FIGURE 1: SEQUENCE OF CDRS OF MOUSE MONOCLONAL 5/44

H1	NYWIH	(SEQ ID NO:1)
H2	GINPGNNYTTYKRNLKG	(SEQ ID NO:2)
H3	EGYGNYGAWFAY	(SEQ ID NO:3)
L1	RSSQSLANSYGNTFLS	(SEQ ID NO:4)
L2	GISNRFS	(SEQ ID NO:5)
L3	LQGTHQPYT	(SEQ ID NO:6)

FIGURE 2: DNA/PROTEIN SEQUENCE OF 5/44 V_L

```
          10                  20                  30                  40                  50
GAT GTT GTG GTG ACT CAA ACT CCA CTC TCC CTG CCT GTC AGC TTT GGA GAT CAA GTT

CTA CAA CAC CAC TGA GTT TGA GGT GAG AGG GAC GGA CAG TCG AAA CCT CTA GTT CAA

 D   V   V   V   T   Q   T   P   L   S   L   P   V   S   F   G   D   Q   V>

 60                  70                  80                  90                  100                 110
TCT ATC TCT TGC AGG TCT AGT CAG AGT CTT GCA AAC AGT TAT GGG AAC ACC TTT TTG
AGA TAG AGA ACG TCC AGA TCA GTC TCA GAA CGT TTG TCA ATA CCC TTG TGG AAA AAC
 S   I   S   C   R   S   S   Q   S   L   A   N   S   Y   G   N   T   F   L>

    120                 130                 140                 150                 160                 170
TCT TGG TAC CTG CAC AAG CCT GGC CAG TCT CCA CAG CTC CTC ATC TAT GGG ATT TCC
AGA ACC ATG GAC GTG TTC GGA CCG GTC AGA GGT GTC GAG GAG TAG ATA CCC TAA AGG
 S   W   Y   L   H   K   P   G   Q   S   P   Q   L   L   I   Y   G   I   S>

        180                 190                 200                 210                 220
AAC AGA TTT TCT GGG GTG CCA GAC AGG TTC ACT GGC AGT GGT TCA GGG ACA GAT TTC
TTG TCT AAA AGA CCC CAC GGT CTG TCC AAG TGA CCG TCA CCA AGT CCC TGT CTA AAG
 N   R   F   S   G   V   P   D   R   F   T   G   S   G   S   G   T   D   F>

230                 240                 250                 260                 270                 280
ACA CTC AAG ATC AGC ACA ATA AAG CCT GAG GAC TTG GGA ATG TAT TAC TGC TTA CAA
TGT GAG TTC TAG TCG TGT TAT TTC GGA CTC CTG AAC CCT TAC ATA ATG ACG AAT GTT
 T   L   K   I   S   T   I   K   P   E   D   L   G   M   Y   Y   C   L   Q>

    290                 300                 310                 320                 330
GGT ACA CAT CAG CCG TAC ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA CGT
CCA TGT GTA GTC GGC ATG TGC AAG CCT CCC CCC TGG TTC GAC CTT TAT TTT GCA
 G   T   H   Q   P   Y   T   F   G   G   G   T   K   L   E   I   K   R>
```

FIGURE 3: DNA/PROTEIN SEQUENCE OF 5/44 V_H

```
           10          20          30          40          50
GAG GTC CAA CTG CAG CAG TCT GGG ACT GTA CTG GCA AGG CCT GGG GCT TCC GTG AAG

CTC CAG GTT GAC GTC GTC AGA CCC TGA CAT GAC CGT TCC GGA CCC CGA AGG CAC TTC
 E   V   Q   L   Q   Q   S   G   T   V   L   A   R   P   G   A   S   V   K>

  60          70          80          90          100         110
ATG TCC TGC AAG GCT TCT GGC TAC AGG TTT ACC AAC TAC TGG ATT CAC TGG GTA AAA
TAC AGG ACG TTC CGA AGA CCG ATG TCC AAA TGG TTG ATG ACC TAA GTG ACC CAT TTT
 M   S   C   K   A   S   G   Y   R   F   T   N   Y   W   I   H   W   V   K>

    120         130         140         150         160         170
CAG AGG CCT GGG CAG GGT CTA GAA TGG ATT GGT GGT ATT AAT CCT GGA AAT AAT TAT
GTC TCC GGA CCC GTC CCA GAT CTT ACC TAA CCA CCA TAA TTA GGA CCT TTA TTA ATA
 Q   R   P   G   Q   G   L   E   W   I   G   G   I   N   P   G   N   N   Y>

        180         190         200         210         220
ACT ACG TAT AAG AGG AAC TTG AAG GGC AAG GCC ACA CTG ACT GCA GTC ACA TCC GCC
TGA TGC ATA TTC TCC TTG AAC TTC CCG TTC CGG TGT GAC TGA CGT CAG TGT AGG CGG
 T   T   Y   K   R   N   L   K   G   K   A   T   L   T   A   V   T   S   A>

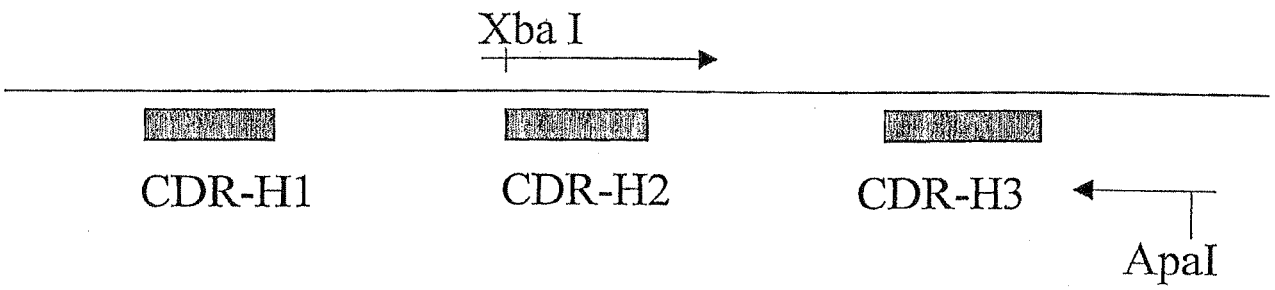
230         240         250         260         270         280
AGC ACT GCC TAC ATG GAC CTC AGC AGC CTG ACA AGT GAG GAC TCT GCG GTC TAT TAC
TCG TGA CGG ATG TAC CTG GAG TCG TCG GAC TGT TCA CTC CTG AGA CGC CAG ATA ATG
 S   T   A   Y   M   D   L   S   S   L   T   S   E   D   S   A   V   Y   Y>

  290         300         310         320         330         340
TGT ACA AGA GAG GGC TAT GGT AAC TAC GGG GCC TGG TTT GCT TAC TGG GGC CAG GGG
ACA TGT TCT CTC CCG ATA CCA TTG ATG CCC CGG ACC AAA CGA ATG ACC CCG GTC CCC
 C   T   R   E   G   Y   G   N   Y   G   A   W   F   A   Y   W   G   Q   G>

       350         360
ACT CTG GTC ACC GTC TCC TCA

TGA GAC CAG TGG CAG AGG AGT
 T   L   V   T   V   S   S>
```

FIGURE 4: REMOVAL OF GLYCOSYLATION SITE AND REACTIVE LYSINE: PCR STRATEGY TO MUTATE CDR-H2 IN CH VECTOR



x

CDR-H2

		55 60 65
		• • •
cH		**GNNYTTYKRNLKG**
N55Q	**H2''**	**GNQYTTYKRNLKG**
T57A	**H2'**	**GNNYATYKRNLKG**
T57V		**GNNYVTYKRNLKG**
K60R		**GNNYTTYRRNLKG**

FIGURE 5: 5/44 LIGHT CHAIN SEQUENCE GRAFT DESIGN

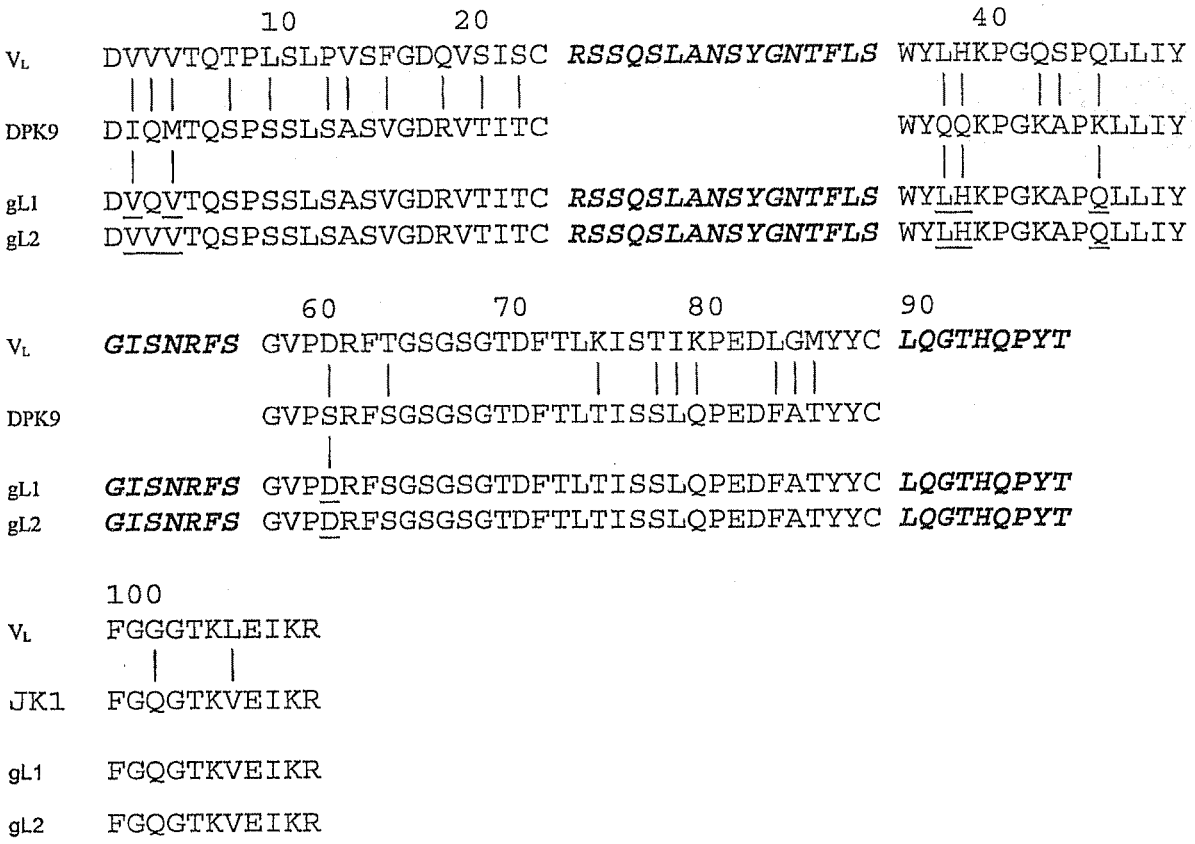


FIGURE 6: 5/44 HEAVY CHAIN SEQUENCE GRAFT DESIGN



FIGURE 7: MAP OF VECTOR PMRR14.

