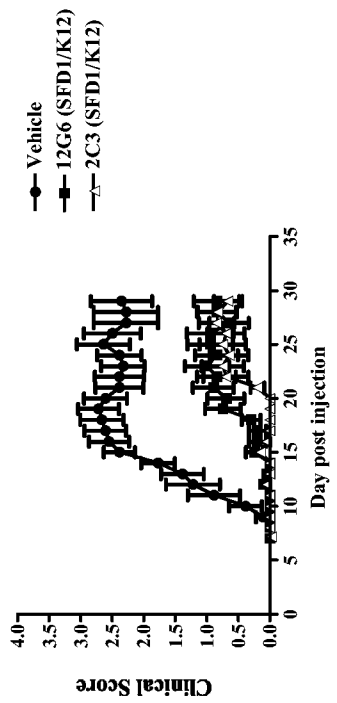

Vehicle
12G6 (SFD1/K12)
2C3 (SFD1/K12)
Clinical Score
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
5
10
15
20
25
30
35
Day post injection

FIG. 97A

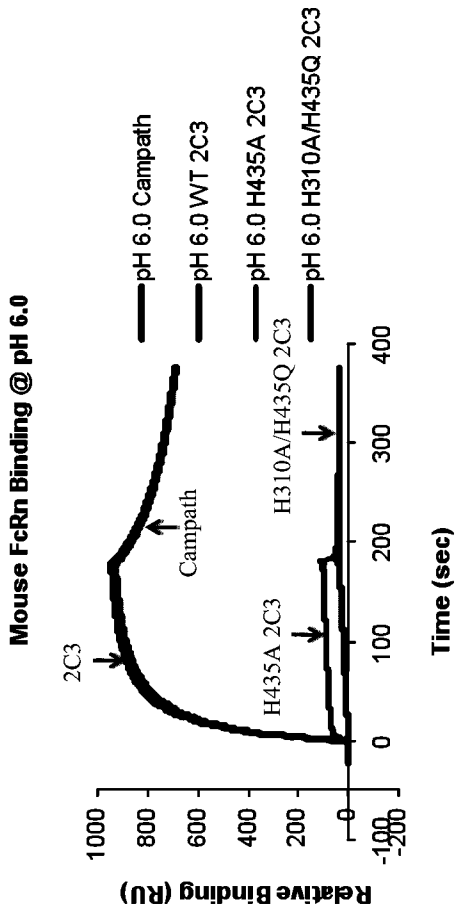

Mouse FcRn Binding @ pH 6.0
pH 6.0 Campath
pH 6.0 WT 2C3
pH 6.0 H435A 2C3
pH 6.0 H310A/H435Q 2C3
2C3
Campath
H435A 2C3
H310A/H435Q 2C3
Relative Binding (RU)
Time (sec)
1000
800
600
400
200
0
-100
-200
0
100
200
300
400

FIG. 97B

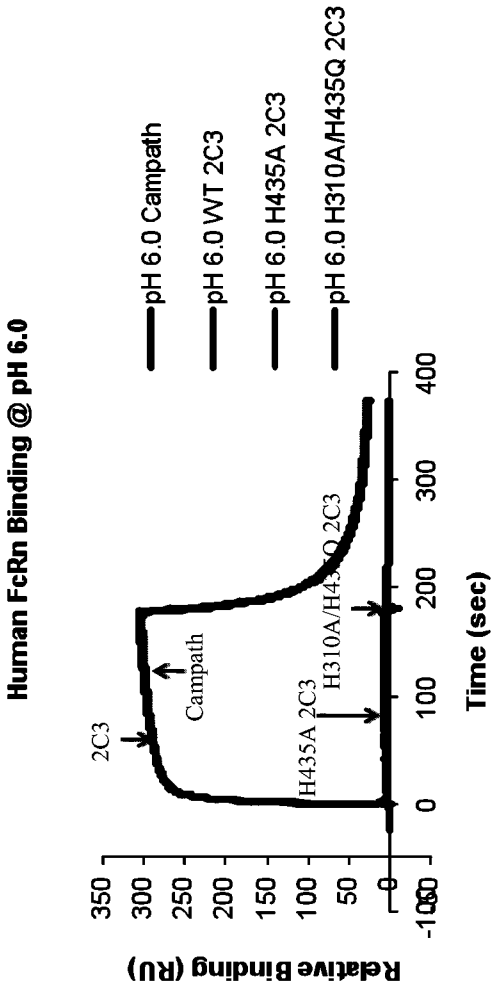

Human FcRn Binding @ pH 6.0
pH 6.0 Campath
pH 6.0 WT 2C3
pH 6.0 H435A 2C3
pH 6.0 H310A/H435Q 2C3
2C3
Campath
H435A 2C3
H310A/H435Q 2C3
Relative Binding (RU)
Time (sec)
350
300
250
200
150
100
50
0
-100
0
100
200
300
400

FIG. 98

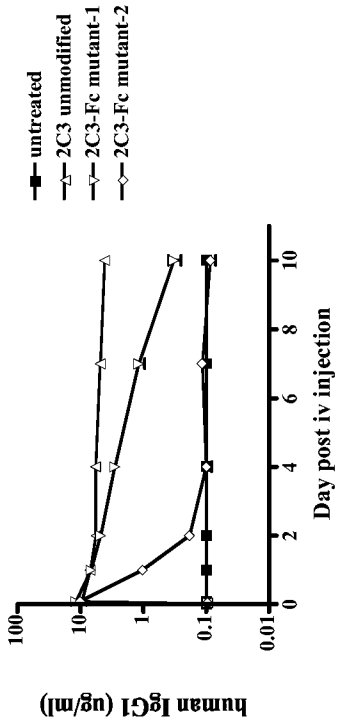

untreated
2C3 unmodified
2C3-Fc mutant-1
2C3-Fc mutant-2
100
10
1
0.1
0.01
0
2
4
6
8
10
Day post iv injection
human IgG1 (ug/ml)

FIG. 99

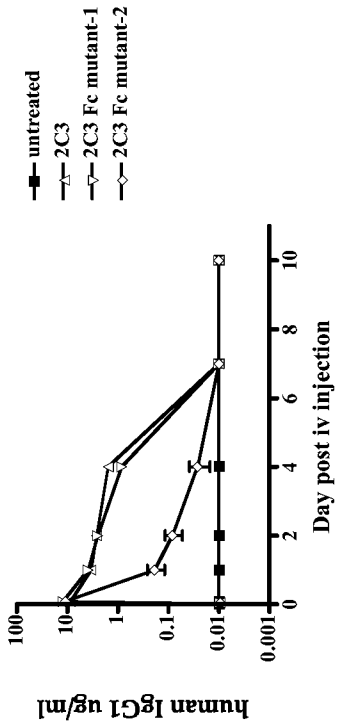
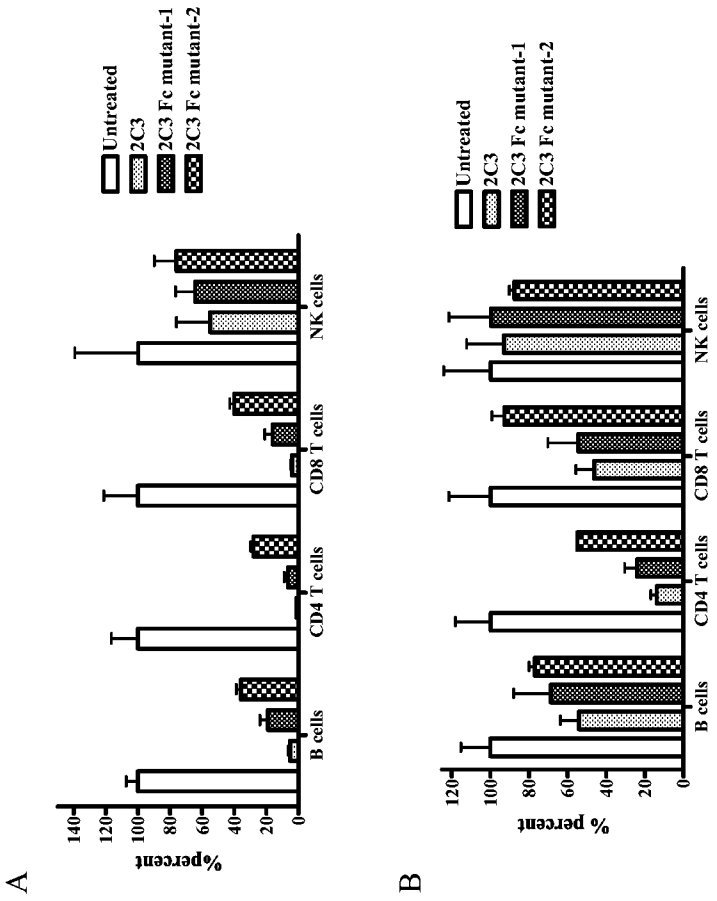

untreated
2C3
2C3 Fc mutant-1
2C3 Fc mutant-2
100
10
1
0.1
0.01
0.001
0
2
4
6
8
10
Day post iv injection
human IgG1 ug/ml

FIG. 100


A
Untreated
2C3
2C3 Fc mutant-1
2C3 Fc mutant-2
%percent
0
20
40
60
80
100
120
140
B cells
CD4 T cells
CD8 T cells
NK cells
B
Untreated
2C3
2C3 Fc mutant-1
2C3 Fc mutant-2
% percent
0
20
40
60
80
100
120
B cells
CD4 T cells
CD8 T cells
NK cells

