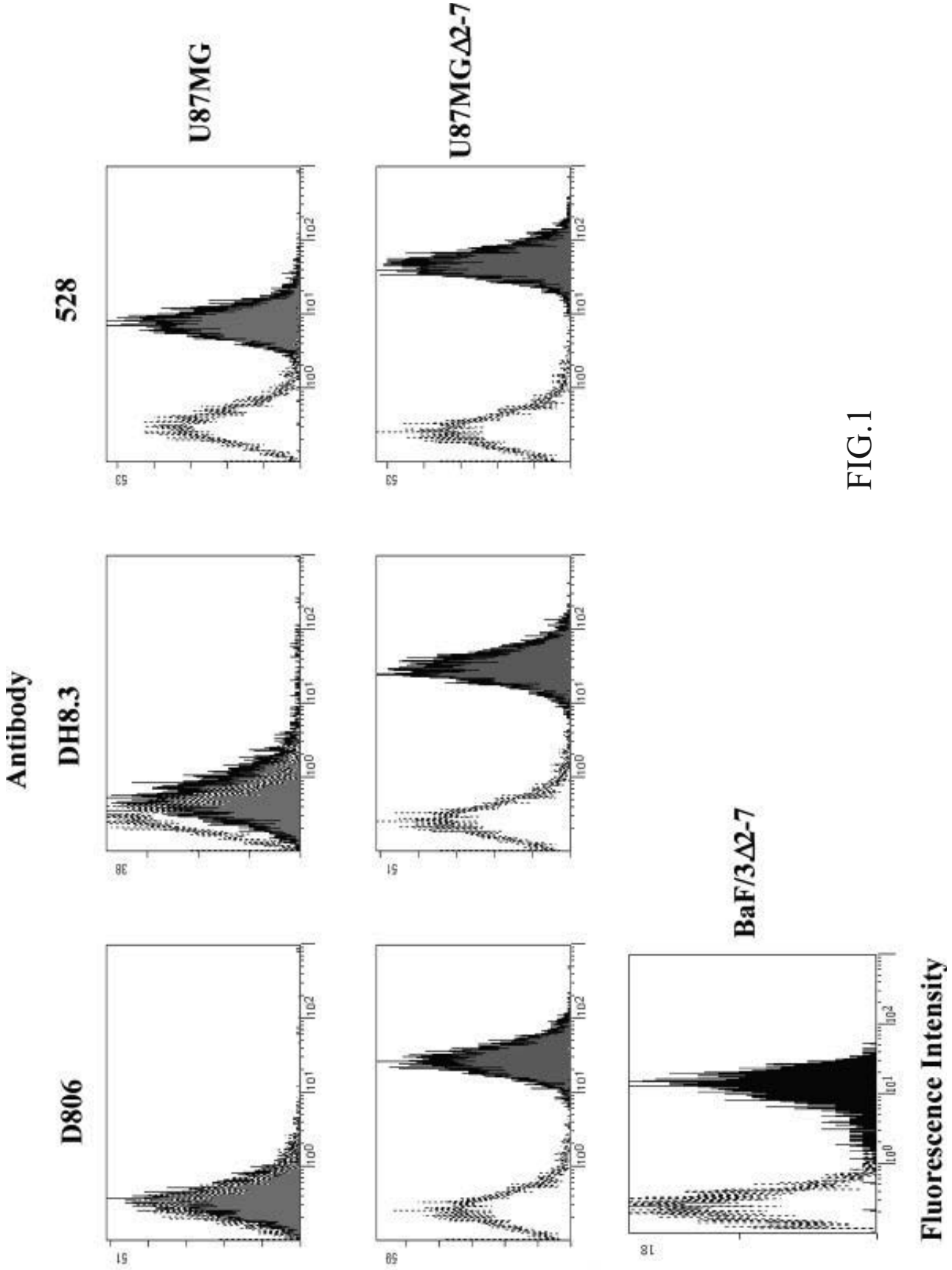

Antibody
D806
DH8.3
528
U87MG
U87MGΔ2-7
BaF/3Δ2-7
Cell Number
Fluorescence Intensity

FIG.1

FIG

FIG.2A

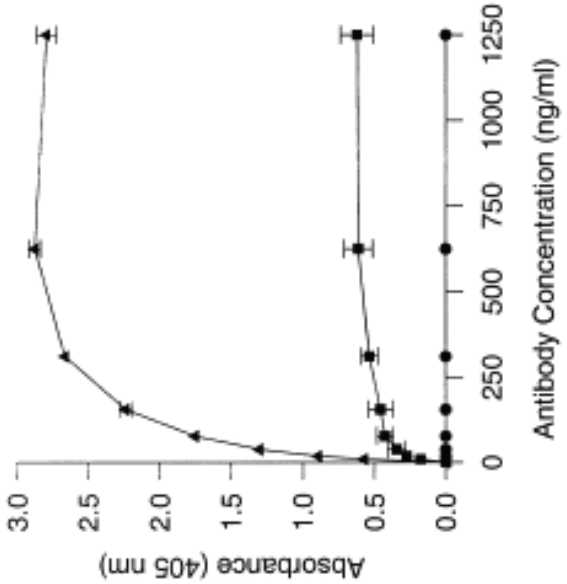


FIG.2B

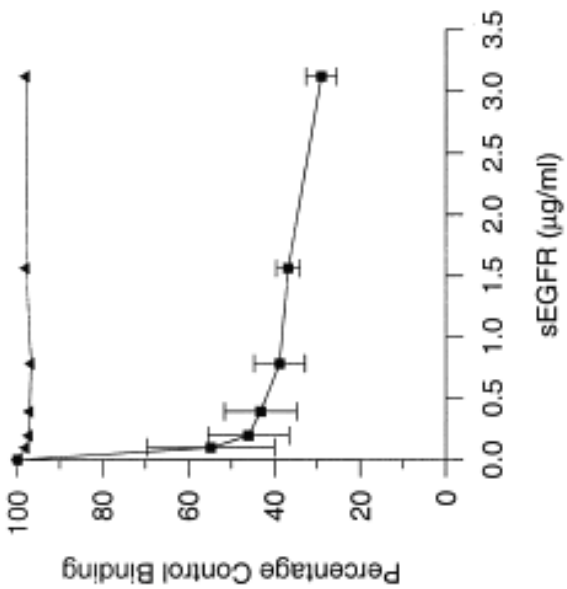


FIG.2C

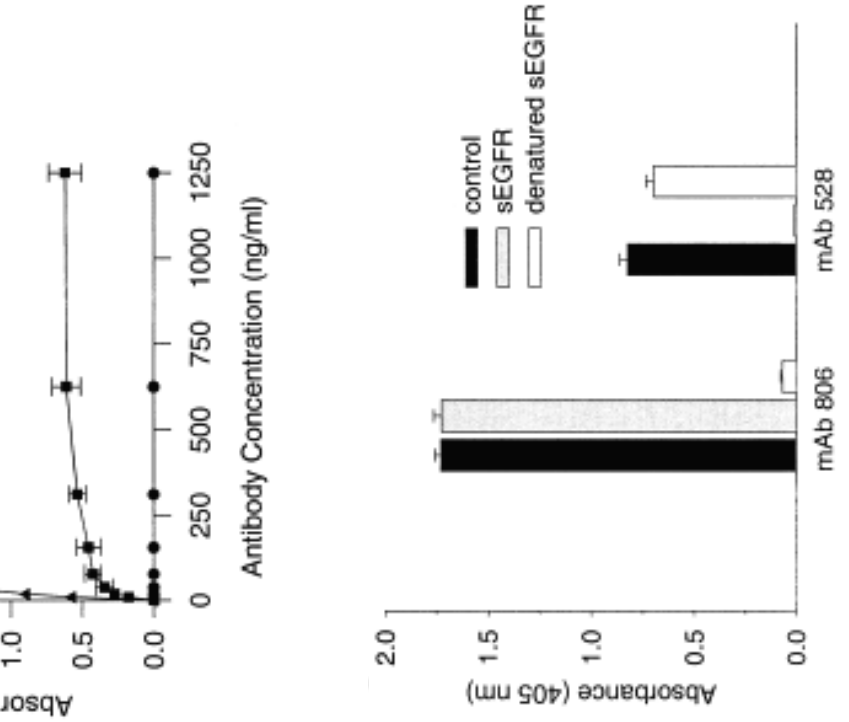
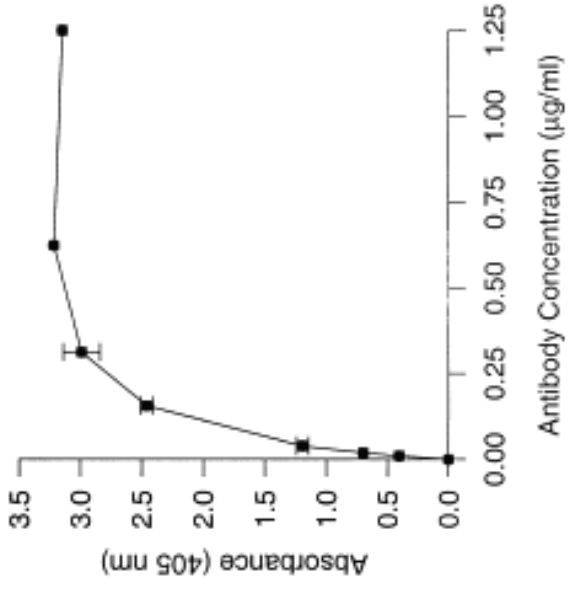


FIG.2D



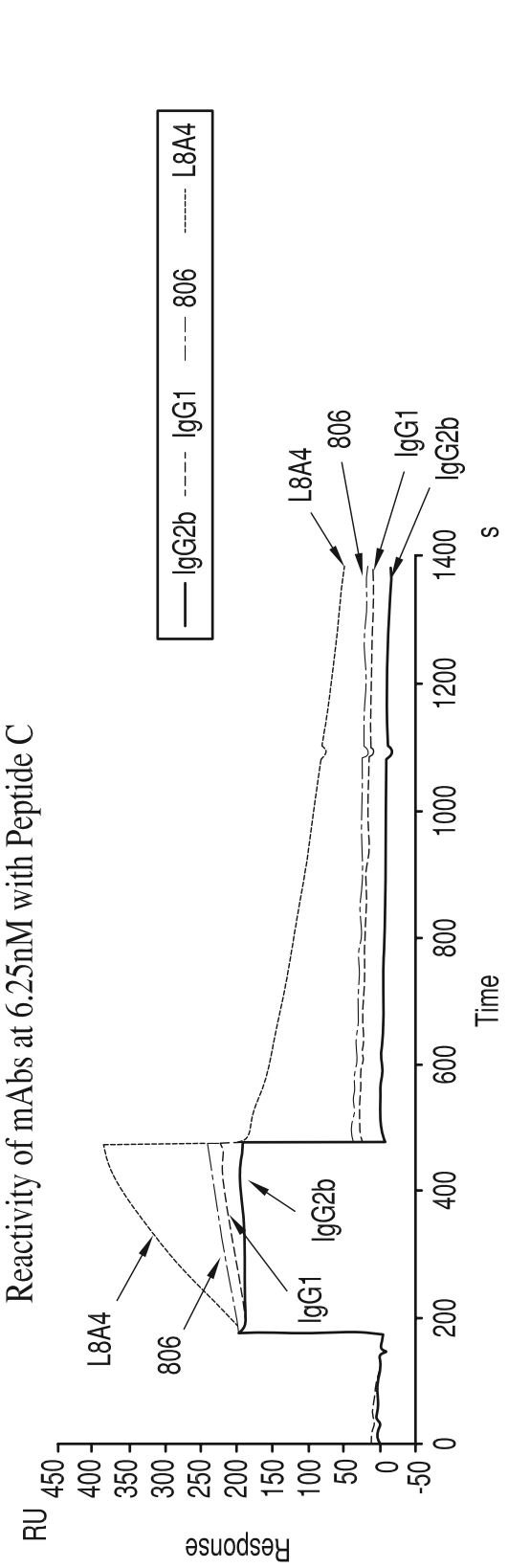

Reactivity of mAbs at 6.25nM with Peptide C
IgG2b
IgG1
806
L8A4
RU
Response
Time
s
L8A4
806
IgG1
IgG2b

FIG. 2E

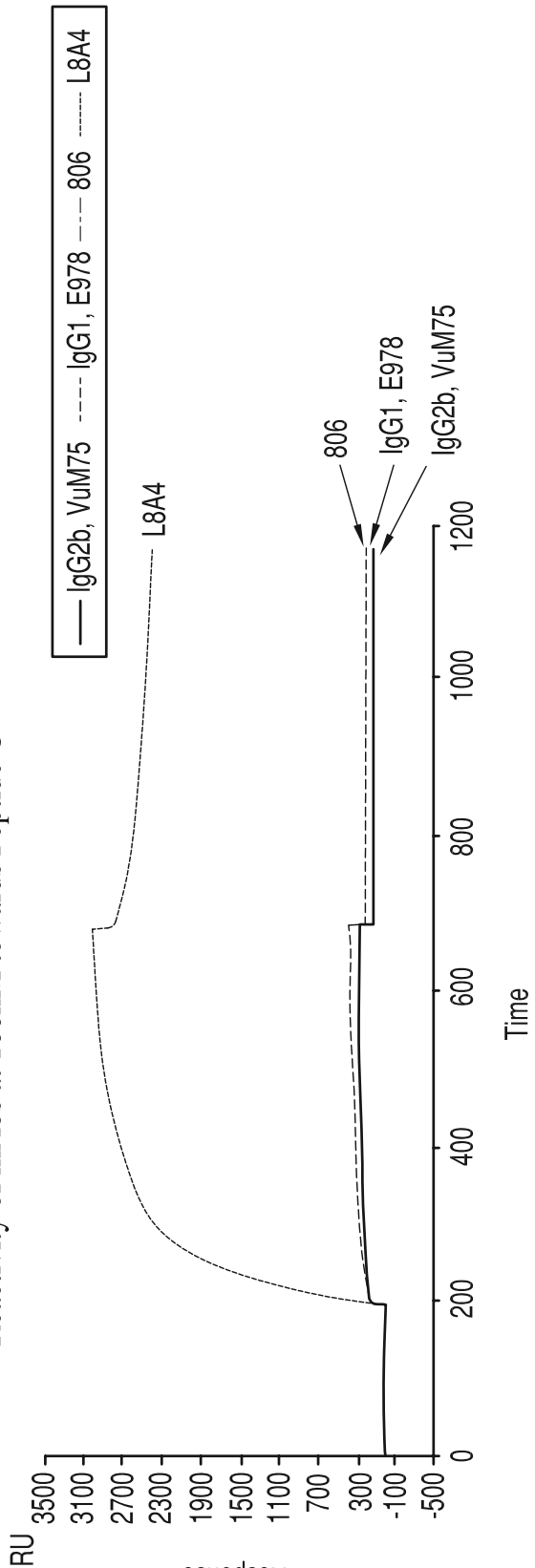

Reactivity of mAbs at 100nM towards Peptide C
IgG2b, VuM75
IgG1, E978
806
L8A4
RU
Response
Time
L8A4
806
IgG1, E978
IgG2b, VuM75

FIG. 2F

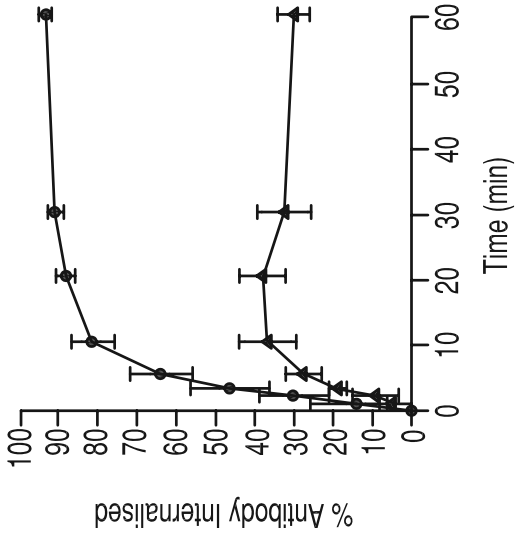

% Antibody Internalised
100
90
80
70
60
50
40
30
20
10
0
0
10
20
30
40
50
60
Time (min)

FIG. 3

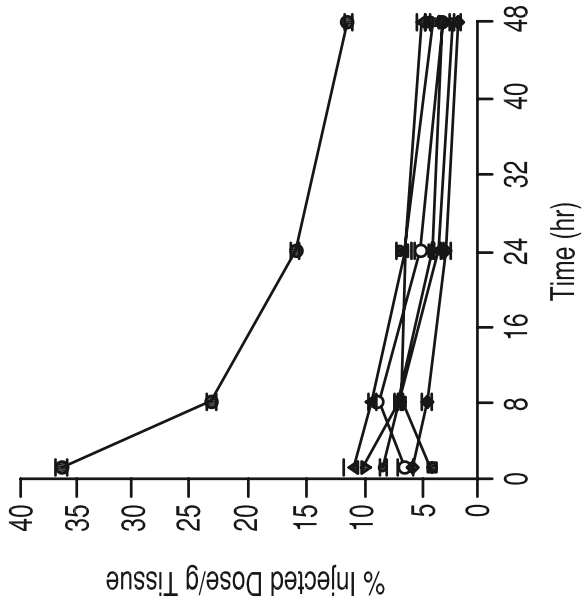

% Injected Dose/g Tissue
0
5
10
15
20
25
30
35
40
0
8
16
24
32
40
48
Time (hr)

FIG. 4B

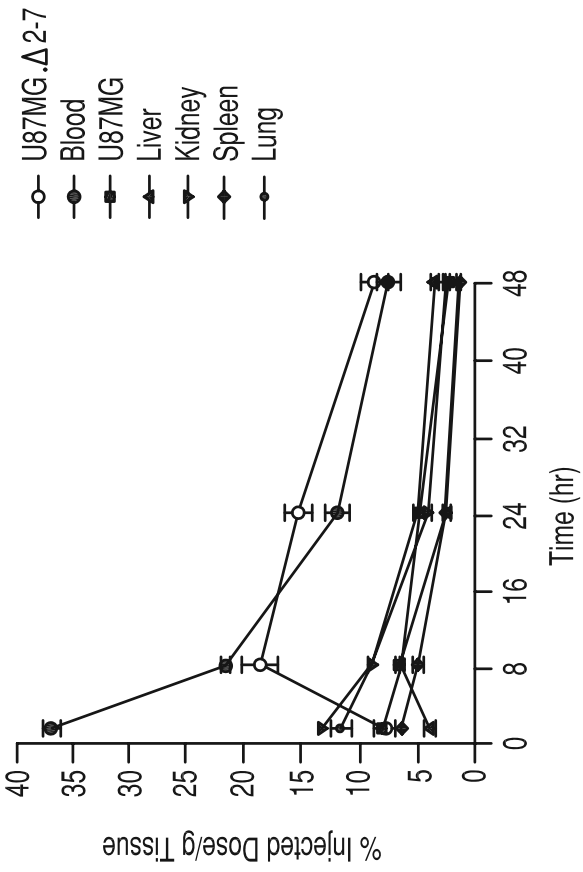

U87MG.Δ2-7
Blood
U87MG
Liver
Kidney
Spleen
Lung
% Injected Dose/g Tissue
0
5
10
15
20
25
30
35
40
0
8
16
24
32
40
48
Time (hr)

FIG. 4A

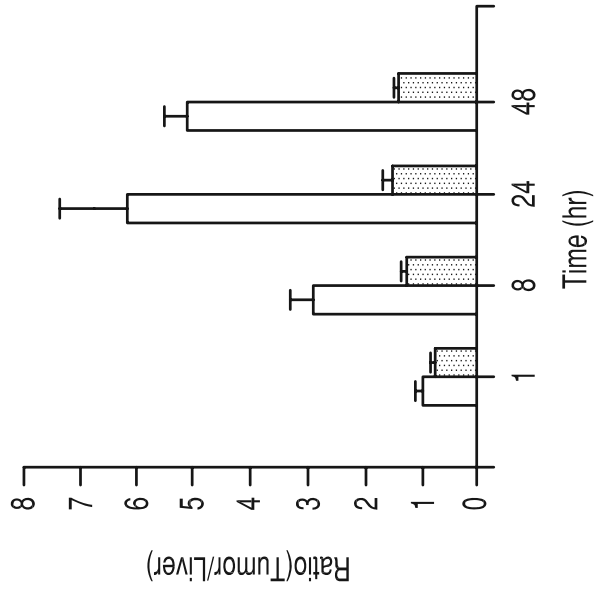

Ratio(Tumor/Liver)
0
1
2
3
4
5
6
7
8
1
8
24
48
Time (hr)

FIG. 5B

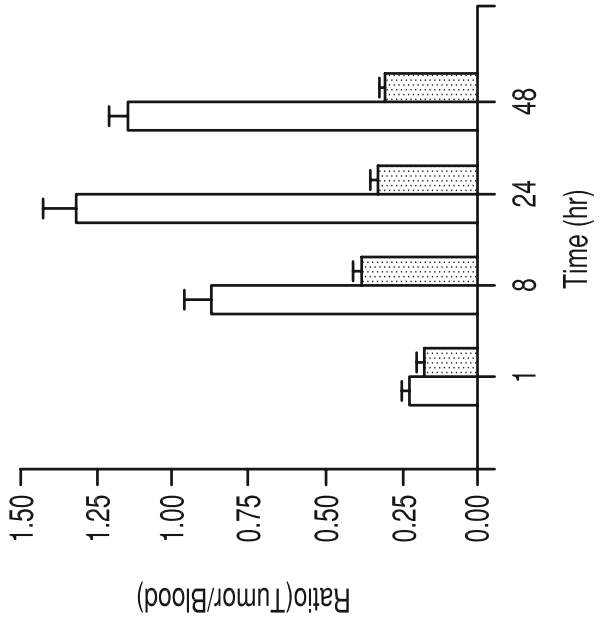
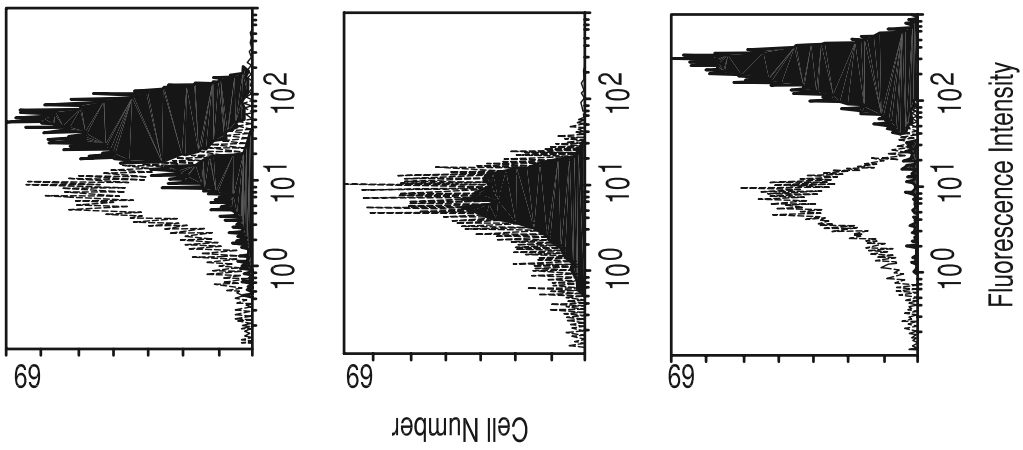

Ratio(Tumor/Blood)
0.00
0.25
0.50
0.75
1.00
1.25
1.50
1
8
24
48
Time (hr)

FIG. 5A

FIG. 6A

FIG. 6B

FIG. 6C



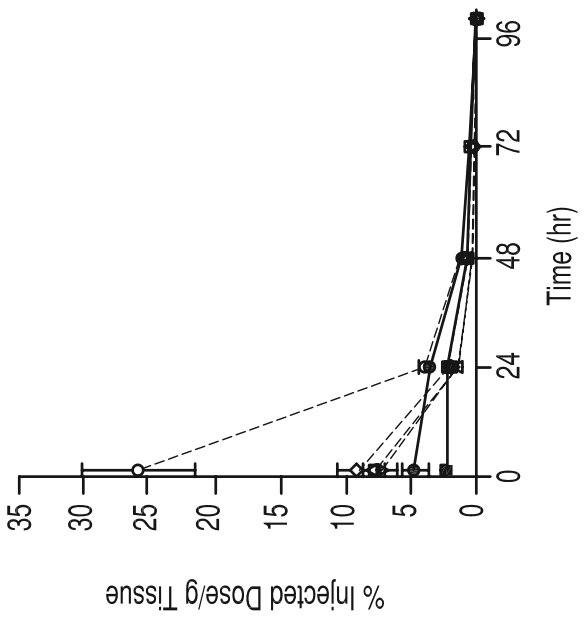

% Injected Dose/g Tissue
0
5
10
15
20
25
30
35
0
24
48
72
96
Time (hr)

FIG. 7B

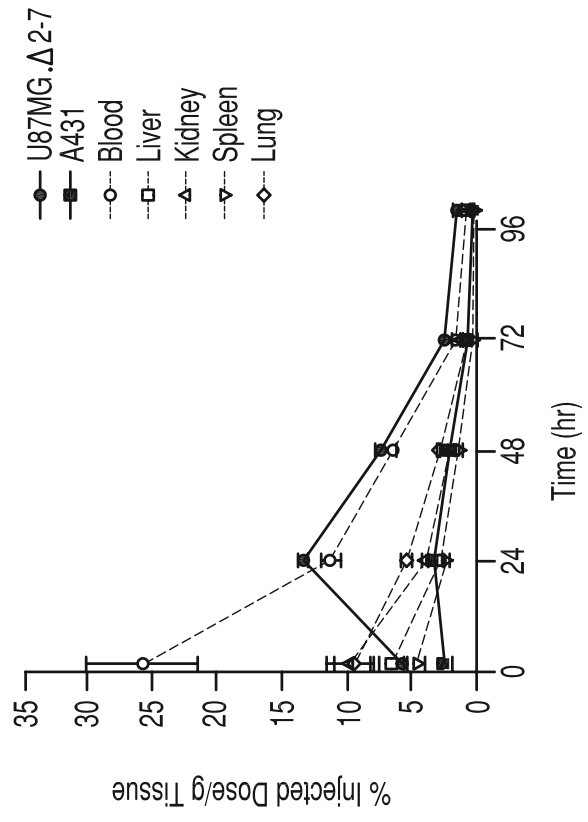

U87MG.Δ2-7
A431
Blood
Liver
Kidney
Spleen
Lung
% Injected Dose/g Tissue
0
5
10
15
20
25
30
35
0
24
48
72
96
Time (hr)

FIG. 7A

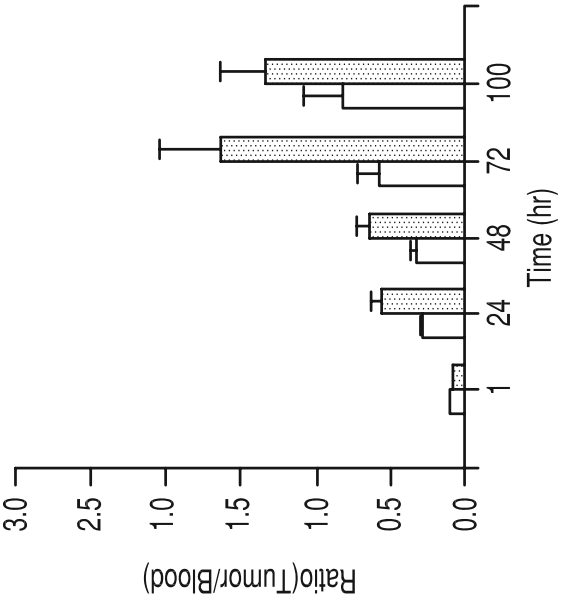


FIG. 8B

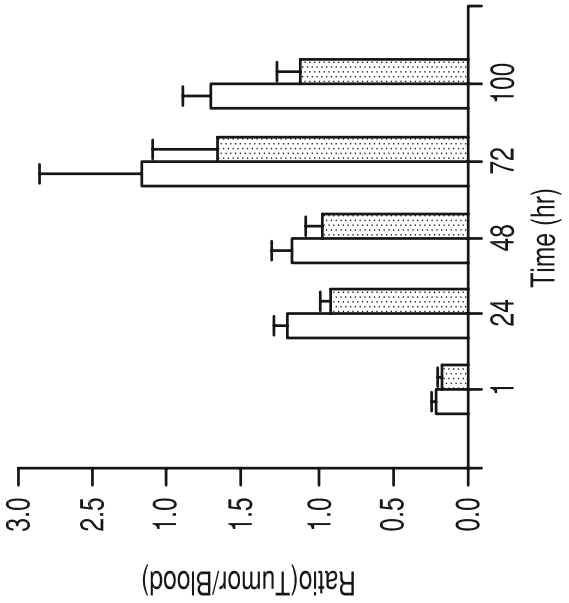


FIG. 8A

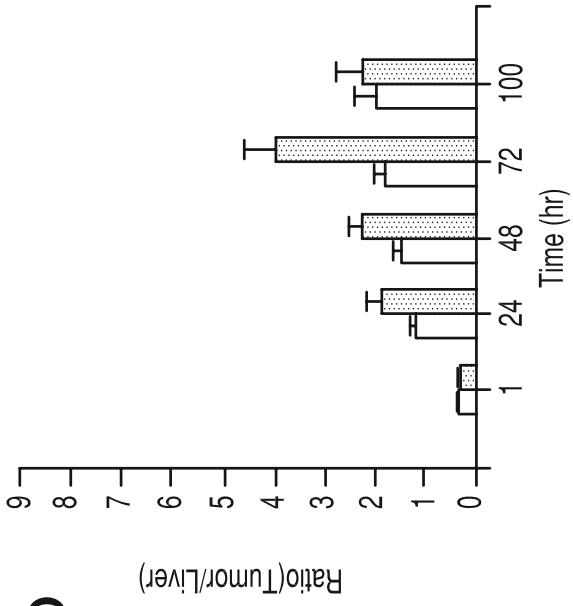


FIG. 8D

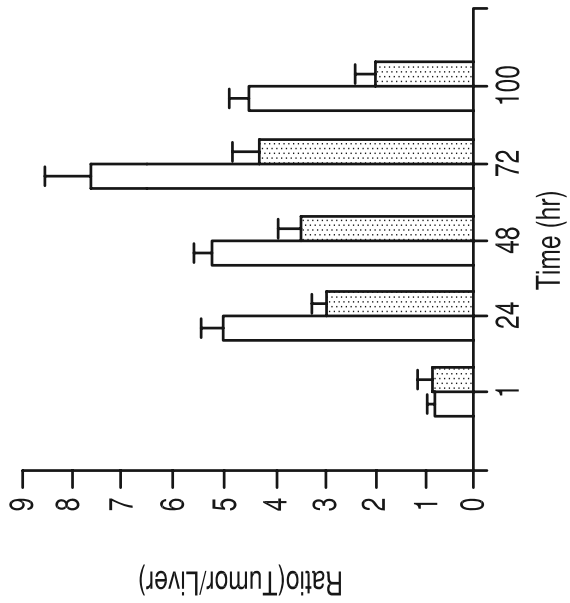


FIG. 8C

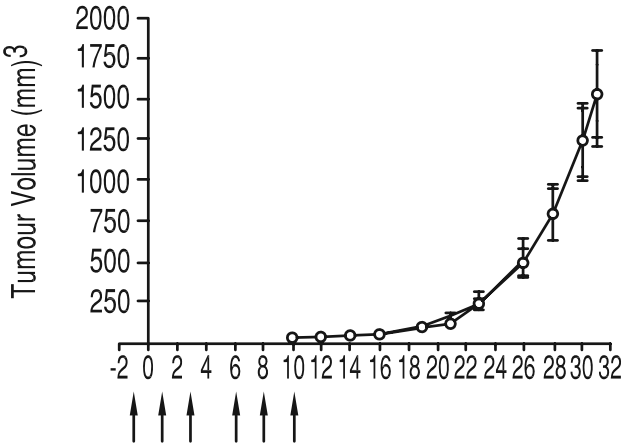

Tumour Volume (mm)3
2000
1750
1500
1250
1000
750
500
250
-2 0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32

FIG. 9A

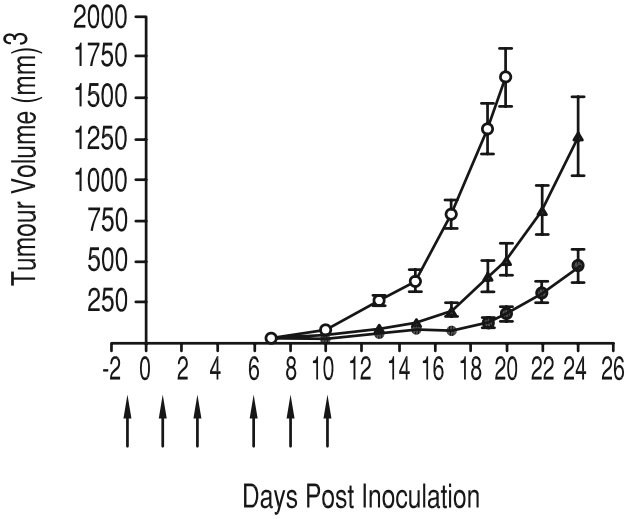

Tumour Volume (mm)3
2000
1750
1500
1250
1000
750
500
250
-2 0 2 4 6 8 10 12 14 16 18 20 22 24 26
Days Post Inoculation

FIG. 9B

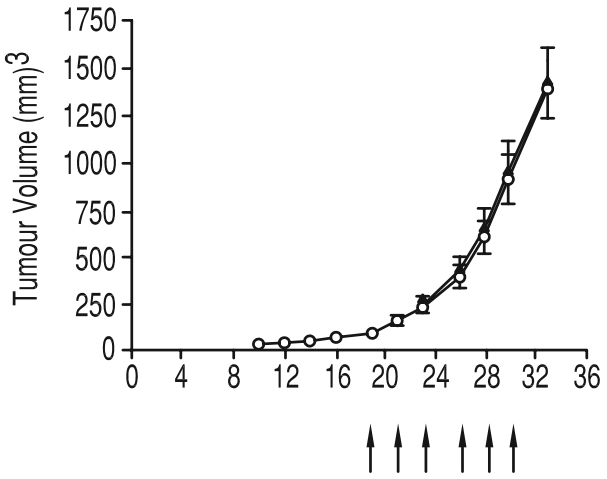


FIG. 10A

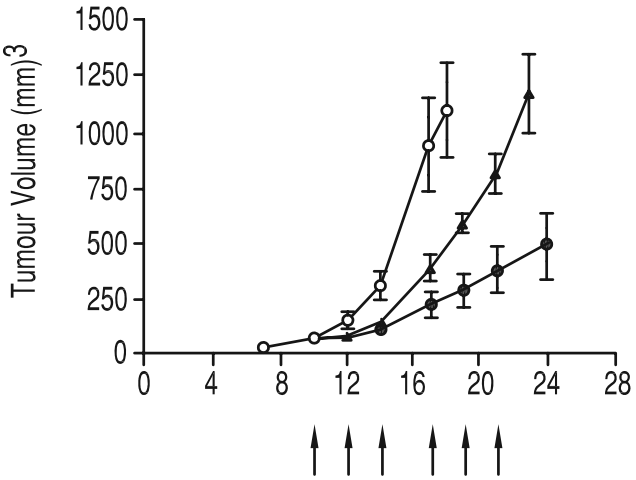


FIG. 10B

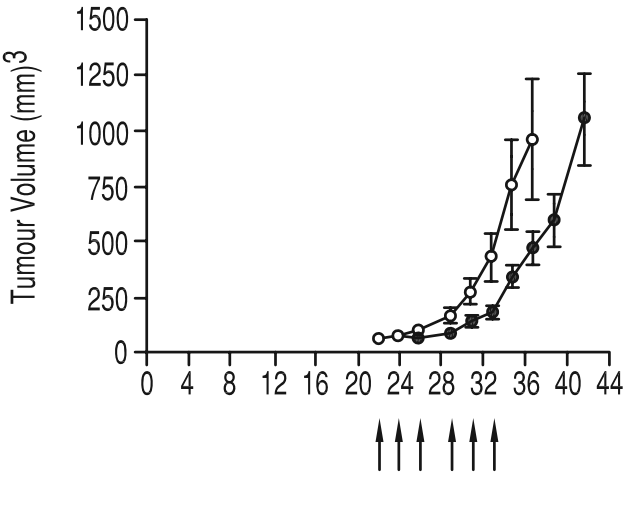


FIG. 10C

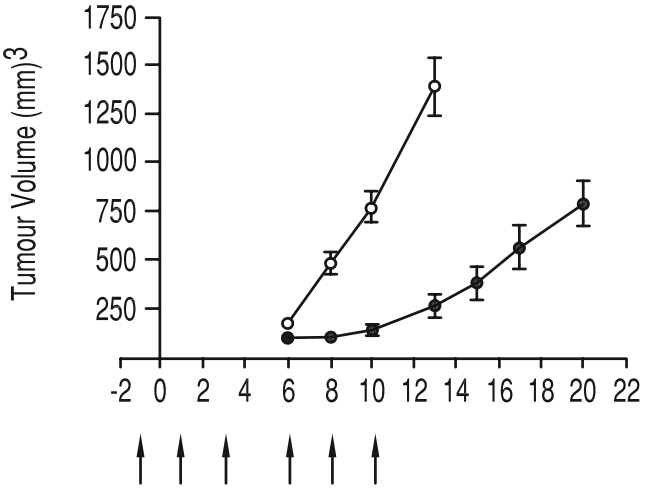


FIG. 11A

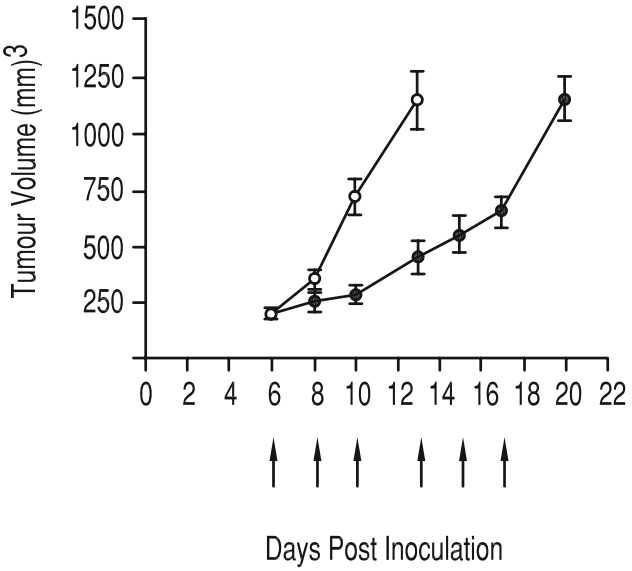


FIG. 11B

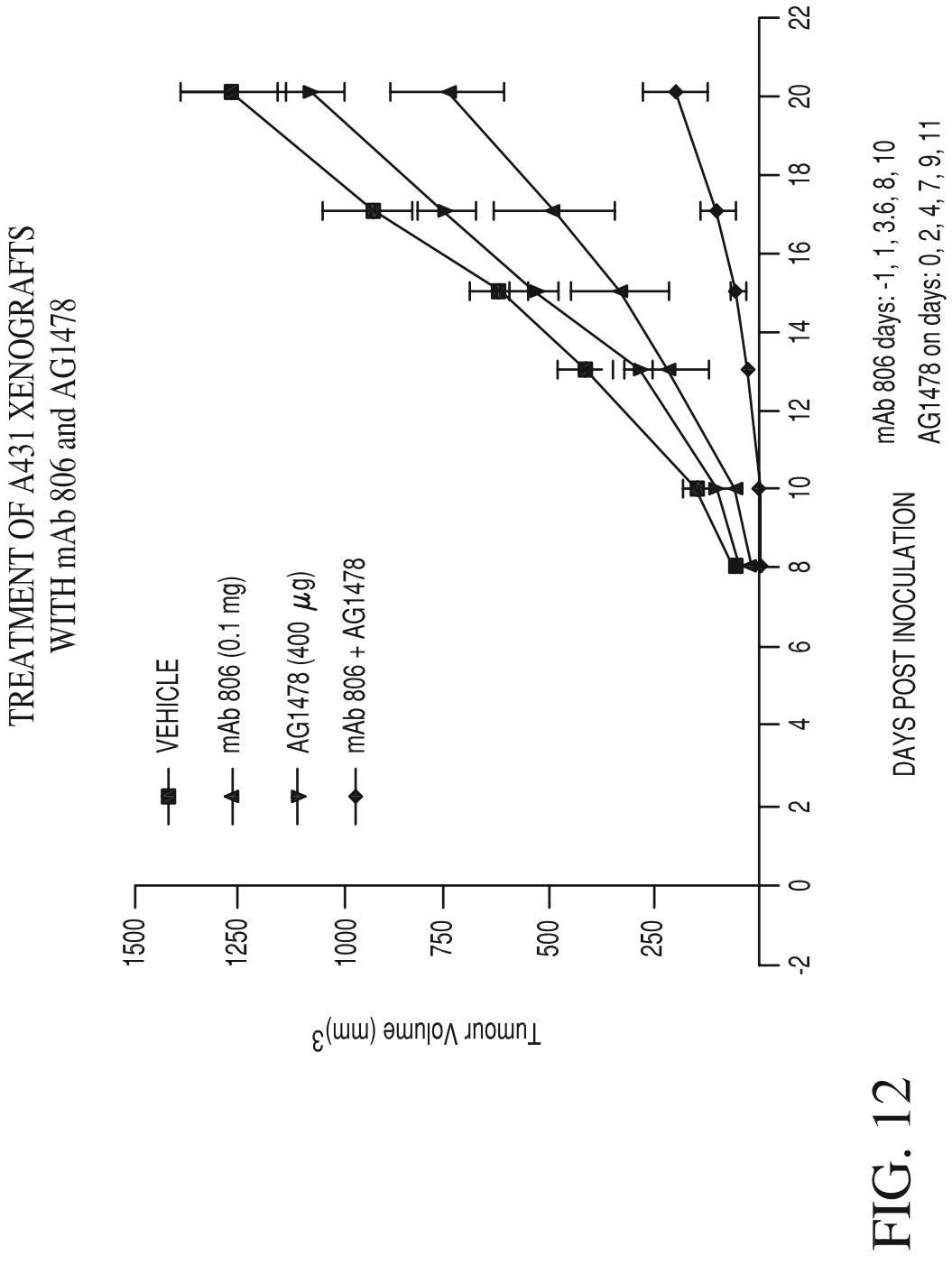

TREATMENT OF A431 XENOGRAFTS
WITH mAb 806 and AG1478
VEHICLE
mAb 806 (0.1 mg)
AG1478 (400 μg)
mAb 806 + AG1478
Tumour Volume (mm)3
1500
1250
1000
750
500
250
-2
0
2
4
6
8
10
12
14
16
18
20
22
DAYS POST INOCULATION
mAb 806 days: -1, 1, 3.6, 8, 10
AG1478 on days: 0, 2, 4, 7, 9, 11

FIG. 12

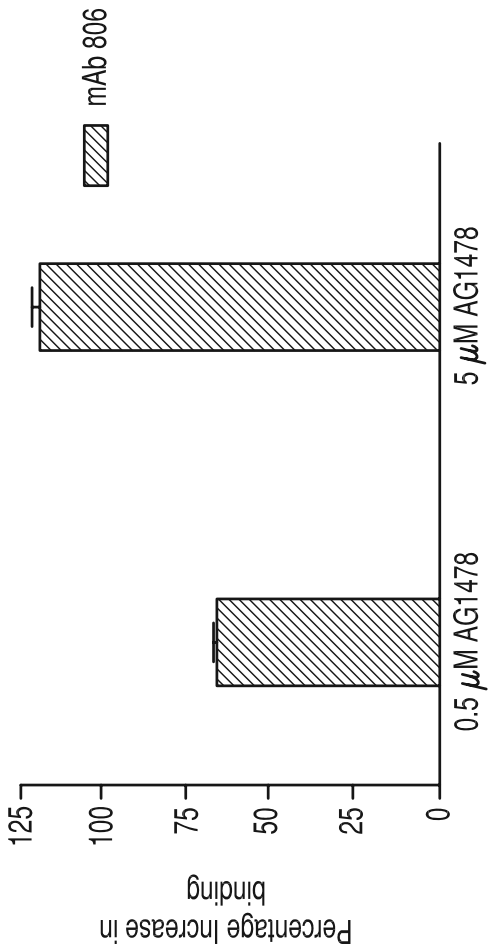

mAb 806
Percentage Increase in binding
125
100
75
50
25
0
0.5 μM AG1478
5 μM AG1478

FIG. 13

mAb806 VH Chain (including signal peptide): Nucleic Acid and Amino Acid Sequences

Nucleic Acid

ATGAGAGTGCTGATTCTTTTGTGGCTGTTCACAGCCTTTCCTGGTGTCCTGTCTGATG
TGCAGCTTCAGGAGTCGGGACCTAGCCTGGTGAAACCTTCTCAGTCTCTGTCCCTCA
CCTGCACTGTCACTGGCTACTCAATCACCAGTGATTTTGCCTGGAACTGGATCCGGC
AGTTTCCAGGAAACAAGCTGGAGTGGATGGGCTACATAAGTTATAGTGGTAACACT
AGGTACAACCCATCTCTCAAAAGTCGAATCTCTATCACTCGAGACACATCCAAGAAC
CAATTCTTCCTGCAGTTGAATTCTGTGACTATTGAGGACACAGCCACATATTACTGT
GTAACGGCGGGACGCGGGTTTCCTTATTGGGGCCAAGGGACTCTGGTCACTGTCTCT
GCA (SEQ ID NO:1)

FIG.14A

Amino Acid

MRVLILLWLFTAFPGVLSDVQLQESGPSLVKPSQSLSLTCTVTGYSITSDFAWNWIRQFP
signal peptide

GNKLEWMGYISYSGNTRYNPSLKSRISITRDTSKNQFFLQLNSVTIEDTATYYCVTAGRG

FPYWGQGTLVTVSA (SEQ ID NO:2)

FIG.14B

mAb806 VL Chain (including signal peptide): Nucleic Acid and Amino Acid Sequences

Nucleic Acid Sequence

ATGGTGTCCACAGCTCAGTTCCTTGCATTCTTGTTGCTTTGGTTTCCAGGTGCAAGAT
GTGACATCCTGATGACCCAATCTCCATCCTCCATGTCTGTATCTCTGGGAGACACAG
TCAGCATCACTTGCCATTCAAGTCAGGACATTAACAGTAATATAGGGTGGTTGCAGC
AGAGACCAGGGAAATCATTTAAGGGCCTGATCTATCATGGAACCAACTTGGACGAT
GAAGTTCCATCAAGGTTCAGTGGCAGTGGATCTGGAGCCGATTATTCTCTCACCATC
AGCAGCCTGGAATCTGAAGATTTTGCAGACTATTACTGTGTACAGTATGCTCAGTTT
CCGTGGACGTTCGGTGGAGGCACCAAGCTGGAAATCAAACGT (SEQ ID NO:3)

FIG.15A

Amino Acid Sequence

MVSTAQFLAFLLLWFPGARCDILMTQSPSSMSVSLGDTVSITCHSSQDINSNIGWLQQRP
Signal Peptide
GKSFKGLIYHGTNLDDEVPSRFSGSGSGADYSLTISSLESEDFADYYCVQYAQFPWTFGG

GTKLEIKR (SEQ ID NO:4)

FIG.15B

mAb806 HL Chain (no signal peptide): Amino Acid Sequence

DVQLQESGPSLVKPSQSLSLTCTVTGYSITSDFAWNWIRQFPGNKLEWMGYISYSGNTRYNPSLKSRISITRDTSKNQFFLQLN
CDR1 *CDR2*
SVTIEDTATYYCVTAGRGFPYWGQGTLVTVSA (SEQ ID NO:11)
CDR3

FIG.16

mAb806 VL Chain (no signal peptide): Amino Acid Sequence

DILMTQSPSSMSVSLGDTVSITC<u>HSSQDINSNIG</u>WLQQRPGKSFKGLIY<u>HGTNLDD</u>EVPSRFSGSGSGADYSLTISSLESEDFAD
CDR1 *CDR2*
YYC<u>VQYAQFPWT</u>FGGGTKLEIKR (SEQ ID NO:12)
CDR3

FIG.17

FIG.18A

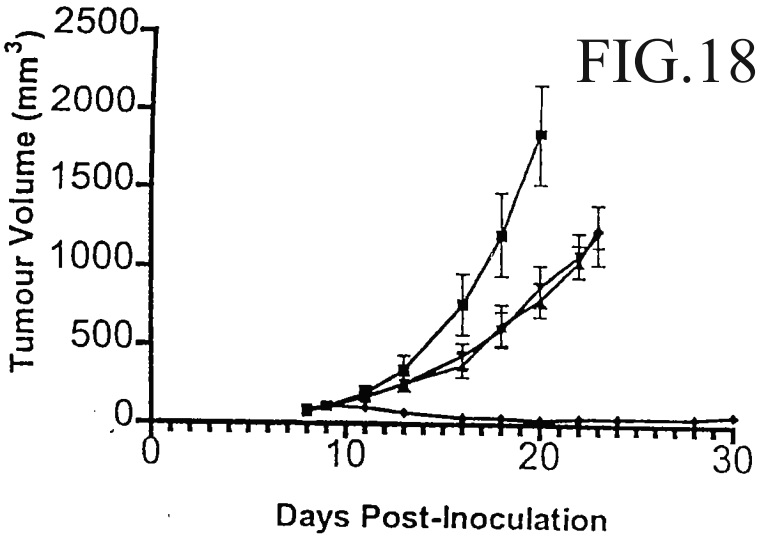


FIG.18B

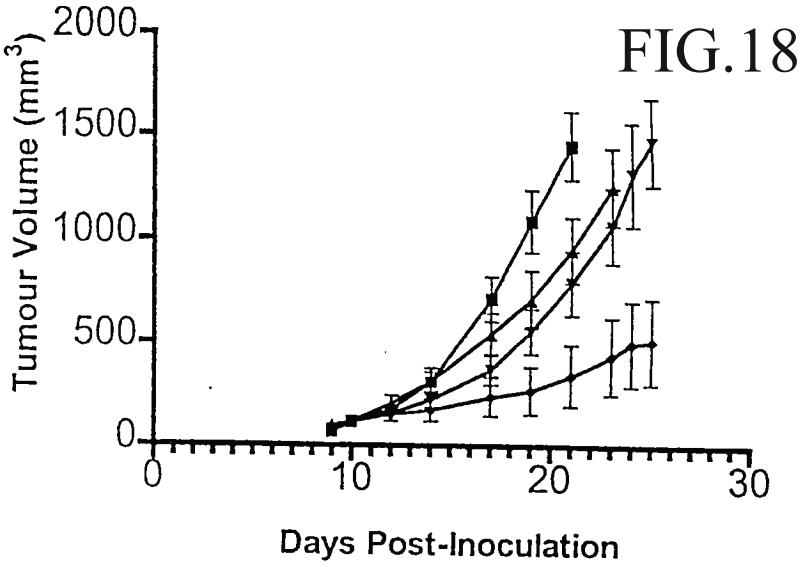


FIG.18C

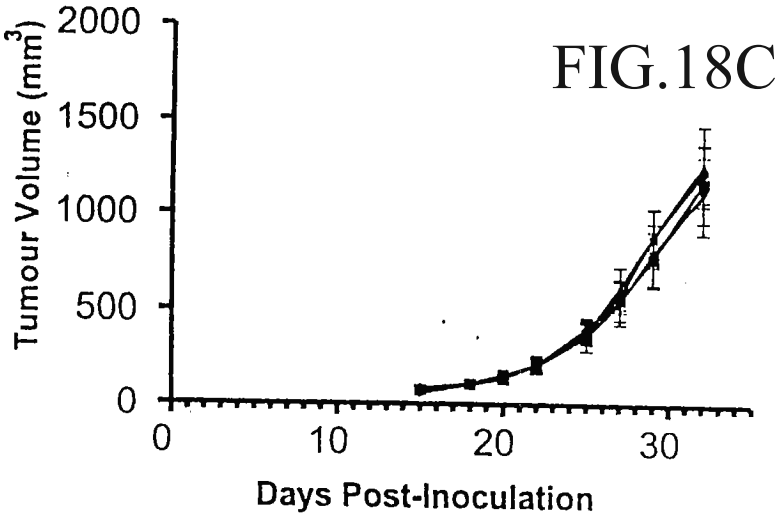
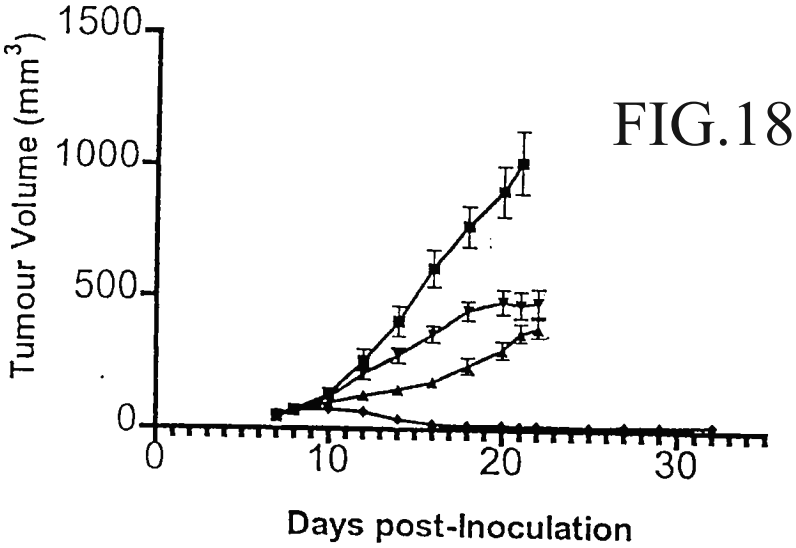


FIG.18D



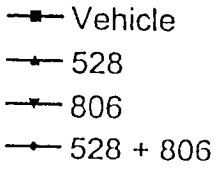


FIG. 19A

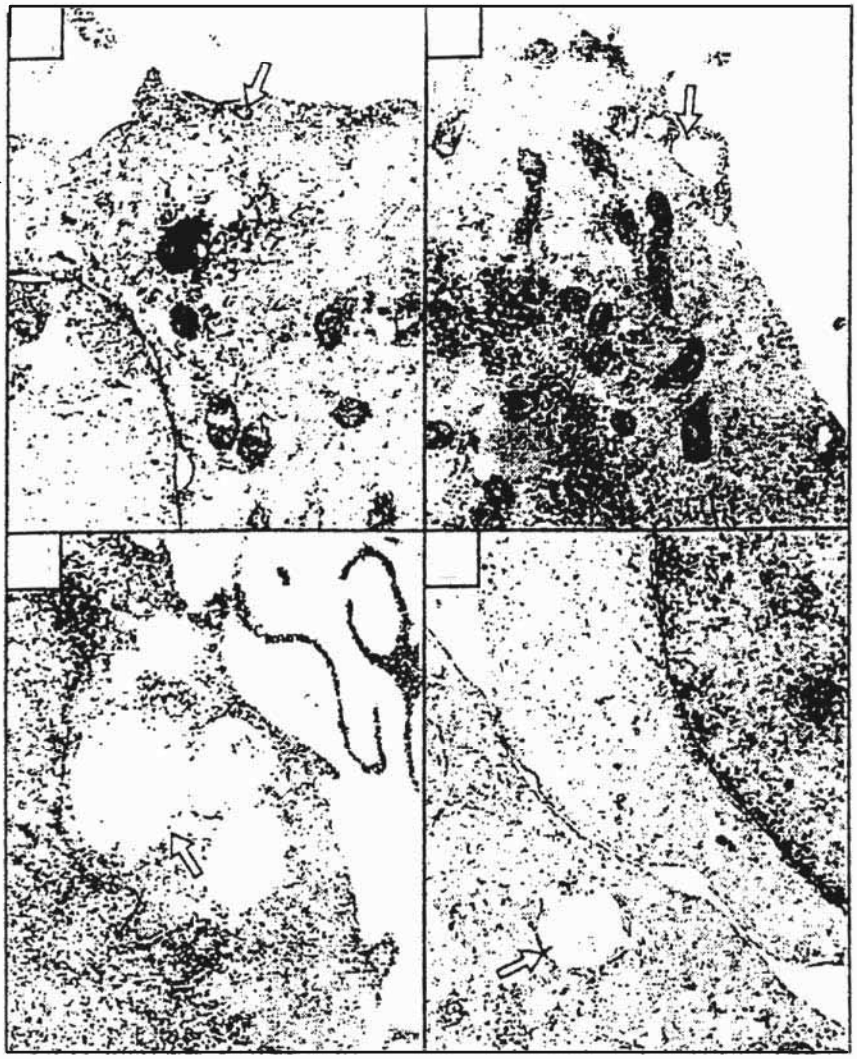


FIG. 19B

FIG. 19C

FIG. 19D

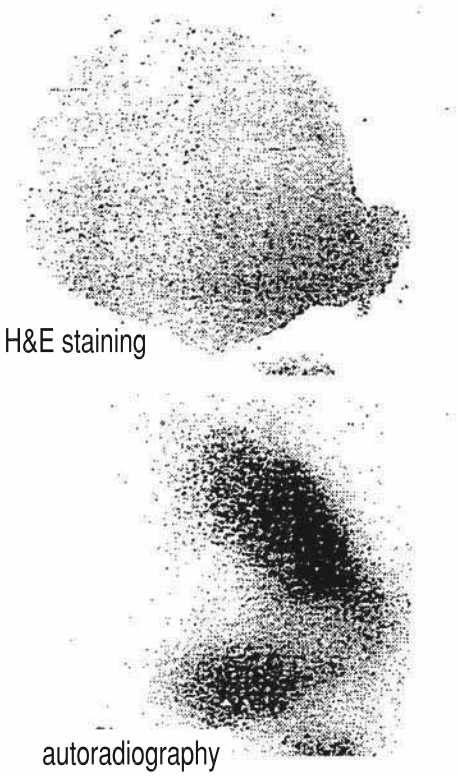


FIG. 20

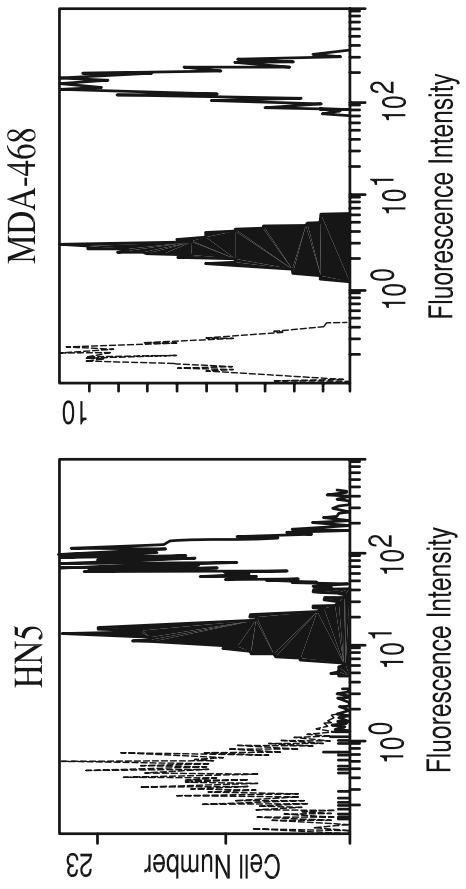

HN5
MDA-468
Cell Number
23
10
10^0
10^1
10^2
Fluorescence Intensity
Fluorescence Intensity

