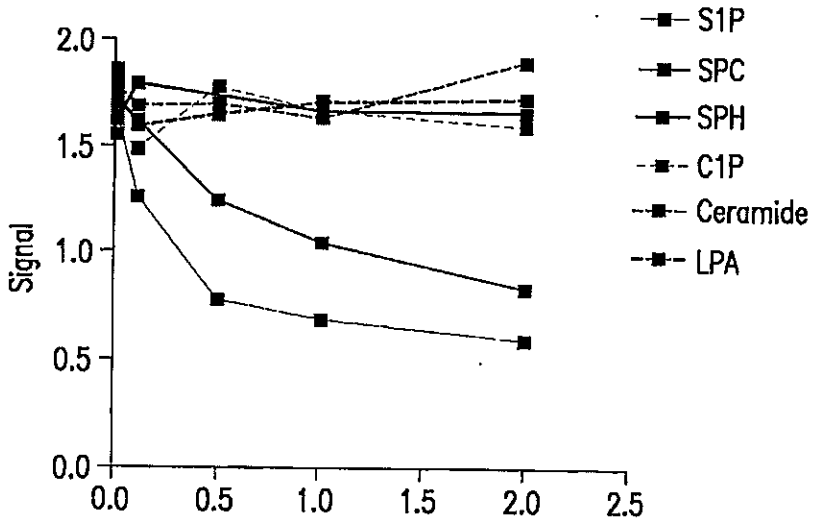

S1P
SPC
SPH
C1P
Ceramide
LPA
Signal
2.0
1.5
1.0
0.5
0.0
0.0
0.5
1.0
1.5
2.0
2.5

FIG.1A

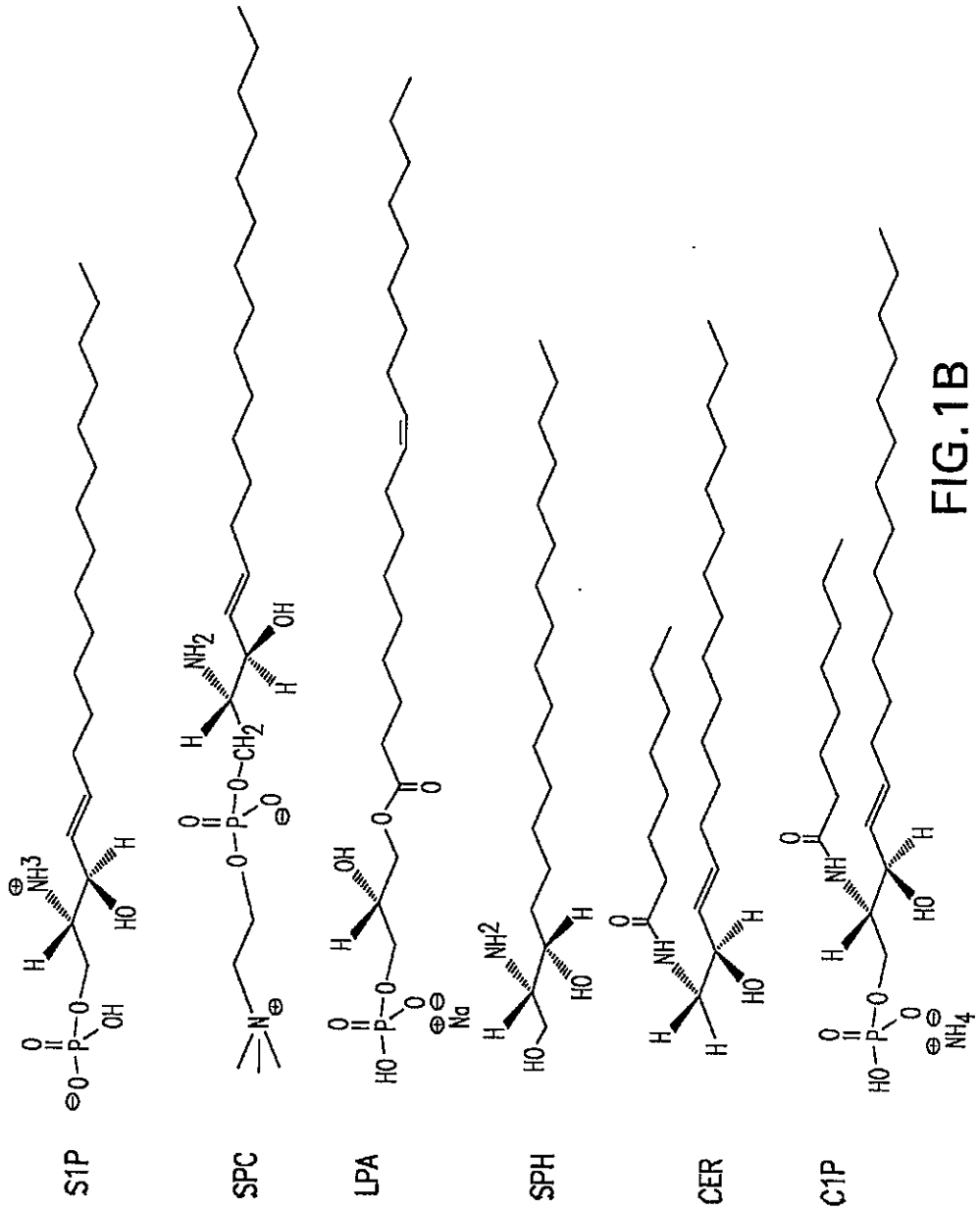


FIG.1B

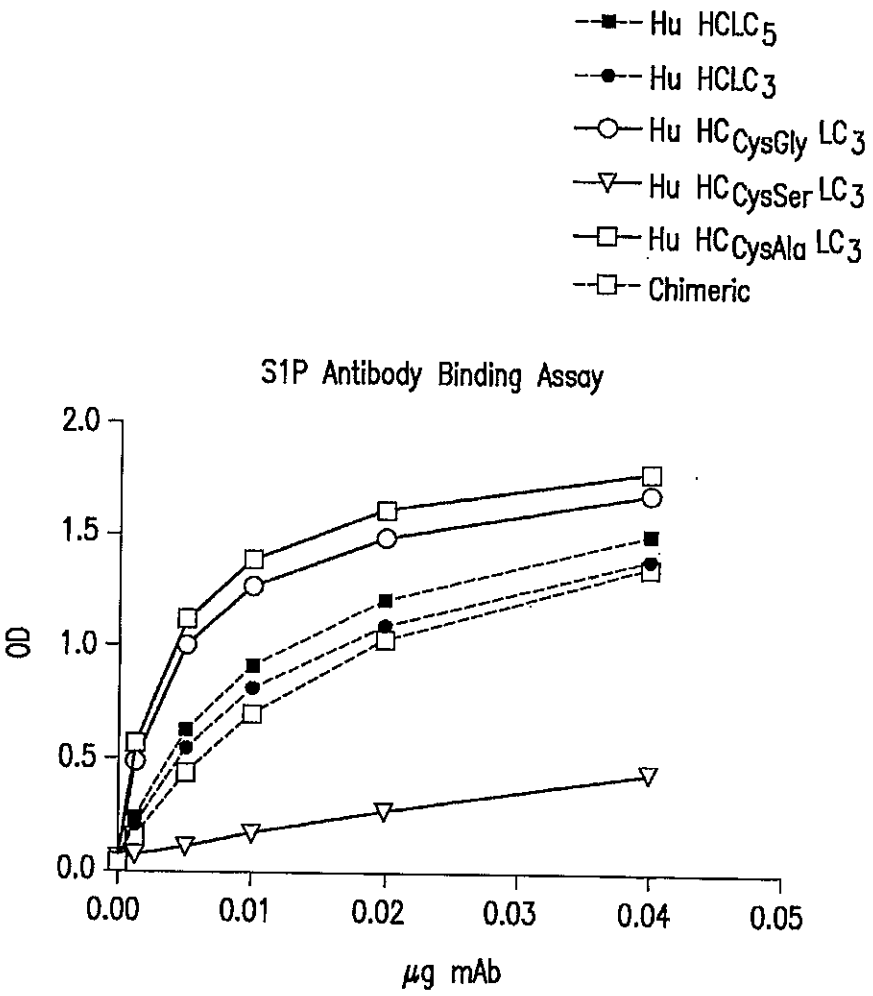

Hu HCLC5
Hu HCLC3
Hu HCCysGly LC3
Hu HCCysSer LC3
Hu HCCysAla LC3
Chimeric
S1P Antibody Binding Assay
OD
2.0
1.5
1.0
0.5
0.0
0.00
0.01
0.02
0.03
0.04
0.05
μg mAb