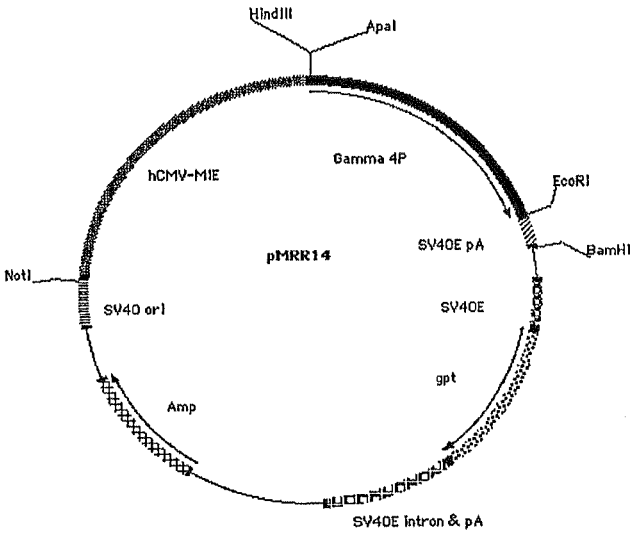


FIGURE 8: MAP OF VECTOR PMRR10.1

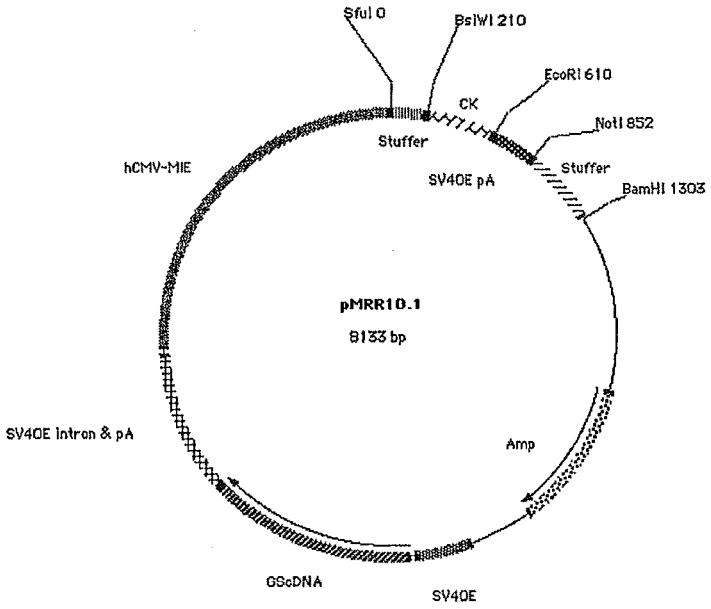


FIGURE 9: BIACORE ASSAY OF CHIMERIC 5/44 AND MUTANTS

5/44	Ka e^{5}	Kd e^{-4}	KD e^{-10}	~KD nM
cLcH	2.9	1.14	3.93	0.4
N55Q	5.81	1.9	3.27	0.3
T57A	7.8	0.51	0.66	0.07
K60R	4.95	1.01	2.04	0.2

FIGURE 10: OLIGONUCLEOTIDES FOR 5/44 GH1 AND GL1 GENE ASSEMBLIES

Heavy Chain

544gH1 T1
AGTGTGAGGTGCAATTGGTCCAGTCAGGAGCAGAGGTTAAGAAGCCTGGTGCTTCCGTC
AAAGTTTCGTGTAAGGCTAGCGGCTACAGGTTCAC

544gH1 T2
GTGGCATTAATCCCGGGAATCAGTACACTACATATAAAAGAAATCTAAAGGGCAGAGCA
ACGCTGACCGCGGACACCTCCACAAGCACTGTCTACA

544gH1 T3
AGAGAAGGCTACGGTAATTACGGAGCCTGGTTCGCCTACTGGGGCCAGGGTACCCTAGT
CACAGTCTCCTCAGCTTCTACAAAGGGCCCAAGAAA

544 gH1 B1
GGACCAATTGCACCTCACACTGCACTCCCTTGAGAATGAGTGCCAGGAACACGAGAGAG
AATCCGAAGTCCATGGTGGCGGCAAGCTTTTATTC

544 gH1 B2
GATTCCCGGGATTAATGCCACCGATCCATTCCAGGCCTTGTCCCGGAGCCTGCCTGACCC
AATGAATCCAATAATTTGTGAACCTGTAGCCGCTAGC

544gH1 B3
CGTAATTACCGTAGCCTTCTCTAGTACAATAGTACACTGCGGTGTCCTCGGATCTCAGAG
ATGACAGCTCCATGTAGACAGTGCTTGTGGAGG

544gH1 F1
GAATAAAAGCTTGCCGCCACC

544gH1 R1
TTTCTTGGGCCCTTTGTAGAAG

FIGURE 10 CONT.

Light Chain

544 gL1 T1
GCTTCCCGGGGTGACGTTCAAGTGACCCAGAGCCCATCCAGCCTGAGCGCATCTGTAGG
AGACCGGGTCACCATCACTTGTAGATCC

544 gL1 T2
TATCTGCACAAACCAGGTAAAGCCCCACAATTGCTCATCTACGGAATCTCTAACAGATTT
AGTGGTGTACCAGACAGGTTCAGCGGTTCC

544gL1 T3
AGATTTCGCCACTTATTACTGTTTACAAGGTACACATCAGCCGTACACATTCGGTCAGGG
TACTAAAGTAGAAATCAAACGTACGGCGTGC

544gL1 B1
GAACGTCACCCCGGGAAGCAGGAATCCAGAACAACAGAAGCACCAACAGCCTAACAGG
CAACTTCATGGTGGCGGCTTCGAATCATCC

544gL1 B2
CTTTACCTGGTTTGTGCAGATACCAAGACAAAAAGGTGTTCCCATAACTGTTTGCAAGAC
TCTGACTGGATCTACAAGTGATGGTGAC

544gL1 B3
AACAGTAATAAGTGGCGAAATCTTCTGGCTGGAGAGACGAGATCGTGAGGGTGAAATCA
GTACCACTTCCGGAACCGCTGAACCTGTCTG

544gL1 F1
GGATGATTCGAAGCCGCCAC

544gL1 R1
GCACGCCGTACGTTTGATTTC

FIGURE 11: PLASMID MAPS OF INTERMEDIATE VECTORS PCR2.1 (544GH1)

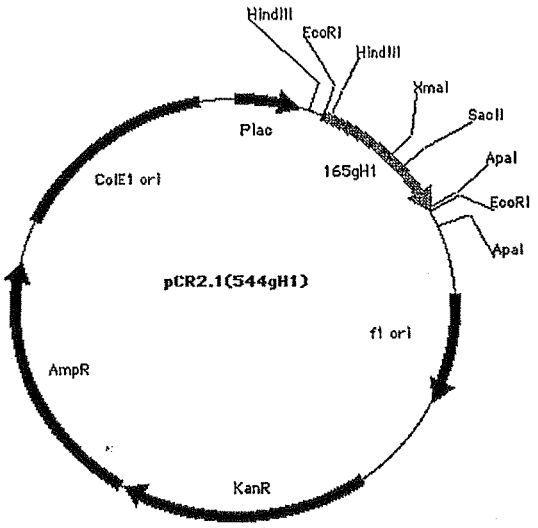


FIGURE 12: PLASMID MAPS OF INTERMEDIATE VECTORS PCR2.1 (544GL1)

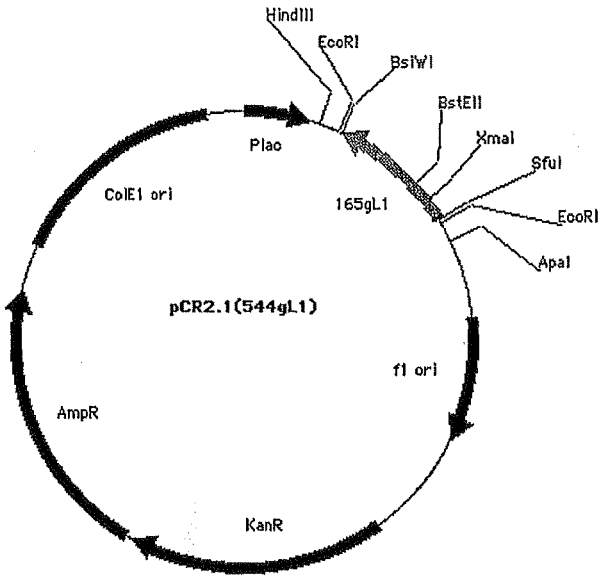


FIGURE 13: OLIGONUCLEOTIDE CASSETTES USED TO MAKE FURTHER GRAFTS

gH4

```
XmaI      10          20          30          40          50        SacII
CC GGG AAT AAC TAC GCT ACA TAT AGG AGA AAT CTA AAG GGC AGA GCA ACG CTG ACC GC
     C TTA TTG ATG CGA TGT ATA TCC TCT TTA GAT TTC CCG TCT CGT TGC GAC TGG
P   G   N   N   Y   A   T   Y   R   R   N   L   K   G   R   A   T   L   T   A
```

gH5

```
XmaI      10          20          30          40          50        SacII
CC GGG AAT AAC TAC GCT ACA TAT AGG AGA AAT CTA AAG GGC AGA GTT ACG ATG ACC GC
     C TTA TTG ATG CGA TGT ATA TCC TCT TTA GAT TTC CCG TCT CAA TGC TAC TGG
P   G   N   N   Y   A   T   Y   R   R   K   F   Q   G   R   V   T   M   T   A
```

gH6

```
XmaI    10          20          30          40          50        SacII
CC GGG AAT AAC TAC GCT ACA TAT AGG AGA AAA TTC CAG GGC AGA GCA ACG CTG ACC GC
     C TTA TTG ATG CGA TGT ATA TCC TCT TTT AAG GTC CCG TCT CGT TGC GAC TGG
P   G   N   N   Y   A   T   Y   R   R   K   F   Q   G   R   A   T   L   T   A
```

gH7

```
XmaI      10          20          30          40          50        SacII
CC GGG AAT AAC TAC GCT ACA TAT AGG AGA AAA TTC CAG GGC AGA GTT ACG ATG ACC GC
     C TTA TTG ATG CGA TGT ATA TCC TCT TTT AAG GTC CCG TCT CAA TGC TAC TGG
P   G   N   N   Y   A   T   Y   R   R   K   F   Q   G   R   V   T   M   T   A
```

gL2

```
      XmaI   10          20          30          40          50          60
BstEII
   C CGG GGT GAC GTT GTC GTG ACC CAG AGC CCA TCC AGC CTG AGC GCA TCT GTA GGA GAC CGG
        CCA CTG CAA CAG CAC TGG GTC TCG GGT AGG TCG GAC TCG CGT AGA CAT CCT CTG GCC CAG TG
  S   R   G   D   V   V   V   T   Q   S   P   S   S   L   S   A   S   V   G   D   R   V   T
```

FIGURE 14: COMPETITION ASSAY, COMPETING BINDING OF FLUORESCENTLY LABELLED MOUSE 5/44 ANTIBODY WITH GRAFTED VARIANTS.