FIG. 21

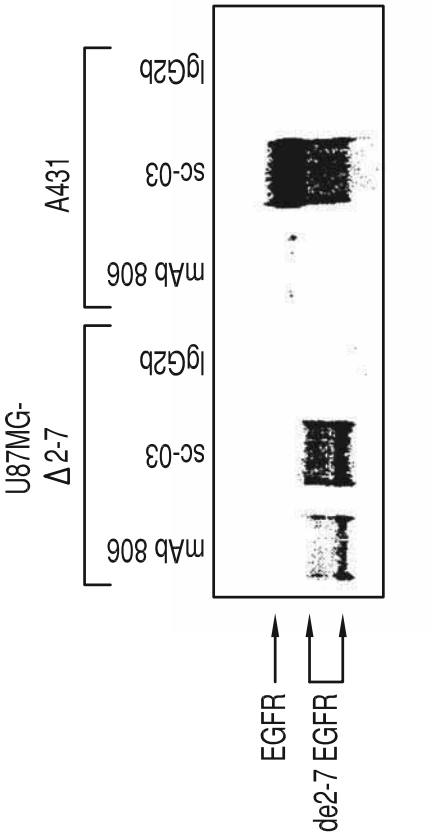

U87MG-
Δ2-7
A431
mAb 806
sc-03
IgG2b
mAb 806
sc-03
IgG2b
EGFR
de2-7 EGFR

FIG. 22

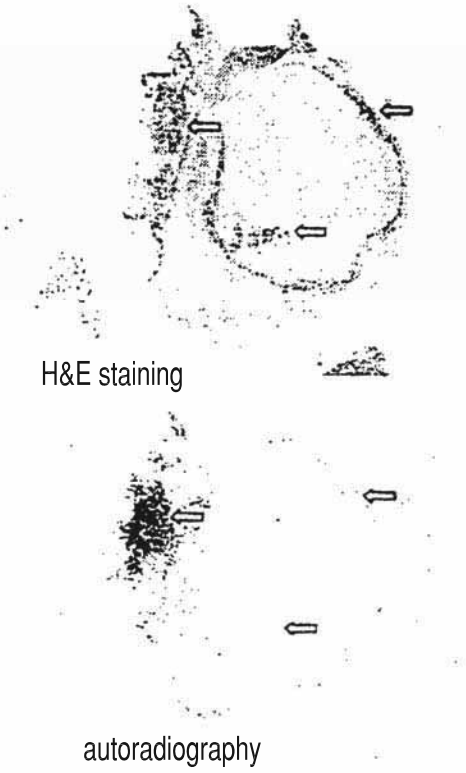


FIG. 23

FIG. 24A

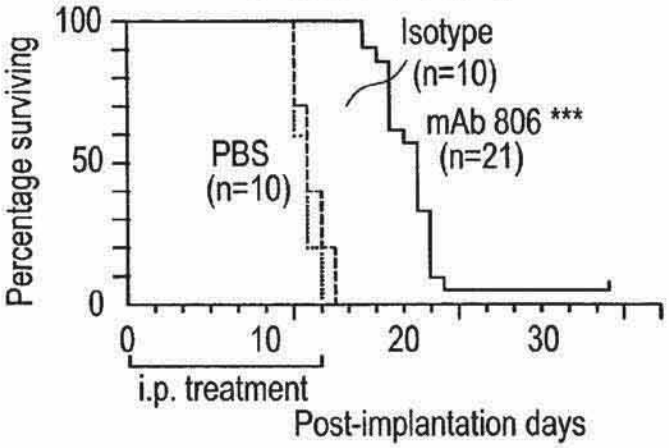


FIG. 24B

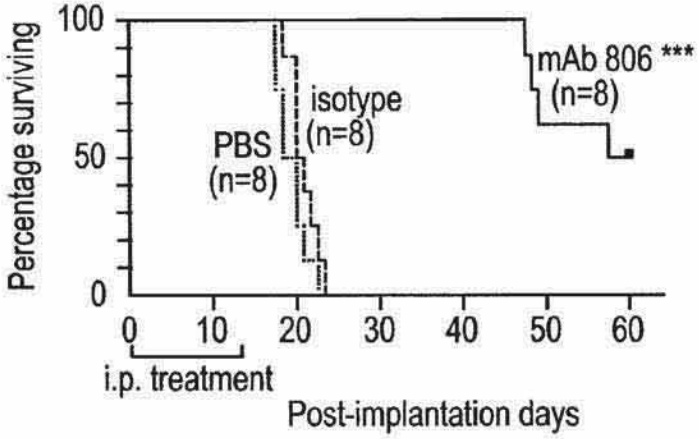


FIG. 24E

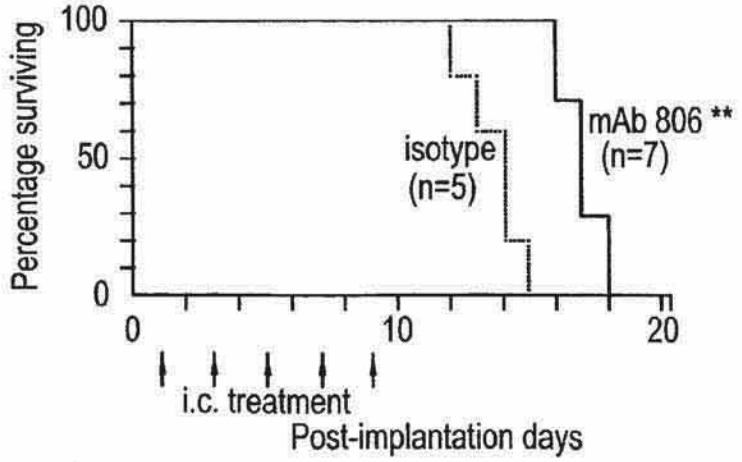


FIG. 24C

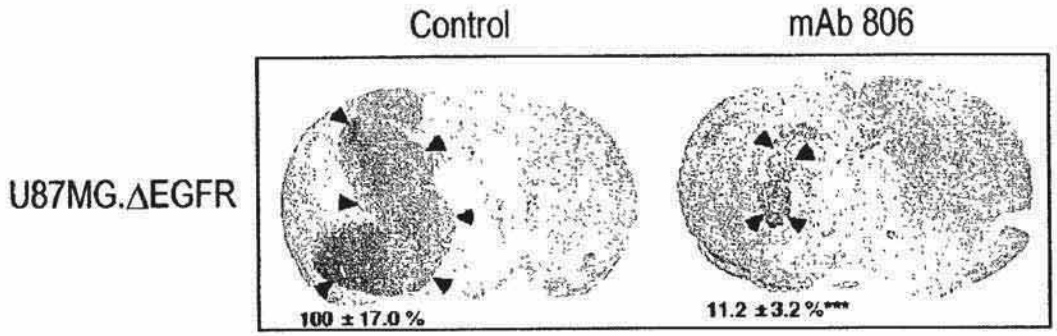


FIG. 24D

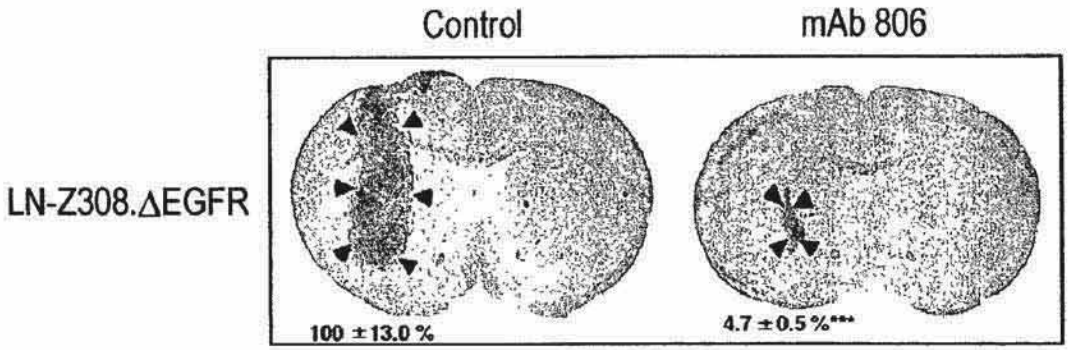


FIG. 25A

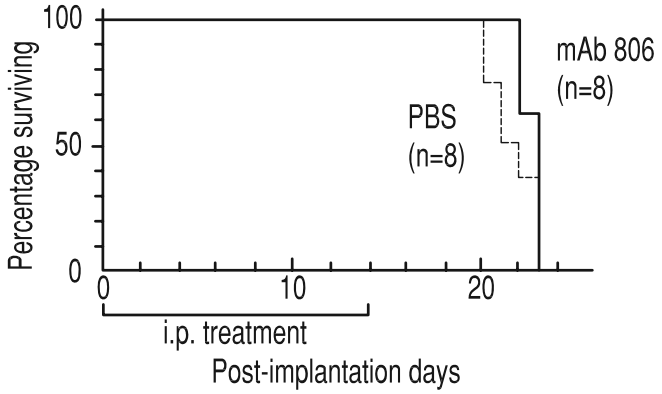


FIG. 25B

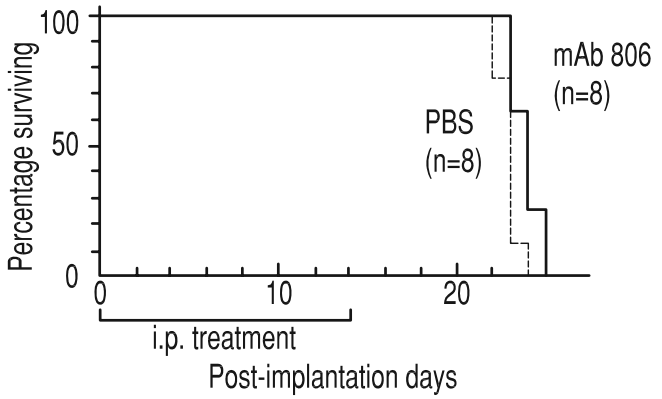
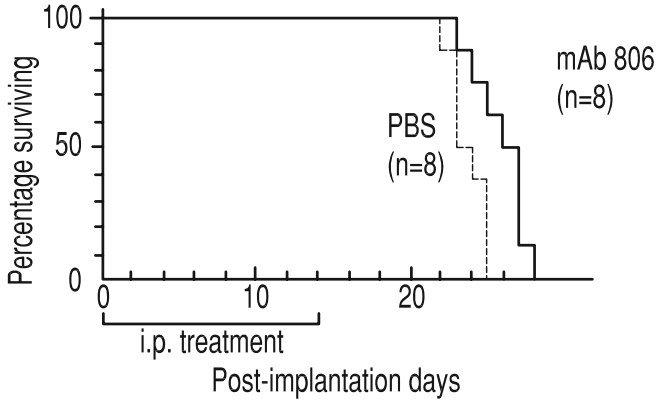


FIG. 25C



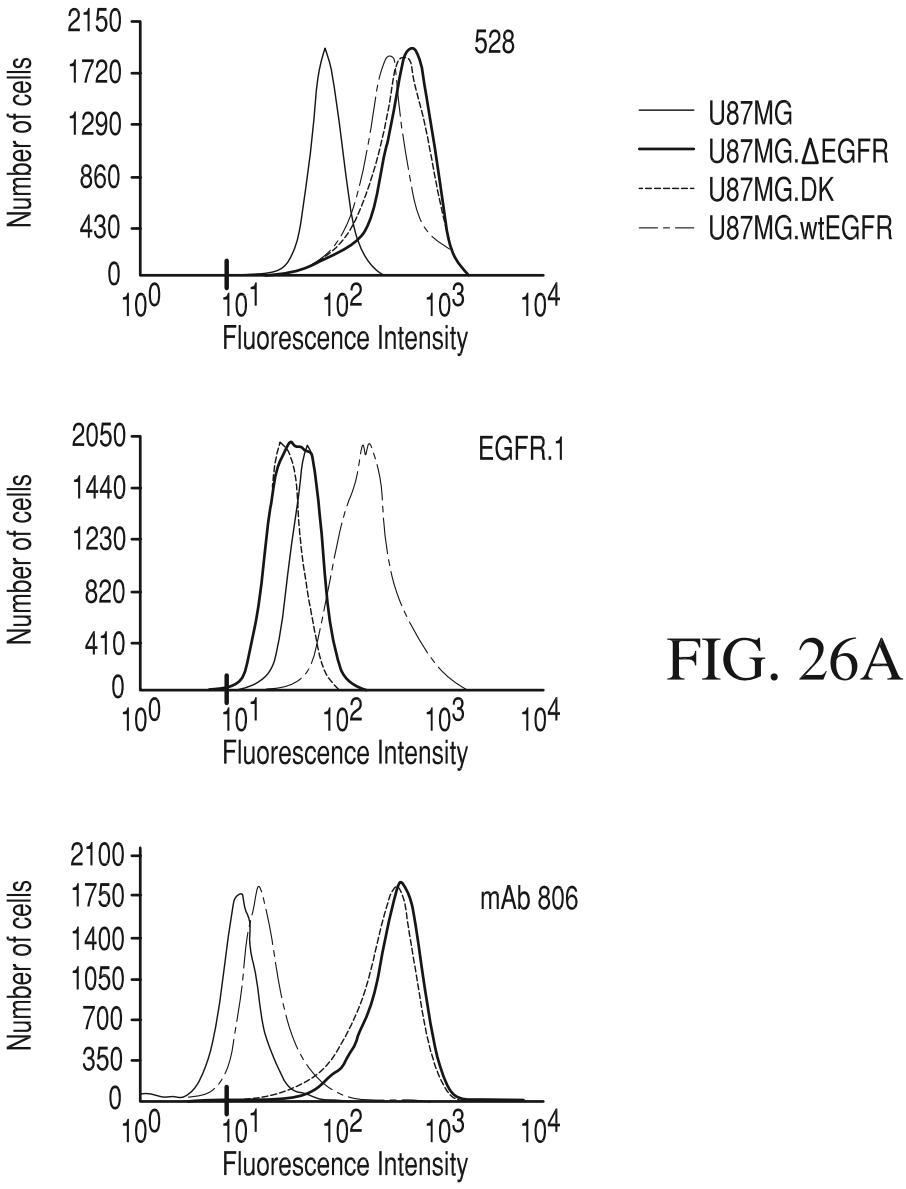


FIG. 26A

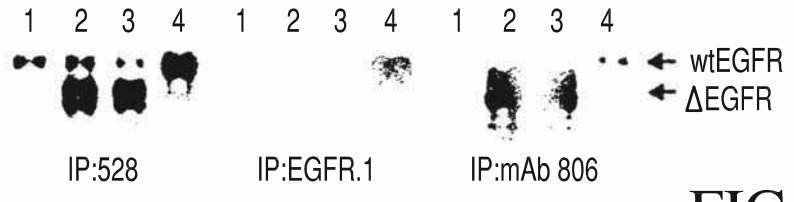


FIG. 26B

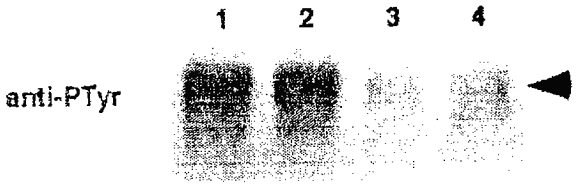


FIG.27A

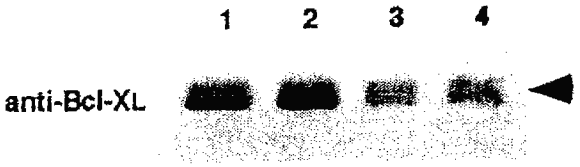


FIG.27B

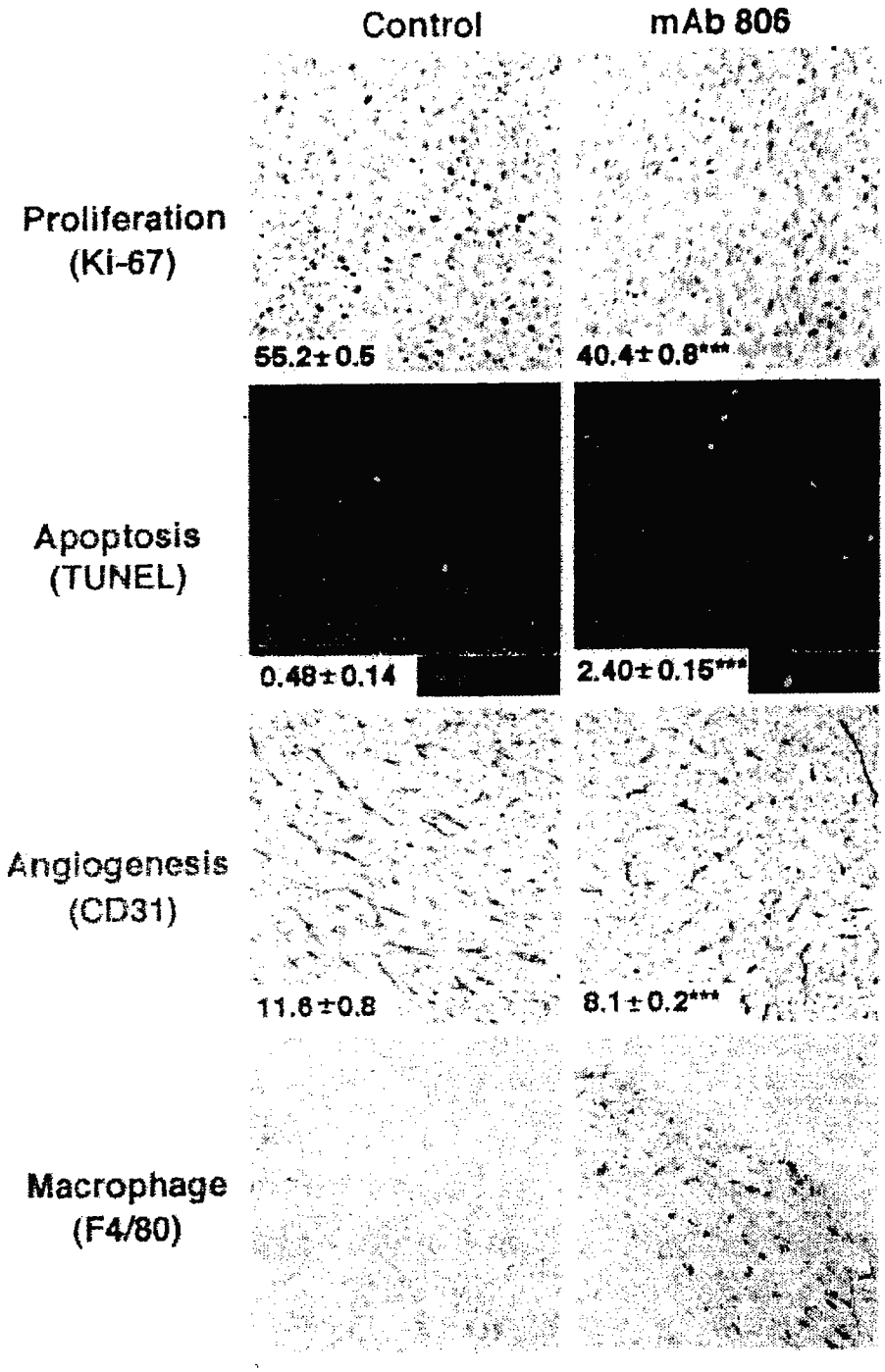

Control
mAb 806
Proliferation
(Ki-67)
55.2± 0.5
40.4± 0.8***
Apoptosis
(TUNEL)
0.48± 0.14
2.40± 0.15***
Angiogenesis
(CD31)
11.6 ±0.8
8.1 ± 0.2***
Macrophage
(F4/80)

FIG.28

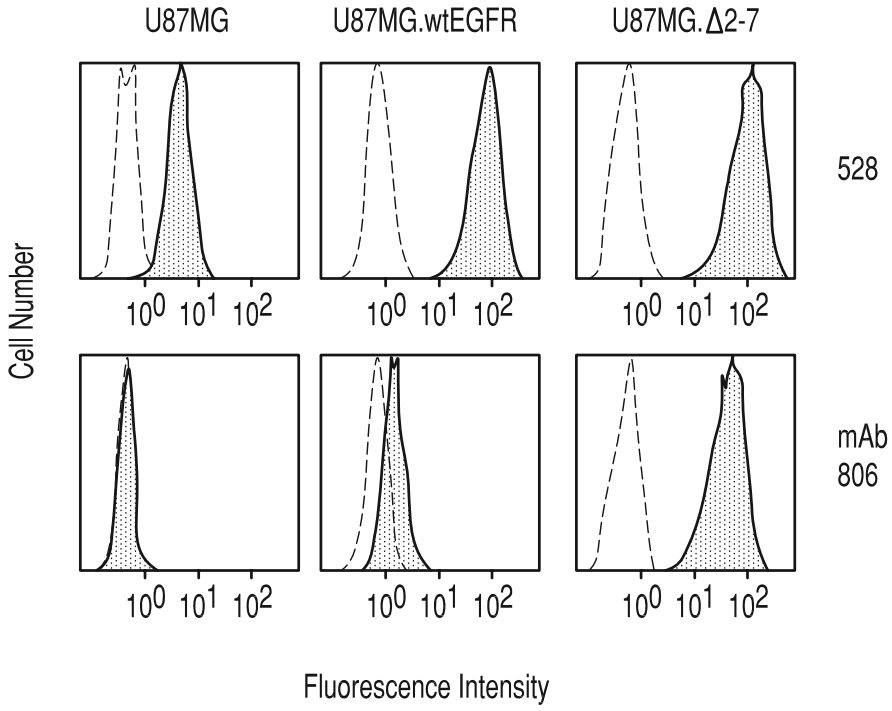

U87MG
U87MG.wtEGFR
U87MG.Δ2-7
528
mAb
806
Cell Number
10^0 10^1 10^2
Fluorescence Intensity

FIG. 29

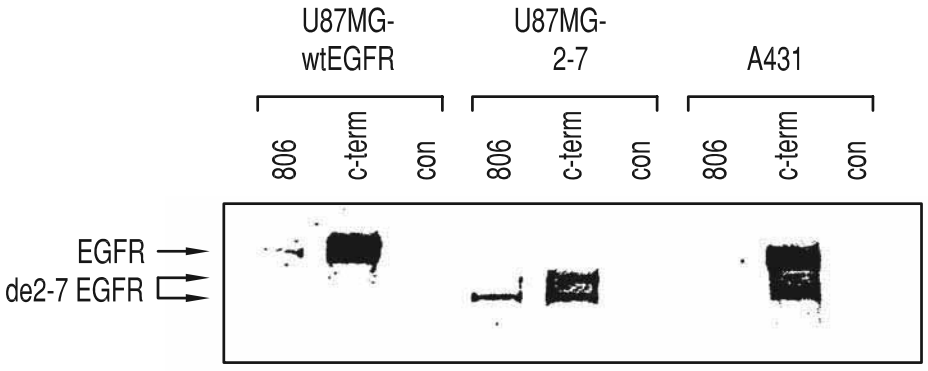

U87MG-
wtEGFR
U87MG-
2-7
A431
806
c-term
con
806
c-term
con
806
c-term
con
EGFR
de2-7 EGFR

FIG. 30

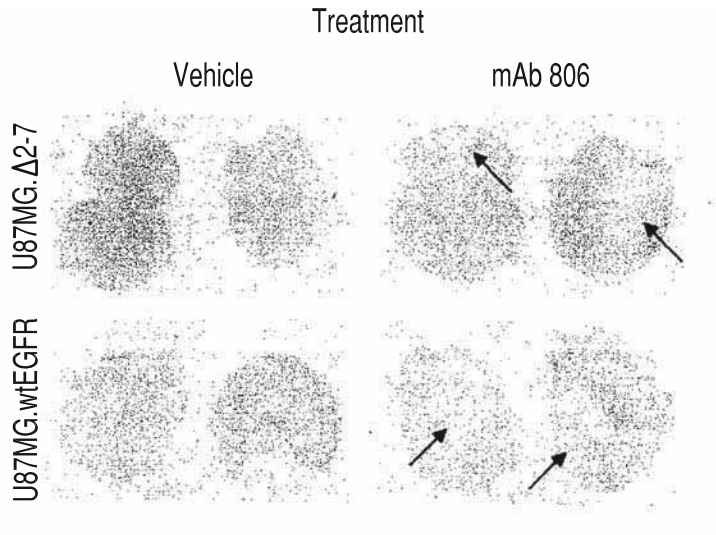


FIG. 31

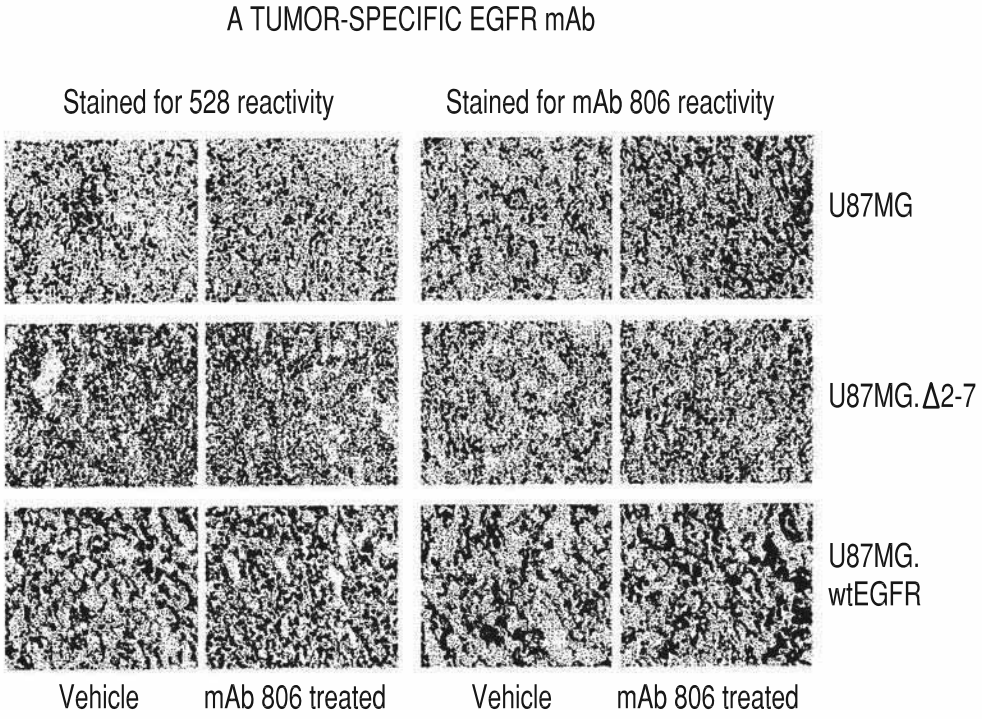

A TUMOR-SPECIFIC EGFR mAb
Stained for 528 reactivity
Stained for mAb 806 reactivity
U87MG
U87MG.Δ2-7
U87MG.
wtEGFR
Vehicle
mAb 806 treated
Vehicle
mAb 806 treated

FIG. 32

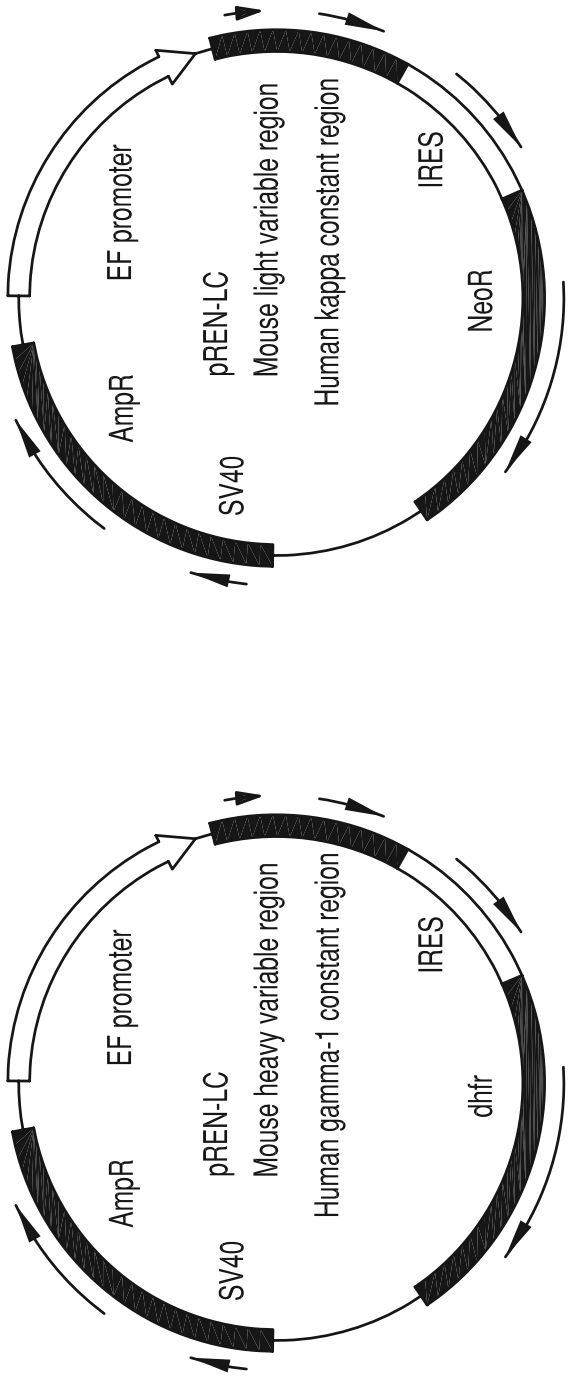

AmpR
EF promoter
pREN-LC
Mouse heavy variable region
Human gamma-1 constant region
IRES
dhfr
SV40
AmpR
EF promoter
pREN-LC
Mouse light variable region
Human kappa constant region
IRES
NeoR
SV40

FIG. 33

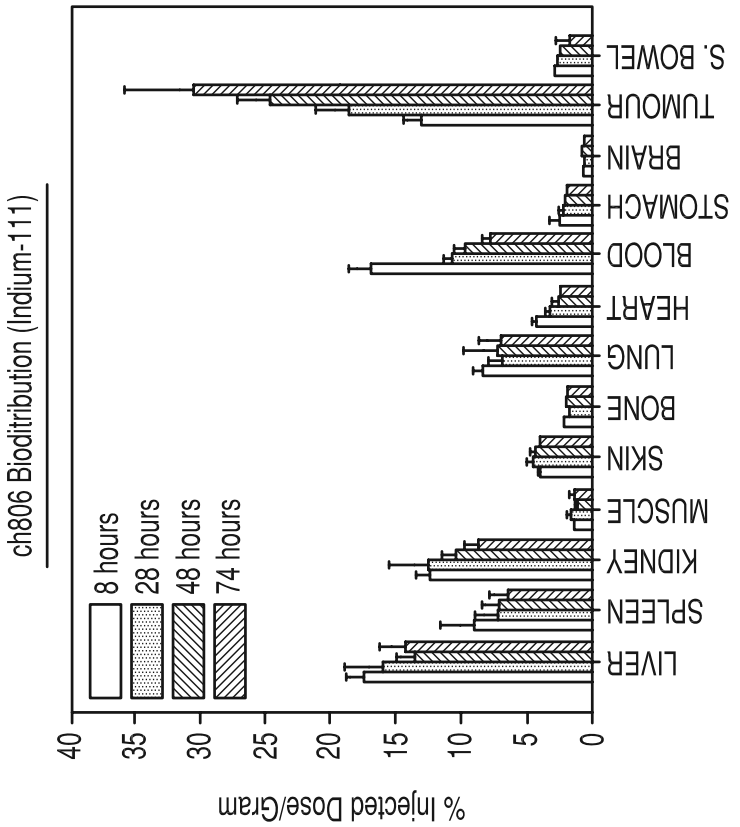


FIG. 34B

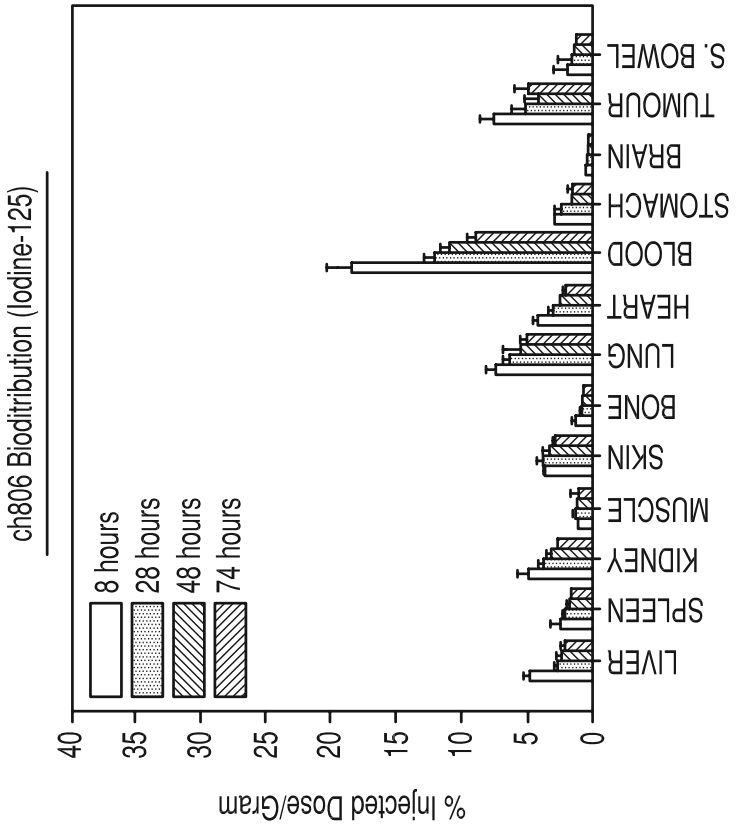


FIG. 34A

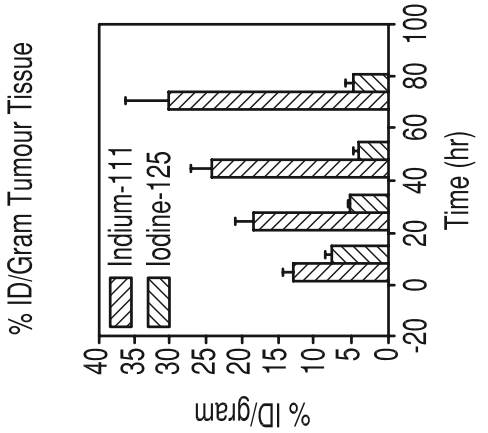


FIG. 35A

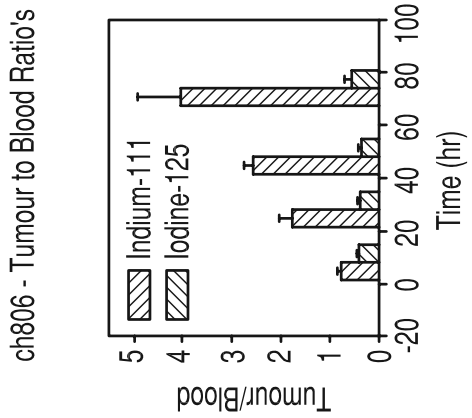


FIG. 35B

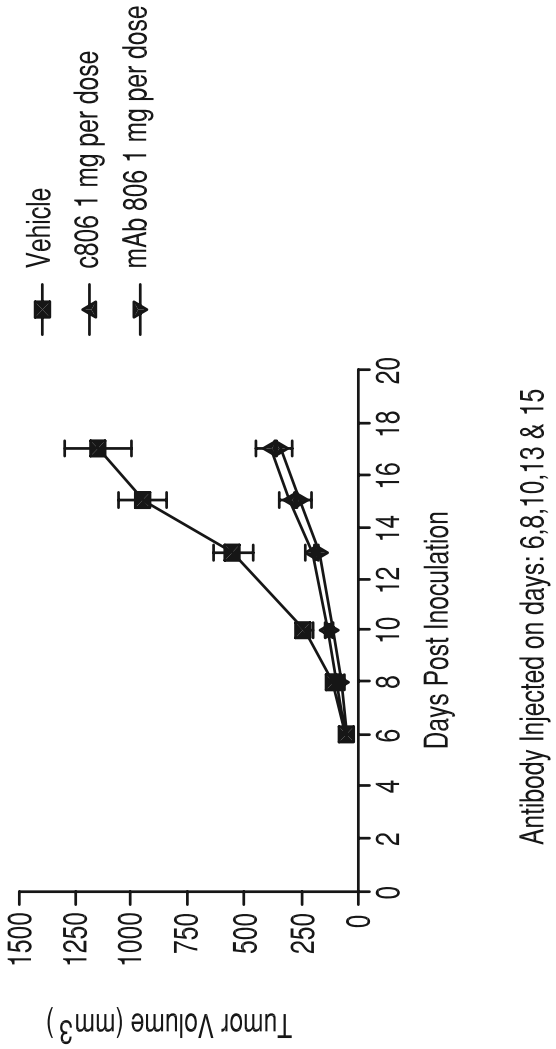

Vehicle
c806 1 mg per dose
mAb 806 1 mg per dose
Tumor Volume (mm3)
1500
1250
1000
750
500
250
0
0 2 4 6 8 10 12 14 16 18 20
Days Post Inoculation
Antibody Injected on days: 6,8,10,13 & 15

FIG. 36

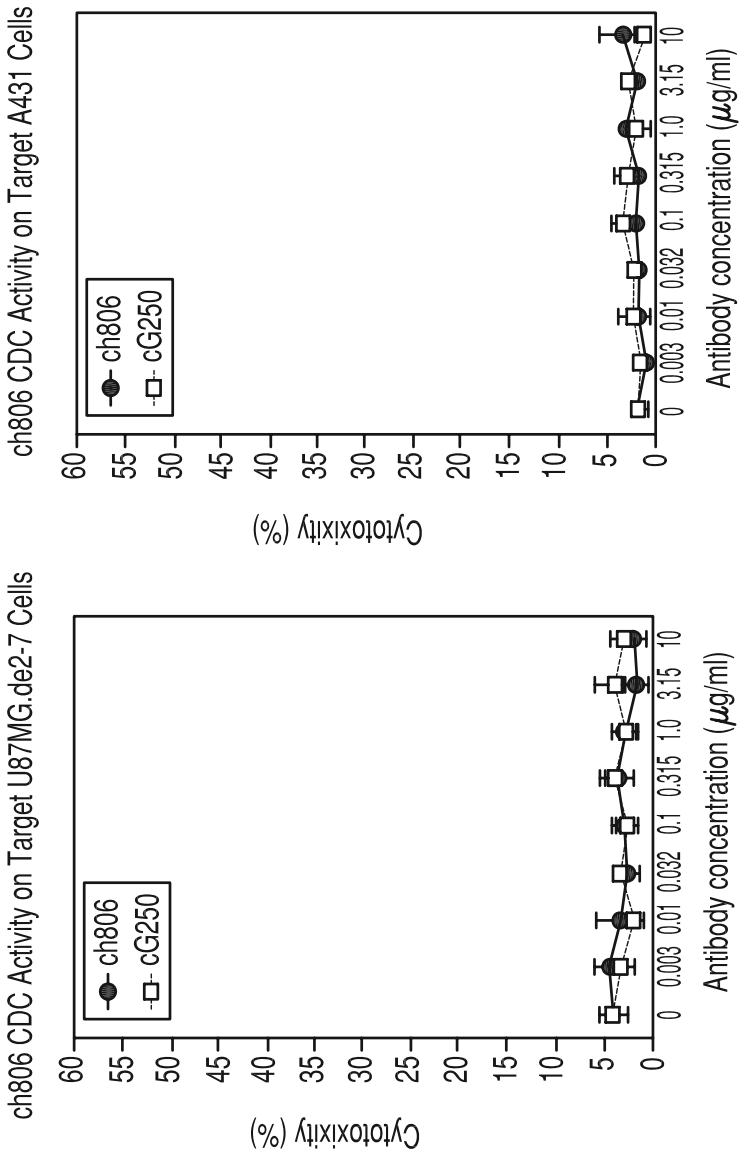

ch806 CDC Activity on Target U87MG.de2-7 Cells
ch806 CDC Activity on Target A431 Cells
ch806
cG250
Cytotoxixity (%)
Antibody concentration (μg/ml)
0
5
10
15
20
25
30
35
40
45
50
55
60
0.003
0.01
0.032
0.1
0.315
1.0
3.15
10

FIG. 37

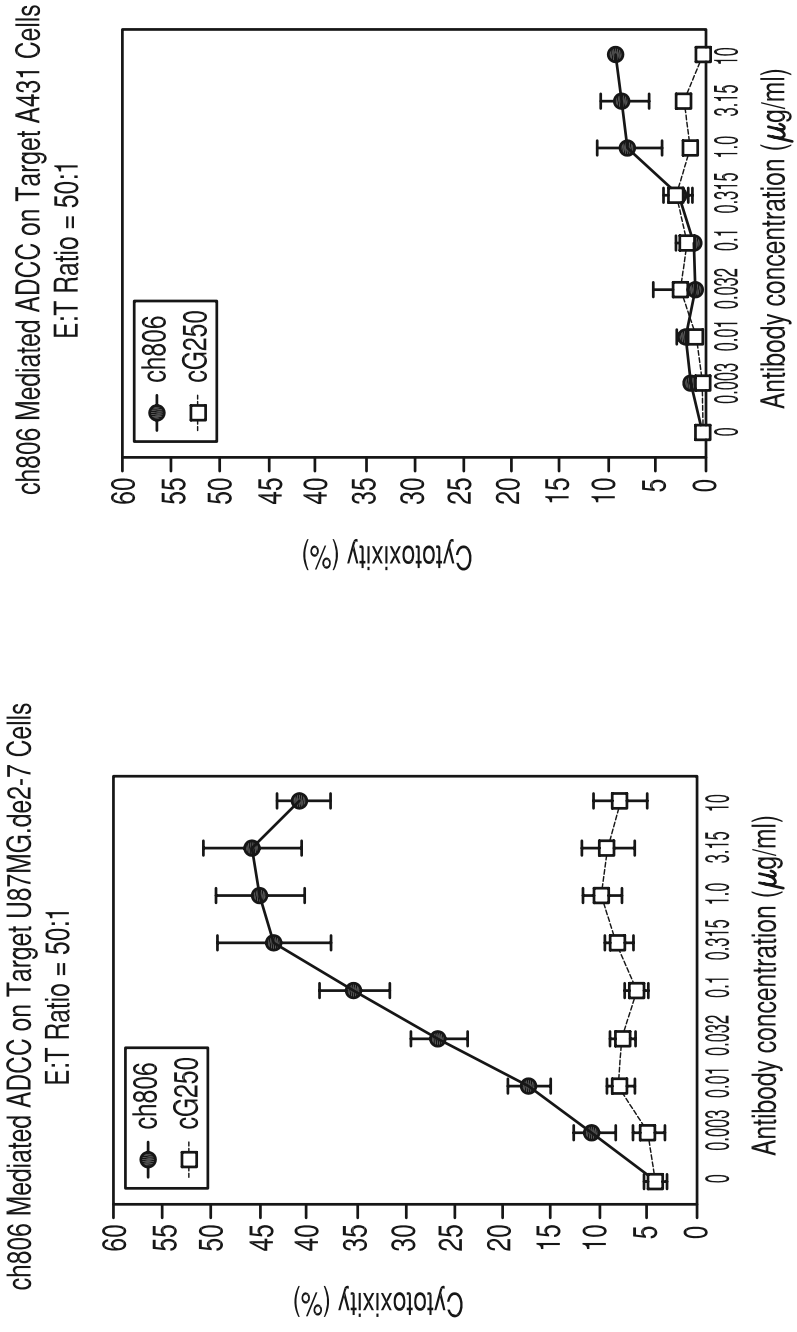

ch806 Mediated ADCC on Target U87MG.de2-7 Cells
E:T Ratio = 50:1
ch806
cG250
Cytotoxixity (%)
Antibody concentration (μg/ml)
0
0.003
0.01
0.032
0.1
0.315
1.0
3.15
10
5
10
15
20
25
30
35
40
45
50
55
60
ch806 Mediated ADCC on Target A431 Cells
E:T Ratio = 50:1
ch806
cG250
Cytotoxixity (%)
Antibody concentration (μg/ml)

FIG. 38

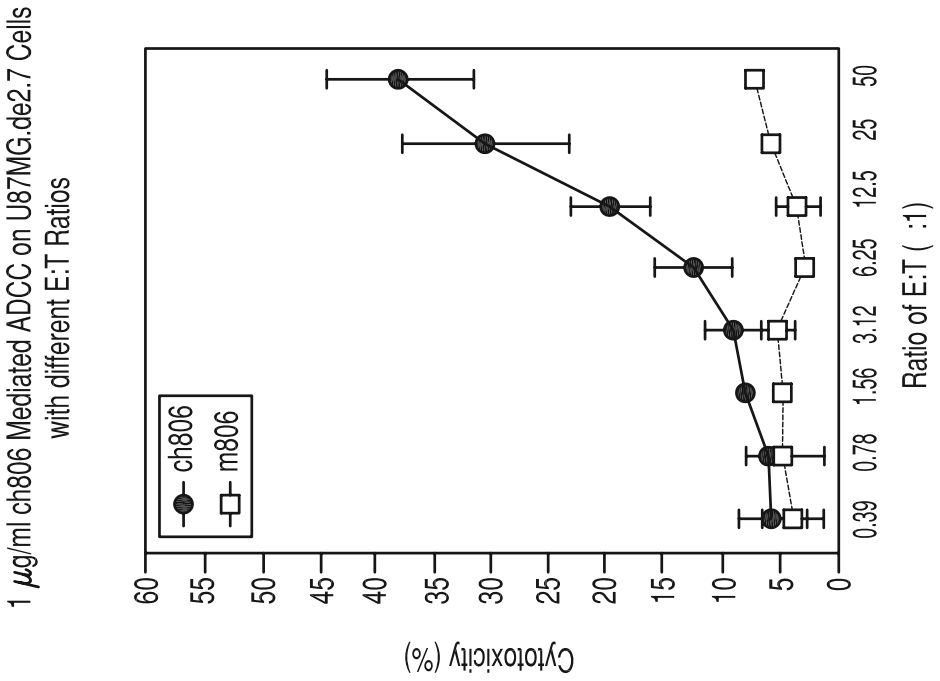

1 μg/ml ch806 Mediated ADCC on U87MG.de2.7 Cells
with different E:T Ratios
ch806
m806
Cytotoxicity (%)
60
55
50
45
40
35
30
25
20
15
10
5
0
0.39
0.78
1.56
3.12
6.25
12.5
25
50
Ratio of E:T (:1)

FIG. 39

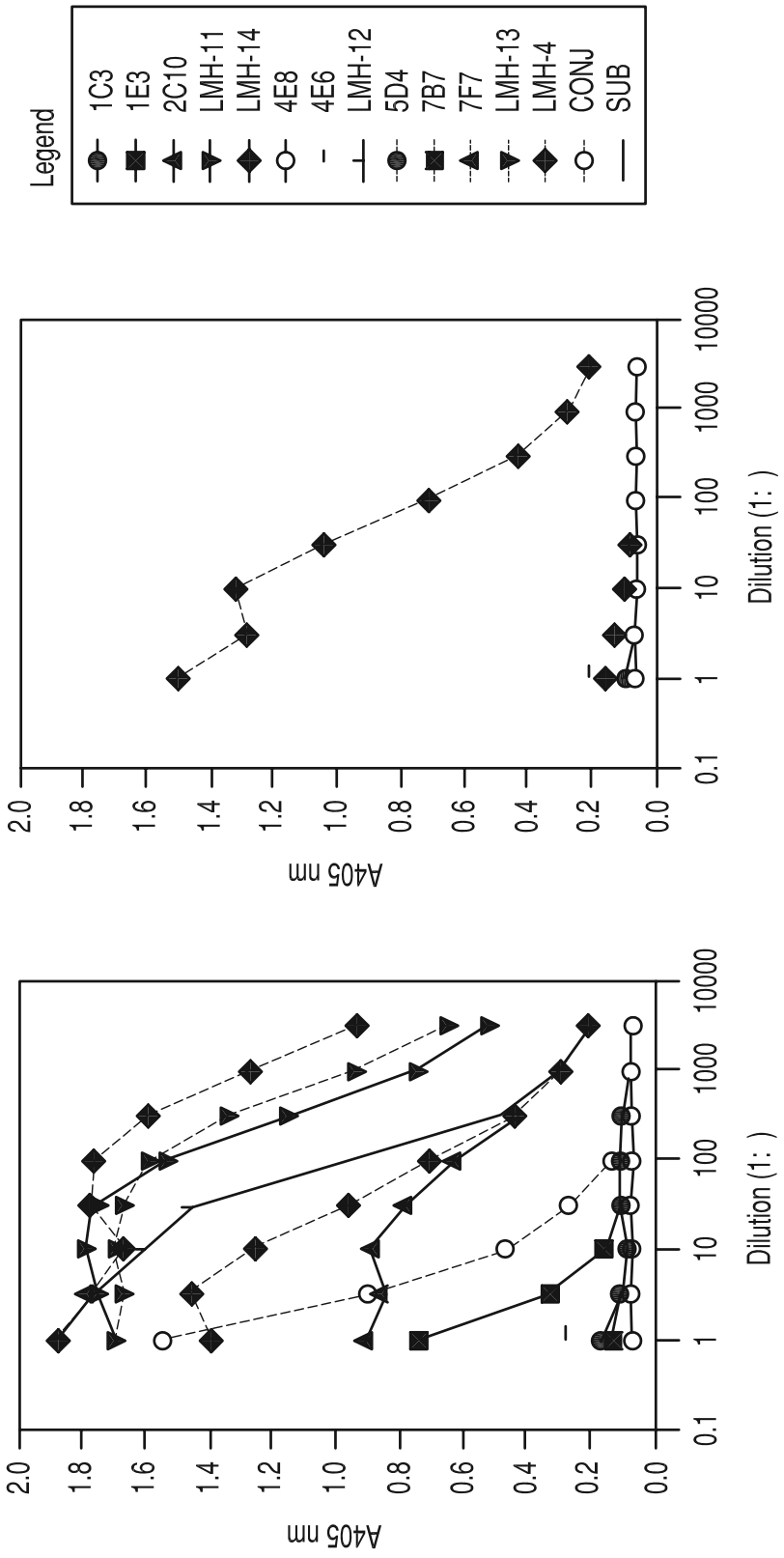
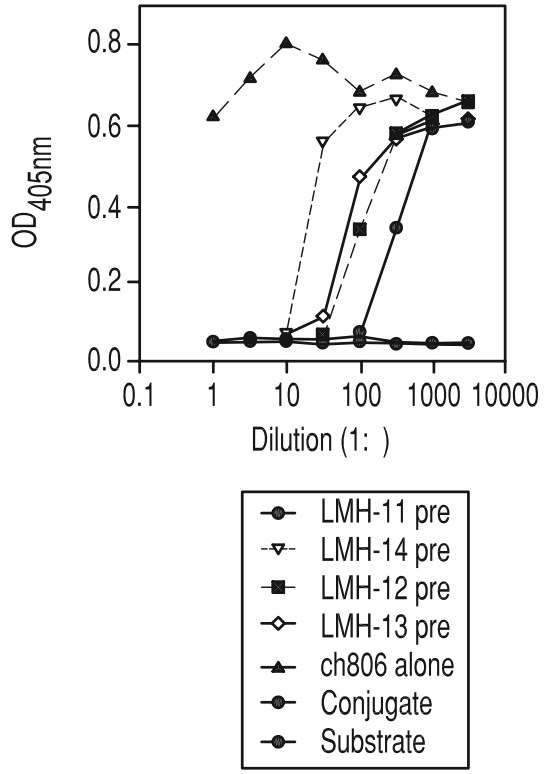

Legend
1C3
1E3
2C10
LMH-11
LMH-14
4E8
4E6
LMH-12
5D4
7B7
7F7
LMH-13
LMH-4
CONJ
SUB
A405 nm
Dilution (1:)
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4
1.6
1.8
2.0
0.1
1
10
100
1000
10000

FIG. 40

FIG. 41A



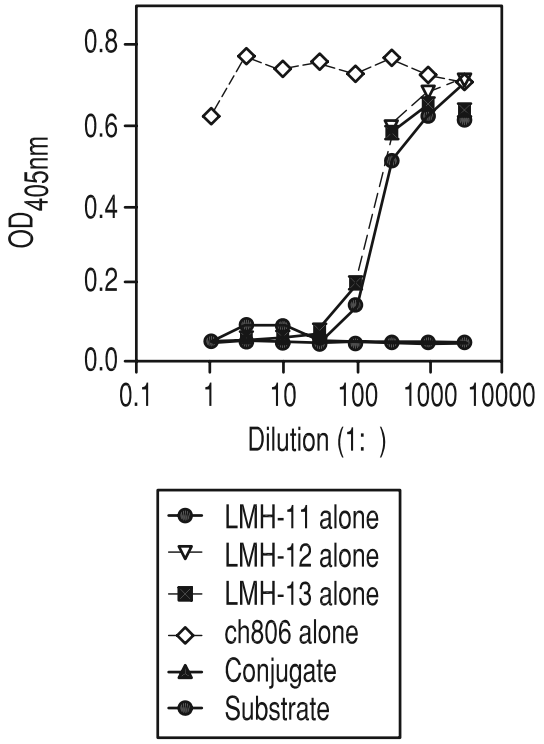


FIG. 41B

FIG. 41C



FIG. 42A

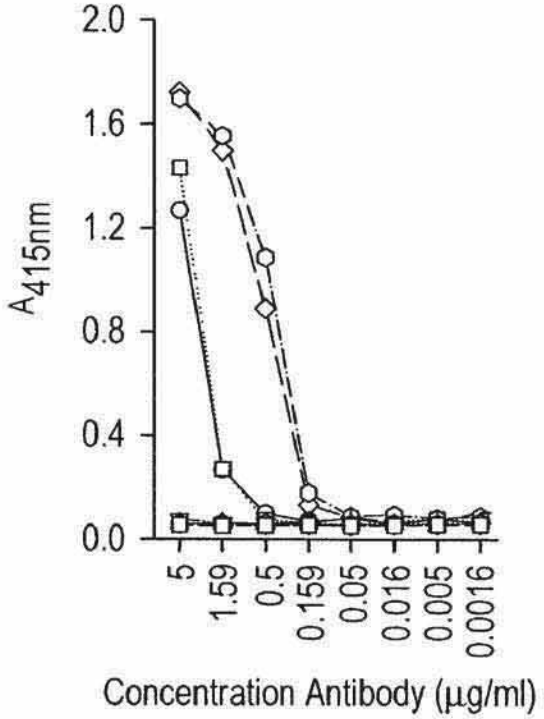


FIG. 42B

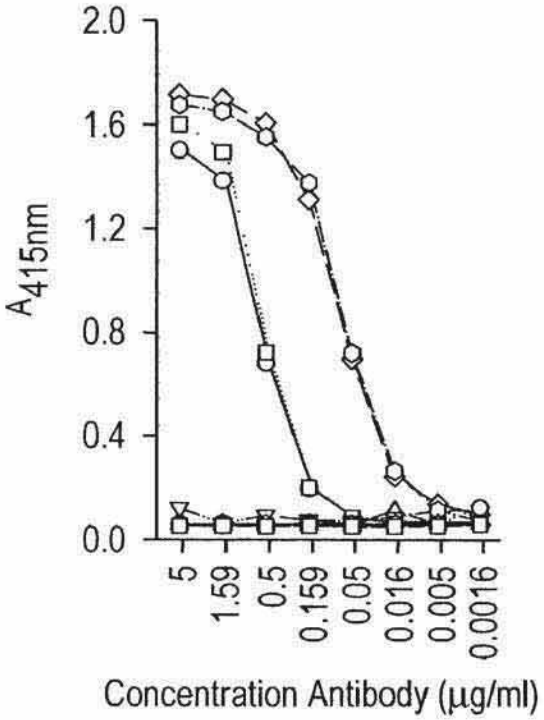
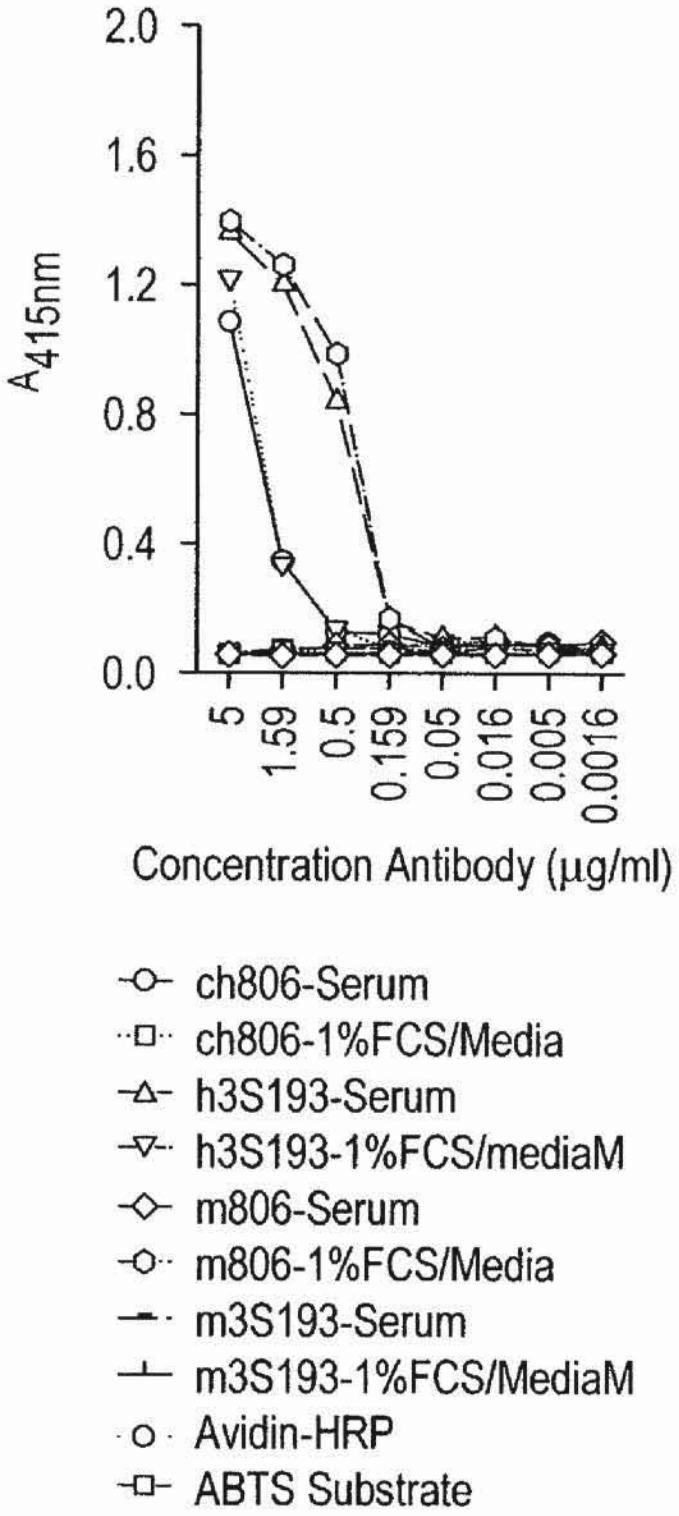


