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>

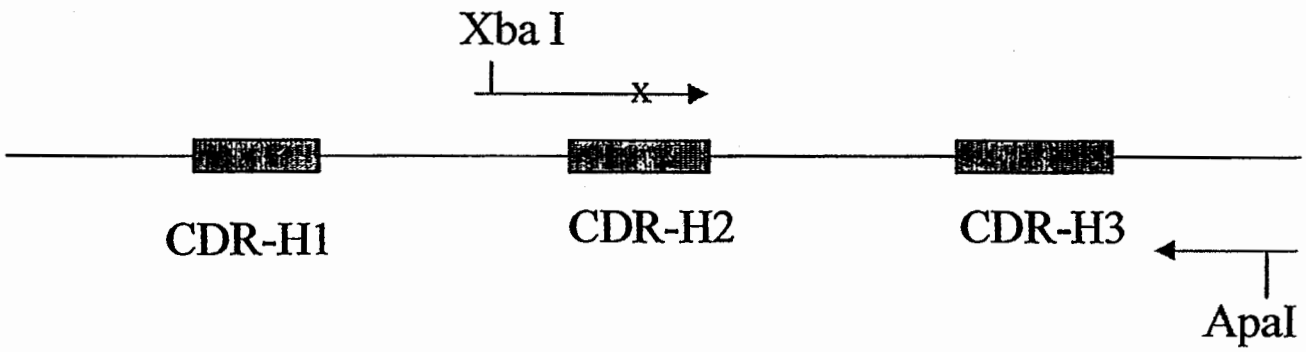
230         240         250         260         270         280
AGC ACT GCC TAC ATG GAC CTC AGC AGC CTG ACA AGT GAG GAC TCT GCG GTC TAT TAC
TCG TGA CGG ATG TAC CTG GAG TCG TCG GAC TGT TCA CTC CTG AGA CGC CAG ATA ATG
 S   T   A   Y   M   D   L   S   S   L   T   S   E   D   S   A   V   Y   Y>

   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



CDR-H2

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

Figure 5: 5/44 Light Chain Sequence Graft design

```
                10        20                            40
VL    DVVVTQTPLSLPVSFGDQVSISC RSSQSLANSYGNTFLS WYLHKPGQSPQLLIY
       |||  | |  || |  | | |                     ||   || |
DPK9  DIQMTQSPSSLSASVGDRVTITC                    WYQQKPGKAPKLLIY
       | |                                       ||       |
gL1   DVQVTQSPSSLSASVGDRVTITC RSSQSLANSYGNTFLS WYLHKPGKAPQLLIY
gL2   DVVVTQSPSSLSASVGDRVTITC RSSQSLANSYGNTFLS WYLHKPGKAPQLLIY

                  60        70        80          90
VL    GISNRFS GVPDRFTGSGSGTDFTLKISTIKPEDLGMYYC LQGTHQPYT
                  |  |          |  |||   |||
DPK9          GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC
                  |
gL1   GISNRFS GVPDRFSGSGSGTDFTLTISSLQPEDFATYYC LQGTHQPYT
gL2   GISNRFS GVPDRFSGSGSGTDFTLTISSLQPEDFATYYC LQGTHQPYT

      100
VL    FGGGTKLEIKR
        |   |
JK1   FGQGTKVEIKR

gL1   FGQGTKVEIKR
gL2   FGQGTKVEIKR
```

DPK-9 is the human germ-line acceptor framework sequence.

Vertical lines indicate differences between mouse and human residues.

Sequences underlined indicate donor residues which have been retained in the graft. CDRs are indicated in blue (not shown for DPK-9).

Graft gL1 has 6 donor framework residues, gL2 has 7.