FIG.2

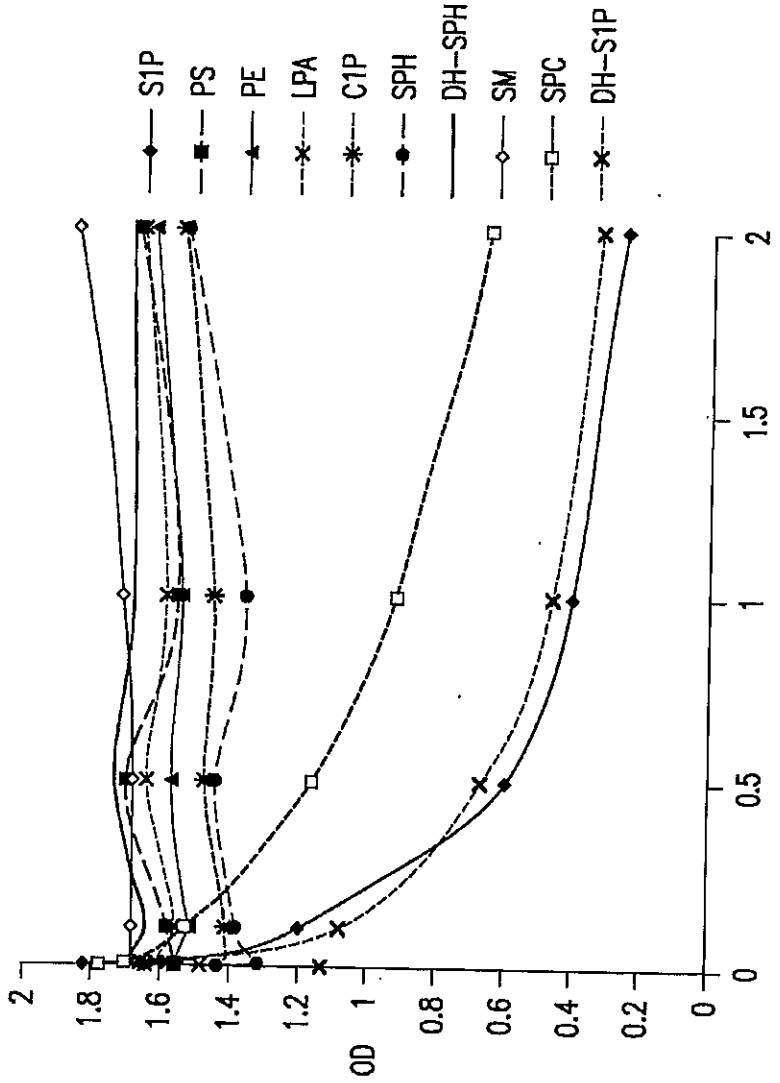

S1P
PS
PE
LPA
C1P
SPH
DH-SPH
SM
SPC
DH-S1P
OD
Lipids [μM]
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
1.8
2
0.5
1.5

FIG.3

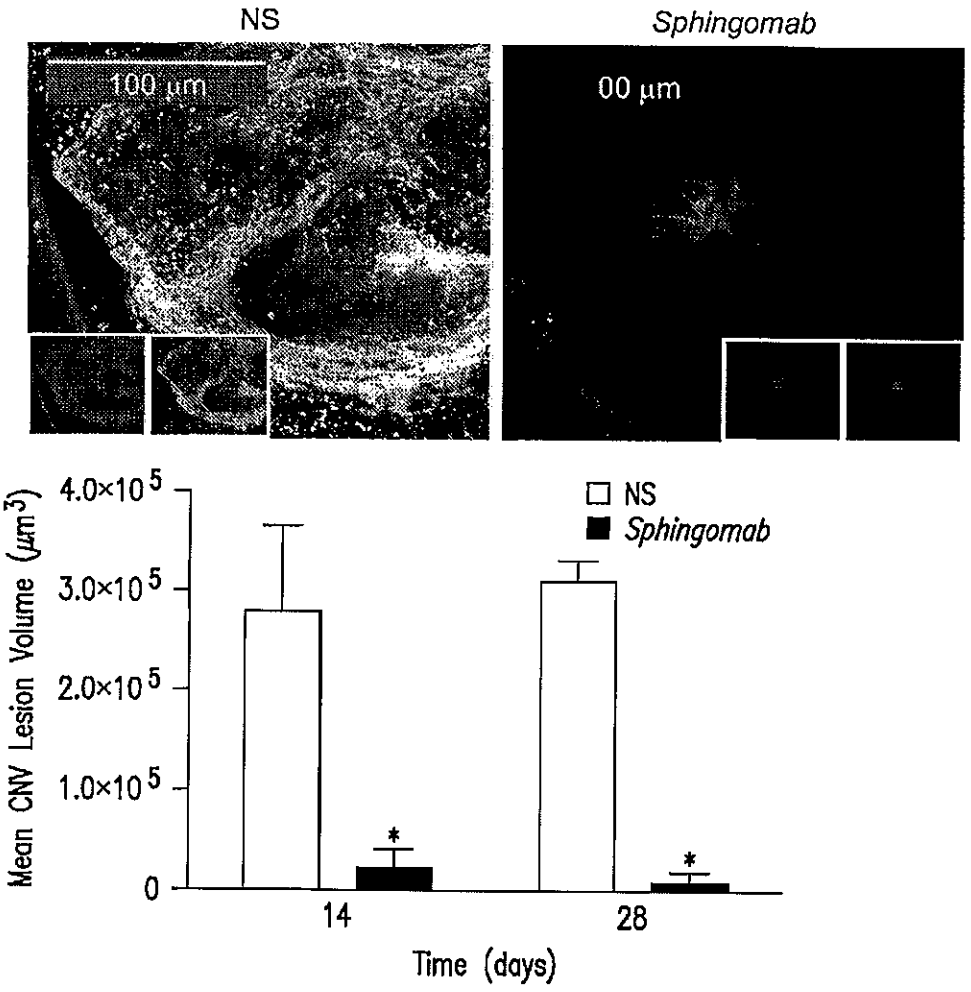

NS
Sphingomab
100 µm
00 µm
Mean CNV Lesion Volume (µm³)
4.0×10⁵
3.0×10⁵
2.0×10⁵
1.0×10⁵
0
NS
Sphingomab
*
*
14
28
Time (days)

FIG.4A

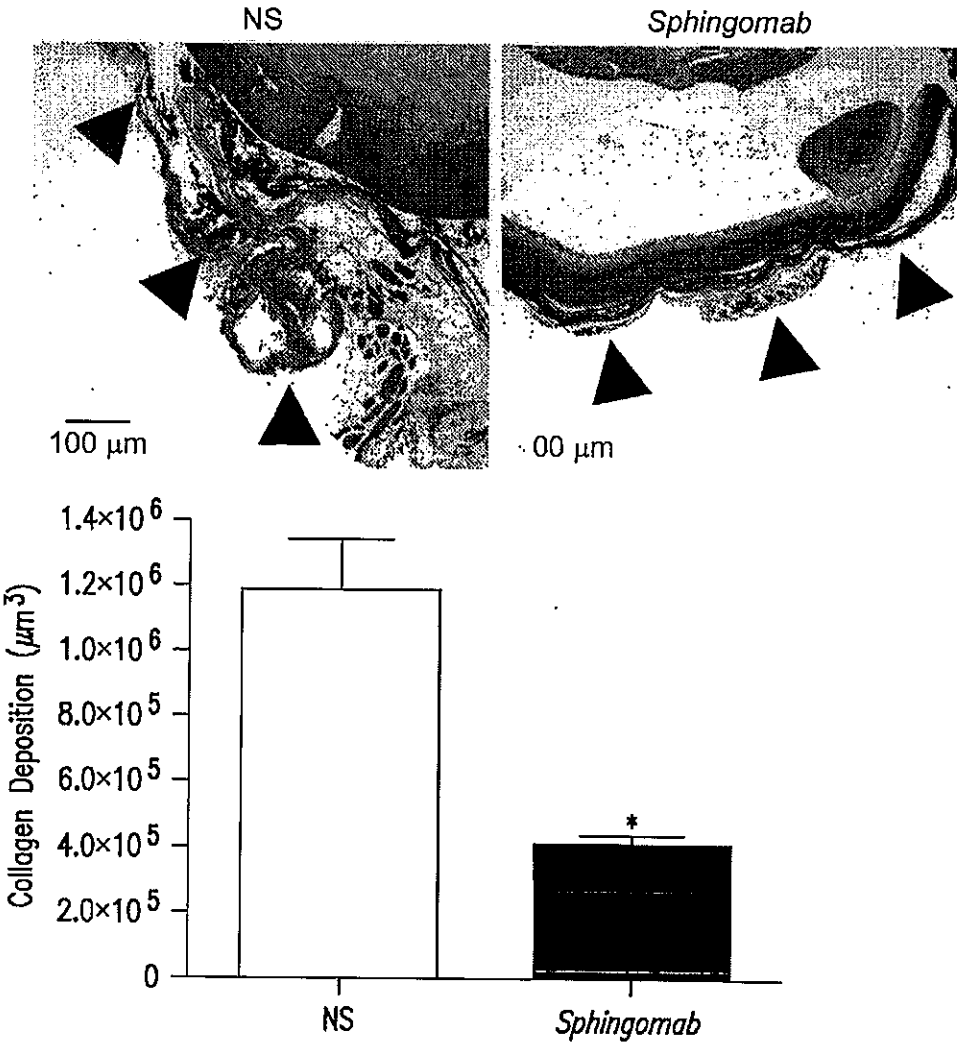

NS
Sphingomab
100 µm
00 µm
Collagen Deposition (µm3)
1.4×10 6
1.2×10 6
1.0×10 6
8.0×10 5
6.0×10 5
4.0×10 5
2.0×10 5
0
*
NS
Sphingomab