FIG. 42C


2.0
1.6
1.2
0.8
0.4
0.0
A415nm
5
1.59
0.5
0.159
0.05
0.016
0.005
0.0016
Concentration Antibody (µg/ml)
ch806-Serum
ch806-1%FCS/Media
h3S193-Serum
h3S193-1%FCS/mediaM
m806-Serum
m806-1%FCS/Media
m3S193-Serum
m3S193-1%FCS/MediaM
Avidin-HRP
ABTS Substrate

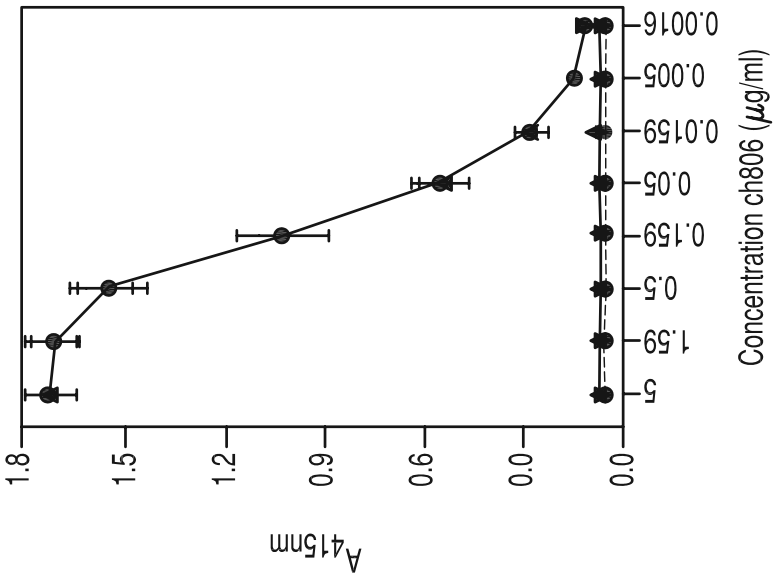

A415nm
1.8
1.5
1.2
0.9
0.6
0.0
0.0
5
1.59
0.5
0.159
0.05
0.0159
0.005
0.0016
Concentration ch806 (μg/ml)

FIG. 43

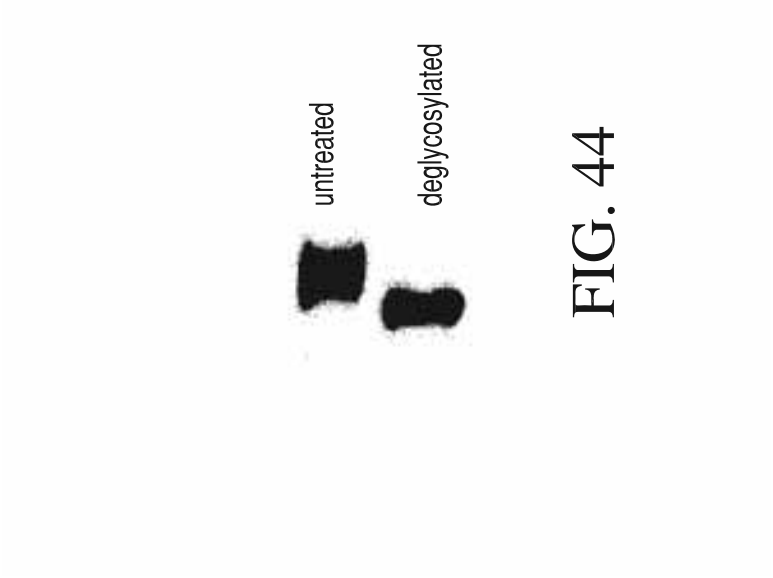


FIG. 44

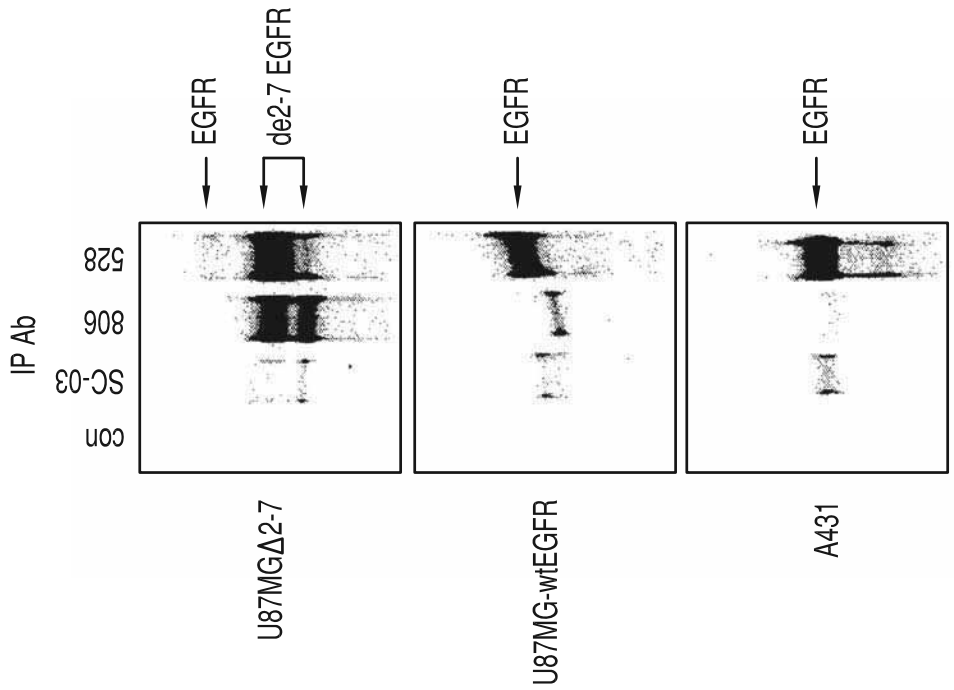

IP Ab
con
SC-03
806
528
EGFR
de2-7 EGFR
EGFR
EGFR
U87MGΔ2-7
U87MG-wtEGFR
A431

FIG. 45

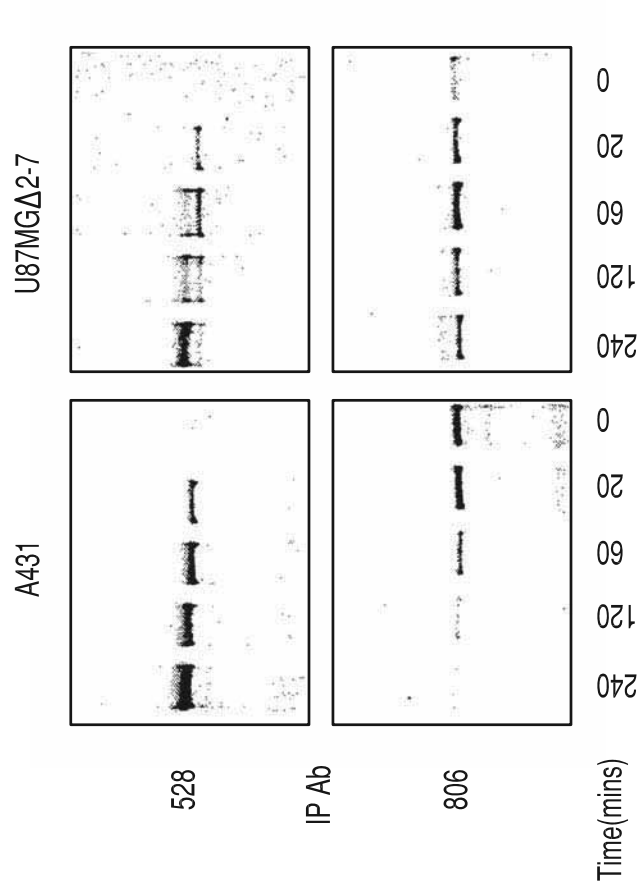

A431
U87MGΔ2-7
528
IP Ab
806
Time(mins)
0
20
60
120
240
0
20
60
120
240

FIG. 46

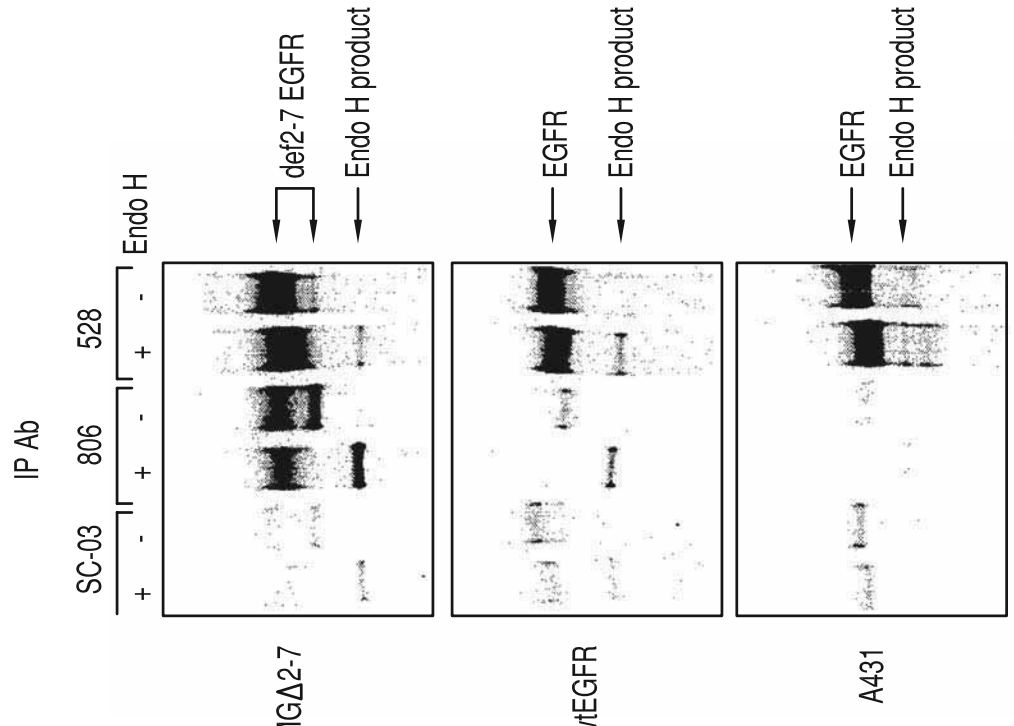

IP Ab
SC-03
806
528
Endo H
+
-
+
-
+
-
def2-7 EGFR
Endo H product
EGFR
Endo H product
EGFR
Endo H product
U87MGΔ2-7
U87MG-wtEGFR
A431

FIG. 47

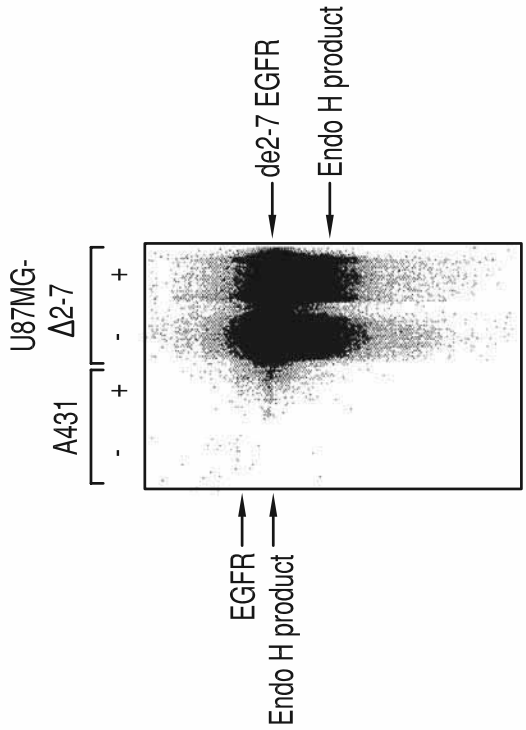


FIG. 48

SEQ ID NO:7 pREN ch806 LC Neo Vector

Xho I

1 CTCGAGAGCGGGCAGTGAGCGCAACGCAATTAATGTGAGTTAGCTCACTC

51 ATTAGGCACCCCAGGCTTTACACTTTATGCTCCCGGCTCGTATGTTGTGT

EcoRI EF1α promoter

101 GGAGATTGTGAGCGGATAACAATTTCACACAGAATTCGTGAGGCTCCGGT

151 GCCCGTCAGTGGGCAGAGCGCACATCGCCCACAGTCCCCGAGAAGTTGGG

201 GGGAGGGGTCGGCAATTGAACCGGTGCCTAGAGAAGGTGGCGCGGGGTAA

251 ACTGGGAAAGTGATGTCGTGTACTGGCTCCGCCTTTTTCCCGAGGGTGGG

301 GGAGAACCGTATATAAGTGCAGTAGTCGCCGTGAACGTTCTTTTTCGCAA

351 CGGGTTTGCCGCCAGAACACAGGTAAGTGCCGTGTGTGGTTCCCGCGGGC

401 CTGGCCTCTTTACGGGTTATGGCCCTTGCGTGCCTTGAATTACTTCCACG

451 CCCCTGGCTGCAGTACGTGATTCTTGATCCCGAGCTTCGGGTTGGAAGTG

501 GGTGGGAGAGTTCGAGGCCTTGCGCTTAAGGAGCCCCTTCGCCTCGTGCT

551 TGAGTTGAGGCCTGGCCTGGGCGCTGGGGCCGCCGCGTGCGAATCTGGTG

601 GCACCTTCGCGCCTGTCTCGCTGCTTTCGATAAGTCTCTAGCCATTTAAA

651 ATTTTTGATGACCTGCTGCGACGCTTTTTTTCTGGCAAGATAGTCTTGTA

701 AATGCGGGCCAAGATCTGCACACTGGTATTTCGGTTTTTGGGGCCGCGGG

751 CGGCGACGGGGCCCGTGCGTCCCAGCGCACATGTTCGGCGAGGCGGGGCC

801 TGCGAGCGCGGCCACCGAGAATCGGACGGGGGTAGTCTCAAGCTGGCCGG

851 CCTGCTCTGGTGCCTGGCCTCGCGCCGCCGTGTATCGCCCCGCCCTGGGC

901 GGCAAGGCTGGCCCGGTCGGCACCAGTTGCGTGAGCGGAAAGATGGCCGC

951 TTCCCGGCCCTGCTGCAGGGAGCTCAAAATGGAGGACGCGGCGCTCGGGA

1001 GAGCGGGCGGGTGAGTCACCCACACAAAGGAAAAGGGCCTTTCCGTCCTC

FIG.49

```
1051  AGCCGTCGCTTCATGTGACTCCACGGAGTACCGGGCGCCGTCCAGGCACC

1101  TCGATTAGTTCTCGAGCTTTTGGAGTACGTCGTCTTTAGGTTGGGGGGAG

1151  GGGTTTTATGCGATGGAGTTTCCCCACACTGAGTGGGTGGAGACTGAAGT

1201  TAGGCCAGCTTGGCACTTGATGTAATTCTCCTTGGAATTTGCCCTTTTTG

1251  AGTTTGGATCTTGGTTCATTCTCAAGCCTCAGACAGTGGTTCAAAGTTTT
                              MluI        HindIII    PmeI
1301  TTTCTTCCATTTCAGGTGTACGCGTCTCGGGAAGCTTTAGTTTAAACGCC

1351  GCCACCATGGTGTCCACAGCTCAGTTCCTTGCATTCTTGTTGCTTTGGTTT
                M  V  S  T  A  Q  F  L  A  F  L  L  L  W  F

1401  CCAGGTGCAAGATGTGACATCCTGATGACCCAATCTCCATCCTCCATGTCT
      P  G  A  R  C  D  I  L  M  T  Q  S  P  S  S  M  S

1451  GTATCTCTGGGAGACACAGTCAGCATCACTTGCCATTCAAGTCAGGACATT
                     V S L G D T V S I T C H S S Q D I

1501  AACAGTAATATAGGGTGGTTGCAGCAGAGACCAGGGAAATCATTTAAGGGC
       N  S  N  I  G  W  L  Q  Q  R  P  G  K  S  F  K  G

1551  CTGATCTATCATGGAACCAACTTGGACGATGAAGTTCCATCAAGGTTCAGT
                     L I Y H G T N L D D E V P S R F S

1601  GGCAGTGGATCTGGAGCCGATTATTCTCTCACCATCAGCAGCCTGGAATCT
                     G S G S G A D Y S L T I S S L E S

1651  GAAGATTTTGCAGACTATTACTGTGTACAGCATGCTCAGTTTCCGTGGACG
       E  D  F  A  D  Y  Y  C  V  Q  H  A  Q  F  P  W  T
                                                    BamHI
1701  TTCGGTGGAGGCACCAAGCTGGAAATCAAACGGGTGAGTGGATCCATCTGGG
       F  G  G  G  T  K  L  E  I  K  R

1751  ATAAGCATGCTGTTTTCTGTCTGTCCCTAACATGCCCTGTGATTATGCGCAAA

1801  CAACACACCCAAGGGCAGAACTTTGTTACTTAAACACCATCCTGTTTGCTTCTT

1851  TCCTCAGGAACTGTGGCTGCACCA
            T  V  A  A  P

1876  TCTGTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAACTGC
       S  V  F  I  F  P  P  S  D  E  Q  L  K  S  G  T  A

1926  CTCTGTTGTGTGCCTGCTGAATAACTTCTATCCCAGAGAGGCCAAAGTAC
```

FIG.49 continued

```
      S  V  V  C  L  L  N  N  F  Y  P  R  E  A  K  V  Q

1976  AGTGGAAGGTGGATAACGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTC
        W  K  V  D  N  A  L  Q  S  G  N  S  Q  E  S  V

2026  ACAGAGCAGGACAGCAAGGACAGCACCTACAGCCTCAGCAGCACCCTGAC
       T  E  Q  D  S  K  D  S  T  Y  S  L  S  S  T  L  T

2076  GCTGAGCAAAGCAGACTACGAGAAACACAAAGTCTACGCCTGCGAAGTCA
        L  S  K  A  D  Y  E  K  H  K  V  Y  A  C  E  V  T

2126  CCCATCAGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAACAGGGGAGAG
        H  Q  G  L  S  S  P  V  T  K  S  F  N  R  G  E
              Nhe/Xba
2176  TGTTGAGCTAGAACTAACTAACTAAGCTAGCAACGGTTTCCCTCTAGCGG
       C  *
2226  GATCAATTCCGCCCCCCCCCCCTAACGTTACTGGCCGAAGCCGCTTGGAA

2276  TAAGGCCGGTGTGCGTTTGTCTATATGTTATTTTCCACCATATTGCCGTC

2326  TTTTGGCAATGTGAGGGCCCGGAAACCTGGCCCTGTCTTCTTGACGAGCA


2376  TTCCTAGGGGTCTTTCCCCTCTCGCCAAAGGAATGCAAGGTCTGTTGAAT

2426  GTCGTGAAGGAAGCAGTTCCTCTGGAAGCTTCTTGAAGACAAACAACGTC

2476  TGTAGCGACCCTTTGCAGGCAGCGGAACCCCCCACCTGGCGACAGGTGCC

2526  TCTGCGGCCAAAAGCCACGTGTATAAGATACACCTGCAAAGGCGGCACAA

2576  CCCCAGTGCCACGTTGTGAGTTGGATAGTTGTGGAAAGAGTCAAATGGCT

2626  CTCCTCAAGCGTATTCAACAAGGGGCTGAAGGATGCCCAGAAGGTACCCC

2676  ATTGTATGGGATCTGATCTGGGGCCTCGGTGCACATGCTTTACGTGTGTT

2751   TAGTCGAGGTTAAAAAACGTCTAGGCCCCCCGAACCACGGGGACGTGGTT

2801   TTCCTTTGAAAAACACGATAATACCATGGTTGAACAAGATGGATTGCACG

2851   CAGGTTCTCCGGCCGCTTGGGTGGAGAGGCTATTCGGCTATGACTGGGCA

2901   CAACAGACAATCGGCTGCTCTGATGCCGCCGTGTTCCGGCTGTCAGCGCA

2951   GGGGCGCCCGGTTCTTTTTGTCAAGACCGACCTGTCCGGTGCCCTGAATG
```

FIG.49 continued

```
3001  AACTGCAGGACGAGGCAGCGCGGCTATCGTGGCTGGCCACGACGGGCGTT
3051  CCTTGCGCAGCTGTGCTCGACGTTGTCACTGAAGCGGGAAGGGACTGGCT
3101  GCTATTGGGCGAAGTGCCGGGGCAGGATCTCCTGTCATCTCACCTTGCTC
3151  CTGCCGAGAAAGTATCCATCATGGCTGATGCAATGCGGCGGCTGCATACG
3201  CTTGATCCGGCTACCTGCCCATTCGACCACCAAGCGAAACATCGCATCGA
3251  GCGAGCACGTACTCGGATGGAAGCCGGTCTTGTCGATCAGGATGATCTGG
3301  ACGAAGAGCATCAGGGGCTCGCGCCAGCCGAACTGTTCGCCAGGCTCAAG
3351  GCGCGCATGCCCGACGGCGAGGATCTCGTCGTGACCCATGGCGATGCCTG
3401  CTTGCCGAATATCATGGTGGAAAATGGCCGCTTTTCTGGATTCATCGACT
3451  GTGGCCGGCTGGGTGTGGCGGACCGCTATCAGGACATAGCGTTGGCTACC
3501  CGTGATATTGCTGAAGAGCTTGGCGGCGAATGGGCTGACCGCTTCCTCGT
3551  GCTTTACGGTATCGCCGCTCCCGATTCGCAGCGCATCGCCTTCTATCGCC
                          blunt end SalI/SalI
3601  TTCTTGACGAGTTCTTCTGAGTCGATCGACCTGGCGTAATAGCGAAGAGG
3651  CCCGCACCGATCGCCCTTCCCAACAGTTGCGCAGCCTGAATGGCGAATGG
3701  GACGCGCCCTGTAGCGGCGCATTAAGCGCGGCGGGTGTGGTGGTTACGCG
3751  CAGCGTGACCGCTACACTTGCCAGCGCCCTAGCGCCCGCTCCTTTCGCTT
3801  TCTTCCCTTCCTTTCTCGCCACGTTCGCCGGCTTTCCCCGTCAAGCTCTA
3851  AATCGGGGGCTCCCTTTAGGGTTCCGATTTAGTGCTTTACGGCACCTCGA
3901  CCCCAAAAAACTTGATTAGGGTGATGGTTCACGTAGTGGGCCATCGCCCT
3951  GATAGACGGTTTTTCGCCTTTGACGTTGGAGTCCACGTTCTTTAATAGTG
4001  GACTCTTGTTCCAAACTGGAACAACACTCAACCCTATCTCGGTCTATTTA
4051  TAAGGGATTTTGCCGATTTCGGCCTATTGGTTAAAAAATGAGCTGATTTA
4101  ACAAAATTTAACGCGAATTTTAACAAAATATTAACGCTTACAATTTAGGT
4151  GGCACTTTTCGGGGAAATGTGCGCGGAACCCCTATATTTGTTTATTTTTC
```

FIG.49 continued

```
4201  TAAATACATTCAAATATGTATCCGCTCATGAGACAATAACCCTGATAAAT
4251  GCTTCAATAATATTGAAAAAGGAAGAGTATGAGTATTCAACATTTCCGTG
4301  TCGCCCTTATTCCCTTTTTTGCGGCATTTTGCCTTACTGTTTTTGCTCAC
4351  CCAGAAACGCTGGTGAAAGTAAAAGATGCTGAAGATCAGTTGGGTGCACG
4401  AGTGGGTTACATCGAACTGGATCTCAACAGCGGTAAGATCCTTGAGAGTT
4451  TTCGCCCCGAAGAACGTTTTCCAATGATGAGCACTTTTAAAGTTCTGCTA
4501  TGTGGCGCGGTATTATCCCGTATTGACGCCGGGCAAGAGCAACTCGGTCG
4551  CCGCATACACTATTCTCAGAATGACTTGGTTGAGTACTCACCAGTCACAG
4601  AAAAGCATATTACGGATGGCATGACAGTAAGAGAATTATGCAGTGCTGCC
4651  ATAACCATGAGTGATAACACTGCGGCCAACTTACTTCTGACAACGATCGG
4701  AGGACCGAAGGAGCTAACCGCTTTTTTGCACAACATGGGGGATCATGTAA
4751  CTCGCCTTGATCGTTGGGAACCGGAGCTGAATGAAGCCATACCAAACGAC
4801  GAGCGTGACACCACGATGCCTGTAGCAATGGCAACAACGTTGCGCAAACT
4851  ATTAACTGGCGAACTACTTACTCTAGCTTCCCGGCAACAATTAATAGACT
4901  GGATGGAGGCGGATAAAGTTGCAGGACCACTTCTGCGCTCGGCCCTTCCG
4951  GCTGGCTGGTTTATTGCTGATAAATCTGGAGCCGGTGAGCGTGGGTCTCG
5001  CGGTATCATTGCAGCACTGGGGCCAGATGGTAAGCCCTCCCGTATCGTAG
5051  TTATCTACACGACGGGGAGTCAGGCAACTATGGATGAACGAAATAGACAG
5101  ATCGCTGAGATAGGTGCCTCACTGATTAAGCATTGGTAACTGTCAGACCA
5151  AGTTTACTCATATATACTTTAGATTGATTTAAAACTTCATTTTTAATTTA
5201  AAAGGATCTAGGTGAAGATCCTTTTTGATAATCTCATGACCAAAATCCCT
5251  TAACGTGAGTTTTCGTTCCACTGAGCGTCAGACCCCGTAGAAAAGATCAA
5301  AGGATGTTCTTGAGATCCTTTTTTTCTGCACGTAATCTGCTGCTTGCAAA
```

FIG.49 continued

```
5351  CAAAAAACCACCGCTACCAGCGGTGGTTTGTTTGCCGGATCAAGAGCTAC
5401  CAACTCTTTTTCCGAAGGTAACTGGCTTCAGCAGAGCGCAGATACCAAAT
5451  ACTGTCCTTCTAGTGTAGCCGTAGTTAGGCCACCACTTCAAGAACTCTGT
5501  AGCACCGCCTACATACCTCGCTCTGCTAATCCTGTTACCAGTGGCTGCTG
5551  CCAGTGGCGATAAGTCGTGTCTTACCGGGTTGGACTCAAGACGATAGTTA
5601  CCGGATAAGGCGCAGCGGTCGGGCTGAACGGGGGGTTCGTGCACACAGCC
5651  CAGCTTGGAGCGAACGACCTACACCGAACTGAGATACCTACAGCGTGAGC
5701  TATGAGAAAGCGCCACGCTTCCCGAAGGGAGAAAGGCGGACAGGTATCCG
5751  GTAAGCGGCAGGGTCGGAACAGGAGAGCGCACGAGGGAGCTTCCAGGGGG
5801  AAACGCCTGGTATCTTTATAGTCCTGTCGGGTTTCGCCACCTCTGACTTG
5851  AGCGTCGATTTTTGTGATGCTCGTCAGGGGGGCGGAGCCTATGGAAAAAC
5901  GCCAGCAACGCGGCCTTTTTACGGTTCCTGGCCTTTTGCTGGCCTTTTGC
5951  TCACATGTTCTTTCCTGCGTTATCCCCTGATTCTGTGGATAACCGTATTA
6001  CCGCCTTTGAGTGAGCTGATACCGCTCGCCGCAGCCGAACGACCGAGCGC
6051  AGCGAGTCAGTGAGCGAGGAAGCGGAAGAGCGCCCAATACGCAAACCGCC
6101  TCTCCCCGCGCGTTGGCCGATTCATTAATGCAGGTATCACGAGGCCCTTT
6151  CGTCTTCAC
```

FIG.49 continued

SEQ ID NO:8 pREN 806 HC DHFR Vector

Xho I

1 CTCGAGAGCGGGCAGTGAGCGCAACGCAATTAATGTGAGTTAGCTCACTC

52 ATTAGGCACCCCAGGCTTTACACTTTATGCTCCCGGCTCGTATGTTGTGT

EcoRI EF1α promoter

102 GGAGATTGTGAGCGGATAACAATTTCACACAGAATTCGTGAGGCTCCGGT

152 GCCCGTCAGTGGGCAGAGCGCACATCGCCCACAGTCCCCGAGAAGTTGGG

202 GGGAGGGGTCGGCAATTGAACCGGTGCCTAGAGAAGGTGGCGCGGGGTAA

252 ACTGGGAAAGTGATGTCGTGTACTGGCTCCGCCTTTTTCCCGAGGGTGGG

302 GGAGAACCGTATATAAGTGCAGTAGTCGCCGTGAACGTTCTTTTTCGCAA

352 CGGGTTTGCCGCCAGAACACAGGTAAGTGCCGTGTGTGGTTCCCGCGGGC

402 CTGGCCTCTTTACGGGTTATGGCCCTTGCGTGCCTTGAATTACTTCCACG

452 CCCCTGGCTGCAGTACGTGATTCTTGATCCCGAGCTTCGGGTTGGAAGTG

502 GGTGGGAGAGTTCGAGGCCTTGCGCTTAAGGAGCCCCTTCGCCTCGTGCT

552 TGAGTTGAGGCCTGGCCTGGGCGCTGGGGCCGCCGCGTGCGAATCTGGTG

602 GCACCTTCGCGCCTGTCTCGCTGCTTTCGATAAGTCTCTAGCCATTTAAA

652 ATTTTTGATGACCTGCTGCGACGCTTTTTTTCTGGCAAGATAGTCTTGTA

702 AATGCGGGCCAAGATCTGCACACTGGTATTTCGGTTTTTGGGGCCGCGGG

752 CGGCGACGGGGCCCGTGCGTCCCAGCGCACATGTTCGGCGAGGCGGGGCC

802 TGCGAGCGCGGCCACCGAGAATCGGACGGGGGTAGTCTCAAGCTGGCCGG

852 CCTGCTCTGGTGCCTGGCCTCGCGCCGCCGTGTATCGCCCCGCCCTGGGC

902 GGCAAGGCTGGCCCGGTCGGCACCAGTTGCGTGAGCGGAAAGATGGCCGC

952 TTCCCGGCCCTGCTGCAGGGAGCTCAAAATGGAGGACGCGGCGCTCGGGA

1002 GAGCGGGCGGGTGAGTCACCCACACAAAGGAAAAGGGCCTTTCCGTCCTC

FIG.50

```
1052  AGCCGTCGCTTCATGTGACTCCACGGAGTACCGGGCGCCGTCCAGGCACC

1102  TCGATTAGTTCTCGAGCTTTTGGAGTACGTCGTCTTTAGGTTGGGGGGAG

1152  GGGTTTTATGCGATGGAGTTTCCCCACACTGAGTGGGTGGAGACTGAAGT

1202  TAGGCCAGCTTGGCACTTGATGTAATTCTCCTTGGAATTTGCCCTTTTTG

1251  AGTTTGGATCTTGGTTCATTCTCAAGCCTCAGACAGTGGTTCAAAGTTTT
                          MluI          HindIII     PmeI
1302  TTTCTTCCATTTCAGGTGTACGCGTCTCGGGAAGCTTTAGTTTAAACGCC

1352  GCCACCATGAGAGTGCTGATTCTTTTGTGGCTGTTCACAGCCTTTCCTGGT
            M  R  V  L  I  L  L  W  L  F  T  A  F  P  G

1401  GTCCTGTCTGATGTGCAGCTTCAGGAGTCGGGACCTAGCCTGGTGAAACCT
            V  L  S  D  V  Q  L  Q  E  S  G  P  S  L  V  K  P

1451  TCTCAGACTCTGTCCCTCACCTGCACTGTCACTGGCTACTCAATCACCAGT
      S  Q  T  L  S  L  T  C  T  V  T  G  Y  S  I  T  S

1501  GATTTTGCCTGGAACTGGATCCGGCAGTTTCCAGGAAACAAGCTGGAGTGG
      D  F  A  W  N  W  I  R  Q  F  P  G  N  K  L  E  W

1551  ATGGGCTACATAAGTTATAGTGGTAACACTAGGTACAACCCATCTCTCAAA
      M  G  Y  I  S  Y  S  G  N  T  R  Y  N  P  S  L  K

1601  AGTCGAATCTCTATCACTCGAGACACATCCAAGAACCAATTCTTCCTGCAG
      S  R  I  S  I  T  R  D  T  S  K  N  Q  F  F  L  Q

1651  TTGAATTCTGTGACTATTGAGGACACAGCCACATATTACTGTGTAACGGCG
         L  N  S  V  T  I  E  D  T  A  T  Y  Y  C  V  T  A

1701  GGACGCGGGTTTCCTTATTGGGGCCAAGGGACTCTGGTCACTGTCTCTGCA
      G  R  G  F  P  Y  W  G  Q  G  T  L  V  T  V  S  A

                  BamHI
1751  CAGTGAGTGGATCCTCTGCGCCTGGGCCCAGCTCTGTC

1801  CCACACCGCGGTCACATGGCACCACCTCTCTTGCAGCCTCCACCAAGGGC
                                                S  T  K  G
1851  CCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCAC
p  s  v  f  p  l  a  p  s  s  k  s  t  s  g  g  t
```

FIG.50 continued

```
1901  AGCGGCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGG
        A  A  L  G  C  L  V  K  D  Y  F  P  E  P  V  T  V

1951  TGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGGCT
  s  w  n  s  g  a  l  t  s  g  v  h  t  f  p  a

2001  GTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCC
v  l  q  s  s  g  l  y  s  l  s  s  v  y  s  v  p

2051  CTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGC
        S  S  S  L  G  T  Q  T  Y  I  C  N  V  N  H  K  P

2101  CCAGCAACACCAAGGTGGACAAGAAAGTTGAGCCCAAATCTTGTGACAAA
        S  N  T  K  V  D  K  K  V  E  P  K  S  C  D  K

2151  ACTCACACATGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACCGTC
      T  H  T  C  P  P  C  P  A  P  E  L  L  G  G  P  S

2201  AGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGA
        V  F  L  F  P  P  K  P  K  D  T  L  M  I  S  R  T

2251  CCCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAG
        P  E  V  T  C  V  V  V  D  V  S  H  E  D  P  E

2301  GTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAACGCCAAGAC
      V  K  F  N  W  Y  V  D  G  V  E  V  H  N  A  K  T

2351  AAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGGGTGGTCAGCGTCC
        K  P  R  E  E  Q  Y  N  S  T  Y  R  V  V  S  V  L

2401  TCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAG
        T  V  L  H  Q  D  W  L  N  G  K  E  Y  K  C  K

2451  GTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGC
      V  S  N  K  A  L  P  A  P  I  E  K  T  I  S  K  A

2501  CAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGG
        K  G  Q  P  R  E  P  Q  V  Y  T  L  P  P  S  R  E

2551  AGGAGATGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTC
        E  M  T  K  N  Q  V  S  L  T  C  L  V  K  G  F

2601  TATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAA
      Y  P  S  D  I  A  V  E  W  E  S  N  G  Q  P  E  N

2651  CAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCC
```

FIG.50 continued

```
          N  Y  K  T  T  P  P  V  L  D  S  D  G  S  F  F  L

2701  TCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTC
        Y  S  K  L  T  V  D  K  S  R  W  Q  Q  G  N  V

2751  TTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAA
      F  S  C  S  V  M  H  E  A  L  H  N  H  Y  T  Q  K
                                                  Nhe/Xba
2801  GAGCCTCTCCCTGTCTCCGGGTAAATGAGCTAGAAACTAACTAAGCTAGC
       S  L  S  L  S  P  G  K  *
2851  AACGGTTTCCCTCTAGCGGGATCAATTCCGCCCCCCCCCCCTAACGTTAC

2901  TGGCCGAAGCCGCTTGGAATAAGGCCGGTGTGCGTTTGTCTATATGTTAT

2951  TTTCCACCATATTGCCGTCTTTTGGCAATGTGAGGGCCCGGAAACCTGGC

3001  CCTGTCTTCTTGACGAGCATTCCTAGGGGTCTTTCCCCTCTCGCCAAAGG

3051  AATGCAAGGTCTGTTGAATGTCGTGAAGGAAGCAGTTCCTCTGGAAGCTT

3101  CTTGAAGACAAACAACGTCTGTAGCGACCCTTTGCAGGCAGCGGAACCCC

3151  CCACCTGGCGACAGGTGCCTCTGCGGCCAAAAGCCACGTGTATAAGATAC

3201  ACCTGCAAAGGCGGCACAACCCCAGTGCCACGTTGTGAGTTGGATAGTTG

3251  TGGAAAGAGTCAAATGGCTCTCCTCAAGCGTATTCAACAAGGGGCTGAAG

3301  GATGCCCAGAAGGTACCCCATTGTATGGGATCTGATCTGGGGCCTCGGTG

3351  CACATGCTTTACGTGTGTTTAGTCGAGGTTAAAAAACGTCTAGGCCCCCC

3401  GAACCACGGGGACGTGGTTTTCCTTTGAAAAACACGATAATACCATGGTT

3451  CGACCATTGAACTGCATCGTCGCCGTGTCCCAAAATATGGGGATTGGCAA

3501  GAACGGAGACCTACCCTGGCCTCCGCTCAGGAACGAGTTCAAGTACTTCC

3551  AAAGAATGACCACAACCTCTTCAGTGGAAGGTAAACAGAATCTGGTGATT

3601  ATGGGTAGGAAAACCTGGTTCTCCATTCCTGAGAAGAATCGACCTTTAAA

3651  GGACAGAATTAATGGTTCGATATAGTTCTCAGTAGAGAACTCAAAGAACC

3701  ACCACGAGGAGCTCATTTTCTTGCCAAAAGTTTGGATGATGCCTTAAGAC

3751  TTATTGAACAACCGGAATTGGCAAGTAAAGTAGACATGGTTTGGATAGTC
```

FIG.50 continued

```
3801   GGAGGCAGTTCTGTTTACCAGGAAGCCATGAATCAACCAGGCCACCTCAG

3851   ACTCTTTGTGACAAGGATCATGCAGGAATTTGAAAGTGACACGTTTTTCC

3901   CAGAAATTGATTTGGGGAAATATAAACTTCTCCCAGAATACCCAGGCGTC

3951   CTCTCTGAGGTCCAGGAGGAAAAAGGCATCAAGTATAAGTTTGAAGTCTA

4001   CGAGAAGAAAGACTAACAGGAAGATGCTTTCAAGTTCTCTGCTCCCCTCC
                                                    Blunt end
SalI/SalI
4051   TAAAGCTATGCATTTTTATAAGACCATGGGACTTTTGCTGGTCGATCGAC

4101   CTGGCGTAATAGCGAAGAGGCCCGCACCGATCGCCCTTCCCAACAGTTGC

4151   GCAGCCTGAATGGCGAATGGGACGCGCCCTGTAGCGGCGCATTAAGCGCG

4201   GCGGGTGTGGTGGTTACGCGCAGCGTGACCGCTACACTTGCCAGCGCCCT

4251   AGCGCCCGCTCCTTTCGCTTTCTTCCCTTCCTTTCTCGCCACGTTCGCCG

4301   GCTTTCCCCGTCAAGCTCTAAATCGGGGGCTCCCTTTAGGGTTCCGATTT

4351   AGTGCTTTACGGCACCTCGACCCCAAAAAACTTGATTAGGGTGATGGTTC

4401   ACGTAGTGGGCCATCGCCCTGATAGACGGTTTTTCGCCTTTGACGTTGGA

4451   GTCCACGTTCTTTAATAGTGGACTCTTGTTCCAAACTGGAACAACACTCA

4501   ACCCTATCTCGGTCTATTTATAAGGGATTTTGCCGATTTCGGCCTATTGG

4551   TTAAAAAATGAGCTGATTTAACAAAATTTAACGCGAATTTTAACAAAATA

4601   TTAACGCTTACAATTTAGGTGGCACTTTTCGGGGAAATGTGCGCGGAACC

4651   CCTATATTTGTTTATTTTTCTAAATACATTCAAATATGTATCCGCTCATG

4701   AGACAATAACCCTGATAAATGCTTCAATAATATTGAAAAAGGAAGAGTAT

4751   GAGTATTCAACATTTCCGTGTCGCCCTTATTCCCTTTTTTGCGGCATTTT

4801   GCCTTACTGTTTTTGCTCACCCAGAAACGCTGGTGAAAGTAAAAGATGCT

4851   GAAGATCAGTTGGGTGCACGAGTGGGTTACATCGAACTGGATCTCAACAG

4901   CGGTAAGATCCTTGAGAGTTTTCGCCCCGAAGAACGTTTTCCAATGATGA
```

FIG.50 continued

```
4951  GCACTTTTAAAGTTCTGCTATGTGGCGCGGTATTATCCCGTATTGACGCC
5001  GGGCAAGAGCAACTCGGTCGCCGCATACACTATTCTCAGAATGACTTGGT
5051  TGAGTACTCACCAGTCACAGAAAAGCATATTACGGATGGCATGACAGTAA
5101  GAGAATTATGCAGTGCTGCCATAACCATGAGTGATAACACTGCGGCCAAC
5151  TTACTTCTGACAACGATCGGAGGACCGAAGGAGCTAACCGCTTTTTTGCA
5201  CAACATGGGGGATCATGTAACTCGCCTTGATCGTTGGGAACCGGAGCTGA
5251  ATGAAGCCATACCAAACGACGAGCGTGACACCACGATGCCTGTAGCAATG
5301  GCAACAACGTTGCGCAAACTATTAACTGGCGAACTACTTACTCTAGCTTC
5351  CCGGCAACAATTAATAGACTGGATGGAGGCGGATAAAGTTGCAGGACCAC
5401  TTCTGCGCTCGGCCCTTCCGGCTGGCTGGTTTATTGCTGATAAATCTGGA
5451  GCCGGTGAGCGTGGGTCTCGCGGTATCATTGCAGCACTGGGGCCAGATGG
5501  TAAGCCCTCCCGTATCGTAGTTATCTACACGACGGGGAGTCAGGCAACTA
5551  TGGATGAACGAAATAGACAGATCGCTGAGATAGGTGCCTCACTGATTAAG
5601  CATTGGTAACTGTCAGACCAAGTTTACTCATATATACTTTAGATTGATTT
5651  AAAACTTCATTTTTAATTTAAAAGGATCTAGGTGAAGATCCTTTTTGATA
5701  ATCTCATGACCAAAATCCCTTAACGTGAGTTTTCGTTCCACTGAGCGTCA
5751  GACCCCGTAGAAAAGATCAAAGGATGTTCTTGAGATCCTTTTTTTCTGCA
5801  CGTAATCTGCTGCTTGCAAACAAAAAACCACCGCTACCAGCGGTGGTTTG
5851  TTTGCCGGATCAAGAGCTACCAACTCTTTTTCCGAAGGTAACTGGCTTCA
5901  GCAGAGCGCAGATACCAAATACTGTCCTTCTAGTGTAGCCGTAGTTAGGC
5951  CACCACTTCAAGAACTCTGTAGCACCGCCTACATACCTCGCTCTGCTAAT
6001  CCTGTTACCAGTGGCTGCTGCCAGTGGCGATAAGTCGTGTCTTACCGGGT
6051  TGGACTCAAGACGATAGTTACCGGATAAGGCGCAGCGGTCGGGCTGAACG
```

FIG.50 continued

```
6101   GGGGGTTCGTGCACACAGCCCAGCTTGGAGCGAACGACCTACACCGAACT
6151   GAGATACCTACAGCGTGAGCTATGAGAAAGCGCCACGCTTCCCGAAGGGA
6201   GAAAGGCGGACAGGTATCCGGTAAGCGGCAGGGTCGGAACAGGAGAGCGC
6251   ACGAGGGAGCTTCCAGGGGGAAACGCCTGGTATCTTTATAGTCCTGTCGG
6301   GTTTCGCCACCTCTGACTTGAGCGTCGATTTTTGTGATGCTCGTCAGGGG
6351   GGCGGAGCCTATGGAAAAACGCCAGCAACGCGGCCTTTTTACGGTTCCTG
6401   GCCTTTTGCTGGCCTTTTGCTCACATGTTCTTTCCTGCGTTATCCCCTGA
6451   TTCTGTGGATAACCGTATTACCGCCTTTGAGTGAGCTGATACCGCTCGCC
6501   GCAGCCGAACGACCGAGCGCAGCGAGTCAGTGAGCGAGGAAGCGGAAGAG
6551   CGCCCAATACGCAAACCGCCTCTCCCCGCGCGTTGGCCGATTCATTAATG
6601   CAGGTATCACGAGGCCCTTTCGTCTTCAC
```

FIG.50 continued

mAb124 VH Chain: Nucleic Acid and Amino Sequences

A. Nucleic Acid Sequence

GATGTGCAGCTTCAGGAGTCGGGACCTAGCCTGGTGAAACCTTCTCAGTCTCTGTCCCTCACCTGCACTGTCACTGGCT
ACTCAATCACCAGTGACTATGCCTGGAACTGGATCCGGCAGTTTCCAGGAAACAAACTGGAGTGGATGGGCTACATAA
GTTACAGTGCTAACACTAGGTACAACCCATCTCTCAAAAGTCGAATCTCTATCACTCGAGACACATCCAAGAACCAATT
CTTCCTGCAGTTGAATTCTGTGACTACTGAGGACACAGCCACATATTACTGTGCAACGGCGGGACGCGGGTTTCCTTAC
TGGGGCCAAGGGACTCTGGTCACTGTCTCTGCA (SEQ ID NO:21)

B. Amino Acid Sequence

DVQLQESGPSLVKPSQSLSLTCTVTGYSITSDYAWNWIRQFPGNKLEWMGYISYSANTRYNPSLKSRISITRDTSKNQFFLQL
CDR1 *CDR2*
NSVTTEDTATYYCATAGRGFPYWGQGTLVTVSA (SEQ ID NO:22)
CDR3

FIG.51

mAb124 VL Chain: Nucleic Acid and Amino Acid Sequences

C. Nucleic Acid Sequence

GACATCCTGATGACCCAATCTCCATCCTCCATGTCTCTATCTCTGGGAGACACAGTCAGTATCACTTGCCATTCAAGTCA
GGACATTAACAGTAATATAGGGTGGTTGCAGCAGAAACCAGGGAAATCATTTAAGGGCCTGATCTATCATGGAACCAA
CTTGGACGATGGAGTTCCATCAAGGTTCAGTGGCAGTGGATCTGGAGCCGATTATTCTCTCACCATCAGCAGCCTGGAA
TCTGAAGATTTTGTAGACTATTACTGTGTACAGTATGGTCAGTTTCCGTGGACGTTCGGTGGAGGCACCAAGCTGGAAA
TCAAACGG (SEQ ID NO:26)

D. Amino Acid Sequence

DILMTQSPSSMSLSLGDTVSITCHSSQDINSNIGWLQQKPGKSFKGLIYHGTNLDDGVPSRFSGSGSGADYSLTISSLESEDFVD
CDR1 *CDR2*

YYCVQYGQFPWTFGGGTKLEIKR (SEQ ID NO:27)
CDR3

FIG.51 continued

mAb1133 VH Chain: Nucleic Acid and Amino Acid Sequences

A. Nucleic Acid Sequence

GATGTGCAGCTTCAGGGGTCGGGACCTAGCCTGGTGAAACCTTCTCAGTCTCTGTCCCTCACCTGCACTGTCACTGGCT
ACTCAATCACCAGTGATTATGCCTGGAACTGGATCCGGCAGTTTCCAGGAAACAAACTGGAGTGGATGGGCTACATAA
GCTACAGTGGTAACACTAGATACAACCCATCTCTCAGAAGTCGAATCTCTATCACTCGAGACACATCCAAGAACCAATT
CTTCCTGCAGTTGAATTCTGTGACTACTGAGGACACAGCCACATATTACTGTGCAACGGCGGGACGCGGATTTCCTTAC
TGGGGCCAAGGGACTCTGGTCACTGTCTCTGCA (SEQ ID NO:31)

B. Amino Acid Sequence

DVQLQGSGPSLVKPSQSLSLTCTVTGYSITSDYAWNWIRQFPGNKLEWMGYISYSGNTRYNPSLRSRISITRDTSKNQFFLQL
CDR1 *CDR2*

NSVTTEDTATYYCATAGRGFPYWGQGTLVTVSA (SEQ ID NO:32)
CDR3

FIG.52

mAb1133 VL Chain: Nucleic Acid and Amino Acid Sequences

C. Nucleic Acid Sequence

GACATCCTGATGACCCAATCTCCATCCTCCATGTCTGTGTCTCTGGGAGACACAGTCAACATCACTTGCCATTCAAGTC
AGGACATTAACAGTAATATAGGGTGGTTGCAGCAGAAACCAGGGAAATCATTTAAGGGCCTGATCTATCATGGAACCA
ACTTGGACGATGGAGTTCCATCAAGGTTCAGTGGCAGTGGATCTGGAGCCGATTATTCTCTCACCATCAGCAGCCTGGA
ATCTGAGGATTTTGCAGACTATTACTGTGTACAGTATGGTCAGTTTCCGTGGACGTTCGGTGGAGGCACCAAGCTGGAA
ATCAAAC (SEQ ID NO:36)

D. Amino Acid Sequence

DILMTQSPSSMSVSLGDTVNITCHSSQDINSNIGWLQQKPGKSFKGLIYHGTNLDDGVPSRFSGSGSGADYSLTISSLESEDFA
CDR1 *CDR2*
DYYCVQYGQFPWTFGGGTKLEIKR (SEQ ID NO:37)
CDR3

FIG.52 continued

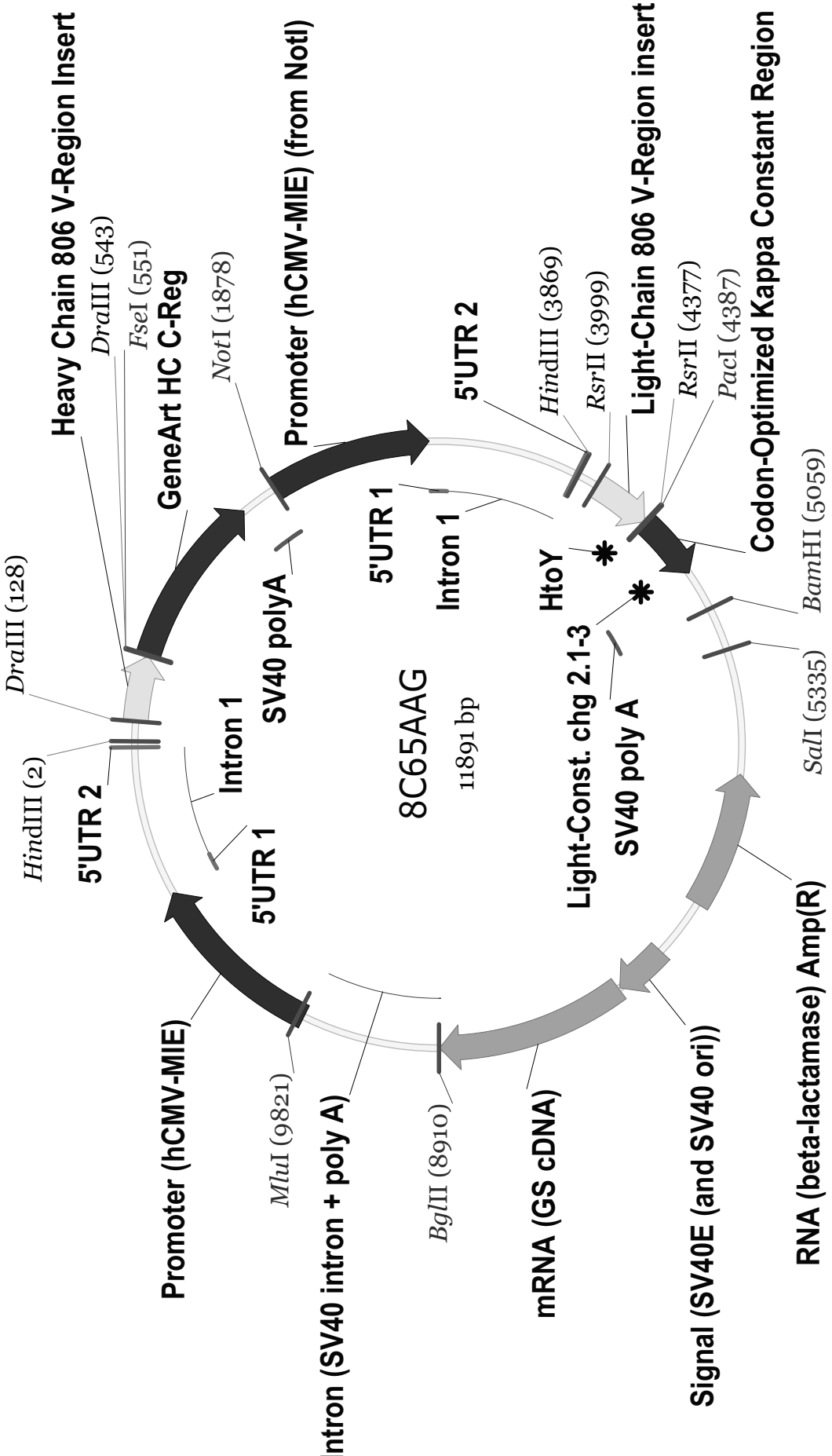

8C65AAG
11891 bp
Heavy Chain 806 V-Region Insert
GeneArt HC C-Reg
Promoter (hCMV-MIE) (from NotI)
5'UTR 2
Intron 1
SV40 polyA
5'UTR 1
Intron 1
HtoY
Light-Const. chg 2.1-3
SV40 poly A
5'UTR 2
Light-Chain 806 V-Region insert
Codon-Optimized Kappa Constant Region
RNA (beta-lactamase) Amp(R)
Signal (SV40E (and SV40 ori))
mRNA (GS cDNA)
Intron (SV40 intron + poly A)
Promoter (hCMV-MIE)
5'UTR 2
Intron 1
5'UTR 1
SV40 polyA
HtoY
Light-Const. chg 2.1-3
SV40 poly A
Light-Chain 806 V-Region insert
Codon-Optimized Kappa Constant Region
RNA (beta-lactamase) Amp(R)
Signal (SV40E (and SV40 ori))
mRNA (GS cDNA)
Intron (SV40 intron + poly A)
Promoter (hCMV-MIE)
HindIII (2)
DraIII (128)
DraIII (543)
FseI (551)
NotI (1878)
HindIII (3869)
RsrII (3999)
RsrII (4377)
PacI (4387)
BamHI (5059)
SalI (5335)
MluI (9821)
BglII (8910)