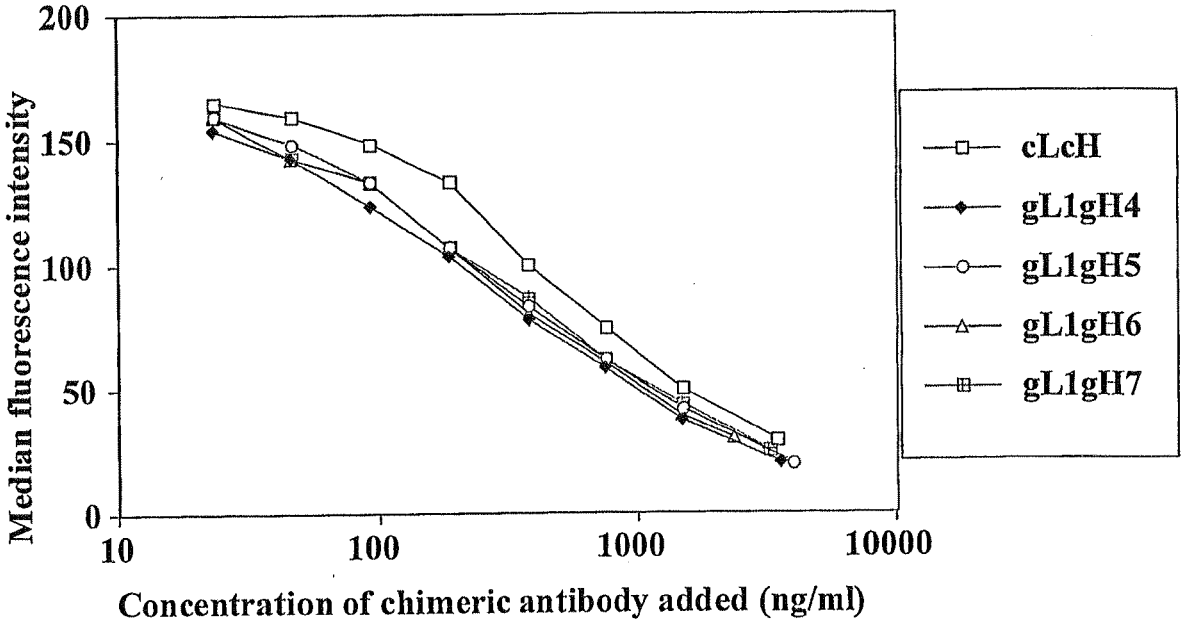


FIGURE 15: COMPETITION ASSAY, COMPETING BINDING OF FLUORESCENTLY LABELLED MOUSE 5/44 ANTIBODY WITH GRAFTED VARIANTS.

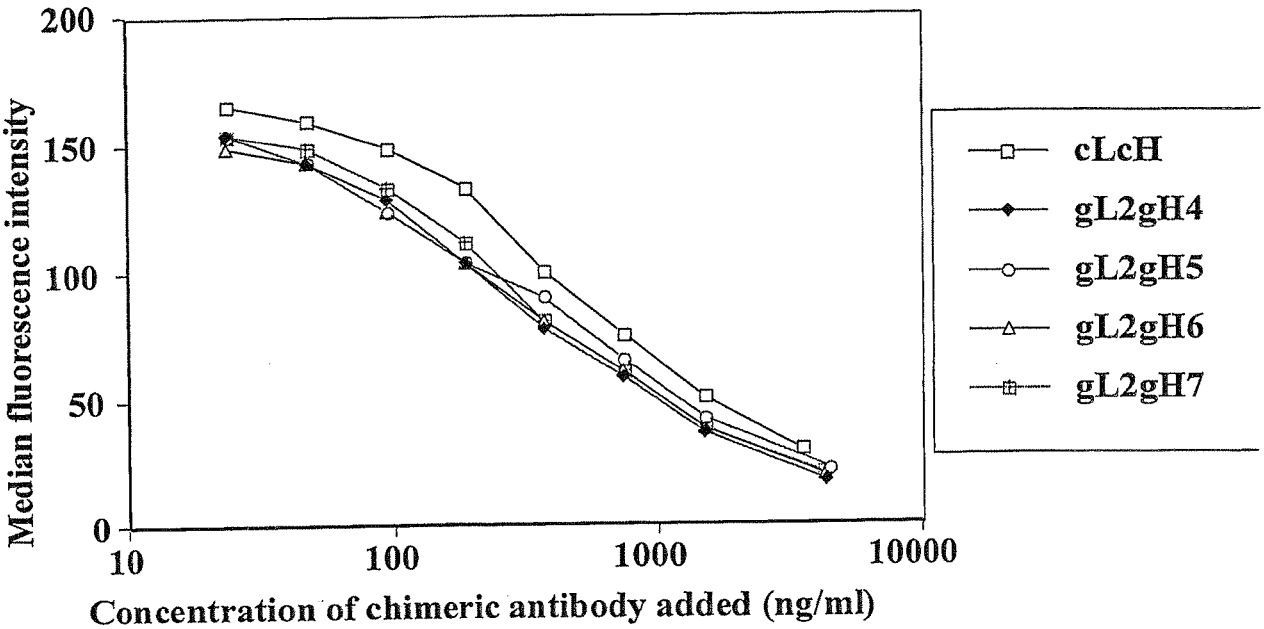


FIGURE 16: FULL DNA SEQUENCE OF GRAFTED HEAVY AND LIGHT CHAINS

a) Heavy Chain

```
        10          20          30          40          50          60
AAGCTTGCCG CCACC ATG GAC TTC GGA TTC TCT CTC GTG TTC CTG GCA CTC ATT CTC AAG
TTCGAACGGC GGTGG TAC CTG AAG CCT AAG AGA GAG CAC AAG GAC CGT GAG TAA GAG TTC
                  M   D   F   G   F   S   L   V   F   L   A   L   I   L   K>

            70          80          90          100         110
GGA GTG CAG TGT GAG GTG CAA TTG GTC CAG TCA GGA GCA GAG GTT AAG AAG CCT GGT
CCT CAC GTC ACA CTC CAC GTT AAC CAG GTC AGT CCT CGT CTC CAA TTC TTC GGA CCA
 G   V   Q   C   E   V   Q   L   V   Q   S   G   A   E   V   K   K   P   G>

120         130         140         150         160         170
GCT TCC GTC AAA GTT TCG TGT AAG GCT AGC GGC TAC AGG TTC ACA AAT TAT TGG ATT
CGA AGG CAG TTT CAA AGC ACA TTC CGA TCG CCG ATG TCC AAG TGT TTA ATA ACC TAA
 A   S   V   K   V   S   C   K   A   S   G   Y   R   F   T   N   Y   W   I>

    180         190         200         210         220         230
CAT TGG GTC AGG CAG GCT CCG GGA CAA GGC CTG GAA TGG ATC GGT GGC ATT AAT CCC
GTA ACC CAG TCC GTC CGA GGC CCT GTT CCG GAC CTT ACC TAG CCA CCG TAA TTA GGG
 H   W   V   R   Q   A   P   G   Q   G   L   E   W   I   G   G   I   N   P>

        240         250         260         270         280
GGG AAT AAC TAC GCT ACA TAT AGG AGA AAA TTC CAG GGC AGA GTT ACG ATG ACC GCG
CCC TTA TTG ATG CGA TGT ATA TCC TCT TTT AAG GTC CCG TCT CAA TGC TAC TGG CGC
 G   N   N   Y   A   T   Y   R   R   K   F   Q   G   R   V   T   M   T   A>

290         300         310         320         330         340
GAC ACC TCC ACA AGC ACT GTC TAC ATG GAG CTG TCA TCT CTG AGA TCC GAG GAC ACC
CTG TGG AGG TGT TCG TGA CAG ATG TAC CTC GAC AGT AGA GAC TCT AGG CTC CTG TGG
D   T   S   T   S   T   V   Y   M   E   L   S   S   L   R   S   E   D   T>

    350         360         370         380         390         400
GCA GTG TAC TAT TGT ACT AGA GAA GGC TAC GGT AAT TAC GGA GCC TGG TTC GCC TAC
CGT CAC ATG ATA ACA TGA TCT CTT CCG ATG CCA TTA ATG CCT CGG ACC AAG CGG ATG
 A   V   Y   Y   C   T   R   E   G   Y   G   N   Y   G   A   W   F   A   Y>

        410         420         430         440         450
TGG GGC CAG GGT ACC CTA GTC ACA GTC TCC TCA GCT TCT ACA AAG GGC CCA TCC GTC
ACC CCG GTC CCA TGG GAT CAG TGT CAG AGG AGT CGA AGA TGT TTC CCG GGT AGG CAG
 W   G   Q   G   T   L   V   T   V   S   S   A   S   T   K   G   P   S   V>

460         470         480         490         500         510
TTC CCC CTG GCG CCC TGC TCC AGG AGC ACC TCC GAG AGC ACA GCC GCC CTG GGC TGC
AAG GGG GAC CGC GGG ACG AGG TCC TCG TGG AGG CTC TCG TGT CGG CGG GAC CCG ACG
 F   P   L   A   P   C   S   R   S   T   S   E   S   T   A   A   L   G   C>

   520         530         540         550         560         570
CTG GTC AAG GAC TAC TTC CCC GAA CCG GTG ACG GTG TCG TGG AAC TCA GGC GCC CTG
GAC CAG TTC CTG ATG AAG GGG CTT GGC CAC TGC CAC AGC ACC TTG AGT CCG CGG GAC
 L   V   K   D   Y   F   P   E   P   V   T   V   S   W   N   S   G   A   L>

        580         590         600         610         620         630
ACC AGC GGC GTG CAC ACC TTC CCG GCT GTC CTA CAG TCC TCA GGA CTC TAC TCC CTC
TGG TCG CCG CAC GTG TGG AAG GGC CGA CAG GAT GTC AGG AGT CCT GAG ATG AGG GAG
 T   S   G   V   H   T   F   P   A   V   L   Q   S   S   G   L   Y   S   L>
```

FIGURE 16 CONT.

```
            640          650          660          670          680
AGC AGC GTG GTG ACC GTG CCC TCC AGC AGC TTG GGC ACG AAG ACC TAC ACC TGC AAC
TCG TCG CAC CAC TGG CAC GGG AGG TCG TCG AAC CCG TGC TTC TGG ATG TGG ACG TTG
 S   S   V   V   T   V   P   S   S   S   L   G   T   K   T   Y   T   C   N>

690           700          710          720          730          740
GTA GAT CAC AAG CCC AGC AAC ACC AAG GTG GAC AAG AGA GTT G GTGAGAGGCC
CAT CTA GTG TTC GGG TCG TTG TGG TTC CAC CTG TTC TCT CAA C CACTCTCCGG
 V   D   H   K   P   S   N   T   K   V   D   K   R   V>

       750          760          770          780          790          800          810
AGCACAGGGA GGGAGGGTGT CTGCTGGAAG CCAGGCTCAG CCCTCCTGCC TGGACGCACC CCGGCTGTGC
TCGTGTCCCT CCCTCCCACA GACGACCTTC GGTCCGAGTC GGGAGGACGG ACCTGCGTGG GGCCGACACG

       820          830          840          850          860          870          880
AGCCCCAGCC CAGGGCAGCA AGGCATGCCC CATCTGTCTC CTCACCCGGA GGCCTCTGAC CACCCCACTC
TCGGGGTCGG GTCCCGTCGT TCCGTACGGG GTAGACAGAG GAGTGGGCCT CCGGAGACTG GTGGGGTGAG

       890          900          910          920          930          940          950
ATGCCCAGGG AGAGGGTCTT CTGGATTTTT CCACCAGGCT CCGGGCAGCC ACAGGCTGGA TGCCCCTACC
TACGGGTCCC TCTCCCAGAA GACCTAAAAA GGTGGTCCGA GGCCCGTCGG TGTCCGACCT ACGGGGATGG

       960          970          980          990         1000         1010         1020
CCAGGCCCTG CGCATACAGG GGCAGGTGCT GCGCTCAGAC CTGCCAAGAG CCATATCCGG GAGGACCCTG
GGTCCGGGAC GCGTATGTCC CCGTCCACGA CGCGAGTCTG GACGGTTCTC GGTATAGGCC CTCCTGGGAC

      1030         1040         1050         1060         1070         1080         1090
CCCCTGACCT AAGCCCACCC CAAAGGCCAA ACTCTCCACT CCCTCAGCTC AGACACCTTC TCTCCTCCCA
GGGGACTGGA TTCGGGTGGG GTTTCCGGTT TGAGAGGTGA GGGAGTCGAG TCTGTGGAAG AGAGGAGGGT

      1100         1110         1120         1130         1140         1150
GATCTGAGTA ACTCCCAATC TTCTCTCTGC A GAG TCC AAA TAT GGT CCC CCA TGC CCA CCA
CTAGACTCAT TGAGGGTTAG AAGAGAGACG T CTC AGG TTT ATA CCA GGG GGT ACG GGT GGT
                                    E   S   K   Y   G   P   P   C   P   P>

1160       1170         1180         1190         1200         1210         1220
    TGC CCA GGT AAGCCAACCC AGGCCTCGCC CTCCAGCTCA AGGCGGGACA GGTGCCCTAG AGTAGCCTGC

    ACG GGT CCA TTCGGTTGGG TCCGGAGCGG GAGGTCGAGT TCCGCCCTGT CCACGGGATC TCATCGGACG
     C   P>

      1230         1240         1250         1260         1270         1280
ATCCAGGGAC AGGCCCCAGC CGGGTGCTGA CGCATCCACC TCCATCTCTT CCTCA GCA CCT GAG TTC
TAGGTCCCTG TCCGGGGTCG GCCCACGACT GCGTAGGTGG AGGTAGAGAA GGAGT CGT GGA CTC AAG
                                                            A   P   E   F>

 1290          1300         1310         1320         1330         1340
CTG GGG GGA CCA TCA GTC TTC CTG TTC CCC CCA AAA CCC AAG GAC ACT CTC ATG ATC
GAC CCC CCT GGT AGT CAG AAG GAC AAG GGG GGT TTT GGG TTC CTG TGA GAG TAC TAG
 L   G   G   P   S   V   F   L   F   P   P   K   P   K   D   T   L   M   I>

    1350         1360         1370         1380         1390         1400
TCC CGG ACC CCT GAG GTC ACG TGC GTG GTG GTG GAC GTG AGC CAG GAA GAC CCC GAG
AGG GCC TGG GGA CTC CAG TGC ACG CAC CAC CAC CTG CAC TCG GTC CTT CTG GGG CTC
 S   R   T   P   E   V   T   C   V   V   V   D   V   S   Q   E   D   P   E>
```