FIG.4B

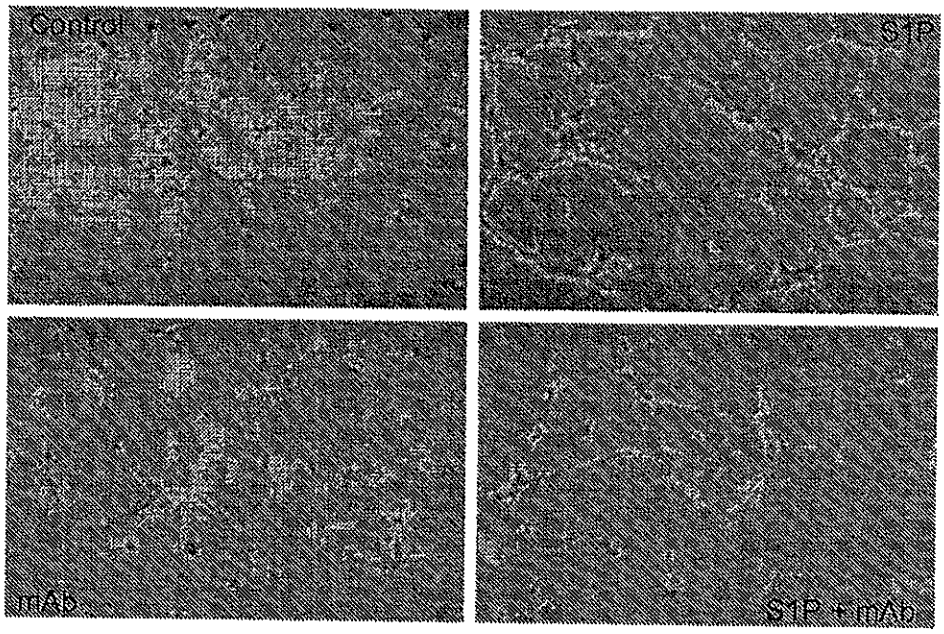

Control
S1P
mAb
S1P + mAb

FIG.5A

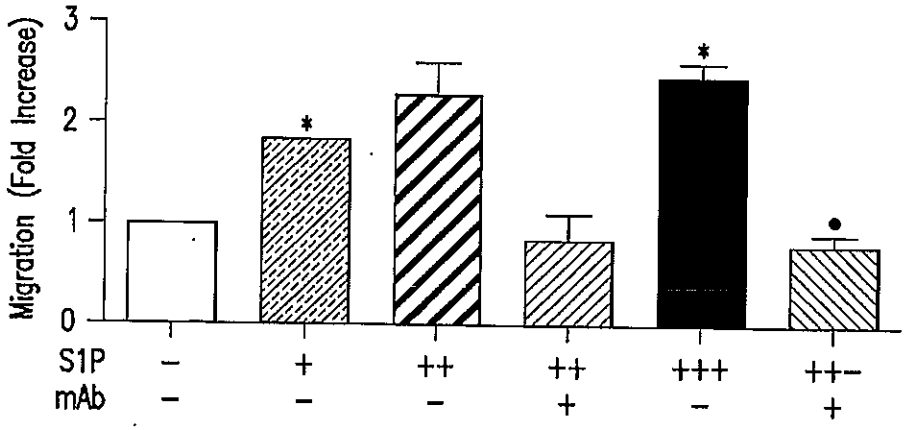

Migration (Fold Increase)
3
2
1
0
*
*
S1P
mAb
–
+
++
++
+++
++–
–
–
–
+
–
+

FIG.5B

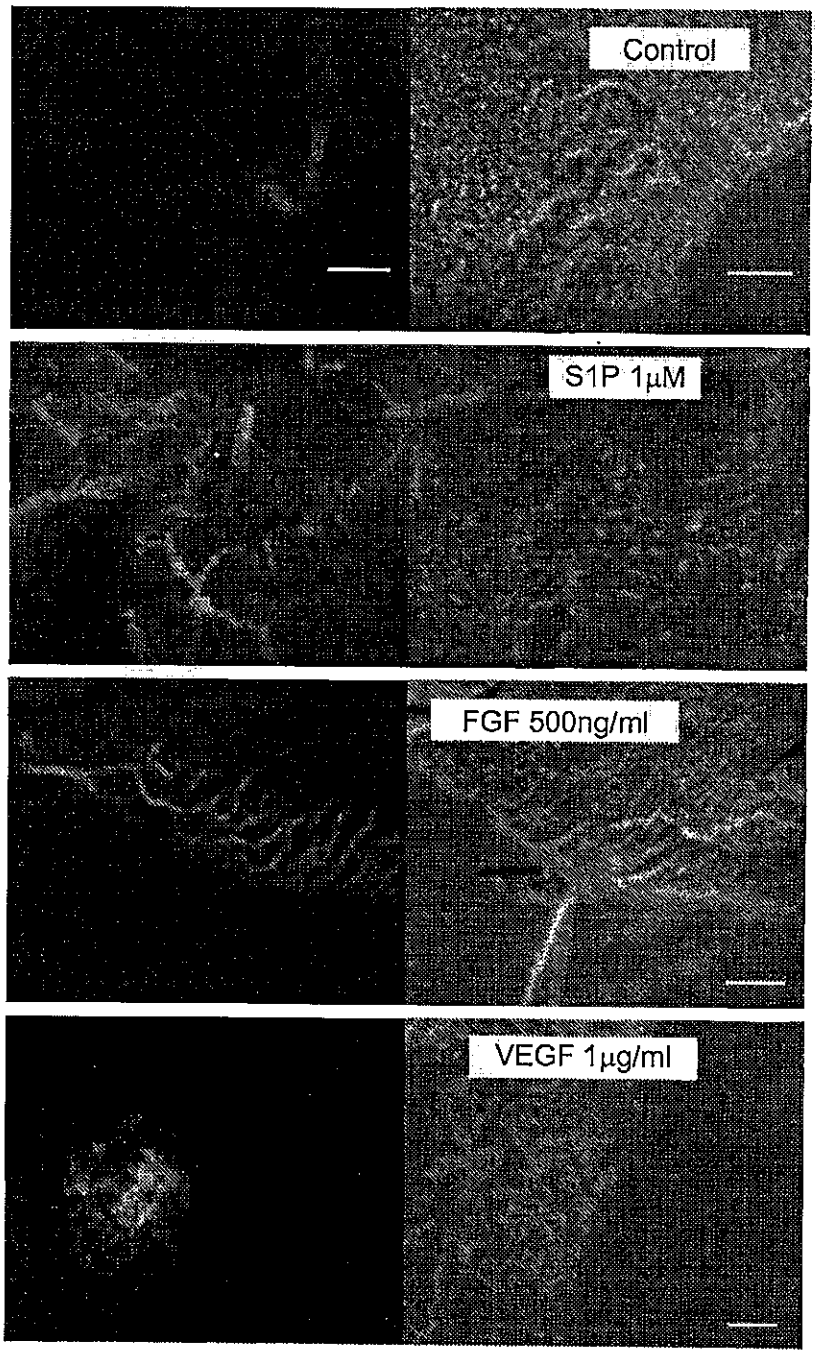


FIG.6A

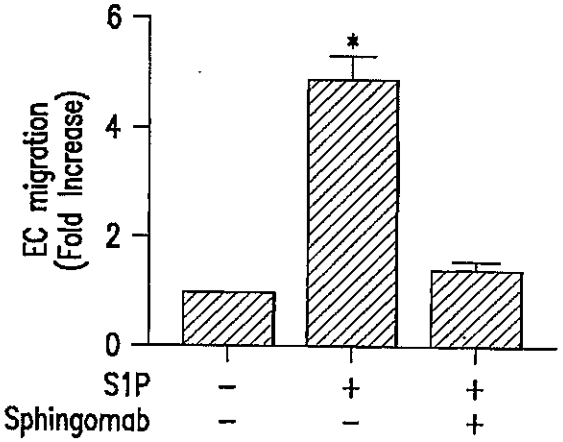

EC migration (Fold Increase)
6
4
2
0
*
S1P – + +
Sphingomab – – +

FIG.6B

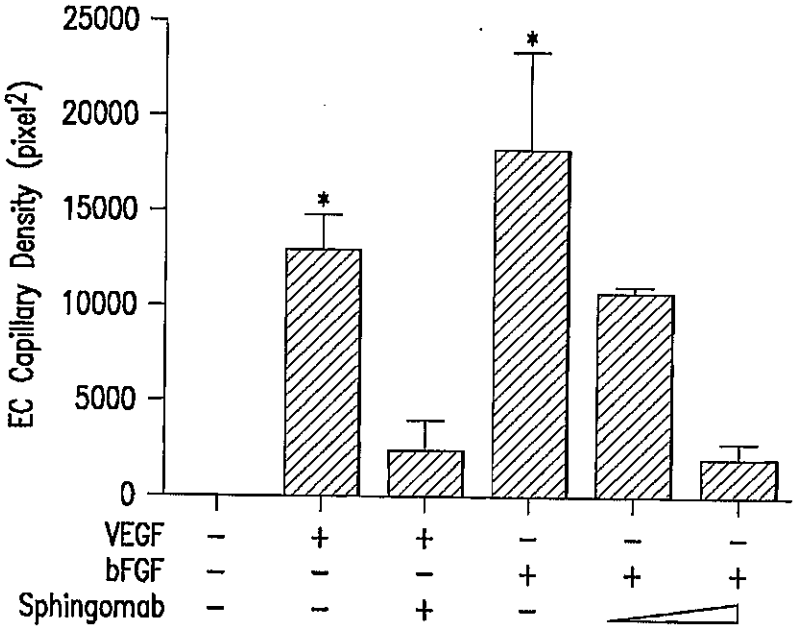

EC Capillary Density (pixel²)
25000
20000
15000
10000
5000
0
*
*
VEGF – + + – – –
bFGF – – – + + +
Sphingomab – – + –