Figure 6: 5/44 Heavy Chain Sequence Graft design

```
                10        20        30        40        50
VH    EVQLQQSGTVLARPGASVKMSCKASGYRFT NYWIH WVKQRPGQGLEWIG GINP
      |   |   |||||       |                  | |       |
DP7   QVQLVQSGAEVKKPGASVKVSCKASGYTFT        WVRQAPGQGLEWMG
      |                               |                  |
gH1   EVQLVQSGAEVKKPGASVKVSCKASGYRFT NYWIH WVRQAPGQGLEWIG GINP
gH4,5,6,7 EVQLVQSGAEVKKPGASVKVSCKASGYRFT NYWIH WVRQAPGQGLEWIG GINP

          60        70        80        90        100
VH    GNNYTTYKRNLKG KATLTAVTSASTAYMDLSSLTSEDSAVYYCTR EGYGNYG
                    || | ||  |  |  |    |   |     |
DP7           KFQG RVTMTRDTSTSTVYMELSSLRSEDTAVYYCAR
                     | | |                        |
gH1   GNQYTTYKRNLKG RATLTADTSTSTVYMELSSLRSEDTAVYYCTR EGYGNYG
gH4   GNNYATYRRNLKG RATLTADTSTSTVYMELSSLRSEDTAVYYCTR EGYGNYG
gH5   GNNYATYRRNLKG RVTMTADTSTSTVYMELSSLRSEDTAVYYCTR EGYGNYG
gH6   GNNYATYRRKFQG RATLTADTSTSTVYMELSSLRSEDTAVYYCTR EGYGNYG
gH7   GNNYATYRRKFQG RVTMTADTSTSTVYMELSSLRSEDTAVYYCTR EGYGNYG

           110
JH4       WGQGTLVTVSS

VH    AWFAY WGQGTLVTVSS

gH1   AWFAY WGQGTLVTVSS
gH4,5,6,7 AWFAY WGQGTLVTVSS
```

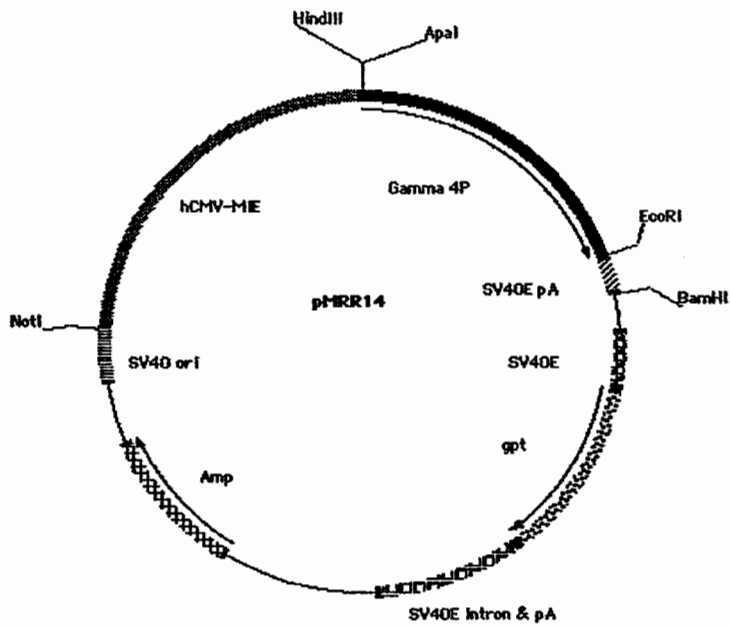
DP7 is the human germ-line acceptor framework sequence.

Vertical lines indicate differences between mouse and human residues.

Sequences underlined indicate donor residues which have been retained in the graft. CDRs are indicated in blue (not shown for DP7)

Grafts gH4 and gH6 have 6 donor framework residues. Grafts gH5 and gH7 have 4.

