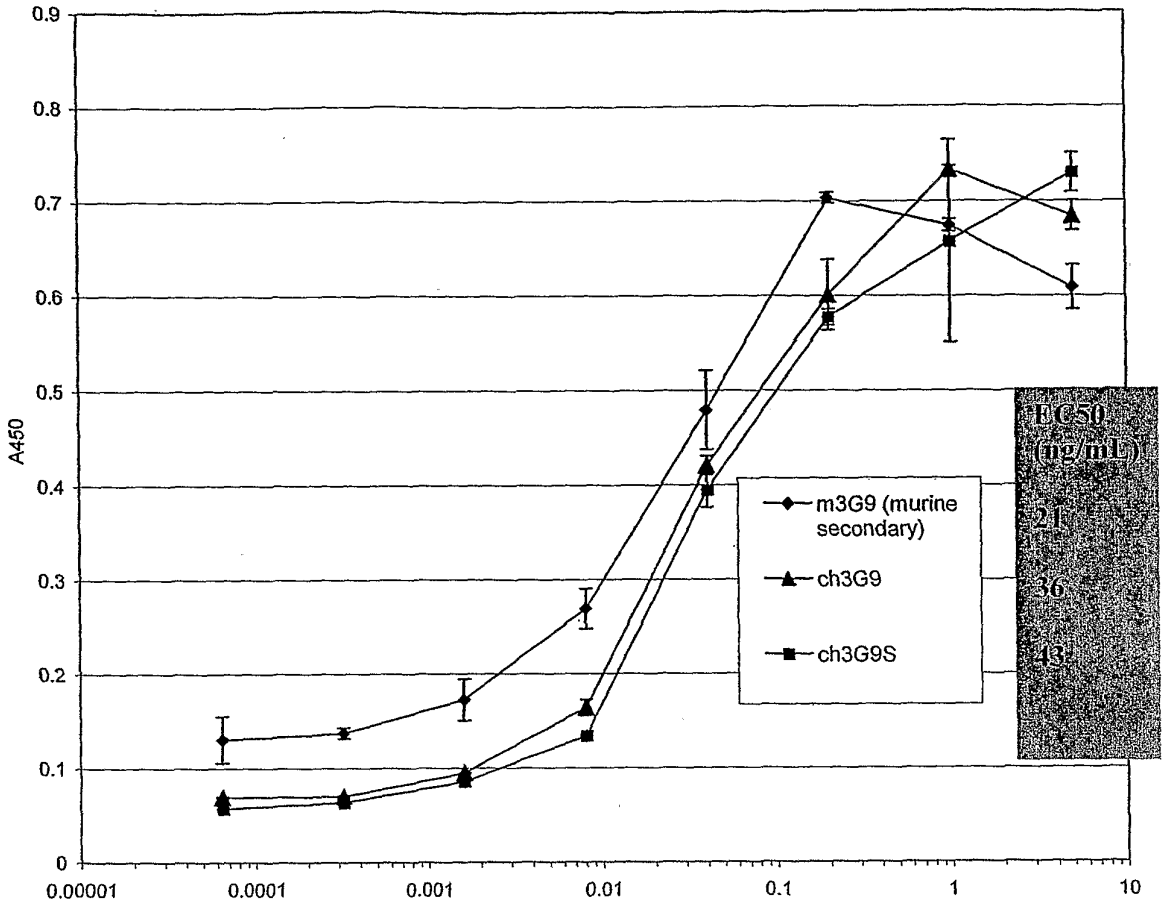


Figure 1. Binding ELISA of purified and chimerized 3G9 antibody variants to $\alpha_v\beta_6$.

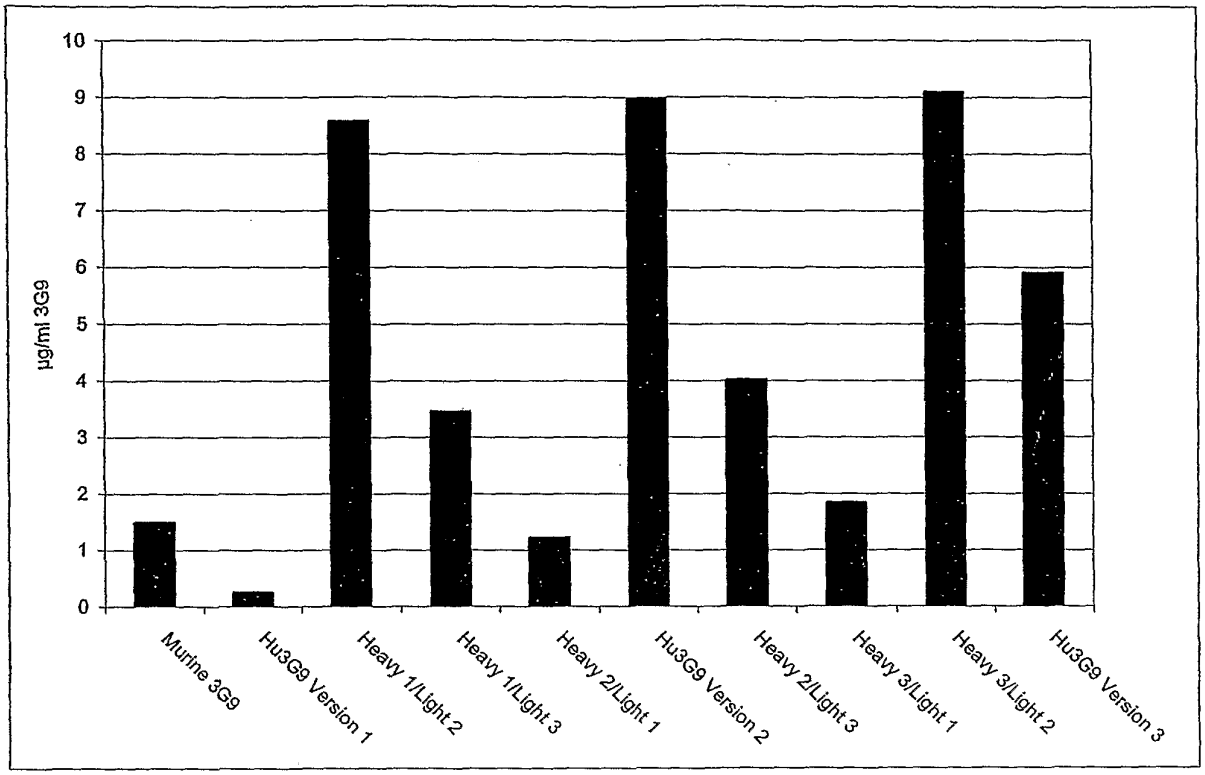


Figure 2. Easy Titer expression analysis of 3G9 humanization variants from transfected 293E cells.

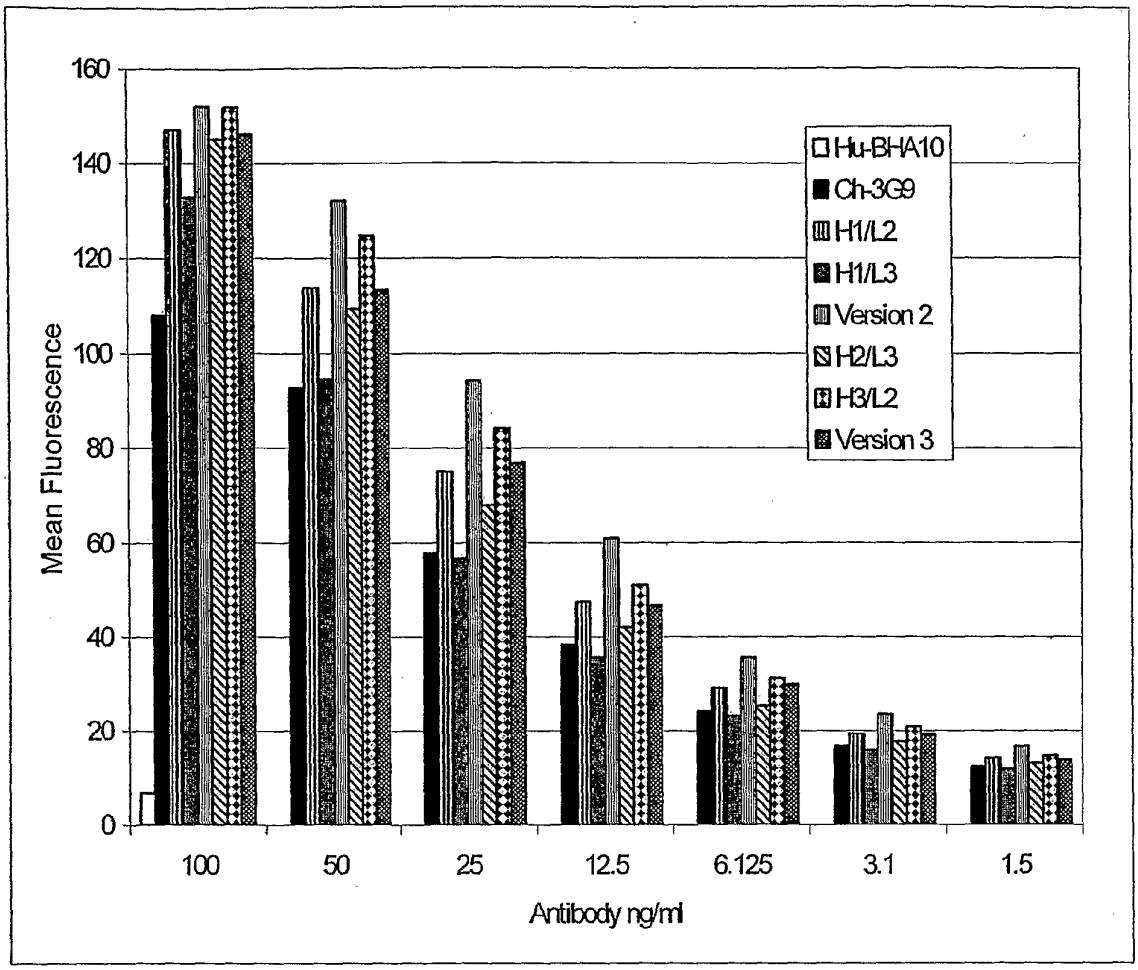


Figure 3. FACS analysis of hu-3G9 antibody variants binding to $\alpha_v\beta_6$ integrin expressing SW480 cells.

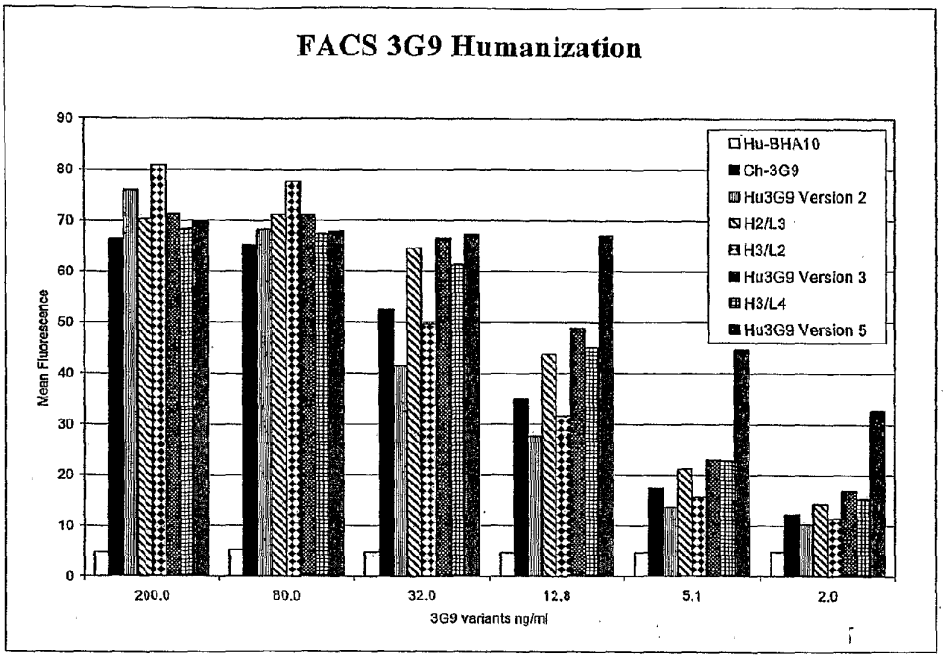


Figure 4. FACS analysis of hu-3G9 antibody versions 2-5 binding to FDCP1-β6 cells.

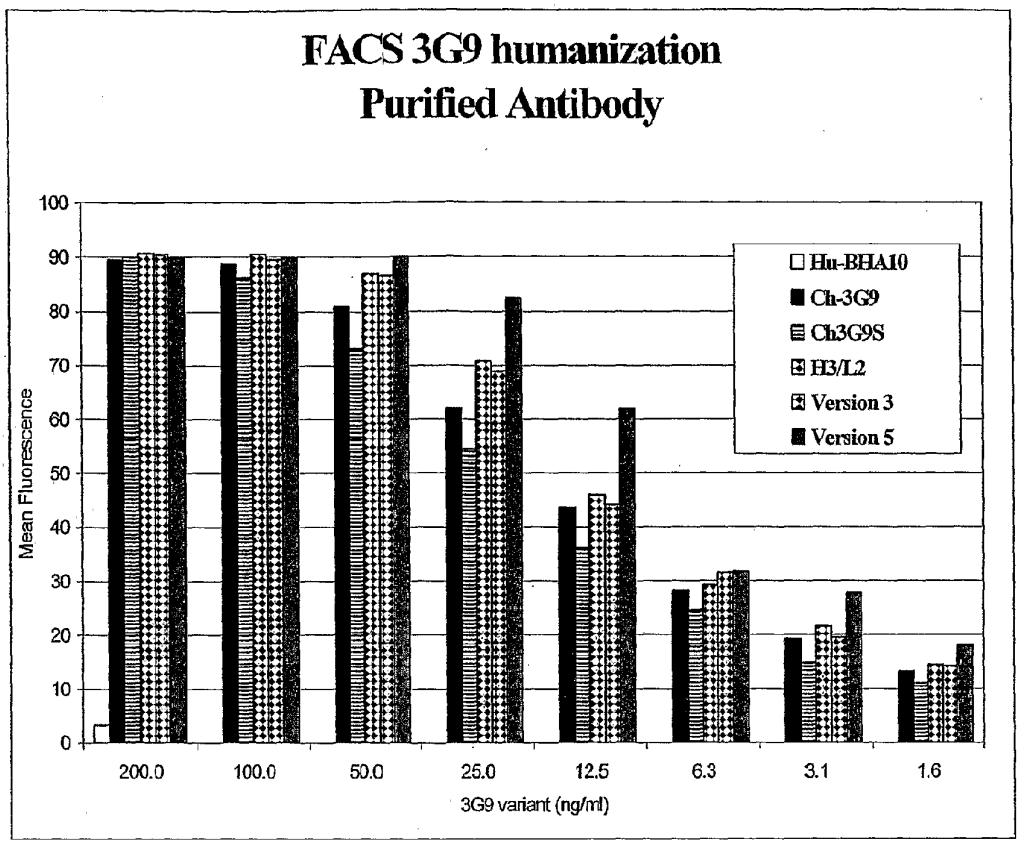


Figure 5. FACS analysis of purified hu-3G9 antibody versions 2-5 binding to FDCP1-β6 cells.