FIG.53

FIG. 54

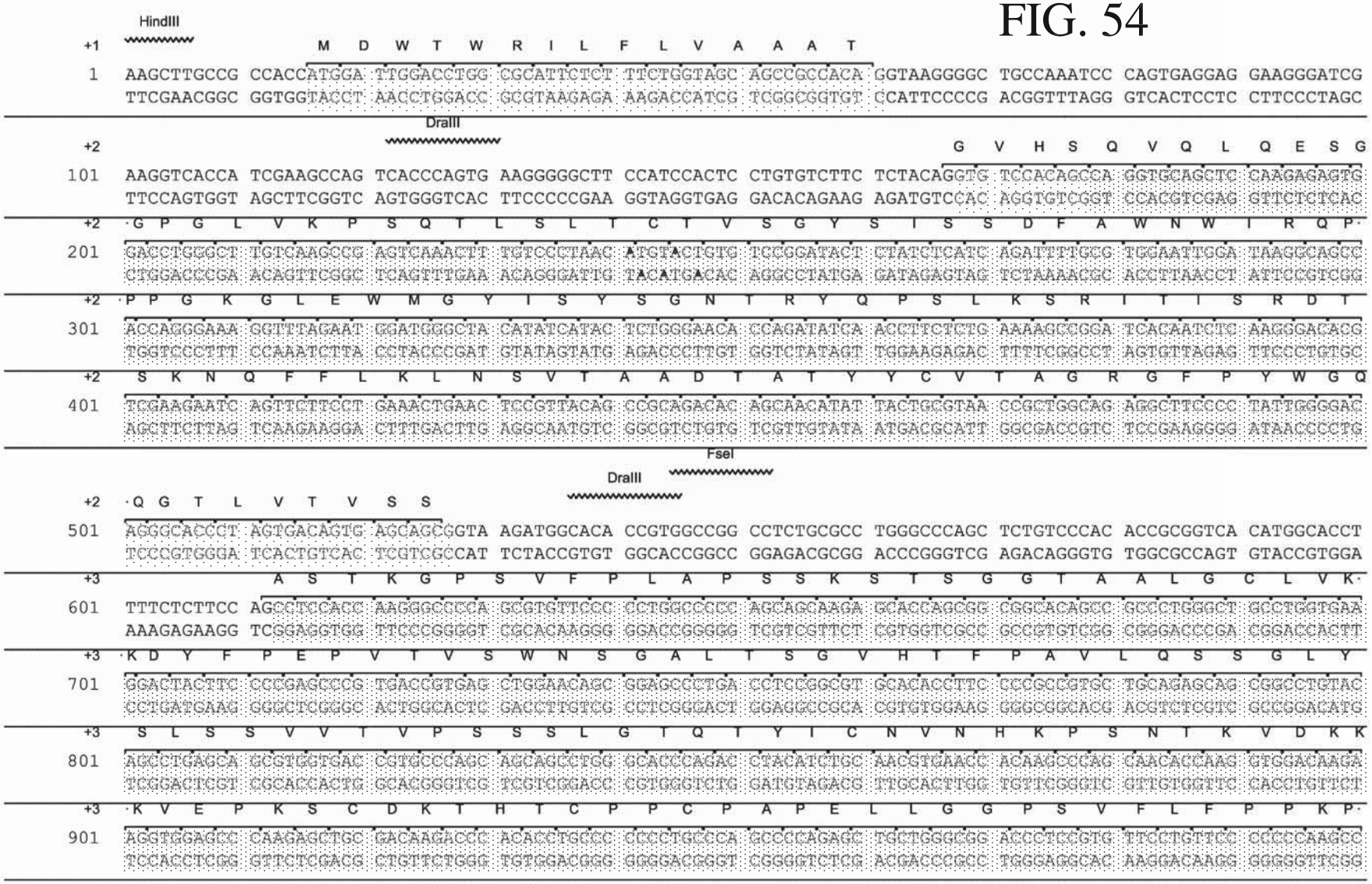


FIG. 54
continued

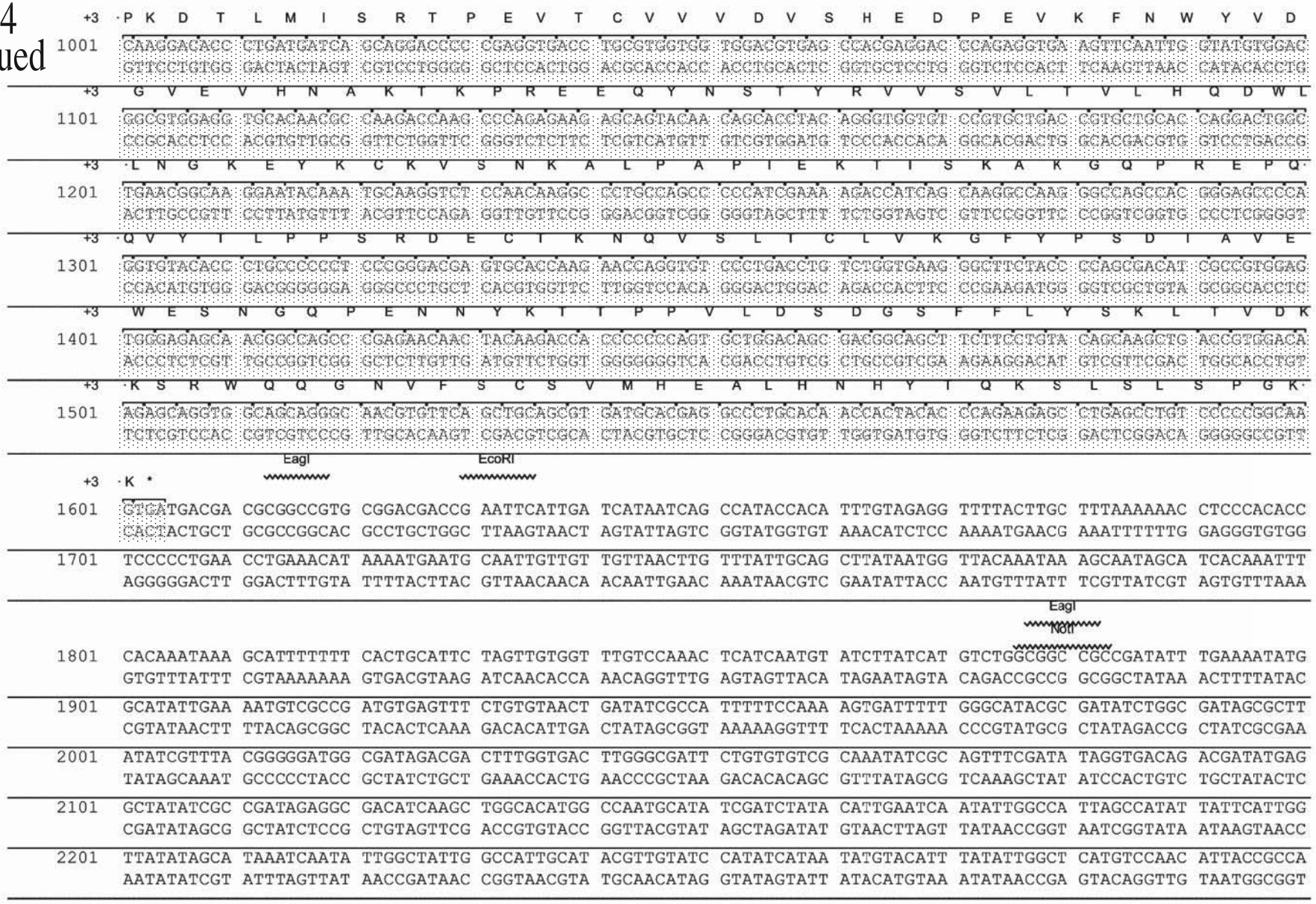


FIG. 54 continued

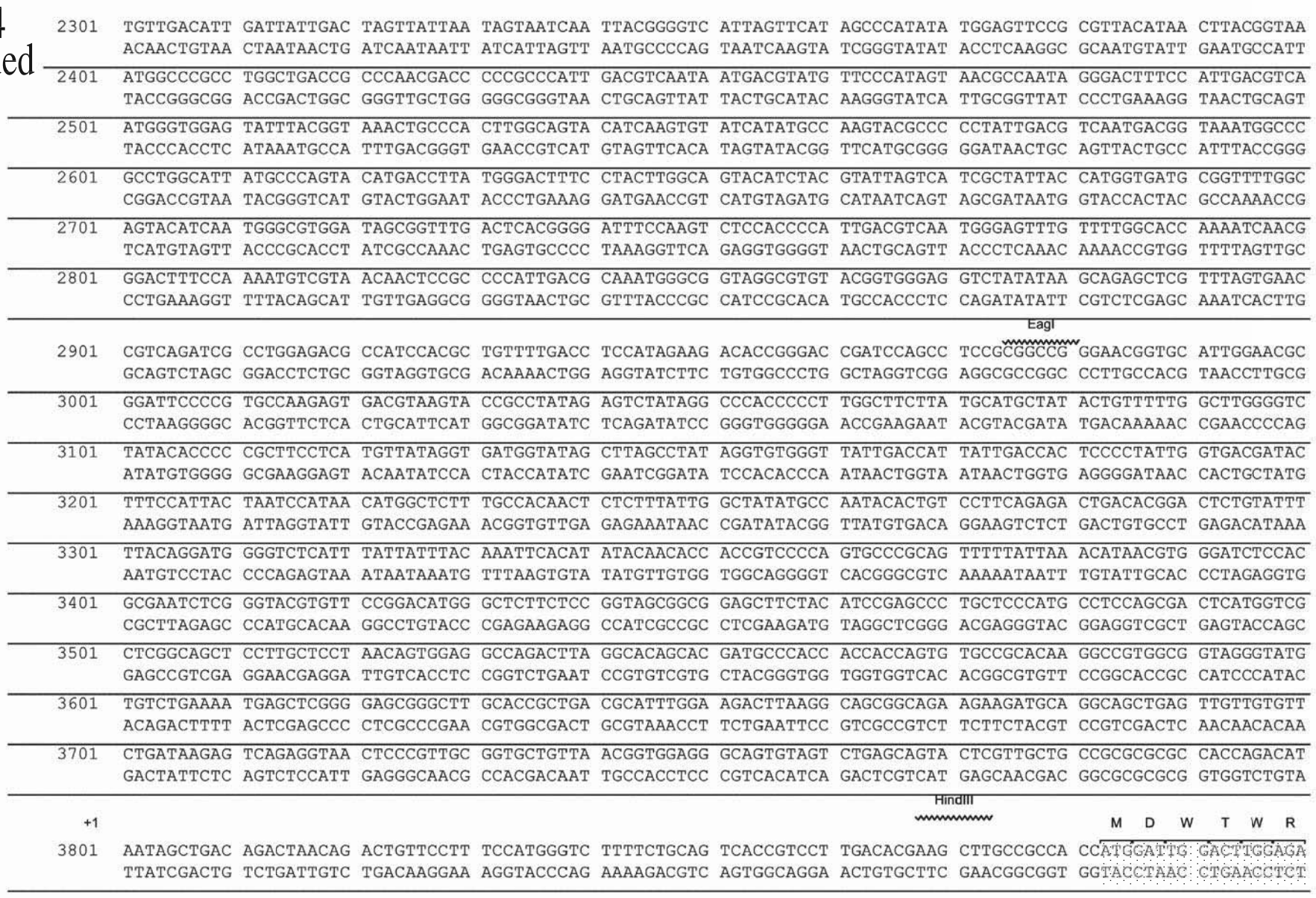


FIG. 54
continued

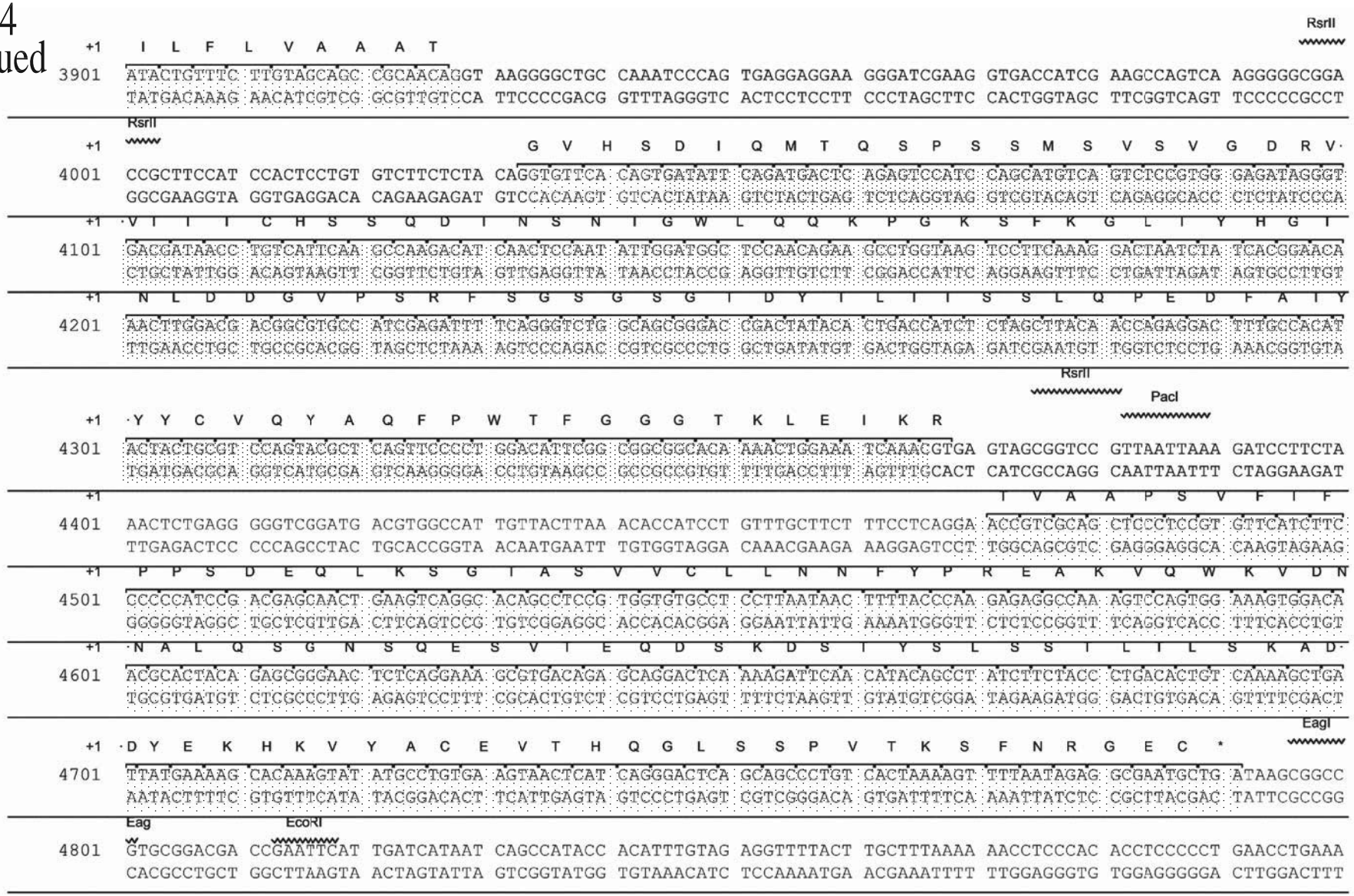


FIG. 54
continued

```
4901  CATAAAATGA ATGCAATTGT TGTTGTTAAC TTGTTTATTG CAGCTTATAA TGGTTACAAA TAAAGCAATA GCATCACAAA TTTCACAAAT AAAGCATTTT
      GTATTTTACT TACGTTAACA ACAACAATTG AACAAATAAC GTCGAATATT ACCAATGTTT ATTTCGTTAT CGTAGTGTTT AAAGTGTTTA TTTCGTAAAA

                                                                                    BamHI
5001  TTTCACTGCA TTCTAGTTGT GGTTTGTCCA AACTCATCAA TGTATCTTAT CATGTCTGGA TCCTCTACGC CGGACGCATC GTGGCCGGCA TCACCGGCGC
      AAAGTGACGT AAGATCAACA CCAAACAGGT TTGAGTAGTT ACATAGAATA GTACAGACCT AGGAGATGCG GCCTGCGTAG CACCGGCCGT AGTGGCCGCG

5101  CACAGGTGCG GTTGCTGGCG CCTATATCGC CGACATCACC GATGGGGAAG ATCGGGCTCG CCACTTCGGG CTCATGAGCG CTTGTTTCGG CGTGGGTATG
      GTGTCCACGC CAACGACCGC GGATATAGCG GCTGTAGTGG CTACCCCTTC TAGCCCGAGC GGTGAAGCCC GAGTACTCGC GAACAAAGCC GCACCCATAC

5201  GTGGCAGGCC CCGTGGCCGG GGGACTGTTG GGCGCCATCT CCTTGCATGC ACCATTCCTT GCGGCGGCGG TGCTCAACGG CCTCAACCTA CTACTGGGCT
      CACCGTCCGG GGCACCGGCC CCCTGACAAC CCGCGGTAGA GGAACGTACG TGGTAAGGAA CGCCGCCGCC ACGAGTTGCC GGAGTTGGAT GATGACCCGA

                                                SalI
5301  GCTTCCTAAT GCAGGAGTCG CATAAGGGAG AGCGTCGACC TCGGGCCGCG TTGCTGGCGT TTTTCCATAG GCTCCGCCCC CCTGACGAGC ATCACAAAAA
      CGAAGGATTA CGTCCTCAGC GTATTCCCTC TCGCAGCTGG AGCCCGGCGC AACGACCGCA AAAAGGTATC CGAGGCGGGG GGACTGCTCG TAGTGTTTTT

5401  TCGACGCTCA AGTCAGAGGT GGCGAAACCC GACAGGACTA TAAAGATACC AGGCGTTTCC CCCTGGAAGC TCCCTCGTGC GCTCTCCTGT TCCGACCCTG
      AGCTGCGAGT TCAGTCTCCA CCGCTTTGGG CTGTCCTGAT ATTTCTATGG TCCGCAAAGG GGGACCTTCG AGGGAGCACG CGAGAGGACA AGGCTGGGAC

5501  CCGCTTACCG GATACCTGTC CGCCTTTCTC CCTTCGGGAA GCGTGGCGCT TTCTCATAGC TCACGCTGTA GGTATCTCAG TTCGGTGTAG GTCGTTCGCT
      GGCGAATGGC CTATGGACAG GCGGAAAGAG GGAAGCCCTT CGCACCGCGA AAGAGTATCG AGTGCGACAT CCATAGAGTC AAGCCACATC CAGCAAGCGA

5601  CCAAGCTGGG CTGTGTGCAC GAACCCCCCG TTCAGCCCGA CCGCTGCGCC TTATCCGGTA ACTATCGTCT TGAGTCCAAC CCGGTAAGAC ACGACTTATC
      GGTTCGACCC GACACACGTG CTTGGGGGGC AAGTCGGGCT GGCGACGCGG AATAGGCCAT TGATAGCAGA ACTCAGGTTG GGCCATTCTG TGCTGAATAG

5701  GCCACTGGCA GCAGCCACTG GTAACAGGAT TAGCAGAGCG AGGTATGTAG GCGGTGCTAC AGAGTTCTTG AAGTGGTGGC CTAACTACGG CTACACTAGA
      CGGTGACCGT CGTCGGTGAC CATTGTCCTA ATCGTCTCGC TCCATACATC CGCCACGATG TCTCAAGAAC TTCACCACCG GATTGATGCC GATGTGATCT

5801  AGAACAGTAT TTGGTATCTG CGCTCTGCTG AAGCCAGTTA CCTTCGGAAA AAGAGTTGGT AGCTCTTGAT CCGGCAAACA AACCACCGCT GGTAGCGGTG
      TCTTGTCATA AACCATAGAC GCGAGACGAC TTCGGTCAAT GGAAGCCTTT TTCTCAACCA TCGAGAACTA GGCCGTTTGT TTGGTGGCGA CCATCGCCAC

5901  GTTTTTTTGT TTGCAAGCAG CAGATTACGC GCAGAAAAAA AGGATCTCAA GAAGATCCTT TGATCTTTTC TACGGGGTCT GACGCTCAGT GGAACGAAAA
      CAAAAAAACA AACGTTCGTC GTCTAATGCG CGTCTTTTTT TCCTAGAGTT CTTCTAGGAA ACTAGAAAAG ATGCCCCAGA CTGCGAGTCA CCTTGCTTTT

6001  CTCACGTTAA GGGATTTTGG TCATGAGATT ATCAAAAAGG ATCTTCACCT AGATCCTTTT AAATTAAAAA TGAAGTTTTA AATCAATCTA AAGTATATAT
      GAGTGCAATT CCCTAAAACC AGTACTCTAA TAGTTTTTCC TAGAAGTGGA TCTAGGAAAA TTTAATTTTT ACTTCAAAAT TTAGTTAGAT TTCATATATA

6101  GAGTAAACTT GGTCTGACAG TTACCAATGC TTAATCAGTG AGGCACCTAT CTCAGCGATC TGTCTATTTC GTTCATCCAT AGTTGCCTGA CTCCCCGTCG
      CTCATTTGAA CCAGACTGTC AATGGTTACG AATTAGTCAC TCCGTGGATA GAGTCGCTAG ACAGATAAAG CAAGTAGGTA TCAACGGACT GAGGGGCAGC

6201  TGTAGATAAC TACGATACGG GAGGGCTTAC CATCTGGCCC CAGTGCTGCA ATGATACCGC GAGACCCACG CTCACCGGCT CCAGATTTAT CAGCAATAAA
      ACATCTATTG ATGCTATGCC CTCCCGAATG GTAGACCGGG GTCACGACGT TACTATGGCG CTCTGGGTGC GAGTGGCCGA GGTCTAAATA GTCGTTATTT

6301  CCAGCCAGCC GGAAGGGCCG AGCGCAGAAG TGGTCCTGCA ACTTTATCCG CCTCCATCCA GTCTATTAAT TGTTGCCGGG AAGCTAGAGT AAGTAGTTCG
      GGTCGGTCGG CCTTCCCGGC TCGCGTCTTC ACCAGGACGT TGAAATAGGC GGAGGTAGGT CAGATAATTA ACAACGGCCC TTCGATCTCA TTCATCAAGC

6401  CCAGTTAATA GTTTGCGCAA CGTTGTTGCC ATTGCTACAG GCATCGTGGT GTCACGCTCG TCGTTTGGTA TGGCTTCATT CAGCTCCGGT TCCCAACGAT
      GGTCAATTAT CAAACGCGTT GCAACAACGG TAACGATGTC CGTAGCACCA CAGTGCGAGC AGCAAACCAT ACCGAAGTAA GTCGAGGCCA AGGGTTGCTA
```

FIG. 54
continued

```
6501  CAAGGCGAGT TACATGATCC CCCATGTTGT GCAAAAAAGC GGTTAGCTCC TTCGGTCCTC CGATCGTTGT CAGAAGTAAG TTGGCCGCAG TGTTATCACT
      GTTCCGCTCA ATGTACTAGG GGGTACAACA CGTTTTTTCG CCAATCGAGG AAGCCAGGAG GCTAGCAACA GTCTTCATTC AACCGGCGTC ACAATAGTGA

6601  CATGGTTATG GCAGCACTGC ATAATTCTCT TACTGTCATG CCATCCGTAA GATGCTTTTC TGTGACTGGT GAGTACTCAA CCAAGTCATT CTGAGAATAG
      GTACCAATAC CGTCGTGACG TATTAAGAGA ATGACAGTAC GGTAGGCATT CTACGAAAAG ACACTGACCA CTCATGAGTT GGTTCAGTAA GACTCTTATC

6701  TGTATGCGGC GACCGAGTTG CTCTTGCCCG GCGTCAATAC GGGATAATAC CGCGCCACAT AGCAGAACTT TAAAAGTGCT CATCATTGGA AAACGTTCTT
      ACATACGCCG CTGGCTCAAC GAGAACGGGC CGCAGTTATG CCCTATTATG GCGCGGTGTA TCGTCTTGAA ATTTTCACGA GTAGTAACCT TTTGCAAGAA

6801  CGGGGCGAAA ACTCTCAAGG ATCTTACCGC TGTTGAGATC CAGTTCGATG TAACCCACTC GTGCACCCAA CTGATCTTCA GCATCTTTTA CTTTCACCAG
      GCCCCGCTTT TGAGAGTTCC TAGAATGGCG ACAACTCTAG GTCAAGCTAC ATTGGGTGAG CACGTGGGTT GACTAGAAGT CGTAGAAAAT GAAAGTGGTC

6901  CGTTTCTGGG TGAGCAAAAA CAGGAAGGCA AAATGCCGCA AAAAAGGGAA TAAGGGCGAC ACGGAAATGT TGAATACTCA TACTCTTCCT TTTTCAATAT
      GCAAAGACCC ACTCGTTTTT GTCCTTCCGT TTTACGGCGT TTTTTCCCTT ATTCCCGCTG TGCCTTTACA ACTTATGAGT ATGAGAAGGA AAAAGTTATA

7001  TATTGAAGCA TTTATCAGGG TTATTGTCTC ATGAGCGGAT ACATATTTGA ATGTATTTAG AAAAATAAAC AAATAGGGGT TCCGCGCACA TTTCCCCGAA
      ATAACTTCGT AAATAGTCCC AATAACAGAG TACTCGCCTA TGTATAAACT TACATAAATC TTTTTATTTG TTTATCCCCA AGGCGCGTGT AAAGGGGCTT

7101  AAGTGCCACC TGACGTCTAA GAAACCATTA TTATCATGAC ATTAACCTAT AAAAATAGGC GTATCACGAG GCCCTGATGG CTCTTTGCGG CACCCATCGT
      TTCACGGTGG ACTGCAGATT CTTTGGTAAT AATAGTACTG TAATTGGATA TTTTTATCCG CATAGTGCTC CGGGACTACC GAGAAACGCC GTGGGTAGCA

7201  TCGTAATGTT CCGTGGCACC GAGGACAACC CTCAAGAGAA AATGTAATCA CACTGGCTCA CCTTCGGGTG GGCCTTTCTG CGTTTATAAG GAGACACTTT
      AGCATTACAA GGCACCGTGG CTCCTGTTGG GAGTTCTCTT TTACATTAGT GTGACCGAGT GGAAGCCCAC CCGGAAAGAC GCAAATATTC CTCTGTGAAA

7301  ATGTTTAAGA AGGTTGGTAA ATTCCTTGCG GCTTTGGCAG CCAAGCTAGA TCCGGCTGTG GAATGTGTGT CAGTTAGGGT GTGGAAAGTC CCCAGGCTCC
      TACAAATTCT TCCAACCATT TAAGGAACGC CGAAACCGTC GGTTCGATCT AGGCCGACAC CTTACACACA GTCAATCCCA CACCTTTCAG GGGTCCGAGG

7401  CCAGCAGGCA GAAGTATGCA AAGCATGCAT CTCAATTAGT CAGCAACCAG GTGTGGAAAG TCCCCAGGCT CCCCAGCAGG CAGAAGTATG CAAAGCATGC
      GGTCGTCCGT CTTCATACGT TTCGTACGTA GAGTTAATCA GTCGTTGGTC CACACCTTTC AGGGGTCCGA GGGGTCGTCC GTCTTCATAC GTTTCGTACG

7501  ATCTCAATTA GTCAGCAACC ATAGTCCCGC CCCTAACTCC GCCCATCCCG CCCCTAACTC CGCCCAGTTC CGCCCATTCT CCGCCCCATG GCTGACTAAT
      TAGAGTTAAT CAGTCGTTGG TATCAGGGCG GGGATTGAGG CGGGTAGGGC GGGGATTGAG GCGGGTCAAG GCGGGTAAGA GGCGGGGTAC CGACTGATTA

7601  TTTTTTTATT TATGCAGAGG CCGAGGCCGC CTCGGCCTCT GAGCTATTCC AGAAGTAGTG AGGAGGCTTT TTTGGAGGCC TAGGCTTTTG CAAAAAGCTA
      AAAAAAATAA ATACGTCTCC GGCTCCGGCG GAGCCGGAGA CTCGATAAGG TCTTCATCAC TCCTCCGAAA AAACCTCCGG ATCCGAAAAC GTTTTTCGAT

7701  GCTTGGGGCC ACCGCTCAGA GCACCTTCCA CCATGGCCAC CTCAGCAAGT TCCCACTTGA ACAAAAACAT CAAGCAAATG TACTTGTGCC TGCCCCAGGG
      CGAACCCCGG TGGCGAGTCT CGTGGAAGGT GGTACCGGTG GAGTCGTTCA AGGGTGAACT TGTTTTTGTA GTTCGTTTAC ATGAACACGG ACGGGGTCCC

7801  TGAGAAAGTC CAAGCCATGT ATATCTGGGT TGATGGTACT GGAGAAGGAC TGCGCTGCAA AACCCGCACC CTGGACTGTG AGCCCAAGTG TGTAGAAGAG
      ACTCTTTCAG GTTCGGTACA TATAGACCCA ACTACCATGA CCTCTTCCTG ACGCGACGTT TTGGGCGTGG GACCTGACAC TCGGGTTCAC ACATCTTCTC

7901  TTACCTGAGT GGAATTTTGA TGGCTCTAGT ACCTTTCAGT CTGAGGGCTC CAACAGTGAC ATGTATCTCA GCCCTGTTGC CATGTTTCGG GACCCCTTCC
      AATGGACTCA CCTTAAAACT ACCGAGATCA TGGAAAGTCA GACTCCCGAG GTTGTCACTG TACATAGAGT CGGGACAACG GTACAAAGCC CTGGGGAAGG

8001  GCAGAGATCC CAACAAGCTG GTGTTCTGTG AAGTTTTCAA GTACAACCGG AAGCCTGCAG AGACCAATTT AAGGCACTCG TGTAAACGGA TAATGGACAT
      CGTCTCTAGG GTTGTTCGAC CACAAGACAC TTCAAAAGTT CATGTTGGCC TTCGGACGTC TCTGGTTAAA TTCCGTGAGC ACATTTGCCT ATTACCTGTA

8101  GGTGAGCAAC CAGCACCCCT GGTTTGGAAT GGAACAGGAG TATACTCTGA TGGGAACAGA TGGGCACCCT TTTGGTTGGC CTTCCAATGG CTTTCCTGGG
      CCACTCGTTG GTCGTGGGGA CCAAACCTTA CCTTGTCCTC ATATGAGACT ACCCTTGTCT ACCCGTGGGA AAACCAACCG GAAGGTTACC GAAAGGACCC
```

FIG. 54
continued

```
8201  CCCCAAGGTC CGTATTACTG TGGTGTGGGC GCAGACAAAG CCTATGGCAG GGATATCGTG GAGGCTCACT ACCGCGCCTG CTTGTATGCT GGGGTCAAGA
      GGGGTTCCAG GCATAATGAC ACCACACCCG CGTCTGTTTC GGATACCGTC CCTATAGCAC CTCCGAGTGA TGGCGCGGAC GAACATACGA CCCCAGTTCT

8301  TTACAGGAAC AAATGCTGAG GTCATGCCTG CCCAGTGGGA ACTCCAAATA GGACCCTGTG AAGGAATCCG CATGGGAGAT CATCTCTGGG TGGCCCGTTT
      AATGTCCTTG TTTACGACTC CAGTACGGAC GGGTCACCCT TGAGGTTTAT CCTGGGACAC TTCCTTAGGC GTACCCTCTA GTAGAGACCC ACCGGGCAAA

8401  CATCTTGCAT CGAGTATGTG AAGACTTTGG GGTAATAGCA ACCTTTGACC CCAAGCCCAT TCCTGGGAAC TGGAATGGTG CAGGCTGCCA TACCAACTTT
      GTAGAACGTA GCTCATACAC TTCTGAAACC CCATTATCGT TGGAAACTGG GGTTCGGGTA AGGACCCTTG ACCTTACCAC GTCCGACGGT ATGGTTGAAA

8501  AGCACCAAGG CCATGCGGGA GGAGAATGGT CTGAAGCACA TCGAGGAGGC CATCGAGAAA CTAAGCAAGC GGCACCGGTA CCACATTCGA GCCTACGATC
      TCGTGGTTCC GGTACGCCCT CCTCTTACCA GACTTCGTGT AGCTCCTCCG GTAGCTCTTT GATTCGTTCG CCGTGGCCAT GGTGTAAGCT CGGATGCTAG

8601  CCAAGGGGGG CCTGGACAAT GCCCGTGGTC TGACTGGGTT CCACGAAACG TCCAACATCA ACGACTTTTC TGCTGGTGTC GCCAATCGCA GTGCCAGCAT
      GGTTCCCCCC GGACCTGTTA CGGGCACCAG ACTGACCCAA GGTGCTTTGC AGGTTGTAGT TGCTGAAAAG ACGACCACAG CGGTTAGCGT CACGGTCGTA

8701  CCGCATTCCC CGGACTGTCG GCCAGGAGAA GAAAGGTTAC TTTGAAGACC GCGGCCCCTC TGCCAATTGT GACCCCTTTG CAGTGACAGA AGCCATCGTC
      GGCGTAAGGG GCCTGACAGC CGGTCCTCTT CTTTCCAATG AAACTTCTGG CGCCGGGGAG ACGGTTAACA CTGGGGAAAC GTCACTGTCT TCGGTAGCAG

8801  CGCACATGCC TTCTCAATGA GACTGGCGAC GAGCCCTTCC AATACAAAAA CTAATTAGAC TTTGAGTGAT CTTGAGCCTT TCCTAGTTCA TCCCACCCCG
      GCGTGTACGG AAGAGTTACT CTGACCGCTG CTCGGGAAGG TTATGTTTTT GATTAATCTG AAACTCACTA GAACTCGGAA AGGATCAAGT AGGGTGGGGC

                BglII
8901  CCCCAGAGAG ATCTTTGTGA AGGAACCTTA CTTCTGTGGT GTGACATAAT TGGACAAACT ACCTACAGAG ATTTAAAGCT CTAAGGTAAA TATAAAATTT
      GGGGTCTCTC TAGAAACACT TCCTTGGAAT GAAGACACCA CACTGTATTA ACCTGTTTGA TGGATGTCTC TAAATTTCGA GATTCCATTT ATATTTTAAA

9001  TTAAGTGTAT AATGTGTTAA ACTACTGATT CTAATTGTTT GTGTATTTTA GATTCCAACC TATGGAACTG ATGAATGGGA GCAGTGGTGG AATGCCTTTA
      AATTCACATA TTACACAATT TGATGACTAA GATTAACAAA CACATAAAAT CTAAGGTTGG ATACCTTGAC TACTTACCCT CGTCACCACC TTACGGAAAT

9101  ATGAGGAAAA CCTGTTTTGC TCAGAAGAAA TGCCATCTAG TGATGATGAG GCTACTGCTG ACTCTCAACA TTCTACTCCT CCAAAAAAGA AGAGAAAGGT
      TACTCCTTTT GGACAAAACG AGTCTTCTTT ACGGTAGATC ACTACTACTC CGATGACGAC TGAGAGTTGT AAGATGAGGA GGTTTTTTCT TCTCTTTCCA

9201  AGAAGACCCC AAGGACTTTC CTTCAGAATT GCTAAGTTTT TTGAGTCATG CTGTGTTTAG TAATAGAACT CTTGCTTGCT TTGCTATTTA CACCACAAAG
      TCTTCTGGGG TTCCTGAAAG GAAGTCTTAA CGATTCAAAA AACTCAGTAC GACACAAATC ATTATCTTGA GAACGAACGA AACGATAAAT GTGGTGTTTC

9301  GAAAAAGCTG CACTGCTATA CAAGAAAATT ATGGAAAAAT ATTCTGTAAC CTTTATAAGT AGGCATAACA GTTATAATCA TAACATACTG TTTTTTCTTA
      CTTTTTCGAC GTGACGATAT GTTCTTTTAA TACCTTTTTA TAAGACATTG GAAATATTCA TCCGTATTGT CAATATTAGT ATTGTATGAC AAAAAAGAAT

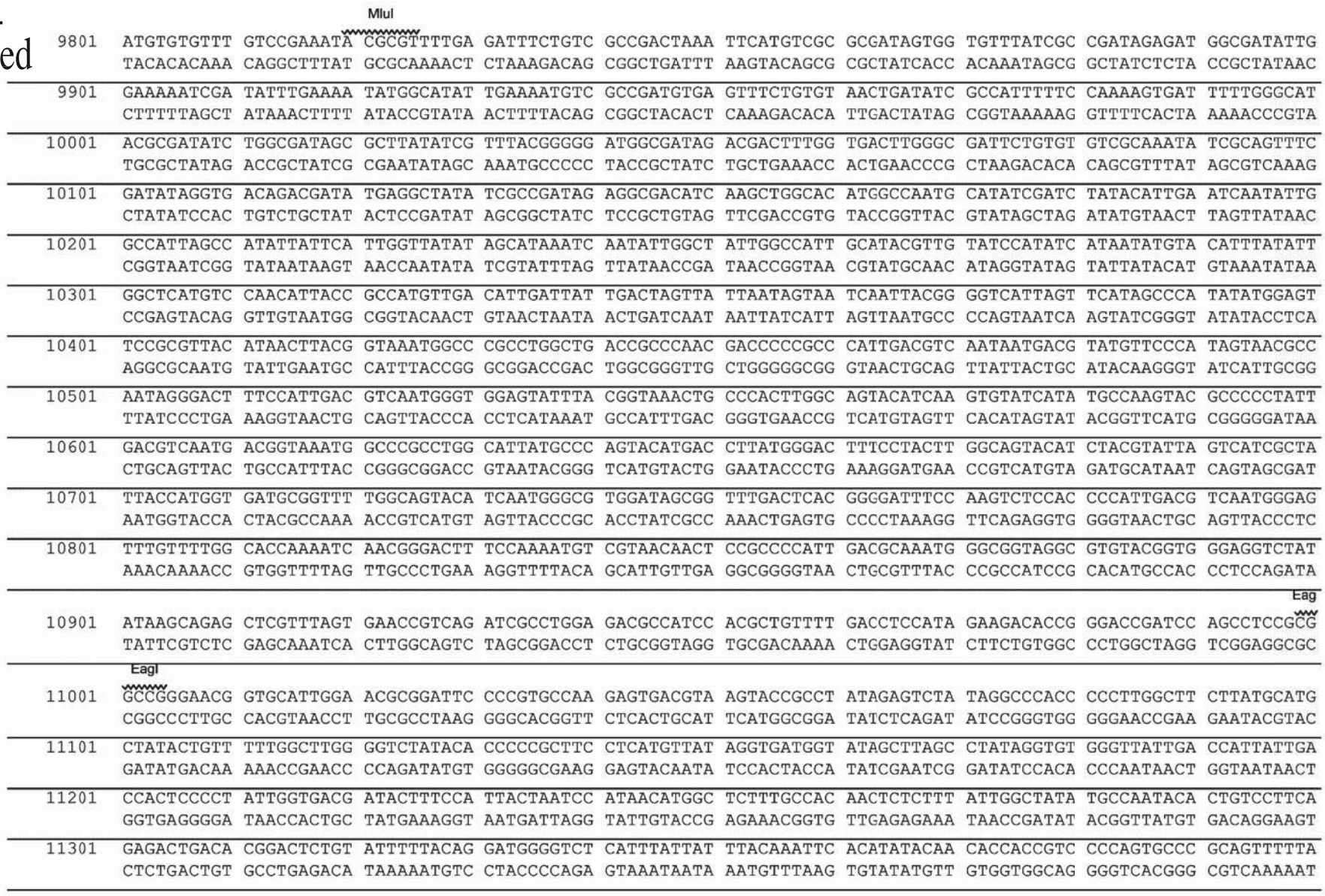
9401  CTCCACACAG GCATAGAGTG TCTGCTATTA ATAACTATGC TCAAAAATTG TGTACCTTTA GCTTTTTAAT TTGTAAAGGG GTTAATAAGG AATATTTGAT
      GAGGTGTGTC CGTATCTCAC AGACGATAAT TATTGATACG AGTTTTTAAC ACATGGAAAT CGAAAAATTA AACATTTCCC CAATTATTCC TTATAAACTA

9501  GTATAGTGCC TTGACTAGAG ATCATAATCA GCCATACCAC ATTTGTAGAG GTTTTACTTG CTTTAAAAAA CCTCCCACAC CTCCCCCTGA ACCTGAAACA
      CATATCACGG AACTGATCTC TAGTATTAGT CGGTATGGTG TAAACATCTC CAAAATGAAC GAAATTTTTT GGAGGGTGTG GAGGGGGACT TGGACTTTGT

9601  TAAAATGAAT GCAATTGTTG TTGTTAACTT GTTTATTGCA GCTTATAATG GTTACAAATA AAGCAATAGC ATCACAAATT TCACAAATAA AGCATTTTTT
      ATTTTACTTA CGTTAACAAC AACAATTGAA CAAATAACGT CGAATATTAC CAATGTTTAT TTCGTTATCG TAGTGTTTAA AGTGTTTATT TCGTAAAAAA

9701  TCACTGCATT CTAGTTGTGG TTTGTCCAAA CTCATCAATG TATCTTATCA TGTCTGGATC TAGCTTCGTG TCAAGGACGG TGACTGCAGT GAATAATAAA
      AGTGACGTAA GATCAACACC AAACAGGTTT GAGTAGTTAC ATAGAATAGT ACAGACCTAG ATCGAAGCAC AGTTCCTGCC ACTGACGTCA CTTATTATTT
```

FIG. 54
continued



```
11401  TTAAACATAA CGTGGGATCT CCACGCGAAT CTCGGGTACG TGTTCCGGAC ATGGGCTCTT CTCCGGTAGC GGCGGAGCTT CTACATCCGA GCCCTGCTCC
       AATTTGTATT GCACCCTAGA GGTGCGCTTA GAGCCCATGC ACAAGGCCTG TACCCGAGAA GAGGCCATCG CCGCCTCGAA GATGTAGGCT CGGGACGAGG

11501  CATGCCTCCA GCGACTCATG GTCGCTCGGC AGCTCCTTGC TCCTAACAGT GGAGGCCAGA CTTAGGCACA GCACGATGCC CACCACCACC AGTGTGCCGC
       GTACGGAGGT CGCTGAGTAC CAGCGAGCCG TCGAGGAACG AGGATTGTCA CCTCCGGTCT GAATCCGTGT CGTGCTACGG GTGGTGGTGG TCACACGGCG

11601  ACAAGGCCGT GGCGGTAGGG TATGTGTCTG AAAATGAGCT CGGGGAGCGG GCTTGCACCG CTGACGCATT TGGAAGACTT AAGGCAGCGG CAGAAGAAGA
       TGTTCCGGCA CCGCCATCCC ATACACAGAC TTTTACTCGA GCCCCTCGCC CGAACGTGGC GACTGCGTAA ACCTTCTGAA TTCCGTCGCC GTCTTCTTCT

11701  TGCAGGCAGC TGAGTTGTTG TGTTCTGATA AGAGTCAGAG GTAACTCCCG TTGCGGTGCT GTTAACGGTG GAGGGCAGTG TAGTCTGAGC AGTACTCGTT
       ACGTCCGTCG ACTCAACAAC ACAAGACTAT TCTCAGTCTC CATTGAGGGC AACGCCACGA CAATTGCCAC CTCCCGTCAC ATCAGACTCG TCATGAGCAA

11801  GCTGCCGCGC GCGCCACCAG ACATAATAGC TGACAGACTA ACAGACTGTT CCTTTCCATG GGTCTTTTCT GCAGTCACCG TCCTTGACAC G
       CGACGGCGCG CGCGGTGGTC TGTATTATCG ACTGTCTGAT TGTCTGACAA GGAAAGGTAC CCAGAAAAGA CGTCAGTGGC AGGAACTGTG C
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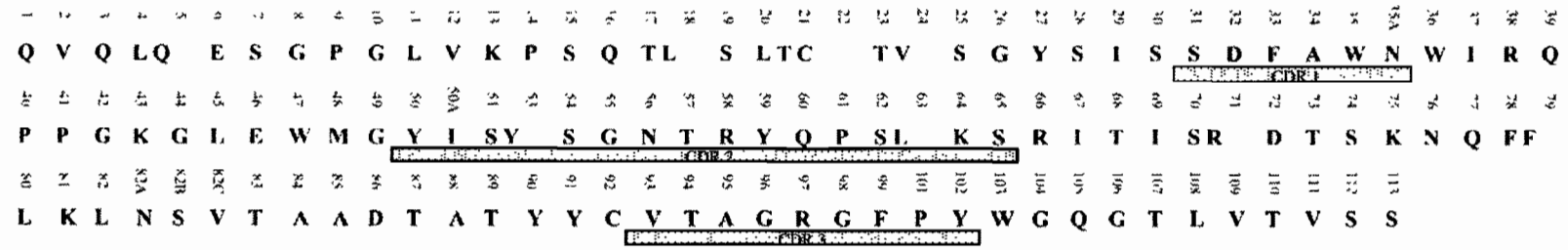
FIG. 54 continued

Heavy Chain

FIG. 55A

Signal **MDWTWRILFLVAAATGVHS**

V_H



C_H

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNV
NHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDECTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain

FIG. 55B

Signal **MDWTWRILFLVAAATGVHS**

V_L



C_L

TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVY
ACEVTHQGLSSPVTKSFNRGEC

Map of Surface-Exposed Residues for Veneering of mAb 806 VH

FIG. 56A

```
mAb 806   Heavy chain  Murine Subgroup VH-I (Homologous to Human Subgroup II)
          *   * ** *  * **      * **              ***              *     **
          * * * ** ** * *** * * * ** * *         ***** *                * *   **
          * * * ** ** ***** * * * ** * *         ***** *            !   * * * * ***    *
mAb 806   DVQLQESGPSLVKPSQTLSLTCTVTGYSITSDFAWNWIRQFPGNKLEWMGYISYSGNTRYNPSLKSRISITRDTSKNQFFLQLN
VH36germ  E                     S   D     Y-     K       Y        S Y                   YY
AAA37941          D      S                GYS H       H         H  S N
CAD26810  E                     S   D    NGF- I   K       Y        S Y                Q   Y

Consensus Q         A             S F  S          P  KA   L                  LT  K       V T
                    G               L                RG   I                  V   V       S K
                    T               G                     M                      R    S  F Q
                                    Y
                                    D

Residues
To change Q         G             S    S          P  KG                     T       S
          QVQLQESGPGLVKPSQTLSLTCTVSGYSISSDFAWNWIRQPPGKGLEWMGYISYSGNTRYQPSLKSRITITRDTSKSQFFLQLN

           *  **                    **
           * ***                    **      **
          ** ***  *                 **  * * **
          SVTIEDTATYYC---VTAGRGFPY---WGQGTLVTVSA
VH36         S       ------------------------
AAA37941     T       ARIYYYGSSYVWFAY
CAD26810     T   G   ACRSYGRTPYYFDF      T    S

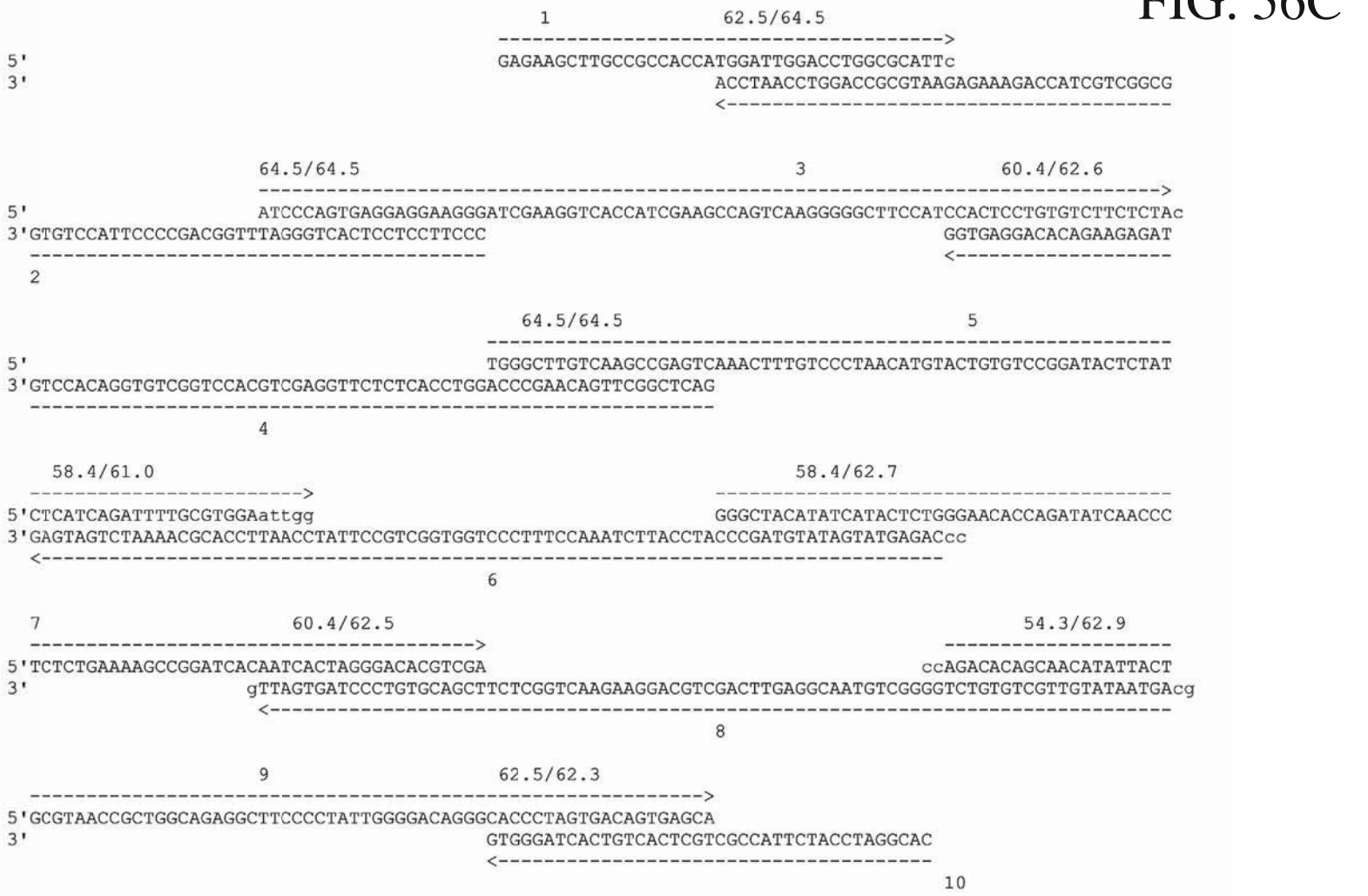
Consensus    PV      AR                        JH1,4,5
             AA
Residues     SE
To change    AP                              S
          SVTAPDTATYYC---VTAGRGFPY---WGQGTLVTVSS
```

FIG. 56B

KEY: CDRs are in RED; ***surface exposed residues (more * indicates greater surface exposure);**
N, potential glycosylation site

Initial Oligonucleotide Overlap Map for Design of Veneered 806 VH

FIG. 56C



KEY: Lower case = add to oligo; Upper case = remove from oligo …this was done to increase the Tm of the overlaps
Oligos used to synthesize the V-region

Map of Surface-Exposed Residues for Veneering of mAb 806 V_L

```
mAb 806   Light chain  Murine Kappa subgroup (Homologous to Human Kappa Subgroup I)
          * *   * **     *                      ***  *           *  *  * ****
          * * * * **   *** *                     ***  *           *  *  * ****
          * * * **** * ***** * *                 ****  *           * **  * ****
mAb 806   DILMTQSPSSMSVSLGDTVSITCHSSQDINSNIGWLQQRPGKSFKGLIYHGTNLDDEVPSRFSGSGSG
CF9germ                          A  G S        K               E G
CAB46157                         A  G S                        E G
AASC1772    Q       V A V  R T   RA  G S WLA Y  K   AP L   DASS QSG

Consensus   Q       L A V  R T              Y  K   AP L          G
                      V P                       S
                      L L                       P

Residues
To change   Q          V  R T                  K                G
          DIQMTQSPSSMSVSVGDRVTITCHSSQDINSNIGWLQQKPGKSFKGLIYHGTNLDDGVPSRFSGSGSG


           *         **                  **    *
          ** *   **  **                  **  * * *
          ** *   ** *** * *             **  * * *
mAb 806   ADYSLTISSLESEDFADYYCVQYAQFPWTFGGGTKLEIK
CF9germ                        Y    -
CAB46157                       Y
AASC1772  T FT      QP    T   Q ANS  L       V