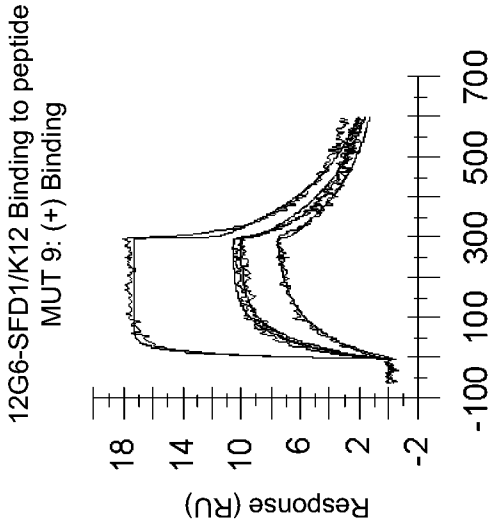


FIG. 101B

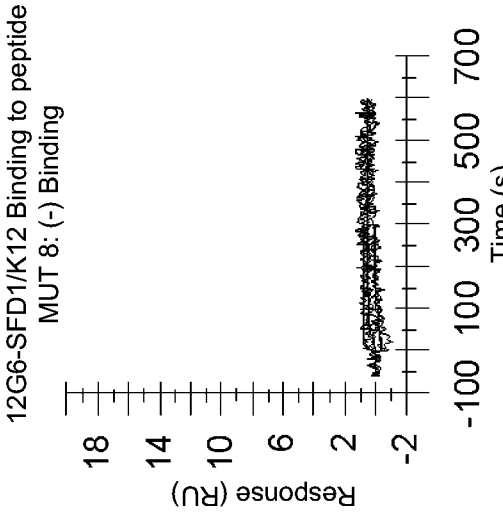


FIG. 101A

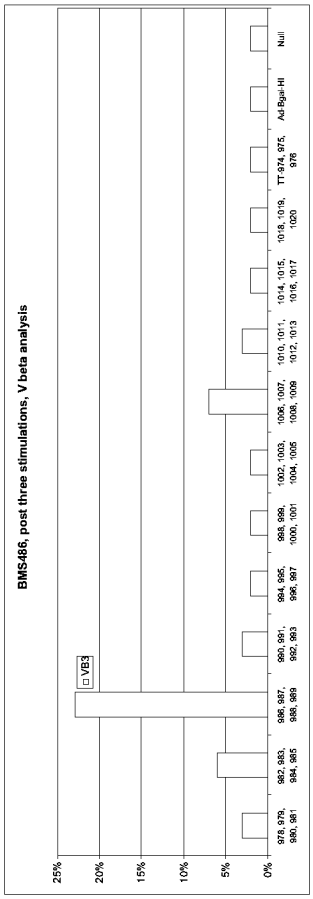

BMS486, post three stimulations, V beta analysis
VB3
25%
20%
15%
10%
5%
0%
978, 979, 980, 981
982, 983, 984, 985
986, 987, 988, 989
990, 991, 992, 993
994, 995, 996, 997
998, 999, 1000, 1001
1002, 1003, 1004, 1005
1006, 1007, 1008, 1009
1010, 1011, 1012, 1013
1014, 1015, 1016, 1017
1018, 1019, 1020
TT-974, 975, 976
AdBgal-HI
Null

FIG. 102

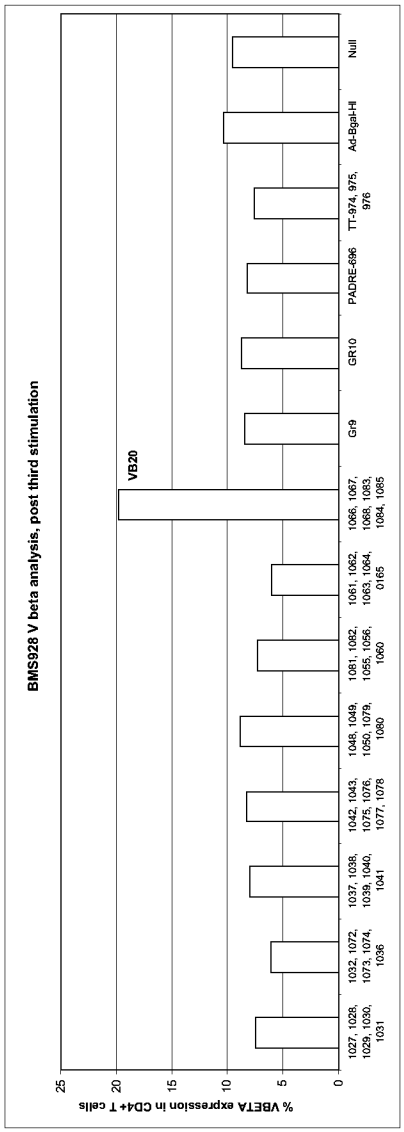

BMS928 V beta analysis, post third stimulation
% VBETA expression in CD4+ T cells
0
5
10
15
20
25
VB20
1027, 1028, 1029, 1030, 1031
1032, 1072, 1073, 1074, 1036
1037, 1038, 1039, 1040, 1041
1042, 1043, 1075, 1076, 1077, 1078
1048, 1049, 1050, 1079, 1080
1081, 1082, 1055, 1056, 1060
1061, 1062, 1063, 1064, 0165
1066, 1067, 1068, 1083, 1084, 1085
Gr9
GR10
PADRE-696
TT-974, 975, 976
Ad-Bgal-HI
Null

FIG. 103

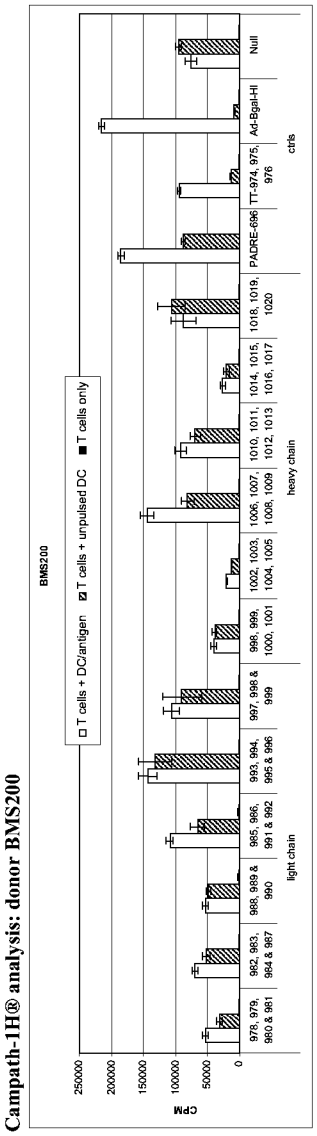

Campath-1H® analysis: donor BMS200
BMS200
T cells + DC/antigen
T cells + unpulsed DC
T cells only
CPM
250000
200000
150000
100000
50000
0
978, 979, 980 & 981
982, 983, 984 & 987
988, 989 & 990
985, 986, 991 & 992
993, 994, 995 & 996
997, 998 & 999
998, 999, 1000, 1001
1002, 1003, 1004, 1005
1006, 1007, 1008, 1009
1010, 1011, 1012, 1013
1014, 1015, 1016, 1017
1018, 1019, 1020
PADRE-696
TT-974, 975, 976
Ad-BgaI-HI
Null
light chain
heavy chain
ctrls

FIG. 104A

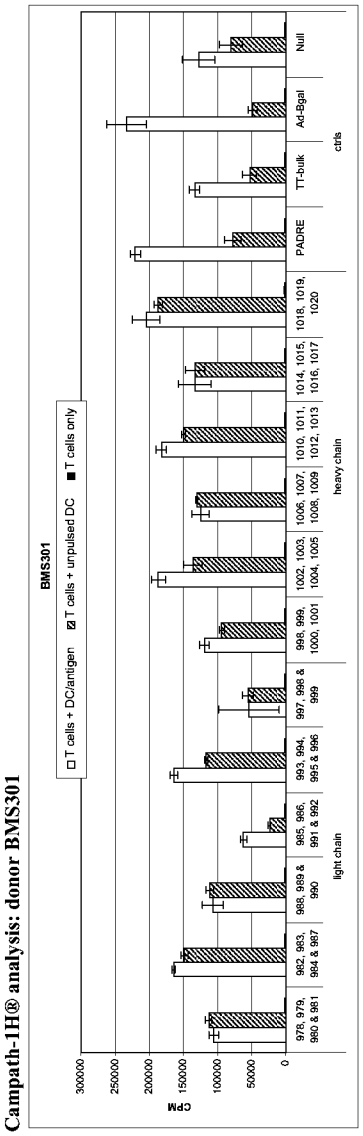

Campath-1H® analysis: donor BMS301
BMS301
T cells + DC/antigen
T cells + unpulsed DC
T cells only
CPM
300000
250000
200000
150000
100000
50000
0
978, 979, 980 & 981
982, 983, 984 & 987
988, 989 & 990
985, 986, 991 & 992
993, 994, 995 & 996
997, 998 & 999
998, 999, 1000, 1001
1002, 1003, 1004, 1005
1006, 1007, 1008, 1009
1010, 1011, 1012, 1013
1014, 1015, 1016, 1017
1018, 1019, 1020
PADRE
TT-bulk
Ad-Bgal
Null
light chain
heavy chain
ctrls

FIG. 104B

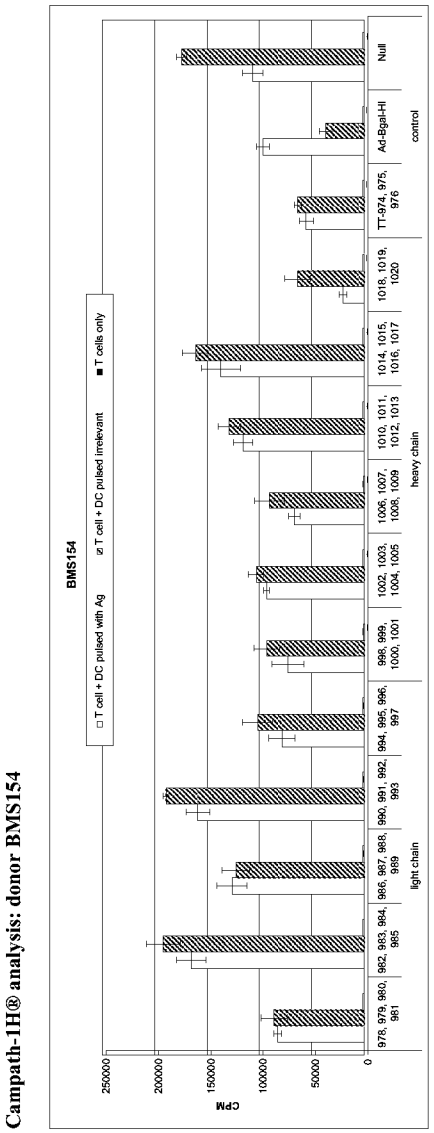

Campath-1H® analysis: donor BMS154
BMS154
□ T cell + DC pulsed with Ag
T cell + DC pulsed irrelevant
■ T cells only
CPM
250000
200000
150000
100000
50000
0
976, 979, 980, 981
982, 983, 984, 985
986, 987, 988, 989
990, 991, 992, 993
994, 995, 996, 997
998, 999, 1000, 1001
1002, 1003, 1004, 1005
1006, 1007, 1008, 1009
1010, 1011, 1012, 1013
1014, 1015, 1016, 1017
1018, 1019, 1020
TT-974, 975, 976
Ad-Bgal-HI
Null
light chain
heavy chain
control