FIGURE 16 CONT.

```
    1410          1420          1430          1440          1450
GTC CAG TTC AAC TGG TAC GTG GAT GGC GTG GAG GTG CAT AAT GCC AAG ACA AAG CCG
CAG GTC AAG TTG ACC ATG CAC CTA CCG CAC CTC CAC GTA TTA CGG TTC TGT TTC GGC
 V   Q   F   N   W   Y   V   D   G   V   E   V   H   N   A   K   T   K   P>

1460          1470          1480          1490          1500          1510
CGG GAG GAG CAG TTC AAC AGC ACG TAC CGT GTG GTC AGC GTC CTC ACC GTC CTG CAC
GCC CTC CTC GTC AAG TTG TCG TGC ATG GCA CAC CAG TCG CAG GAG TGG CAG GAC GTG
 R   E   E   Q   F   N   S   T   Y   R   V   V   S   V   L   T   V   L   H>

  1520          1530          1540          1550          1560          1570
CAG GAC TGG CTG AAC GGC AAG GAG TAC AAG TGC AAG GTC TCC AAC AAA GGC CTC CCG
GTC CTG ACC GAC TTG CCG TTC CTC ATG TTC ACG TTC CAG AGG TTG TTT CCG GAG GGC
 Q   D   W   L   N   G   K   E   Y   K   C   K   V   S   N   K   G   L   P>

      1580          1590          1600          1610          1620          1630
TCC TCC ATC GAG AAA ACC ATC TCC AAA GCC AAA GGTGG GACCCACGGG GTGCGAGGGC
AGG AGG TAG CTC TTT TGG TAG AGG TTT CGG TTT CCACC CTGGGTGCCC CACGCTCCCG
 S   S   I   E   K   T   I   S   K   A   K>

      1640          1650          1660          1670          1680          1690          1700
CACATGGACA GAGGTCAGCT CGGCCCACCC TCTGCCCTGG GAGTGACCGC TGTGCCAACC TCTGTCCCTA
GTGTACCTGT CTCCAGTCGA GCCGGGTGGG AGACGGGACC CTCACTGGCG ACACGGTTGG AGACAGGGAT

          1710          1720          1730          1740          1750
CA GGG CAG CCC CGA GAG CCA CAG GTG TAC ACC CTG CCC CCA TCC CAG GAG GAG ATG
GT CCC GTC GGG GCT CTC GGT GTC CAC ATG TGG GAC GGG GGT AGG GTC CTC CTC TAC
    G   Q   P   R   E   P   Q   V   Y   T   L   P   P   S   Q   E   E   M>

 1760          1770          1780          1790          1800          1810
ACC AAG AAC CAG GTC AGC CTG ACC TGC CTG GTC AAA GGC TTC TAC CCC AGC GAC ATC
TGG TTC TTG GTC CAG TCG GAC TGG ACG GAC CAG TTT CCG AAG ATG GGG TCG CTG TAG
 T   K   N   Q   V   S   L   T   C   L   V   K   G   F   Y   P   S   D   I>

     1820          1830          1840          1850          1860          1870
GCC GTG GAG TGG GAG AGC AAT GGG CAG CCG GAG AAC AAC TAC AAG ACC ACG CCT CCC
CGG CAC CTC ACC CTC TCG TTA CCC GTC GGC CTC TTG TTG ATG TTC TGG TGC GGA GGG
 A   V   E   W   E   S   N   G   Q   P   E   N   N   Y   K   T   T   P   P>

          1880          1890          1900          1910          1920
GTG CTG GAC TCC GAC GGC TCC TTC TTC CTC TAC AGC AGG CTA ACC GTG GAC AAG AGC
CAC GAC CTG AGG CTG CCG AGG AAG AAG GAG ATG TCG TCC GAT TGG CAC CTG TTC TCG
 V   L   D   S   D   G   S   F   F   L   Y   S   R   L   T   V   D   K   S>

1930          1940          1950          1960          1970          1980
AGG TGG CAG GAG GGG AAT GTC TTC TCA TGC TCC GTG ATG CAT GAG GCT CTG CAC AAC
TCC ACC GTC CTC CCC TTA CAG AAG AGT ACG AGG CAC TAC GTA CTC CGA GAC GTG TTG
 R   W   Q   E   G   N   V   F   S   C   S   V   M   H   E   A   L   H   N>

  1990          2000          2010          2020          2030          2040
CAC TAC ACA CAG AAG AGC CTC TCC CTG TCT CTG GGT AAA TGA GTGC CAGGGCCGGC
GTG ATG TGT GTC TTC TCG GAG AGG GAC AGA GAC CCA TTT ACT CACG GTCCCGGCCG
 H   Y   T   Q   K   S   L   S   L   S   L   G   K   *>

      2050          2060          2070          2080          2090          2100          2110
AAGCCCCCGC TCCCCGGGCT CTCGGGGTCG CGCGAGGATG CTTGGCACGT ACCCCGTCTA CATACTTCCC
TTCGGGGGCG AGGGGCCCGA GAGCCCCAGC GCGCTCCTAC GAACCGTGCA TGGGGCAGAT GTATGAAGGG
```

FIGURE 16 CONT

```
      2120       2130       2140       2150       2160
AGGCACCCAG CATGGAAATA AAGCACCCAC CACTGCCCTG GCTCGAATTC
TCCGTGGGTC GTACCTTTAT TTCGTGGGTG GTGACGGGAC CGAGCTTAAG
```

FIGURE 16 CONT.

b) Light Chain

```
         10          20          30          40          50          60
TTCGAAGCCG CCACC ATG AAG TTG CCT GTT AGG CTG TTG GTG CTT CTG TTG TTC TGG ATT
AAGCTTCGGC GGTGG TAC TTC AAC GGA CAA TCC GAC AAC CAC GAA GAC AAC AAG ACC TAA
                   M   K   L   P   V   R   L   L   V   L   L   L   F   W   I>

             70          80          90          100         110
CCT GCT TCC CGG GGT GAC GTT CAA GTG ACC CAG AGC CCA TCC AGC CTG AGC GCA TCT
GGA CGA AGG GCC CCA CTG CAA GTT CAC TGG GTC TCG GGT AGG TCG GAC TCG CGT AGA
 P   A   S   R   G   D   V   Q   V   T   Q   S   P   S   S   L   S   A   S>

120         130         140         150         160         170
GTA GGA GAC CGG GTC ACC ATC ACT TGT AGA TCC AGT CAG AGT CTT GCA AAC AGT TAT
CAT CCT CTG GCC CAG TGG TAG TGA ACA TCT AGG TCA GTC TCA GAA CGT TTG TCA ATA
 V   G   D   R   V   T   I   T   C   R   S   S   Q   S   L   A   N   S   Y>

    180         190         200         210         220         230
GGG AAC ACC TTT TTG TCT TGG TAT CTG CAC AAA CCA GGT AAA GCC CCA CAA TTG CTC
CCC TTG TGG AAA AAC AGA ACC ATA GAC GTG TTT GGT CCA TTT CGG GGT GTT AAC GAG
 G   N   T   F   L   S   W   Y   L   H   K   P   G   K   A   P   Q   L   L>

        240         250         260         270         280
ATC TAC GGA ATC TCT AAC AGA TTT AGT GGT GTA CCA GAC AGG TTC AGC GGT TCC GGA
TAG ATG CCT TAG AGA TTG TCT AAA TCA CCA CAT GGT CTG TCC AAG TCG CCA AGG CCT
 I   Y   G   I   S   N   R   F   S   G   V   P   D   R   F   S   G   S   G>

290         300         310         320         330         340
AGT GGT ACT GAT TTC ACC CTC ACG ATC TCG TCT CTC CAG CCA GAA GAT TTC GCC ACT
TCA CCA TGA CTA AAG TGG GAG TGC TAG AGC AGA GAG GTC GGT CTT CTA AAG CGG TGA
 S   G   T   D   F   T   L   T   I   S   S   L   Q   P   E   D   F   A   T>

   350         360         370         380         390         400
TAT TAC TGT TTA CAA GGT ACA CAT CAG CCG TAC ACA TTC GGT CAG GGT ACT AAA GTA
ATA ATG ACA AAT GTT CCA TGT GTA GTC GGC ATG TGT AAG CCA GTC CCA TGA TTT CAT
 Y   Y   C   L   Q   G   T   H   Q   P   Y   T   F   G   Q   G   T   K   V>

       410         420         430         440         450
GAA ATC AAA CGT ACG GTA GCG GCC CCA TCT GTC TTC ATC TTC CCG CCA TCT GAT GAG
CTT TAG TTT GCA TGC CAT CGC CGG GGT AGA CAG AAG TAG AAG GGC GGT AGA CTA CTC
 E   I   K   R   T   V   A   A   P   S   V   F   I   F   P   P   S   D   E>

460         470         480         490         500         510
CAG TTG AAA TCT GGA ACT GCC TCT GTT GTG TGC CTG CTG AAT AAC TTC TAT CCC AGA
GTC AAC TTT AGA CCT TGA CGG AGA CAA CAC ACG GAC GAC TTA TTG AAG ATA GGG TCT
 Q   L   K   S   G   T   A   S   V   V   C   L   L   N   N   F   Y   P   R>

   520         530         540         550         560         570
GAG GCC AAA GTA CAG TGG AAG GTG GAT AAC GCC CTC CAA TCG GGT AAC TCC CAG GAG
CTC CGG TTT CAT GTC ACC TTC CAC CTA TTG CGG GAG GTT AGC CCA TTG AGG GTC CTC
 E   A   K   V   Q   W   K   V   D   N   A   L   Q   S   G   N   S   Q   E>

       580         590         600         610         620         630
AGT GTC ACA GAG CAG GAC AGC AAG GAC AGC ACC TAC AGC CTC AGC AGC ACC CTG ACG
TCA CAG TGT CTC GTC CTG TCG TTC CTG TCG TGG ATG TCG GAG TCG TCG TGG GAC TGC
 S   V   T   E   Q   D   S   K   D   S   T   Y   S   L   S   S   T   L   T>

           640         650         660         670         680
```