Figure 7: Maps of pMRR14 and pMRR10.1



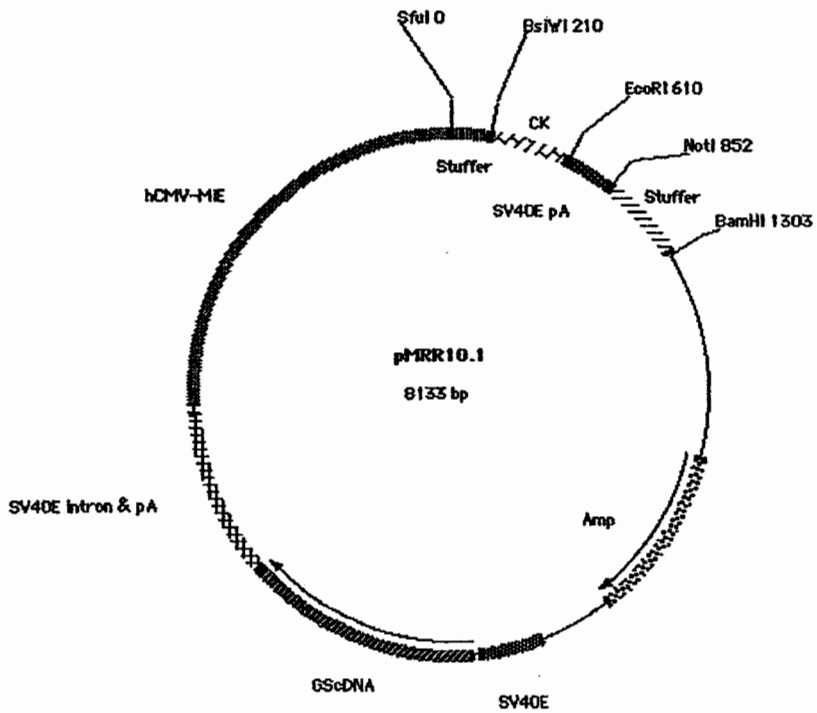


Figure 8: **Biacore assay of chimeric 5/44 and mutants**

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 9: Oligonucleotides for 5/44 gH1 and gL1 gene assemblies

Heavy Chain

544gH1 T1

AGTGTGAGGTGCAATTGGTCCAGTCAGGAGCAGAGGTTAAGAAGCCTGGTGCTTCCGTCA
AAGTTTCGTGTAAGGCTAGCGGCTACAGGTTCAC

544gH1 T2

GTGGCATTAATCCCGGGAATCAGTACACTACATATAAAAGAAATCTAAAGGGCAGAGCA
ACGCTGACCGCGGACACCTCCACAAGCACTGTCTACA

544gH1 T3

AGAGAAGGCTACGGTAATTACGGAGCCTGGTTCGCCTACTGGGGCCAGGGTACCCTAGTC
ACAGTCTCCTCAGCTTCTACAAAGGGCCCAAGAAA

544 gH1 B1

GGACCAATTGCACCTCACACTGCACTCCCTTGAGAATGAGTGCCAGGAACACGAGAGAG
AATCCGAAGTCCATGGTGGCGGCAAGCTTTTATTC

544 gH1 B2

GATTCCCGGGATTAATGCCACCGATCCATTCCAGGCCTTGTCCCGGAGCCTGCCTGACCC
AATGAATCCAATAATTTGTGAACCTGTAGCCGCTAGC

544gH1 B3

CGTAATTACCGTAGCCTTCTCTAGTACAATAGTACACTGCGGTGTCCTCGGATCTCAGAG
ATGACAGCTCCATGTAGACAGTGCTTGTGGAGG

544gH1 F1

GAATAAAAGCTTGCCGCCACC

544gH1 R1

TTTCTTGGGCCCTTTGTAGAAG

Figure 9 cont.