FIG. 104C

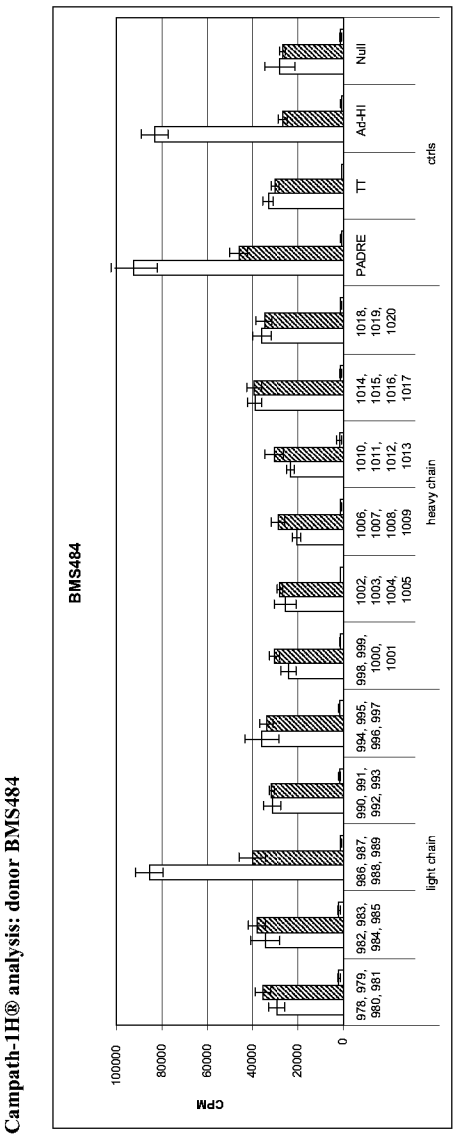

Campath-1H® analysis: donor BMS484
BMS484
CPM
100000
80000
60000
40000
20000
0
978, 979, 980, 981
982, 983, 984, 985
986, 987, 988, 989
990, 991, 992, 993
994, 995, 996, 997
998, 999, 1000, 1001
1002, 1003, 1004, 1005
1006, 1007, 1008, 1009
1010, 1011, 1012, 1013
1014, 1015, 1016, 1017
1018, 1019, 1020
PADRE
TT
Ad-HI
Null
light chain
heavy chain
ctrls

FIG. 104D

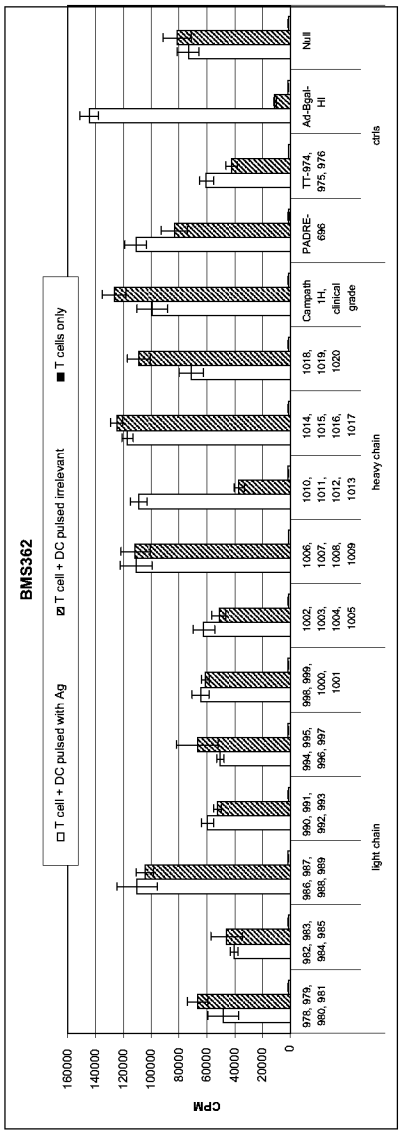

Campath-1H® analysis: donor BMS362
BMS362
T cell + DC pulsed with Ag
T cell + DC pulsed irrelevant
T cells only
CPM
160000
140000
120000
100000
80000
60000
40000
20000
0
978, 979, 980, 981
982, 983, 984, 985
986, 987, 988, 989
990, 991, 992, 993
994, 995, 996, 997
998, 999, 1000, 1001
1002, 1003, 1004, 1005
1006, 1007, 1008, 1009
1010, 1011, 1012, 1013
1014, 1015, 1016, 1017
1018, 1019, 1020
Campath 1H, clinical grade
PADRE-696
TT-974, 975, 976
Ad-BgaI-HI
Null
light chain
heavy chain
ctrls

FIG. 104E

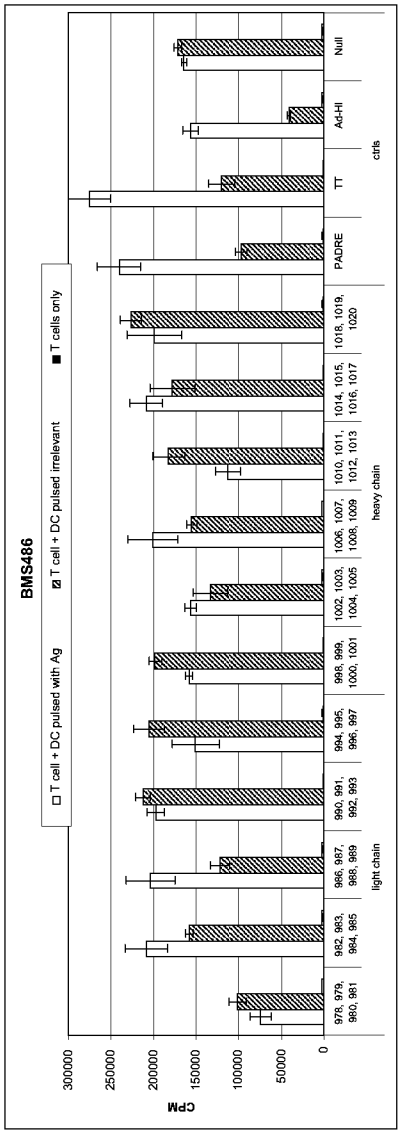

Campath-1H® analysis: donor BMS486
BMS486
T cell + DC pulsed with Ag
T cell + DC pulsed irrelevant
T cells only
CPM
300000
250000
200000
150000
100000
50000
0
978, 979, 980, 981
982, 983, 984, 985
986, 987, 988, 989
990, 991; 992, 993
994, 995, 996, 997
998, 999, 1000, 1001
1002, 1003, 1004, 1005
1006, 1007, 1008, 1009
1010, 1011, 1012, 1013
1014, 1015, 1016, 1017
1018, 1019, 1020
PADRE
TT
Ad-HI
Null
light chain
heavy chain
ctrls

FIG. 104F

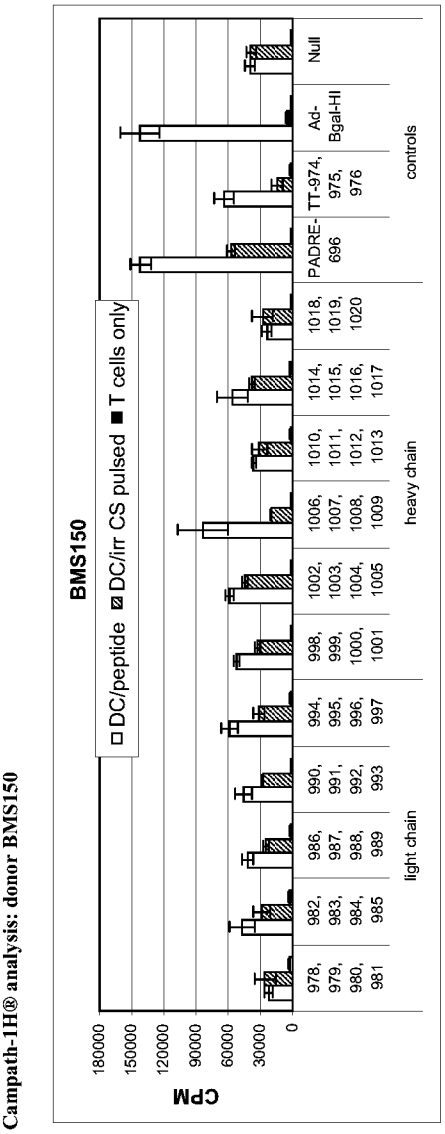

Campath-1H® analysis: donor BMS150
BMS150
DC/peptide
DC/irr CS pulsed
T cells only
CPM
180000
150000
120000
90000
60000
30000
0
978, 979, 980, 981
982, 983, 984, 985
986, 987, 988, 989
990, 991, 992, 993
994, 995, 996, 997
998, 999, 1000, 1001
1002, 1003, 1004, 1005
1006, 1007, 1008, 1009
1010, 1011, 1012, 1013
1014, 1015, 1016, 1017
1018, 1019, 1020
PADRE-696
TT-974, 975, 976
Ad-Bgal-HI
Null
light chain
heavy chain
controls