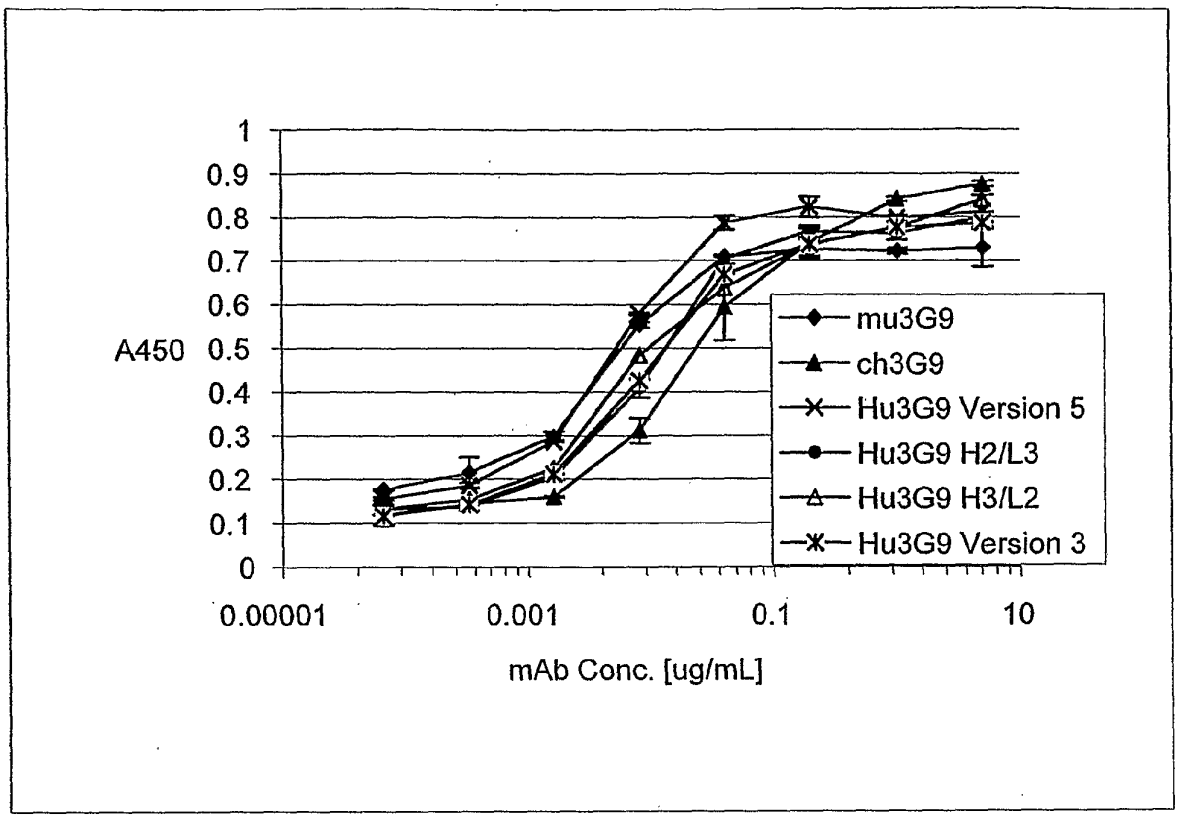


Figure 6. Binding ELISA of purified hu-3G9 antibody versions 2-5 binding to $\alpha_V\beta_6$.

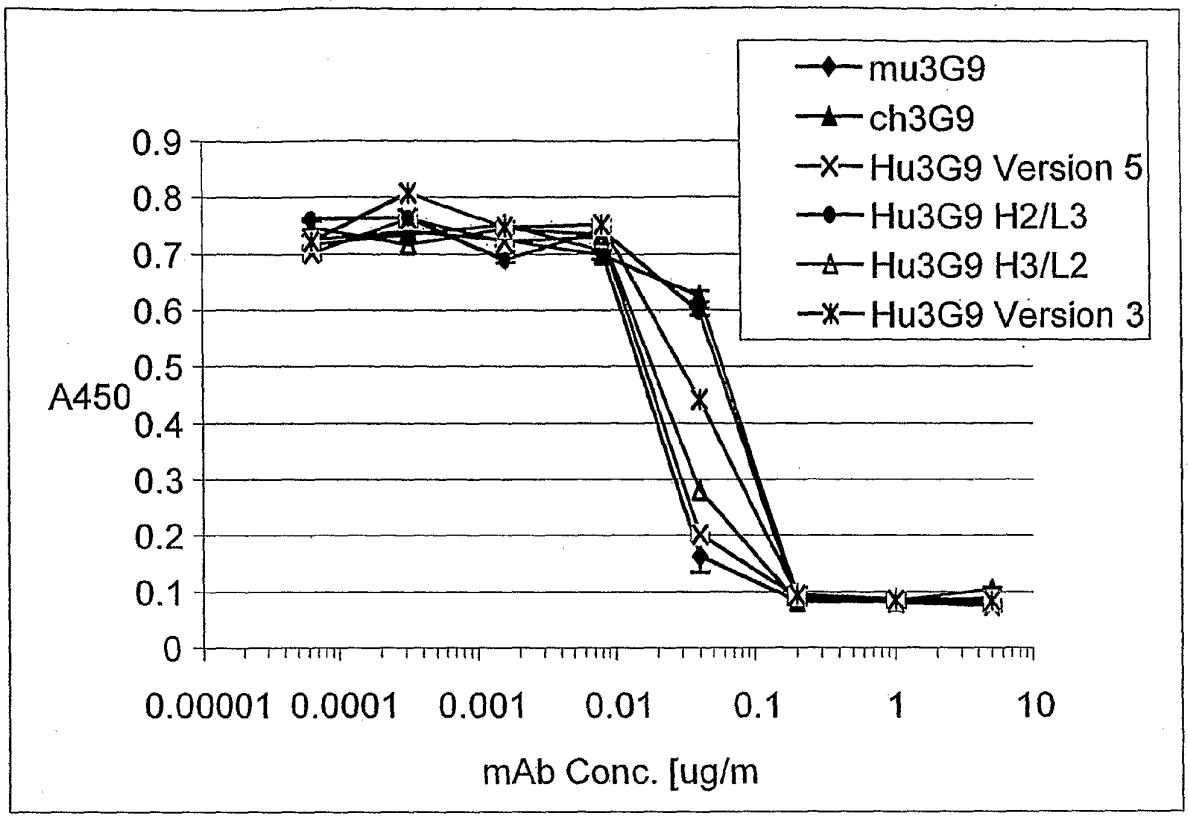


Figure 7. Blocking ELISA of purified hu-3G9 antibody versions 2-5 binding to $\alpha_V\beta_6$.

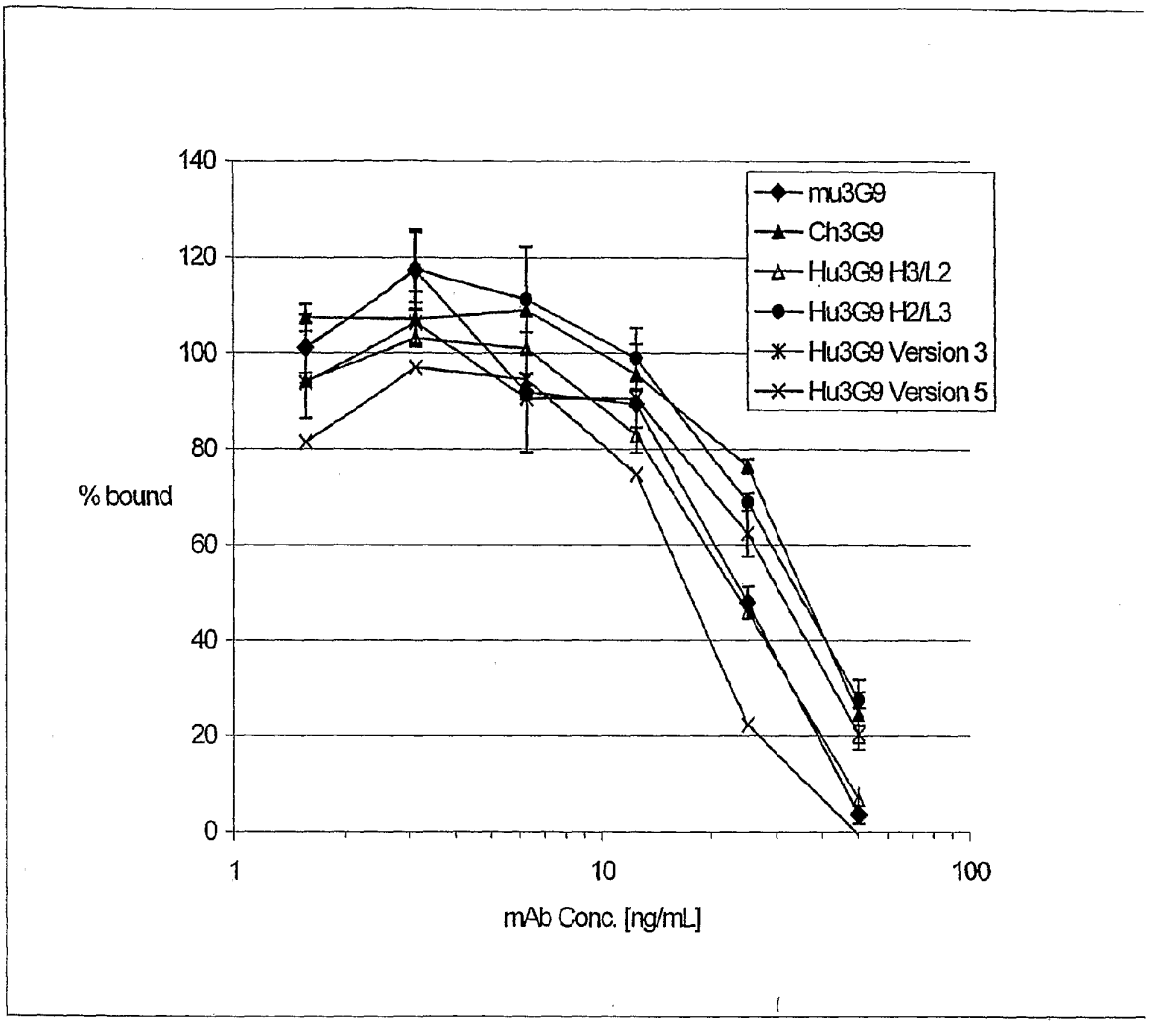
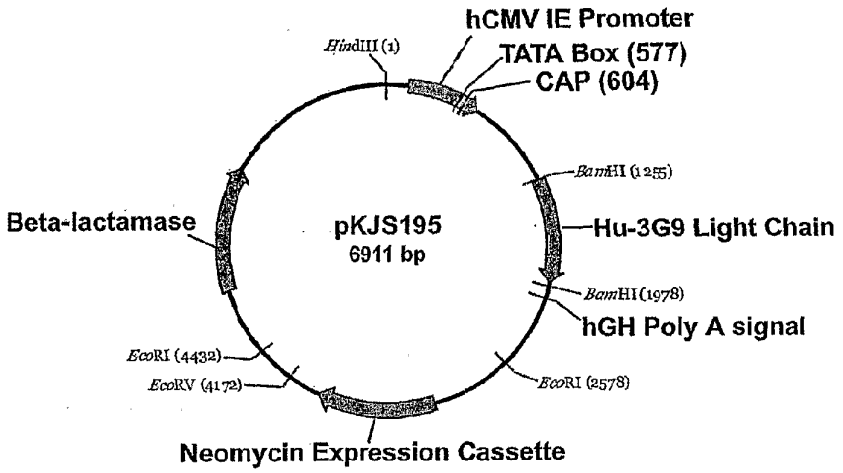


Figure 8. Cell-adhesion assay of purified hu-3G9 antibody versions 2-5.




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1       Met Asp Phe Gln Val Gln Ile Phe Ser Phe Leu Leu Ile Ser Val Ser Val Ile Met Ser Arg Gly Glu Ile Val Leu Thr Gln

1347    AGC CCC GCC ACC CTG AGC CTG AGC CCC GGC GAG AGG GCC ACC CTG AGC TGC AGC GCC AGC AGC AGC GTG AGC AGC AGC TAC CTG
29      Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Ser Ala Ser Ser Ser Val Ser Ser Ser Tyr Leu

1431    TAC TGG TAC CAG CAG AAG CCC GGC CAG GCC CCC AGG CTG CTG ATC TAC AGC ACC AGC AAC CTG GCC AGC GGC ATC CCC GCC CGC
56      Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg

1515    TTC AGC GGC AGC GGC AGC GGC ACC GAC TTC ACC CTG ACC ATC AGC AGC CTG GAG CCC GAG GAC TTC GCC GTG TAC TAC TGC CAC
83      Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys His

1599    CAG TGG AGC ACC TAC CCC CCC ACC TTC GGC GGC GGC ACC AAG GTG GAG ATC AAG CGT ACG GTG GCT GCA CCA TCT GTC TTC ATC
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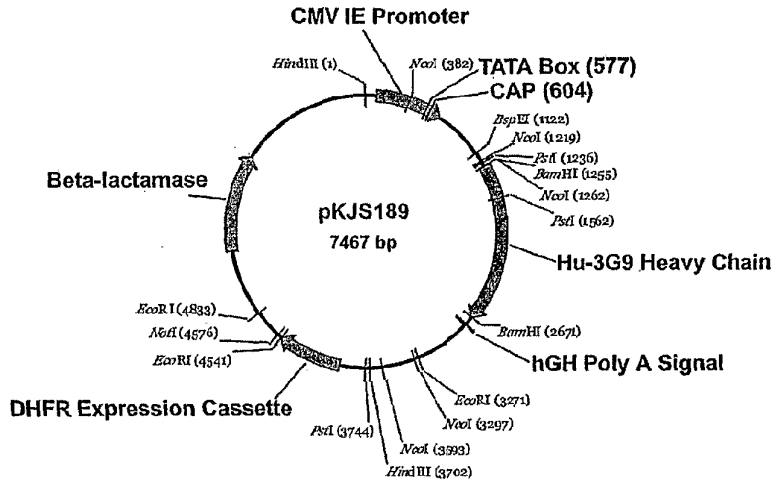
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1767    GTA CAG TGG AAG GTG GAT AAC GCC CTC CAA TCG GGT AAC TCC CAG GAG AGT GTC ACA GAG CAG GAC AGC AAG GAC AGC ACC TAC
164     Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr

1851    AGC CTC AGC AGC ACC CTG ACG CTG AGC AAA GCA GAC TAC GAG AAA CAC AAA GTC TAC GCC TGC GAA GTC ACC CAT CAG GGC CTG
191     Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu

1935    AGC TCG CCC GTC ACA AAG AGC TTC AAC AGG GGA GAG TGT
218     Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
```

Figure 9. Plasmid map of pKJS195 and 3G9 version 5 Light Chain Sequence.