FIGURE 16 CONT

```
CTG AGC AAA GCA GAC TAC GAG AAA CAC AAA GTC TAC GCC TGC GAA GTC ACC CAT CAG
GAC TCG TTT CGT CTG ATG CTC TTT GTG TTT CAG ATG CGG ACG CTT CAG TGG GTA GTC
 L   S   K   A   D   Y   E   K   H   K   V   Y   A   C   E   V   T   H   Q>

690           700           710           720           730           740
GGC CTG AGC TCG CCC GTC ACA AAG AGC TTC AAC AGG GGA GAG TGT TAG AGGGA
CCG GAC TCG AGC GGG CAG TGT TTC TCG AAG TTG TCC CCT CTC ACA ATC TCCCT
 G   L   S   S   P   V   T   K   S   F   N   R   G   E   C   *>

        750         760         770         780
GAAGTGCCCC CACCTGCTCC TCAGTTCCAG CCTGGGAATT C
CTTCACGGGG GTGGACGAGG AGTCAAGGTC GGACCCTTAA G
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FIGURE 17: STRUCTURE OF AN ANTIBODY-NAC-GAMMA CALICHEAMICIN DMH CONJUGATE

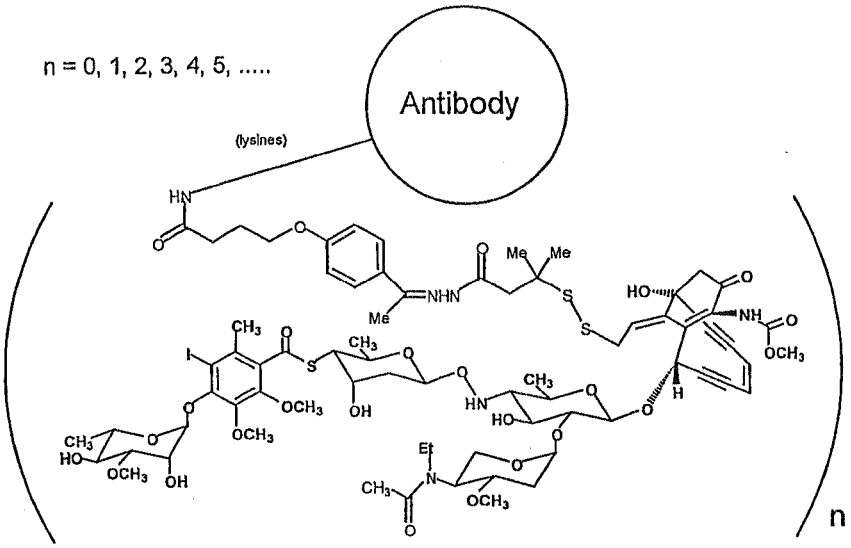
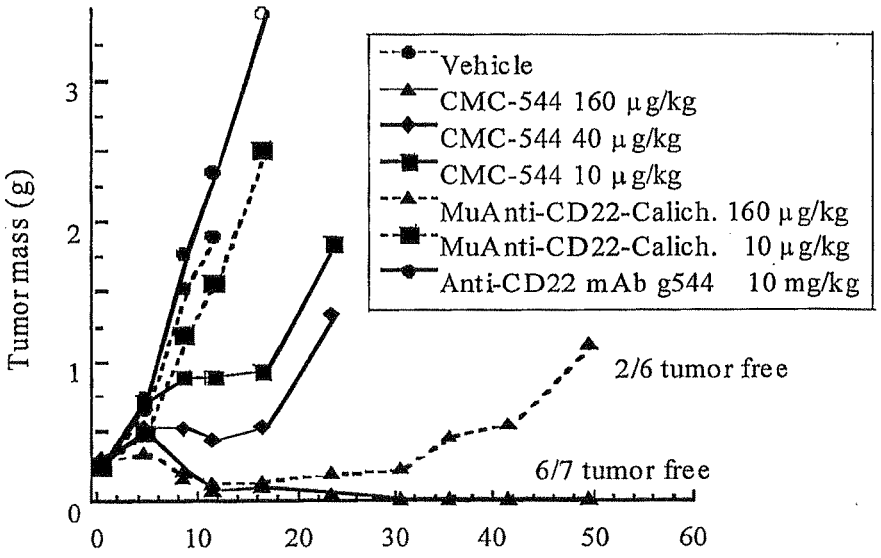


FIGURE 18: EFFECT OF CMC-544 ON GROWTH OF RAMOS B-CELL LYMPHOMA



Treatment: ip on days 1, 5, and 9

FIGURE 19: EFFECT OF CMC-544 ON LARGE B-CELL LYMPHOMAS

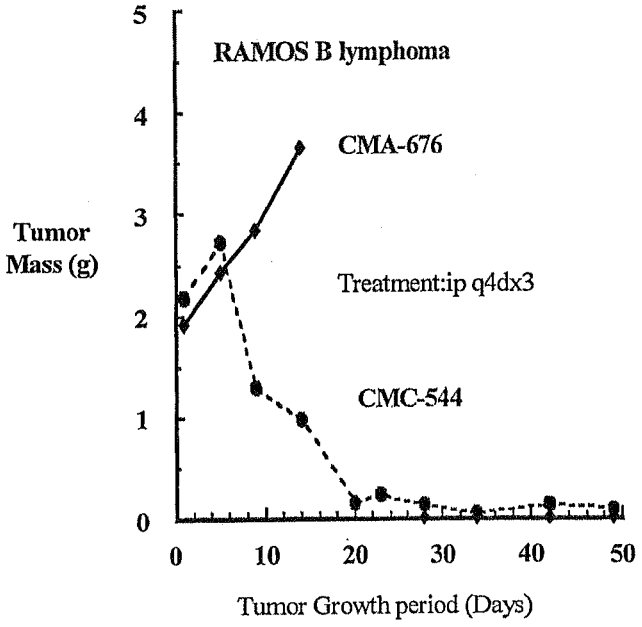


FIGURE 20: EFFECT OF CMC-544 MADE WITH THE CMA AND CMC CONJUGATION PROCEDURES ON THE GROWTH OF RL LYMPHOMA

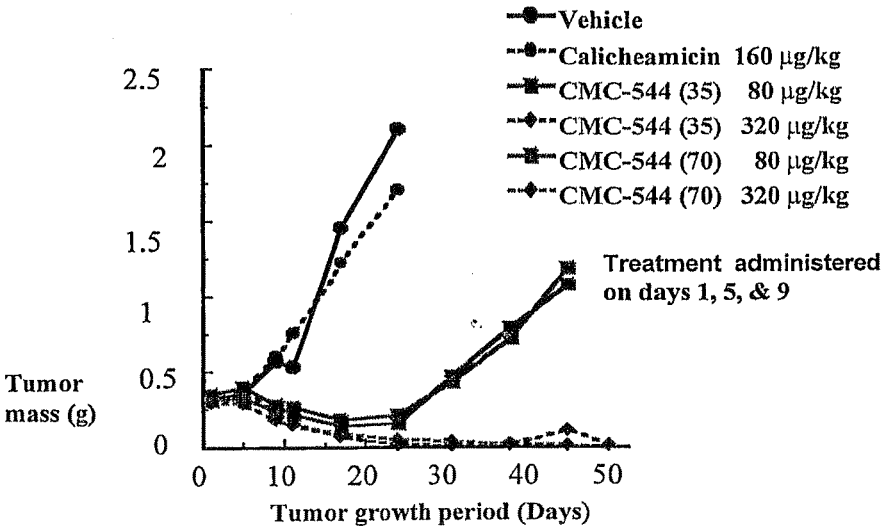


FIGURE 21: RITUXIMAB (RITUXAN™)-TREATED LARGE RL LYMPHOMA IS SUSCEPTIBLE TO CMC-544

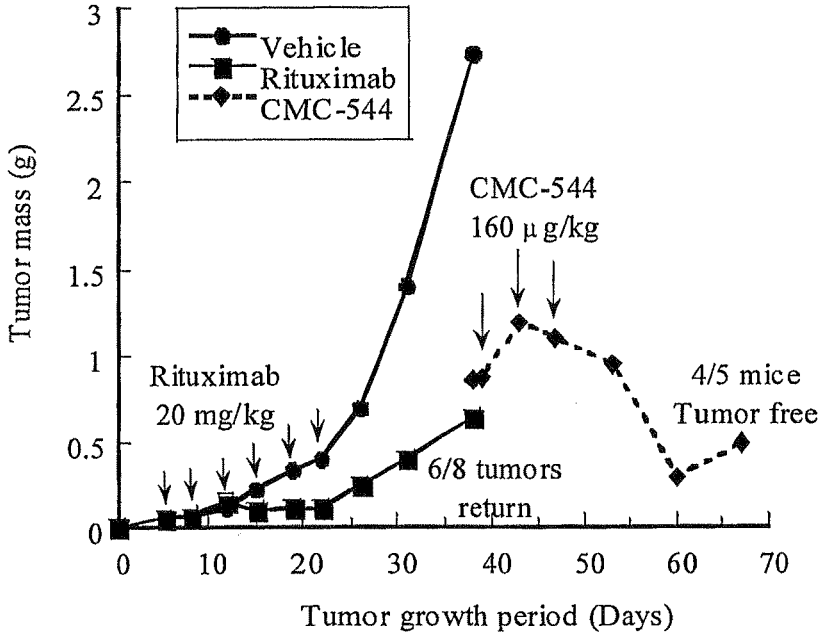


FIGURE 22: EFFECT OF RITUXIMAB (RITUXAN™) ON THE CYTOTOXIC ACTIVITY OF CMC-544

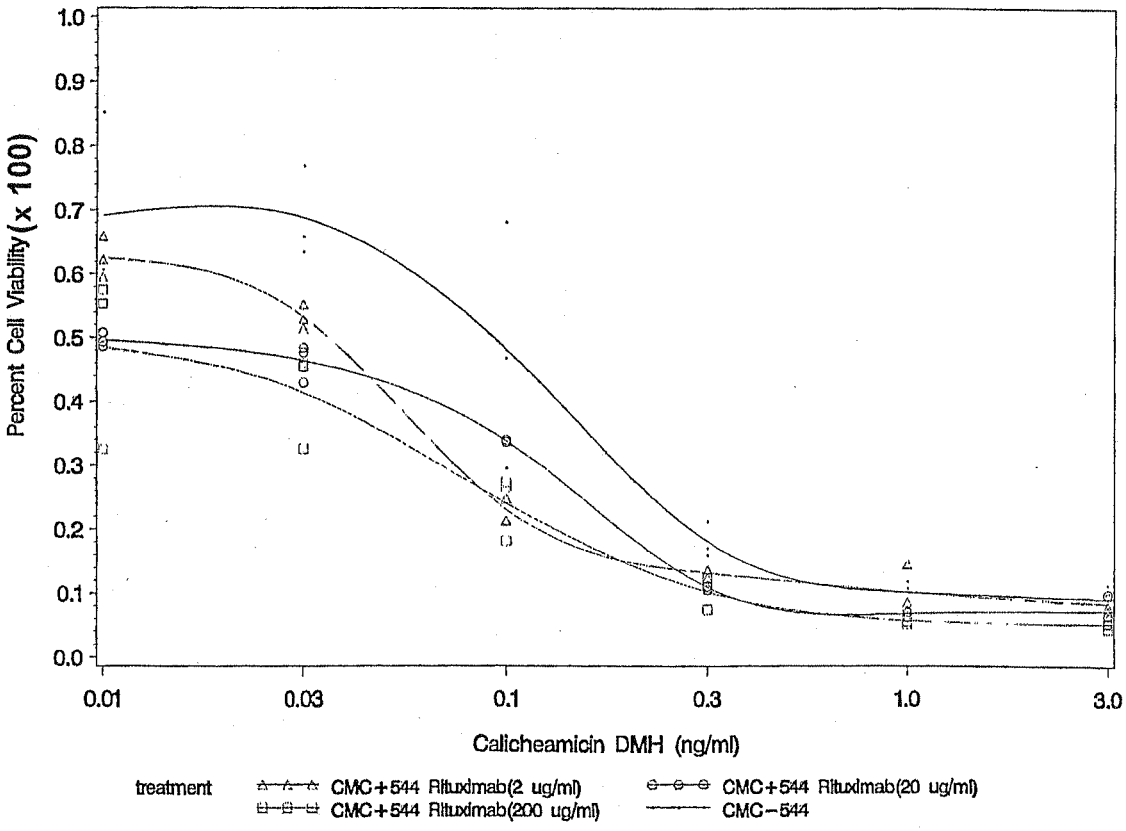


FIGURE 23: EFFECT OF CMC-544, RITUXIMAB (RITUXAN™)-, AND CMA-676 ON SURVIVAL OF SCID MICE WITH DISSEMINATED EARLY RAMOS B LYMPHOMA

Ramos B lymphoma cells
IV in SCID mice on Day 0

Treatment IP on Days 3, 7, 11
Q4Dx3

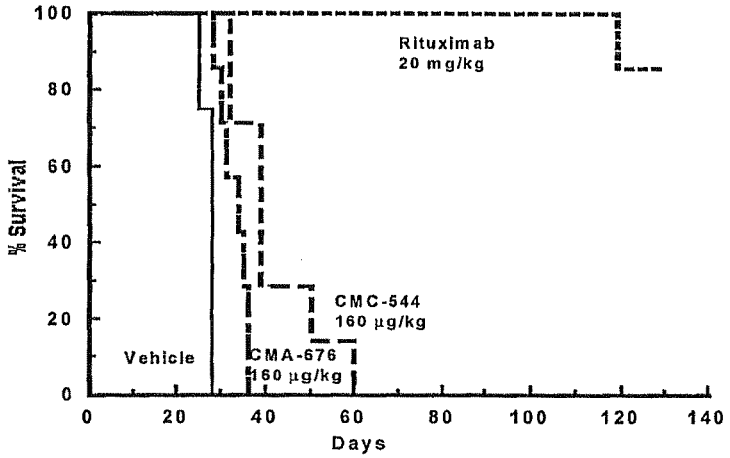


FIGURE 24: EFFECT OF CMC-544, RITUXIMAB (RITUXAN™), AND CMA-676 ON SURVIVAL OF SCID MICE WITH DISSEMINATED LATE RAMOS B LYMPHOMA

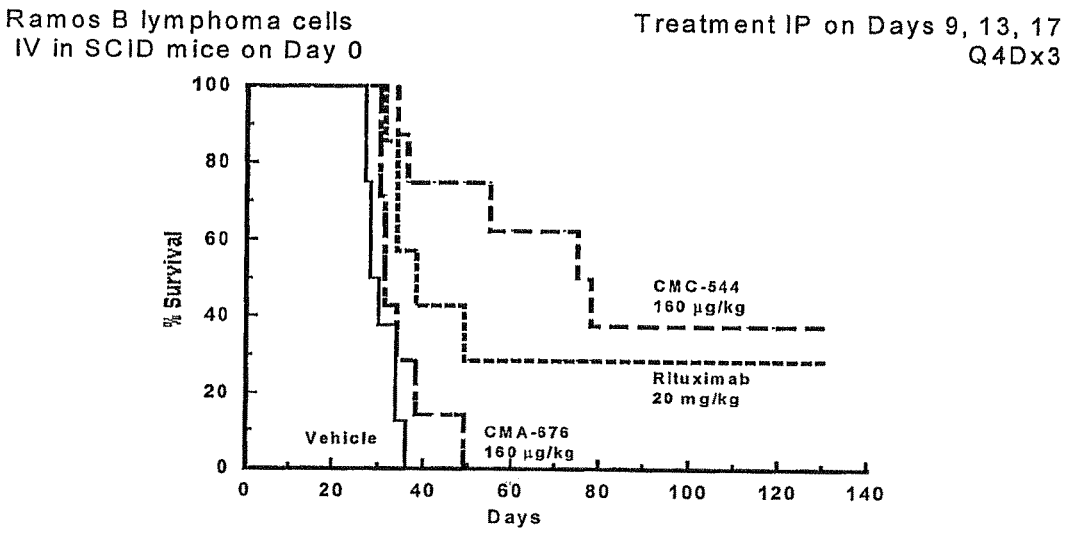


FIGURE 25: EFFECT OF CMC-544, RITUXIMAB (RITUXAN™), AND CMA-676 ON SURVIVAL OF SCID MICE WITH DISSEMINATED LATE RAMOS B LYMPHOMA

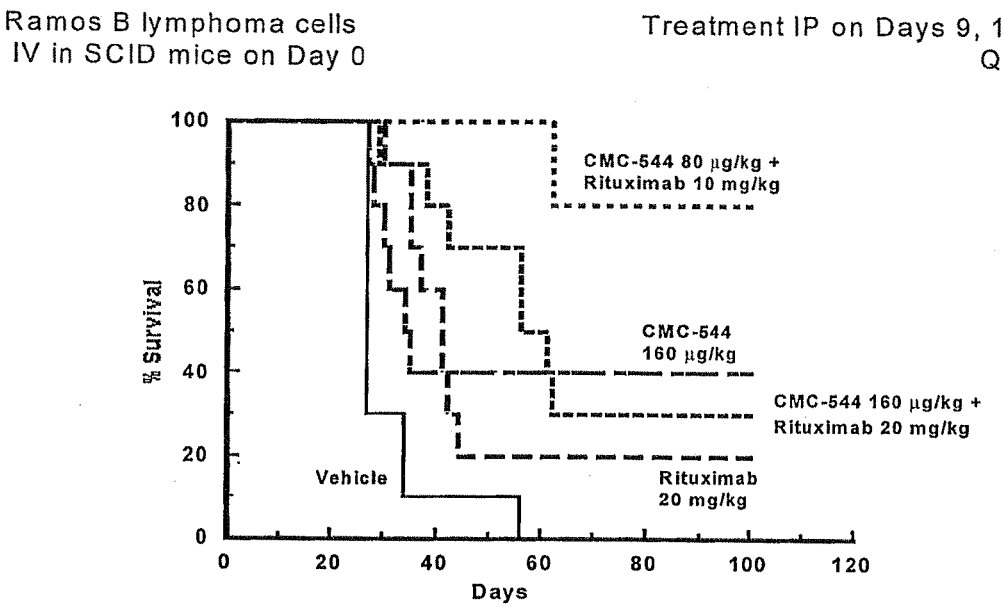


FIGURE 26: EFFECT OF CMC-544, RITUXIMAB (RITUXAN™), AND CMA-676 ON SURVIVAL OF SCID MICE WITH DISSEMINATED LATE RAMOS B LYMPHOMA

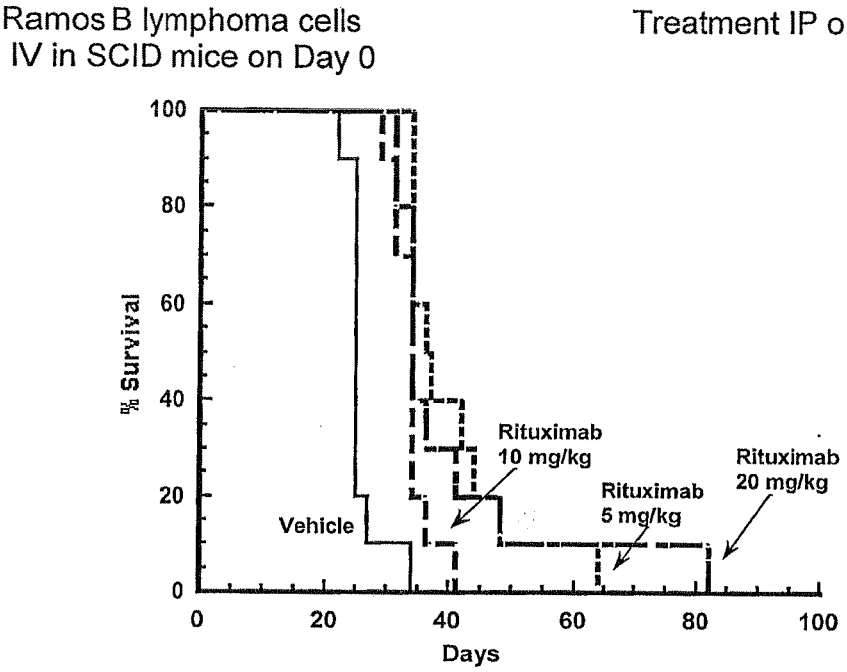


FIGURE 27: EFFECT OF CMC-544, RITUXIMAB (RITUXAN™), AND CMA-676 ON SURVIVAL OF SCID MICE WITH DISSEMINATED LATE RAMOS B LYMPHOMA

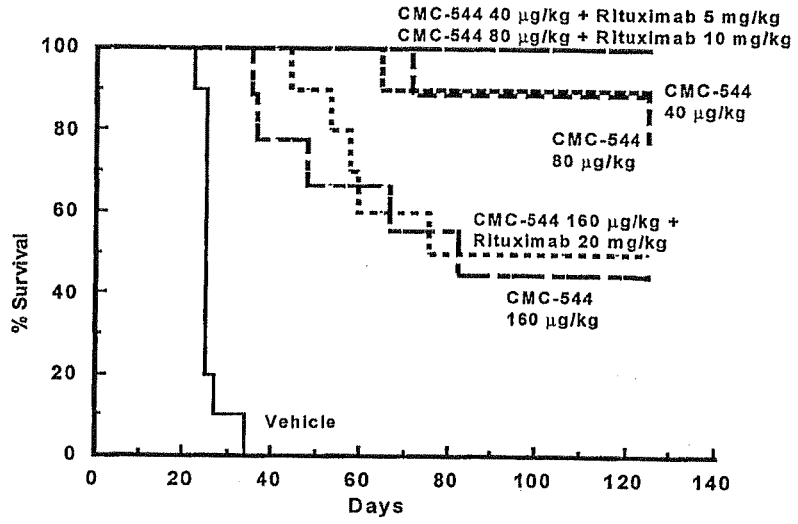


FIGURE 28: ANTI-TUMOR ACTIVITY OF CMC-544 WITH/WITHOUT RITUXIMAB (RITUXAN™) ON RL NON-HODGKINS LYMPHOMA

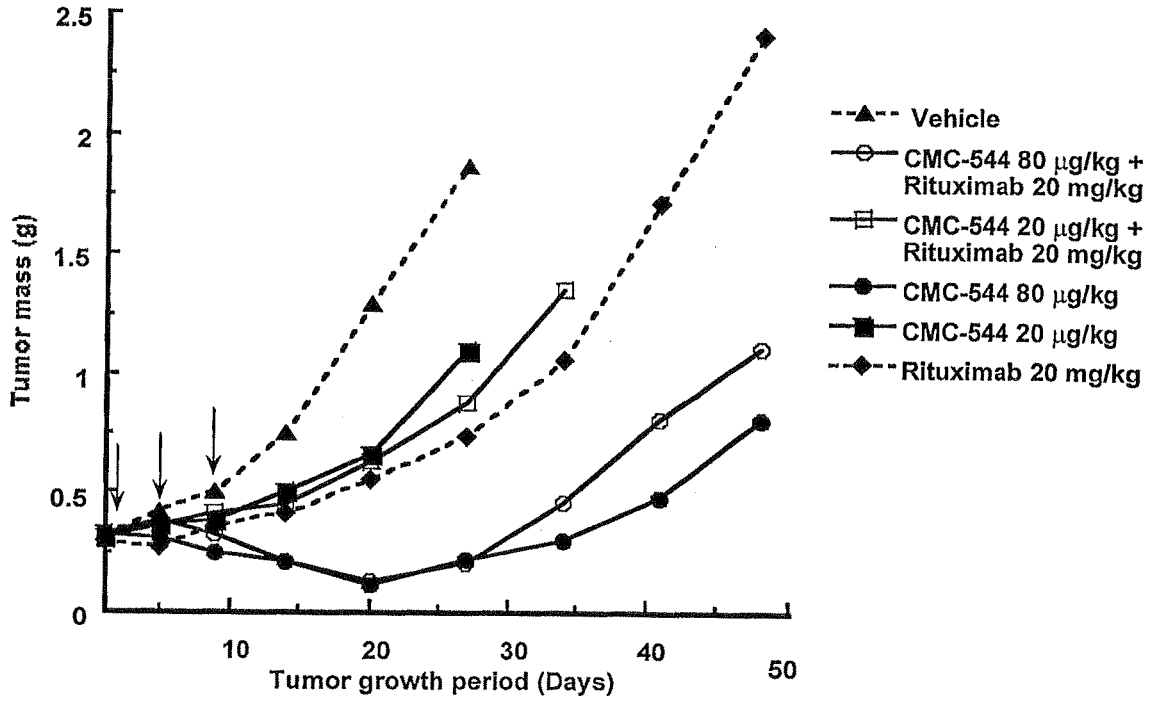
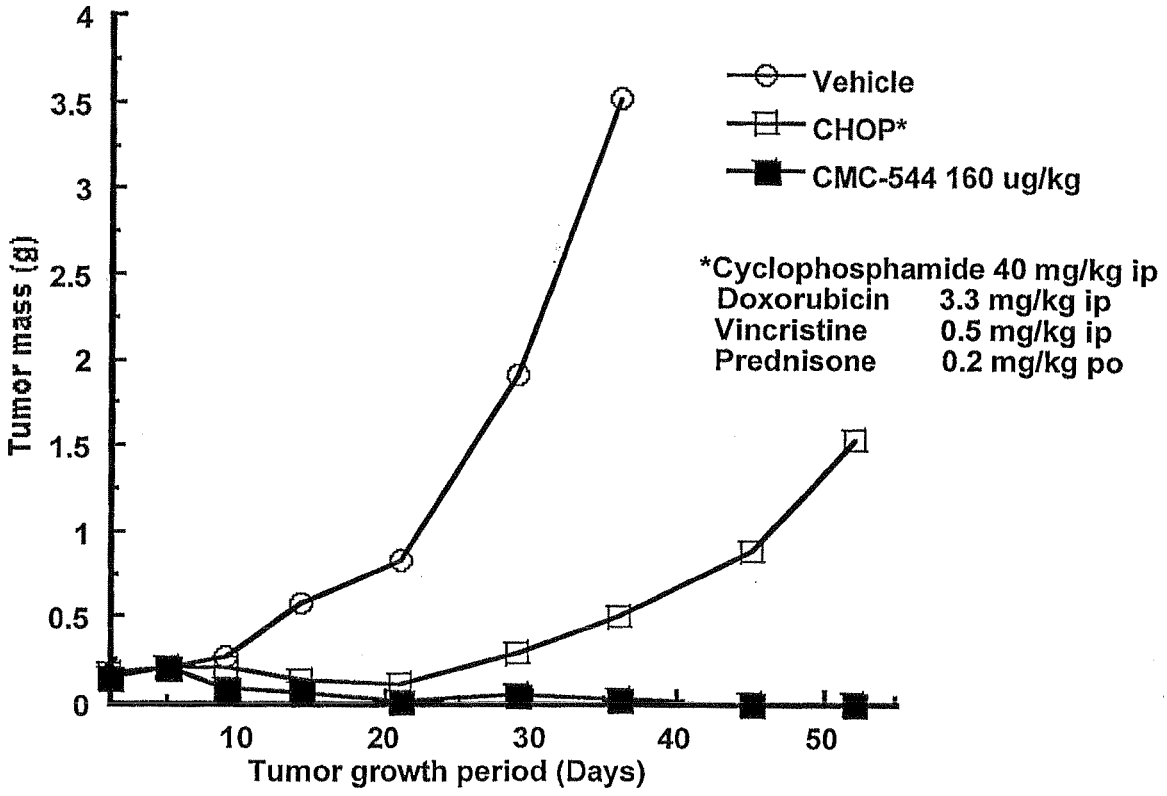


FIGURE 29: ANTI-TUMOR ACTIVITY OF CMC-544 AND CHOP ON RL NON-HODGKINS LYMPHOMA



SEQUENCE LISTING

<110> WYETH HOLDINGS CORPORATION.; KUNZ, ARTHUR ET AL.

<120> CALICHEAMICIN DERIVATIVE-CARRIER CONJUGATES
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Gly

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20 25 30

Tyr Gly Asn Thr Phe Leu Ser Trp Tyr Leu His Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Gly Ile Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Thr Ile Lys Pro Glu Asp Leu Gly Met Tyr Tyr Cys Leu Gln Gly
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Thr His Gln Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
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Arg

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35 40 45

Gly Gly Ile Asn Pro Gly Asn Asn Tyr Thr Thr Tyr Lys Arg Asn Leu
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Val Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Met Asp Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Thr Arg Glu Gly Tyr Gly Asn Tyr Gly Ala Trp Phe Ala Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
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Gly

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Gly

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20 25 30

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35 40 45

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50 55 60

Phe Ala Thr Tyr Tyr Cys
65 70

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20 25 30

Tyr Gly Asn Thr Phe Leu Ser Trp Tyr Leu His Lys Pro Gly Lys Ala
35 40 45

Pro Gln Leu Leu Ile Tyr Gly Ile Ser Asn Arg Phe Ser Gly Val Pro

50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
65 70 75 80

Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Gly
85 90 95

Thr His Gln Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

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20 25 30

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35 40 45

Pro Gln Leu Leu Ile Tyr Gly Ile Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