FIG. 104G

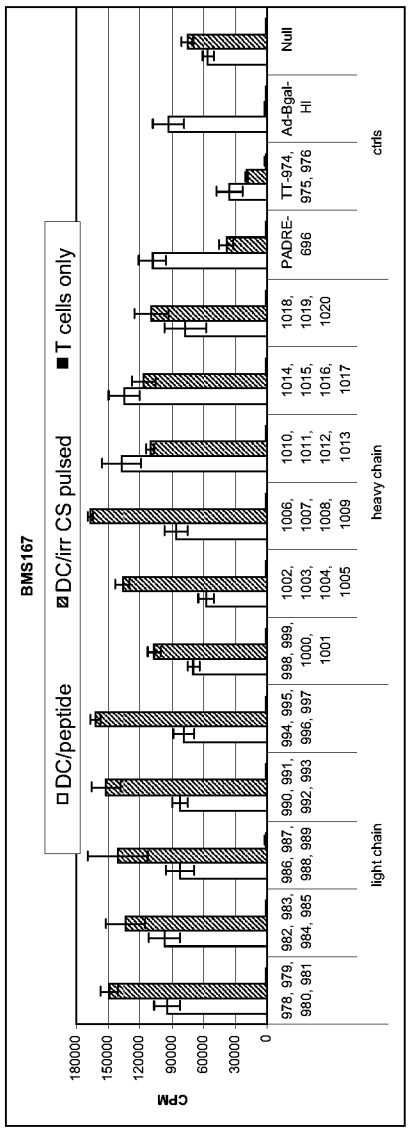

Campath-1H® analysis: donor BMS167
BMS167
DC/peptide
DC/irr CS pulsed
T cells only
CPM
180000
150000
120000
90000
60000
30000
0
978, 979, 980, 981
982, 983, 984, 985
986, 987, 988, 989
990, 991, 992, 993
994, 995, 996, 997
998, 999, 1000, 1001
1002, 1003, 1004, 1005
1006, 1007, 1008, 1009
1010, 1011, 1012, 1013
1014, 1015, 1016, 1017
1018, 1019, 1020
PADRE-696
TT-974, 975, 976
Ad-Bgal-HI
Null
light chain
heavy chain
ctrls

FIG. 104H

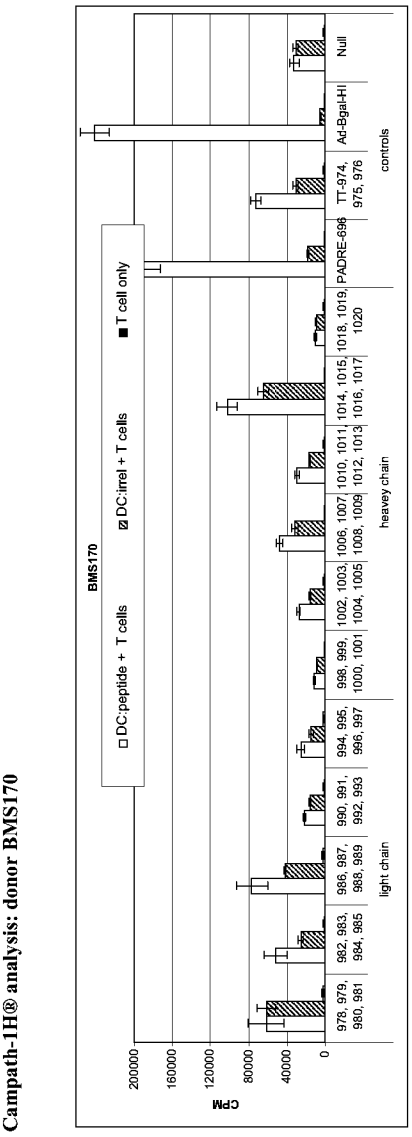

Campath-1H® analysis: donor BMS170
BMS170
DC:peptide + T cells
DC:irrel + T cells
T cell only
CPM
200000
160000
120000
80000
40000
0
978, 979, 980, 981
982, 983, 984, 985
986, 987, 988, 989
990, 991, 992, 993
994, 995, 996, 997
998, 999, 1000, 1001
1002, 1003, 1004, 1005
1006, 1007, 1008, 1009
1010, 1011, 1012, 1013
1014, 1015, 1016, 1017
1018, 1019, 1020
PADRE-698
TT-974, 975, 976
Ad-Bgal-HI
Null
light chain
heavey chain
controls

FIG. 104I

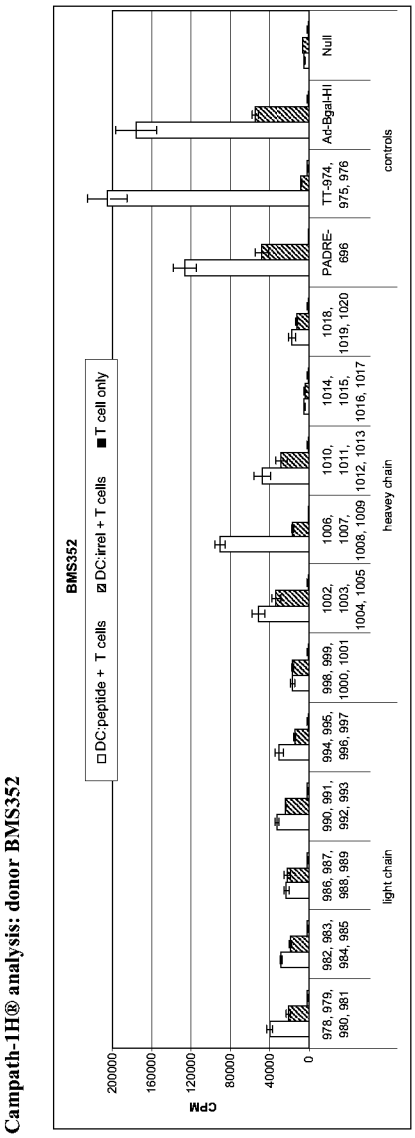

Campath-1H® analysis: donor BMS352
BMS352
DC:peptide + T cells
DC:irrel + T cells
T cell only
CPM
200000
160000
120000
80000
40000
0
978, 979, 980, 981
982, 983, 984, 985
986, 987, 988, 989
990, 991, 992, 993
994, 995, 996, 997
998, 999, 1000, 1001
1002, 1003, 1004, 1005
1006, 1007, 1008, 1009
1010, 1011, 1012, 1013
1014, 1015, 1016, 1017
1018, 1019, 1020
PADRE-696
TT-974, 975, 976
Ad-Bgal-HI
Null
light chain
heavey chain
controls

FIG. 104J

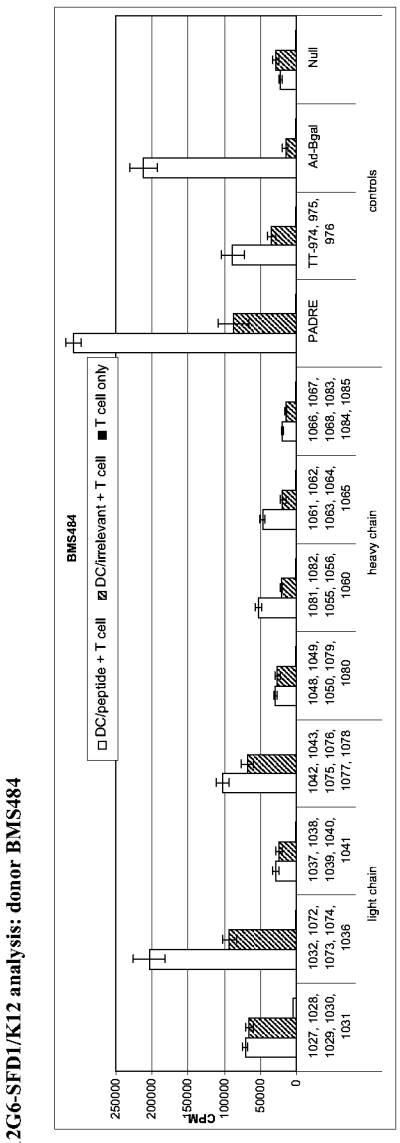

12G6-SFD1/K12 analysis: donor BMS484
BMS484
DC/peptide + T cell
DC/irrelevant + T cell
T cell only
CPM
250000
200000
150000
100000
50000
0
1027, 1028, 1029, 1030, 1031
1032, 1072, 1073, 1074, 1036
1037, 1038, 1039, 1040, 1041
1042, 1043, 1075, 1076, 1077, 1078
1048, 1049, 1050, 1079, 1080
1081, 1082, 1055, 1056, 1060
1061, 1062, 1063, 1064, 1065
1066, 1067, 1068, 1083, 1084, 1085
PADRE
TT-974, 975, 976
Ad-Bgal
Null
light chain
heavy chain
controls

FIG. 105A

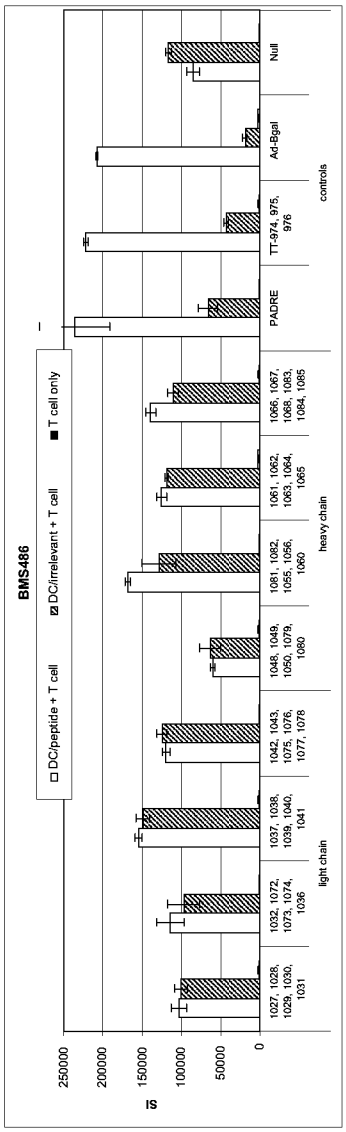

12G6-SFD1/K12 analysis: donor BMS486
BMS486
DC/peptide + T cell
DC/irrelevant + T cell
T cell only
IS
250000
200000
150000
100000
50000
0
1027, 1028, 1029, 1030, 1031
1032, 1072, 1073, 1074, 1036
1037, 1038, 1039, 1040, 1041
1042, 1043, 1075, 1076, 1077, 1078
1048, 1049, 1050, 1079, 1080
1061, 1082, 1055, 1056, 1060
1061, 1062, 1063, 1064, 1065
1066, 1067, 1068, 1083, 1084, 1085
PADRE
TT-974, 975, 976
Ad-Bgal
Null
light chain
heavy chain
controls