FIG.6C

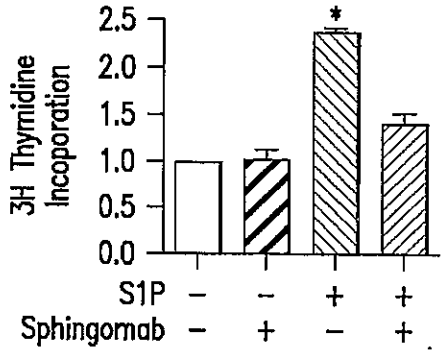


FIG.7A

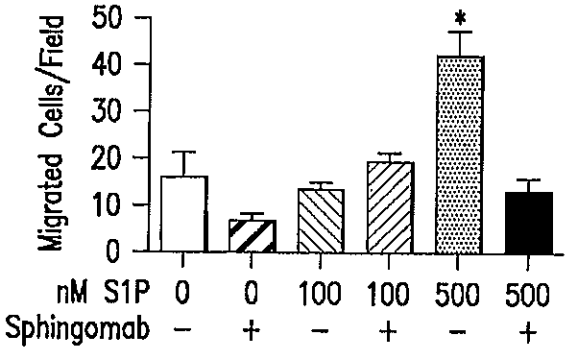


FIG.7B

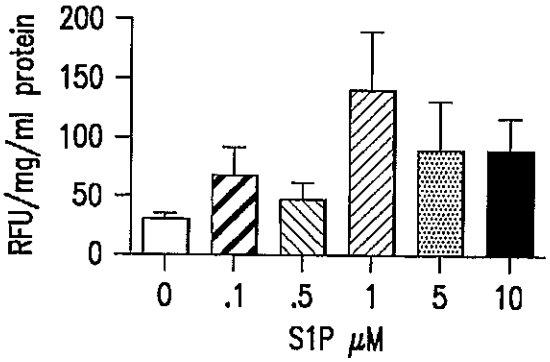


FIG.7C

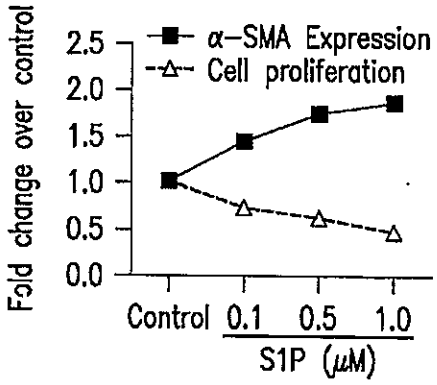

Fold change over control
2.5
2.0
1.5
1.0
0.5
0.0
α–SMA Expression
Cell proliferation
Control
0.1
0.5
1.0
S1P (μM)

FIG.7D

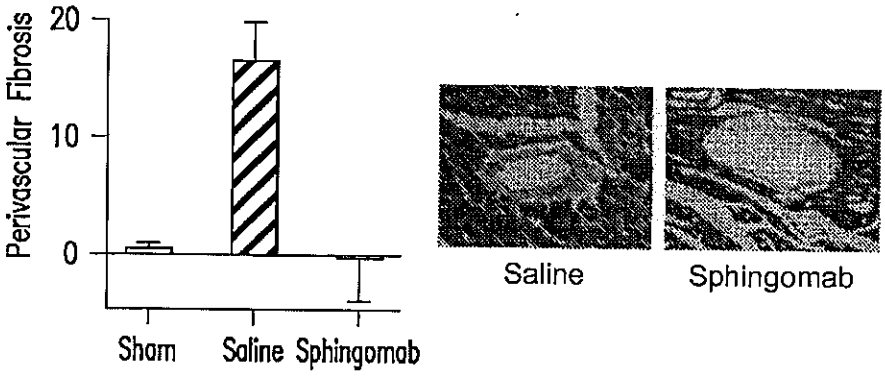

Perivascular Fibrosis
20
10
0
Sham
Saline
Sphingomab
Saline
Sphingomab

FIG.7E

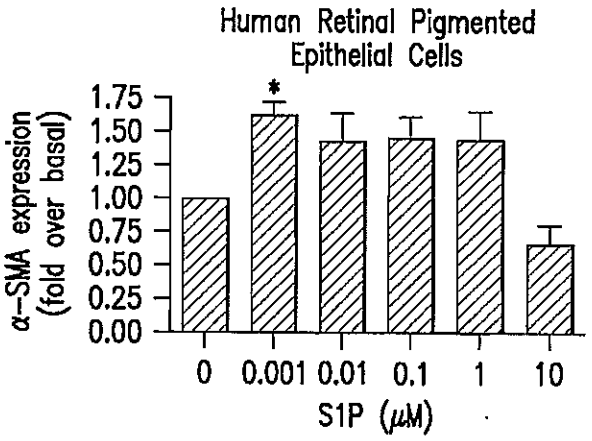


FIG.8A

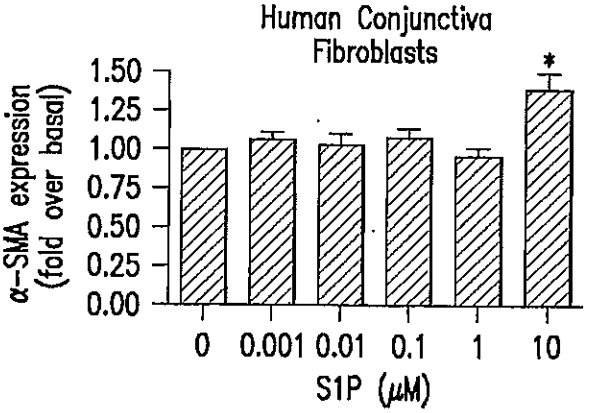


FIG.8B

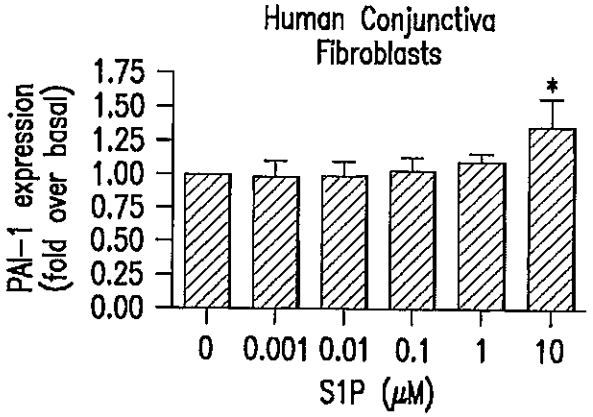


FIG.8C

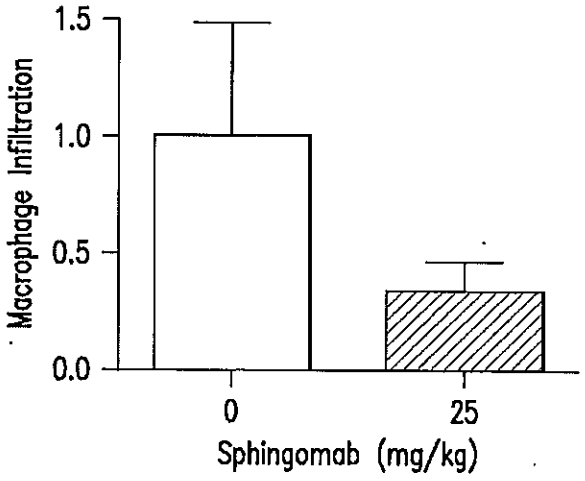

1.5
1.0
0.5
0.0
Macrophage Infiltration
0
25
Sphingomab (mg/kg)