Consensus T FT      QP    T                 V      JL-4
                    E

Residues
To change T  T       P    T
          TDYTLTISSLEPEDFATYYCVQYAQFPWTFGGGTKLEIK
```

KEY : CDRs are in RED

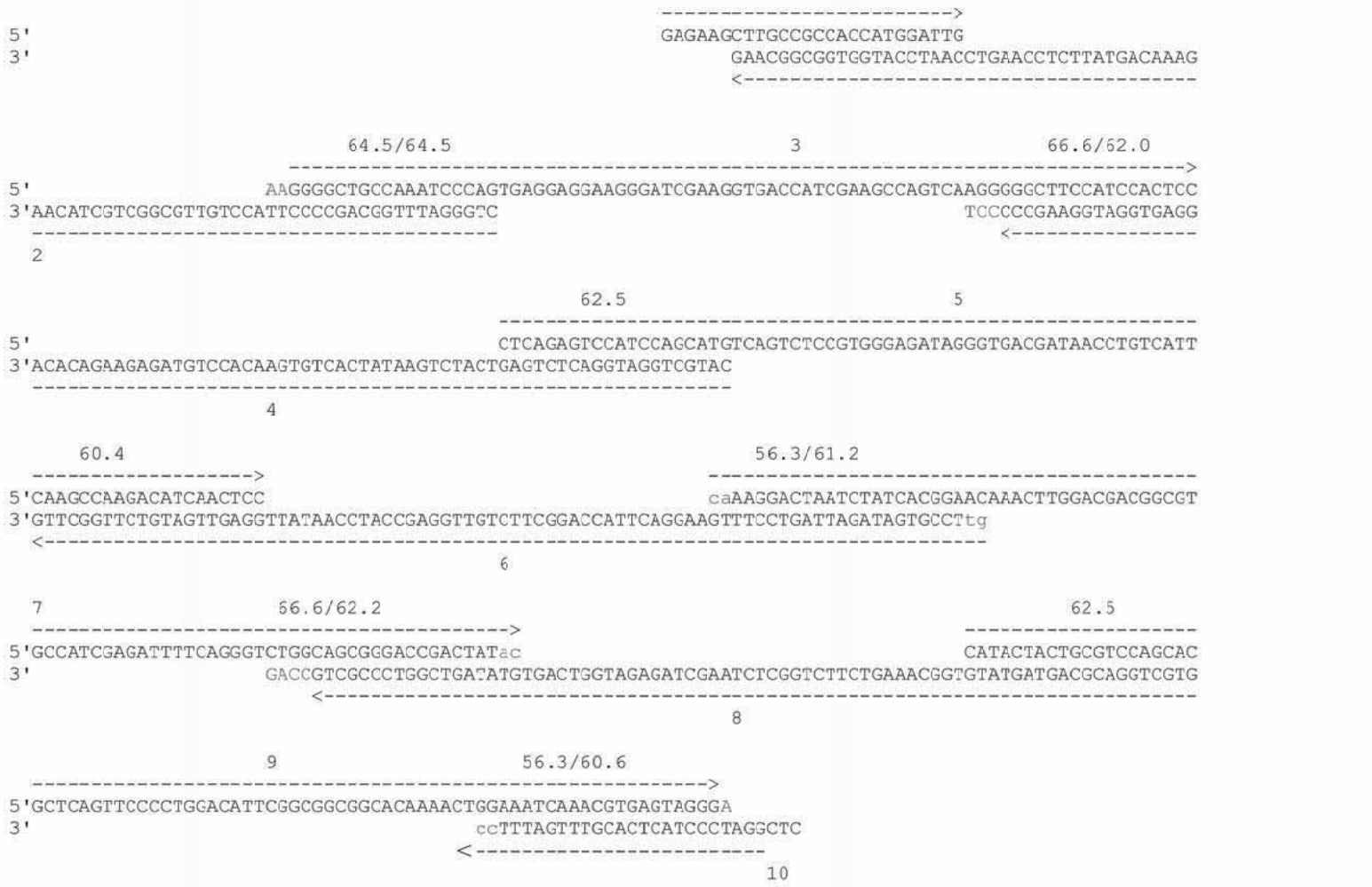
***surface exposed residues (more * indicates greater surface exposure)**

FIG. 57A

FIG. 57B

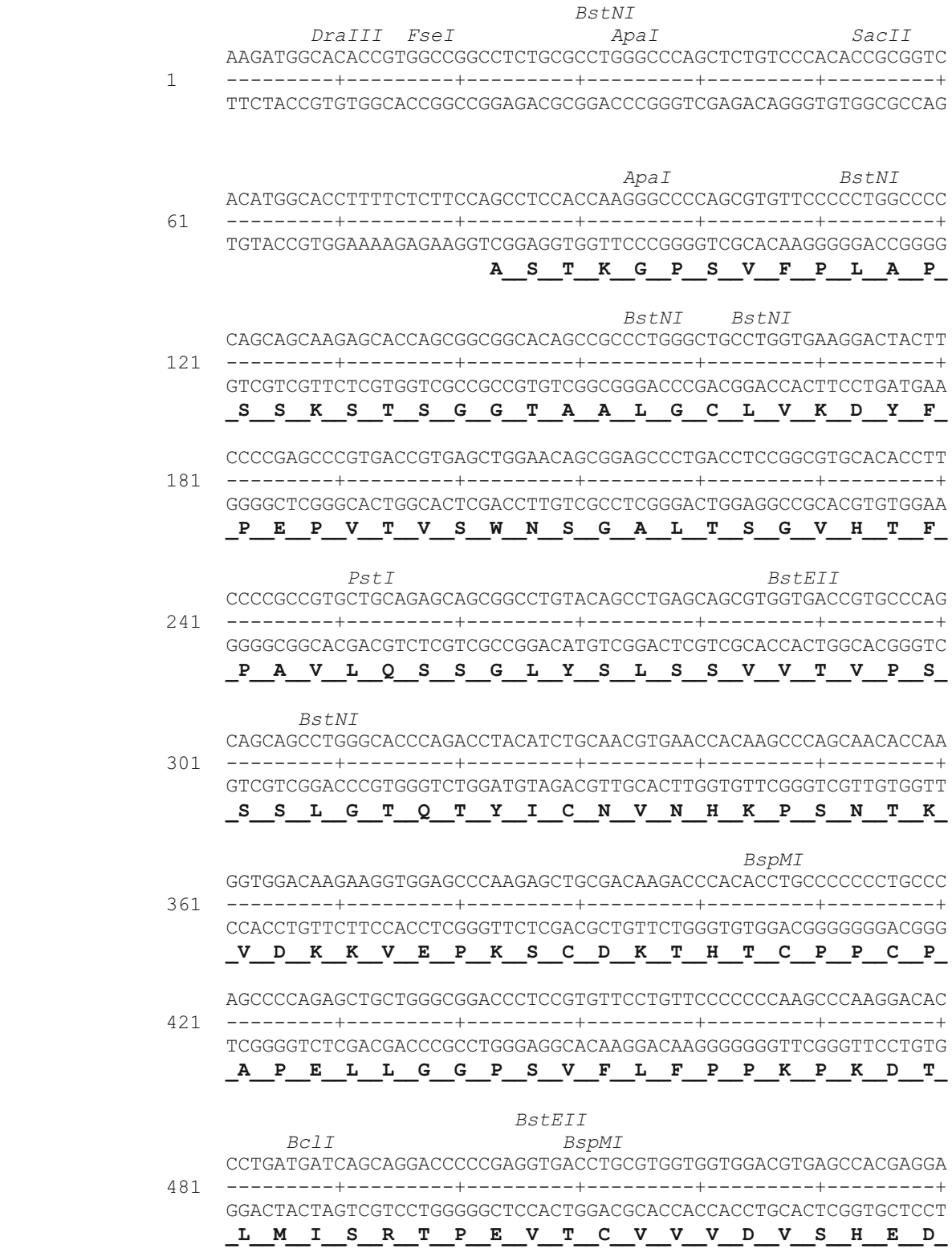
Initial Oligonucleotide Overlap Map for Design of Veneered 806 VL

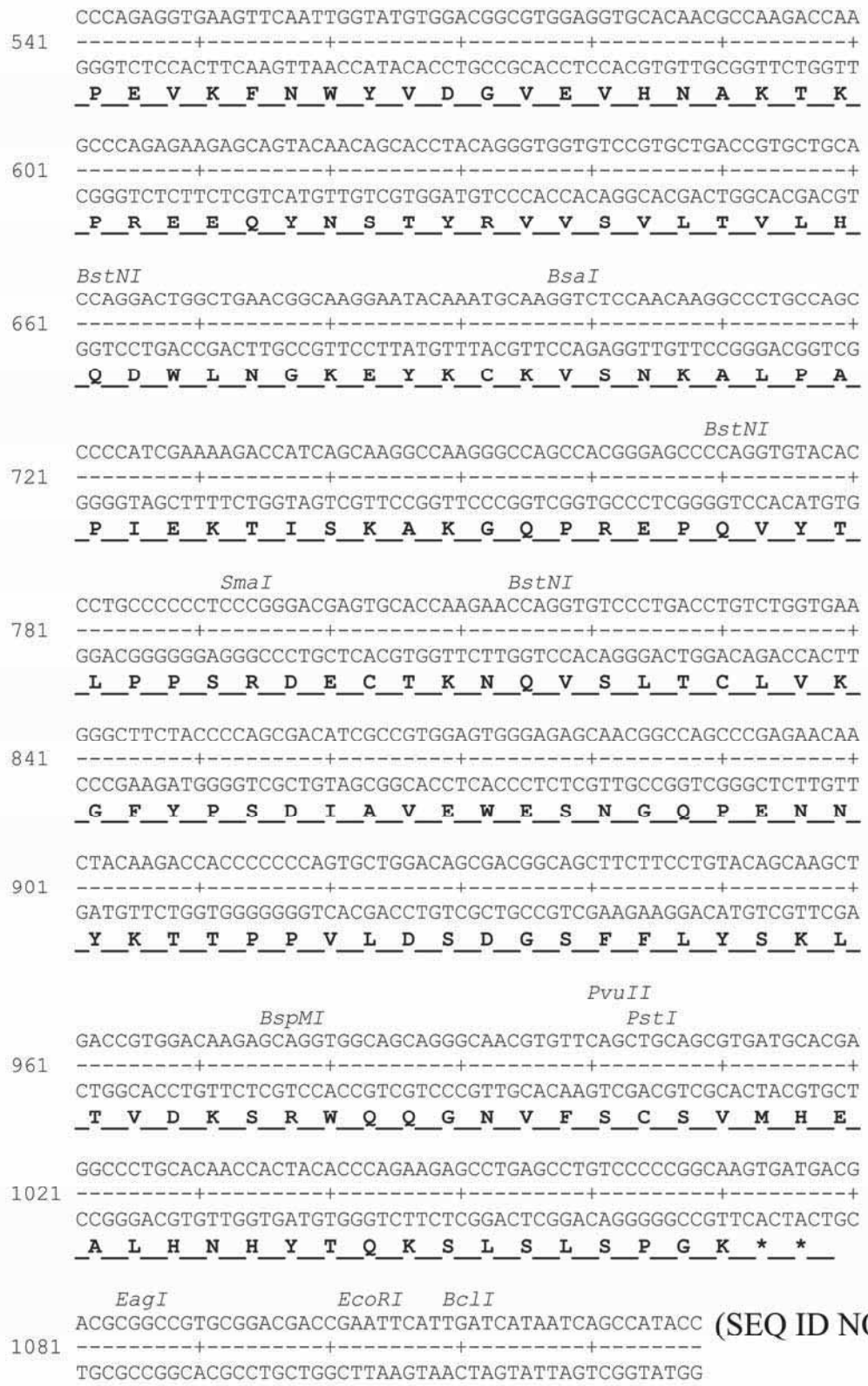
FIG. 57C



KEY: Lower case = add to oligo; Upper case = remove from oligo …this was done to increase the Tm of the overlaps
Oligos used to synthesize the V-region

FIG.58


BstNI
DraIII FseI ApaI SacII
AAGATGGCACACCGTGGCCGGCCTCTGCGCCTGGGCCCAGCTCTGTCCCACACCGCGGTC
1
TTCTACCGTGTGGCACCGGCCGGAGACGCGGACCCGGGTCGAGACAGGGTGTGGCGCCAG
ApaI BstNI
ACATGGCACCTTTTCTCTTCCAGCCTCCACCAAGGGCCCCAGCGTGTTCCCCCTGGCCCC
61
TGTACCGTGGAAAAGAGAAGGTCGGAGGTGGTTCCCGGGGTCGCACAAGGGGGACCGGGG
A S T K G P S V F P L A P
BstNI BstNI
CAGCAGCAAGAGCACCAGCGGCGGCACAGCCGCCCTGGGCTGCCTGGTGAAGGACTACTT
121
GTCGTCGTTCTCGTGGTCGCCGCCGTGTCGGCGGGACCCGACGGACCACTTCCTGATGAA
S S K S T S G G T A A L G C L V K D Y F
CCCCGAGCCCGTGACCGTGAGCTGGAACAGCGGAGCCCTGACCTCCGGCGTGCACACCTT
181
GGGGCTCGGGCACTGGCACTCGACCTTGTCGCCTCGGGACTGGAGGCCGCACGTGTGGAA
P E P V T V S W N S G A L T S G V H T F
PstI BstEII
CCCCGCCGTGCTGCAGAGCAGCGGCCTGTACAGCCTGAGCAGCGTGGTGACCGTGCCCAG
241
GGGGCGGCACGACGTCTCGTCGCCGGACATGTCGGACTCGTCGCACCACTGGCACGGGTC
P A V L Q S S G L Y S L S S V V T V P S
BstNI
CAGCAGCCTGGGCACCCAGACCTACATCTGCAACGTGAACCACAAGCCCAGCAACACCAA
301
GTCGTCGGACCCGTGGGTCTGGATGTAGACGTTGCACTTGGTGTTCGGGTCGTTGTGGTT
S S L G T Q T Y I C N V N H K P S N T K
BspMI
GGTGGACAAGAAGGTGGAGCCCAAGAGCTGCGACAAGACCCACACCTGCCCCCCCTGCCC
361
CCACCTGTTCTTCCACCTCGGGTTCTCGACGCTGTTCTGGGTGTGGACGGGGGGGACGGG
V D K K V E P K S C D K T H T C P P C P
AGCCCCAGAGCTGCTGGGCGGACCCTCCGTGTTCCTGTTCCCCCCCAAGCCCAAGGACAC
421
TCGGGGTCTCGACGACCCGCCTGGGAGGCACAAGGACAAGGGGGGGTTCGGGTTCCTGTG
A P E L L G G P S V F L F P P K P K D T
BstEII
BclI BspMI
CCTGATGATCAGCAGGACCCCCGAGGTGACCTGCGTGGTGGTGGACGTGAGCCACGAGGA
481
GGACTACTAGTCGTCCTGGGGGCTCCACTGGACGCACCACCACCTGCACTCGGTGCTCCT
L M I S R T P E V T C V V V D V S H E D



(SEQ ID NO:80)

FIG.58 continued

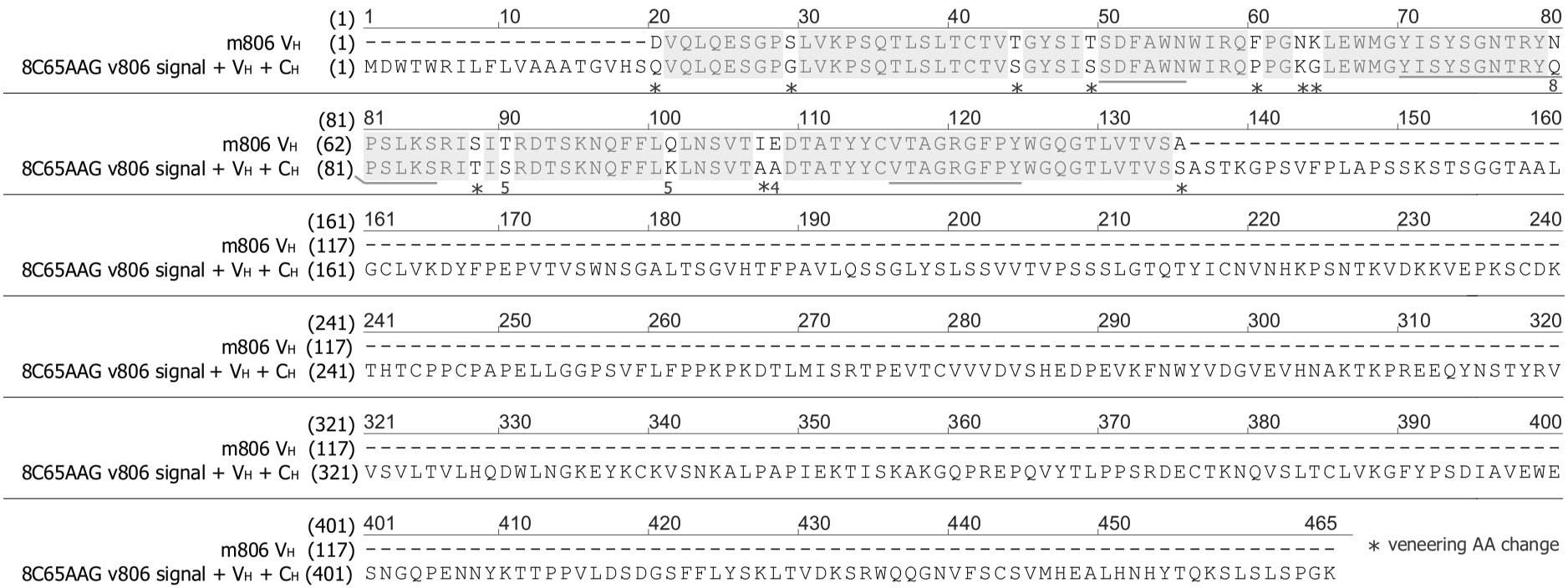


FIG.59

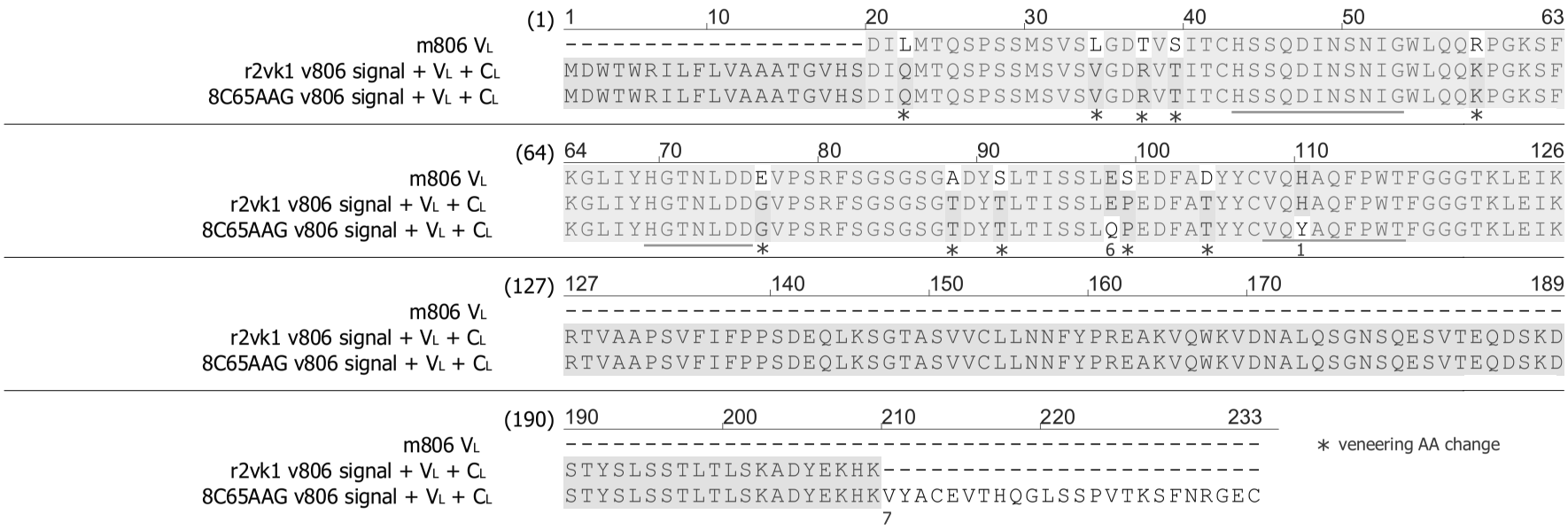

(1) 1 10 20 30 40 50 63
m806 VL ----------DILMTQSPSSMSVSLGDTVSITCHSSQDINSNIGWLQQRPGKSF
r2vk1 v806 signal + VL + CL MDWTWRILFLVAAATGVHSDIQMTQSPSSMSVSVGDRVTITCHSSQDINSNIGWLQQKPGKSF
8C65AAG v806 signal + VL + CL MDWTWRILFLVAAATGVHSDIQMTQSPSSMSVSVGDRVTITCHSSQDINSNIGWLQQKPGKSF
(64) 64 70 80 90 100 110 126
m806 VL KGLIYHGTNLDDEVPSRFSGSGSGADYSLTISSLESEDFADYYCVQHAQFPWTFGGGTKLEIK
r2vk1 v806 signal + VL + CL KGLIYHGTNLDDGVPSRFSGSGSGTDYTLTISSLEPEDFATYYCVQHAQFPWTFGGGTKLEIK
8C65AAG v806 signal + VL + CL KGLIYHGTNLDDGVPSRFSGSGSGTDYTLTISSLQPEDFATYYCVQYAQFPWTFGGGTKLEIK
(127) 127 140 150 160 170 189
m806 VL ----------
r2vk1 v806 signal + VL + CL RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKD
8C65AAG v806 signal + VL + CL RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKD
(190) 190 200 210 220 233
m806 VL ----------
r2vk1 v806 signal + VL + CL STYSLSSTLTLSKADYEKHK----------
8C65AAG v806 signal + VL + CL STYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
∗ veneering AA change

FIG.60

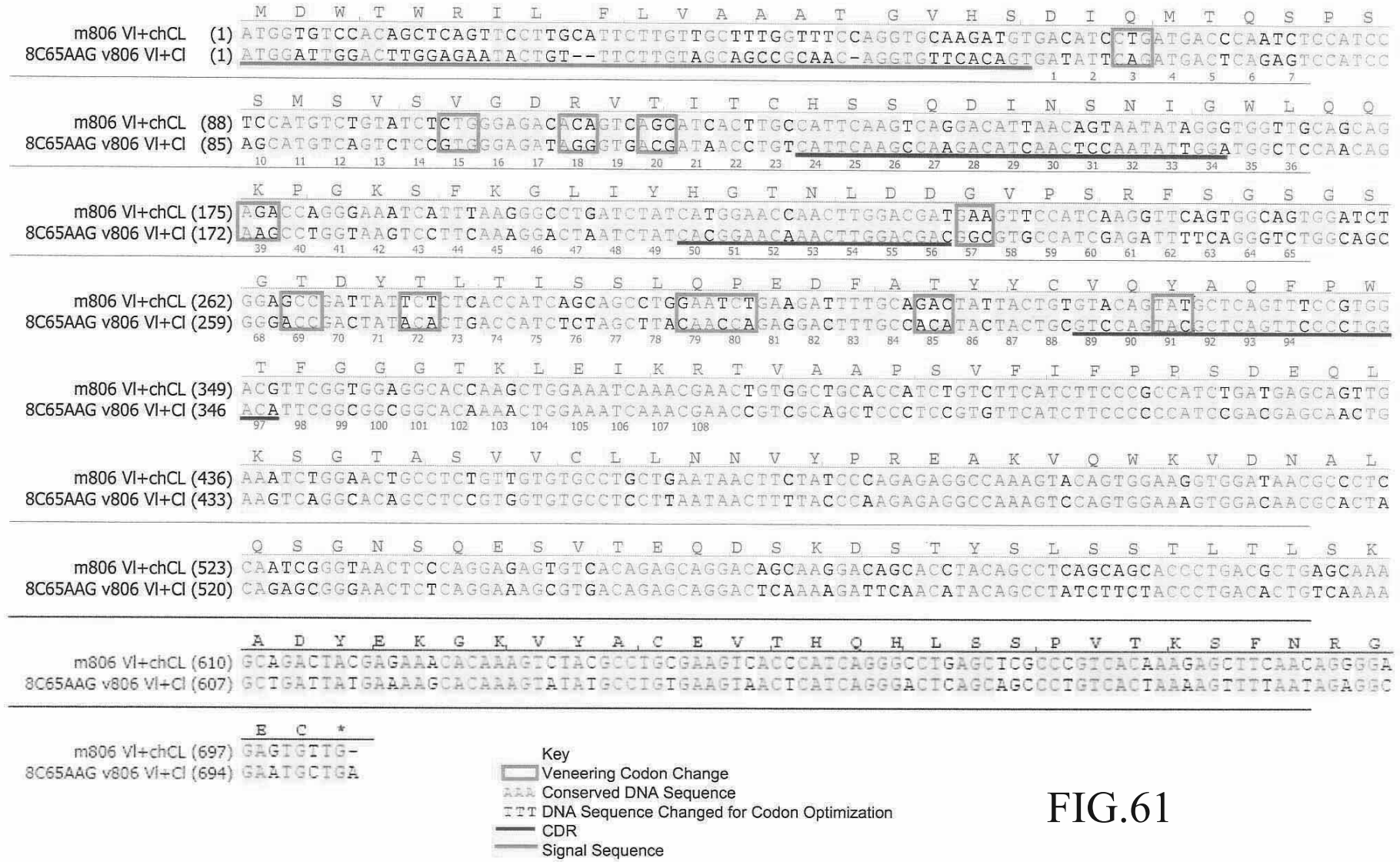

m806 Vl+chCL (1)
8C65AAG v806 Vl+Cl (1)
m806 Vl+chCL (88)
8C65AAG v806 Vl+Cl (85)
m806 Vl+chCL (175)
8C65AAG v806 Vl+Cl (172)
m806 Vl+chCL (262)
8C65AAG v806 Vl+Cl (259)
m806 Vl+chCL (349)
8C65AAG v806 Vl+Cl (346
m806 Vl+chCL (436)
8C65AAG v806 Vl+Cl (433)
m806 Vl+chCL (523)
8C65AAG v806 Vl+Cl (520)
m806 Vl+chCL (610)
8C65AAG v806 Vl+Cl (607)
m806 Vl+chCL (697)
8C65AAG v806 Vl+Cl (694)
Key
Veneering Codon Change
AAA Conserved DNA Sequence
TTT DNA Sequence Changed for Codon Optimization
CDR
Signal Sequence

FIG.61

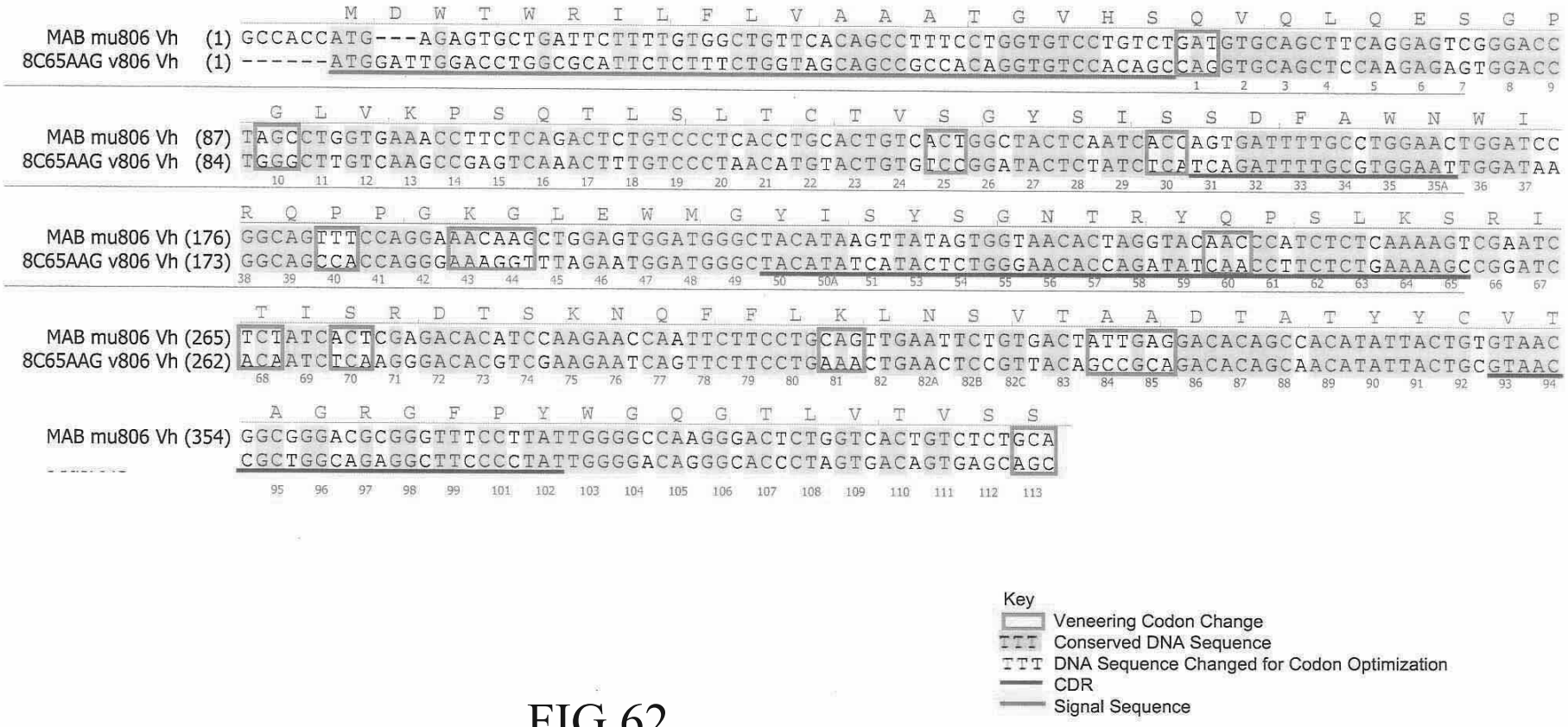

MAB mu806 Vh (1) GCCACCATG---AGAGTGCTGATTCTTTTGTGGCTGTTCACAGCCTTTCCTGGTGTCCTGTCTGATGTGCAGCTTCAGGAGTCGGGACC
8C65AAG v806 Vh (1) ------ATGGATTGGACCTGGCGCATTCTCTTTCTGGTAGCAGCCGCCACAGGTGTCCACAGCCAGGTGCAGCTCCAAGAGAGTGGACC
MAB mu806 Vh (87) TAGCCTGGTGAAACCTTCTCAGACTCTGTCCCTCACCTGCACTGTCACTGGCTACTCAATCACCAGTGATTTTGCCTGGAACTGGATCC
8C65AAG v806 Vh (84) TGGGCTTGTCAAGCCGAGTCAAACTTTGTCCCTAACATGTACTGTGTCCGGATACTCTATCTCATCAGATTTTGCGTGGAATTGGATAA
MAB mu806 Vh (176) GGCAGTTTCCAGGAAACAAGCTGGAGTGGATGGGCTACATAAGTTATAGTGGTAACACTAGGTACAACCCATCTCTCAAAAGTCGAATC
8C65AAG v806 Vh (173) GGCAGCCACCAGGGAAAGGTTTAGAATGGATGGGCTACATATCATACTCTGGGAACACCAGATATCAACCTTCTCTGAAAAGCCGGATC
MAB mu806 Vh (265) TCTATCACTCGAGACACATCCAAGAACCAATTCTTCCTGCAGTTGAATTCTGTGACTATTGAGGACACAGCCACATATTACTGTGTAAC
8C65AAG v806 Vh (262) ACAATCTCAAGGGACACGTCGAAGAATCAGTTCTTCCTGAAACTGAACTCCGTTACAGCCGCAGACACAGCAACATATTACTGCGTAAC
MAB mu806 Vh (354) GGCGGGACGCGGGTTTCCTTATTGGGGCCAAGGGACTCTGGTCACTGTCTCTGCA
CGCTGGCAGAGGCTTCCCCTATTGGGGACAGGGCACCCTAGTGACAGTGAGCAGC
Key
Veneering Codon Change
Conserved DNA Sequence
DNA Sequence Changed for Codon Optimization
CDR
Signal Sequence

FIG.62

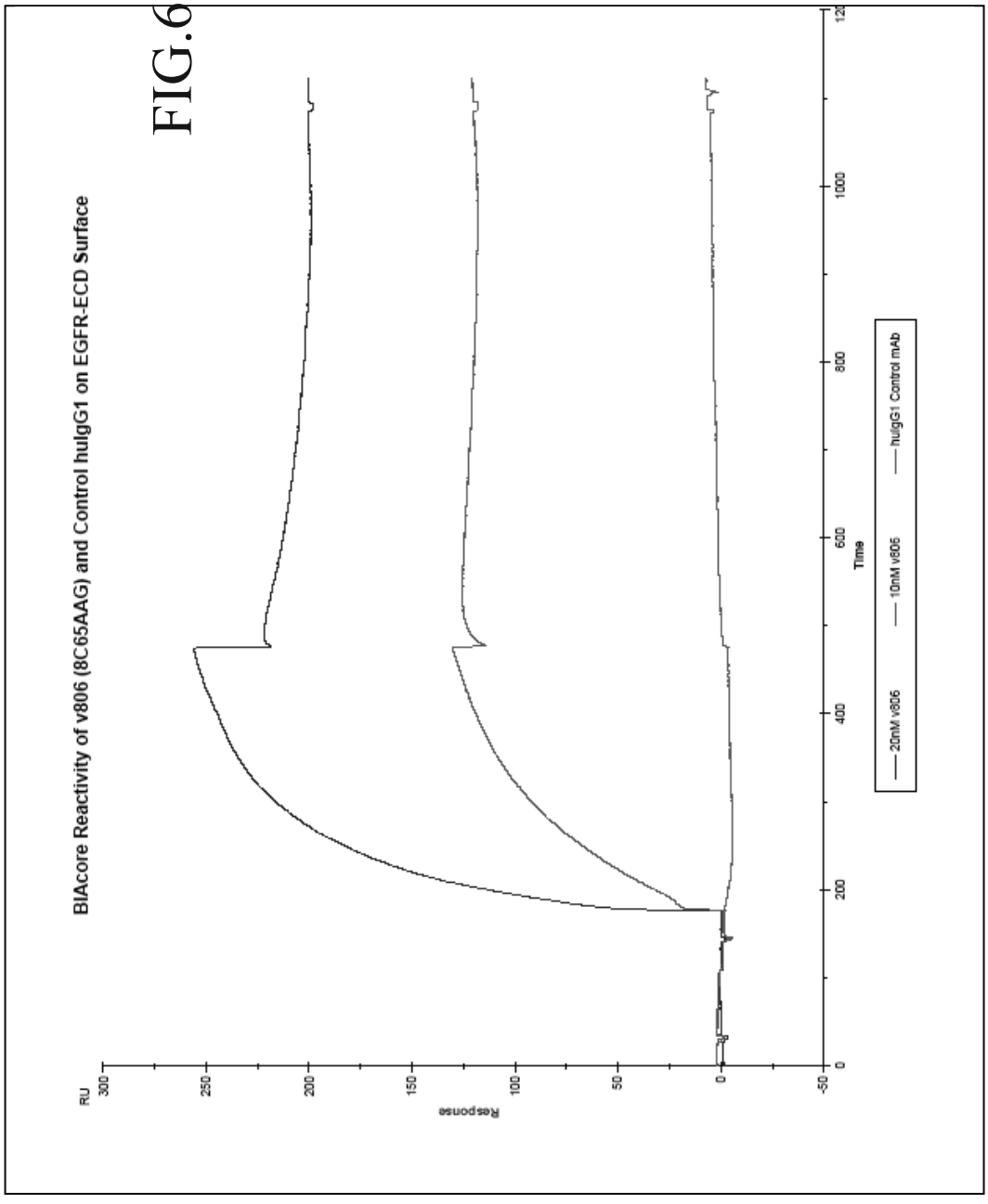


FIG.63

FIG.63

Demonstrates binding of purified hu806 antibody obtained from transient transfectant 293 cells to recombinant EGFR-ECD as determined by Biacore. No binding to the EGFR-ECD was observed with purified control human IgG1 antibody.

FIG.64

```
LOCUS
8C65AAG                11891 bp    DNA     circular     27-NOV-2006
      DEFINITION  veneered 806 HC variable region, GeneArt human HC constant
region, veneered LC variable region, cod-opt LC constant region, combined in
large Lonza Vector.
SOURCE
  ORGANISM
COMMENT     This file is created by Vector NTI
            http://www.invitrogen.com/
COMMENT     VNTDATE|418148572|
COMMENT     VNTDBDATE|428174363|
COMMENT     LSOWNER|
COMMENT     VNTNAME|8C65AAG|
COMMENT     VNTAUTHORNAME|Anne Murray|
COMMENT     VNTAUTHORTEL|646 888-2342|
COMMENT     VNTAUTHORFAX|646 422-0492|
COMMENT     VNTAUTHOREML|murraya1@mskcc.org|
COMMENT     VNTAUTHORAD1|Ludwig Inst. at Memorial Sloan Kettering Cancer Center|
COMMENT     VNTAUTHORAD2|1275 York Ave.|
COMMENT     VNTAUTHORAD3|New York, NY 10021 |
COMMENT     VNTAUTHORAD4|USA|
COMMENT     VNTREPLTYPE|Plasmid
COMMENT     Vector_NTI_Display_Data_(Do_Not_Edit!)
COMMENT     (SXF
COMMENT      (CGexDoc "8C65AAG" 0 11891
COMMENT       (CDBMol 0 0 1 6558 1 0 0 1 0 "" "" 0 0 0 0 (CObList) (CObList)
(CObList)
COMMENT        (CObList) -1 "")
COMMENT       (CDocSetData 1 1 0 0 0 0 "MAIN" 1 1 1 1 0 0 1 1 1 0 10 10 40 50 0
1 0
COMMENT        (CHomObj 0 0 0 3 75) (CWordArray) (CWordArray)
COMMENT        (CStringList "BamHI" "BglII" "DraIII" "FseI" "HindIII" "MluI"
"NotI"
COMMENT         "PacI" "RsrII" "SalI") (CStringList "atg" "gtg")
COMMENT        (CStringList "taa" "tga" "tag") (CObList) 1 "{(0,1),2}" 0 0 "" 0
COMMENT        4294967295 0 1 0 0 0 0 1 "MAIN" 0 0 30 0
COMMENT        (CProteinMotifSearchObject 100 10 1 1 1 1 1 0 1 0 0 0 0 0))
COMMENT       (CMolPar 1 0 0 0 0 1 11891 0 0 0 0 0 0 0 0) (CStringList)
(CStringList)
COMMENT       (CObList) (COAPar 25 250 50 0 6 4 3 7) (COAPar 25 250 50 0 6 4 3
7)
COMMENT       (COAPar 25 250 50 0 6 4 3 7)
COMMENT       (CObList #0=(CRSite (CStringList) "BamHI" "ggatcc" 2 0 1 5059 0 0
"")
COMMENT        #1=(CRSite (CStringList) "BglII" "agatct" 2 0 1 8910 0 0 "")
COMMENT        #2=(CRSite (CStringList) "DraIII" "cacnnngtg" 7 0 2 128 0 543 0 0
"")
COMMENT        #3=(CRSite (CStringList) "FseI" "ggccggcc" 7 0 1 551 0 0 "")
COMMENT        #4=(CRSite (CStringList) "HindIII" "aagctt" 2 0 2 2 0 3869 0 0
"")
COMMENT        #5=(CRSite (CStringList) "MluI" "acgcgt" 2 0 1 9821 0 0 "")
COMMENT        #6=(CRSite (CStringList) "NotI" "gcggccgc" 3 0 1 1878 0 0 "")
COMMENT        #7=(CRSite (CStringList) "PacI" "ttaattaa" 6 0 1 4387 0 0 "")
COMMENT        #8=(CRSite (CStringList) "RsrII" "cggwccg" 3 0 2 3999 0 4377 0 0
"")
```

```
COMMENT         #9=(CRSite (CStringList) "SalI" "gtcgac" 2 0 1 5335 0 0 ""))
COMMENT        (CObList
COMMENT         #10=(CFSignal (CObList) "GeneArt HC C-Reg" 2 0 0 553 1643 0
COMMENT              (CStringList) (CStringList) 1 1 1 1 "")
COMMENT         #11=(CFSignal (CObList) "SV40 polyA" 25 0 0 1644 1875 0
(CStringList)
COMMENT              (CStringList) 1 1 1 1 "")
COMMENT         #12=(CFSignal (CObList) "Signal (SV40E (and SV40 ori))" 21 0 0
7356 7699
COMMENT              0 (CStringList) (CStringList) 1 1 1 1 "")
COMMENT         #13=(CFSignal (CObList) "RNA (beta-lactamase) Amp(R)" 53 0 1 6121
6981 0
COMMENT              (CStringList) (CStringList) 1 1 1 1 "")
COMMENT         #14=(CFSignal (CObList) "mRNA (GS cDNA)" 54 0 0 7707 8906 0
COMMENT              (CStringList) (CStringList) 1 1 1 1 "")
COMMENT         #15=(CFSignal (CObList) "Promoter (hCMV-MIE)" 30 0 0 9784 10926 0
COMMENT              (CStringList) (CStringList) 1 1 1 1 "")
COMMENT         #16=(CFSignal (CObList) "Intron (SV40 intron + poly A)" 15 0 0
8909 9760
COMMENT              0 (CStringList) (CStringList) 1 1 1 1 "")
COMMENT         #17=(CFSignal (CObList) "5'UTR_1" 52 0 0 10927 11047 0
(CStringList)
COMMENT              (CStringList) 1 1 1 1 "")
COMMENT         #18=(CFSignal (CObList) "Intron_1" 15 0 0 11048 11874 0
(CStringList)
COMMENT              (CStringList) 1 1 1 1 "")
COMMENT         #19=(CFSignal (CObList) "5'UTR_2" 52 0 0 11875 11891 0
(CStringList)
COMMENT              (CStringList) 1 1 1 1 "")
COMMENT         #20=(CFSignal (CObList) "Heavy Chain 806 V-Region Insert" 45 0 0
128 542
COMMENT              0 (CStringList) (CStringList) 1 1 1 1 "")
COMMENT         #21=(CFSignal (CObList) "HtoY" 23 0 0 4315 4315 0 (CStringList)
COMMENT              (CStringList) 1 1 1 1 "")
COMMENT         #22=(CFSignal (CObList) "Light-Const. chg 2.1-3" 23 0 0 4716 4716
0
COMMENT              (CStringList) (CStringList) 1 1 1 1 "")
COMMENT         #23=(CFSignal (CObList) "Light-Chain 806 V-Region insert" 45 0 0
3999
COMMENT              4376 0 (CStringList) (CStringList) 1 1 1 1 "")
COMMENT         #24=(CFSignal (CObList) "Promoter (hCMV-MIE) (from NotI)" 30 0 0
1884
COMMENT              2902 0 (CStringList) (CStringList) 1 1 1 1 "")
COMMENT         #25=(CFSignal (CObList) "5'UTR_2" 52 0 0 3851 3867 0
(CStringList)
COMMENT              (CStringList) 1 1 1 1 "")
COMMENT         #26=(CFSignal (CObList) "Intron_1" 15 0 0 3024 3850 0
(CStringList)
COMMENT              (CStringList) 1 1 1 1 "")
COMMENT         #27=(CFSignal (CObList) "5'UTR_1" 52 0 0 2903 3023 0
(CStringList)
COMMENT              (CStringList) 1 1 1 1 "")
COMMENT         #28=(CFSignal (CObList) "SV40 poly A" 25 0 0 4827 5063 0
(CStringList)
COMMENT              (CStringList) 1 1 1 1 "")
COMMENT         #29=(CFSignal (CObList) "Codon-Optimized Kappa Constant Region" 2
```

FIG.64 continued

```
0 0
COMMENT             4390 4800 0 (CStringList) (CStringList) 1 1 1 1 ""))
(CObList)
COMMENT       (CObList) (CObList) (CObList) (CObList) (CObList)
COMMENT       (CTextView 0
COMMENT        #30=(CGroupPar (CParagraph 0 (0 0) 1 2 0 0 180)
COMMENT             (CObjectList
COMMENT              #31=(CRefLinePar
COMMENT                   (CLinePar (CParagraph 0 (0 0) 0 2 0 1 233) "8C65AAG"
2) 5 ""
COMMENT                   0 4)
COMMENT              #32=(CFolderPar
COMMENT                   (CGroupPar (CParagraph 1 (0 0) 1 1 0 0 178)
COMMENT                    (CObjectList
COMMENT                     #33=(CLinePar (CParagraph 0 (0 0) 1 2 1 0 180)
COMMENT                          "DNA Plasmid '8C65AAG'" 1)
COMMENT                     #34=(CLinePar (CParagraph 0 (0 0) 1 2 1 0 180)
COMMENT                          "veneered 806 HC variable region, GeneArt human
HC constant region, veneered LC variable region, cod-opt LC constant region,
combined in large Lonza Vector"
COMMENT                          1)
COMMENT                     #35=(CLinePar (CParagraph 0 (0 0) 1 2 1 0 180)
COMMENT                          "Currently local object. Original author: Anne"
1)
COMMENT                     #36=(CLinePar (CParagraph 0 (0 0) 1 2 1 0 180)
COMMENT                          "Created: 08/07/06 04:22PM" 1)
COMMENT                     #37=(CLinePar (CParagraph 0 (0 0) 1 2 1 0 180)
COMMENT                          "Last Modified: 11/27/06 05:19PM" 1)
COMMENT                     #38=(CLinePar (CParagraph 0 (0 0) 1 2 1 0 180)
COMMENT                          "length: 11891 bp" 1)
COMMENT                     #39=(CLinePar (CParagraph 0 (0 0) 1 2 1 0 180)
COMMENT                          "storage type: Basic" 1)
COMMENT                     #40=(CLinePar (CParagraph 0 (0 0) 1 2 1 0 180)
COMMENT                          "form: Circular" 1))) "General Description")
COMMENT              #41=(CFolderPar
COMMENT                   (CGroupPar (CParagraph 2 (0 0) 1 1 0 0 178)
(CObjectList))
COMMENT                   "Standard Fields")
COMMENT              #42=(CFolderPar
COMMENT                   (CGroupPar (CParagraph 5 (0 0) 1 1 0 0 178)
COMMENT                    (CObjectList
COMMENT                     #43=(CLinePar (CParagraph 0 (0 0) 1 2 1 0 180)
"Anne" 1)))
COMMENT                   "Original Author")
COMMENT              #44=(CRefLinePar
COMMENT                   (CLinePar (CParagraph 0 (0 0) 0 2 0 0 233) "Comments"
2) 1 ""
COMMENT                   0 0)
COMMENT              #45=(CFolderPar
COMMENT                   (CGroupPar (CParagraph 8 (0 0) 1 2 0 0 178)
(CObjectList))
COMMENT                   "Annotations")
COMMENT              #46=(CFolderPar
COMMENT                   (CGroupPar (CParagraph 12 (6 0) 1 1 0 0 178)
COMMENT                    (CObjectList
COMMENT                     #47=(CFolderPar
```

FIG.64 continued

```
COMMENT                          (CGroupPar (CParagraph 2 (7 2 0) 1 1 1 0 178)
COMMENT                           (CObjectList
COMMENT                            #48=(CFolderPar
COMMENT                                 (CGroupPar
COMMENT                                  (CParagraph 553 (3 #10# 0) 1 2 2 0 194)
COMMENT                                  (CObjectList
COMMENT                                   #49=(CLinePar
COMMENT                                        (CParagraph 0 (0 0) 1 2 3 0 180)
COMMENT                                        "Start: 553   End: 1643" 1)
COMMENT                                   #50=(CLinePar
COMMENT                                        (CParagraph 0 (0 0) 1 2 3 0 180)
COMMENT                                        "GeneArt human HC C-Reg" 1)))
COMMENT                                "GeneArt HC C-Reg")
COMMENT                            #51=(CFolderPar
COMMENT                                 (CGroupPar
COMMENT                                  (CParagraph 4390 (3 #29# 0) 1 2 2 0
194)
COMMENT                                  (CObjectList
COMMENT                                   #52=(CLinePar
COMMENT                                        (CParagraph 0 (0 0) 1 2 3 0 180)
COMMENT                                        "Start: 4390  End: 4800" 1)))
COMMENT                                "Codon-Optimized Kappa Constant
Region")))
COMMENT                          "C-Region (2 total)")
COMMENT                     #53=(CFolderPar
COMMENT                          (CGroupPar (CParagraph 15 (7 15 0) 1 1 1 0 178)
COMMENT                           (CObjectList
COMMENT                            #54=(CFolderPar
COMMENT                                 (CGroupPar
COMMENT                                  (CParagraph 3024 (3 #26# 0) 1 2 2 0
194)
COMMENT                                  (CObjectList
COMMENT                                   #55=(CLinePar
COMMENT                                        (CParagraph 0 (0 0) 1 2 3 0 180)
COMMENT                                        "Start: 3024  End: 3850" 1)
COMMENT                                   #56=(CLinePar
COMMENT                                        (CParagraph 0 (0 0) 1 2 3 0 180)
COMMENT                                        "intron" 1))) "Intron_1")
COMMENT                            #57=(CFolderPar
COMMENT                                 (CGroupPar
COMMENT                                  (CParagraph 8909 (3 #16# 0) 1 2 2 0
194)
COMMENT                                  (CObjectList
COMMENT                                   #58=(CLinePar
COMMENT                                        (CParagraph 0 (0 0) 1 2 3 0 180)
COMMENT                                        "Start: 8909  End: 9760" 1)
COMMENT                                   #59=(CLinePar
COMMENT                                        (CParagraph 0 (0 0) 1 2 3 0 180)
COMMENT                                        "SV40 intron + poly A" 1)))
COMMENT                                "Intron (SV40 intron + poly A)")
COMMENT                            #60=(CFolderPar
COMMENT                                 (CGroupPar
COMMENT                                  (CParagraph 11048 (3 #18# 0) 1 2 2 0
194)
COMMENT                                  (CObjectList
COMMENT                                   #61=(CLinePar
```

FIG.64 continued

```
COMMENT                                        (CParagraph 0 (0 0) 1 2 3 0 180)
COMMENT                                        "Start: 11048  End: 11874" 1)
COMMENT                                    #62=(CLinePar
COMMENT                                        (CParagraph 0 (0 0) 1 2 3 0 180)
COMMENT                                        "intron" 1))) "Intron_1")))
COMMENT                               "Intron (3 total)")
COMMENT                          #63=(CFolderPar
COMMENT                               (CGroupPar (CParagraph 21 (7 21 0) 1 1 1 0 178)
COMMENT                                (CObjectList
COMMENT                                 #64=(CFolderPar
COMMENT                                      (CGroupPar
COMMENT                                       (CParagraph 7356 (3 #12# 0) 1 2 2 0
194)
COMMENT                                       (CObjectList
COMMENT                                        #65=(CLinePar
COMMENT                                             (CParagraph 0 (0 0) 1 2 3 0 180)
COMMENT                                             "Start: 7356  End: 7699" 1)
COMMENT                                        #66=(CLinePar
COMMENT                                             (CParagraph 0 (0 0) 1 2 3 0 180)
COMMENT                                             "SV40E (and SV40 ori)" 1)))
COMMENT                                    "Signal (SV40E (and SV40 ori))")))
COMMENT                               "Misc. Feature (1 total)")
COMMENT                          #67=(CFolderPar
COMMENT                               (CGroupPar (CParagraph 23 (7 23 0) 1 1 1 0 178)
COMMENT                                (CObjectList
COMMENT                                 #68=(CFolderPar
COMMENT                                      (CGroupPar
COMMENT                                       (CParagraph 4315 (3 #21# 0) 1 2 2 0
194)
COMMENT                                       (CObjectList
COMMENT                                        #69=(CLinePar
COMMENT                                             (CParagraph 0 (0 0) 1 2 3 0 180)
COMMENT                                             "Start: 4315  End: 4315" 1)
COMMENT                                        #70=(CLinePar
COMMENT                                             (CParagraph 0 (0 0) 1 2 3 0 180)
COMMENT                                             "Histidine-to-Tyrosine change in
the 806 Light-Chain variable CDR3 region"
COMMENT                                             1))) "HtoY")
COMMENT                                 #71=(CFolderPar
COMMENT                                      (CGroupPar
COMMENT                                       (CParagraph 4716 (3 #22# 0) 1 2 2 0
194)
COMMENT                                       (CObjectList
COMMENT                                        #72=(CLinePar
COMMENT                                             (CParagraph 0 (0 0) 1 2 3 0 180)
COMMENT                                             "Start: 4716  End: 4716" 1)
COMMENT                                        #73=(CLinePar
COMMENT                                             (CParagraph 0 (0 0) 1 2 3 0 180)
COMMENT                                             "Light-chain c-region change 2.1-
3" 1)))
COMMENT                                    "Light-Const. chg 2.1-3")))
COMMENT                               "Modified Base (2 total)")
COMMENT                          #74=(CFolderPar
COMMENT                               (CGroupPar (CParagraph 25 (7 25 0) 1 1 1 0 178)
COMMENT                                (CObjectList
COMMENT                                 #75=(CFolderPar
```

FIG.64 continued

```
COMMENT                                (CGroupPar
COMMENT                                 (CParagraph 1644 (3 #11# 0) 1 2 2 0
194)
COMMENT                                 (CObjectList
COMMENT                                  #76=(CLinePar
COMMENT                                       (CParagraph 0 (0 0) 1 2 3 0 180)
COMMENT                                       "Start: 1644  End: 1875" 1)))
COMMENT                                "SV40 polyA")
COMMENT                           #77=(CFolderPar
COMMENT                                (CGroupPar
COMMENT                                 (CParagraph 4827 (3 #28# 0) 1 2 2 0
194)
COMMENT                                 (CObjectList
COMMENT                                  #78=(CLinePar
COMMENT                                       (CParagraph 0 (0 0) 1 2 3 0 180)
COMMENT                                       "Start: 4827  End: 5063" 1)
COMMENT                                  #79=(CLinePar
COMMENT                                       (CParagraph 0 (0 0) 1 2 3 0 180)
COMMENT                                       "SV40 poly A" 1))) "SV40 poly
A")))
COMMENT                           "PolyA Signal (2 total)")
COMMENT                      #80=(CFolderPar
COMMENT                           (CGroupPar (CParagraph 30 (7 30 0) 1 1 1 0 178)
COMMENT                            (CObjectList
COMMENT                             #81=(CFolderPar
COMMENT                                  (CGroupPar
COMMENT                                   (CParagraph 1884 (3 #24# 0) 1 2 2 0
194)
COMMENT                                   (CObjectList
COMMENT                                    #82=(CLinePar
COMMENT                                         (CParagraph 0 (0 0) 1 2 3 0 180)
COMMENT                                         "Start: 1884  End: 2902" 1)
COMMENT                                    #83=(CLinePar
COMMENT                                         (CParagraph 0 (0 0) 1 2 3 0 180)
COMMENT                                         "Promoter (hCMV-MIE) (from NotI)"
1)))
COMMENT                                "Promoter (hCMV-MIE) (from NotI)")
COMMENT                           #84=(CFolderPar
COMMENT                                (CGroupPar
COMMENT                                 (CParagraph 9784 (3 #15# 0) 1 2 2 0
194)
COMMENT                                 (CObjectList
COMMENT                                  #85=(CLinePar
COMMENT                                       (CParagraph 0 (0 0) 1 2 3 0 180)
COMMENT                                       "Start: 9784  End: 10926" 1)
COMMENT                                  #86=(CLinePar
COMMENT                                       (CParagraph 0 (0 0) 1 2 3 0 180)
COMMENT                                       "hCMV-MIE promoter" 1)))
COMMENT                                "Promoter (hCMV-MIE)")))
COMMENT                           "Promoter Prokaryotic (2 total)")
COMMENT                      #87=(CFolderPar
COMMENT                           (CGroupPar (CParagraph 45 (7 45 0) 1 1 1 0 178)
COMMENT                            (CObjectList
COMMENT                             #88=(CFolderPar
COMMENT                                  (CGroupPar
COMMENT                                   (CParagraph 128 (3 #20# 0) 1 2 2 0 194)
```

FIG.64 continued

```
COMMENT                                  (CObjectList
COMMENT                                   #89=(CLinePar
COMMENT                                        (CParagraph 0 (0 0) 1 2 3 0 180)
COMMENT                                        "Start: 128   End: 542 " 1)))
COMMENT                                 "Heavy Chain 806 V-Region Insert")
COMMENT                            #90=(CFolderPar
COMMENT                                 (CGroupPar
COMMENT                                  (CParagraph 3999 (3 #23# 0) 1 2 2 0
194)
COMMENT                                  (CObjectList
COMMENT                                   #91=(CLinePar
COMMENT                                        (CParagraph 0 (0 0) 1 2 3 0 180)
COMMENT                                        "Start: 3999  End: 4376" 1)))
COMMENT                                 "Light-Chain 806 V-Region insert")))
COMMENT                       "V-Region (2 total)")
COMMENT                  #92=(CFolderPar
COMMENT                       (CGroupPar (CParagraph 52 (7 52 0) 1 1 1 0 178)
COMMENT                        (CObjectList
COMMENT                         #93=(CFolderPar
COMMENT                              (CGroupPar
COMMENT                               (CParagraph 2903 (3 #27# 0) 1 2 2 0
194)
COMMENT                               (CObjectList
COMMENT                                #94=(CLinePar
COMMENT                                     (CParagraph 0 (0 0) 1 2 3 0 180)
COMMENT                                     "Start: 2903  End: 3023" 1)
COMMENT                                #95=(CLinePar
COMMENT                                     (CParagraph 0 (0 0) 1 2 3 0 180)
"5'UT"
COMMENT                                     1))) "5'UTR_1")
COMMENT                            #96=(CFolderPar
COMMENT                                 (CGroupPar
COMMENT                                  (CParagraph 3851 (3 #25# 0) 1 2 2 0
194)
COMMENT                                  (CObjectList
COMMENT                                   #97=(CLinePar
COMMENT                                        (CParagraph 0 (0 0) 1 2 3 0 180)
COMMENT                                        "Start: 3851  End: 3867" 1)
COMMENT                                   #98=(CLinePar
COMMENT                                        (CParagraph 0 (0 0) 1 2 3 0 180)
"5'UT"
COMMENT                                        1))) "5'UTR_2")
COMMENT                            #99=(CFolderPar
COMMENT                                 (CGroupPar
COMMENT                                  (CParagraph 10927 (3 #17# 0) 1 2 2 0
194)
COMMENT                                  (CObjectList
COMMENT                                   #100=(CLinePar
COMMENT                                         (CParagraph 0 (0 0) 1 2 3 0 180)
COMMENT                                         "Start: 10927  End: 11047" 1)
COMMENT                                   #101=(CLinePar
COMMENT                                         (CParagraph 0 (0 0) 1 2 3 0 180)
"5'UT"
COMMENT                                         1))) "5'UTR_1")
COMMENT                            #102=(CFolderPar
COMMENT                                  (CGroupPar
```

FIG.64 continued

```
COMMENT                                    (CParagraph 11875 (3 #19# 0) 1 2 2 0
194)
COMMENT                                    (CObjectList
COMMENT                                     #103=(CLinePar
COMMENT                                           (CParagraph 0 (0 0) 1 2 3 0
180)
COMMENT                                           "Start: 11875  End: 11891" 1)
COMMENT                                     #104=(CLinePar
COMMENT                                           (CParagraph 0 (0 0) 1 2 3 0
180)
COMMENT                                           "5'UT" 1))) "5'UTR_2")))
COMMENT                              "5' UTR (4 total)")
COMMENT                         #105=(CFolderPar
COMMENT                               (CGroupPar (CParagraph 53 (7 53 0) 1 1 1 0
178)
COMMENT                                (CObjectList
COMMENT                                 #106=(CFolderPar
COMMENT                                       (CGroupPar
COMMENT                                        (CParagraph 6121 (3 #13# 0) 1 2 2 0
194)
COMMENT                                        (CObjectList
COMMENT                                         #107=(CLinePar
COMMENT                                               (CParagraph 0 (0 0) 1 2 3 0
180)
COMMENT                                               "Start: 6121  End: 6981
(Complementary)"
COMMENT                                               1)
COMMENT                                         #108=(CLinePar
COMMENT                                               (CParagraph 0 (0 0) 1 2 3 0
180)
COMMENT                                               "beta-lactamase" 1)))
COMMENT                                      "RNA (beta-lactamase) Amp(R)")))
COMMENT                               "RNA - Misc. (1 total)")
COMMENT                         #109=(CFolderPar
COMMENT                               (CGroupPar (CParagraph 54 (7 54 0) 1 1 1 0
178)
COMMENT                                (CObjectList
COMMENT                                 #110=(CFolderPar
COMMENT                                       (CGroupPar
COMMENT                                        (CParagraph 7707 (3 #14# 0) 1 2 2 0
194)
COMMENT                                        (CObjectList
COMMENT                                         #111=(CLinePar
COMMENT                                               (CParagraph 0 (0 0) 1 2 3 0
180)
COMMENT                                               "Start: 7707  End: 8906" 1)
COMMENT                                         #112=(CLinePar
COMMENT                                               (CParagraph 0 (0 0) 1 2 3 0
180)
COMMENT                                               "GS cDNA" 1))) "mRNA (GS
cDNA)")))
COMMENT                              "mRNA (1 total)"))) "Feature Map")
COMMENT                    #113=(CFolderPar
COMMENT                          (CGroupPar (CParagraph 13 (0 0) 1 1 0 0 178)
COMMENT                           (CObjectList
COMMENT                            #114=(CRSFolderPar
```

FIG.64 continued

```
COMMENT                         (CFolderPar
COMMENT                          (CGroupPar (CParagraph 37104496 (8 0) 1 1 1
0 178)
COMMENT                           (CObjectList
COMMENT                            #115=(CGroupPar
COMMENT                                  (CParagraph 0 (10 #0# 0) 1 2 2 0
180)
COMMENT                                  (CObjectList
COMMENT                                   #116=(CLinePar
COMMENT                                         (CParagraph 0 (1 #0# 1) 1 2 2
0 191)
COMMENT                                         " N1: 5059 " 1))))) "BamHI: 1
site")
COMMENT                        1 5 "GGATCC" "CCTAGG")
COMMENT                  #117=(CRSFolderPar
COMMENT                        (CFolderPar
COMMENT                         (CGroupPar (CParagraph 37104336 (8 0) 1 1 1
0 178)
COMMENT                          (CObjectList
COMMENT                           #118=(CGroupPar
COMMENT                                 (CParagraph 0 (10 #1# 0) 1 2 2 0
180)
COMMENT                                 (CObjectList
COMMENT                                  #119=(CLinePar
COMMENT                                        (CParagraph 0 (1 #1# 1) 1 2 2
0 191)
COMMENT                                        " N1: 8910 " 1))))) "BglII: 1
site")
COMMENT                        1 5 "AGATCT" "TCTAGA")
COMMENT                  #120=(CRSFolderPar
COMMENT                        (CFolderPar
COMMENT                         (CGroupPar (CParagraph 18147408 (8 0) 1 1 1
0 178)
COMMENT                          (CObjectList
COMMENT                           #121=(CGroupPar
COMMENT                                 (CParagraph 0 (10 #2# 0) 1 2 2 0
180)
COMMENT                                 (CObjectList
COMMENT                                  #122=(CLinePar
COMMENT                                        (CParagraph 0 (1 #2# 1) 1 2 2
0 191)
COMMENT                                        " N1: 128 " 1)
COMMENT                                  #123=(CLinePar
COMMENT                                        (CParagraph 0 (1 #2# 2) 1 2 2
0 191)
COMMENT                                        " N2: 543 " 1))))) "DraIII: 2
sites")
COMMENT                        6 3 "CACNNNGTG" "GTGNNNCAC")
COMMENT                  #124=(CRSFolderPar
COMMENT                        (CFolderPar
COMMENT                         (CGroupPar (CParagraph 37104736 (8 0) 1 1 1
0 178)
COMMENT                          (CObjectList
COMMENT                           #125=(CGroupPar
COMMENT                                 (CParagraph 0 (10 #3# 0) 1 2 2 0
180)
```

FIG.64 continued