FIG. 105B

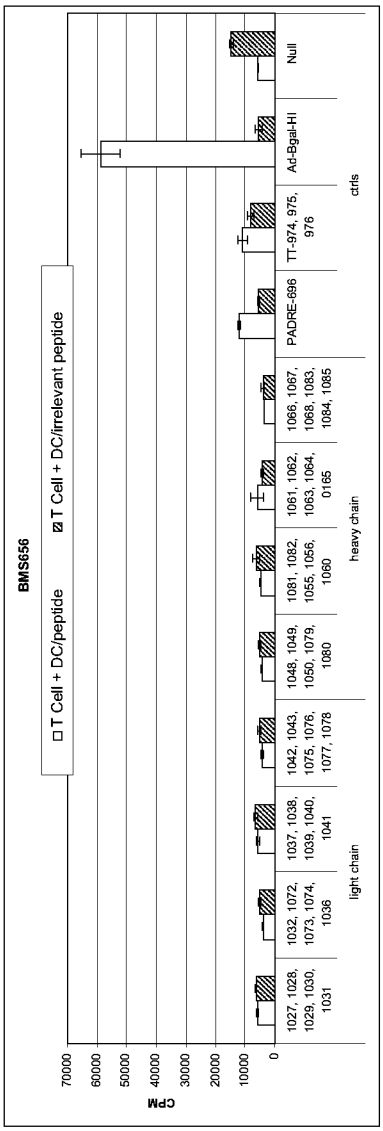

12G6-SFD1/K12 analysis: donor BMS656
BMS656
T Cell + DC/peptide
T Cell + DC/irrelevant peptide
CPM
70000
60000
50000
40000
30000
20000
10000
0
1027, 1028, 1029, 1030, 1031
1032, 1072, 1073, 1074, 1036
1037, 1038, 1039, 1040, 1041
1042, 1043, 1075, 1076, 1077, 1078
1048, 1049, 1050, 1079, 1080
1081, 1082, 1055, 1056, 1060
1061, 1062, 1063, 1064, 0165
1066, 1067, 1068, 1083, 1084, 1085
PADRE-896
TT-974, 975, 976
Ad-Bgal-HI
Null
light chain
heavy chain
ctrls

FIG. 105C

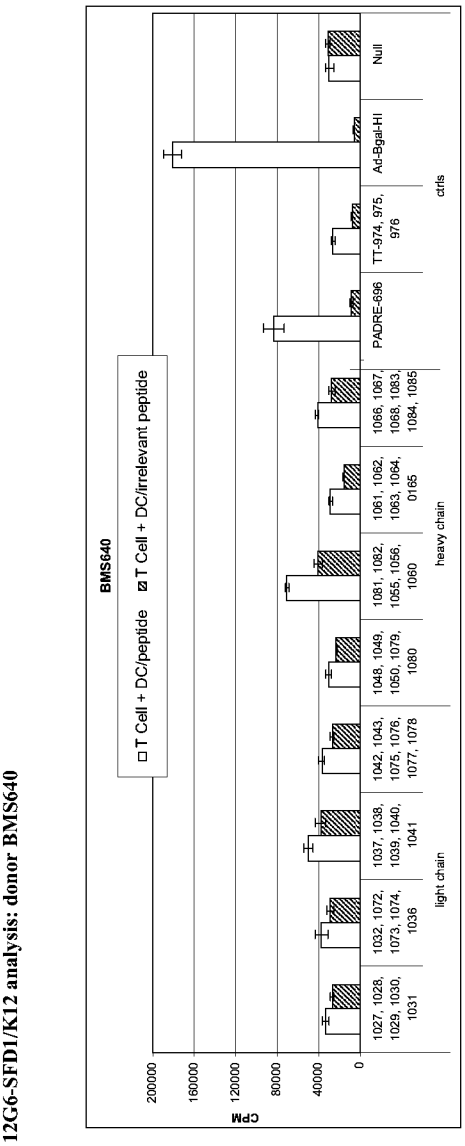

12G6-SFD1/K12 analysis: donor BMS640
BMS640
T Cell + DC/peptide
T Cell + DC/irrelevant peptide
CPM
200000
160000
120000
80000
40000
0
1027, 1028, 1029, 1030, 1031
1032, 1072, 1073, 1074, 1036
1037, 1038, 1039, 1040, 1041
1042, 1043, 1075, 1076, 1077, 1078
1048, 1049, 1050, 1079, 1080
1081, 1082, 1055, 1056, 1060
1061, 1062, 1063, 1064, 0165
1066, 1067, 1068, 1083, 1084, 1085
PADRE-896
TT-974, 975, 976
Ad-Bgal-HI
Null
light chain
heavy chain
ctrls

FIG. 105D

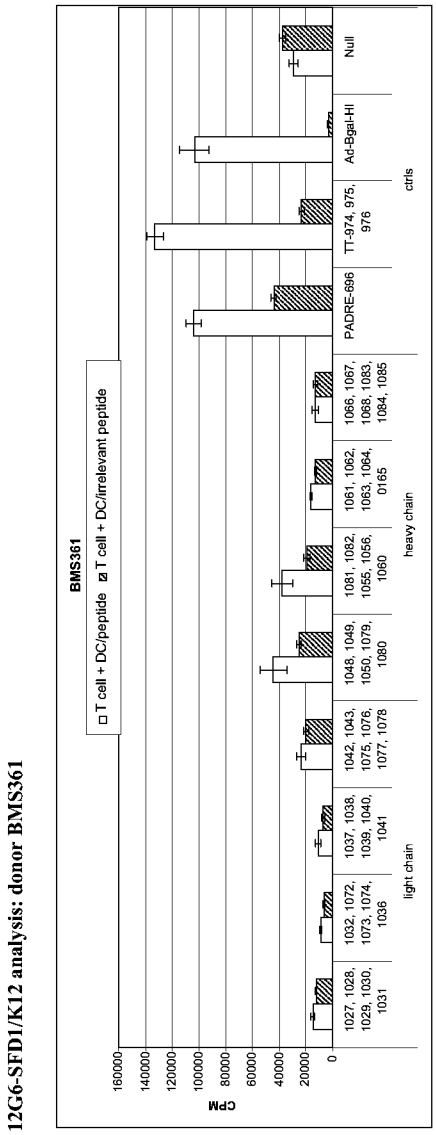

12G6-SFD1/K12 analysis: donor BMS361
BMS361
T cell + DC/peptide
T cell + DC/irrelevant peptide
CPM
160000
140000
120000
100000
80000
60000
40000
20000
0
1027, 1028, 1029, 1030, 1031
1032, 1072, 1073, 1074, 1036
1037, 1038, 1039, 1040, 1041
1042, 1043, 1075, 1076, 1077, 1078
1048, 1049, 1050, 1079, 1080
1081, 1082, 1055, 1056, 1060
1061, 1062, 1063, 1064, 0165
1066, 1067, 1068, 1083, 1084, 1085
PADRE-696
TT-974, 975, 976
Ad-Bgal-HI
Null
light chain
heavy chain
ctrls

FIG. 105E

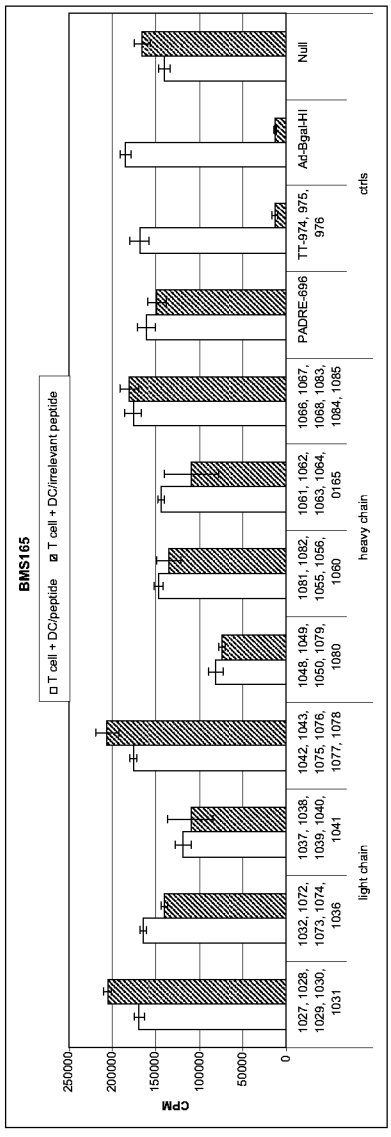

12G6-SFD1/K12 analysis: donor BMS165
BMS165
T cell + DC/peptide
T cell + DC/irrelevant peptide
CPM
250000
200000
150000
100000
50000
0
1027, 1028, 1029, 1030, 1031
1032, 1072, 1073, 1074, 1036
1037, 1038, 1039, 1040, 1041
1042, 1043, 1075, 1076, 1077, 1078
1048, 1049, 1050, 1079, 1080
1081, 1082, 1055, 1056, 1060
1061, 1062, 1063, 1064, 0165
1066, 1067, 1068, 1083, 1084, 1085
PADRE-696
TT-974, 975, 976
Ad-Bgal-HI
Null
light ch'ain
heavy ch'ain
ctrls