65 70 75 80

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Thr His Gln Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
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20 25 30

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Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr Met Glu
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20 25 30

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35 40 45

Gly Gly Ile Asn Pro Gly Asn Gln Tyr Thr Thr Tyr Lys Arg Asn Leu
50 55 60

Lys Gly Arg Ala Thr Leu Thr Ala Asp Thr Ser Thr Ser Thr Val Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Thr Arg Glu Gly Tyr Gly Asn Tyr Gly Ala Trp Phe Ala Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Arg Phe Thr Asn Tyr
20 25 30

Trp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile

35 40 45

Gly Gly Ile Asn Pro Gly Asn Asn Tyr Ala Thr Tyr Arg Arg Asn Leu
50 55 60

Lys Gly Arg Ala Thr Leu Thr Ala Asp Thr Ser Thr Ser Thr Val Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Thr Arg Glu Gly Tyr Gly Asn Tyr Gly Ala Trp Phe Ala Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 25
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<223> gH5

<220>
<221>

<400> 25
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Arg Phe Thr Asn Tyr
20 25 30

Trp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Gly Ile Asn Pro Gly Asn Asn Tyr Ala Thr Tyr Arg Arg Asn Leu
50 55 60

Lys Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Val Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Thr Arg Glu Gly Tyr Gly Asn Tyr Gly Ala Trp Phe Ala Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 26
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<223> gH6

<220>
<221>

<400> 26
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Arg Phe Thr Asn Tyr
20 25 30

Trp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Gly Ile Asn Pro Gly Asn Asn Tyr Ala Thr Tyr Arg Arg Lys Phe
50 55 60

Gln Gly Arg Ala Thr Leu Thr Ala Asp Thr Ser Thr Ser Thr Val Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Thr Arg Glu Gly Tyr Gly Asn Tyr Gly Ala Trp Phe Ala Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 27
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<223> gH7

<220>
<221>

<400> 27
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Arg Phe Thr Asn Tyr
20 25 30

Trp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Gly Ile Asn Pro Gly Asn Asn Tyr Ala Thr Tyr Arg Arg Lys Phe

50 55 60

Gln Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser Thr Val Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Thr Arg Glu Gly Tyr Gly Asn Tyr Gly Ala Trp Phe Ala Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 28
<211> 239
<212> PRT
<213> Artificial Sequence

<220>
<223> Full sequence of grafted light chain

<220>
<221>

<400> 28
Met Lys Leu Pro Val Arg Leu Leu Val Leu Leu Leu Phe Trp Ile Pro
1 5 10 15

Ala Ser Arg Gly Asp Val Gln Val Thr Gln Ser Pro Ser Ser Leu Ser
20 25 30

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ser Ser Gln Ser
35 40 45

Leu Ala Asn Ser Tyr Gly Asn Thr Phe Leu Ser Trp Tyr Leu His Lys
50 55 60

Pro Gly Lys Ala Pro Gln Leu Leu Ile Tyr Gly Ile Ser Asn Arg Phe
65 70 75 80

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
85 90 95

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
100 105 110

Cys Leu Gln Gly Thr His Gln Pro Tyr Thr Phe Gly Gln Gly Thr Lys
115 120 125

Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro
130 135 140

Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu
145 150 155 160

Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp
165 170 175

Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp
180 185 190

Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys
195 200 205

Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln
210 215 220

Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
225 230 235

<210> 29
<211> 781
<212> DNA

<213> Artificial Sequence

<220>
<223> Full sequence of grafted light chain

<220>
<221>

<400> 29
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cctgcttccc ggggtgacgt tcaagtgacc cagagcccat ccagcctgag cgcatctgta 120
ggagaccggg tcaccatcac ttgtagatcc agtcagagtc ttgcaaacag ttatgggaac 180
acctttttgt cttggtatct gcacaaacca ggtaaagccc cacaattgct catctacgga 240
atctctaaca gatttagtgg tgtaccagac aggttcagcg gttccggaag tggtactgat 300
ttcaccctca cgatctcgtc tctccagcca gaagatttcg ccacttatta ctgtttacaa 360
ggtacacatc agccgtacac attcggtcag ggtactaaag tagaaatcaa acgtacggta 420
gcggccccat ctgtcttcat cttcccgcca tctgatgagc agttgaaatc tggaactgcc 480
tctgttgtgt gcctgctgaa taacttctat cccagagagg ccaaagtaca gtggaaggtg 540
gataacgccc tccaatcggg taactcccag gagagtgtca cagagcagga cagcaaggac 600