```
1263  ATG GAC TTC GGC CTG AGC TGG GTG TTC CTG GTG CTG GTG CTG AAG GGC GTG CAG TGC GAG GTG CAG CTG GTG GAG AGC GGC GGC
1     Met Asp Phe Gly Leu Ser Trp Val Phe Leu Val Leu Val Leu Lys Gly Val Gln Cys Glu Val Gln Leu Val Glu Ser Gly Gly

1347  GGC CTG GTG CAG CCC GGC GGC AGC CTG AGG CTG AGC TGC GCC GCC AGC GGC TTC ACC TTC AGC CGC TAC GTG ATG AGC TGG GTG
29    Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Arg Tyr Val Met Ser Trp Val

1431  CGC CAG GCC CCC GGC AAG GGC CTG GAG TGG GTG GCC AGC ATC AGC AGC GGA GGC CGC ATG TAC TAC CCC GAC ACC GTG AAG GGC
57    Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ser Ile Ser Ser Gly Gly Arg Met Tyr Tyr Pro Asp Thr Val Lys Gly

1515  CGC TTC ACC ATC AGC CGC GAC AAC GCC AAG AAC AGC CTG TAC CTG CAG ATG AAC AGC CTG CGC GCC GAG GAC ACC GCC GTG TAC
85    Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr

1599  TAC TGC GCC CGC GGC AGC ATC TAC GAC GGC TAC TAC GTG TTC CCC TAC TGG GGC CAG GGC ACC CTG GTG ACC GTG AGC TCC GCC
113   Tyr Cys Ala Arg Gly Ser Ile Tyr Asp Gly Tyr Tyr Val Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala

1683  AGC ACC AAG GGC CCC AGC GTG TTC CCC CTG GCC CCC AGC AGC AAG AGC ACC AGC GGC GGC ACC GCC GCC CTG GGC TGC CTG GTG
141   Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val

1767  AAG GAC TAC TTC CCC GAA CCG GTG ACG GTG TCG TGG AAC TCA GGC GCC CTG ACC AGC GGC GTG CAC ACC TTC CCG GCT GTC CTA
169   Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu

1851  CAG TCC TCA GGA CTC TAC TCC CTC AGC AGC GTG GTG ACC GTG CCC TCC AGC AGC TTG GGC ACC CAG ACC TAC ATC TGC AAC GTG
197   Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val

1935  AAT CAC AAG CCC AGC AAC ACC AAG GTG GAC AAG AAA GTT GAG CCC AAA TCT TGT GAC AAG ACT CAC ACA TGC CCA CCG TGC CCA
225   Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro

2019  GCA CCT GAA CTC CTG GGG GGA CCG TCA GTC TTC CTC TTC CCC CCA AAA CCC AAG GAC ACC CTC ATG ATC TCC CGG ACC CCT GAG
253   Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu

2103  GTC ACA TGC GTG GTG GTG GAC GTG AGC CAC GAA GAC CCT GAG GTC AAG TTC AAC TGG TAC GTG GAC GGC GTG GAG GTG CAT AAT
281   Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn

2187  GCC AAG ACA AAG CCG CGG GAG GAG CAG TAC AAC AGC ACG TAC CGT GTG GTC AGC GTC CTC ACC GTC CTG CAC CAG GAC TGG CTG
309   Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu

2271  AAT GGC AAG GAG TAC AAG TGC AAG GTC TCC AAC AAA GCC CTC CCA GCC CCC ATC GAG AAA ACC ATC TCC AAA GCC AAA GGG CAG
337   Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln

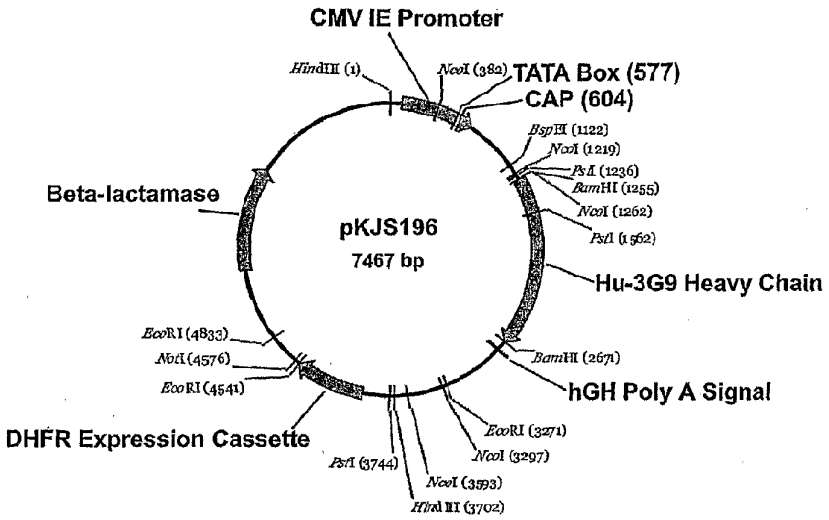
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365   Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys

2439  GGC TTC TAT CCC AGC GAC ATC GCC GTG GAG TGG GAG AGC AAT GGG CAG CCG GAG AAC AAC TAC AAG ACC ACG CCT CCC GTG TTG
393   Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu

2523  GAC TCC GAC GGC TCC TTC TTC CTC TAC AGC AAG CTC ACC GTG GAC AAG AGC AGG TGG CAG CAG GGG AAC GTC TTC TCA TGC TCC
421   Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser

2607  GTG ATG CAT GAG GCT CTG CAC AAC CAC TAC ACG CAG AAG AGC CTC TCC CTG TCT CCC GGT
449   Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
```

Figure 10. Plasmid map of pKJS189 and 3G9 version 3 Heavy Chain Sequence.




```
1263  ATG GAC TTC GGC CTG AGC TGG GTG TTC CTG GTG CTG GTG CTG AAG GGC GTG CAG TGC GAG GTG CAG CTG GTG GAG AGC GGC GGC
1     Met Asp Phe Gly Leu Ser Trp Val Phe Leu Val Leu Val Leu Lys Gly Val Gln Cys Glu Val Gln Leu Val Glu Ser Gly Gly
1347  GGC CTG GTG CAG CCC GGC GGC AGC CTG AGG CTG AGC TGC GCC GCC AGC GGC TTC ACC TTC AGC CGC TAC GTG ATG AGC TGG GTG
29    Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Arg Tyr Val Met Ser Trp Val
1431  CGC CAG GCC CCC GGC AAG GGC CTG GAG TGG GTG GCC AGC ATC AGC AGC GGA GGC CGC ATG TAC TAC CCC GAC ACC GTG AAG GGC
57    Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Ser Ile Ser Ser Gly Gly Arg Met Tyr Tyr Pro Asp Thr Val Lys Gly
1515  CGC TTC ACC ATC AGC CGC GAC AAC GCC AAG AAC AGC CTG TAC CTG CAG ATG AAC AGC CTG CGC GCC GAG GAC ACC GCC GTG TAC
85    Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
1599  TAC TGC GCC CGC GGC AGC ATC TAC GAC GGC TAC TAC GTG TTC CCC TAC TGG GGC CAG GGC ACC CTG GTG ACC GTG AGC TCC GCC
113   Tyr Cys Ala Arg Gly Ser Ile Tyr Asp Gly Tyr Tyr Val Phe Pro Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala
1683  AGC ACC AAG GGC CCC AGC GTG TTC CCC CTG GCC CCC AGC AGC AAG AGC ACC AGC GGC GGC ACC GCC GCC CTG GGC TGC CTG GTG
141   Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
1767  AAG GAC TAC TTC CCC GAA CCG GTG ACG GTG TCG TGG AAC TCA GGC GCC CTG ACC AGC GGC GTG CAC ACC TTC CCG GCT GTC CTA
169   Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
1851  CAG TCC TCA GGA CTC TAC TCC CTC AGC AGC GTG GTG ACC GTG CCC TCC AGC AGC TTG GGC ACC CAG ACC TAC ATC TGC AAC GTG
197   Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
1935  AAT CAC AAG CCC AGC AAC ACC AAG GTG GAC AAG AAA GTT GAG CCC AAA TCT TGT GAC AAG ACT CAC ACA TGC CCA CCG TGC CCA
225   Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro
2019  GCA CCT GAA CTC CTG GGG GGA CCG TCA GTC TTC CTC TTC CCC CCA AAA CCC AAG GAC ACC CTC ATG ATC TCC CGG ACC CCT GAG
253   Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
2103  GTC ACA TGC GTG GTG GTG GAC GTG AGC CAC GAA GAC CCT GAG GTC AAG TTC AAC TGG TAC GTG GAC GGC GTG GAG GTG CAT AAT
281   Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
2187  GCC AAG ACA AAG CCG CGG GAG GAG CAG TAC CAG AGC ACG TAC CGT GTG GTC AGC GTC CTC ACC GTC CTG CAC CAG GAC TGG CTG
309   Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gln Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
2271  AAT GGC AAG GAG TAC AAG TGC AAG GTC TCC AAC AAA GCC CTC CCA GCC CCC ATC GAG AAA ACC ATC TCC AAA GCC AAA GGG CAG
337   Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
2355  CCC CGA GAA CCA CAG GTG TAC ACC CTG CCC CCA TCC CGG GAT GAG CTG ACC AAG AAC CAG GTC AGC CTG ACC TGC CTG GTC AAA
365   Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
2439  GGC TTC TAT CCC AGC GAC ATC GCC GTG GAG TGG GAG AGC AAT GGG CAG CCG GAG AAC AAC TAC AAG ACC ACG CCT CCC GTG TTG
393   Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
2523  GAC TCC GAC GGC TCC TTC TTC CTC TAC AGC AAG CTC ACC GTG GAC AAG AGC AGG TGG CAG CAG GGG AAC GTC TTC TCA TGC TCC
421   Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
2607  GTG ATG CAT GAG GCT CTG CAC AAC CAC TAC ACG CAG AAG AGC CTC TCC CTG TCT CCC GGT
449   Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
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Figure 11. Plasmid map of pKJS196 and Aglycosyl 3G9 version 3 Heavy Chain Sequence.

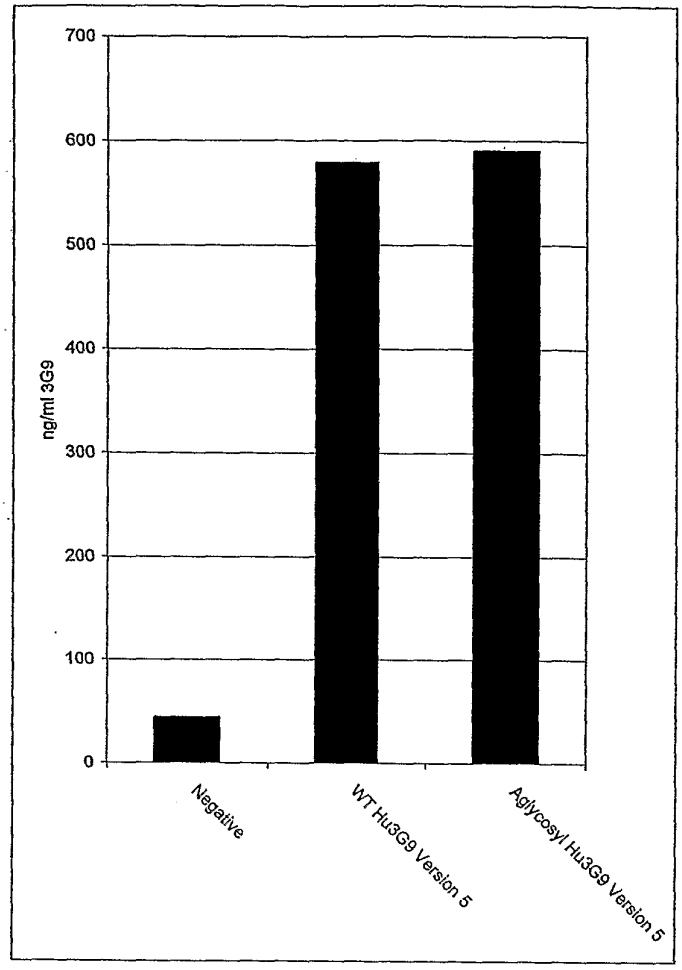


Figure 12. Easy Titer assay of CHO cells transiently transfected with hu-3G9 CHO expression vectors.