FIG. 105F

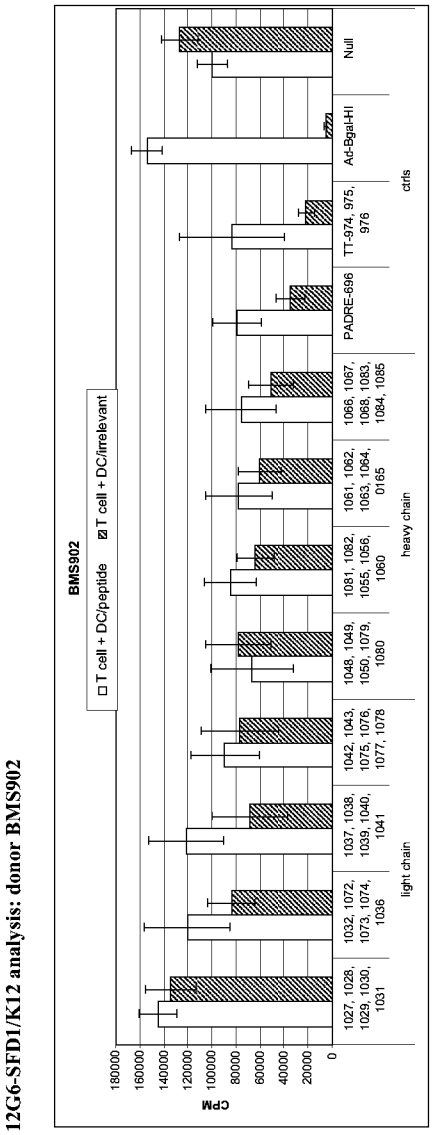

12G6-SFD1/K12 analysis: donor BMS902
BMS902
T cell + DC/peptide
T cell + DC/irrelevant
CPM
180000
160000
140000
120000
100000
80000
60000
40000
20000
0
1027, 1028, 1029, 1030, 1031
1032, 1072, 1073, 1074, 1036
1037, 1038, 1039, 1040, 1041
1042, 1043, 1075, 1076, 1077, 1078
1048, 1049, 1050, 1079, 1080
1081, 1082, 1055, 1056, 1060
1061, 1062, 1063, 1064, 0165
1066, 1067, 1068, 1083, 1084, 1085
PADRE-696
TT-974, 975, 976
Ad-Bgal-HI
Null
light chain
heavy chain
ctrls

FIG. 105G

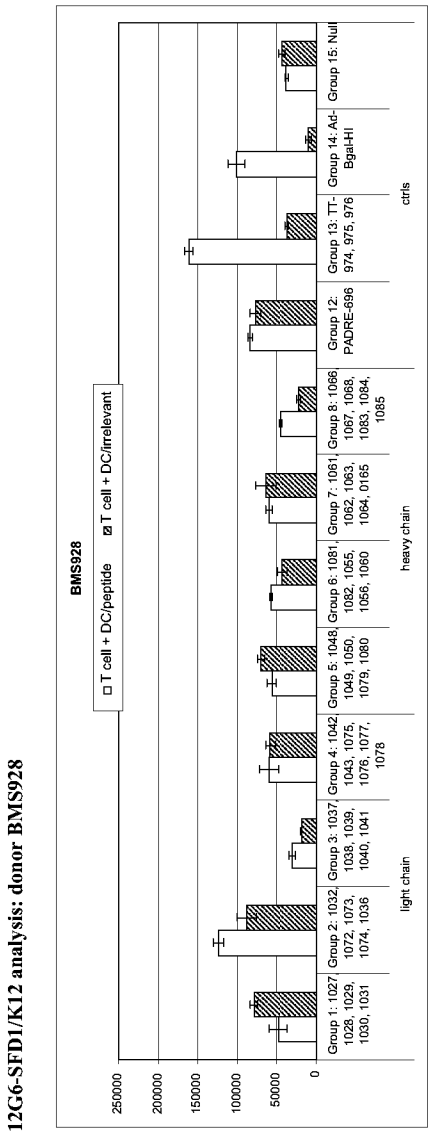

12G6-SFD1/K12 analysis: donor BMS928
BMS928
T cell + DC/peptide
T cell + DC/irrelevant
250000
200000
150000
100000
50000
0
Group 1: 1027, 1028, 1029, 1030, 1031
Group 2: 1032, 1072, 1073, 1074, 1036
Group 3: 1037, 1038, 1039, 1040, 1041
Group 4: 1042, 1043, 1075, 1076, 1077, 1078
Group 5: 1048, 1049, 1050, 1079, 1080
Group 6: 1081, 1082, 1055, 1056, 1060
Group 7: 1061, 1062, 1063, 1064, 0165
Group 8: 1066, 1067, 1068, 1083, 1084, 1085
Group 12: PADRE-696
Group 13: TT-974, 975, 976
Group 14: Ad-BgaI-HI
Group 15: Null
light chain
heavy chain
ctrls

FIG. 105H

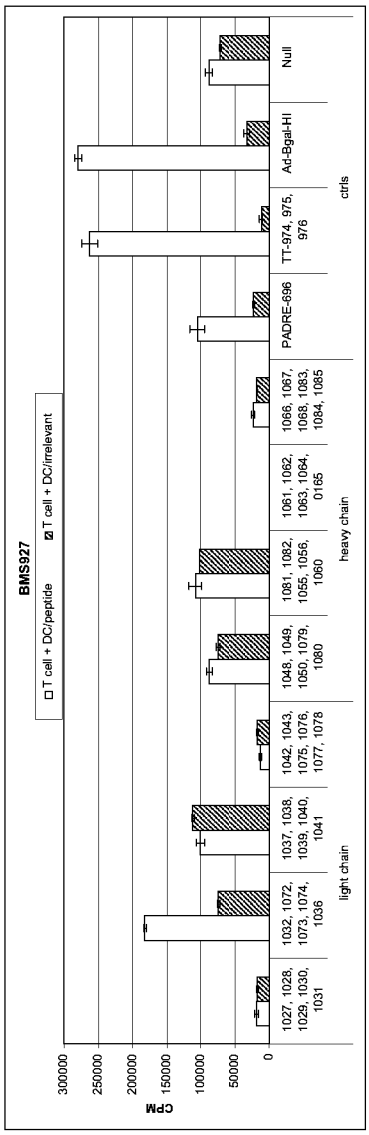

12G6-SFD1/K12 analysis: donor BMS927
BMS927
T cell + DC/peptide
T cell + DC/irrelevant
CPM
300000
250000
200000
150000
100000
50000
0
1027, 1028, 1029, 1030, 1031
1032, 1072, 1073, 1074, 1036
1037, 1038, 1039, 1040, 1041
1042, 1043, 1075, 1076, 1077, 1078
1048, 1049, 1050, 1079, 1080
1081, 1082, 1055, 1056, 1060
1061, 1062, 1063, 1064, 0165
1066, 1067, 1068, 1083, 1084, 1085
PADRE-696
TT-974, 975, 976
Ad-Bgal-HI
Null
light chain
heavy chain
ctrls

FIG. 105I

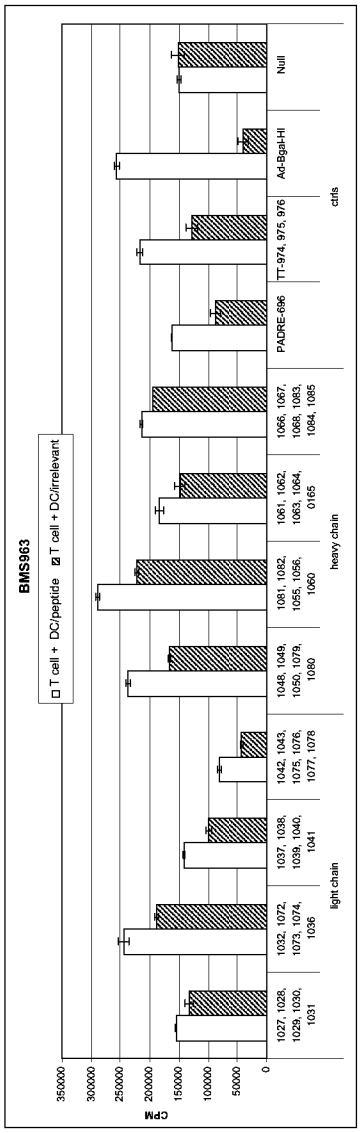

12G6-SFD1/K12 analysis: donor BMS963
BMS963
T cell + DC/peptide
T cell + DC/irrelevant
CPM
350000
300000
250000
200000
150000
100000
50000
0
1027, 1028, 1029, 1030, 1031
1032, 1072, 1073, 1074, 1036
1037, 1038, 1039, 1040, 1041
1042, 1043, 1075, 1076, 1077, 1078
1048, 1049, 1050, 1079, 1080
1051, 1052, 1055, 1056, 1060
1061, 1062, 1063, 1064, 0165
1066, 1067, 1068, 1083, 1084, 1085
PADRE-596
TT-974, 975, 976
Ad-Bgal-HI
Null
light chain
heavy chain
ctrls

FIG. 105J

Humanized 2C3 clone full-length heavy chain sequence

2C3-SFD1
MEAPAQLLFLLLLWLPDTTGEVQLVESGGGLVQPGGSLRLSCAASGFTFNTYWMNWV
RQAPGKGLEWVGQIRLKSNNYATHYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAV
YYCTPVDFWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVE
PKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFN
WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIE
KTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
(SEQ ID NO: 272)

Humanized 2C3 clone full-length light chain sequence

2C3-K12
MEAPAQLLFLLLLWLPDTTGDIVMTQTPLSLSVTPGQPASISCKSSQSLLYSNGKTYLNW
LLQKPGQSPQRLIYLVSKLDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCVQGTHL
HTFGQGTRLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNAL
QSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGE
C (SEQ ID NO: 273)