Light Chain

544 gL1 T1

GCTTCCCGGGGTGACGTTCAAGTGACCCAGAGCCCATCCAGCCTGAGCGCATCTGTAGGA
GACCGGGTCACCATCACTTGTAGATCC

544 gL1 T2

TATCTGCACAAACCAGGTAAAGCCCCACAATTGCTCATCTACGGAATCTCTAACAGATTT
AGTGGTGTACCAGACAGGTTCAGCGGTTCC

544gL1 T3

AGATTTCGCCACTTATTACTGTTTACAAGGTACACATCAGCCGTACACATTCGGTCAGGG
TACTAAAGTAGAAATCAAACGTACGGCGTGC

544gL1 B1

GAACGTCACCCCGGGAAGCAGGAATCCAGAACAACAGAAGCACCAACAGCCTAACAGG
CAACTTCATGGTGGCGGCTTCGAATCATCC

544gL1 B2

CTTTACCTGGTTTGTGCAGATACCAAGACAAAAAGGTGTTCCCATAACTGTTTGCAAGAC
TCTGACTGGATCTACAAGTGATGGTGAC

544gL1 B3

AACAGTAATAAGTGGCGAAATCTTCTGGCTGGAGAGACGAGATCGTGAGGGTGAAATCA
GTACCACTTCCGGAACCGCTGAACCTGTCTG

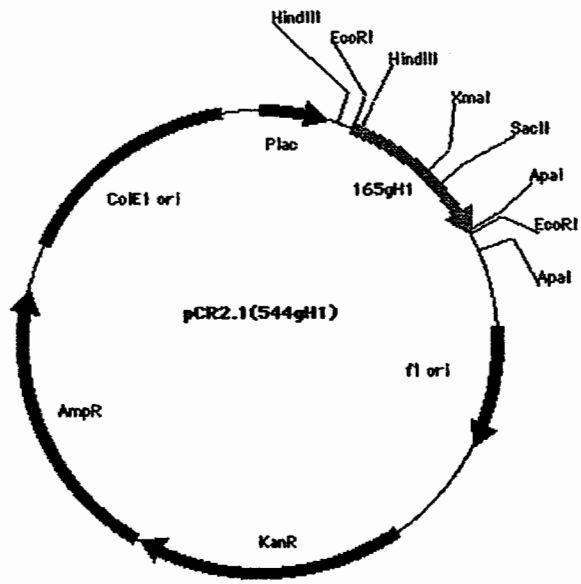
544gL1 F1

GGATGATTCGAAGCCGCCAC

544gL1 R1

GCACGCCGTACGTTTGATTTC

Figure 10: Plasmid maps of intermediate vectors pCR2.1 (544gH1) and pCR2.1(544gL1)



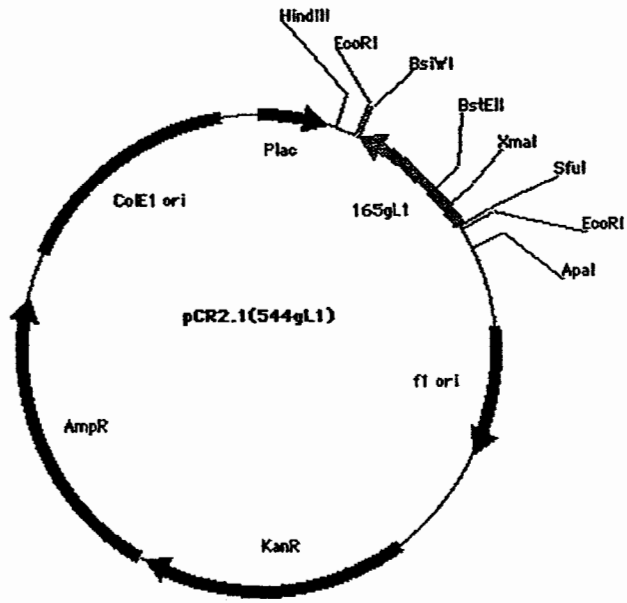


Figure 11: Oligonucleotide cassettes used to make further grafts

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
```

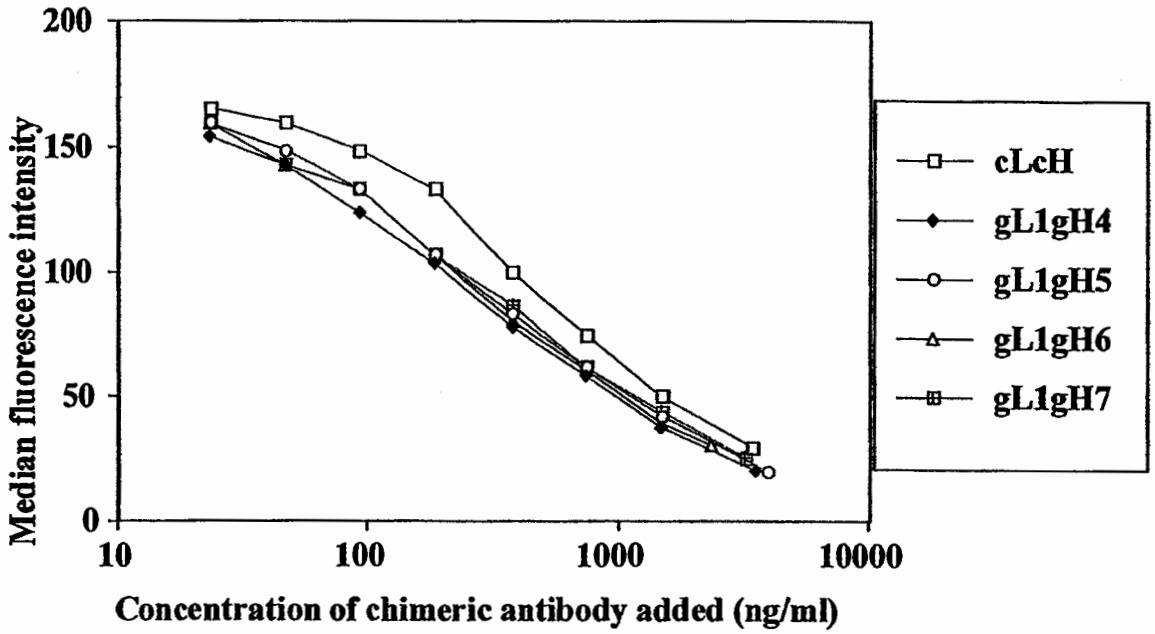
gH7