```
COMMENT                                 (CObjectList
COMMENT                                  #126=(CLinePar
COMMENT                                        (CParagraph 0 (1 #3# 1) 1 2 2
0 191)
COMMENT                                        " N1: 551 " 1))))) "FseI: 1
site") 6
COMMENT                               2 "GGCCGGCC" "CCGGCCGG")
COMMENT                         #127=(CRSFolderPar
COMMENT                               (CFolderPar
COMMENT                                (CGroupPar (CParagraph 37104576 (8 0) 1 1 1
0 178)
COMMENT                                 (CObjectList
COMMENT                                  #128=(CGroupPar
COMMENT                                        (CParagraph 0 (10 #4# 0) 1 2 2 0
180)
COMMENT                                        (CObjectList
COMMENT                                         #129=(CLinePar
COMMENT                                               (CParagraph 0 (1 #4# 1) 1 2 2
0 191)
COMMENT                                               " N1: 2 " 1)
COMMENT                                         #130=(CLinePar
COMMENT                                               (CParagraph 0 (1 #4# 2) 1 2 2
0 191)
COMMENT                                               " N2: 3869 " 1)))))
COMMENT                                "HindIII: 2 sites") 1 5 "AAGCTT" "TTCGAA")
COMMENT                         #131=(CRSFolderPar
COMMENT                               (CFolderPar
COMMENT                                (CGroupPar (CParagraph 27521208 (8 0) 1 1 1
0 178)
COMMENT                                 (CObjectList
COMMENT                                  #132=(CGroupPar
COMMENT                                        (CParagraph 0 (10 #5# 0) 1 2 2 0
180)
COMMENT                                        (CObjectList
COMMENT                                         #133=(CLinePar
COMMENT                                               (CParagraph 0 (1 #5# 1) 1 2 2
0 191)
COMMENT                                               " N1: 9821 " 1))))) "MluI: 1
site")
COMMENT                               1 5 "ACGCGT" "TGCGCA")
COMMENT                         #134=(CRSFolderPar
COMMENT                               (CFolderPar
COMMENT                                (CGroupPar (CParagraph 37104976 (8 0) 1 1 1
0 178)
COMMENT                                 (CObjectList
COMMENT                                  #135=(CGroupPar
COMMENT                                        (CParagraph 0 (10 #6# 0) 1 2 2 0
180)
COMMENT                                        (CObjectList
COMMENT                                         #136=(CLinePar
COMMENT                                               (CParagraph 0 (1 #6# 1) 1 2 2
0 191)
COMMENT                                               " N1: 1878 " 1))))) "NotI: 1
site")
COMMENT                               2 6 "GCGGCCGC" "CGCCGGCG")
COMMENT                         #137=(CRSFolderPar
```

FIG.64 continued

```
COMMENT                              (CFolderPar
COMMENT                               (CGroupPar (CParagraph 37104816 (8 0) 1 1 1
0 178)
COMMENT                                (CObjectList
COMMENT                                 #138=(CGroupPar
COMMENT                                       (CParagraph 0 (10 #7# 0) 1 2 2 0
180)
COMMENT                                       (CObjectList
COMMENT                                        #139=(CLinePar
COMMENT                                              (CParagraph 0 (1 #7# 1) 1 2 2
0 191)
COMMENT                                              " N1: 4387 " 1))))) "PacI: 1
site")
COMMENT                              5 3 "TTAATTAA" "AATTAATT")
COMMENT                        #140=(CRSFolderPar
COMMENT                              (CFolderPar
COMMENT                               (CGroupPar (CParagraph 37104256 (8 0) 1 1 1
0 178)
COMMENT                                (CObjectList
COMMENT                                 #141=(CGroupPar
COMMENT                                       (CParagraph 0 (10 #8# 0) 1 2 2 0
180)
COMMENT                                       (CObjectList
COMMENT                                        #142=(CLinePar
COMMENT                                              (CParagraph 0 (1 #8# 1) 1 2 2
0 191)
COMMENT                                              " N1: 3999 " 1)
COMMENT                                        #143=(CLinePar
COMMENT                                              (CParagraph 0 (1 #8# 2) 1 2 2
0 191)
COMMENT                                              " N2: 4377 " 1))))) "RsrII: 2
sites")
COMMENT                              2 5 "CGGWCCG" "GCCWGGC")
COMMENT                        #144=(CRSFolderPar
COMMENT                              (CFolderPar
COMMENT                               (CGroupPar (CParagraph 18147328 (8 0) 1 1 1
0 178)
COMMENT                                (CObjectList
COMMENT                                 #145=(CGroupPar
COMMENT                                       (CParagraph 0 (10 #9# 0) 1 2 2 0
180)
COMMENT                                       (CObjectList
COMMENT                                        #146=(CLinePar
COMMENT                                              (CParagraph 0 (1 #9# 1) 1 2 2
0 191)
COMMENT                                              " N1: 5335 " 1))))) "SalI: 1
site")
COMMENT                              1 5 "GTCGAC" "CAGCTG")))
COMMENT                        "Restriction/Methylation Map"))))
COMMENT       (CGraphView
COMMENT        (CWStyleSheet
COMMENT         (CObjectList
COMMENT          #147=(CWidgetStyle "RSite Label" 1 (LOGPEN 0 0 13408563) 1 0 1
COMMENT                (LOGFONT 0 0 0 0 400 0 0 0 0 3 2 1 18 "Georgia") 0.555556
0 1 5
COMMENT                "@N (@S)" 0)
```

FIG.64 continued

```
COMMENT          #148=(CWidgetStyle "Signal Label" 1 (LOGPEN 0 0 0) 1 0 1
COMMENT                (LOGFONT 0 0 0 0 700 0 0 0 0 3 2 1 34 "Arial") 0.666667 0
1 1
COMMENT                "@N" 0)
COMMENT          #149=(CWidgetStyle "Molecule Label 2" 0 0 1
COMMENT                (LOGFONT 0 0 0 0 400 0 0 0 0 3 2 1 18 "Georgia") 0.555556
0 1 16
COMMENT                "@L bp" 0)
COMMENT          #150=(CWidgetStyle "Molecule Label 1" 0 0 1
COMMENT                (LOGFONT 0 0 0 0 400 0 0 0 0 3 2 1 34 "Verdana") 0.833333
0 1 1
COMMENT                "@N" 0)
COMMENT          #151=(CWidgetStyle "Shape 3" 1 (LOGPEN 0 0 3355545) 1 1
COMMENT                (LOGBRUSH 0 6724095 0) 0 0 1 (LOGSHAPE 9 1 0.8 1.8 0))
COMMENT          #152=(CWidgetStyle "Shape 1" 1 (LOGPEN 0 0 6723840) 1 1
COMMENT                (LOGBRUSH 0 10079334 0) 0 0 1 (LOGSHAPE 9 1 0.8 1.8 0))
COMMENT          #153=(CWidgetStyle "Axis" 1 (LOGPEN 0 0 10079436) 2 1
COMMENT                (LOGBRUSH 0 13434879 0) 0 0 1 (LOGSHAPE 10 1 0 0 0))
COMMENT          #154=(CWidgetStyle "Line 2" 1 (LOGPEN 0 0 6723840) 8 0 0 0 1
COMMENT                (LOGSHAPE 1 1.9 0 0 0))
COMMENT          #155=(CWidgetStyle "RSite" 1 (LOGPEN 0 0 10053171) 8 0 0 0 1
COMMENT                (LOGSHAPE 1 1.9 0 0 0))
COMMENT          #156=(CWidgetStyle "Short Signal" 1 (LOGPEN 0 0 13395507) 10 0
0 0 1
COMMENT                (LOGSHAPE 1 1.9 0 0 0))
COMMENT          #157=(CWidgetStyle "Uniq RSite Label" 1 (LOGPEN 0 0 153) 1 0 1
COMMENT                (LOGFONT 0 0 0 0 400 0 0 0 0 3 2 1 18 "Georgia") 0.555556
128 1
COMMENT                5 "@N (@S)" 0)
COMMENT          #158=(CWidgetStyle "Vanilla" 1 (LOGPEN 0 0 0) 1 1
COMMENT                (LOGBRUSH 0 16777215 0) 1
COMMENT                (LOGFONT 0 0 0 0 400 0 0 0 0 7 48 2 18 "Times New Roman")
0.8 0
COMMENT                1 2 "?" 0)
COMMENT          #159=(CWidgetStyle "Mark 1" 0 0 1
COMMENT                (LOGFONT 0 0 0 0 400 0 0 0 2 7 48 2 2 "Windings") 0.7 0 1
2 "?"
COMMENT                0)
COMMENT          #160=(CWidgetStyle "Motif Label" 1 (LOGPEN 0 0 16744512) 1 0 1
COMMENT                (LOGFONT 0 0 0 0 400 0 0 0 0 3 2 1 34 "Arial") 0.611111
8388608
COMMENT                1 65535 "@N (@H)" 0)
COMMENT          #161=(CWidgetStyle "Fragment Label 2" 1 (LOGPEN 0 0 0) 1 0 1
COMMENT                (LOGFONT 0 0 0 0 400 0 0 0 0 3 2 1 49 "Courier New") 1.05
0 1 48
COMMENT                "@F bp (molecule @L bp)" 0)
COMMENT          #162=(CWidgetStyle "Fragment Label 1" 1 (LOGPEN 0 0 0) 1 0 1
COMMENT                (LOGFONT 0 0 0 0 400 0 0 0 0 3 2 1 34 "Arial") 0.91 0 1 1
COMMENT                "Fragment of @N" 0)
COMMENT          #163=(CWidgetStyle "Shape 4" 1 (LOGPEN 0 0 0) 1 1
COMMENT                (LOGBRUSH 2 8388608 5) 0 0 0)
COMMENT          #164=(CWidgetStyle "Shape 2" 1 (LOGPEN 0 0 0) 1 1 (LOGBRUSH 0
128 0) 0
COMMENT                0 0)
COMMENT          #165=(CWidgetStyle "Shape 0" 1 (LOGPEN 0 0 0) 1 1 (LOGBRUSH 0 0
0) 0 0
```

FIG.64 continued

```
COMMENT                0)
COMMENT           #166=(CWidgetStyle "ORF" 1 (LOGPEN 0 0 16384) 8 0 0 0 1
COMMENT                (LOGSHAPE 7 0.2 3.41182 2.86186 0.609808))
COMMENT           #167=(CWidgetStyle "Line 4" 1 (LOGPEN 0 0 32768) 8 0 0 0 0)
COMMENT           #168=(CWidgetStyle "Line 3" 1 (LOGPEN 0 0 16711680) 8 0 0 0 0)
COMMENT           #169=(CWidgetStyle "Line 1" 1 (LOGPEN 0 0 16711680) 1 0 0 0 0)
COMMENT           #170=(CWidgetStyle "Short Promoter" 1 (LOGPEN 0 0 128) 6 0 0 0
0)
COMMENT           #171=(CWidgetStyle "Motif" 1 (LOGPEN 0 0 0) 1 0 0 0 0)
COMMENT           #172=(CWidgetStyle "Line 0" 1 (LOGPEN 0 0 0) 8 0 0 0 0)
COMMENT           #173=(CWidgetStyle "Void" 0 0 0 0 0)
COMMENT           #174=(CWidgetStyle "General Label" 1 (LOGPEN 0 0 0) 1 0 1
COMMENT                (LOGFONT 0 0 0 0 400 0 0 0 0 3 2 1 18 "Times New Roman")
0.91 0
COMMENT                1 3 "@T @N " 0)
COMMENT           #175=(CWidgetStyle "Position" 1 (LOGPEN 0 0 0) 1 0 0 0 0)
COMMENT           #176=(CWidgetStyle "Annotation" 0 0 1
COMMENT                (LOGFONT 0 0 0 0 400 0 0 0 0 3 2 1 18 "Times New Roman")
0.91 0
COMMENT                0 0)
COMMENT           #177=(CWidgetStyle "Position Label" 1 (LOGPEN 0 0 8388608) 1 0
1
COMMENT                (LOGFONT 0 0 0 0 400 0 1 0 0 3 2 1 34 "Arial") 0.63
8388608 1 1
COMMENT                "@N" 0)
COMMENT           #178=(CWidgetStyle "Range" 1 (LOGPEN 0 0 0) 1 1
COMMENT                (LOGBRUSH 0 16777215 0) 0 0 0)
COMMENT           #179=(CWidgetStyle "Range Label" 1 (LOGPEN 0 0 8388608) 1 0 1
COMMENT                (LOGFONT 0 0 0 0 400 0 1 0 0 3 2 1 34 "Arial") 0.63
8388608 1 1
COMMENT                "@N" 0)
COMMENT           #180=(CWidgetStyle "ORF Label" 1 (LOGPEN 0 0 49216) 1 0 1
COMMENT                (LOGFONT 0 0 0 0 400 0 0 0 0 3 2 1 18 "Times New Roman")
COMMENT                0.611111 0 1 65535 "@N" 0)
COMMENT           #181=(CWidgetStyle "CDS Label" 1 (LOGPEN 0 0 4227264) 1 0 1
COMMENT                (LOGFONT 0 0 0 0 400 0 0 0 0 3 2 1 34 "Arial") 0.555556
255 1 1
COMMENT                "@N" 0)
COMMENT           #182=(CWidgetStyle "Shape 5" 1 (LOGPEN 0 0 0) 3 1
COMMENT                (LOGBRUSH 0 16777113 0) 1
COMMENT                (LOGFONT 0 0 0 0 400 0 0 0 0 7 48 2 50 "Arial") 0.9 0 0 1
COMMENT                (LOGSHAPE 9 1 0.8 1.8 0))
COMMENT           #183=(CWidgetStyle "CDS" 1 (LOGPEN 0 0 0) 1 1 (LOGBRUSH 2 39423
3) 0 0
COMMENT                1 (LOGSHAPE 9 1 0.8 1.8 0))
COMMENT           #184=(CWidgetStyle "Label 2" 1 (LOGPEN 0 0 4227264) 1 0 1
COMMENT                (LOGFONT 0 0 0 0 400 0 0 0 0 3 2 1 34 "Arial") 0.944444
8388608
COMMENT                1 1 "@N" 0)
COMMENT           #185=(CWidgetStyle "Label 3" 1 (LOGPEN 0 0 8421376) 1 0 1
COMMENT                (LOGFONT 0 0 0 0 700 255 0 0 0 3 2 1 34 "Arial") 0.833333
255 1
COMMENT                5 "@N (@S)" 0)
COMMENT           #186=(CWidgetStyle "Label 4" 1 (LOGPEN 0 0 8437824) 1 0 1
COMMENT                (LOGFONT 0 0 0 0 400 0 0 0 0 3 2 1 34 "Arial") 0.722222 0
1 5
```

FIG.64 continued

```
COMMENT                 "@N (@S)" 0)
COMMENT           #187=(CWidgetStyle "Shape 6" 1 (LOGPEN 0 0 0) 1 1
COMMENT                 (LOGBRUSH 0 3394713 0) 1
COMMENT                 (LOGFONT 0 0 0 0 400 0 0 0 0 7 48 2 50 "Arial") 0.9 0 0
0)
COMMENT           #188=(CWidgetStyle "Shape 7" 1 (LOGPEN 0 0 0) 1 1
COMMENT                 (LOGBRUSH 0 3407871 0) 1
COMMENT                 (LOGFONT 0 0 0 0 400 0 0 0 0 7 48 2 50 "Arial") 0.9 0 0
0)
COMMENT           #189=(CWidgetStyle "Shape 8" 1 (LOGPEN 0 0 52275) 1 1
COMMENT                 (LOGBRUSH 0 3407871 0) 1
COMMENT                 (LOGFONT 0 0 0 0 400 0 0 0 0 7 48 2 50 "Arial") 0.9 0 0
0)
COMMENT           #190=(CWidgetStyle "Shape 9" 1 (LOGPEN 0 0 0) 1 1
COMMENT                 (LOGBRUSH 0 10040064 0) 1
COMMENT                 (LOGFONT 0 0 0 0 400 0 0 0 0 7 48 2 50 "Arial") 0.9 0 0
0))
COMMENT          0.164644 1.74233 0.164644 2.53336
COMMENT          (2 (CShapeMapEntry 0 "Shape 9" 1 "Signal Label") 45
COMMENT           (CShapeMapEntry 0 "Shape 8" 1 "Signal Label") 70
COMMENT           (CShapeMapEntry 0 "Unique RSite" 1 "Uniq RSite Label") 67
COMMENT           (CShapeMapEntry 0 "ORF" 0 "ORF Label")) 40.0378 40.0378 39 39
0.1
COMMENT          -11891) 1 0 1 1 1
COMMENT         (mapper: 26.6862 -31.9823 39 39 0.01 10 14 11891 11891 1 0 0)
COMMENT         #191=(CGroupWidget (CWidget 0 (0 0) 1 2 0 0 Nil -317 100)
COMMENT               (CObjectList
COMMENT                #192=(CGroupWidget (CWidget 1 (0 0) 1 2 0 0 Nil -639 100)
COMMENT                      (CObjectList
COMMENT                       #193=(CAxis
COMMENT                             (CWideLine
COMMENT                              (CWidget 0 (0 0) 1 2 0 0 #153# 37106252 0)
COMMENT                              (LOGPEN 0 0 10079436) 2 (LOGBRUSH 0 13434879
0) 1
COMMENT                              6.27471 6.27271 1 0.0214037) 0.0527557)
COMMENT                       #194=(CLabel
COMMENT                             (CWidget 1001 (0 0) 1 2 0 0 #150# 28370780
100)
COMMENT                             (LOGPEN 0 0 0) 1
COMMENT                             (LOGFONT 41 15 0 0 400 0 0 0 0 3 2 1 34
"Verdana")
COMMENT                             2.53336 0.833333 0 "8C65AAG" "@N" 1 0 0.5 0 -
6.206
COMMENT                             3.84615 1.07692 Nil)
COMMENT                       #195=(CLabel (CWidget 1002 (0 0) 1 2 0 0 #149# 0
100)
COMMENT                             (LOGPEN 0 0 0) 1
COMMENT                             (LOGFONT 27 10 0 0 400 0 0 0 0 3 2 1 18
"Georgia")
COMMENT                             2.53336 0.555556 0 "11891 bp" "@L bp" 16 0 -
0.8 0
COMMENT                             -7.47268 2.30769 0.692308 Nil))
(CObjectList))
COMMENT                #196=(CGroupWidget (CWidget 10 (6 0) 1 2 0 0 Nil 393219
100)
COMMENT                      (CObjectList
```

FIG.64 continued

```
COMMENT                    #197=(CGroupWidget
COMMENT                          (CWidget 2 (7 2 0) 1 2 0 0 Nil -108 100)
COMMENT                          (CObjectList
COMMENT                           #198=(CWideArrow
COMMENT                                 (CWideLine
COMMENT                                  (CWidget 0 (3 #10# 0) 1 2 0 0 #190# 0
100)
COMMENT                                  (LOGPEN 0 0 0) 1 (LOGBRUSH 0 10040064
0) 1
COMMENT                                  5.40641 5.98197 1 0.082322) 0.8 1.8
0)
COMMENT                                 #199=(CLabel
COMMENT                                 (CWidget 0 (0 0) 1 2 0 0 #148#
37745700 100)
COMMENT                                 (LOGPEN 0 0 0) 1
COMMENT                                 (LOGFONT 32 12 0 0 700 0 0 0 0 3 2 1
34
COMMENT                                  "Arial") 2.53336 0.666667 0
COMMENT                                 "GeneArt HC C-Reg" "@N" 1 0 0 -15.0455
COMMENT                                 8.30913 6.28205 0.846154 #198#)
COMMENT                                 #200=(CWideArrow
COMMENT                                 (CWideLine
COMMENT                                  (CWidget 0 (3 #29# 0) 1 2 0 0 #190#
393235
COMMENT                                   100) (LOGPEN 0 0 0) 1
COMMENT                                  (LOGBRUSH 0 10040064 0) 1 3.74091
3.95774 1
COMMENT                                  0.082322) 0.8 1.8 0)
COMMENT                                 #201=(CLabel
COMMENT                                 (CWidget 0 (0 0) 1 2 0 0 #148#
28396148 100)
COMMENT                                 (LOGPEN 0 0 0) 1
COMMENT                                 (LOGFONT 32 12 0 0 700 0 0 0 0 3 2 1
34
COMMENT                                  "Arial") 2.53336 0.666667 0
COMMENT                                 "Codon-Optimized Kappa Constant
Region" "@N"
COMMENT                                 1 0 0 -11.1884 24.776 14.4872 0.846154
#200#))
COMMENT                          (CObjectList))
COMMENT                    #202=(CGroupWidget
COMMENT                          (CWidget 15 (7 15 0) 1 2 0 0 Nil 18088376
100)
COMMENT                          (CObjectList
COMMENT                           #203=(CLine
COMMENT                                 (CWidget 0 (3 #16# 0) 1 2 0 0 #169#
18088384
COMMENT                                  100) (LOGPEN 0 0 16711680) 1 0.835356
COMMENT                                 1.12422 1.5737)
COMMENT                           #204=(CLabel
COMMENT                                 (CWidget 0 (0 0) 1 2 0 0 #148#
18088512 100)
COMMENT                                 (LOGPEN 0 0 0) 1
COMMENT                                 (LOGFONT 32 12 0 0 700 0 0 0 0 3 2 1
34
COMMENT                                  "Arial") 2.53336 0.666667 0
```

FIG.64 continued

```
COMMENT                                   "Intron (SV40 intron + poly A)" "@N" 1
0 0
COMMENT                                   13.1146 8.30913 9.74359 0.846154
#203#)
COMMENT                                 #205=(CLine
COMMENT                                   (CWidget 0 (3 #18# 0) 1 2 0 0 #169# -
1215 100)
COMMENT                                   (LOGPEN 0 0 16711680) 1 0.835356
0.00896848
COMMENT                                  0.445258)
COMMENT                                 #206=(CLabel
COMMENT                                   (CWidget 0 (0 0) 1 2 0 0 #148#
27471448 100)
COMMENT                                   (LOGPEN 0 0 0) 1
COMMENT                                   (LOGFONT 32 12 0 0 700 0 0 0 0 3 2 1
34
COMMENT                                    "Arial") 2.53336 0.666667 0 "Intron
1" "@N"
COMMENT                                   1 0 0 14.7731 3.24241 2.74359 0.846154
#205#)
COMMENT                                 #207=(CLine
COMMENT                                   (CWidget 0 (3 #26# 0) 1 2 0 0 #169#
268634520
COMMENT                                    100) (LOGPEN 0 0 16711680) 1 0.835356
COMMENT                                  4.24209 4.67838)
COMMENT                                 #208=(CLabel
COMMENT                                   (CWidget 0 (0 0) 1 2 0 0 #148#
37615420 100)
COMMENT                                   (LOGPEN 0 0 0) 1
COMMENT                                   (LOGFONT 32 12 0 0 700 0 0 0 0 3 2 1
34
COMMENT                                    "Arial") 2.53336 0.666667 0 "Intron
1" "@N"
COMMENT                                   1 0 0 -7.95233 14.6425 2.74359
0.846154 #207#))
COMMENT                               (CObjectList))
COMMENT                             #209=(CGroupWidget
COMMENT                               (CWidget 21 (7 21 0) 1 2 0 0 Nil 327685 100)
COMMENT                               (CObjectList
COMMENT                                #210=(CWideArrow
COMMENT                                   (CWideLine
COMMENT                                    (CWidget 0 (3 #12# 0) 1 2 0 0 #152# 0
100)
COMMENT                                    (LOGPEN 0 0 6723840) 1
COMMENT                                    (LOGBRUSH 0 10079334 0) 1 2.21152
2.393 1
COMMENT                                    0.082322) 0.8 1.8 0)
COMMENT                                 #211=(CLabel
COMMENT                                   (CWidget 0 (0 0) 1 2 0 0 #148#
18088608 100)
COMMENT                                   (LOGPEN 0 0 0) 1
COMMENT                                   (LOGFONT 32 12 0 0 700 0 0 0 0 3 2 1
34
COMMENT                                    "Arial") 2.53336 0.666667 0
COMMENT                                   "Signal (SV40E (and SV40 ori))" "@N" 1
0 0
```

FIG.64 continued

```
COMMENT                                   8.88505 12.1092 10.0513 0.846154
#210#))
COMMENT                             (CObjectList))
COMMENT                          #212=(CGroupWidget
COMMENT                             (CWidget 23 (7 23 0) 1 2 0 0 Nil 27986056
100)
COMMENT                             (CObjectList
COMMENT                              #213=(CShape
COMMENT                                   (CWidget 0 (3 #21# 0) 1 2 0 0 #172# 0
100)
COMMENT                                   (LOGPEN 0 6 0) 8 (LOGBRUSH 0 0 4)
0.835356
COMMENT                                  3.9973 0.7 2)
COMMENT                              #214=(CLabel
COMMENT                                   (CWidget 0 (0 0) 1 2 0 0 #148#
37029036 100)
COMMENT                                   (LOGPEN 0 0 0) 1
COMMENT                                   (LOGFONT 32 12 0 0 700 0 0 0 0 3 2 1
34
COMMENT                                    "Arial") 2.53336 0.666667 0 "HtoY"
"@N" 1 0
COMMENT                                  0 -5.40373 20.9759 1.64103 0.846154
#213#)
COMMENT                              #215=(CShape
COMMENT                                   (CWidget 0 (3 #22# 0) 1 2 0 0 #172# 0
100)
COMMENT                                   (LOGPEN 0 6 0) 8 (LOGBRUSH 0 0 4)
0.835356
COMMENT                                  3.78575 0.7 2)
COMMENT                              #216=(CLabel
COMMENT                                   (CWidget 0 (0 0) 1 2 0 0 #148#
18088616 100)
COMMENT                                   (LOGPEN 0 0 0) 1
COMMENT                                   (LOGFONT 32 12 0 0 700 0 0 0 0 3 2 1
34
COMMENT                                    "Arial") 2.53336 0.666667 0
COMMENT                                  "Light-Const. chg 2.1-3" "@N" 1 0 0 -
7.491
COMMENT                                  26.0426 7.64103 0.846154 #215#))
COMMENT                             (CObjectList))
COMMENT                          #217=(CGroupWidget
COMMENT                             (CWidget 25 (7 25 0) 1 2 0 0 Nil -736 100)
COMMENT                             (CObjectList
COMMENT                              #218=(CLine
COMMENT                                   (CWidget 0 (3 #11# 0) 1 2 0 0 #167#
18088376
COMMENT                                    100) (LOGPEN 0 6 32768) 8 0.835356
5.28402
COMMENT                                  5.40641)
COMMENT                              #219=(CLabel (CWidget 0 (0 0) 1 2 0 0 #148#
0 100)
COMMENT                                   (LOGPEN 0 0 0) 1
COMMENT                                   (LOGFONT 32 12 0 0 700 0 0 0 0 3 2 1
34
COMMENT                                    "Arial") 2.53336 0.666667 0 "SV40
polyA"
```

FIG.64 continued

```
COMMENT                                "@N" 1 0 0 -12.2962 9.57581 3.79487
0.846154
COMMENT                                #218#)
COMMENT                          #220=(CLine
COMMENT                                (CWidget 0 (3 #28# 0) 1 2 0 0 #167#
18088384
COMMENT                                 100) (LOGPEN 0 6 32768) 8 0.670712
3.60216
COMMENT                                3.72719)
COMMENT                          #221=(CLabel
COMMENT                                (CWidget 0 (0 0) 1 2 0 0 #148#
37126836 100)
COMMENT                                (LOGPEN 0 0 0) 1
COMMENT                                (LOGFONT 32 12 0 0 700 0 0 0 0 3 2 1
34
COMMENT                                 "Arial") 2.53336 0.666667 0 "SV40
poly A"
COMMENT                                "@N" 1 0 0 -5.16093 27.3093 4.02564
0.846154
COMMENT                                #220#)) (CObjectList))
COMMENT                     #222=(CGroupWidget
COMMENT                           (CWidget 30 (7 30 0) 1 2 0 0 Nil 18088376
100)
COMMENT                           (CObjectList
COMMENT                            #223=(CWideArrow
COMMENT                                 (CWideLine
COMMENT                                  (CWidget 0 (3 #15# 0) 1 2 0 0 #164#
28358516
COMMENT                                   100) (LOGPEN 0 0 0) 1 (LOGBRUSH 0
128 0) 1
COMMENT                                  0.509093 1.11209 1 0.082322) 0.8 1.8
0)
COMMENT                            #224=(CLabel
COMMENT                                 (CWidget 0 (0 0) 1 2 0 0 #148#
18088512 100)
COMMENT                                 (LOGPEN 0 0 0) 1
COMMENT                                 (LOGFONT 32 12 0 0 700 0 0 0 0 3 2 1
34
COMMENT                                  "Arial") 2.53336 0.666667 0
COMMENT                                 "Promoter (hCMV-MIE)" "@N" 1 0 0
14.3466
COMMENT                                 5.77577 7.25641 0.846154 #223#)
COMMENT                            #225=(CWideArrow
COMMENT                                 (CWideLine
COMMENT                                  (CWidget 0 (3 #24# 0) 1 2 0 0 #164#
196625
COMMENT                                   100) (LOGPEN 0 0 0) 1 (LOGBRUSH 0
128 0) 1
COMMENT                                  4.74221 5.27979 1 0.082322) 0.8 1.8
0)
COMMENT                            #226=(CLabel
COMMENT                                 (CWidget 0 (0 0) 1 2 0 0 #148#
37176452 100)
COMMENT                                 (LOGPEN 0 0 0) 1
COMMENT                                 (LOGFONT 32 12 0 0 700 0 0 0 0 3 2 1
34
```

FIG.64 continued

```
COMMENT                                  "Arial") 2.53336 0.666667 0
COMMENT                                 "Promoter (hCMV-MIE) (from NotI)" "@N"
1 0 0
COMMENT                                 -14.5466 12.1092 11.1795 0.846154
#225#))
COMMENT                           (CObjectList))
COMMENT                         #227=(CGroupWidget
COMMENT                           (CWidget 45 (7 45 0) 1 2 0 0 Nil -1015 100)
COMMENT                           (CObjectList
COMMENT                            #228=(CWideArrow
COMMENT                                  (CWideLine
COMMENT                                   (CWidget 0 (3 #20# 0) 1 2 0 0 #189#
37110564
COMMENT                                    100) (LOGPEN 0 0 52275) 1
COMMENT                                   (LOGBRUSH 0 3407871 0) 1 5.98725
6.20619 1
COMMENT                                   0.082322) 0.8 1.8 0)
COMMENT                            #229=(CLabel (CWidget 0 (0 0) 1 2 0 0 #148#
0 100)
COMMENT                                  (LOGPEN 0 0 0) 1
COMMENT                                  (LOGFONT 32 12 0 0 700 0 0 0 0 3 2 1
34
COMMENT                                   "Arial") 2.53336 0.666667 0
COMMENT                                  "Heavy Chain 806 V-Region Insert" "@N"
1 0 0
COMMENT                                  -19.2693 4.50909 11.2564 0.846154
#228#)
COMMENT                            #230=(CWideArrow
COMMENT                                  (CWideLine
COMMENT                                   (CWidget 0 (3 #23# 0) 1 2 0 0 #189#
37186028
COMMENT                                    100) (LOGPEN 0 0 52275) 1
COMMENT                                   (LOGBRUSH 0 3407871 0) 1 3.96459
4.16401 1
COMMENT                                   0.082322) 0.8 1.8 0)
COMMENT                            #231=(CLabel
COMMENT                                  (CWidget 0 (0 0) 1 2 0 0 #148#
18088608 100)
COMMENT                                  (LOGPEN 0 0 0) 1
COMMENT                                  (LOGFONT 32 12 0 0 700 0 0 0 0 3 2 1
34
COMMENT                                   "Arial") 2.53336 0.666667 0
COMMENT                                  "Light-Chain 806 V-Region insert" "@N"
1 0 0
COMMENT                                  -10.3851 19.7092 11.0256 0.846154
#230#))
COMMENT                           (CObjectList))
COMMENT                         #232=(CGroupWidget
COMMENT                           (CWidget 52 (7 52 0) 1 2 0 0 Nil 18088352
100)
COMMENT                           (CObjectList
COMMENT                            #233=(CLine
COMMENT                                  (CWidget 0 (3 #17# 0) 1 2 0 0 #154#
37060948
COMMENT                                   100) (LOGPEN 0 6 6723840) 8 0.835356
COMMENT                                  0.445258 0.509093)
```

FIG.64 continued

```
COMMENT                                  #234=(CLabel
COMMENT                                        (CWidget 0 (0 0) 1 2 0 0 #148#
18088512 100)
COMMENT                                        (LOGPEN 0 0 0) 1
COMMENT                                        (LOGFONT 32 12 0 0 700 0 0 0 0 3 2 1
34
COMMENT                                         "Arial") 2.53336 0.666667 0 "5'UTR 1"
"@N" 1
COMMENT                                        0 0 13.5592 4.50909 2.61538 0.846154
#233#)
COMMENT                                  #235=(CScratch
COMMENT                                        (CWidget 0 (3 #19# 0) 1 2 0 0 #154# 0
100)
COMMENT                                        (LOGPEN 0 6 6723840) 8 1 0.00896848
1.9
COMMENT                                       0.082322 1)
COMMENT                                  #236=(CLabel
COMMENT                                        (CWidget 0 (0 0) 1 2 0 0 #148#
18088528 100)
COMMENT                                        (LOGPEN 0 0 0) 1
COMMENT                                        (LOGFONT 32 12 0 0 700 0 0 0 0 3 2 1
34
COMMENT                                         "Arial") 2.53336 0.666667 0 "5'UTR 2"
"@N" 1
COMMENT                                       0 0 15.7121 1.97573 2.61538 0.846154
#235#)
COMMENT                                  #237=(CScratch
COMMENT                                        (CWidget 0 (3 #25# 0) 1 2 0 0 #154# 0
100)
COMMENT                                        (LOGPEN 0 6 6723840) 8 1 4.24209 1.9
0.082322
COMMENT                                       1)
COMMENT                                  #238=(CLabel
COMMENT                                        (CWidget 0 (0 0) 1 2 0 0 #148#
18088600 100)
COMMENT                                        (LOGPEN 0 0 0) 1
COMMENT                                        (LOGFONT 32 12 0 0 700 0 0 0 0 3 2 1
34
COMMENT                                         "Arial") 2.53336 0.666667 0 "5'UTR 2"
"@N" 1
COMMENT                                       0 0 -6.94704 15.9092 2.61538 0.846154
#237#)
COMMENT                                  #239=(CLine
COMMENT                                        (CWidget 0 (3 #27# 0) 1 2 0 0 #154#
268634520
COMMENT                                         100) (LOGPEN 0 6 6723840) 8 0.835356
4.67838
COMMENT                                       4.74221)
COMMENT                                  #240=(CLabel
COMMENT                                        (CWidget 0 (0 0) 1 2 0 0 #148#
18088584 100)
COMMENT                                        (LOGPEN 0 0 0) 1
COMMENT                                        (LOGFONT 32 12 0 0 700 0 0 0 0 3 2 1
34
COMMENT                                         "Arial") 2.53336 0.666667 0 "5'UTR 1"
"@N" 1
```

FIG.64 continued

```
COMMENT                                    0 0 -8.96711 13.3758 2.61538 0.846154
#239#))
COMMENT                             (CObjectList))
COMMENT                          #241=(CGroupWidget
COMMENT                             (CWidget 53 (7 53 0) 1 2 0 0 Nil 18088360
100)
COMMENT                             (CObjectList
COMMENT                              #242=(CWideArrow
COMMENT                                    (CWideLine
COMMENT                                     (CWidget 0 (3 #13# 0) 1 2 0 0 #152# 0
100)
COMMENT                                     (LOGPEN 0 0 6723840) 1
COMMENT                                     (LOGBRUSH 0 10079334 0) 1 2.59031
3.04453 1
COMMENT                                     0.082322) 0.8 1.8 1)
COMMENT                              #243=(CLabel
COMMENT                                    (CWidget 0 (0 0) 1 2 0 0 #148#
18088592 100)
COMMENT                                    (LOGPEN 0 0 0) 1
COMMENT                                    (LOGFONT 32 12 0 0 700 0 0 0 0 3 2 1
34
COMMENT                                     "Arial") 2.53336 0.666667 0
COMMENT                                    "RNA (beta-lactamase) Amp(R)" "@N" 1 0
0
COMMENT                                    6.3624 13.3758 9.74359 0.846154
#242#))
COMMENT                             (CObjectList))
COMMENT                          #244=(CGroupWidget
COMMENT                             (CWidget 54 (7 54 0) 1 2 0 0 Nil 268634520
100)
COMMENT                             (CObjectList
COMMENT                              #245=(CWideArrow
COMMENT                                    (CWideLine
COMMENT                                     (CWidget 0 (3 #14# 0) 1 2 0 0 #152# 0
100)
COMMENT                                     (LOGPEN 0 0 6723840) 1
COMMENT                                     (LOGBRUSH 0 10079334 0) 1 1.57476
2.20783 1
COMMENT                                     0.082322) 0.8 1.8 0)
COMMENT                              #246=(CLabel
COMMENT                                    (CWidget 0 (0 0) 1 2 0 0 #148#
18088520 100)
COMMENT                                    (LOGPEN 0 0 0) 1
COMMENT                                    (LOGFONT 32 12 0 0 700 0 0 0 0 3 2 1
34
COMMENT                                     "Arial") 2.53336 0.666667 0 "mRNA (GS
cDNA)"
COMMENT                                    "@N" 1 0 0 8.63373 10.8425 5.76923
0.846154
COMMENT                                    #245#)) (CObjectList))) (CObjectList))
COMMENT                #247=(CGroupWidget (CWidget 11 (8 0) 1 2 0 0 Nil -1088
100)
COMMENT                       (CObjectList
COMMENT                        #248=(CGroupWidget
COMMENT                             (CWidget 1 (10 #0# 0) 1 2 0 0 Nil -1227 100)
COMMENT                             (CObjectList
```

FIG.64 continued

```
COMMENT                          #249=(CScratch
COMMENT                                (CWidget 1 (1 #0# 1) 1 2 0 0 #155# 0
100)
COMMENT                                (LOGPEN 0 6 10053171) 8 1 3.6048 1.9
0.082322
COMMENT                                1)
COMMENT                          #250=(CLabel (CWidget 0 (0 0) 1 2 0 0 #157#
0 100)
COMMENT                                (LOGPEN 0 0 153) 1
COMMENT                                (LOGFONT 27 10 0 0 400 0 0 0 0 3 2 1
18
COMMENT                                 "Georgia") 2.53336 0.555556 128
COMMENT                                "{\\i Bam}HI (5059)" "@N (@S)" 5 0 0 -
4.92823
COMMENT                                28.576 4.07692 0.692308 #249#))
(CObjectList))
COMMENT                     #251=(CGroupWidget
COMMENT                           (CWidget 1 (10 #1# 0) 1 2 0 0 Nil 678 100)
COMMENT                           (CObjectList
COMMENT                            #252=(CScratch
COMMENT                                (CWidget 1 (1 #1# 1) 1 2 0 0 #155# 0
100)
COMMENT                                (LOGPEN 0 6 10053171) 8 1 1.57318 1.9
COMMENT                                0.082322 1)
COMMENT                            #253=(CLabel (CWidget 0 (0 0) 1 2 0 0 #157#
0 100)
COMMENT                                (LOGPEN 0 0 153) 1
COMMENT                                (LOGFONT 27 10 0 0 400 0 0 0 0 3 2 1
18
COMMENT                                 "Georgia") 2.53336 0.555556 128
COMMENT                                "{\\i Bgl}II (8910)" "@N (@S)" 5 0 0
8.917
COMMENT                                9.57581 3.41026 0.692308 #252#))
COMMENT                           (CObjectList))
COMMENT                     #254=(CGroupWidget
COMMENT                           (CWidget 1 (10 #3# 0) 1 2 0 0 Nil -320 100)
COMMENT                           (CObjectList
COMMENT                            #255=(CScratch
COMMENT                                (CWidget 1 (1 #3# 1) 1 2 0 0 #155# 669
100)
COMMENT                                (LOGPEN 0 6 10053171) 8 1 5.98303 1.9
COMMENT                                0.082322 1)
COMMENT                            #256=(CLabel
COMMENT                                (CWidget 0 (0 0) 1 2 0 0 #157#
18146168 100)
COMMENT                                (LOGPEN 0 0 153) 1
COMMENT                                (LOGFONT 27 10 0 0 400 0 0 0 0 3 2 1
18
COMMENT                                 "Georgia") 2.53336 0.555556 128
COMMENT                                "{\\i Fse}I (551)" "@N (@S)" 5 0 0 -
14.4711
COMMENT                                7.04245 2.64103 0.692308 #255#))
COMMENT                           (CObjectList))
COMMENT                     #257=(CGroupWidget
COMMENT                           (CWidget 1 (10 #5# 0) 1 2 0 0 Nil 1368 100)
COMMENT                           (CObjectList
```

FIG.64 continued

```
COMMENT                          #258=(CScratch
COMMENT                                (CWidget 1 (1 #5# 1) 1 2 0 0 #155#
1170 100)
COMMENT                                (LOGPEN 0 6 10053171) 8 1 1.09257 1.9
COMMENT                               0.082322 1)
COMMENT                          #259=(CLabel
COMMENT                                (CWidget 0 (0 0) 1 2 0 0 #157#
37574220 100)
COMMENT                                (LOGPEN 0 0 153) 1
COMMENT                                (LOGFONT 27 10 0 0 400 0 0 0 0 3 2 1
18
COMMENT                                 "Georgia") 2.53336 0.555556 128
COMMENT                               "{\\i Mlu}I (9821)" "@N (@S)" 5 0 0
11.05
COMMENT                               7.04245 3.25641 0.692308 #258#))
COMMENT                        (CObjectList))
COMMENT                   #260=(CGroupWidget
COMMENT                        (CWidget 1 (10 #6# 0) 1 2 0 0 Nil -739 100)
COMMENT                        (CObjectList
COMMENT                         #261=(CScratch
COMMENT                                (CWidget 1 (1 #6# 1) 1 2 0 0 #155# 898
100)
COMMENT                                (LOGPEN 0 6 10053171) 8 1 5.28296 1.9
COMMENT                               0.082322 1)
COMMENT                         #262=(CLabel
COMMENT                                (CWidget 0 (0 0) 1 2 0 0 #157#
37173948 100)
COMMENT                                (LOGPEN 0 0 153) 1
COMMENT                                (LOGFONT 27 10 0 0 400 0 0 0 0 3 2 1
18
COMMENT                                 "Georgia") 2.53336 0.555556 128
COMMENT                               "{\\i Not}I (1878)" "@N (@S)" 5 0 0 -
11.7199
COMMENT                               10.8425 3.17949 0.692308 #261#))
COMMENT                        (CObjectList))
COMMENT                   #263=(CGroupWidget
COMMENT                        (CWidget 1 (10 #7# 0) 1 2 0 0 Nil 27987292
100)
COMMENT                        (CObjectList
COMMENT                         #264=(CScratch
COMMENT                                (CWidget 1 (1 #7# 1) 1 2 0 0 #155# 0
100)
COMMENT                                (LOGPEN 0 6 10053171) 8 1 3.95932 1.9
COMMENT                               0.082322 1)
COMMENT                         #265=(CLabel
COMMENT                                (CWidget 0 (0 0) 1 2 0 0 #157#
37188964 100)
COMMENT                                (LOGPEN 0 0 153) 1
COMMENT                                (LOGFONT 27 10 0 0 400 0 0 0 0 3 2 1
18
COMMENT                                 "Georgia") 2.53336 0.555556 128
COMMENT                               "{\\i Pac}I (4387)" "@N (@S)" 5 0 0 -
6.086
COMMENT                               23.5093 3.33333 0.692308 #264#))
COMMENT                        (CObjectList))
COMMENT                   #266=(CGroupWidget
```

FIG.64 continued

```
COMMENT                          (CWidget 1 (10 #9# 0) 1 2 0 0 Nil 18088384
100)
COMMENT                          (CObjectList
COMMENT                           #267=(CScratch
COMMENT                                 (CWidget 1 (1 #9# 1) 1 2 0 0 #155# 0
100)
COMMENT                                 (LOGPEN 0 6 10053171) 8 1 3.45919 1.9
COMMENT                                0.082322 1)
COMMENT                           #268=(CLabel
COMMENT                                 (CWidget 0 (0 0) 1 2 0 0 #157#
18088352 100)
COMMENT                                 (LOGPEN 0 0 153) 1
COMMENT                                 (LOGFONT 27 10 0 0 400 0 0 0 0 3 2 1
18
COMMENT                                  "Georgia") 2.53336 0.555556 128
COMMENT                                "{\\i Sal}I (5335)" "@N (@S)" 5 0 0 -
3.73591
COMMENT                                29.8427 2.94872 0.692308 #267#))
COMMENT                          (CObjectList))
COMMENT                    #269=(CGroupWidget
COMMENT                          (CWidget 2 (10 #2# 0) 1 2 0 0 Nil -181 100)
COMMENT                          (CObjectList
COMMENT                           #270=(CScratch
COMMENT                                 (CWidget 1 (1 #2# 1) 1 2 0 0 #155# 0
100)
COMMENT                                 (LOGPEN 0 6 10053171) 8 1 6.20619 1.9
COMMENT                                0.082322 1)
COMMENT                           #271=(CLabel
COMMENT                                 (CWidget 0 (0 0) 1 2 0 0 #147# 393229
100)
COMMENT                                 (LOGPEN 0 0 13408563) 1
COMMENT                                 (LOGFONT 27 10 0 0 400 0 0 0 0 3 2 1
18
COMMENT                                  "Georgia") 2.53336 0.555556 0
COMMENT                                "{\\i Dra}III (128)" "@N (@S)" 5 0 0 -
15.8185
COMMENT                                3.24241 3.41026 0.692308 #270#)
COMMENT                           #272=(CScratch
COMMENT                                 (CWidget 2 (1 #2# 2) 1 2 0 0 #155# 508
100)
COMMENT                                 (LOGPEN 0 6 10053171) 8 1 5.98725 1.9
COMMENT                                0.082322 1)
COMMENT                           #273=(CLabel
COMMENT                                 (CWidget 0 (0 0) 1 2 0 0 #147# 945
100)
COMMENT                                 (LOGPEN 0 0 13408563) 1
COMMENT                                 (LOGFONT 27 10 0 0 400 0 0 0 0 3 2 1
18
COMMENT                                  "Georgia") 2.53336 0.555556 0
COMMENT                                "{\\i Dra}III (543)" "@N (@S)" 5 0 0 -
14.9124
COMMENT                                5.77577 3.48718 0.692308 #272#))
COMMENT                          (CObjectList))
COMMENT                    #274=(CGroupWidget
COMMENT                          (CWidget 2 (10 #4# 0) 1 2 0 0 Nil 678 100)
COMMENT                          (CObjectList
```

FIG.64 continued

```
COMMENT                          #275=(CScratch
COMMENT                                (CWidget 1 (1 #4# 1) 1 2 0 0 #155#
1393 100)
COMMENT                                (LOGPEN 0 6 10053171) 8 1 6.27266 1.9
COMMENT                                0.082322 1)
COMMENT                          #276=(CLabel
COMMENT                                (CWidget 0 (0 0) 1 2 0 0 #147#
37174492 100)
COMMENT                                (LOGPEN 0 0 13408563) 1
COMMENT                                (LOGFONT 27 10 0 0 400 0 0 0 0 3 2 1
18
COMMENT                                 "Georgia") 2.53336 0.555556 0
COMMENT                                "{\\i Hin}dIII (2)" "@N (@S)" 5 0 0 -
15.9515
COMMENT                                1.97573 3.10256 0.692308 #275#)
COMMENT                          #277=(CScratch
COMMENT                                (CWidget 2 (1 #4# 2) 1 2 0 0 #155# 0
100)
COMMENT                                (LOGPEN 0 6 10053171) 8 1 4.23259 1.9
COMMENT                                0.082322 1)
COMMENT                          #278=(CLabel
COMMENT                                (CWidget 0 (0 0) 1 2 0 0 #147#
28387876 100)
COMMENT                                (LOGPEN 0 0 13408563) 1
COMMENT                                (LOGFONT 27 10 0 0 400 0 0 0 0 3 2 1
18
COMMENT                                 "Georgia") 2.53336 0.555556 0
COMMENT                                "{\\i Hin}dIII (3869)" "@N (@S)" 5 0 0
COMMENT                                -7.71376 17.1759 4.23077 0.692308
#277#))
COMMENT                                (CObjectList))
COMMENT                    #279=(CGroupWidget
COMMENT                          (CWidget 2 (10 #8# 0) 1 2 0 0 Nil 1 100)
COMMENT                          (CObjectList
COMMENT                           #280=(CScratch
COMMENT                                (CWidget 1 (1 #8# 1) 1 2 0 0 #155#
37028212
COMMENT                                 100) (LOGPEN 0 6 10053171) 8 1
4.16401 1.9
COMMENT                                0.082322 1)
COMMENT                           #281=(CLabel
COMMENT                                (CWidget 0 (0 0) 1 2 0 0 #147#
28372436 100)
COMMENT                                (LOGPEN 0 0 13408563) 1
COMMENT                                (LOGFONT 27 10 0 0 400 0 0 0 0 3 2 1
18
COMMENT                                 "Georgia") 2.53336 0.555556 0
COMMENT                                "{\\i Rsr}II (3999)" "@N (@S)" 5 0 0 -
7.08453
COMMENT                                18.4426 3.5641 0.692308 #280#)
COMMENT                           #282=(CScratch
COMMENT                                (CWidget 2 (1 #8# 2) 1 2 0 0 #155# 0
100)
COMMENT                                (LOGPEN 0 6 10053171) 8 1 3.96459 1.9
COMMENT                                0.082322 1)
COMMENT                           #283=(CLabel
```

FIG.64 continued

```
COMMENT                                    (CWidget 0 (0 0) 1 2 0 0 #147#
28374716 100)
COMMENT                                    (LOGPEN 0 0 13408563) 1
COMMENT                                    (LOGFONT 27 10 0 0 400 0 0 0 0 3 2 1
18
COMMENT                                     "Georgia") 2.53336 0.555556 0
COMMENT                                    "{\\i Rsr}II (4377)" "@N (@S)" 5 0 0 -
6.14723
COMMENT                                    22.2426 3.41026 0.692308 #282#))
COMMENT                              (CObjectList))) (CObjectList))
COMMENT                #284=(CGroupWidget (CWidget 14 (16 0) 1 2 0 0 Nil 18088384
100)
COMMENT                      (CObjectList) (CObjectList))
COMMENT                #285=(CGroupWidget (CWidget 12 (0 0) 1 2 0 0 Nil 18088384
100)
COMMENT                      (CObjectList) (CObjectList))) (CObjectList)))
COMMENT       (CSeqView 10 10 (CObjectList) (CObList) 1 (CObList)) (CObList)
1095072823
COMMENT       (CStringList) 1145656400 2084918081 (CObList)))
FEATURES             Location/Qualifiers
     C_region        553..1643
                     /vntifkey="2"
                     /label=GeneArt\HC\C-Reg
                     /note="GeneArt human HC C-Reg"
     polyA_signal    1644..1875
                     /vntifkey="25"
                     /label=SV40\polyA
     misc_feature    7356..7699
                     /vntifkey="21"
                     /label=Signal\(SV40E\(and\SV40\ori))
                     /note="SV40E (and SV40 ori)"
     misc_RNA        complement(6121..6981)
                     /vntifkey="53"
                     /label=RNA\(beta-lactamase)\Amp(R)
                     /note="beta-lactamase"
     mRNA            7707..8906
                     /vntifkey="54"
                     /label=mRNA\(GS\cDNA)
                     /note="GS cDNA"
     promoter        9784..10926
                     /vntifkey="30"
                     /label=Promoter\(hCMV-MIE)
                     /note="hCMV-MIE promoter"
     intron          8909..9760
                     /vntifkey="15"
                     /label=Intron\(SV40\intron\+\poly\A)
                     /note="SV40 intron + poly A"
     5'UTR           10927..11047
                     /vntifkey="52"
                     /label=5'UTR_1
                     /note="5'UT"
     intron          11048..11874
                     /vntifkey="15"
                     /label=Intron_1
                     /note="intron"
     5'UTR           11875..11891
```

FIG.64 continued

```
                     /vntifkey="52"
                     /label=5'UTR_2
                     /note="5'UT"
     V_region        128..542
                     /vntifkey="45"
                     /label=Heavy\Chain\806\V-Region\Insert
     modified_base   4315..4315
                     /vntifkey="23"
                     /label=HtoY
                     /note="Histidine-to-Tyrosine change in the 806 Light-Chain
variable CDR3 region"
     modified_base   4716..4716
                     /vntifkey="23"
                     /label=Light-Const.\chg\2.1-3
                     /note="Light-chain c-region change 2.1-3"
     V_region        3999..4376
                     /vntifkey="45"
                     /label=Light-Chain\806\V-Region\insert
     promoter        1884..2902
                     /vntifkey="30"
                     /label=Promoter\(hCMV-MIE)\(from\NotI)
                     /note="Promoter (hCMV-MIE) (from NotI)"
     5'UTR           3851..3867
                     /vntifkey="52"
                     /label=5'UTR_2
                     /note="5'UT"
     intron          3024..3850
                     /vntifkey="15"
                     /label=Intron_1
                     /note="intron"
     5'UTR           2903..3023
                     /vntifkey="52"
                     /label=5'UTR_1
                     /note="5'UT"
     polyA_signal    4827..5063
                     /vntifkey="25"
                     /label=SV40\poly\A
                     /note="SV40 poly A"
     C_region        4390..4800
                     /vntifkey="2"
                     /label=Codon-Optimized\Kappa\Constant\Region
BASE COUNT     3000 a      3039 c      2868 g      2984 t
ORIGIN
        1 aagcttgccg ccaccatgga ttggacctgg cgcattctct ttctggtagc agccgccaca
       61 ggtaaggggc tgccaaatcc cagtgaggag gaagggatcg aaggtcacca tcgaagccag
      121 tcacccagtg aaggggggctt ccatccactc ctgtgtcttc tctacaggtg tccacagcca
      181 ggtgcagctc caagagagtg gacctgggct tgtcaagccg agtcaaactt tgtccctaac
      241 atgtactgtg tccggatact ctatctcatc agattttgcg tggaattgga taaggcagcc
      301 accagggaaa ggtttagaat ggatgggcta catatcatac tctgggaaca ccagatatca
      361 accttctctg aaaagccgga tcacaatctc aagggacacg tcgaagaatc agttcttcct
      421 gaaactgaac tccgttacag ccgcagacac agcaacatat tactgcgtaa ccgctggcag
      481 aggcttcccc tattggggac agggcaccct agtgacagtg agcagcggta agatggcaca
      541 ccgtggccgg cctctgcgcc tgggcccagc tctgtcccac accgcggtca catggcacct
      601 tttctcttcc agcctccacc aagggcccca gcgtgttccc cctggccccc agcagcaaga
      661 gcaccagcgg cggcacagcc gccctgggct gcctggtgaa ggactacttc cccgagcccg
      721 tgaccgtgag ctggaacagc ggagccctga cctccggcgt gcacaccttc cccgccgtgc
```

FIG.64 continued

```
 781 tgcagagcag cggcctgtac agcctgagca gcgtggtgac cgtgcccagc agcagcctgg
 841 gcacccagac ctacatctgc aacgtgaacc acaagcccag caacaccaag gtggacaaga
 901 aggtggagcc caagagctgc gacaagaccc acacctgccc cccctgccca gccccagagc
 961 tgctgggcgg accctccgtg ttcctgttcc cccccaagcc caaggacacc ctgatgatca
1021 gcaggacccc cgaggtgacc tgcgtggtgg tggacgtgag ccacgaggac ccagaggtga
1081 agttcaattg gtatgtggac ggcgtggagg tgcacaacgc caagaccaag cccagagaag
1141 agcagtacaa cagcacctac agggtggtgt ccgtgctgac cgtgctgcac caggactggc
1201 tgaacggcaa ggaatacaaa tgcaaggtct ccaacaaggc cctgccagcc cccatcgaaa
1261 agaccatcag caaggccaag ggccagccac gggagcccca ggtgtacacc ctgccccccct
1321 cccgggacga gtgcaccaag aaccaggtgt ccctgacctg tctggtgaag ggcttctacc
1381 ccagcgacat cgccgtggag tgggagagca acggccagcc cgagaacaac tacaagacca
1441 ccccccccagt gctggacagc gacggcagct tcttcctgta cagcaagctg accgtggaca
1501 agagcaggtg gcagcagggc aacgtgttca gctgcagcgt gatgcacgag gccctgcaca
1561 accactacac ccagaagagc ctgagcctgt cccccggcaa gtgatgacga cgcggccgtg
1621 cggacgaccg aattcattga tcataatcag ccataccaca tttgtagagg ttttacttgc
1681 tttaaaaaac ctcccacacc tccccctgaa cctgaaacat aaaatgaatg caattgttgt
1741 tgttaacttg tttattgcag cttataatgg ttacaaataa agcaatagca tcacaaattt
1801 cacaaataaa gcatttttt cactgcattc tagttgtggt ttgtccaaac tcatcaatgt
1861 atcttatcat gtctggcggc cgccgatatt tgaaaatatg gcatattgaa aatgtcgccg
1921 atgtgagttt ctgtgtaact gatatcgcca tttttccaaa agtgattttt gggcatacgc
1981 gatatctggc gatagcgctt atatcgttta cgggggatgg cgatagacga ctttggtgac
2041 ttgggcgatt ctgtgtgtcg caaatatcgc agtttcgata taggtgacag acgatatgag
2101 gctatatcgc cgatagaggc gacatcaagc tggcacatgg ccaatgcata tcgatctata
2161 cattgaatca atattggcca ttagccatat tattcattgg ttatatagca taaatcaata
2221 ttggctattg gccattgcat acgttgtatc catatcataa tatgtacatt tatattggct
2281 catgtccaac attaccgcca tgttgacatt gattattgac tagttattaa tagtaatcaa
2341 ttacggggtc attagttcat agcccatata tggagttccg cgttacataa cttacggtaa
2401 atggcccgcc tggctgaccg cccaacgacc cccgcccatt gacgtcaata atgacgtatg
2461 ttcccatagt aacgccaata gggactttcc attgacgtca atgggtggag tatttacggt
2521 aaactgccca cttggcagta catcaagtgt atcatatgcc aagtacgccc cctattgacg
2581 tcaatgacgg taaatggccc gcctggcatt atgcccagta catgacctta tgggactttc
2641 ctacttggca gtacatctac gtattagtca tcgctattac catggtgatg cggttttggc
2701 agtacatcaa tgggcgtgga tagcggtttg actcacgggg atttccaagt ctccacccca
2761 ttgacgtcaa tgggagtttg ttttggcacc aaaatcaacg ggactttcca aaatgtcgta
2821 acaactccgc cccattgacg caaatgggcg gtaggcgtgt acggtgggag gtctatataa
2881 gcagagctcg tttagtgaac cgtcagatcg cctggagacg ccatccacgc tgttttgacc
2941 tccatagaag acaccgggac cgatccagcc tccgcggccg ggaacggtgc attggaacgc
3001 ggattccccg tgccaagagt gacgtaagta ccgcctatag agtctatagg cccacccccct
3061 tggcttctta tgcatgctat actgtttttg gcttggggtc tatacacccc cgcttcctca
3121 tgttataggt gatggtatag cttagcctat aggtgtgggt tattgaccat tattgaccac
3181 tcccctattg gtgacgatac tttccattac taatccataa catggctctt tgccacaact
3241 ctctttattg gctatatgcc aatacactgt ccttcagaga ctgacacgga ctctgtattt
3301 ttacaggatg gggtctcatt tattatttac aaattcacat atacaacacc accgtcccca
3361 gtgcccgcag tttttattaa acataacgtg ggatctccac gcgaatctcg ggtacgtgtt
3421 ccggacatgg gctcttctcc ggtagcggcg gagcttctac atccgagccc tgctcccatg
3481 cctccagcga ctcatggtcg ctcggcagct ccttgctcct aacagtggag gccagactta
3541 ggcacagcac gatgcccacc accaccagtg tgccgcacaa ggccgtggcg gtagggtatg
3601 tgtctgaaaa tgagctcggg gagcgggctt gcaccgctga cgcatttgga agacttaagg
3661 cagcggcaga agaagatgca ggcagctgag ttgttgtgtt ctgataagag tcagaggtaa
3721 ctcccgttgc ggtgctgtta acggtggagg gcagtgtagt ctgagcagta ctcgttgctg
3781 ccgcgcgcgc caccagacat aatagctgac agactaacag actgttcctt tccatgggtc
3841 ttttctgcag tcaccgtcct tgacacgaag cttgccgcca ccatggattg gacttggaga
3901 atactgtttc ttgtagcagc cgcaacaggt aaggggctgc caaatcccag tgaggaggaa
3961 gggatcgaag gtgaccatcg aagccagtca agggggcgga ccgcttccat ccactcctgt
4021 gtcttctcta caggtgttca cagtgatatt cagatgactc agagtccatc cagcatgtca
4081 gtctccgtgg gagatagggt gacgataacc tgtcattcaa gccaagacat caactccaat
```

FIG.64 continued