FIG. 106

Humanized 7F11 clone full-length heavy chain sequence

7F11-SFD1
MEAPAQLLFLLLLWLPDTTGEVQLVESGGGLVQPGGSLRLSCAASGFTFTDYYMSWV
RQAPGKGLEWVGFIRNKANGYTTEYNASVKGRFTISRDDSKNSLYLQMNSLKTEDTA
VYYCTRYIFFDYWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEP
VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV
DKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHED
PEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSN
KALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESN
GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
SLSPGK (SEQ ID NO: 274)

Humanized 7F11 clone full-length light chain sequence

7F11-K2
MEAPAQLLFLLLLWLPDTTGDIVMTQTPLSLSVTPGQPASISCRSSQSLVHTNGNSYLH
WYLQKPGQSPQLLIYMVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTH
VPFTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN
ALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNR
GEC (SEQ ID NO: 275)

FIG. 107

Humanized 9D9 clone full-length heavy chain sequences

9D9-H16
MEAPAQLLFLLLLWLPDTTGEVQLLESGGGLVQPGGSLRLSCAASGFTFSDAWMDWV
RQAPGKGLELVSEIRNKAKNHATYYAESVKGRFTISRDNSKNTLYLQMNSLRAEDTAV
YYCTTLDSWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVE
PKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFN
WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIE
KTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
(SEQ ID NO: 276)

9D9-H18
MEAPAQLLFLLLLWLPDTTGEVQLLESGGGLVQPGGSLRLSCAASGFTFSDAWMDWV
RQAPGKGLELVAEIRNKAKNHATYYAESVKGRFTISRDNSKNTLYLQMNSLRAEDTAV
YYCTTLDSWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVE
PKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFN
WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIE
KTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK
TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
(SEQ ID NO: 277)

Humanized 9D9 clone full-length light chain sequence

9D9-K13
MEAPAQLLFLLLLWLPDTTGDIVMTQTPLSLSVTPGQPASISCKSSQSLLDSDGKTYLNW
LLQKPGQSPQRLIYLVSALDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCWQGTHF
PWTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNA
LQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG
EC (SEQ ID NO: 278)

FIG. 108

Humanized 12G6 clone full-length heavy chain sequence

12G6-SFD1
MEAPAQLLFLLLLWLPDTTGEVQLVESGGGLVQPGGSLRLSCAASGFPFSNYWMN
WVRQAPGKGLEWVGQIRLKSNNYATHYAESVKGRFTISRDDSKNSLYLQMNSLKTE
DTAVYYCTPIDYWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNT
KVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS
HEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKC
KVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAV
EWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNH
YTQKSLSLSPGK (SEQ ID NO: 279)

Humanized 12G6 clone full-length light chain sequence

12G6-K12
MEAPAQLLFLLLLWLPDTTGDIVMTQTPLSLSVTPGQPASISCKSSQSLLYSNGKTYL
NWVLQKPGQSPQRLIYLVSKLDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCVQ
GSHFHTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWK
VDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVT
KSFNRGEC (SEQ ID NO: 280)

FIG. 109

Humanized 4B10 clone full-length heavy chain sequence

4B10-H1
MEAPAQLLFLLLLWLPDTTGEVQLVESGGGLVQPGGSLRLSCAASGFTFSDYYMSW
VRQAPGKGLEWVGFIRNKANGYTTEYSASVKGRFTISRDDSKNSLYLQMNSLKTED
TAVYYCARYIWFDYWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKD
YFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKP
SNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVV
DVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSD
IAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL
HNHYTQKSLSLSPGK (SEQ ID NO: 281)

Humanized 4B10 clone full-length light chain sequence

4B10-K1
MEAPAQLLFLLLLWLPDTTGDIVMTQTPLSLSVTPGQPASISCRSSQSLVHTNGNTYL
HWYLQKPGQSPQLLIYMVSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQ
SAHVPPLTFGQGTRLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQ
WKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSS
PVTKSFNRGEC (SEQ ID NO: 282)

FIG. 110

Humanized 2C3 clone full-length heavy chain nucleic acid sequence

2C3-SFD1
ATGGAAGCCCCAGCGCAGCTTCTCTTCCTCCTGCTACTCTGGCTCCCTGATACCACCGGA
GAGGTACAGCTGGTGGAGTCGGGAGGAGGCTTGGTACAGCCTGGGGGTTCTCTGA
GACTCTCCTGTGCAGCTTCTGGATTCACTTTCAATACCTACTGGATGAACTGGGTCC
GCCAGGCTCCAGGGAAGGGACTTGAGTGGGTGGGTCAAATTAGATTGAAATCTAAT
AATTATGCAACACATTATGCGGAGTCTGTGAAAGGGCGGTTCACCATCTCCAGAGA
TGATTCCAAAAACAGCCTCTATCTTCAAATGAATTCCCTGAAAACTGAAGACACTGC
CGTTTATTACTGTACCCCAGTTGACTTTTGGGGCCAAGGCACCACTGTCACAGTCTC
CTCA*GCCTCCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG*
GGGGTACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCG
TGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGG
ACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACAT
CTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACAAGAAAGTTGAGCCCAAATCTTG
TGACAAAACTCACACATGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTT
CCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGT
GGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGG
AGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTC
AGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCC
AACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAA
CCACAGGTGTACACCCTGCCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGAC
ATGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGC
CGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCTACA
GCAAGCTCACCGTGGACAAGTCCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATG
*CATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTAAA*TGA
(SEQ ID NO: 283)

Humanized 2C3 clone full-length light chain nucleic acid sequence

2C3-K12
ATGGAAGCCCCAGCGCAGCTTCTCTTCCTCCTGCTACTCTGGCTCCCTGATACCACCGGA
GACATTGTGATGACCCAGACTCCACTCAGTTTGTCAGTTACCCCTGGACAACCAGC
CTCAATCTCTTGCAAGTCAAGTCAGAGCCTCTTATATAGTAATGGAAAAACCTATTT
GAACTGGTTATTACAGAAGCCAGGCCAGTCTCCACAGCGCCTAATCTATCTGGTGT
CTAAATTGGACTCTGGAGTCCCTGACAGGTTCAGTGGCAGTGGATCAGGAACAGAT
TTTACACTGAAAATCAGCAGAGTGGAGGCTGAGGATGTGGGAGTTTATTACTGCGT
GCAAGGTACACATCTGCACACGTTCGGTCAAGGGACCAGGCTGGAGATAAAA*CGAA*
CTGTGGCAGCACCAAGCGTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAACTGC
CTCTGTTGTGTGCCTGCTGAATAACTTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTGGAT
AACGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCACAGAGCAGGACAGCAAGGACAGCAC
CTACAGCCTCAGCAGCACCCTGACGCTGAGCAAAGCAGACTACGAGAAACACAAAGTCTACGC
CTGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAACAGGGGAGAGT
*GT*TAG **(SEQ ID NO: 284)**

FIG. 111

Humanized 7F11 clone full-length heavy chain nucleic acid sequence

7F11-SFD1
ATGGAAGCCCCAGCGCAGCTTCTCTTCCTCCTGCTACTCTGGCTCCCTGATACCACCGGA
GAGGTACAGCTGGTGGAGTCGGGAGGAGGCTTGGTACAGCCTGGGGGTTCTCTGA
GACTCTCCTGTGCAGCTTCTGGCTTCACATTCACCGACTATTACATGAGCTGGGTCC
GCCAGGCTCCAGGGAAGGGACTTGAGTGGGTGGGTTTCATAAGGAACAAGGCTAA
CGGTTATACAACCGAGTACAACGCTTCCGTTAAAGGCCGGTTCACCATCTCCAGAG
ATGATTCCAAAAACAGCCTCTATCTTCAAATGAATTCCCTGAAAACTGAAGACACTG
CCGTTTATTACTGTACCAGGTATATCTTTTTCGATTACTGGGGCCAAGGCACCACTG
TCACAGTCTCCTCA*GCCTCCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAA*
GAGCACCTCTGGGGGTACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGG
TGACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTA
CAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACC
CAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACAAGAAAGTTGAG
CCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGGA
CCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAG
GTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTG
GACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTA
CCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGT
GCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGC
AGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAG
GTCAGCCTGACATGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAG
CAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCT
TCTTCCTCTACAGCAAGCTCACCGTGGACAAGTCCAGGTGGCAGCAGGGGAACGTCTTCTCAT
GCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGG
*GTAAA*TGA **(SEQ ID NO: 285)**

Humanized 7F11 clone full-length light chain nucleic acid sequence

7F11-K2
ATGGAAGCCCCAGCGCAGCTTCTCTTCCTCCTGCTACTCTGGCTCCCTGATACCACCGGA
GATATTGTAATGACCCAAACACCCCTCTCTCTTTCAGTCACACCTGGACAGCCAGCG
TCCATCTCCTGCAGGTCCTCACAGAGTCTCGTGCACACCAATGGCAATTCCTACCTG
CATTGGTACCTGCAGAAGCCCGGGCAGAGCCCCCAGTTGCTGATCTATATGGTGTC
TAATCGGTTCTCCGGAGTCCCCGACAGATTTTCTGGTTCAGGGTCTGGAACTGATTT
TACACTGAAGATTAGTCGGGTCGAGGCCGAGGATGTAGGCGTGTATTACTGCTCAC
AAAGCACACATGTGCCGTTCACTTTCGGCCAAGGAACAAAGCTCGAAATCAAG*CGAA*
CTGTGGCAGCACCAAGCGTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAACTGC
CTCTGTTGTGTGCCTGCTGAATAACTTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTGGAT
AACGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCACAGAGCAGGACAGCAAGGACAGCAC
CTACAGCCTCAGCAGCACCCTGACGCTGAGCAAAGCAGACTACGAGAAACACAAAGTCTACGC
CTGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAACAGGGGAGAGT
*GT*TAG **(SEQ ID NO: 286)**