FIG.9A

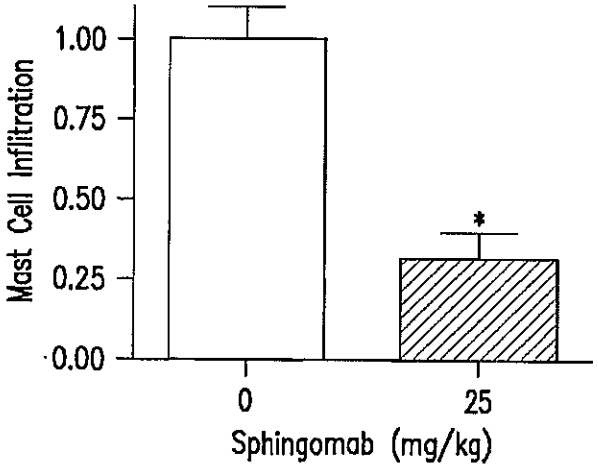

1.00
0.75
0.50
0.25
0.00
Mast Cell Infiltration
*
0
25
Sphingomab (mg/kg)

FIG.9B

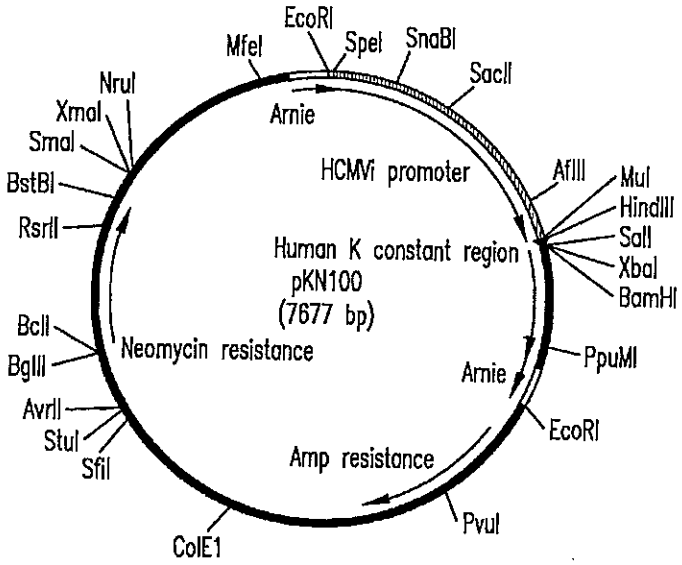


FIG.10A

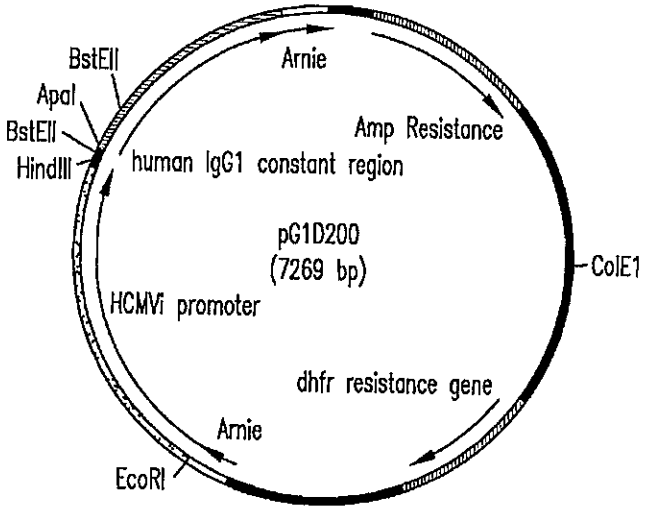


FIG.10B

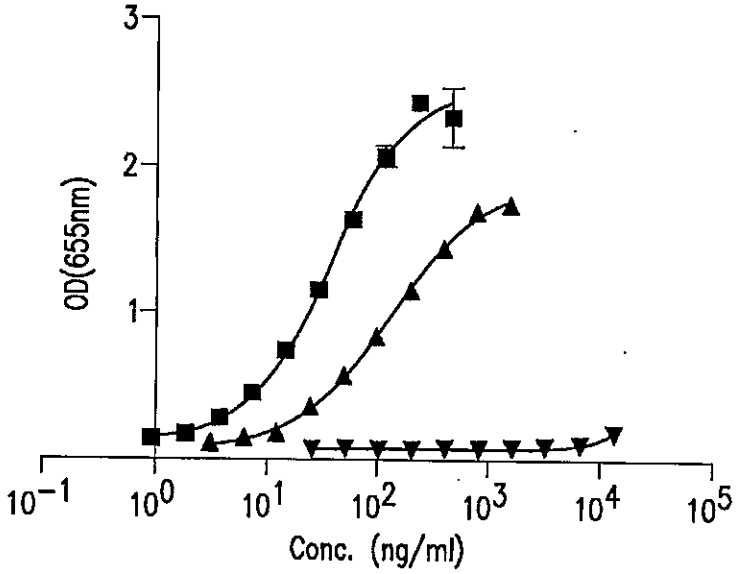


FIG.11

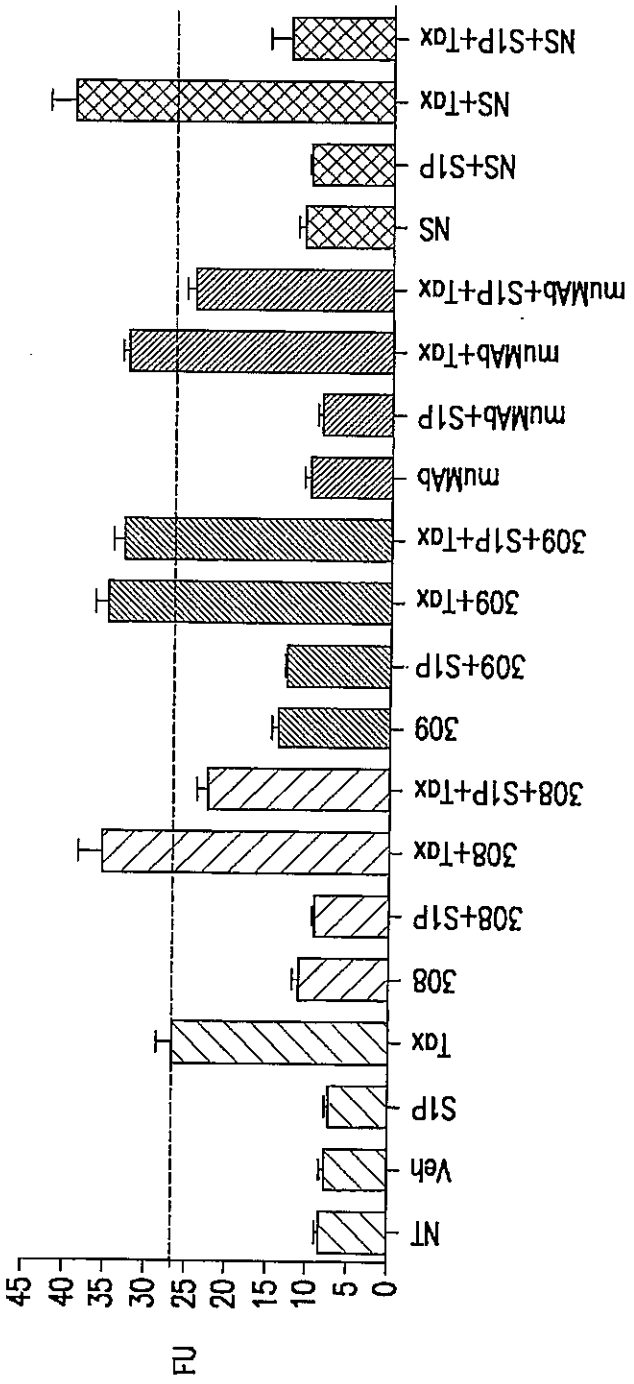

NT
Veh
S1P
Tax
308
308+S1P
308+Tax
308+S1P+Tax
309
309+S1P
309+Tax
309+S1P+Tax
muMAb
muMAb+S1P
muMAb+Tax
muMAb+S1P+Tax
NS
NS+S1P
NS+Tax
NS+S1P+Tax
FU
0
5
10
15
20
25
30
35
40
45

FIG.12A

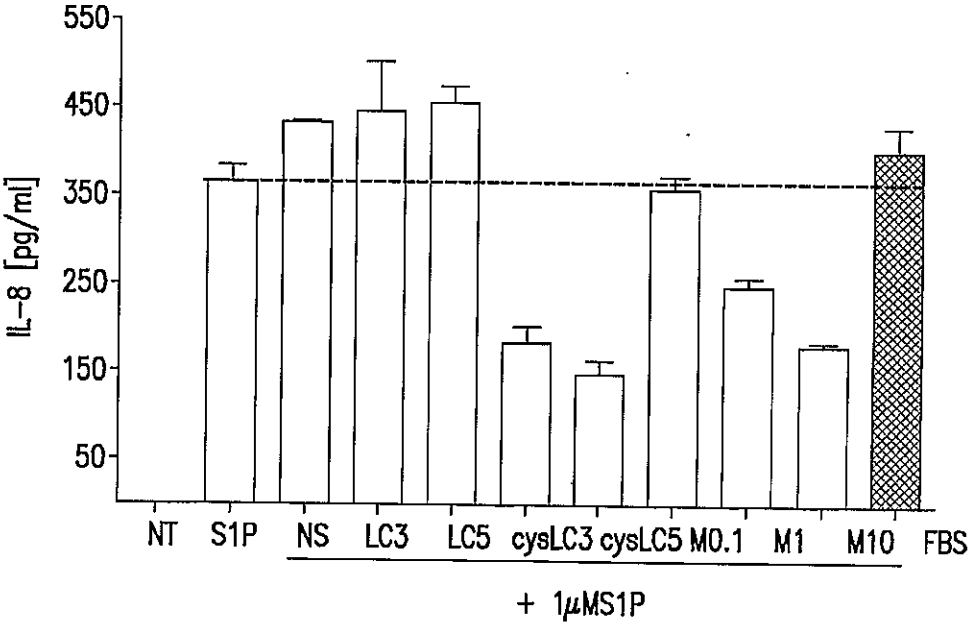

550
450
350
250
150
50
IL-8 [pg/ml]
NT
S1P
NS
LC3
LC5
cysLC3
cysLC5
M0.1
M1
M10
FBS
+ 1μMS1P