Figure 13

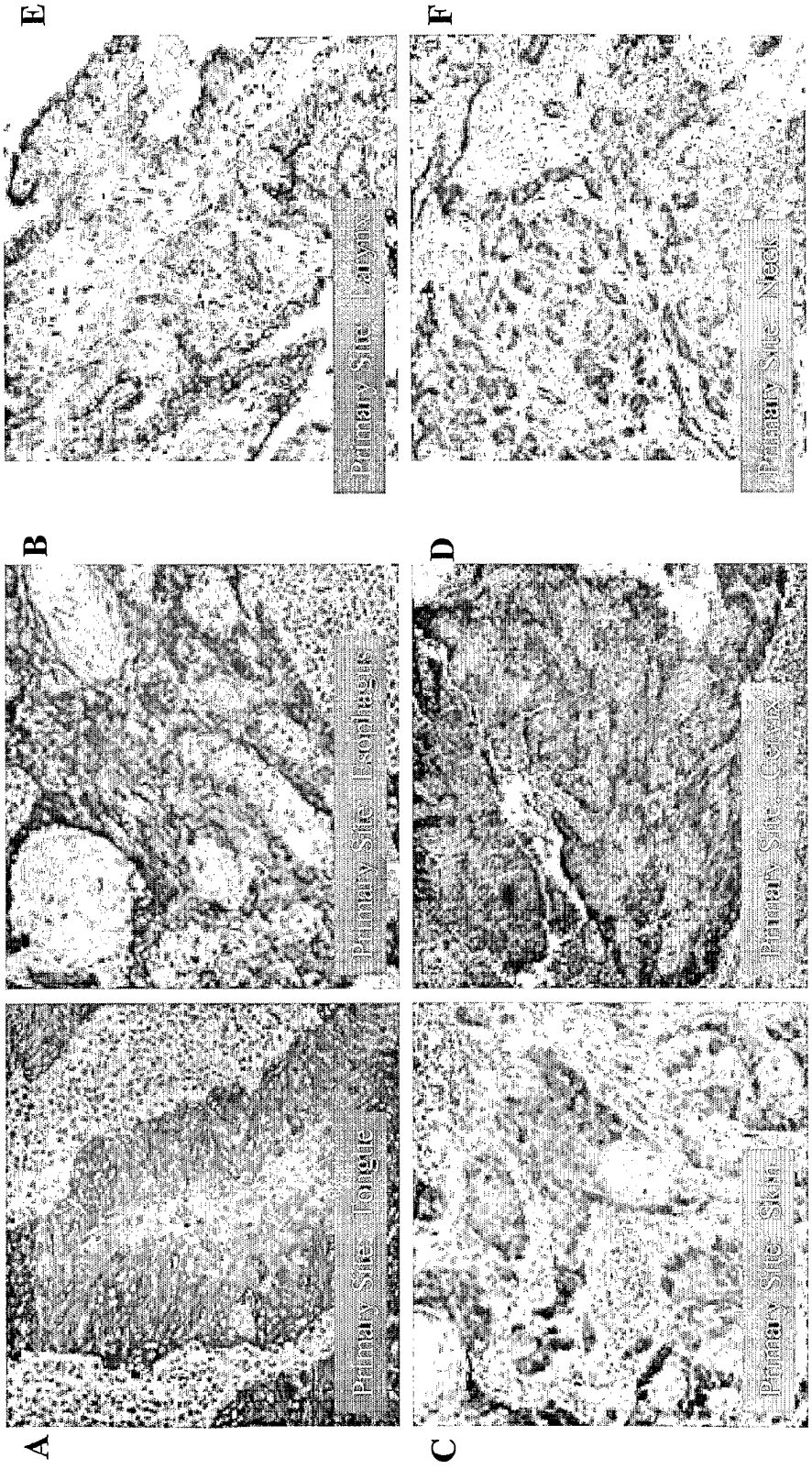
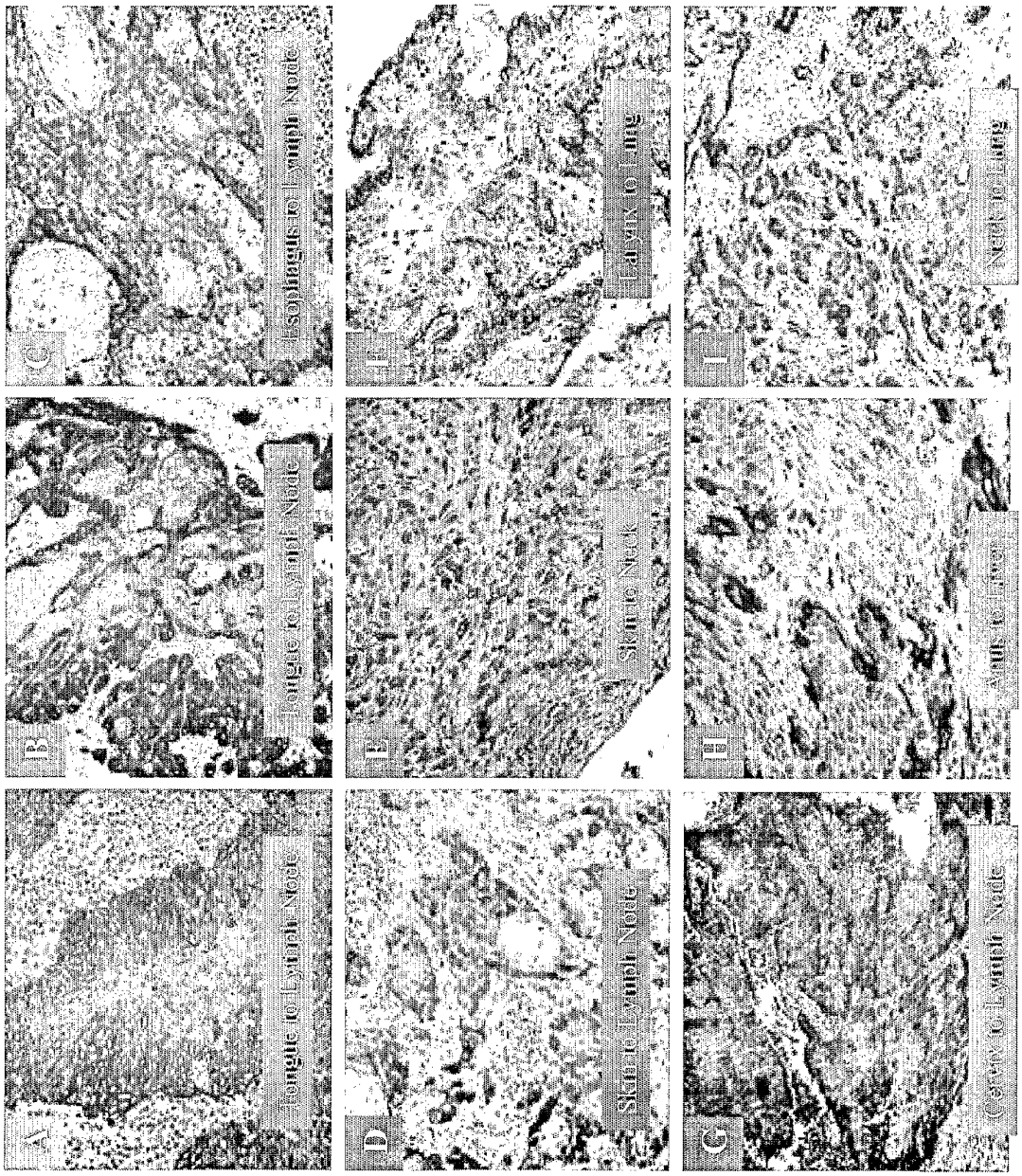

Lymph Node
Lung
A
Primary Site: Tongue
B
Primary Site: Esophagus
C
Primary Site: Skin
D
Primary Site: Cervix
E
Primary Site: Larynx
F
Primary Site: Neck

Figure 14


A
Tongue to Lymph Node
B
Tongue to Lymph Node
C
Esophagus to Lymph Node
D
Skin to Lymph Node
E
Skin to Neck
F
Esophagus to Lung
G
Esophagus to Lymph Node
H
Skin to Lymph Node
I
Neck to Lung

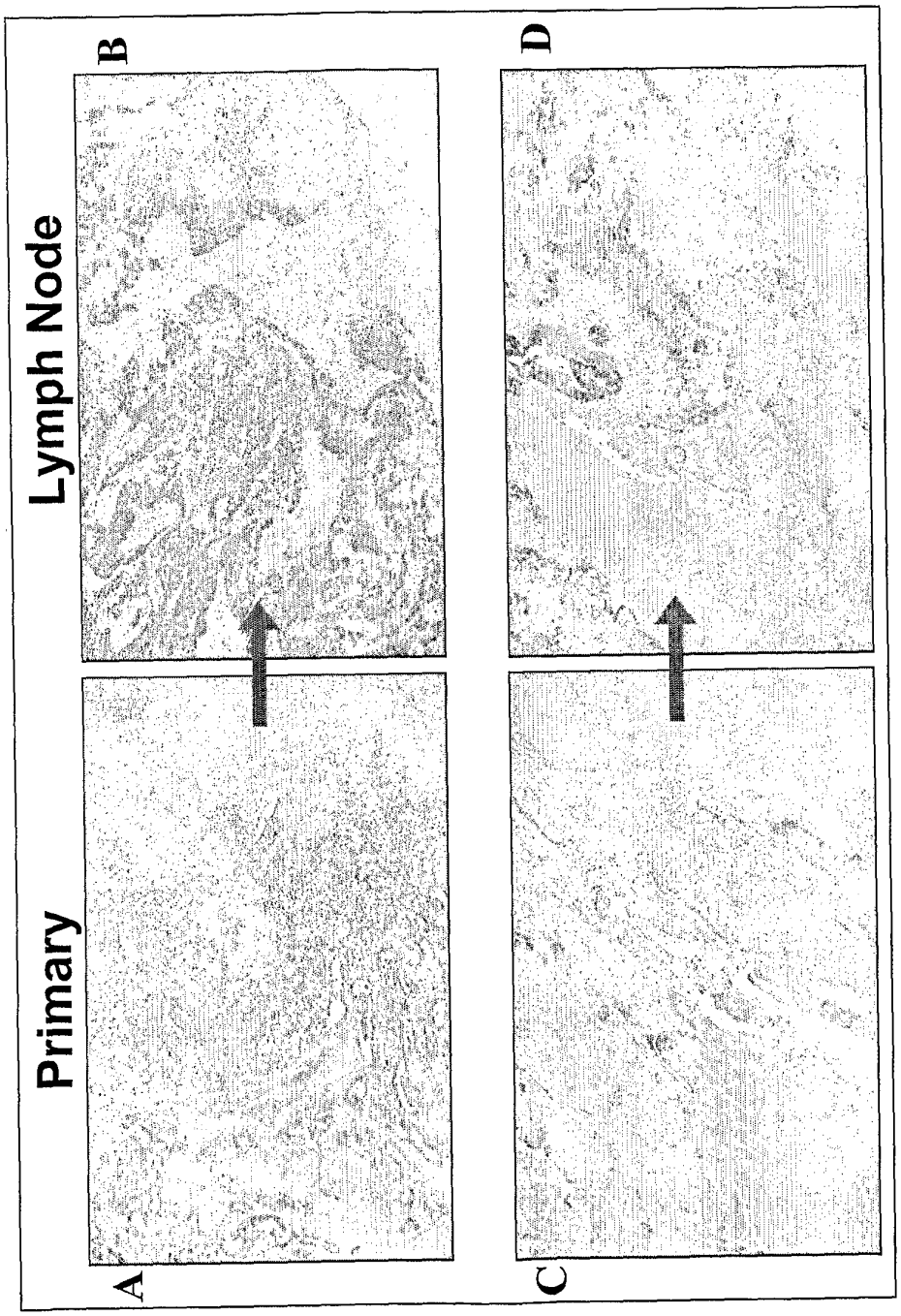


Figure 15

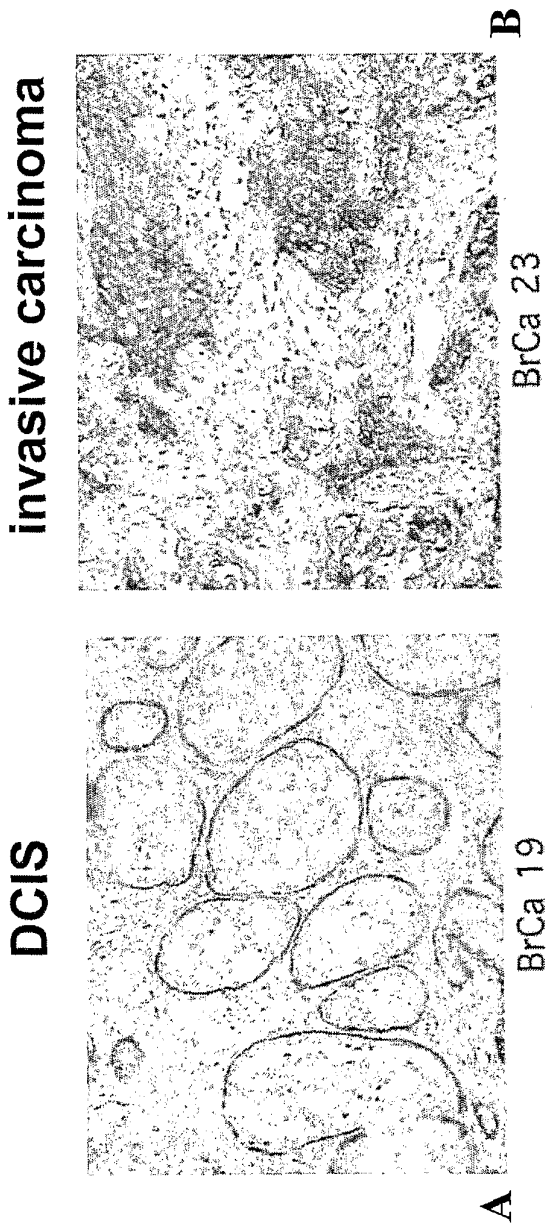


Figure 16

Figure 17

Matched cases
Pancreatic Adenocarcinoma, *Ductal*

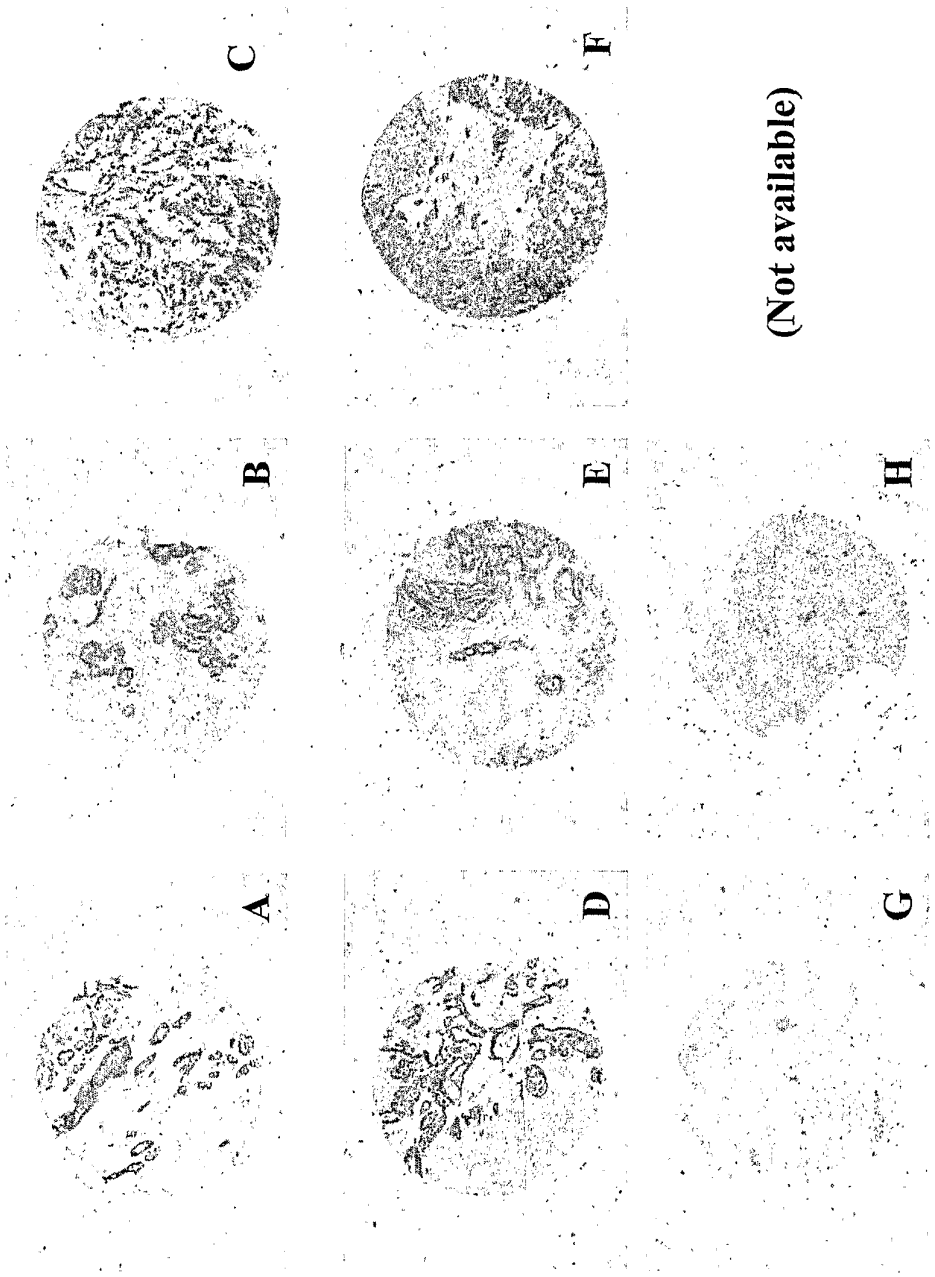


Figure 18

Matched cases Pancreatic Carcinoma



$\alpha_v\beta_6$ mAb inhibits tumor growth in xenograft model of human pancreatic cancer (BxPC-3)