FIG. 112

Humanized 9D9 clone full-length heavy chain nucleic acid sequences

9D9-H16

ATGGAAGCCCCAGCGCAGCTTCTCTTCCTCCTGCTACTCTGGCTCCCTGATACCACCGGA**GAG**
GTACAGCTTCTTGAAAGTGGAGGTGGCCTTGTCCAACCCGGAGGGTCATTGCGGTTGAG
CTGTGCGGCAAGTGGCTTCACCTTCTCTGACGCTTGGATGGACTGGGTGAGACAAGCCC
CCGGTAAGGGACTGGAGTTGGTTTCTGAAATCAGGAACAAGGCCAAGAACCATGCAAC
ATATTATGCCGAAAGTGTGAAGGGAAGGTTCACAATCAGTAGAGATAACAGCAAGAACA
CACTGTACCTCCAGATGAACAGCCTCAGAGCTGAGGACACCGCCGTCTATTATTGTACC
ACTCTCGATTCATGGGGGCAGGGTACCACCGTTACAGTCAGCAGC*GCCTCCACCAAGGGC*
CCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGTACAGCGGCCCTGGGCTG
CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCG
GCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCG
TGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCA
AGGTGGACAAGAAAGTTGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCAGCAC
CTGAACTCCTGGGGGGACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCT
CCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTC
AACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAA
CAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGT
ACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAG
GGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAG
GTCAGCCTGACATGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAAT
GGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTC
TACAGCAAGCTCACCGTGGACAAGTCCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATG
*CATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTAAA*TGA **(SEQ ID NO: 287)**

9D9-H18

ATGGAAGCCCCAGCGCAGCTTCTCTTCCTCCTGCTACTCTGGCTCCCTGATACCACCGGA**GAG**
GTACAGCTTCTTGAAAGTGGAGGTGGCCTTGTCCAACCCGGAGGGTCATTGCGGTTGAG
CTGTGCGGCAAGTGGCTTCACCTTCTCTGACGCTTGGATGGACTGGGTGAGACAAGCCC
CCGGTAAGGGACTGGAGTTGGTTGCTGAAATCAGGAACAAGGCCAAGAACCATGCAAC
ATATTATGCCGAAAGTGTGAAGGGAAGGTTCACAATCAGTAGAGATAACAGCAAGAACA
CACTGTACCTCCAGATGAACAGCCTCAGAGCTGAGGACACCGCCGTCTATTATTGTACC
ACTCTCGATTCATGGGGGCAGGGTACCACCGTTACAGTCAGCAGC*GCCTCCACCAAGGGC*
CCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGTACAGCGGCCCTGGGCTG
CCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCG
GCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCG
TGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCA
AGGTGGACAAGAAAGTTGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCAGCAC
CTGAACTCCTGGGGGGACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCT
CCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTC
AACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAA
CAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGT
ACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAG
GGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAG
GTCAGCCTGACATGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAAT
GGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTC
TACAGCAAGCTCACCGTGGACAAGTCCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATG
*CATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTAAA*TGA **(SEQ ID NO: 288)**

FIG. 113

Humanized 9D9 clone full-length light chain nucleic acid sequence

9D9-K13
ATGGAAGCCCCAGCGCAGCTTCTCTTCCTCCTGCTACTCTGGCTCCCTGATACCACCGGA
GATATCGTGATGACACAAACTCCCCTGTCTCTGTCTGTAACTCCAGGTCAGCCCGC
GAGTATTTCATGTAAGAGCAGCCAATCCCTGCTGGACAGCGACGGGAAGACCTACC
TGAACTGGTTACTCCAAAAGCCAGGACAAAGTCCCCAACGCCTTATTTACCTGGTGT
CAGCCCTGGACTCTGGCGTGCCCGATCGATTTAGCGGCAGCGGGAGTGGCACAGAT
TTCACCCTGAAAATATCCCGCGTCGAGGCCGAAGATGTGGGCGTGTACTACTGCTG
GCAGGGCACACATTTCCCCTGGACATTTGGTCAGGGGACAAAGCTGGAAATTAAA*C*
GAACTGTGGCAGCACCAAGCGTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAAC
TGCCTCTGTTGTGTGCCTGCTGAATAACTTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTG
GATAACGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCACAGAGCAGGACAGCAAGGACAG
CACCTACAGCCTCAGCAGCACCCTGACGCTGAGCAAAGCAGACTACGAGAAACACAAAGTCTA
CGCCTGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAACAGGGGAG
*AGTGT*TAG **(SEQ ID NO: 289)**

FIG. 114

Humanized 12G6 clone full-length heavy chain nucleic acid sequence

12G6-SFD1
ATGGAAGCCCCAGCGCAGCTTCTCTTCCTCCTGCTACTCTGGCTCCCTGATACCACCGGA
GAGGTACAGCTGGTGGAGTCGGGAGGAGGCTTGGTACAGCCTGGGGGTTCTCTGA
GACTCTCCTGTGCAGCTTCTGGATTCCCATTCAGTAACTACTGGATGAACTGGGTCC
GCCAGGCTCCAGGGAAGGGACTTGAGTGGGTGGGTCAAATTAGATTGAAATCTAAT
AATTATGCAACACATTATGCGGAGTCTGTGAAAGGGCGGTTCACCATCTCCAGAGA
TGATTCCAAAAACAGCCTCTATCTTCAAATGAATTCCCTGAAAACTGAAGACACTGC
CGTTTATTACTGTACCCCAATTGACTATTGGGGCCAAGGCACCACTGTCACAGTCTC
CTCA*GCCTCCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG*
GGGGTACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCG
TGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGG
ACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACAT
CTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACAAGAAAGTTGAGCCCAAATCTTG
TGACAAAACTCACACATGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTT
CCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGT
GGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGG
AGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTC
AGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCC
AACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAA
CCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGAC
ATGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGC
CGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCTACA
GCAAGCTCACCGTGGACAAGTCCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATG
*CATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTAAA*TGA
(SEQ ID NO: 290)

Humanized 12G6 clone full-length light chain nucleic acid sequence

12G6-K12
ATGGAAGCCCCAGCGCAGCTTCTCTTCCTCCTGCTACTCTGGCTCCCTGATACCACCGGA
GACATTGTGATGACCCAGACTCCACTCAGTTTGTCAGTTACCCCTGGGCAACCAGC
CTCTATCTCTTGCAAGTCAAGTCAGAGCCTCTTATATAGTAATGGAAAAACCTATTT
GAACTGGGTTTTACAGAAGCCAGGCCAGTCTCCACAGCGCCTAATCTATCTGGTGT
CTAAACTGGACTCTGGAGTCCCTGACAGGTTCTCTGGCAGTGGATCAGGAACAGAT
TTTACACTGAAAATCAGCAGAGTGGAGGCTGAGGATGTGGGAGTTTATTACTGCGT
GCAAGGTTCACATTTTCACACGTTCGGTCAAGGGACCAAGCTGGAGATTAAA*CGAAC*
TGTGGCAGCACCAAGCGTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAACTGCC
TCTGTTGTGTGCCTGCTGAATAACTTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTGGATA
ACGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCACAGAGCAGGACAGCAAGGACAGCACC
TACAGCCTCAGCAGCACCCTGACGCTGAGCAAAGCAGACTACGAGAAACACAAAGTCTACGCC
TGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAACAGGGGAGAGTG
*T*TAG **(SEQ ID NO: 291)**

FIG. 115

Humanized 4B10 clone full-length heavy chain nucleic acid sequence

4B10-H1

ATGGAAGCCCCAGCGCAGCTTCTCTTCCTCCTGCTACTCTGGCTCCCTGATACCACCGGA
GAGGTACAGCTGGTGGAGTCGGGAGGAGGCTTGGTACAGCCTGGGGGTTCTCTGA
GACTCTCCTGTGCAGCTTCTGGATTCACCTTTTCTGATTACTACATGAGCTGGGTCC
GCCAGGCTCCAGGGAAGGGACTTGAGTGGGTGGGTTTTATTAGAAACAAAGCTAAT
GGTTACACAACAGAGTACAGTGCATCTGTGAAGGGTCGGTTCACCATCTCCAGAGA
TGATTCCAAAAACAGCCTCTATCTTCAAATGAATTCCCTGAAAACTGAAGACACTGC
CGTTTATTACTGTGCAAGATATATCTGGTTTGACTACTGGGGCCAAGGCACCACTGT
CACAGTCTCCTCA*GCCTCCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAG*
AGCACCTCTGGGGGTACAGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGT
GACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCTGTCCTAC
AGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCC
AGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACAAGAAAGTTGAGC
CCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGAC
CGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGG
TCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGG
ACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTAC
CGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTG
CAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCA
GCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGG
TCAGCCTGACATGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCA
ATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCT
TCCTCTACAGCAAGCTCACCGTGGACAAGTCCAGGTGGCAGCAGGGGAACGTCTTCTCATGCT
CCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTA
*AA*TGA **(SEQ ID NO: 292)**

Humanized 4B10 clone full-length light chain nucleic acid sequence

4B10-K1

ATGGAAGCCCCAGCGCAGCTTCTCTTCCTCCTGCTACTCTGGCTCCCTGATACCACCGGA
GACATTGTGATGACCCAAACTCCACTCTCCCTGTCTGTCACTCCTGGACAACCAGCC
TCCATCTCTTGCAGATCTAGTCAGAGCCTTGTACACACTAATGGAAACACCTATTTA
CATTGGTACCTGCAGAAGCCAGGCCAGTCTCCACAGCTCCTGATTTATATGGTTTCC
AACCGATTTTCTGGGGTCCCAGACAGGTTCAGTGGCAGTGGATCAGGGACAGATTT
CACACTCAAGATCAGCAGAGTGGAGGCTGAGGATGTGGGAGTTTATTACTGCTCTC
AAAGTGCACATGTTCCTCCGCTCACGTTCGGTCAAGGGACCAGGCTGGAGATTAAA
CGAACTGTGGCAGCACCAAGCGTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAA
CTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGT
GGATAACGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCACAGAGCAGGACAGCAAGGACA
GCACCTACAGCCTCAGCAGCACCCTGACGCTGAGCAAAGCAGACTACGAGAAACACAAAGTCT
ACGCCTGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAACAGGGGA
*GAGTGT*TAG **(SEQ ID NO: 293)**

FIG. 116