```
4141 attggatggc tccaacagaa gcctggtaag tccttcaaag gactaatcta tcacggaaca
4201 aacttggacg acggcgtgcc atcgagattt tcagggtctg gcagcgggac cgactataca
4261 ctgaccatct ctagcttaca accagaggac tttgccacat actactgcgt ccagtacgct
4321 cagttcccct ggacattcgg cggcggcaca aaactggaaa tcaaacgtga gtagcggtcc
4381 gttaattaaa gatccttcta aactctgagg gggtcggatg acgtggccat tgttacttaa
4441 acaccatcct gtttgcttct ttcctcagga accgtcgcag ctccctccgt gttcatcttc
4501 cccccatccg acgagcaact gaagtcaggc acagcctccg tggtgtgcct ccttaataac
4561 ttttacccaa gagaggccaa agtccagtgg aaagtggaca acgcactaca gagcgggaac
4621 tctcaggaaa gcgtgacaga gcaggactca aaagattcaa catacagcct atcttctacc
4681 ctgacactgt caaaagctga ttatgaaaag cacaaagtat atgcctgtga agtaactcat
4741 cagggactca gcagccctgt cactaaaagt tttaatagag gcgaatgctg ataagcggcc
4801 gtgcggacga ccgaattcat tgatcataat cagccatacc acatttgtag aggttttact
4861 tgctttaaaa aacctcccac acctcccccc gaacctgaaa cataaaatga atgcaattgt
4921 tgttgttaac ttgtttattg cagcttataa tggttacaaa taaagcaata gcatcacaaa
4981 tttcacaaat aaagcatttt tttcactgca ttctagttgt ggtttgtcca aactcatcaa
5041 tgtatcttat catgtctgga tcctctacgc cggacgcatc gtggccggca tcaccggcgc
5101 cacaggtgcg gttgctggcg cctatatcgc cgacatcacc gatggggaag atcgggctcg
5161 ccacttcggg ctcatgagcg cttgtttcgg cgtgggtatg gtggcaggcc ccgtggccgg
5221 gggactgttg ggcgccatct ccttgcatgc accattcctt gcggcggcgg tgctcaacgg
5281 cctcaaccta ctactgggct gcttcctaat gcaggagtcg cataagggag agcgtcgacc
5341 tcgggccgcg ttgctggcgt ttttccatag gctccgcccc cctgacgagc atcacaaaaa
5401 tcgacgctca agtcagaggt ggcgaaaccc gacaggacta taaagatacc aggcgtttcc
5461 ccctggaagc tccctcgtgc gctctcctgt tccgaccctg ccgcttaccg gatacctgtc
5521 cgcctttctc ccttcgggaa gcgtggcgct ttctcatagc tcacgctgta ggtatctcag
5581 ttcggtgtag gtcgttcgct ccaagctggg ctgtgtgcac gaaccccccg ttcagcccga
5641 ccgctgcgcc ttatccggta actatcgtct tgagtccaac ccggtaagac acgacttatc
5701 gccactggca gcagccactg gtaacaggat tagcagagcg aggtatgtag gcggtgctac
5761 agagttcttg aagtggtggc ctaactacgg ctacactaga agaacagtat ttggtatctg
5821 cgctctgctg aagccagtta ccttcggaaa aagagttggt agctcttgat ccggcaaaca
5881 aaccaccgct ggtagcggtg gtttttttgt ttgcaagcag cagattacgc gcagaaaaaa
5941 aggatctcaa gaagatcctt tgatcttttc tacggggtct gacgctcagt ggaacgaaaa
6001 ctcacgttaa gggattttgg tcatgagatt atcaaaaagg atcttcacct agatcctttt
6061 aaattaaaaa tgaagtttta aatcaatcta aagtatatat gagtaaactt ggtctgacag
6121 ttaccaatgc ttaatcagtg aggcacctat ctcagcgatc tgtctatttc gttcatccat
6181 agttgcctga ctccccgtcg tgtagataac tacgatacgg gagggcttac catctggccc
6241 cagtgctgca atgataccgc gagacccacg ctcaccggct ccagatttat cagcaataaa
6301 ccagccagcc ggaagggccg agcgcagaag tggtcctgca actttatccg cctccatcca
6361 gtctattaat tgttgccggg aagctagagt aagtagttcg ccagttaata gtttgcgcaa
6421 cgttgttgcc attgctacag gcatcgtggt gtcacgctcg tcgtttggta tggcttcatt
6481 cagctccggt tcccaacgat caaggcgagt tacatgatcc cccatgttgt gcaaaaaagc
6541 ggttagctcc ttcggtcctc cgatcgttgt cagaagtaag ttggccgcag tgttatcact
6601 catggttatg gcagcactgc ataattctct tactgtcatg ccatccgtaa gatgcttttc
6661 tgtgactggt gagtactcaa ccaagtcatt ctgagaatag tgtatgcggc gaccgagttg
6721 ctcttgcccg gcgtcaatac gggataatac cgcgccacat agcagaactt taaaagtgct
6781 catcattgga aaacgttctt cggggcgaaa actctcaagg atcttaccgc tgttgagatc
6841 cagttcgatg taacccactc gtgcacccaa ctgatcttca gcatctttta ctttcaccag
6901 cgtttctggg tgagcaaaaa caggaaggca aaatgccgca aaaaagggaa taagggcgac
6961 acggaaatgt tgaatactca tactcttcct ttttcaatat tattgaagca tttatcaggg
7021 ttattgtctc atgagcggat acatatttga atgtatttag aaaaataaac aaataggggt
7081 tccgcgcaca tttccccgaa aagtgccacc tgacgtctaa gaaaccatta ttatcatgac
7141 attaacctat aaaaataggc gtatcacgag gccctgatgg ctctttgcgg cacccatcgt
7201 tcgtaatgtt ccgtggcacc gaggacaacc ctcaagagaa aatgtaatca cactggctca
7261 ccttcgggtg ggcctttctg cgtttataag gagacacttt atgtttaaga aggttggtaa
7321 attccttgcg gctttggcag ccaagctaga tccggctgtg gaatgtgtgt cagttagggt
7381 gtggaaagtc cccaggctcc ccagcaggca gaagtatgca aagcatgcat ctcaattagt
7441 cagcaaccag gtgtggaaag tccccaggct ccccagcagg cagaagtatg caaagcatgc
```

FIG.64 continued

```
 7501 atctcaatta gtcagcaacc atagtcccgc ccctaactcc gcccatcccg cccctaactc
 7561 cgcccagttc cgcccattct ccgccccatg gctgactaat ttttttttatt tatgcagagg
 7621 ccgaggccgc ctcggcctct gagctattcc agaagtagtg aggaggcttt tttggaggcc
 7681 taggcttttg caaaaagcta gcttggggcc accgctcaga gcaccttcca ccatggccac
 7741 ctcagcaagt tcccacttga acaaaaacat caagcaaatg tacttgtgcc tgccccaggg
 7801 tgagaaagtc caagccatgt atatctgggt tgatggtact ggagaaggac tgcgctgcaa
 7861 aacccgcacc ctggactgtg agcccaagtg tgtagaagag ttacctgagt ggaattttga
 7921 tggctctagt acctttcagt ctgagggctc caacagtgac atgtatctca gccctgttgc
 7981 catgtttcgg gacccccttcc gcagagatcc caacaagctg gtgttctgtg aagttttcaa
 8041 gtacaaccgg aagcctgcag agaccaattt aaggcactcg tgtaaacgga taatggacat
 8101 ggtgagcaac cagcacccct ggtttggaat ggaacaggag tatactctga tgggaacaga
 8161 tgggcaccct tttggttggc cttccaatgg ctttcctggg ccccaaggtc cgtattactg
 8221 tggtgtgggc gcagacaaag cctatggcag ggatatcgtg gaggctcact accgcgcctg
 8281 cttgtatgct ggggtcaaga ttacaggaac aaatgctgag gtcatgcctg cccagtggga
 8341 actccaaata ggaccctgtg aaggaatccg catgggagat catctctggg tggcccgttt
 8401 catcttgcat cgagtatgtg aagactttgg ggtaatagca acctttgacc ccaagcccat
 8461 tcctgggaac tggaatggtg caggctgcca taccaacttt agcaccaagg ccatgcggga
 8521 ggagaatggt ctgaagcaca tcgaggaggc catcgagaaa ctaagcaagc ggcaccggta
 8581 ccacattcga gcctacgatc ccaaggggcg cctggacaat gcccgtggtc tgactgggtt
 8641 ccacgaaacg tccaacatca acgacttttc tgctggtgtc gccaatcgca gtgccagcat
 8701 ccgcattccc cggactgtcg gccaggagaa gaaaggttac tttgaagacc gcggcccctc
 8761 tgccaattgt gacccctttg cagtgacaga agccatcgtc cgcacatgcc ttctcaatga
 8821 gactggcgac gagcccttcc aatacaaaaa ctaattagac tttgagtgat cttgagcctt
 8881 tcctagttca tcccaccccg ccccagagag atctttgtga aggaacctta cttctgtggt
 8941 gtgacataat tggacaaact acctacagag atttaaagct ctaaggtaaa tataaaattt
 9001 ttaagtgtat aatgtgttaa actactgatt ctaattgttt gtgtatttta gattccaacc
 9061 tatggaactg atgaatggga gcagtggtgg aatgccttta atgaggaaaa cctgttttgc
 9121 tcagaagaaa tgccatctag tgatgatgag gctactgctg actctcaaca ttctactcct
 9181 ccaaaaaaga agagaaaggt agaagacccc aaggactttc cttcagaatt gctaagtttt
 9241 ttgagtcatg ctgtgtttag taatagaact cttgcttgct ttgctattta caccacaaag
 9301 gaaaaagctg cactgctata caagaaaatt atggaaaaat attctgtaac ctttataagt
 9361 aggcataaca gttataatca taacatactg ttttttctta ctccacacag gcatagagtg
 9421 tctgctatta ataactatgc tcaaaaattg tgtaccttta gctttttaat ttgtaaaggg
 9481 gttaataagg aatatttgat gtatagtgcc ttgactagag atcataatca gccataccac
 9541 atttgtagag gttttacttg ctttaaaaaa cctcccacac ctccccctga acctgaaaca
 9601 taaaatgaat gcaattgttg ttgttaactt gtttattgca gcttataatg gttacaaata
 9661 aagcaatagc atcacaaatt tcacaaataa agcatttttt tcactgcatt ctagttgtgg
 9721 tttgtccaaa ctcatcaatg tatcttatca tgtctggatc tagcttcgtg tcaaggacgg
 9781 tgactgcagt gaataataaa atgtgtgttt gtccgaaata cgcgttttga gatttctgtc
 9841 gccgactaaa ttcatgtcgc gcgatagtgg tgtttatcgc cgatagagat ggcgatattg
 9901 gaaaaatcga tatttgaaaa tatggcatat tgaaaatgtc gccgatgtga gtttctgtgt
 9961 aactgatatc gccatttttc caaaagtgat ttttgggcat acgcgatatc tggcgatagc
10021 gcttatatcg tttacggggg atggcgatag acgactttgg tgacttgggc gattctgtgt
10081 gtcgcaaata tcgcagtttc gatataggtg acagacgata tgaggctata tcgccgatag
10141 aggcgacatc aagctggcac atggccaatg catatcgatc tatacattga atcaatattg
10201 gccattagcc atattattca ttggttatat agcataaatc aatattggct attggccatt
10261 gcatacgttg tatccatatc ataatatgta catttatatt ggctcatgtc caacattacc
10321 gccatgttga cattgattat tgactagtta ttaatagtaa tcaattacgg ggtcattagt
10381 tcatagccca tatatggagt tccgcgttac ataacttacg gtaaatggcc cgcctggctg
10441 accgcccaac gacccccgcc cattgacgtc aataatgacg tatgttccca tagtaacgcc
10501 aatagggact ttccattgac gtcaatgggt ggagtattta cggtaaactg cccacttggc
10561 agtacatcaa gtgtatcata tgccaagtac gccccctatt gacgtcaatg acggtaaatg
10621 gcccgcctgg cattatgccc agtacatgac cttatgggac tttcctactt ggcagtacat
10681 ctacgtatta gtcatcgcta ttaccatggt gatgcggttt tggcagtaca tcaatgggcg
10741 tggatagcgg tttgactcac ggggatttcc aagtctccac cccattgacg tcaatgggag
10801 tttgttttgg caccaaaatc aacgggactt tccaaaatgt cgtaacaact ccgccccatt
```

FIG.64 continued