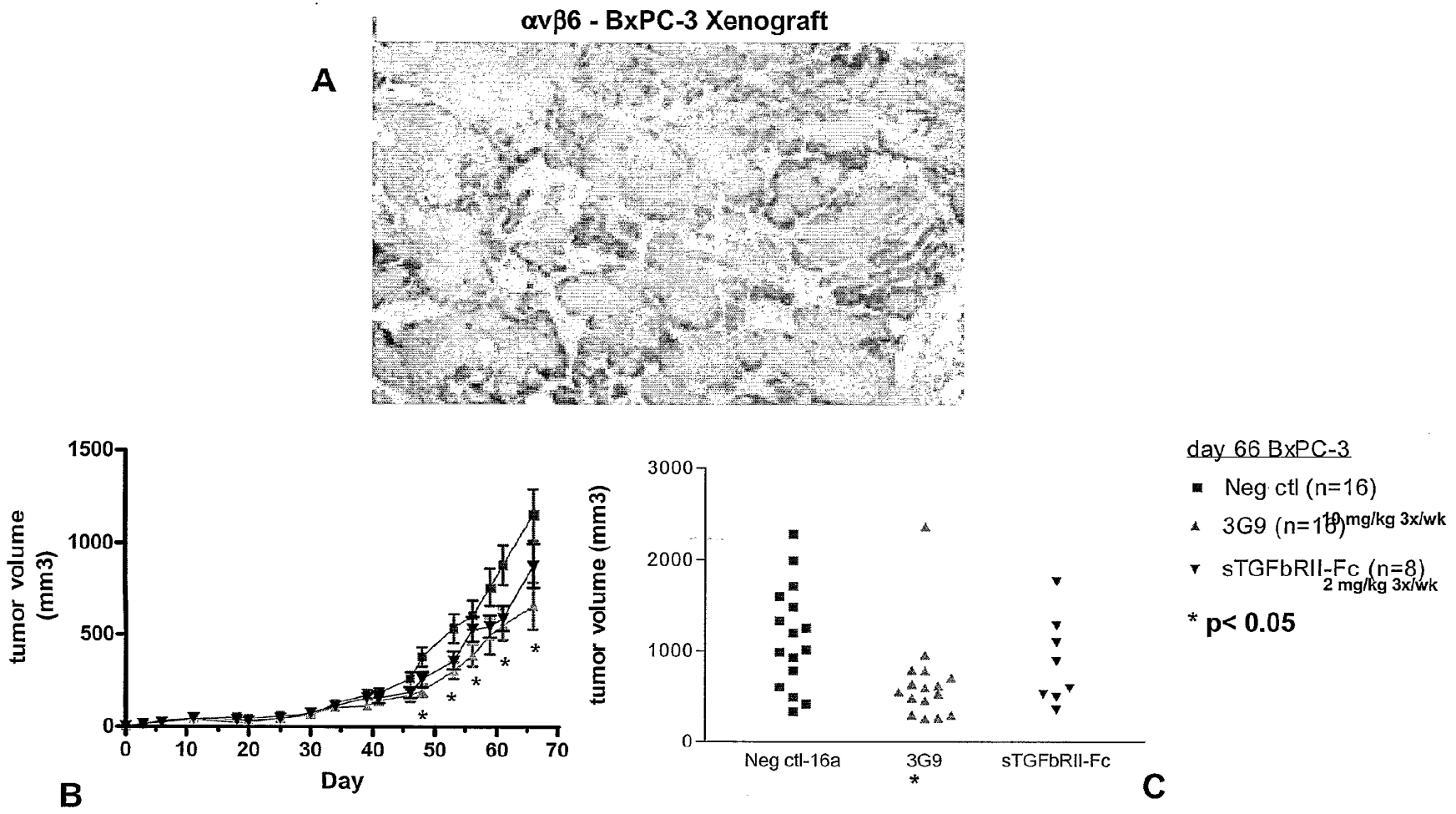
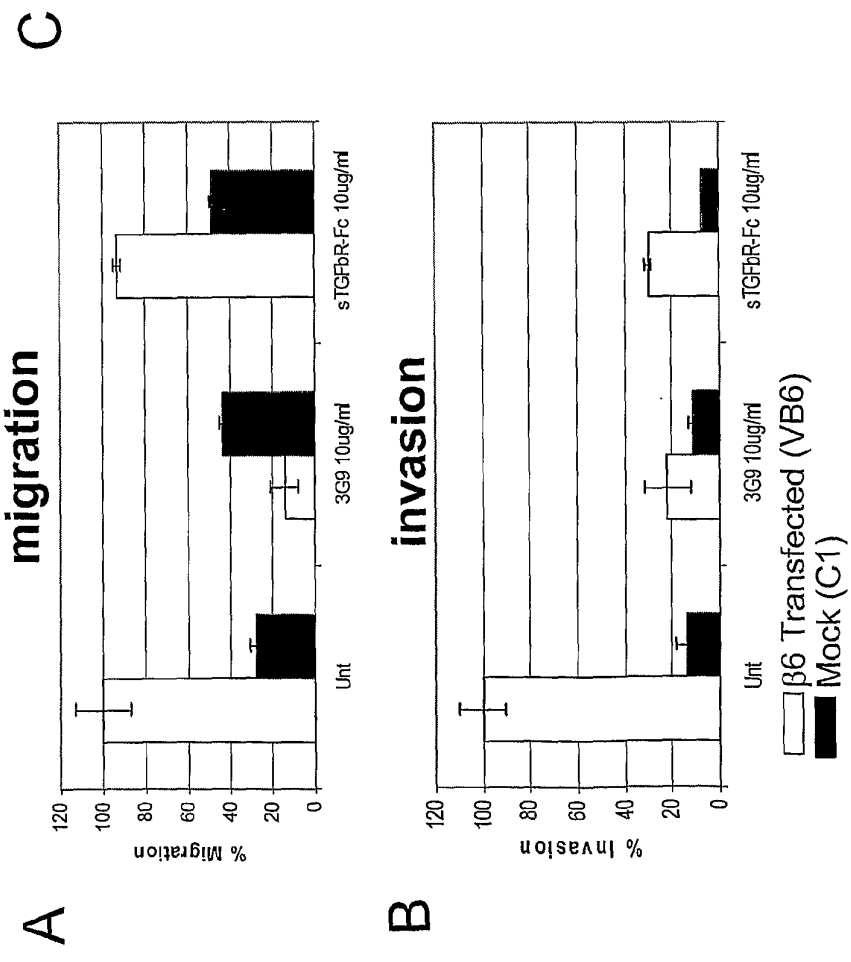


Figure 19

Figure 20


A
migration
% Migration
120
100
80
60
40
20
0
Unt
3G9 10ug/ml
sTGFbR-Fc 10ug/ml
B
invasion
% Invasion
β6 Transfected (VB6)
Mock (C1)
C
MMP9 production
MMP9 Conc (ng/mL)
3.5
3
2.5
2
1.5
1
0.5
0
untreated
3G9
sTGFβRII-Fc
Mock (C1)
β6 (VB6)

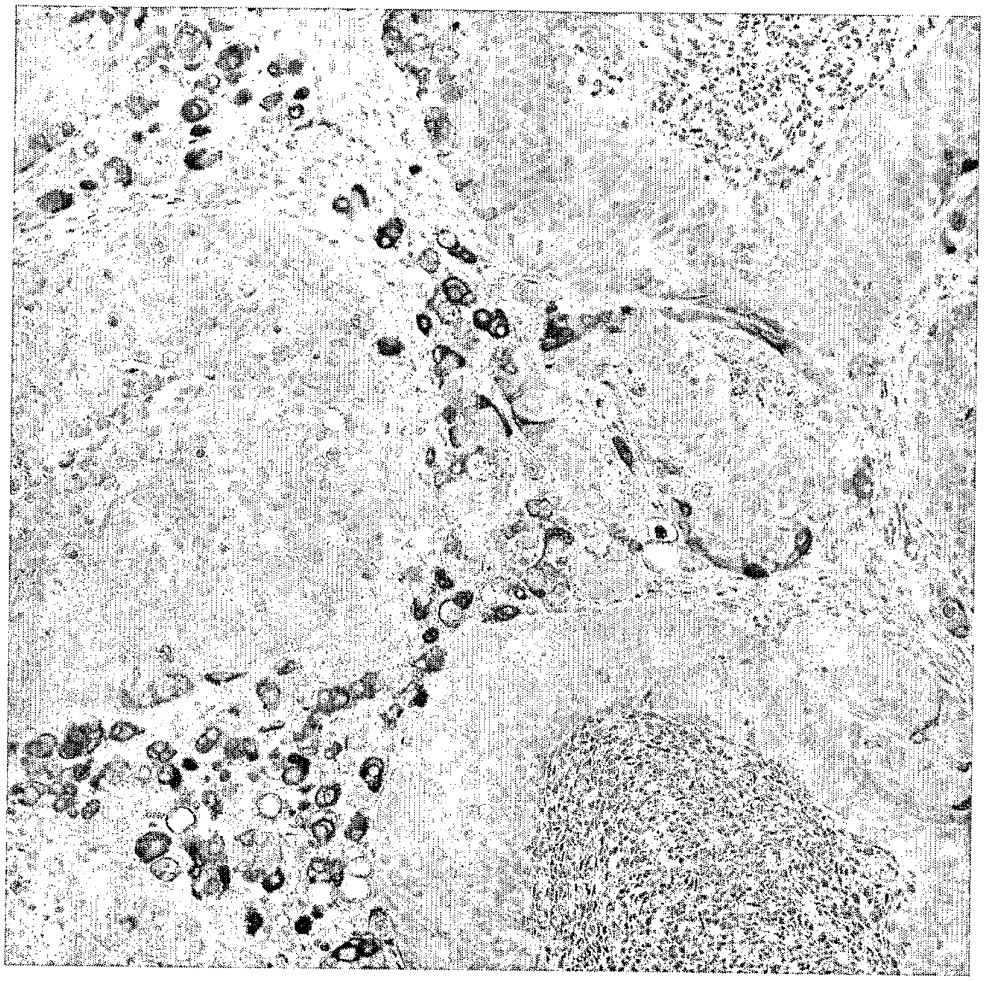
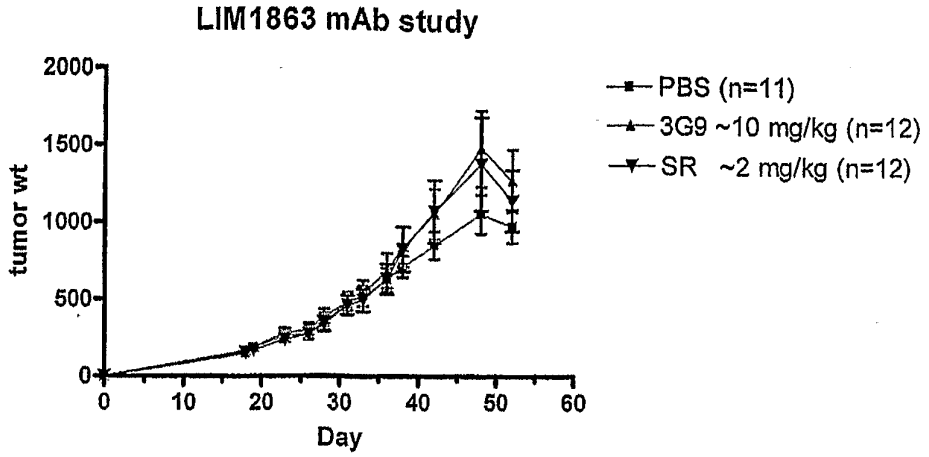
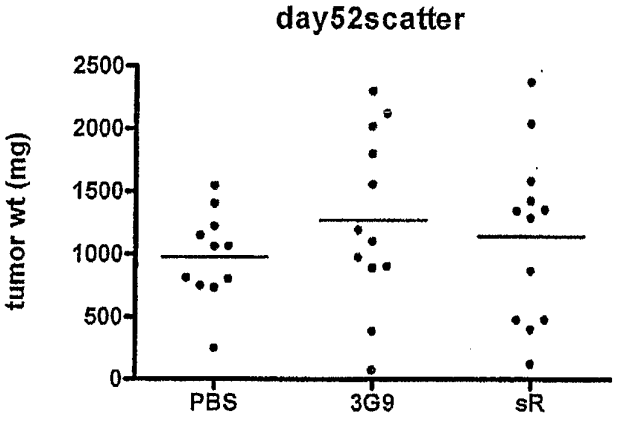