FIG.12B

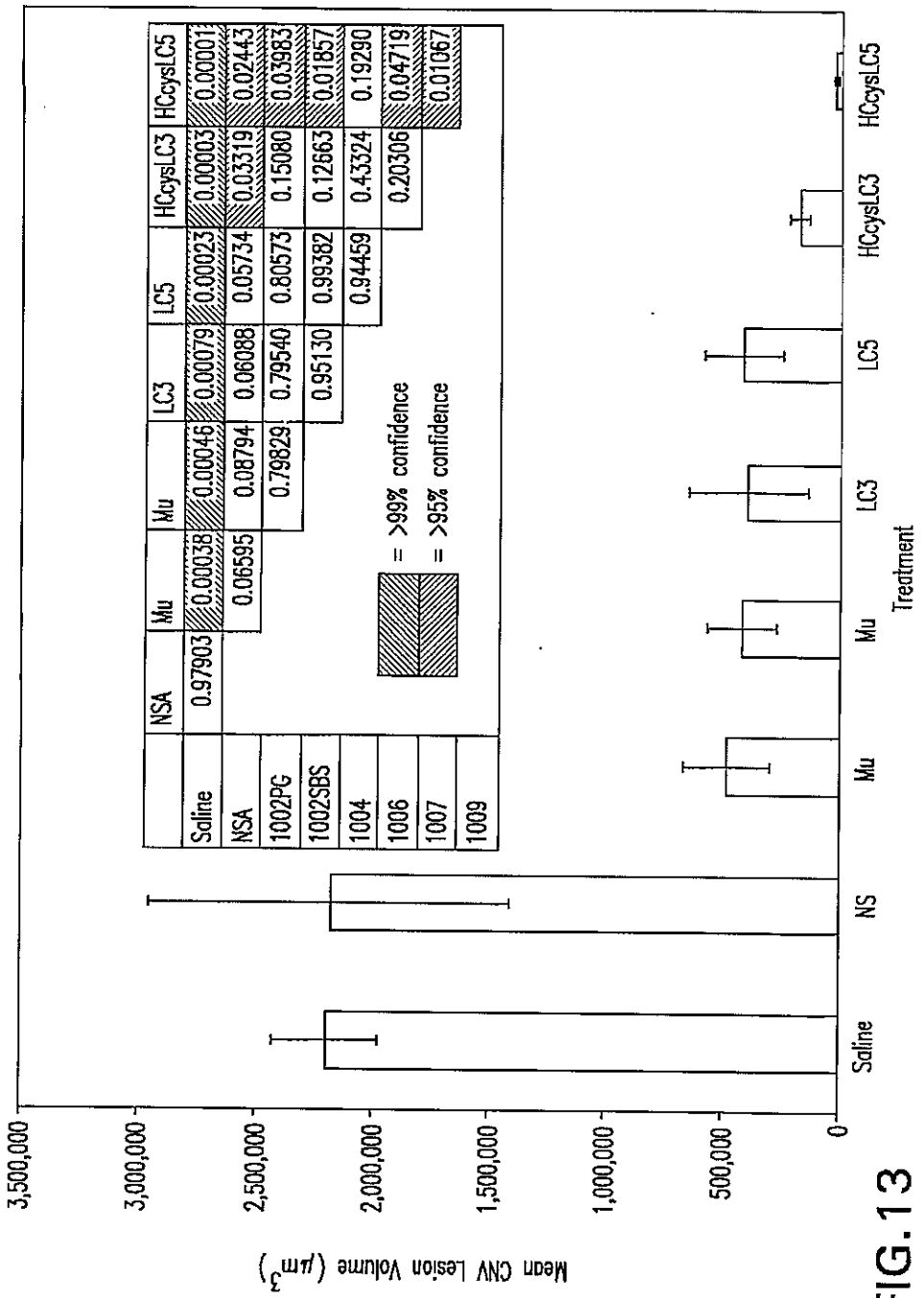


FIG.13

AMENDED SHEET - IPEA/US

SEQUENCE LISTING

<110> Lpath, Inc.
Sabbadini, Roger
Garland, Wiliam A.
Hansen, Genevieve
Jones, Steven Tarran
Williams, David

<120> COMPOSITIONS AND METHODS FOR BINDING SPHINGOSINE-1-PHOSPHATE

<130> LPT-3010-PC

<150> 60/854,971
<151> 2006-10-27

<160> 37

<170> PatentIn version 3.4

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<213> Artificial

<220>
<223> Primer

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<211> 21
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<213> Artificial

<220>
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<400> 2
cagtggatag acagatgggg g 21

<210> 3
<211> 21
<212> DNA
<213> Artificial

<220>
<223> Primer

<400> 3
cagtggatag accgatgggg c 21

<210> 4
<211> 21
<212> DNA
<213> Artificial

<220>
<223> Primer

<400> 4
cagtggatag actgatgggg g 21

<210> 5
<211> 21
<212> DNA
<213> Artificial

<220>
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<400> 5
caagggatag acagatgggg c 21

<210> 6
<211> 18
<212> DNA
<213> Artificial

<220>
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<400> 6
gtctctgatt ctagggca 18

<210> 7
<211> 20
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<213> Artificial

<220>
<223> Primer

<400> 7
actggatggt gggaagatgg 20

<210> 8
<211> 120
<212> PRT
<213> Mus sp.

<400> 8

Gln Ala His Leu Gln Gln Ser Asp Ala Glu Leu Val Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Val Ser Gly Phe Ile Phe Ile Asp His
20 25 30

Thr Ile His Trp Met Lys Gln Arg Pro Glu Gln Gly Leu Glu Trp Ile
35 40 45

Gly Cys Ile Ser Pro Arg His Asp Ile Thr Lys Tyr Asn Glu Met Phe
50 55 60

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

Ile Gln Val Asn Ser Leu Thr Phe Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Gly Gly Phe Tyr Gly Ser Thr Ile Trp Phe Asp Phe Trp Gly

100 105 110

Gln Gly Thr Thr Leu Thr Val Ser
115 120

<210> 9
<211> 107
<212> PRT
<213> Mus sp.

<400> 9

Glu Thr Thr Val Thr Gln Ser Pro Ala Ser Leu Ser Met Ala Ile Gly
1 5 10 15

Glu Lys Val Thr Ile Arg Cys Ile Thr Thr Thr Asp Ile Asp Asp Asp
20 25 30

Met Asn Trp Phe Gln Gln Lys Pro Gly Glu Pro Pro Asn Leu Leu Ile
35 40 45

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

Ser Gly Tyr Gly Thr Asp Phe Leu Phe Thr Ile Glu Asn Met Leu Ser
65 70 75 80

Glu Asp Val Ala Asp Tyr Tyr Cys Leu Gln Ser Asp Asn Leu Pro Phe
85 90 95

Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 10
<211> 11
<212> PRT
<213> Mus sp.

<400> 10

Ile Thr Thr Thr Asp Ile Asp Asp Asp Met Asn
1 5 10

<210> 11
<211> 7
<212> PRT
<213> Mus sp.

<400> 11

Glu Gly Asn Ile Leu Arg Pro
1 5

<210> 12
<211> 9
<212> PRT
<213> Mus sp.

<400> 12

Leu Gln Ser Asp Asn Leu Pro Phe Thr
1 5

<210> 13
<211> 5
<212> PRT
<213> Mus sp.

<400> 13

Asp His Thr Ile His
1 5

<210> 14
<211> 17
<212> PRT
<213> Mus sp.