agcacctaca gcctcagcag caccctgacg ctgagcaaag cagactacga gaaacacaaa 660
gtctacgcct gcgaagtcac ccatcagggc ctgagctcgc ccgtcacaaa gagcttcaac 720
aggggagagt gttagaggga gaagtgcccc cacctgctcc tcagttccag cctgggaatt 780
c 781

<210> 30
<211> 467
<212> PRT
<213> Artificial Sequence

<220>
<223> Full sequence of grafted heavy chain

<220>
<221>

<400> 30
Met Asp Phe Gly Phe Ser Leu Val Phe Leu Ala Leu Ile Leu Lys Gly

1 5 10 15

Val Gln Cys Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
20 25 30

Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Arg Phe
35 40 45

Thr Asn Tyr Trp Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
50 55 60

Glu Trp Ile Gly Gly Ile Asn Pro Gly Asn Asn Tyr Ala Thr Tyr Arg
65 70 75 80

Arg Lys Phe Gln Gly Arg Val Thr Met Thr Ala Asp Thr Ser Thr Ser
85 90 95

Thr Val Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Thr Arg Glu Gly Tyr Gly Asn Tyr Gly Ala Trp Phe Ala
115 120 125

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys
130 135 140

Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu
145 150 155 160

Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
165 170 175

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
180 185 190

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
195 200 205

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn
210 215 220

Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser
225 230 235 240

Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Leu Gly
245 250 255

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
260 265 270

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln
275 280 285

Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val
290 295 300

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr
305 310 315 320

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
325 330 335

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile
340 345 350

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
355 360 365

Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser
370 375 380

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
385 390 395 400

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
405 410 415

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val
420 425 430

Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met
435 440 445

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
450 455 460

Leu Gly Lys
465

<210> 31
<211> 2160
<212> DNA
<213> Artificial Sequence

<220>
<223> Full DNA sequence of grafted heavy chain

<220>
<221>

<400> 31
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ggagtgcagt gtgaggtgca attggtccag tcaggagcag aggttaagaa gcctggtgct 120
tccgtcaaag tttcgtgtaa ggctagcggc tacaggttca caaattattg gattcattgg 180
gtcaggcagg ctccgggaca aggcctggaa tggatcggtg gcattaatcc cgggaataac 240
tacgctacat ataggagaaa attccagggc agagttacga tgaccgcgga cacctccaca 300
agcactgtct acatggagct gtcatctctg agatccgagg acaccgcagt gtactattgt 360
actagagaag gctacggtaa ttacggagcc tggttcgcct actggggcca gggtacccta 420
gtcacagtct cctcagcttc tacaaagggc ccatccgtct tccccctggc gccctgctcc 480
aggagcacct ccgagagcac agccgccctg ggctgcctgg tcaaggacta cttccccgaa 540
ccggtgacgg tgtcgtggaa ctcaggcgcc ctgaccagcg gcgtgcacac cttcccggct 600

gtcctacagt cctcaggact ctactccctc agcagcgtgg tgaccgtgcc ctccagcagc 660
ttgggcacga agacctacac ctgcaacgta gatcacaagc ccagcaacac caaggtggac 720
aagagagttg gtgagaggcc agcacaggga gggagggtgt ctgctggaag ccaggctcag 780
ccctcctgcc tggacgcacc ccggctgtgc agccccagcc cagggcagca aggcatgccc 840
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ctggattttt ccaccaggct ccgggcagcc acaggctgga tgcccctacc ccaggccctg 960
cgcatacagg ggcaggtgct gcgctcagac ctgccaagag ccatatccgg gaggaccctg 1020
cccctgacct aagcccaccc caaaggccaa actctccact ccctcagctc agacaccttc 1080
tctcctccca gatctgagta actcccaatc ttctctctgc agagtccaaa tatggtcccc 1140
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ggtgccctag agtagcctgc atccagggac aggccccagc cgggtgctga cgcatccacc 1260
tccatctctt cctcagcacc tgagttcctg gggggaccat cagtcttcct gttccccccа 1320
aaacccaagg acactctcat gatctcccgg acccctgagg tcacgtgcgt ggtggtggac 1380
gtgagccagg aagaccccga ggtccagttc aactggtacg tggatggcgt ggaggtgcat 1440
aatgccaaga caaagccgcg ggaggagcag ttcaacagca cgtaccgtgt ggtcagcgtc 1500
ctcaccgtcc tgcaccagga ctggctgaac ggcaaggagt acaagtgcaa ggtctccaac 1560
aaaggcctcc cgtcctccat cgagaaaacc atctccaaag ccaaaggtgg gacccacggg 1620
gtgcgagggc cacatggaca gaggtcagct cggcccaccc tctgccctgg gagtgaccgc 1680
tgtgccaacc tctgtcccta cagggcagcc ccgagagcca caggtgtaca ccctgccccc 1740
atcccaggag gagatgacca agaaccaggt cagcctgacc tgcctggtca aaggcttcta 1800
ccccagcgac atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac 1860
cacgcctccc gtgctggact ccgacggctc cttcttcctc tacagcaggc taaccgtgga 1920