Figure 21

A



B



C

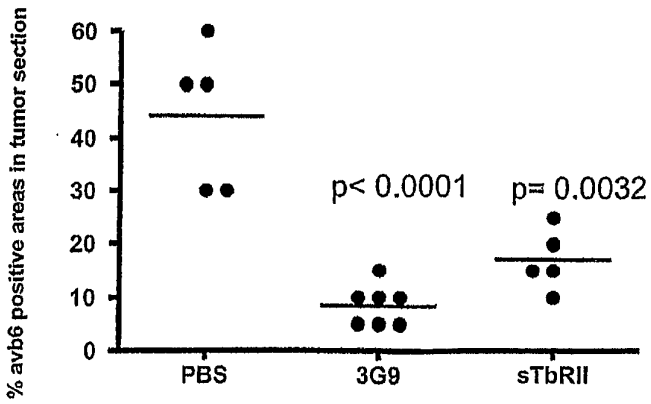


Figure 22A-22C

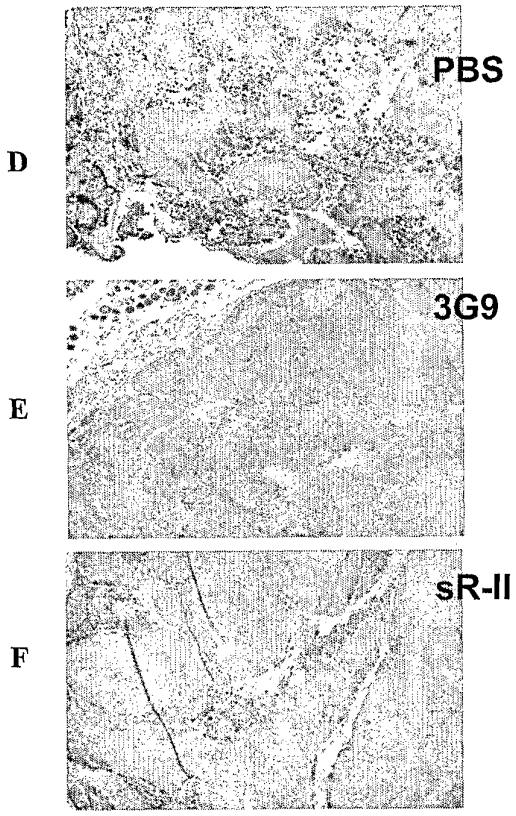


Figure 22D-22F

Figure 23

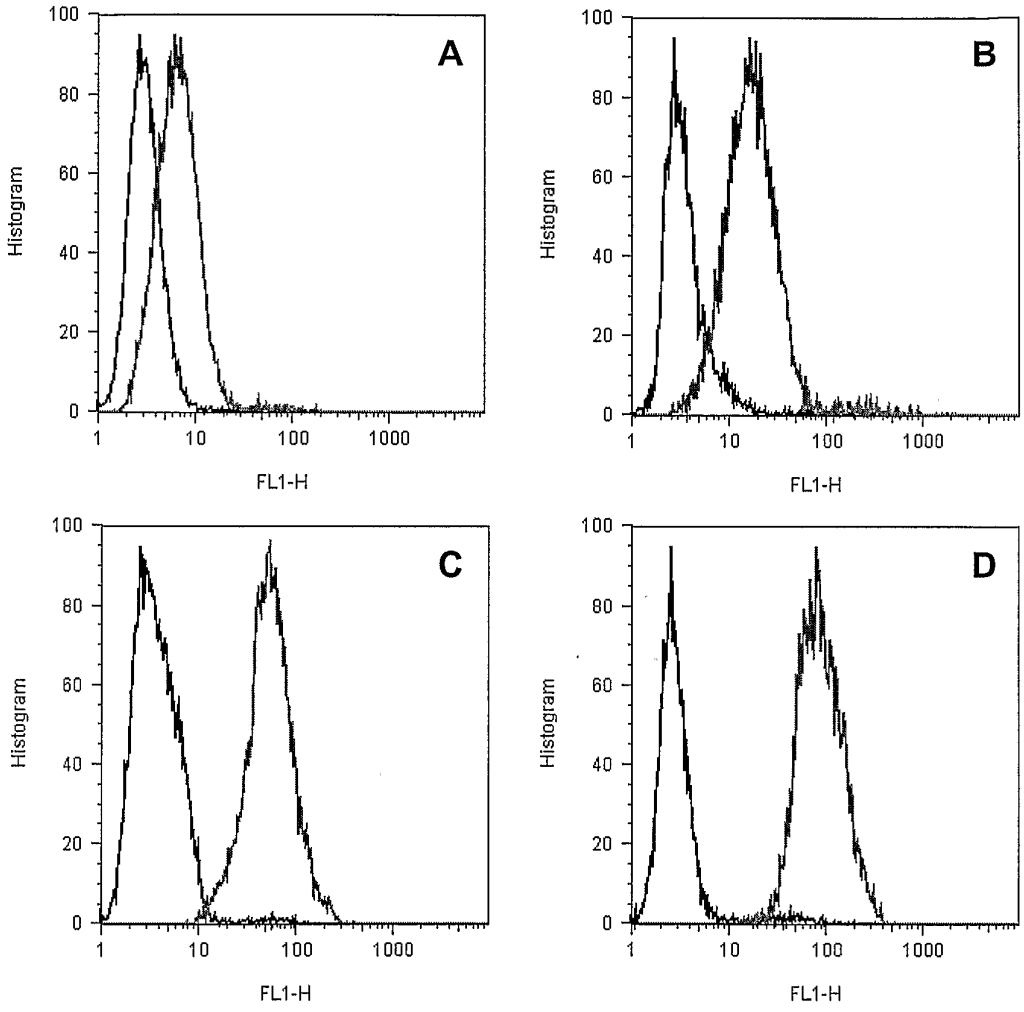


Figure 24

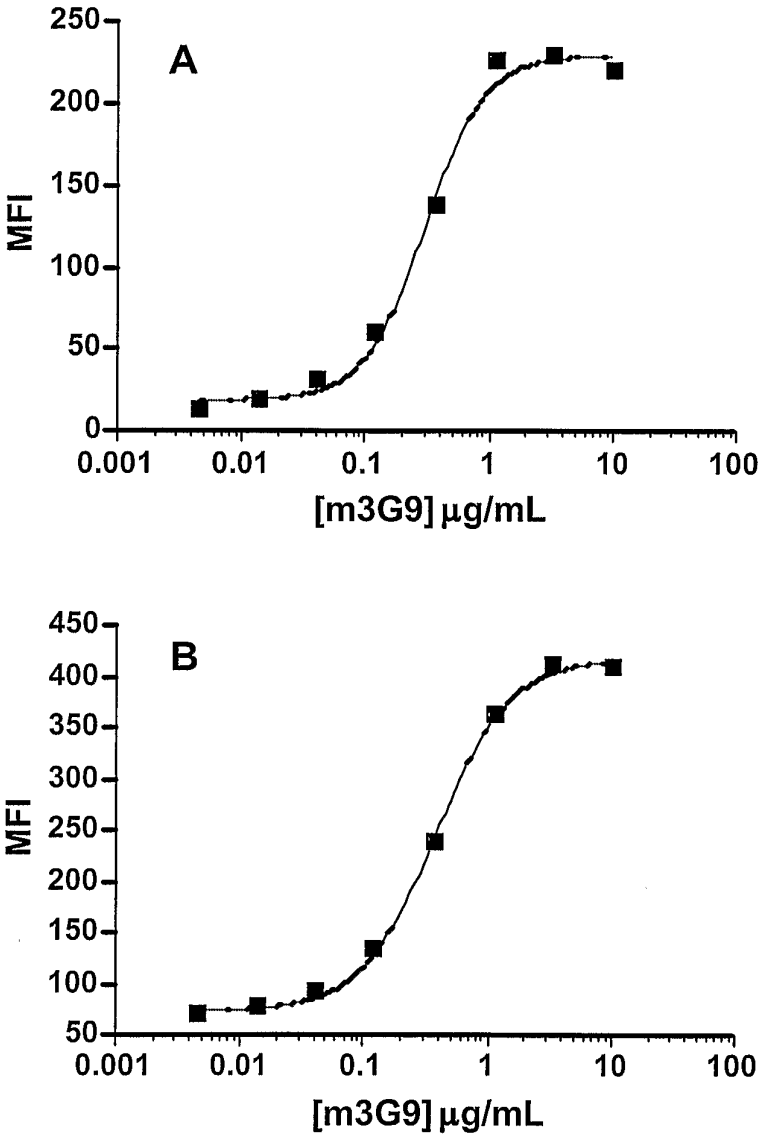

A
MFI
250
200
150
100
50
0
0.001
0.01
0.1
1
10
100
[m3G9] µg/mL
B
MFI
450
400
350
300
250
200
150
100
50
0.001
0.01
0.1
1
10
100
[m3G9] µg/mL

Figure 25

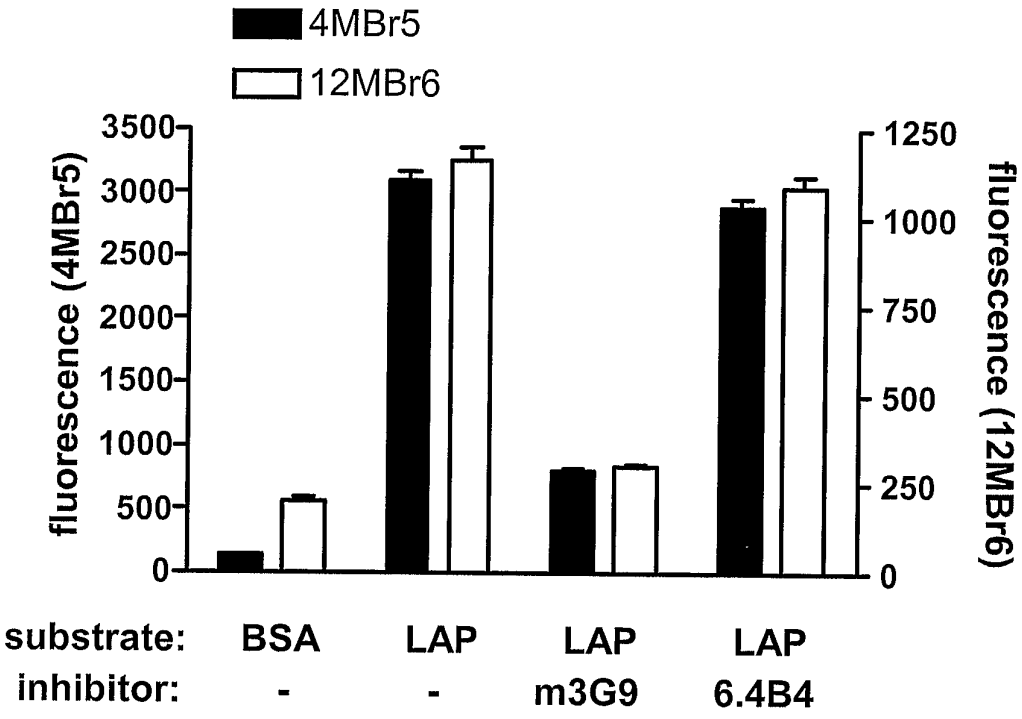

4MBr5
12MBr6
fluorescence (4MBr5)
3500
3000
2500
2000
1500
1000
500
0
1250
1000
750
500
250
0
fluorescence (12MBr6)
substrate: BSA LAP LAP LAP
inhibitor: - - m3G9 6.4B4

Figure 26

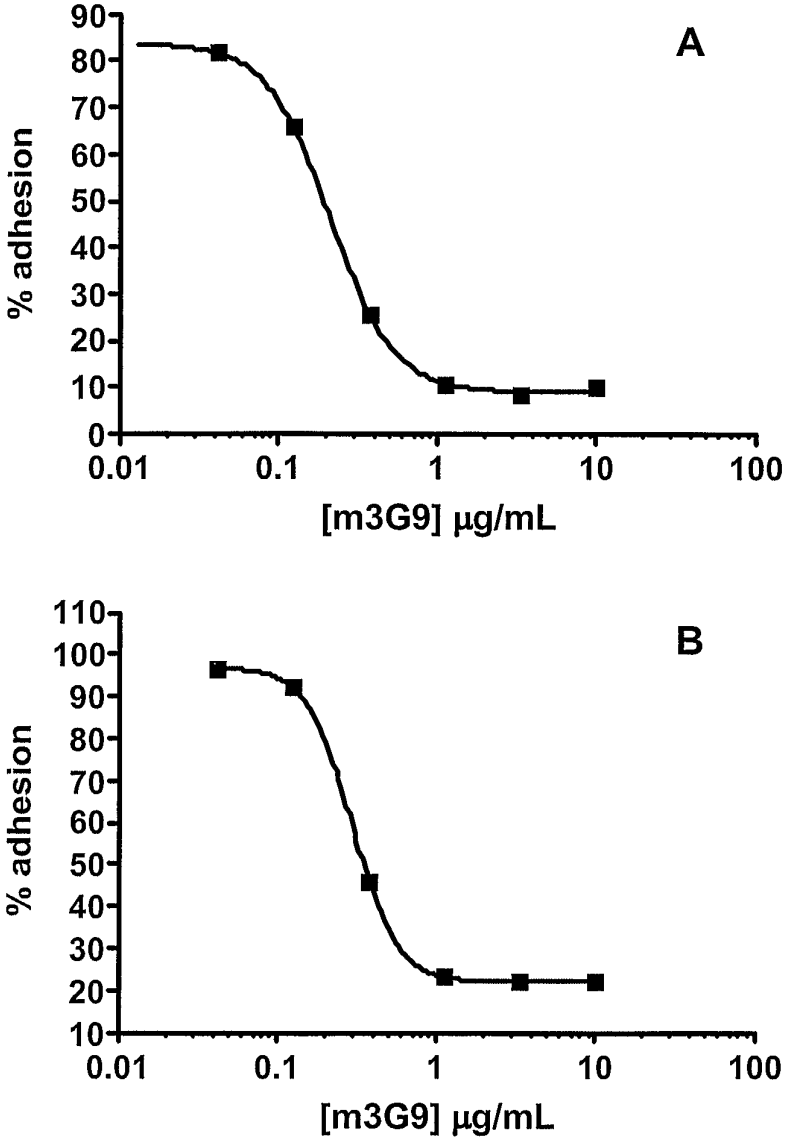

A
% adhesion
90
80
70
60
50
40
30
20
10
0
0.01
0.1
1
10
100
[m3G9] µg/mL
B
% adhesion
110
100
90
80
70
60
50
40
30
20
10
0.01
0.1
1
10
100
[m3G9] µg/mL

Figure 27

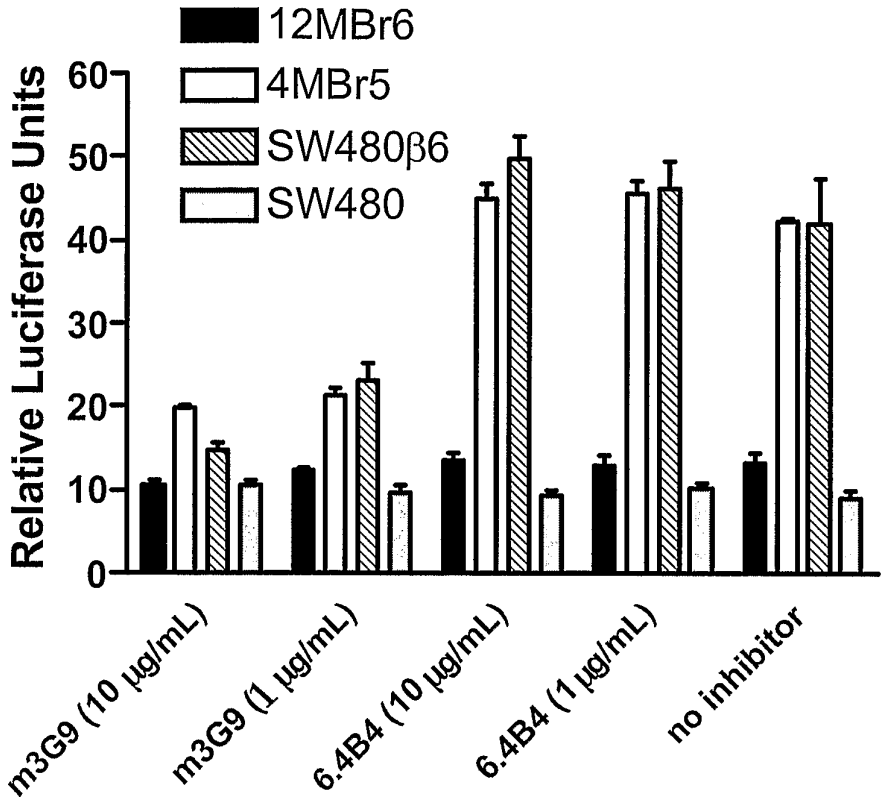

12MBr6
4MBr5
SW480β6
SW480
Relative Luciferase Units
60
50
40
30
20
10
0
m3G9 (10 μg/mL)
m3G9 (1 μg/mL)
6.4B4 (10 μg/mL)
6.4B4 (1 μg/mL)
no inhibitor