<400> 14

Cys Ile Ser Pro Arg His Asp Ile Thr Lys Tyr Asn Glu Met Phe Arg
1 5 10 15

Gly

<210> 15
<211> 12
<212> PRT
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<400> 15

Gly Gly Phe Tyr Gly Ser Thr Ile Trp Phe Asp Phe
1 5 10

<210> 16
<211> 147
<212> PRT
<213> Artificial

<220>
<223> Humanized murine antibody variable domains

<400> 16

Met Gly Ser Thr Ala Ile Leu Ala Leu Leu Leu Ala Val Leu Gln Gly
1 5 10 15

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

Pro Gly Glu Ser Leu Lys Ile Ser Cys Gln Ser Phe Gly Tyr Ile Phe
35 40 45

Ile Asp His Thr Ile His Trp Val Arg Gln Met Pro Gly Gln Gly Leu
50 55 60

```
Glu Trp Met Gly Cys Ile Ser Pro Arg His Asp Ile Thr Lys Tyr Asn
65                  70                  75                  80

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

Thr Ala Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met
            100                 105                 110

Tyr Phe Cys Ala Arg Gly Gly Phe Tyr Gly Ser Thr Ile Trp Phe Asp
        115                 120                 125

Phe Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys
    130                 135                 140

Gly Pro Ser
145
```

<210> 17
<211> 134
<212> PRT
<213> Artificial

<220>
<223> Humanized murine antibody variable domains

<400> 17

```
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1               5                   10                  15

Leu Pro Gly Ala Arg Cys Glu Thr Thr Leu Thr Gln Ser Pro Ser Phe
            20                  25                  30

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

Thr Asp Ile Asp Asp Asp Met Asn Trp Tyr Gln Gln Glu Pro Gly Lys
    50                  55                  60

Ala Pro Lys Leu Leu Ile Tyr Glu Gly Asn Ile Leu Arg Pro Gly Val
65                  70                  75                  80

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

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

Ser Asp Asn Leu Pro Phe Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile
        115                 120                 125
```