caagagcagg tggcaggagg ggaatgtctt ctcatgctcc gtgatgcatg aggctctgca 1980
caaccactac acacagaaga gcctctccct gtctctgggt aaatgagtgc cagggccggc 2040
aagccccccgc tccccgggct ctcggggtcg cgcgaggatg cttggcacgt accccgtcta 2100
catacttccc aggcacccag catggaaata aagcacccac cactgccctg gctcgaattc 2160

<210> 32
<211> 94
<212> DNA
<213> Artificial Sequence

<220>
<223> 544gH1 T1

<220>
<221>

<400> 32
agtgtgaggt gcaattggtc cagtcaggag cagaggttaa gaagcctggt gcttccgtca 60
aagtttcgtg taaggctagc ggctacaggt tcac 94

<210> 33
<211> 96
<212> DNA
<213> Artificial Sequence

<220>
<223> 544gH1 T2

<220>
<221>

<400> 33
gtggcattaa tcccgggaat cagtacacta catataaaag aaatctaaag ggcagagcaa 60
cgctgaccgc ggacacctcc acaagcactg tctaca 96

<210> 34
<211> 95
<212> DNA
<213> Artificial Sequence

<220>
<223> 544gH1 T3

<220>
<221>

<400> 34
agagaaggct acggtaatta cggagcctgg ttcgcctact ggggccaggg taccctagtc 60
acagtctcct cagcttctac aaagggccca agaaa 95

<210> 35
<211> 94

<212> DNA
<213> Artificial Sequence

<220>
<223> 544 gH1 B1

<220>
<221>

<400> 35
ggaccaattg cacctcacac tgcactccct tgagaatgag tgccaggaac acgagagaga 60
atccgaagtc catggtggcg gcaagctttt attc 94

<210> 36
<211> 97
<212> DNA
<213> Artificial Sequence

<220>
<223> 544gH1 B2

<220>
<221>

<400> 36
gattcccggg attaatgcca ccgatccatt ccaggccttg tcccggagcc tgcctgaccc 60
aatgaatcca ataatttgtg aacctgtagc cgctagc 97

<210> 37
<211> 93
<212> DNA
<213> Artificial Sequence

<220>
<223> 544gH1B3

<220>

<221>

<400> 37
cgtaattacc gtagccttct ctagtacaat agtacactgc ggtgtcctcg gatctcagag 60
atgacagctc catgtagaca gtgcttgtgg agg 93

<210> 38
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> 544gH1 F1

<220>
<221>

<400> 38
gaataaaagc ttgccgccac c 21

<210> 39
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> 544gH1 R1

<220>
<221>

<400> 39
tttcttgggc cctttgtaga ag 22

<210> 40
<211> 87
<212> DNA

<213> Artificial Sequence

<220>
<223> 544gL1 T1

<220>
<221>

<400> 40
gcttcccggg gtgacgttca agtgacccag agcccatcca gcctgagcgc atctgtagga 60
gaccgggtca ccatcacttg tagatcc 87

<210> 41
<211> 90
<212> DNA
<213> Artificial Sequence

<220>
<223> 544gL1 T2

<220>
<221>

<400> 41
tatctgcaca aaccaggtaa agccccacaa ttgctcatct acggaatctc taacagattt 60
agtggtgtac cagacaggtt cagcggttcc 90

<210> 42
<211> 91
<212> DNA
<213> Artificial Sequence

<220>
<223> 544gL1 T3

<220>
<221>

<400> 42
agatttcgcc acttattact gtttacaagg tacacatcag ccgtacacat tcggtcaggg 60
tactaaagta gaaatcaaac gtacggcgtg c 91

<210> 43
<211> 88
<212> DNA
<213> Artificial Sequence

<220>
<223> 544gL1 B1

<220>
<221>

<400> 43
gaacgtcacc ccgggaagca ggaatccaga acaacagaag caccaacagc ctaacaggca 60
acttcatggt ggcggcttcg aatcatcc 88

<210> 44
<211> 88
<212> DNA
<213> Artificial Sequence

<220>
<223> 544gL1 B2

<220>
<221>

<400> 44
ctttacctgg tttgtgcaga taccaagaca aaaaggtgtt cccataactg tttgcaagac 60
tctgactgga tctacaagtg atggtgac 88

<210> 45
<211> 90

<212> DNA
<213> Artificial Sequence

<220>
<223> 544gL1B3

<220>
<221>

<400> 45
aacagtaata agtggcgaaa tcttctggct ggagagacga gatcgtgagg gtgaaatcag 60
taccacttcc ggaaccgctg aacctgtctg 90

<210> 46
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> 544gL1 F1

<220>
<221>

<400> 46
ggatgattcg aagccgccac 20

<210> 47
<211> 21
<212> DNA
<213> Artificial sequence

<220>
<223> 544gL1 R1

<220>
<221>

<400> 47
gcacgccgta cgtttgattt c 21

<210> 48
<211> 339
<212> DNA
<213> mouse

<220>
<223> DNA sequence of mouse monoclonal 5/44 VL

<220>
<221>

<400> 48
gatgttgtgg tgactcaaac tccactctcc ctgcctgtca gctttggaga tcaagtttct 60
atctcttgca ggtctagtca gagtcttgca aacagttatg ggaacacctt tttgtcttgg 120
tacctgcaca agcctggcca gtctccacag ctcctcatct atgggatttc caacagattt 180
tctggggtgc cagacaggtt cactggcagt ggttcaggga cagatttcac actcaagatc 240
agcacaataa agcctgagga cttgggaatg tattactgct tacaaggtac acatcagccg 300
tacacgttcg gaggggggac caagctggaa ataaaacgt 339

<210> 49
<211> 363
<212> DNA
<213> mouse

<220>
<223> DNA sequence of mouse monoclonal 5/44 VH

<220>
<221>

<400> 49
gaggtccaac tgcagcagtc tgggactgta ctggcaaggc ctggggcttc cgtgaagatg 60
tcctgcaagg cttctggcta caggtttacc aactactgga ttcactgggt aaaacagagg 120

cctgggcagg gtctagaatg gattggtggt attaatcctg gaaataatta tactacgtat 180
aagaggaact tgaagggcaa ggccacactg actgcagtca catccgccag cactgcctac 240
atggacctca gcagcctgac aagtgaggac tctgcggtct attactgtac aagagagggc 300
tatggtaact acggggcctg gtttgcttac tggggccagg ggactctggt caccgtctcc 360
tca 363

<210> 50
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> sequence within oligonucleotide primer

<400> 50
gccgccacc 9

<210> 51
<211> 101
<212> DNA
<213> Artificial Sequence

<220>
<223> 5' oligonucleotide primer

<400> 51
gcgcgcaagc ttgccgccac catggacttc ggattctctc tcgtgttcct ggcactcatt 60
ctcaagggag tgcagtgtga ggtgcagctc gtcgagtctg g 101