Figure 28

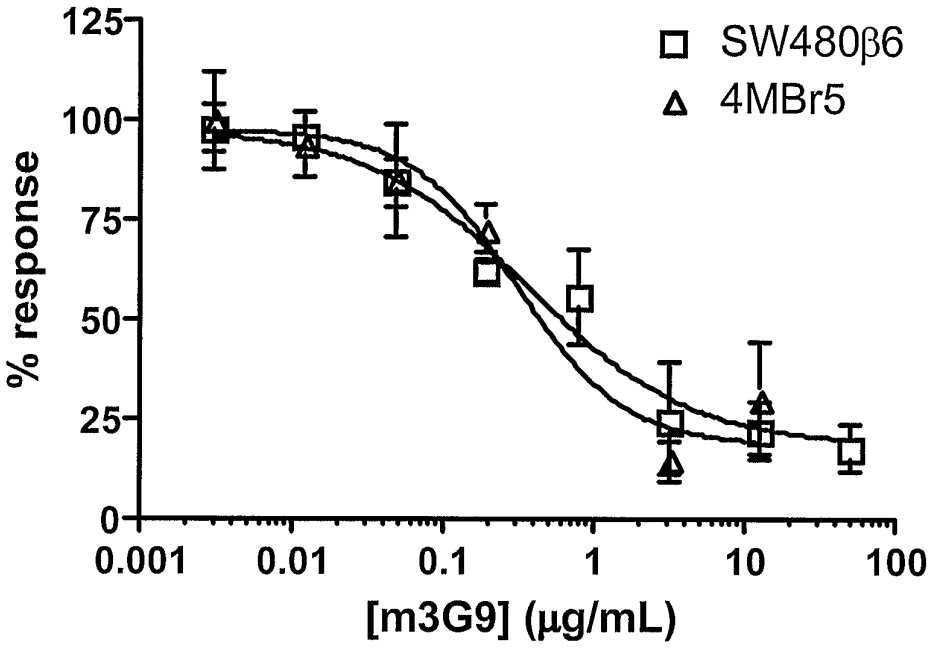

125
100
75
50
25
0
% response
0.001
0.01
0.1
1
10
100
[m3G9] (µg/mL)
SW480β6
4MBr5

Figure 29

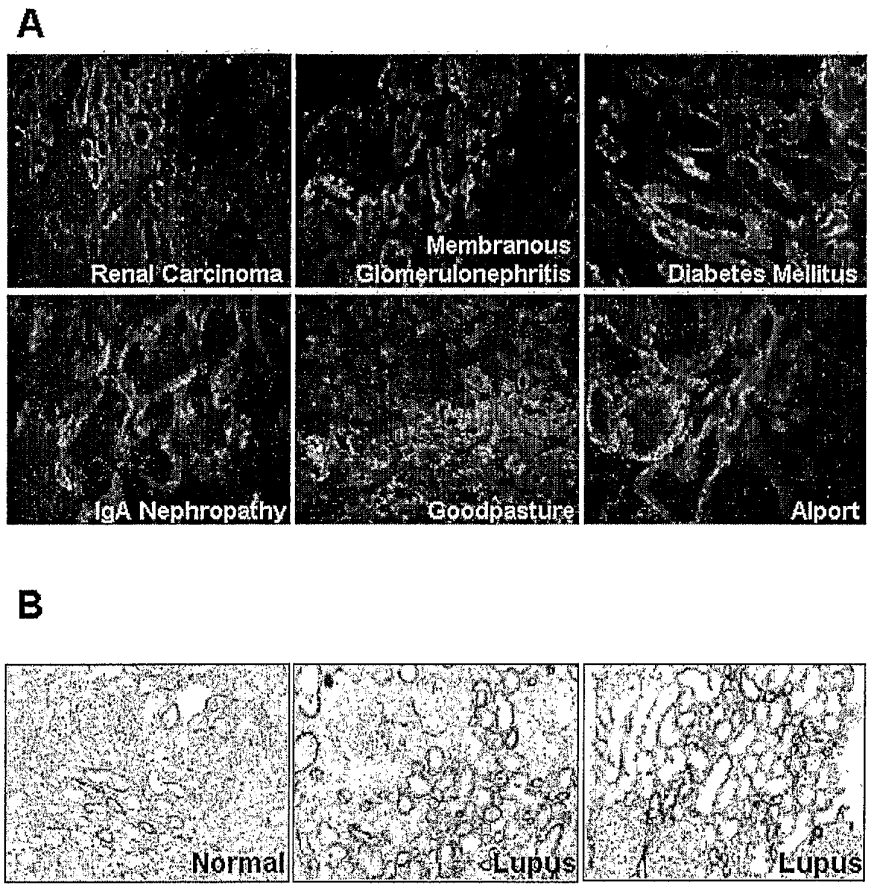

A
Renal Carcinoma
Membranous Glomerulonephritis
Diabetes Mellitus
IgA Nephropathy
Goodpasture
Alport
B
Normal
Lupus
Lupus

Figure 30A-30B

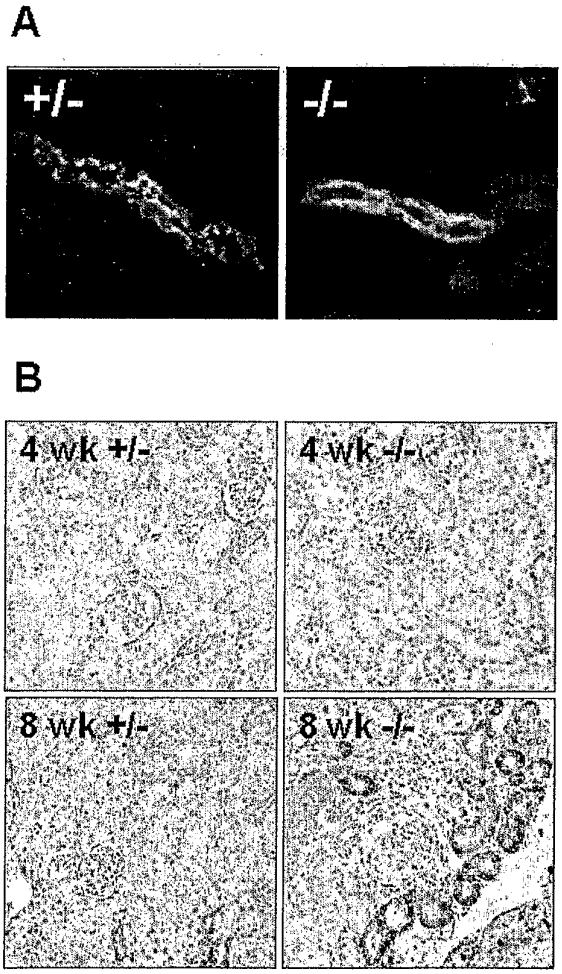


Figure 30C

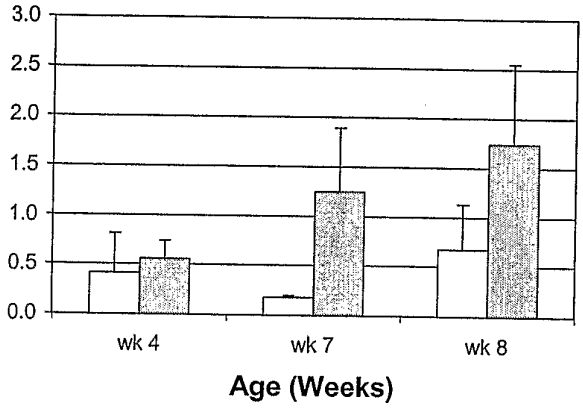


Figure 31A

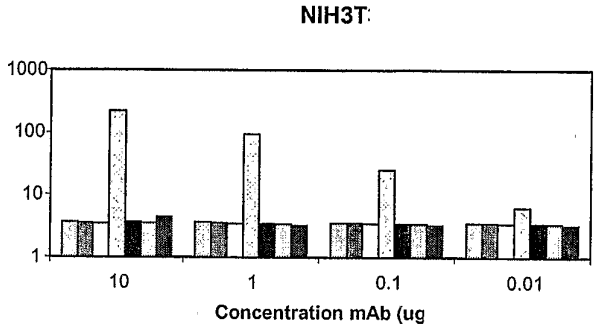


Figure 31B-31C

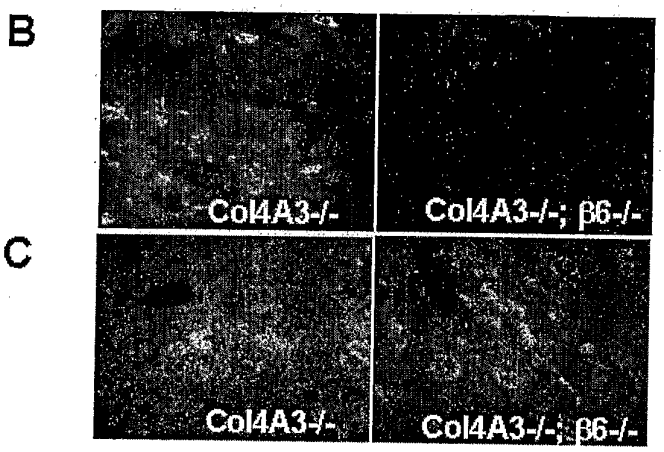


Figure 32A

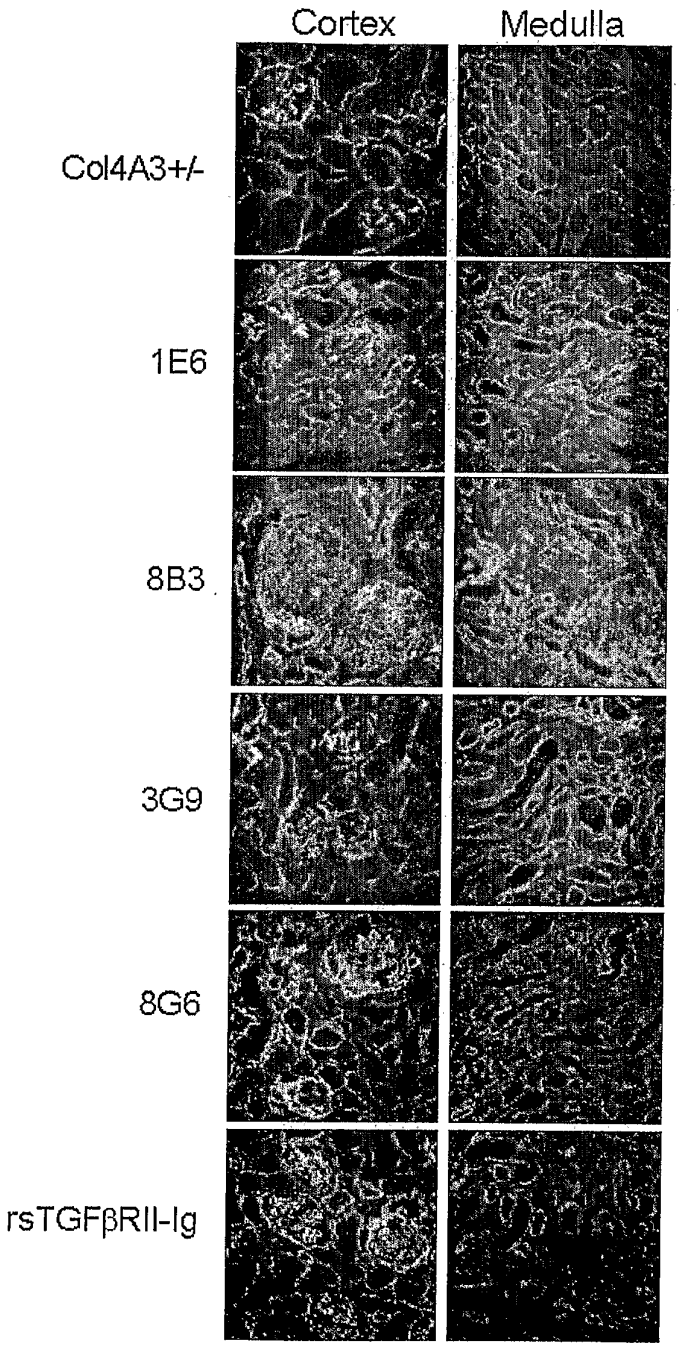


Figure 32B-32C

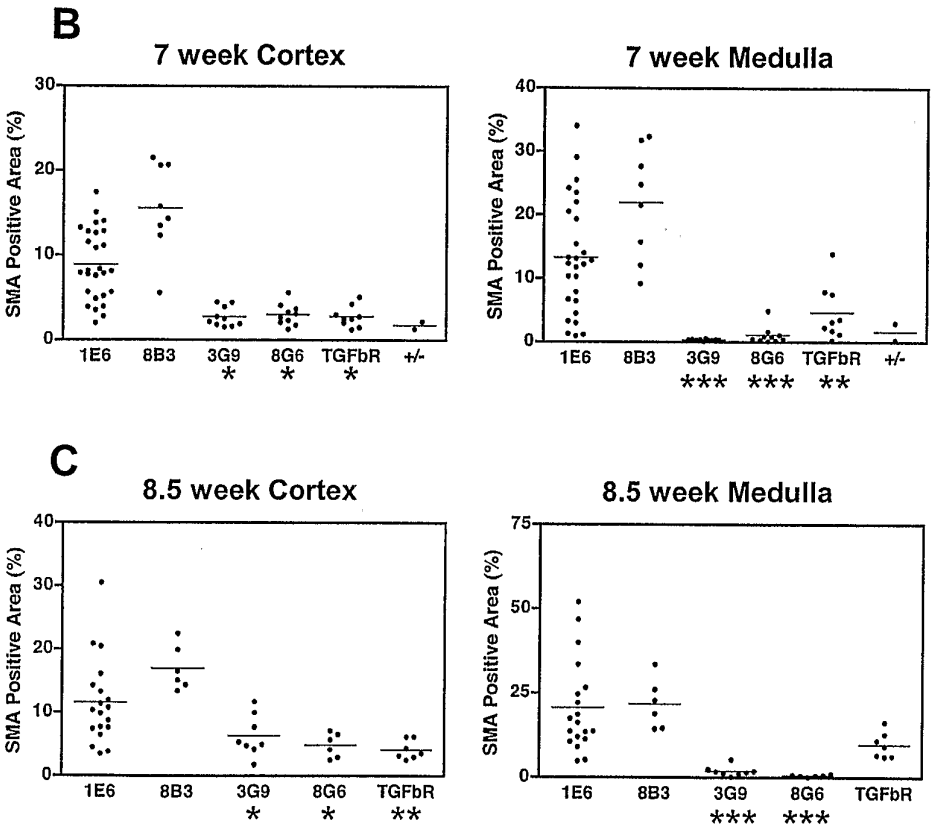


Figure 33

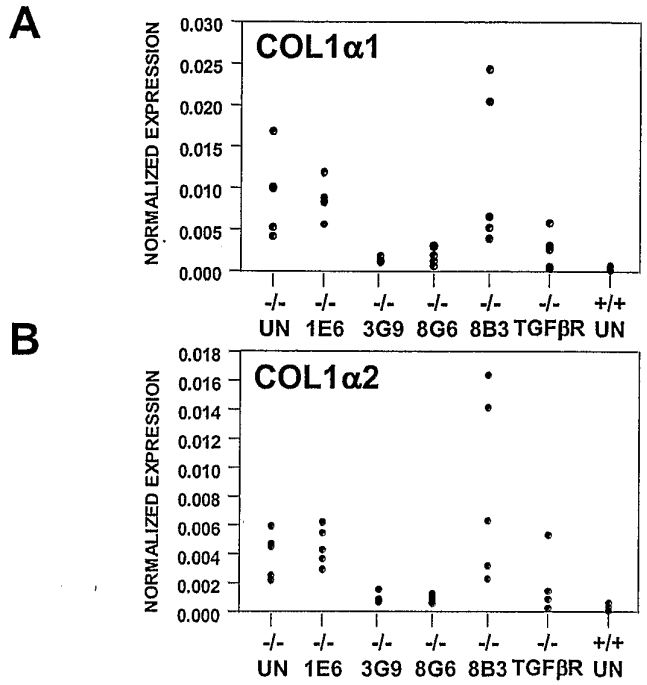

A
B
COL1α1
COL1α2
NORMALIZED EXPRESSION
0.030
0.025
0.020
0.015
0.010
0.005
0.000
0.018
0.016
0.014
0.012
0.010
0.008
0.006
0.004
0.002
0.000
-/- -/- -/- -/- -/- -/- +/+
UN 1E6 3G9 8G6 8B3 TGFβR UN