```
    10861 gacgcaaatg ggcggtaggc gtgtacggtg ggaggtctat ataagcagag ctcgtttagt
    10921 gaaccgtcag atcgcctgga gacgccatcc acgctgtttt gacctccata gaagacaccg
    10981 ggaccgatcc agcctccgcg gccgggaacg gtgcattgga acgcggattc cccgtgccaa
    11041 gagtgacgta agtaccgcct atagagtcta taggcccacc cccttggctt cttatgcatg
    11101 ctatactgtt tttggcttgg ggtctataca cccccgcttc ctcatgttat aggtgatggt
    11161 atagcttagc ctataggtgt gggttattga ccattattga ccactcccct attggtgacg
    11221 atactttcca ttactaatcc ataacatggc tctttgccac aactctcttt attggctata
    11281 tgccaataca ctgtccttca gagactgaca cggactctgt atttttacag gatggggtct
    11341 catttattat ttacaaattc acatatacaa caccaccgtc cccagtgccc gcagttttta
    11401 ttaaacataa cgtgggatct ccacgcgaat ctcgggtacg tgttccggac atgggctctt
    11461 ctccggtagc ggcggagctt ctacatccga gccctgctcc catgcctcca gcgactcatg
    11521 gtcgctcggc agctccttgc tcctaacagt ggaggccaga cttaggcaca gcacgatgcc
    11581 caccaccacc agtgtgccgc acaaggccgt ggcggtaggg tatgtgtctg aaaatgagct
    11641 cggggagcgg gcttgcaccg ctgacgcatt tggaagactt aaggcagcgg cagaagaaga
    11701 tgcaggcagc tgagttgttg tgttctgata agagtcagag gtaactcccg ttgcggtgct
    11761 gttaacggtg gagggcagtg tagtctgagc agtactcgtt gctgccgcgc gcgccaccag
    11821 acataatagc tgacagacta acagactgtt cctttccatg ggtcttttct gcagtcaccg
    11881 tccttgacac g
//
```

FIG.64 continued

Light Chain

CDR1-806 $_{23}$HSSQDI**N**SNIG
CDR1-175 $_{23}$HSSQDI**S**SNIG
CDR2-806 $_{49}$YHGTNL**D**D
CDR2-175 $_{49}$YHGTNL**E**D
CDR3-806 $_{89}$VQY**A**QFPWT
CDR3-175 $_{89}$VQY**G**QFPWT

Heavy Chain

CDR1-806 $_{31}$SD**F**AWN
CDR1-175 $_{31}$SD**Y**AWN
CDR2-806 $_{51}$YISYS**G**NTRYNPSLKS
CDR2-175 $_{51}$YISYS**A**NTRYNPSLKS
CDR3-806 $_{97}$**V**TAGRGFPY
CDR3-175 $_{97}$**A**TAGRGFPY

First residue number is given.
Underline indicates the residues which contact EGFR287-302

FIG.65



FIG.66A

FIG.66B

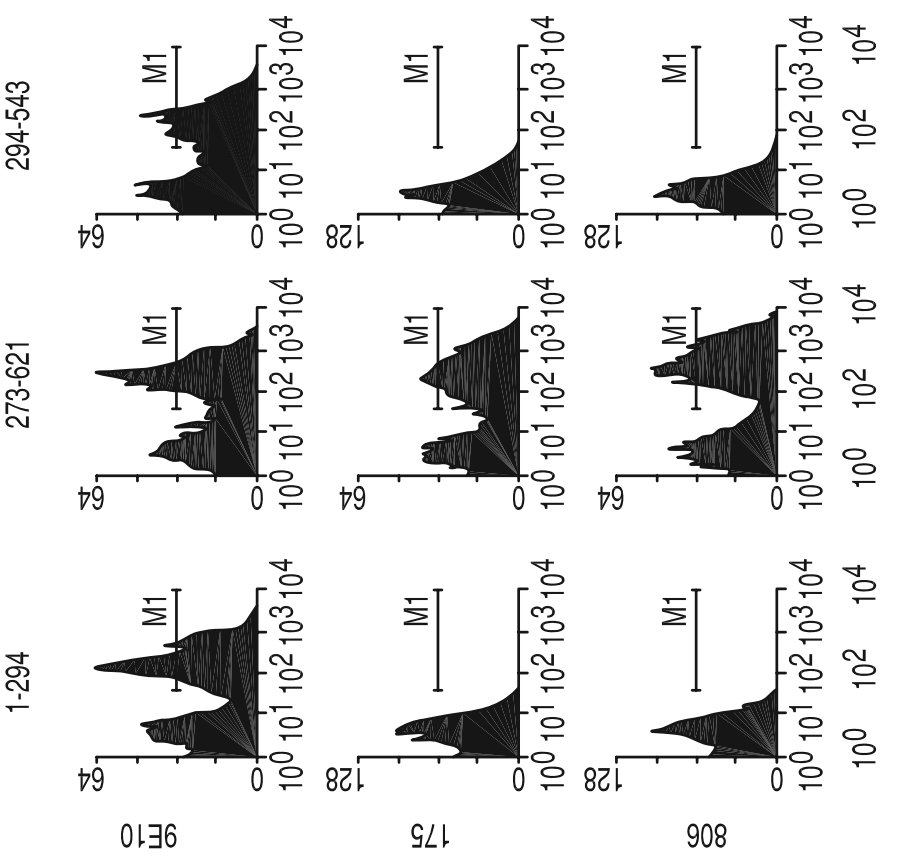


FIG. 67A

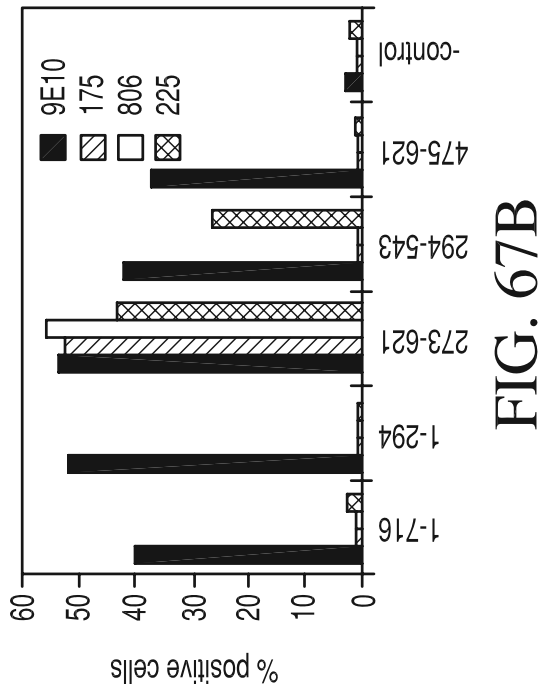


FIG. 67B

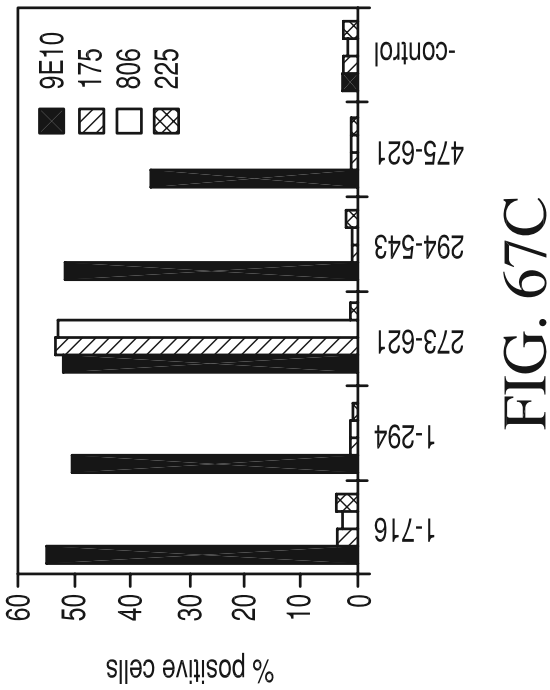


FIG. 67C

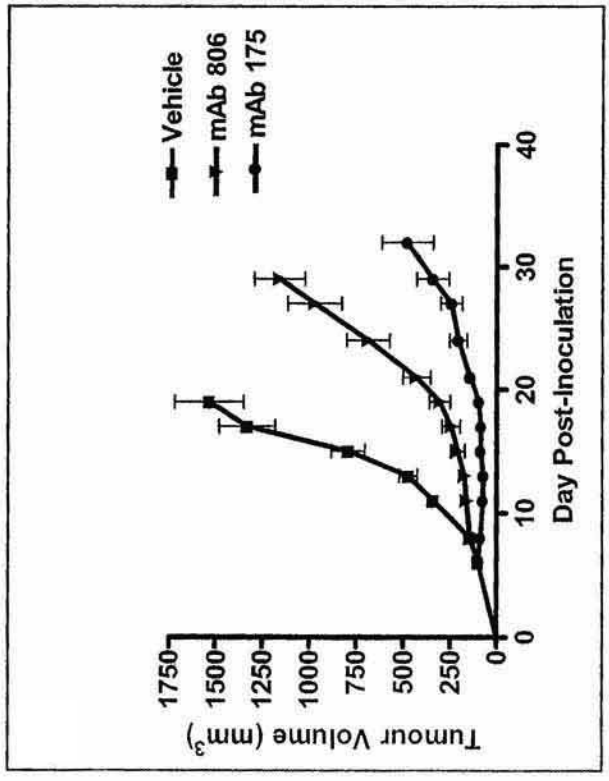


FIG.68A

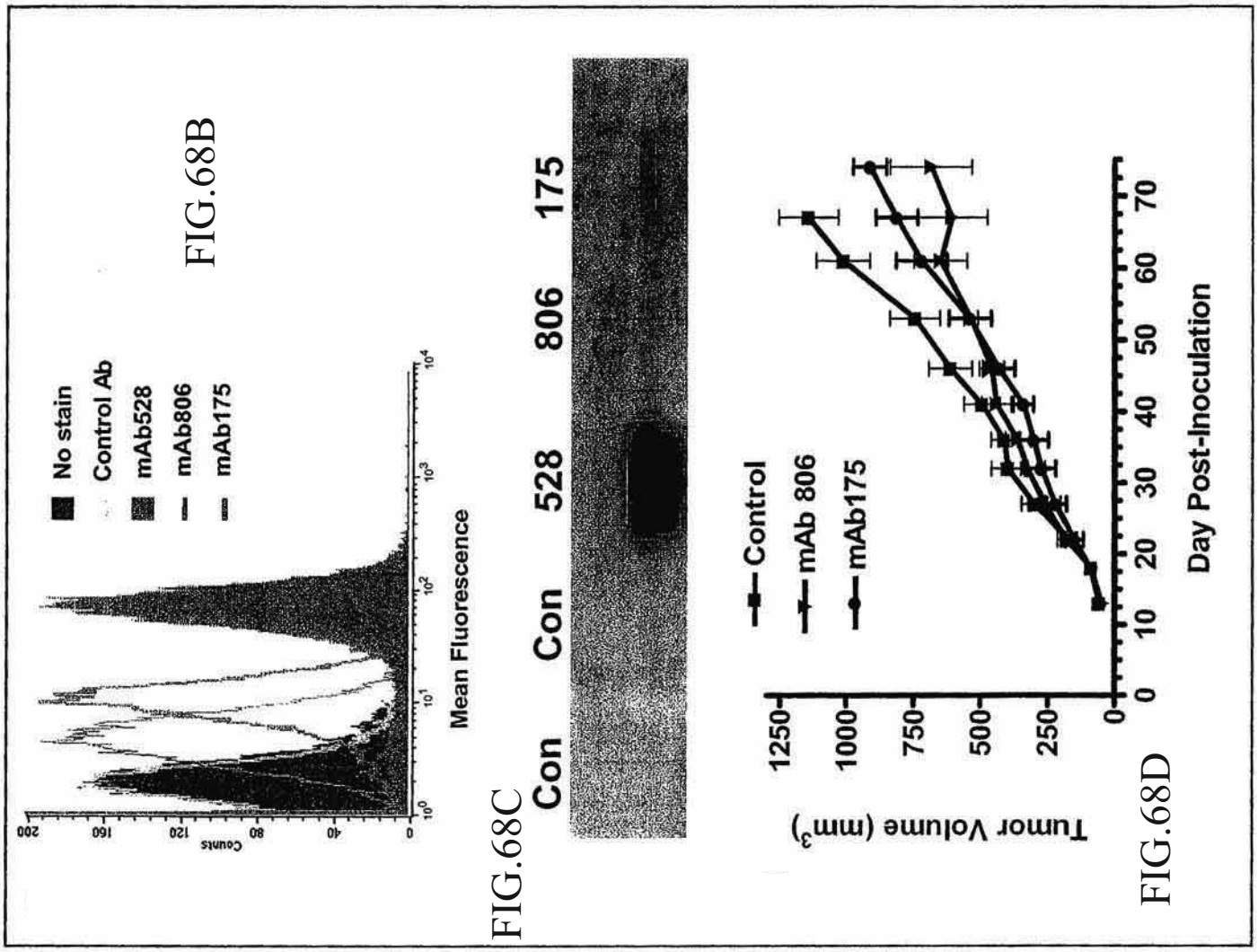
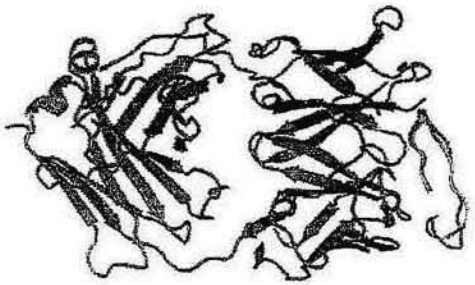


FIG.68B

FIG.68C

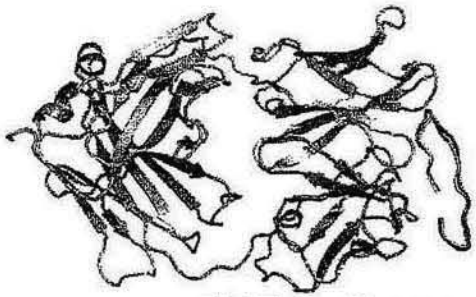
FIG.68D

FIG.69A



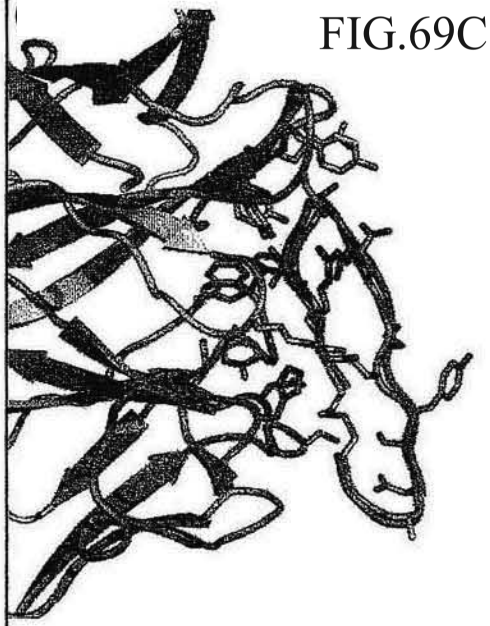
806 epitope

FIG.69B



175 epitope

FIG.69C



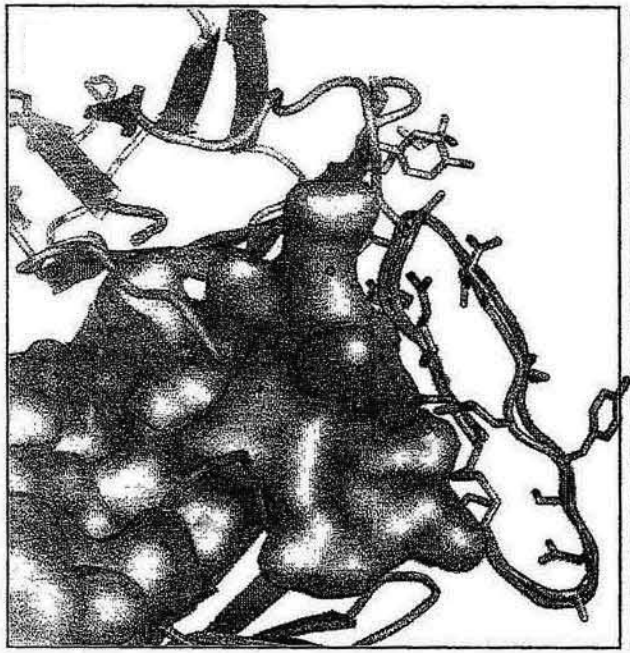


FIG.69D

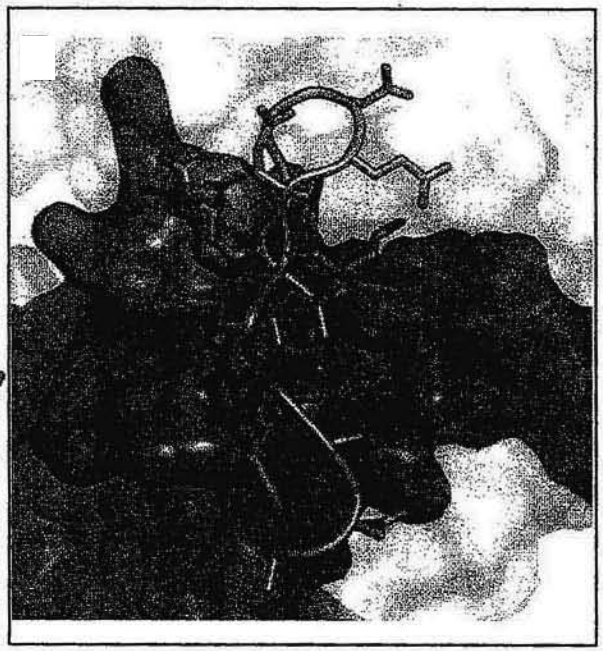


FIG.69E

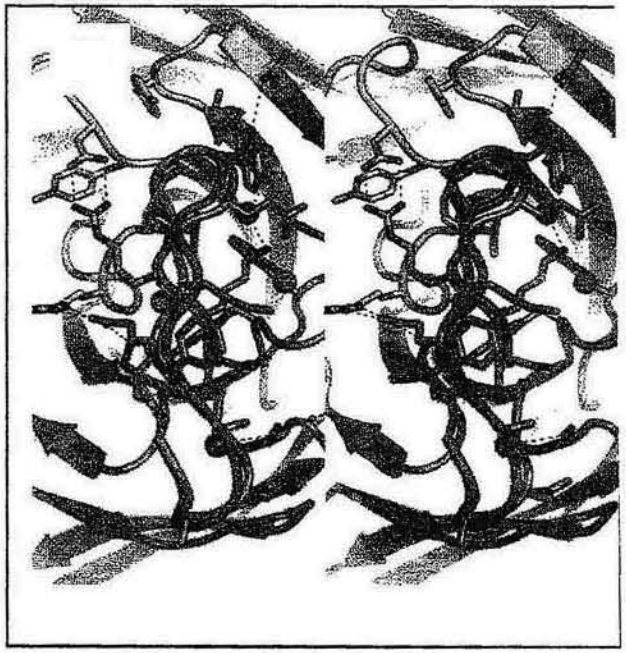


FIG.69F

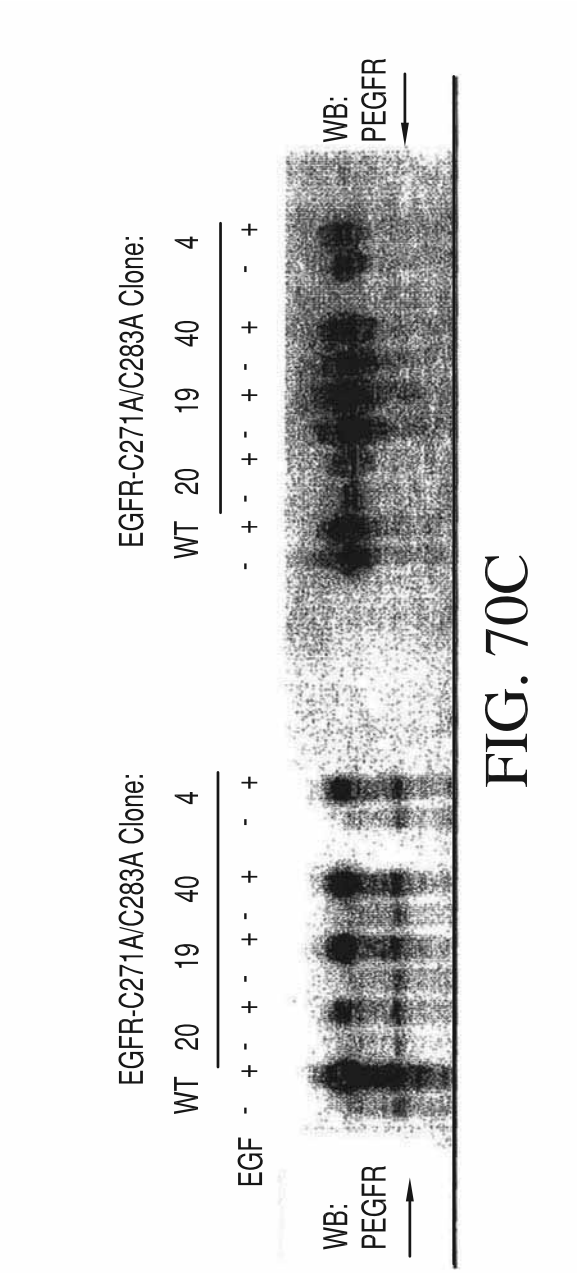


FIG. 70A

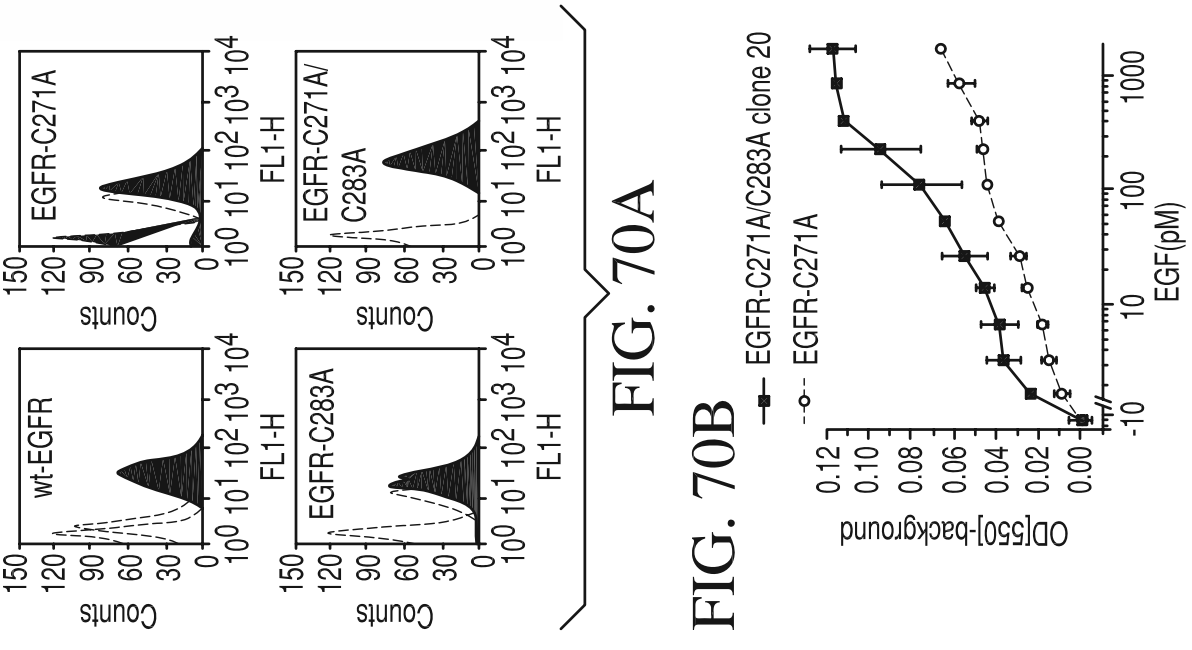


FIG. 70B

FIG. 70C

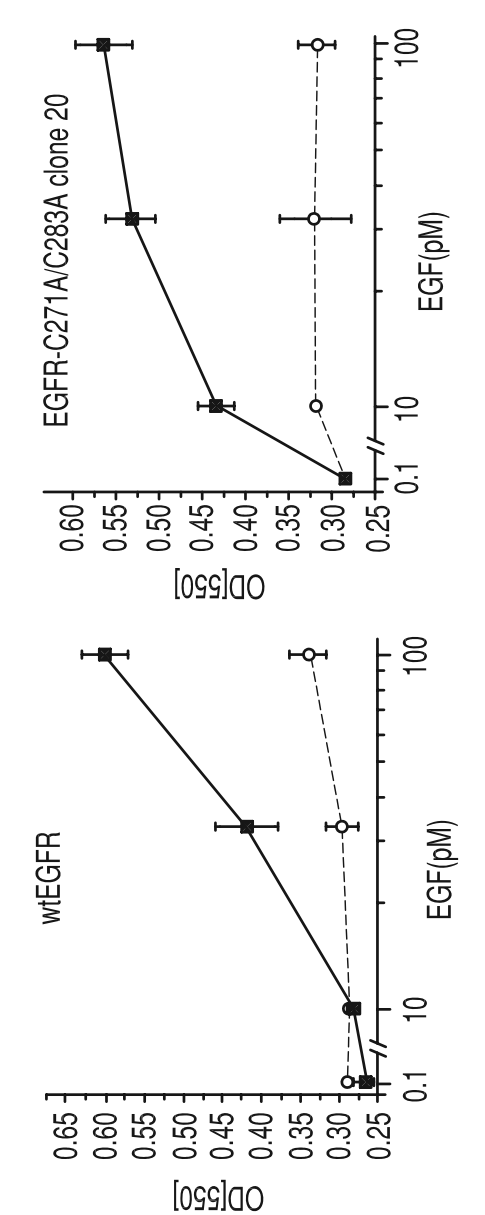


FIG. 70D

FIG.71A

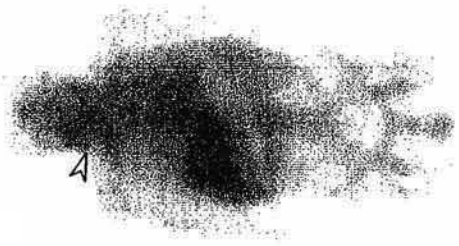


FIG.71B



FIG.71C



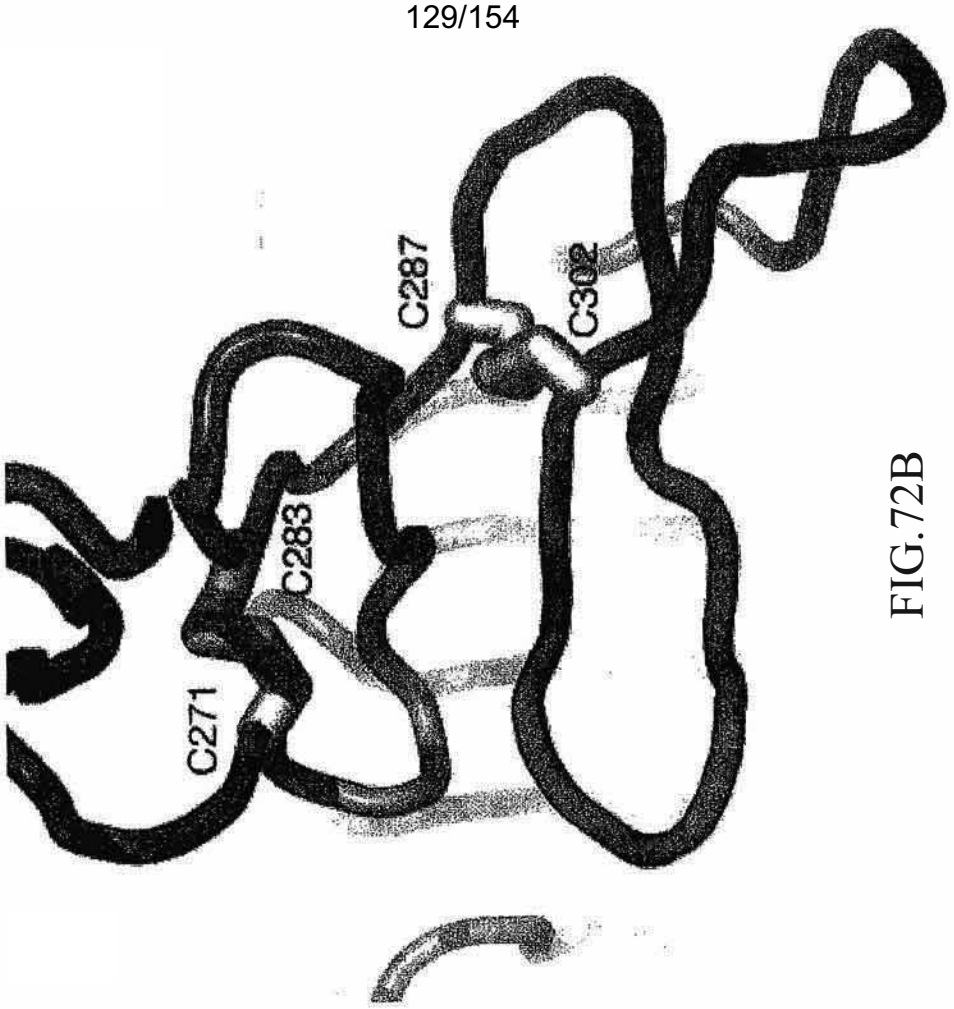


FIG.72B

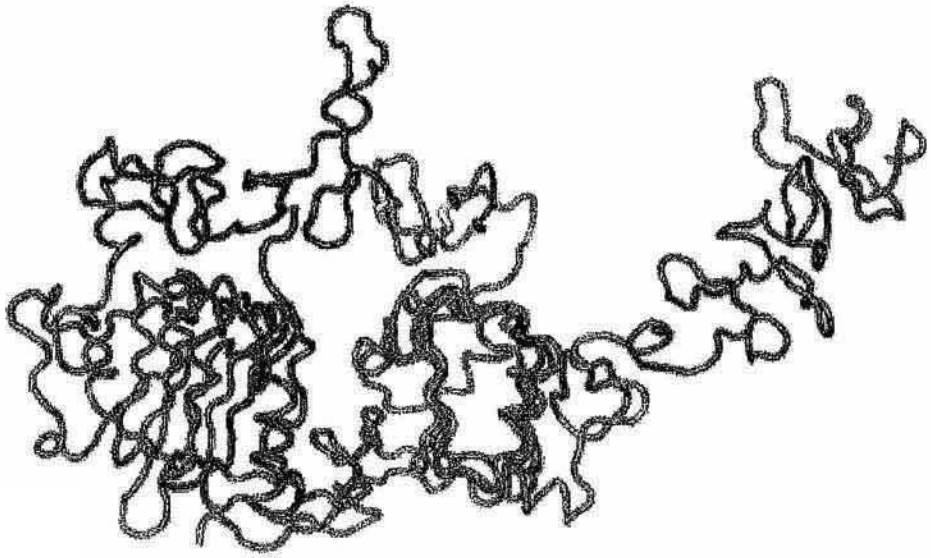


FIG.72A

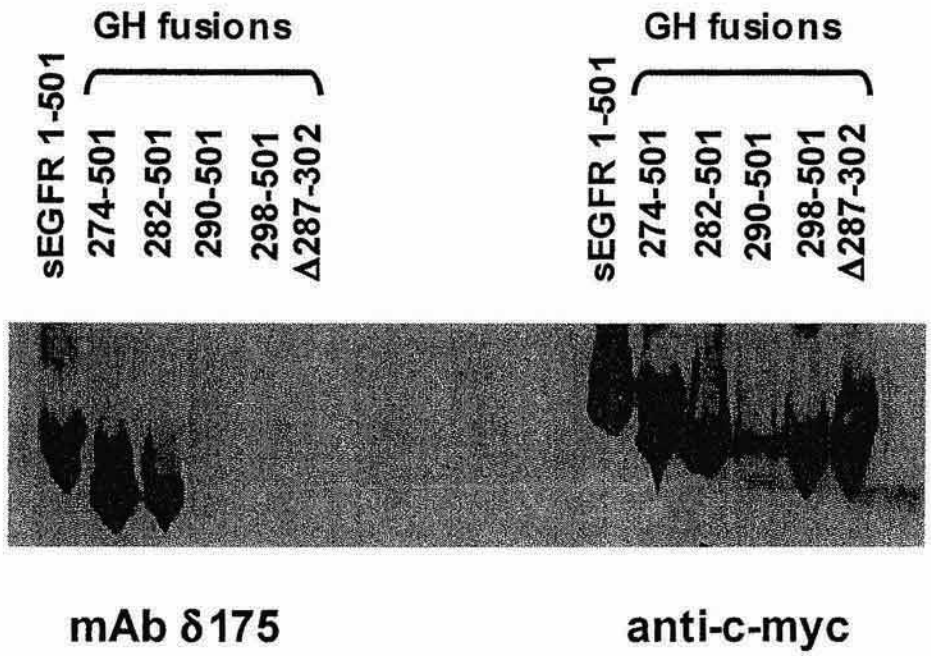

GH fusions
sEGFR 1-501
274-501
282-501
290-501
298-501
Δ287-302
GH fusions
sEGFR 1-501
274-501
282-501
290-501
298-501
Δ287-302
mAb δ175
anti-c-myc

FIG.73

mAb175 VH Chain: Nucleic Acid and Amino Sequences

Nucleic Acid Sequence

TTAGTCAAGCTGCAGGAGTCTGGACCTAGCCTGGTGAAACCTTCTCAGTCTCTGTCCCTCACCTGCACTGTCACTGGCTA
CTCAATCACCAGTGACTATGCCTGGAACTGGATCCGGCAGTTTCCAGGAAACAAACTGGAGTGGATGGGCTACATAAG
TTACAGTGCTAACACTAGGTACAACCCATCTCTCAAAAGTCGAATCTCTATCACTCGAGACACATCCAAGAACCAATTC
TTCCTGCAGTTGAATTCTGTGACTACTGAGGACACAGCCACATATTACTGTGCAACGGCGGGACGCGGGTTTCCTTACT
GGGGCCAAGGGACTCTGGTCACTGTCTCTGCAGCCAAAACGACACCC (SEQ ID NO:128)

FIG.74A

Amino Acid Sequence

LVKLQESGPSLVKPSQSLSLTCTVTGYSITSDYAWNWIRQFPGNKLEWMGYISYSANTRYNPSLKSRISITRDTSKNQFFLQLN
CDR1 *CDR2*
SVTTEDTATYYCATAGRGFPYWGQGTLVTVSA (SEQ ID NO:129)
CDR3

FIG.72B

mAb175 VL Chain: Nucleic Acid and Amino Sequences

Nucleic Acid Sequence

GACATTGTGCTGACCCAGTCTCCATCCTCCATGTCTCTATCTCTGGGAGACACAGTCAGTATCACTTGCCATTCAAGTCA
GGACATTAACAGTAATATAGGGTGGTTGCAGCAGAAACCAGGGAAATCATTTAAGGGCCTGATCTATCATGGAACCAA
CTTGGACGATGGAGTTCCATCAAGGTTCAGTGGCAGTGGATCTGGAGCCGATTATTCTCTCACCATCAGCAGCCTGGAA
TCTGAAGATTTTGTAGACTATTACTGTGTACAGTATGGTCAGTTTCCGTGGACGTTCGGTGGAGGCACCAAGCTGGAAA
TCAAACGG (SEQ ID NO:133)

FIG.75A

Amino Acid Sequence

DIVLTQSPSSMSLSLGDTVSITCHSSQDISSNIGWLQQKPGKSFKGLIYHGTNLEDGVPSRFSGSGSGADYSLTISSLESEDFVD
CDR1 *CDR2*
YYCVQYGQFPWTFGGGTKLEIKR (SEQ ID NO:134)
CDR3

FIG.75B

Volumetric product concentration and **B)** viable cell concentration of GS-CHO (14D8, 15B2 and 40A10) and GS-NS0 (36) hu806 transfectants in small scale (100mL) shake flasks cultures. Product concentration was estimated by ELISA using the 806 anti-idiotype as coating antibody and ch806 Clinical Lot: J06024 as standard.

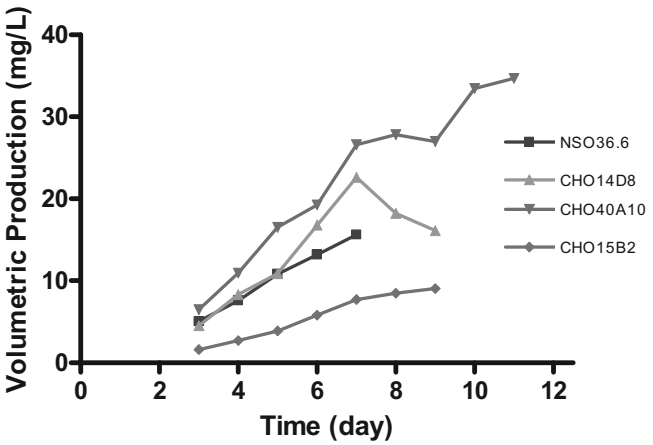


FIG.76A

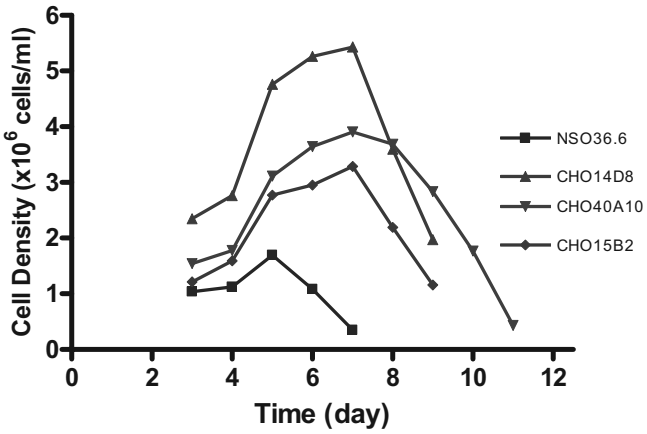


FIG.76B

GS-CHO 40A10 transfectant cell growth and volumetric production in a 15L stirred tank bioreactor. Viable cell density (◆x 10^5 cell/mL), cell viability (■) and production (▲mg/L)

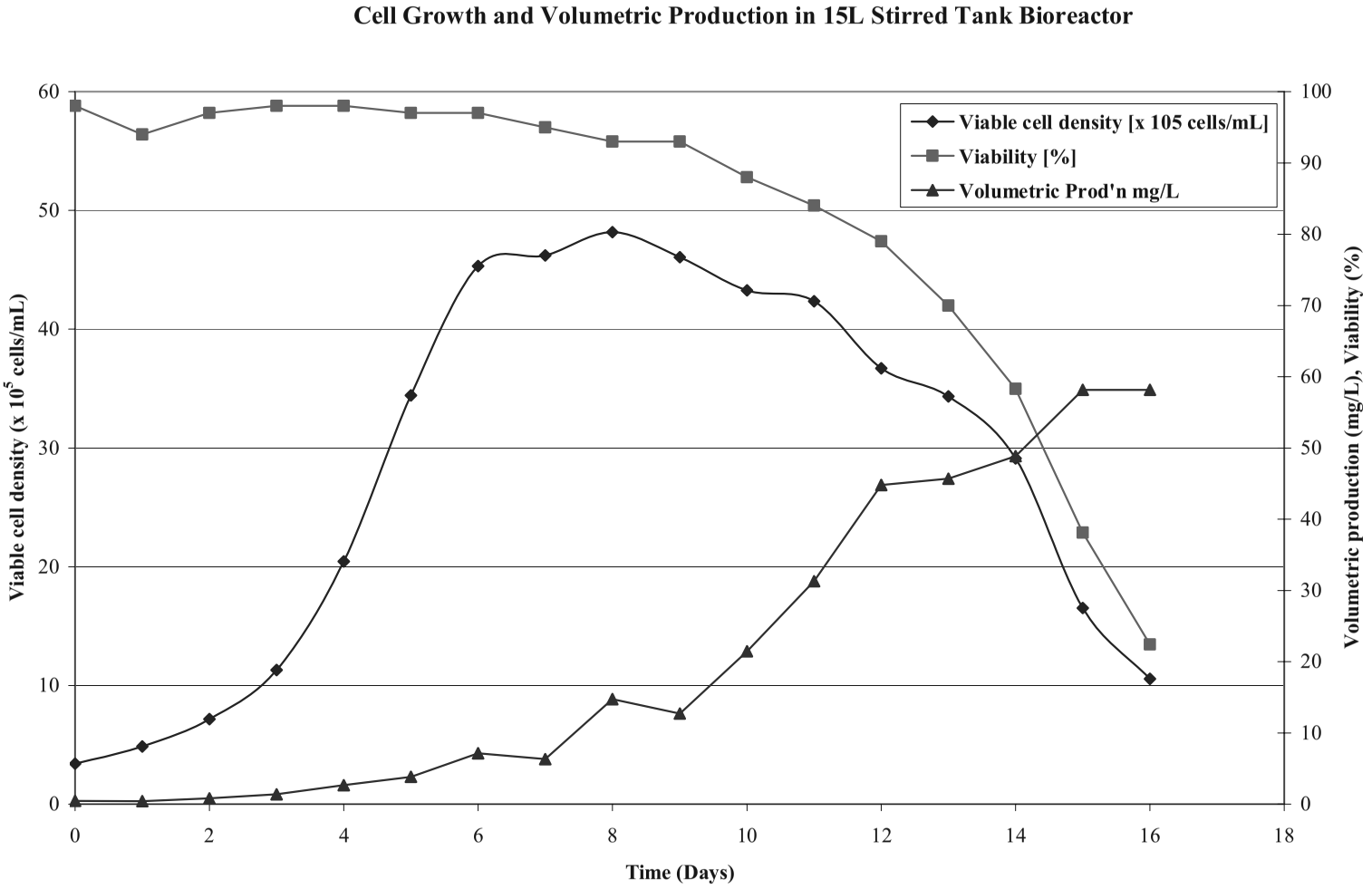


FIG.76C

Size exclusion Chromatography (Biosep SEC-S3000) Analysis of Protein-A purified hu806 antibody constructs produced by small scale culture and control ch806 and mAb 806. Chromatograms at A214nm are presented in the upper panels and at A280nm in the lower panel of each Figure.

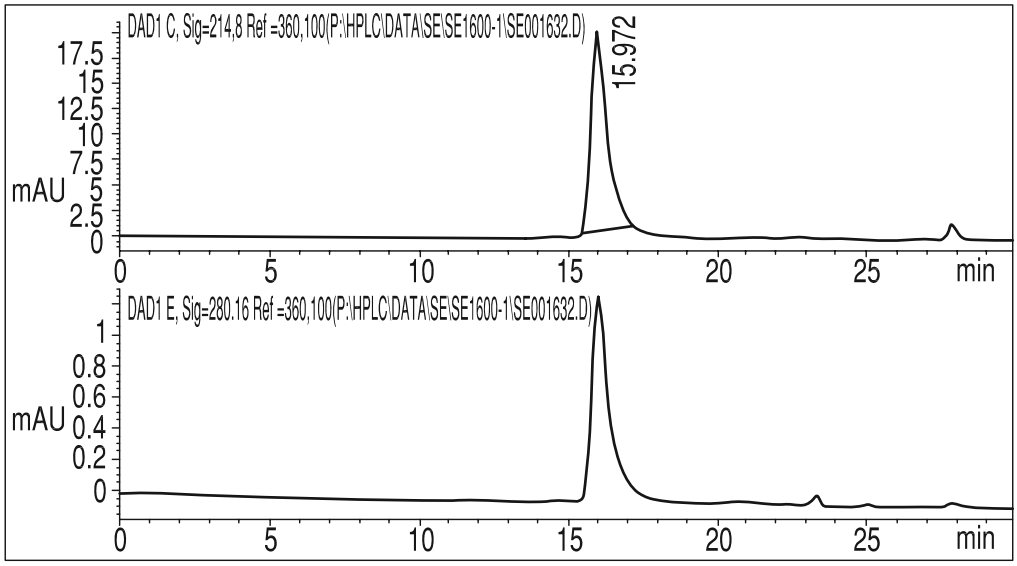


FIG. 77A

A) Control ch806, lot J06024

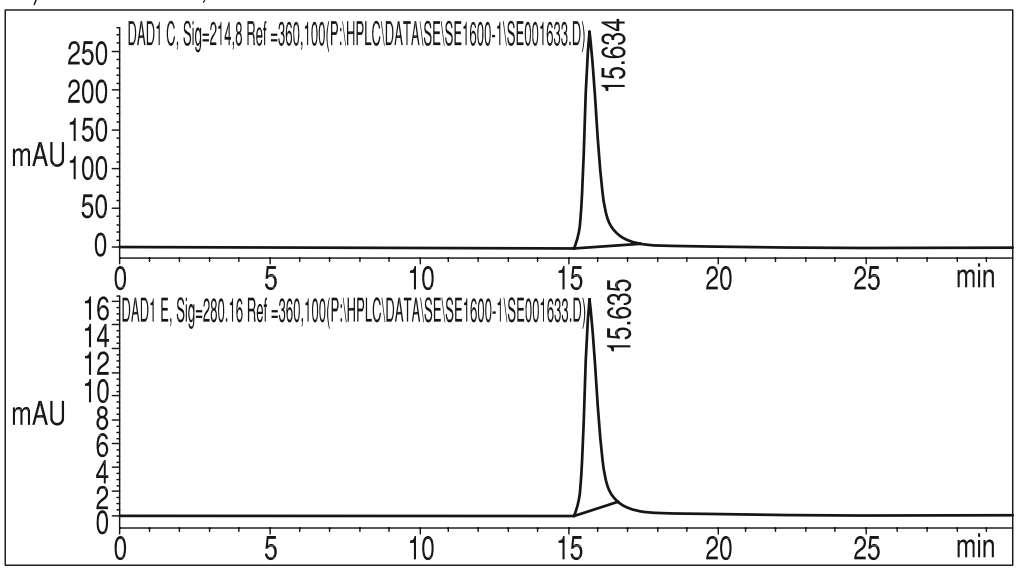


FIG. 77B

B) Control mAb806

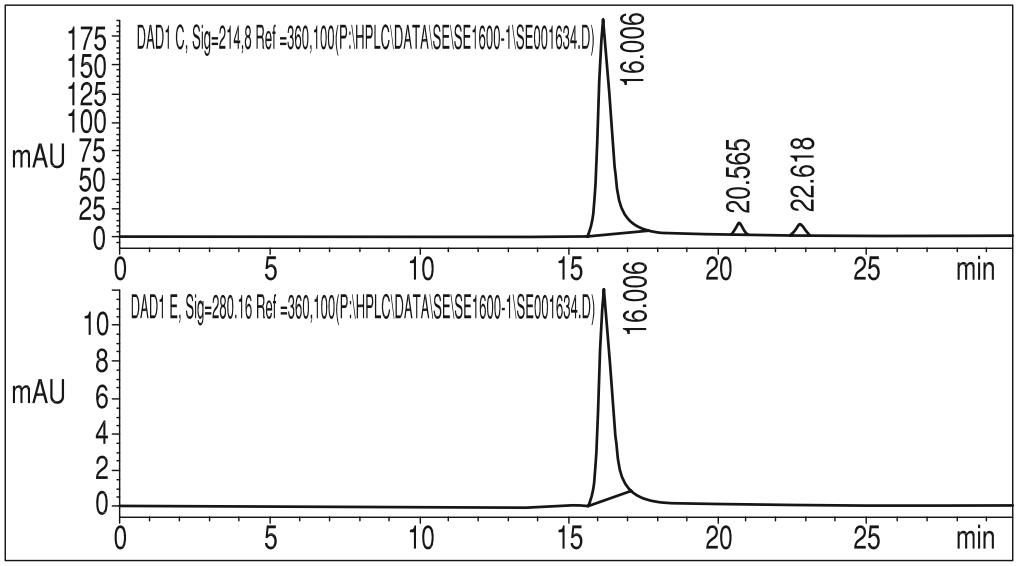
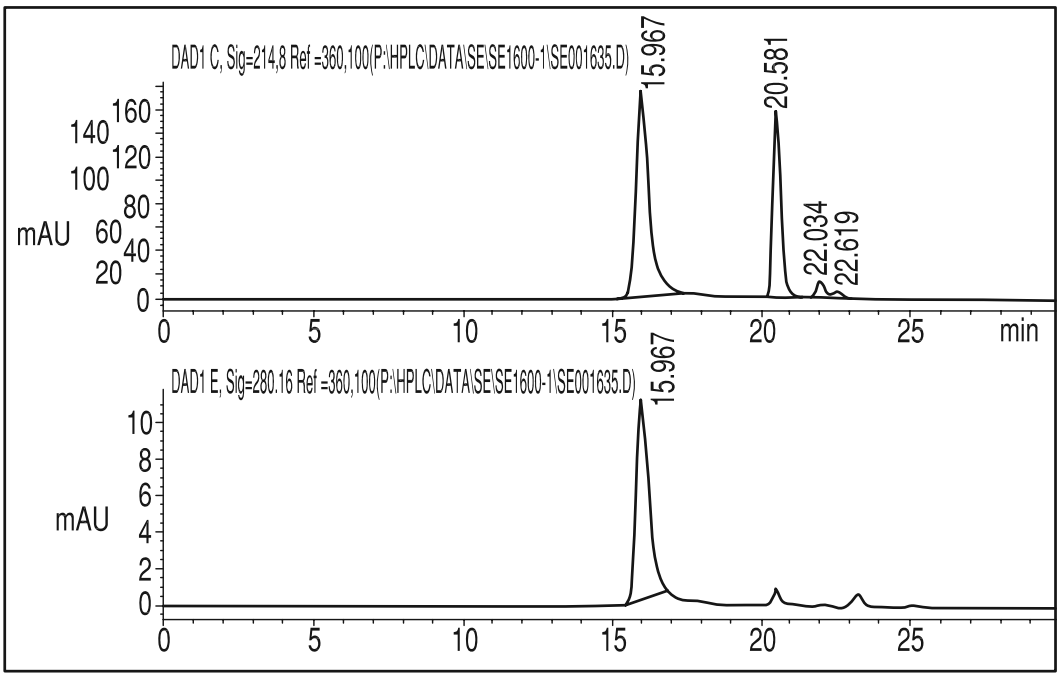


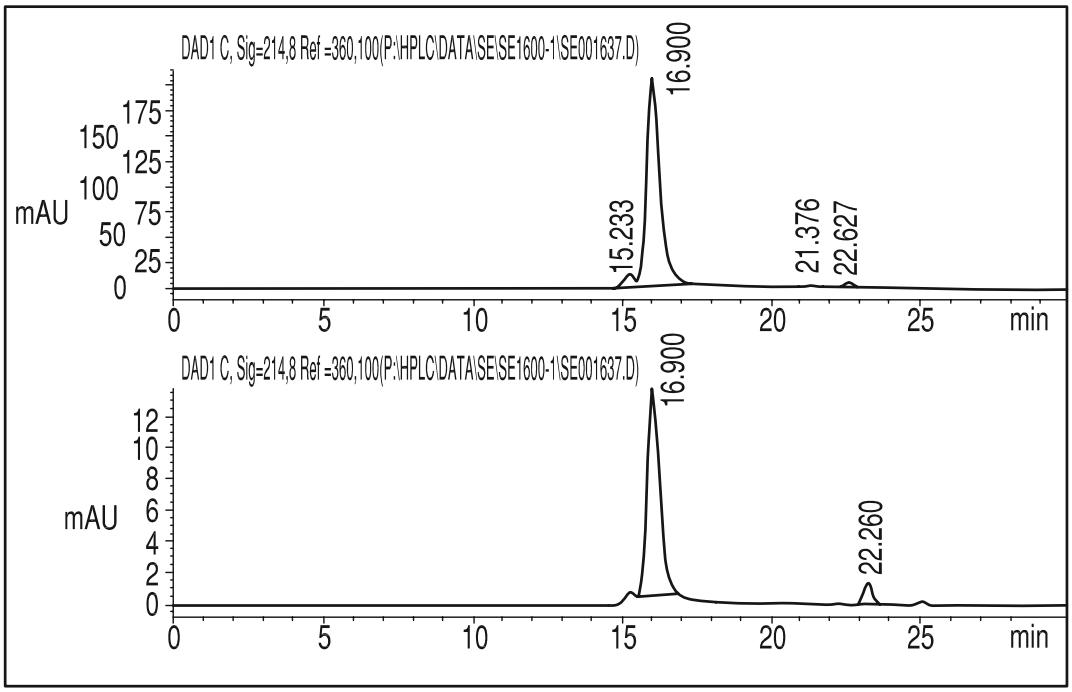
FIG. 77C

C) Purified GS-CHO hu806 14D8 transfectant product.



D): Purified GS-CHO hu806 15B2 transfectant product

FIG. 77D



E): Purified GS-NSO hu806 36 transfectant product

FIG. 77E

Figure 3. Size Exclusion Chromatography (Biosep SEC-S3000) Analysis of Protein-A purified hu806 antibody construct 40A10 following large scale production and protein A purification. chromatogram at A214nm is presented indicating 98.8% purity with 1.2% aggregate present.

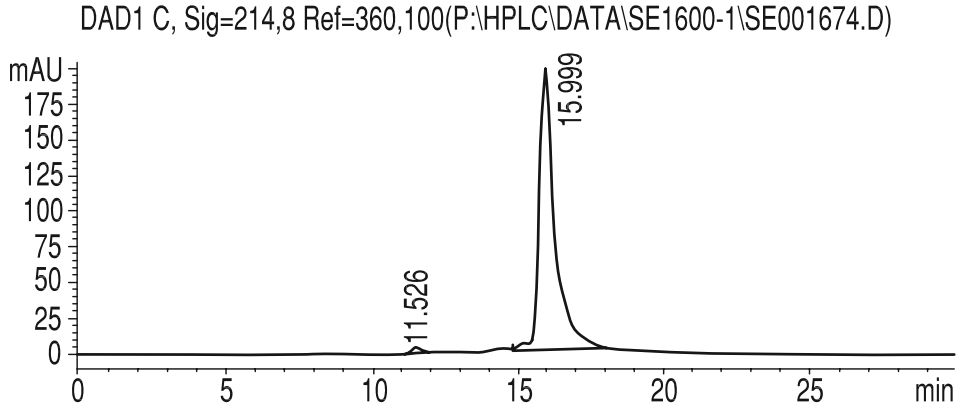


FIG. 78

Precast 4-20% Tris/Glycine Gels from Novex, USA were used under standard SDS-PAGE conditions to analyse purified transfectant hu806 preparations (5μg) GS CHO (14D8, 15B2 and 40A10) and GS-NSO (36) hu806 under reduced conditions. Proteins detected by Coomassie Blue Stain.

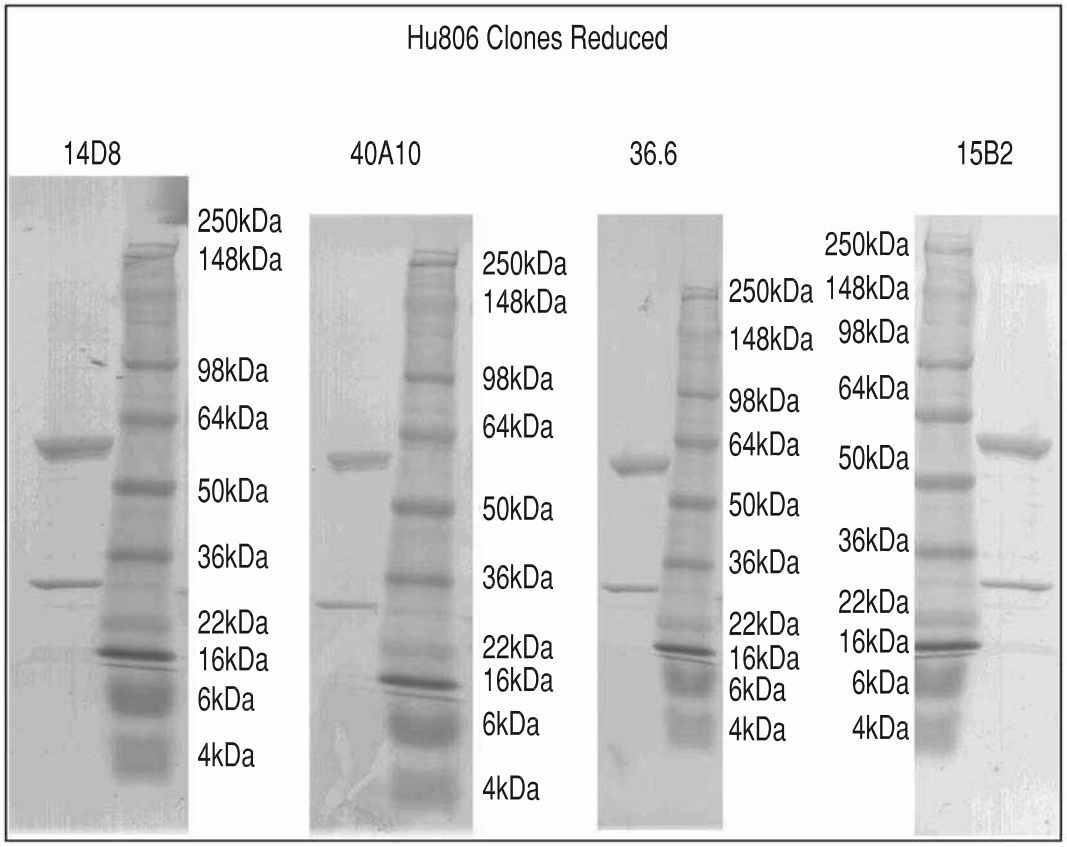


FIG. 79

Precast 4-20% Tris/Glycene Gels were used under standard SDS-PAGE conditions to analyse purified transfectant hu806 preparations (5μg) GS CHO (14D8, 15B2 and 40A10) and GS-NSO (36) under non-reduced conditions. Proteins detected by Coomassie Blue Stain.

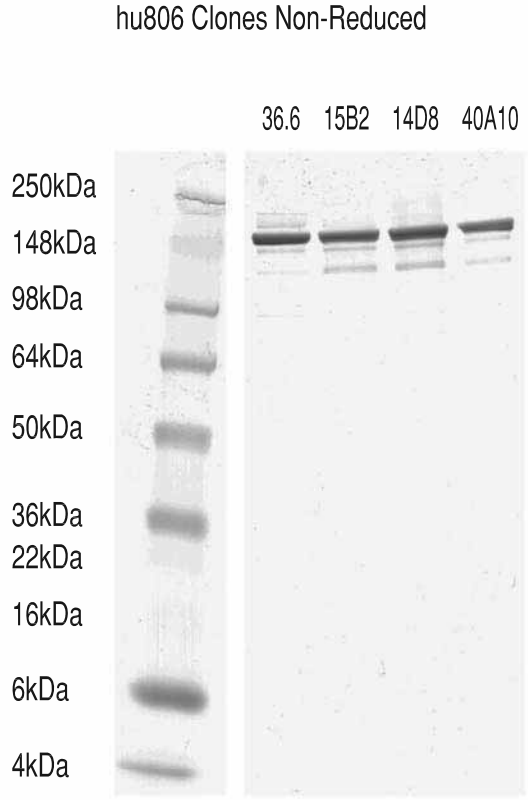


FIG. 80

Precast 4-20% Tris/Glycine Gels were used under standard SDS-PAGE conditions to analyze purified transfectant hu806 GS CHO 40A10 (5 μg) following large scale production. Proteins detected by Coomassie Blue Stain.

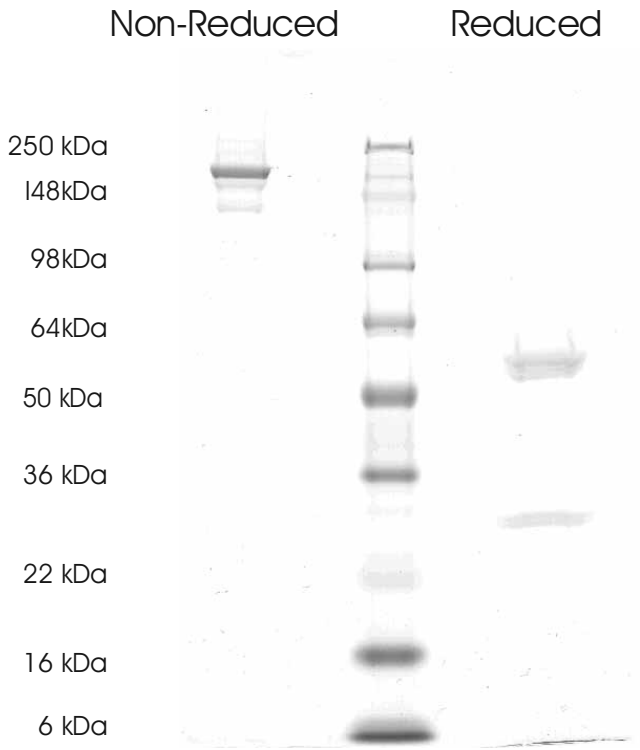


FIG.81

Isoelectric Focusing gel analysis of purified transfectant hu806 GS CHO 40A10 (5 μg) following 15L production. Proteins detected by Coomassie Blue Stain. Lane 1, pI markers; Lane 2, hu806 (three isoforms, pI 8.66 to 8.82); Lane 3, pI markers.

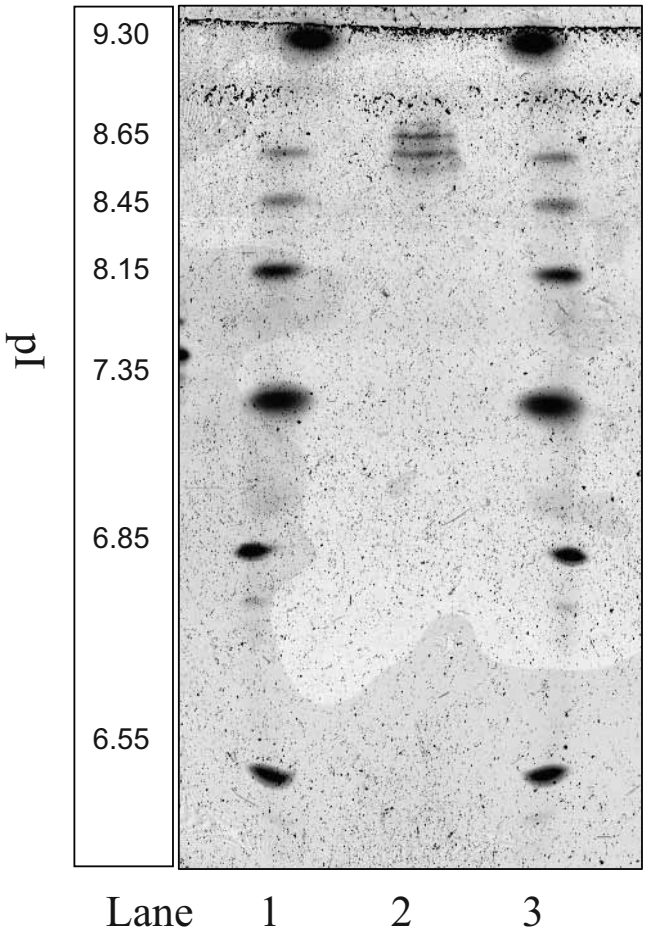


FIG.82

Binding to A431 cells: Flow Cytometry analysis of Protein-A purified hu806 antibody preparations (20 μg/ml), and isotype control huA33 (20 μg/ml). Controls include secondary antibody alone (green) and ch806 (red). Hu806 constructs were produced by small scale culture.

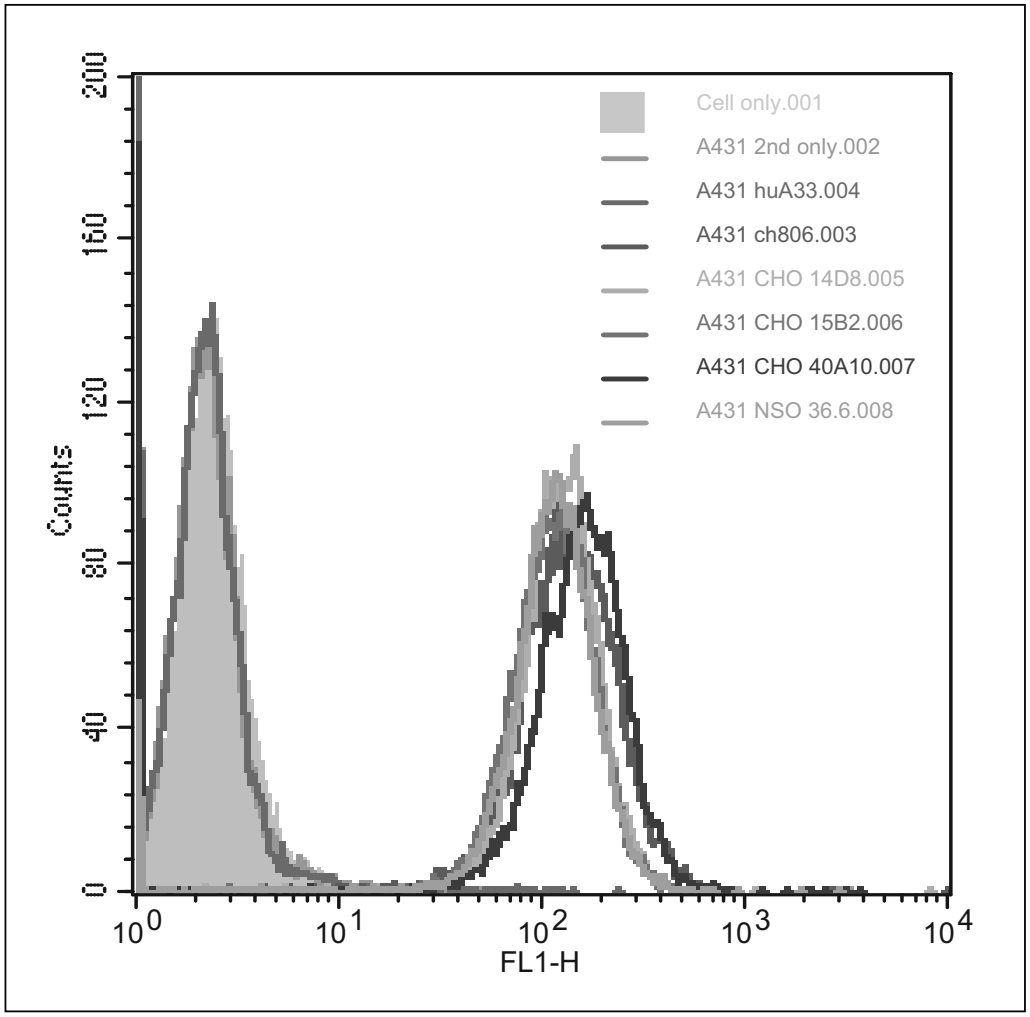
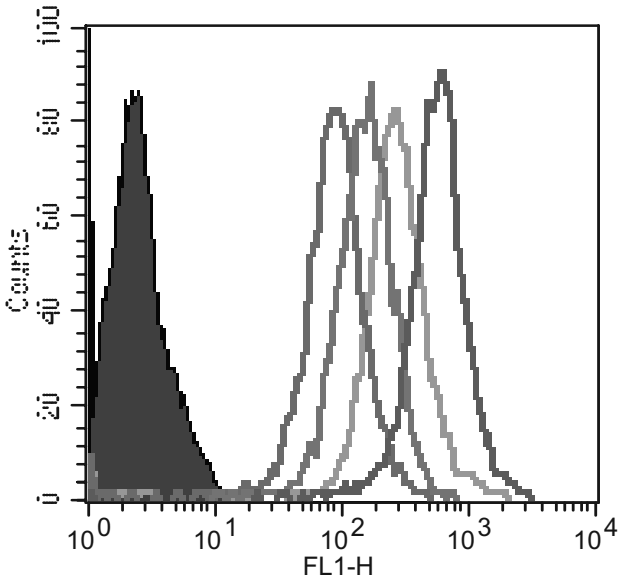


FIG.83

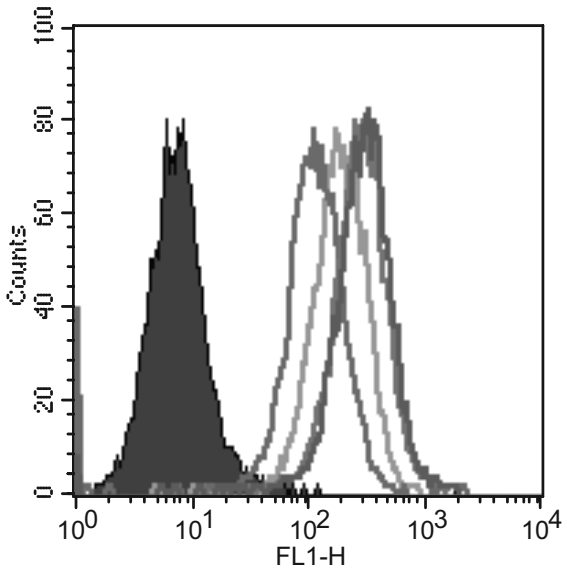
Binding to A431 cells: Flow Cytometry analysis of purified mAb806, ch806 and hu806 40A10 antibody preparations (20 μg/ml) that bind ~ 10% of wild type EGFR on cell surface, 528 (binds both wild type and de2-7 EGFR) and irrelevant control antibody (20 μg/ml) as indicated.



Key	Name	Parameter	Gate
	A431 2B.003	FL1-H	No Gate
	A431 m528.004	FL1-H	No Gate
	A431 m806.005	FL1-H	No Gate
	A431 ch806.006	FL1-H	No Gate
	A431 Hu806.007	FL1-H	No Gate

FIG.84

Binding to U87MG.de2-7 glioma cells. Flow Cytometry analysis of purified mAb806, ch806 and hu806 40A10 antibody preparations (20 μg/ml) and 528 anti-EGFR and irrelevant control antibody (20 μg/ml).



Key	Name	Parameter	Gate
	U87MG.d2-7 2B.009	FL1-H	No Gate
	U87MG.d2-7 m528.011	FL1-H	No Gate
	U87MG.d2-7 m806.012	FL1-H	No Gate
	U87MG.d2-7 ch806.013	FL1-H	No Gate
	U87MG.d2-7 Hu806.014	FL1-H	No Gate

FIG.85

FIG.86

Specific binding of ^{125}I-radiolabelled 806 antibody constructs to:
A) U87MG.de2-7 glioma cells and **B)** A431 carcinoma cells.

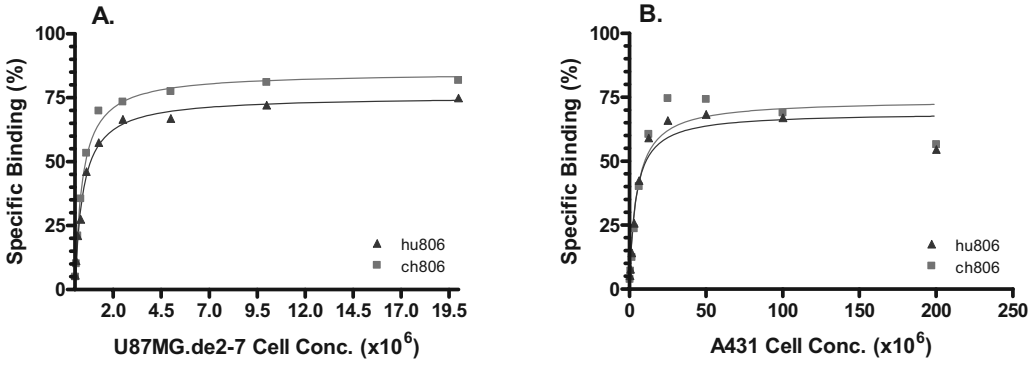


Figure 12. Scatchard Analyses: ^{125}I- radiolabelled **A)** ch806 and **B)** hu806 antibody constructs binding to U87MG.de2-7 cells.

FIG.87

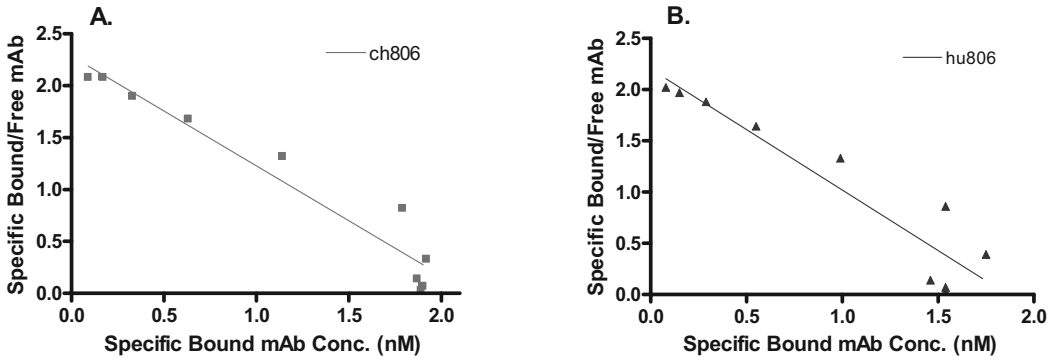
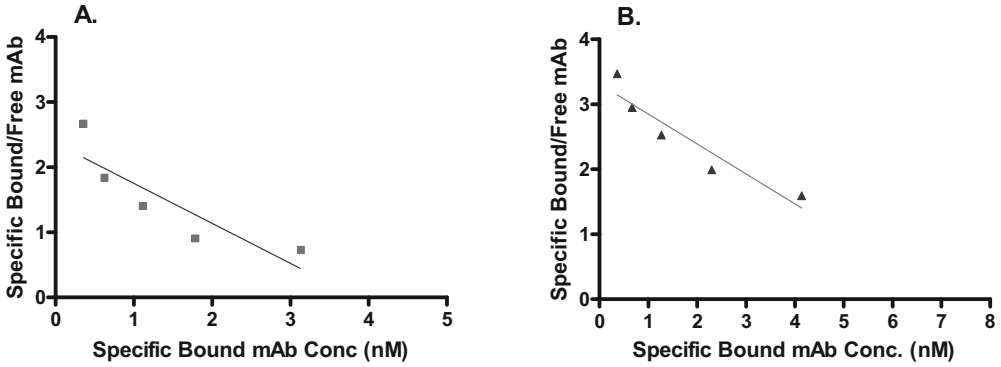


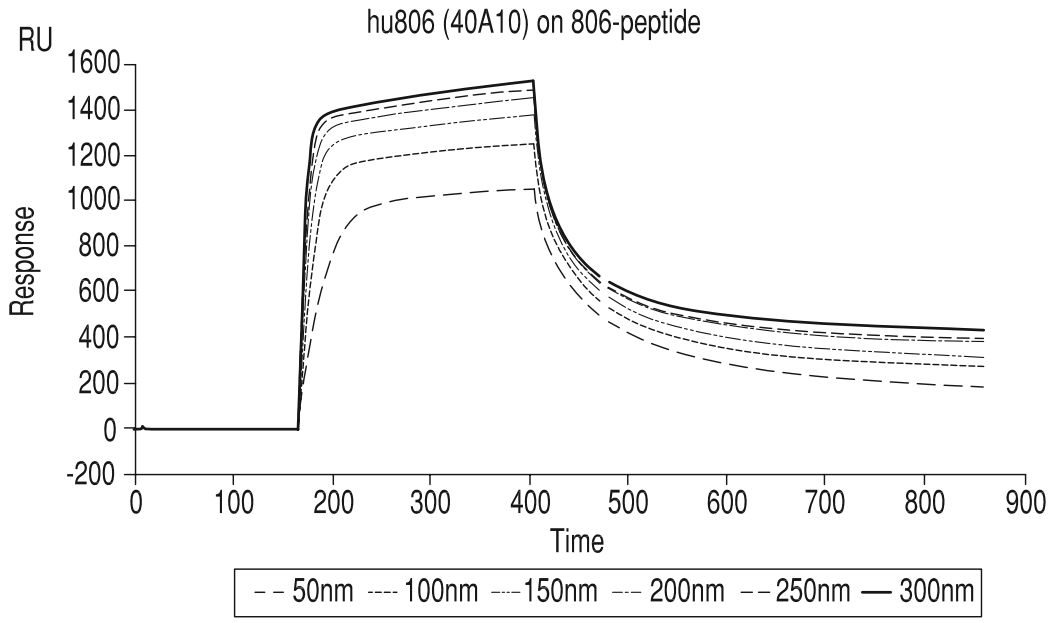
Figure 13. Scatchard Analyses: ^{125}I-radiolabelled **A)** ch806 and **B)** hu806 antibody constructs binding to A431 cells.

FIG.88



BIAcore analysis of binding to 287-302 EGFR 806 peptide epitope by A) hu806 and B) ch806 passing over the immobilised peptide in increasing concentrations of 50nM, 100nM, 150nM, 200nM, 250nM and 300nM.

A.



B.

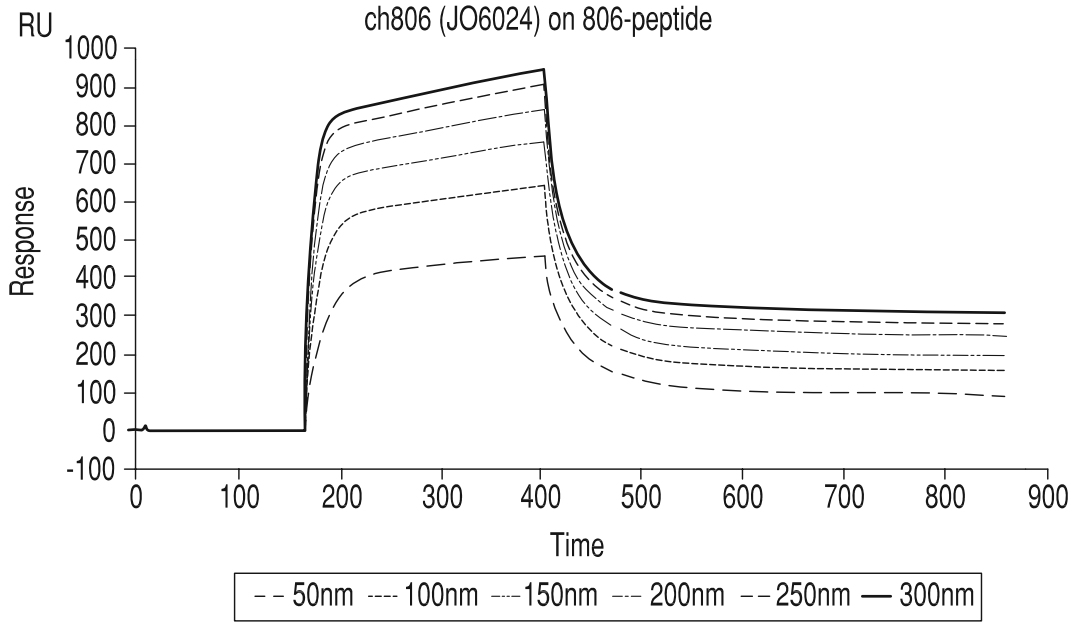


FIG. 89

Ch806- and hu806- mediated Antibody Dependant Cellular Cytotoxicity on target A431 cells determined at **A)** 1 μg/ml each antibody over a range of effector to target cell ratios (E:T = 0.78:1 to 100:1); **B)** at E:T = 50:1 over a concentration range of each antibody (3.15 ng/ml - 10 μg/ml).a on target A431

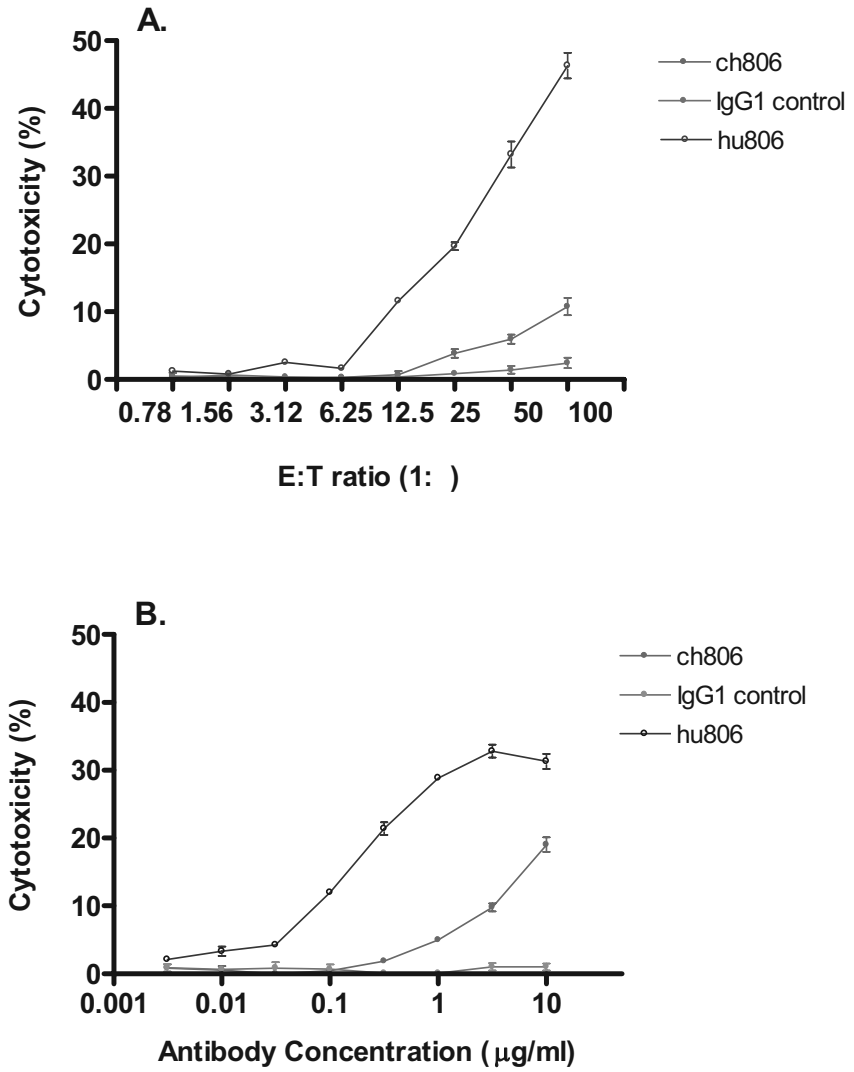


FIG.90

Treatment of established A431 xenografts in BALB/c nude mice. Groups of 5 mice received 6 × 1 mg dose over 2 weeks antibody therapy as indicated (arrows). Mean ± SEM tumour volume is presented until study termination.

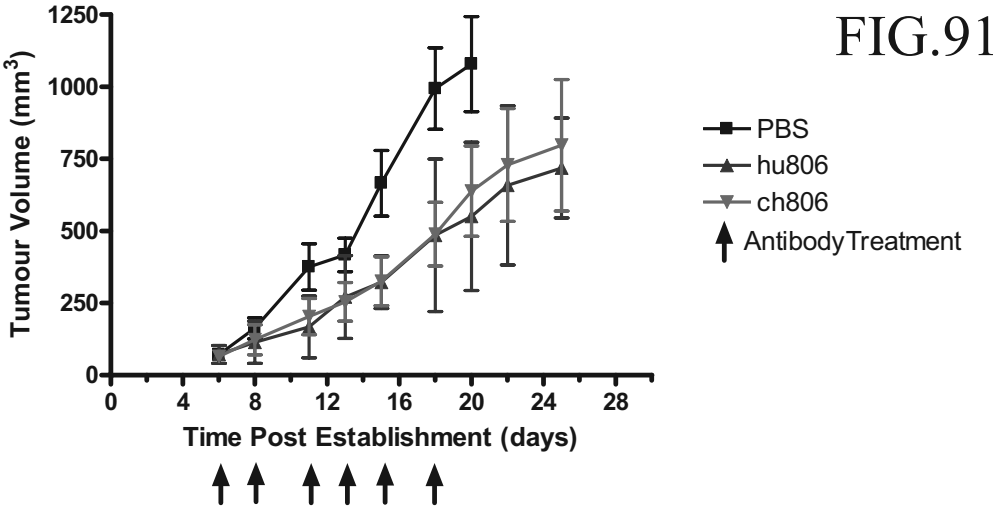


FIG.91

Figure 17. Treatment of established U87MG.de2-7 xenografts in BALB/c nude mice. Groups of 5 mice received 6 × 1 mg dose over 2 weeks antibody therapy as indicated (arrows). Mean ± SEM tumour volume is presented until study termination.

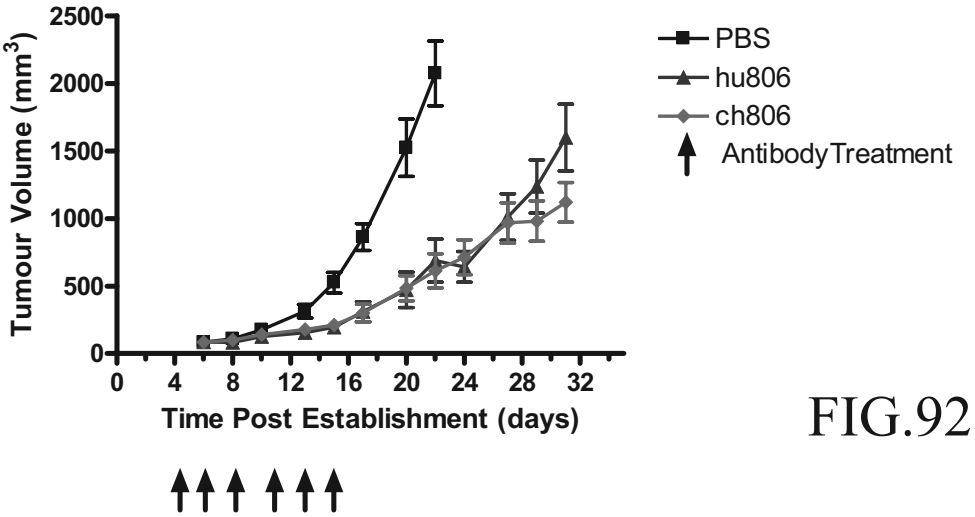


FIG.92

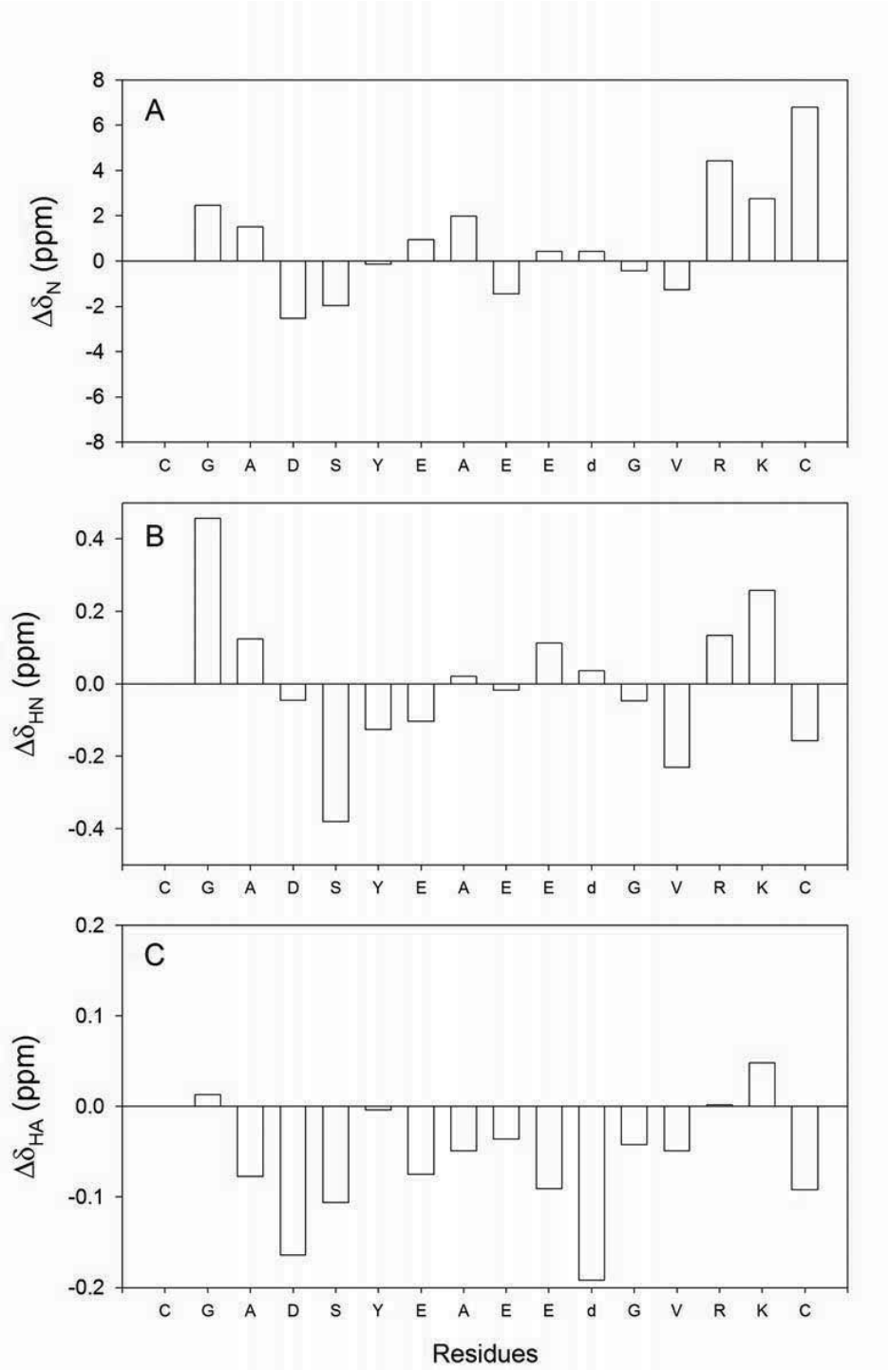

A
B
C
$\Delta\delta_N$ (ppm)
$\Delta\delta_{HN}$ (ppm)
$\Delta\delta_{HA}$ (ppm)
8
6
4
2
0
-2
-4
-6
-8
0.4
0.2
0.0
-0.2
-0.4
0.2
0.1
0.0
-0.1
-0.2
C G A D S Y E A E E d G V R K C
Residues

FIG.93

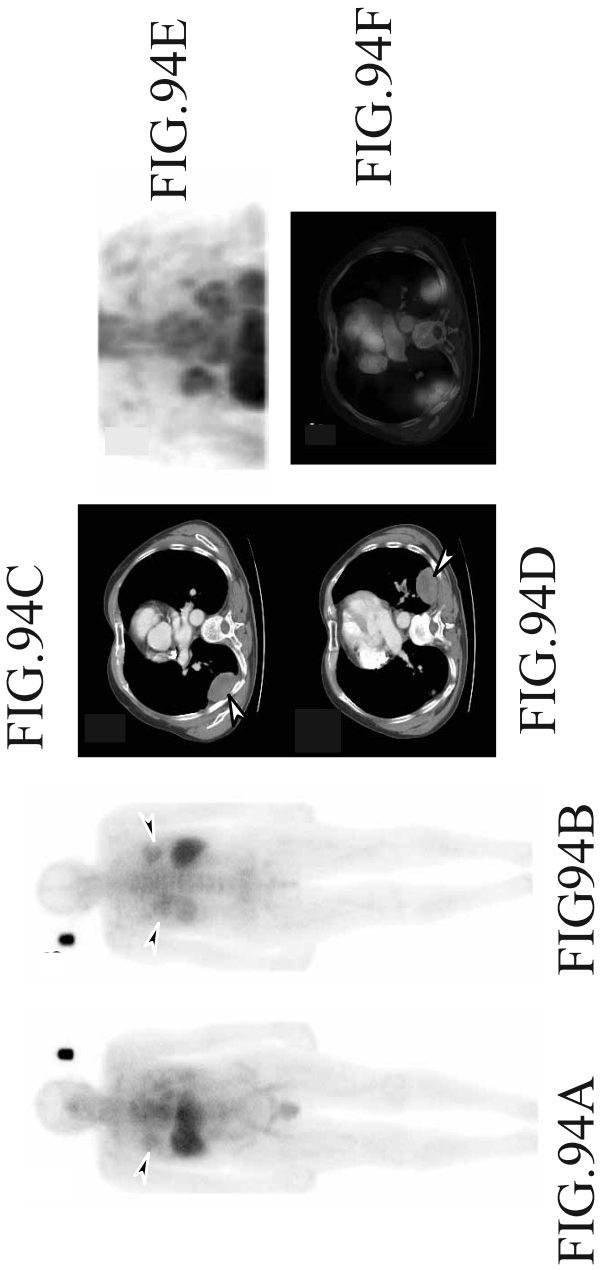


FIG.94A FIG94B FIG.94C FIG.94D FIG.94E FIG.94F

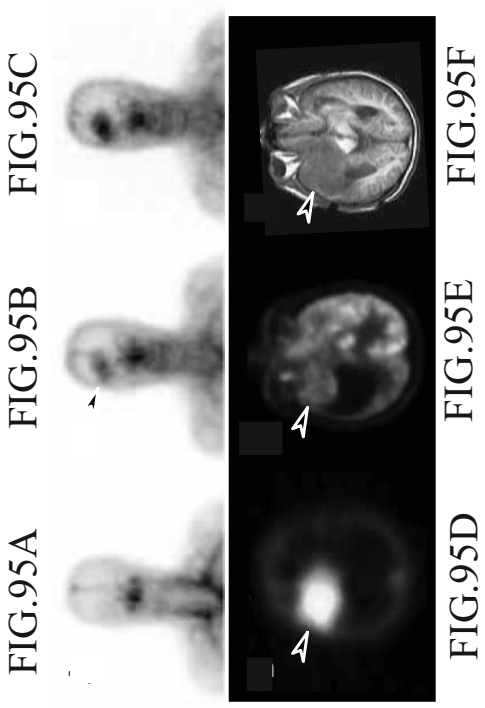


FIG.95A FIG.95B FIG.95C FIG.95D FIG.95E FIG.95F

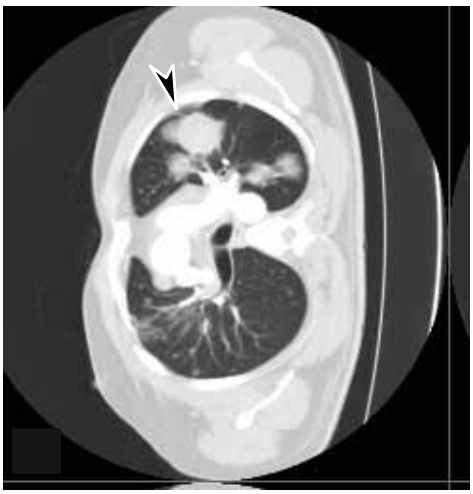


FIG.96B

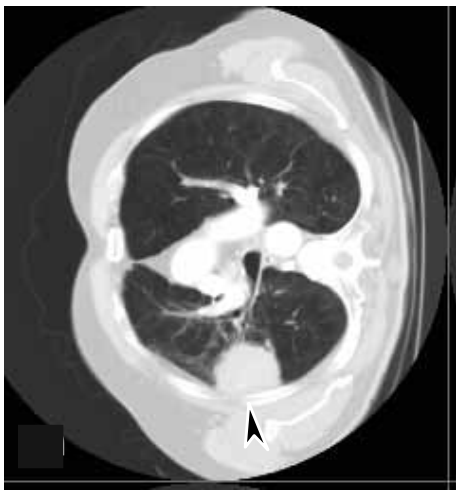


FIG.96D



FIG.96A

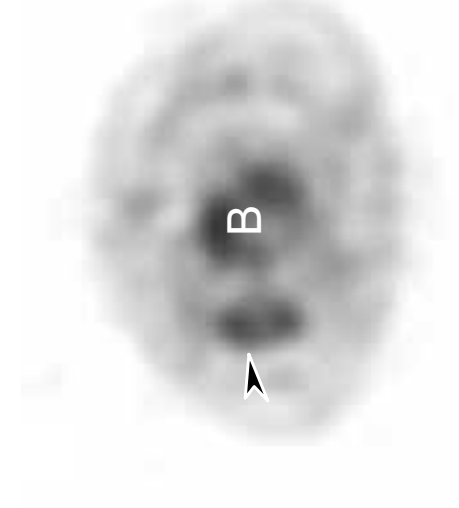


FIG.96C

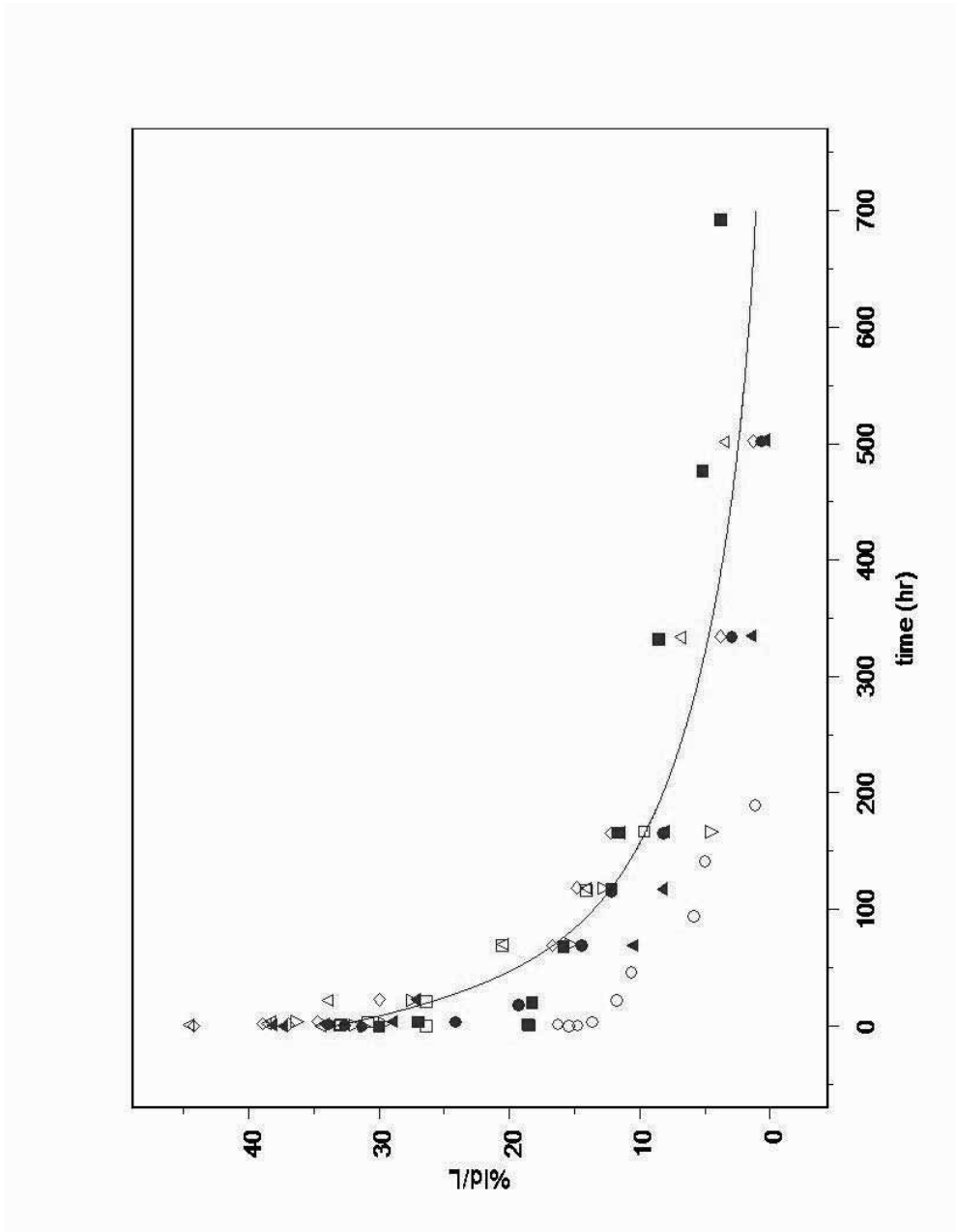


FIG.97

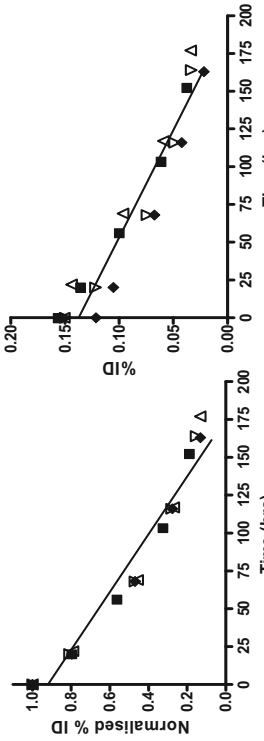


FIG.98A

FIG.98B