```
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 12: Competition assay, competing binding of fluorescently labelled mouse 5/44 antibody with grafted variants.



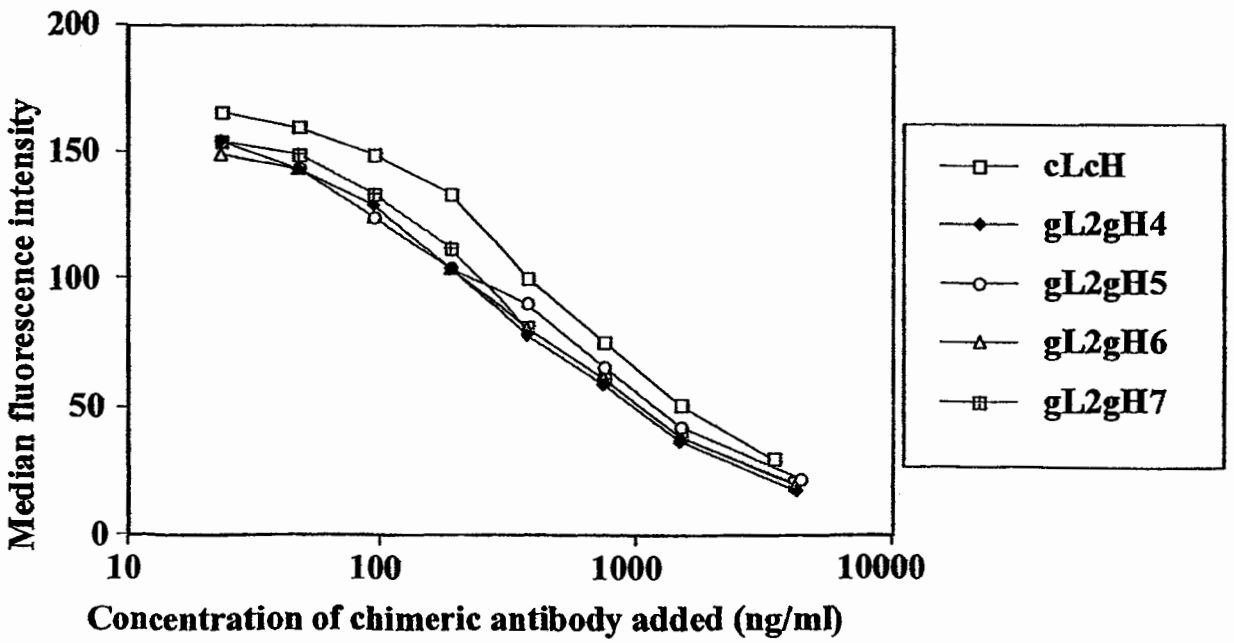


Figure 13: Full DNA sequence of grafted heavy and light chains

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>
```

Figure 13 cont.

```
  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>

          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>
```

Figure 13 cont.

```
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>

         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
```

Figure 13 cont.

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          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

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

Figure 13 cont.

b) Light Chain

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        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>
```

Figure 13 cont.

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  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
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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