Lys Arg Glu Trp Ile Pro
130

<210> 18
<211> 33
<212> DNA
<213> Artificial

<220>
<223> Humanized murine mAb CDR nucleotide sequence

<400> 18
ataaccacca ctgatattga tgatgatatg aac 33

<210> 19
<211> 21
<212> DNA
<213> Artificial

<220>
<223> Humanized murine mAb CDR nucleotide sequence

<400> 19
gaaggcaata ttcttcgtcc t 21

<210> 20
<211> 27
<212> DNA
<213> Artificial

<220>
<223> Humanized murine mAb CDR nucleotide sequence

<400> 20
ttgcagagtg ataacttacc attcacg 27

<210> 21
<211> 13
<212> DNA
<213> Artificial

<220>
<223> Humanized murine mAb CDR nucleotide sequence

<400> 21
gaccatactt cac 13

<210> 22
<211> 51
<212> DNA
<213> Artificial

<220>
<223> Humanized murine mAb CDR nucleotide sequence

<400> 22
tgtatttctc ccagacatga tattactaaa tacaatgaga tgttcagggg c 51

<210> 23
<211> 36
<212> DNA
<213> Artificial

<220>
<223> Humanized murine mAb CDR nucleotide sequence

<400> 23
gggggttct acggtagtac tatctggttt gacttt 36

<210> 24
<211> 36
<212> DNA
<213> Artificial

<220>
<223> Humanized murine mAb CDR nucleotide sequence

<400> 24
gggggttct acggtagtac tatctggttt gacttt 36

<210> 25
<211> 455
<212> DNA
<213> Artificial

<220>
<223> Humanized murine mAb nucleotide sequence

<400> 25
cgccaagctt gccgccacca tggggtcaac cgccatcctc gccctcctcc tggctgttct 60

ccaaggagtc tgttccgagg tgcagctggt gcagtctgga gcagaggtga aaaagcccgg 120

ggagtctctg aagatctcct gtcagagttt tggatacatc tttatcgacc atacttcact 180

gggtgcgcca gatgcccggg caaggcctgg agtggatgtg tatttctccc agacatgata 240

ttactaaata caatgagatg ttcaggggcc aggtcaccat ctcagccgac aagtccagca 300

gcaccgccta cttgcagtgg agcagcctga aggcctcgga caccgccatg tatttctgtg 360

cgagaggggg gttctacggt agtactatct ggtttgactt ttggggccaa gggacaatgg 420

tcaccgtctc ttcagcctcc accaagggcc catcg 455

<210> 26
<211> 452
<212> DNA
<213> Artificial

<220>
<223> Humanized murine mAb nucleotide sequence

<400> 26
cgccaagctt gccgccacca tggggtcaac cgccatcctc gccctcctcc tggctgttct 60

ccaaggagtc tgttccgagg tgcagctggt gcagtctgga gcagaggtga aaaagcccgg 120

ggagtctctg aagatctcct gtcagagttt tggatacatc gaccatactt cactggatgc 180

gccagatgcc cgggcaaggc ctggagtgga tgggggctat ttctcccaga catgatatta 240

ctaaatacaa tgagatgttc aggggccagg tcaccatctc agccgacaag tccagcagca 300

ccgcctactt gcagtggagc agcctgaagg cctcggacac cgccatgtat ttctgtgcga 360

gaggggggtt ctacggtagt actatctggt ttgacttttg gggccaaggg acaatggtca 420

ccgtctcttc agcctccacc aagggcccat cg 452

<210> 27
<211> 147
<212> PRT
<213> Artificial

<220>
<223> Humanized murine mAb sequence

<400> 27

Met Gly Ser Thr Ala Ile Leu Ala Leu Leu Leu Ala Val Leu Gln Gly
1 5 10 15

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

Pro Gly Glu Ser Leu Lys Ile Ser Cys Gln Ser Phe Gly Tyr Ile Phe
35 40 45

Ile Asp His Thr Ile His Trp Met Arg Gln Met Pro Gly Gln Gly Leu
50 55 60

Glu Trp Met Gly Ala Ile Ser Pro Arg His Asp Ile Thr Lys Tyr Asn
65 70 75 80

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

Thr Ala Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met
100 105 110

Tyr Phe Cys Ala Arg Gly Gly Phe Tyr Gly Ser Thr Ile Trp Phe Asp
115 120 125

Phe Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys
130 135 140

Gly Pro Ser
145

<210> 28
<211> 419
<212> DNA
<213> Artificial

<220>
<223> Humanized murine mAb sequence

<400> 28
cgccaagctt gccgccacca tggacatgag ggtccccgct cagctcctgg ggctcctgct 60

gctctggctc ccaggtgcca gatgtgaaac gacactcacg cagtctccat ccttcctgtc 120

tgcatctgta ggagacagag tcaccatcac ataaccacca ctgatattga tgatgatatg 180

aactggtatc agcaggaacc agggaaagcc cctaagctcc tgatctatga aggcaatatt 240

cttcgtcctg gggtcccatc aaggttcagc ggcagtggat ctggcacaga tttcactctc 300

accatcagca aattgcagcc tgaagatttt gcaacttatt actgtttgca gagtgataac 360

ttaccattca cgttcggcca agggaccaag ctggagatca aacgtgagtg gatcccgcg 419

<210> 29
<211> 407
<212> DNA
<213> Artificial

<220>
<223> Humanized murine mAb sequence

<400> 29
cgccaagctt gccgccacca tggacatgag ggtccccgct cagctcctgg ggctcctgct 60

gctctggctc ccaggggcca gatgtgaaac gacagtgacg cagtctccat ccttcctgtc 120

tgcatctgta ggagacagag tcaccatcac ttgcataacc accactgata ttgatgatga 180

tatgaactgg ttccagcagg aaccagggaa agcccctaag ctcctgatct ccgaaggcaa 240

tattcttcgt cctggggtcc catcaagatt cagcagcagt ggatatggca cagatttcac 300

tctcaccatc agcaaattgc agcctgaaga ttttgcaact tattactgtt tgcagagtga 360

taacttacca ttcactttcg gccaagggac caagctggag atcaaac 407

<210> 30
<211> 126
<212> PRT
<213> Artificial

<220>
<223> Humanized murine mAb sequence

<400> 30

Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp Leu Pro
1 5 10 15

Gly Ala Arg Cys Glu Thr Thr Val Thr Gln Ser Pro Ser Phe Leu Ser
20 25 30

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

Ile Asp Asp Asp Met Asn Trp Phe Gln Glu Pro Gly Lys Ala Pro Lys
50 55 60

Leu Leu Ile Ser Glu Gly Asn Ile Leu Arg Pro Gly Val Pro Ser Arg
65 70 75 80

Phe Ser Ser Ser Gly Tyr Gly Thr Asp Phe Thr Leu Thr Ile Ser Lys
85 90 95

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

Leu Pro Phe Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
115 120 125

<210> 31
<211> 17
<212> PRT
<213> Artificial

<220>
<223> Humanized murine mAb sequence

<400> 31

Ala Ile Ser Pro Arg His Asp Ile Thr Lys Tyr Asn Glu Met Phe Arg
1 5 10 15

Gly

<210> 32
<211> 140
<212> PRT
<213> Artificial

<220>
<223> Humanized murine mAb sequence

<400> 32

Met Glu Trp Ser Trp Val Phe Leu Phe Phe Leu Ser Val Thr Thr Gly
1 5 10 15

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

Pro Gly Glu Ser Leu Lys Ile Ser Cys Gln Ser Phe Gly Tyr Ile Phe
35 40 45

Ile Asp His Thr Ile His Trp Met Arg Gln Met Pro Gly Gln Gly Leu
50 55 60

Glu Trp Met Gly Ala Ile Ser Pro Arg His Asp Ile Thr Lys Tyr Asn
65 70 75 80

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

Thr Ala Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met
100 105 110

Tyr Phe Cys Ala Arg Gly Gly Phe Tyr Gly Ser Thr Ile Trp Phe Asp
115 120 125

Phe Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
130 135 140

<210> 33
<211> 127
<212> PRT
<213> Artificial

<220>
<223> Humanized murine mAb sequence

<400> 33

Met Ser Val Pro Thr Gln Val Leu Gly Leu Leu Leu Leu Trp Leu Thr
1 5 10 15

Asp Ala Arg Cys Glu Thr Thr Val Thr Gln Ser Pro Ser Phe Leu Ser
20 25 30

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

Ile Asp Asp Asp Met Asn Trp Phe Gln Gln Glu Pro Gly Lys Ala Pro
50 55 60

Lys Leu Leu Ile Ser Glu Gly Asn Ile Leu Arg Pro Gly Val Pro Ser
65 70 75 80

Arg Phe Ser Ser Ser Gly Tyr Gly Thr Asp Phe Thr Leu Thr Ile Ser
85 90 95

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

Asn Leu Pro Phe Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
115 120 125

<210> 34
<211> 2034
<212> DNA
<213> Artificial

<220>
<223> Humanized murine mAb sequence

<400> 34
aagcttgccg ccaccatgga atggagctgg gtgttcctgt tctttctgtc cgtgaccaca 60

ggcgtgcatt ctgaggtgca gctggtgcag tctggagcag aggtgaaaaa gcccggggag 120

tctctgaaga tctcctgtca gagttttgga tacatcttta tcgaccatac tattcactgg 180

atgcgccaga tgcccgggca aggcctggag tggatggggg ctatttctcc cagacatgat 240

attactaaat acaatgagat gttcaggggc caggtcacca tctcagccga caagtccagc 300

agcaccgcct acttgcagtg gagcagcctg aaggcctcgg acaccgccat gtatttctgt 360

gcgagagggg ggttctacgg tagtactatc tggtttgact tttggggcca agggacaatg 420

gtcaccgtct cttcagcctc caccaagggc ccatcggtct tcccctggc accctcctcc 480

aagagcacct ctgggggcac agcggccctg ggctgcctgg tcaaggacta cttccccgaa 540

ccggtgacgg tgtcgtggaa ctcaggcgcc ctgaccagcg gcgtgcacac cttcccggct 600

gtcctacagt cctcaggact ctactccctc agcagcgtgg tgaccgtgcc ctccagcagc 660

ttgggcaccc agacctacat ctgcaacgtg aatcacaagc ccagcaacac caaggtggac 720

aagagagttg gtgagaggcc agcacaggga gggagggtgt ctgctggaag ccaggctcag 780

cgctcctgcc tggacgcatc ccggctatgc agtcccagtc cagggcagca aggcaggccc 840

cgtctgcctc ttcacccgga ggcctctgcc cgccccactc atgctcaggg agagggtctt 900

ctggcttttt ccccaggctc tgggcaggca caggctaggt gcccctaacc caggccctgc 960

acacaaaggg gcaggtgctg ggctcagacc tgccaagagc catatccggg aggaccctgc 1020

ccctgaccta agcccacccc aaaggccaaa ctctccactc cctcagctcg gacaccttct 1080

ctcctcccag attccagtaa ctcccaatct tctctctgca gagcccaaat cttgtgacaa 1140

aactcacaca tgcccaccgt gcccaggtaa gccagcccag gcctcgccct ccagctcaag 1200

gcgggacagg tgccctagag tagcctgcat ccagggacag gccccagccg ggtgctgaca 1260

cgtccacctc catctcttcc tcagcacctg aactcctggg gggaccgtca gtcttcctct 1320

tccccccaaa acccaaggac accctcatga tctcccggac ccctgaggtc acatgcgtgg 1380

tggtggacgt gagccacgaa gaccctgagg tcaagttcaa ctggtacgtg gacggcgtgg 1440

aggtgcataa tgccaagaca aagccgcggg aggagcagta caacagcacg taccgtgtgg 1500

tcagcgtcct caccgtcctg caccaggact ggctgaatgg caaggagtac aagtgcaagg 1560

tctccaacaa agccctccca gcccccatcg agaaaaccat ctccaaagcc aaaggtggga 1620

cccgtggggt gcgagggcca catggacaga ggccggctcg gcccaccctc tgccctgaga 1680

gtgaccgctg taccaacctc tgtccctaca gggcagcccc gagaaccaca ggtgtacacc 1740

ctgccccccat cccgggagga gatgaccaag aaccaggtca gcctgacctg cctggtcaaa 1800

ggcttctatc ccagcgacat cgccgtggag tgggagagca atgggcagcc ggagaacaac 1860

tacaagacca cgcctcccgt gctggactcc gacggctcct tcttcctcta tagcaagctc 1920

accgtggaca agagcaggtg gcagcagggg aacgtcttct catgctccgt gatgcatgag 1980

gctctgcaca accactacac gcagaagagc ctctccctgt ctccgggtaa atag 2034

<210> 35
<211> 455
<212> PRT
<213> Artificial

<220>
<223> Humanized murine mAb sequence

<400> 35

Met Glu Trp Ser Trp Val Phe Leu Phe Phe Leu Ser Val Thr Thr Gly
1 5 10 15

```
Val His Ser Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
            20                  25                  30

Pro Gly Glu Ser Leu Lys Ile Ser Cys Gln Ser Phe Gly Tyr Ile Phe
        35                  40                  45

Ile Asp His Thr Ile His Trp Met Arg Gln Met Pro Gly Gln Gly Leu
    50                  55                  60

Glu Trp Met Gly Ala Ile Ser Pro Arg His Asp Ile Thr Lys Tyr Asn
65                  70                  75                  80

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

Thr Ala Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met
            100                 105                 110

Tyr Phe Cys Ala Arg Gly Gly Phe Tyr Gly Ser Thr Ile Trp Phe Asp
        115                 120                 125

Phe Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys
    130                 135                 140

Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly
145                 150                 155                 160

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

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

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

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

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

Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
                245                 250                 255

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
            260                 265                 270

Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
        275                 280                 285
```

```
Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
    290                 295                 300

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
305                 310                 315                 320

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
                325                 330                 335

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
            340                 345                 350

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
        355                 360                 365

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
    370                 375                 380

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
385                 390                 395                 400

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
                405                 410                 415

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
            420                 425                 430

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
        435                 440                 445

Leu Ser Leu Ser Pro Gly Lys
    450                 455
```

<210> 36
<211> 720
<212> DNA
<213> Artificial

<220>
<223> Humanized murine mAb sequence

<400> 36

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aagcttgccg ccaccatgtc tgtgcctacc caggtgctgg gactgctgct gctgtggctg     60

acagacgccc gctgtgaaac gacagtgacg cagtctccat ccttcctgtc tgcatctgta    120

ggagacagag tcaccatcac ttgcataacc accactgata ttgatgatga tatgaactgg    180

ttccagcagg aaccagggaa agcccctaag ctcctgatct ccgaaggcaa tattcttcgt    240

cctggggtcc catcaagatt cagcagcagt ggatatggca cagatttcac tctcaccatc    300

agcaaattgc agcctgaaga ttttgcaact tattactgtt tgcagagtga taacttacca    360

ttcactttcg gccaagggac caagctggag atcaaacgta cggtggctgc accatctgtc    420
```

ttcatcttcc cgccatctga tgagcagttg aaatctggaa ctgcctctgt tgtgtgcctg 480

ctgaataact tctatcccag agaggccaaa gtacagtgga aggtggataa cgccctccaa 540

tcgggtaact cccaggagag tgtcacagag caggacagca aggacagcac ctacagcctc 600

agcagcaccc tgacgctgag caaagcagac tacgagaaac acaaagtcta cgcctgcgaa 660

gtcacccatc agggcctgag ctcgcccgtc acaaagagct tcaacagggg agagtgttag 720

<210> 37
<211> 234
<212> PRT
<213> Artificial

<220>
<223> Humanized murine mAb sequence

<400> 37

Met Ser Val Pro Thr Gln Val Leu Gly Leu Leu Leu Leu Trp Leu Thr
1 5 10 15

Asp Ala Arg Cys Glu Thr Thr Val Thr Gln Ser Pro Ser Phe Leu Ser
20 25 30

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

Ile Asp Asp Asp Met Asn Trp Phe Gln Gln Glu Pro Gly Lys Ala Pro
50 55 60

Lys Leu Leu Ile Ser Glu Gly Asn Ile Leu Arg Pro Gly Val Pro Ser
65 70 75 80

Arg Phe Ser Ser Ser Gly Tyr Gly Thr Asp Phe Thr Leu Thr Ile Ser
85 90 95

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

Asn Leu Pro Phe Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg
115 120 125

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
130 135 140

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
145 150 155 160

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

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
180 185 190

```
Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
        195                 200                 205

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
    210                 215                 220

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
225                 230
```