Figure 34

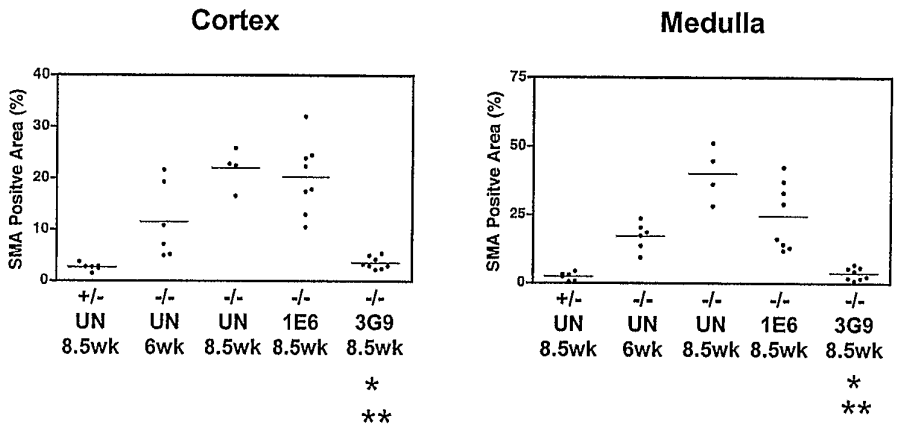

Cortex
Medulla
SMA Positve Area (%)
40
30
20
10
0
75
50
25
+/- UN 8.5wk
-/- UN 6wk
-/- UN 8.5wk
-/- 1E6 8.5wk
-/- 3G9 8.5wk
*
**

Figure 35

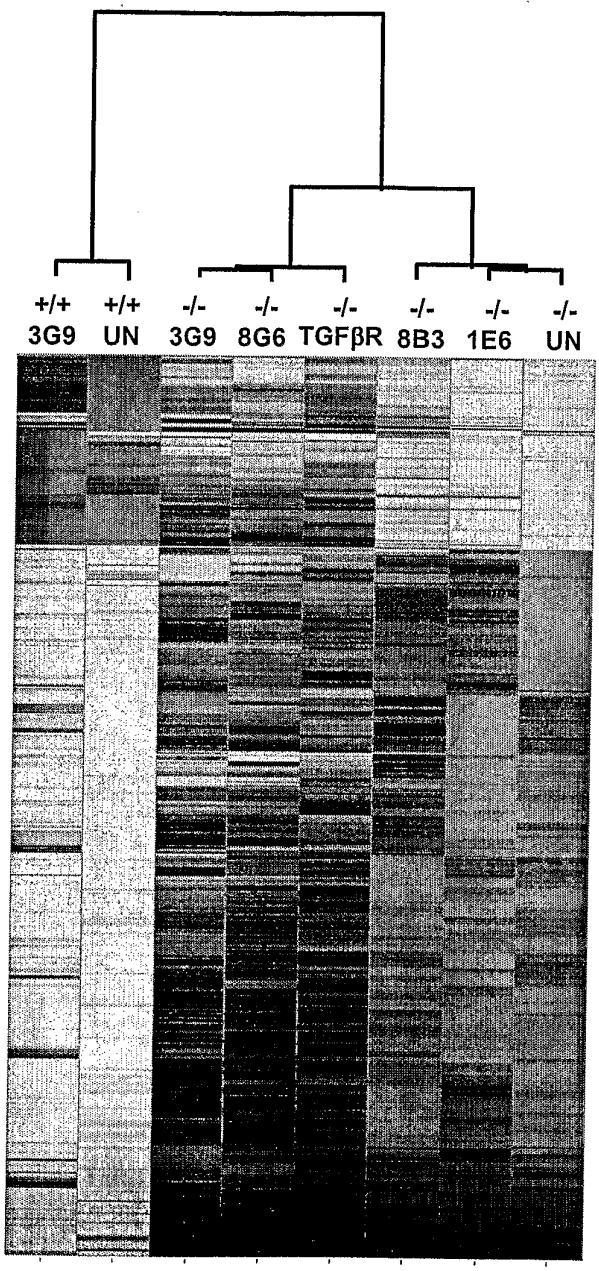


Figure 36

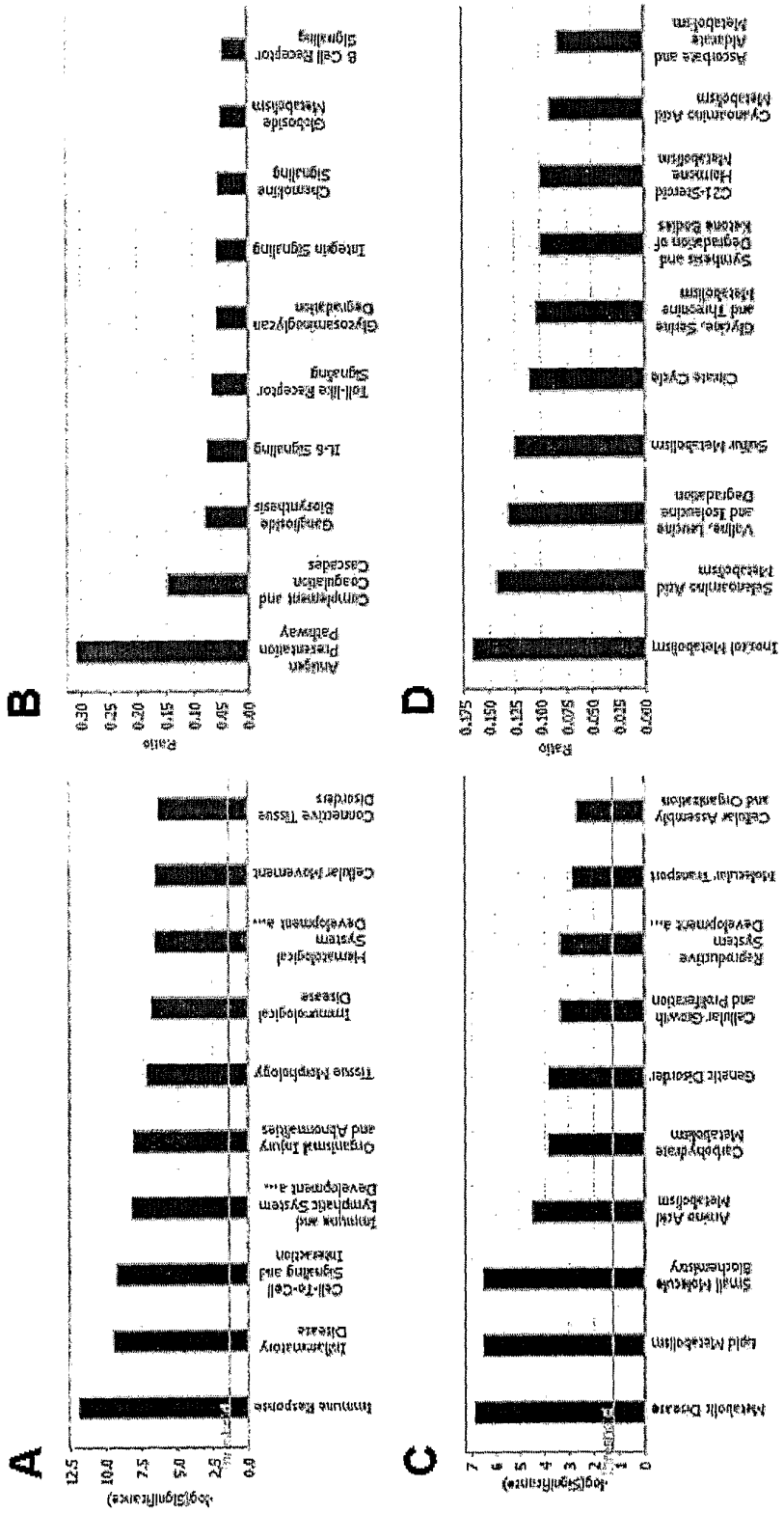

A
-log(SignificanceValue)
12.5
10.0
7.5
5.0
2.5
0.0
Immune Response
Inflammatory Disease
Cell-To-Cell Signaling and Interaction
Hematopoietic System Development a...
Organismal Injury and Abnormalities
Tissue Morphology
Immunological Disease
Hematological System Development a...
Cellular Movement
Connective Tissue Disorders
B
Ratio
0.30
0.25
0.20
0.15
0.10
0.05
0.00
Antigen Presentation Pathway
Complement and Coagulation Cascades
Ganglioside Biosynthesis
IL-6 Signaling
Toll-like Receptor Signaling
Glycosaminoglycan Degradation
Integrin Signaling
Chemokine Signaling
Glycoside Metabolism
B Cell Receptor Signaling
C
-log(SignificanceValue)
7
6
5
4
3
2
1
0
Metabolic Disease
Lipid Metabolism
Small Molecule Biochemistry
Amino Acid Metabolism
Carbohydrate Metabolism
Genetic Disorder
Cellular Growth and Proliferation
Reproductive System Development a...
Molecular Transport
Cellular Assembly and Organization
D
Ratio
0.175
0.150
0.125
0.100
0.075
0.050
0.025
0.000
Inositol Metabolism
Selenoamino Acid Metabolism
Valine, Leucine and Isoleucine Degradation
Sulfur Metabolism
Citrate Cycle
Glycine, Serine and Threonine Metabolism
Synthesis and Degradation of Ketone Bodies
C21-Steroid Hormone Metabolism
Cyanoamino Acid Metabolism
Ascorbate and Aldarate Metabolism

Figure 37

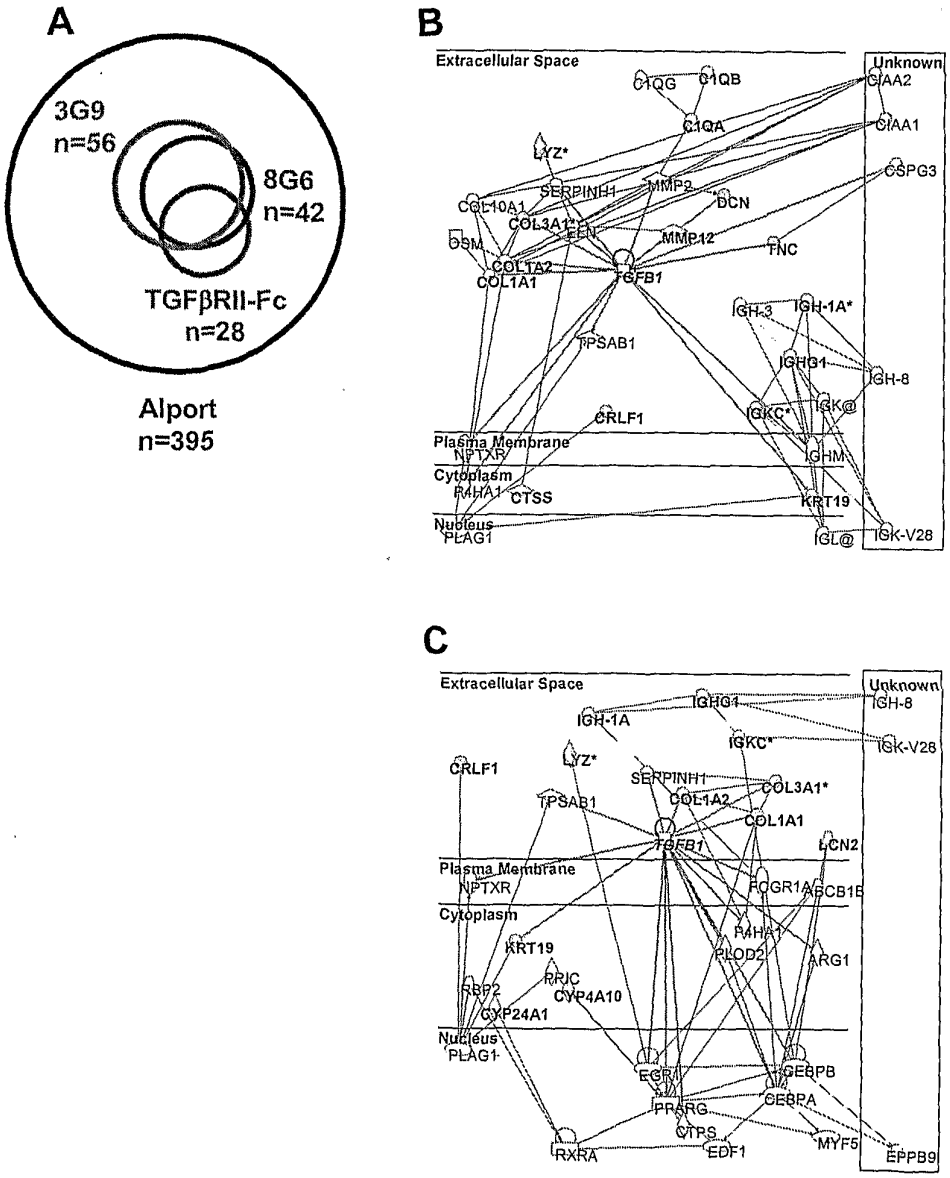

A
3G9
n=56
8G6
n=42
TGFβRII-Fc
n=28
Alport
n=395
B
Extracellular Space
Unknown
C1QG
C1QB
C1QA
CIAA2
CIAA1
LYZ*
CSPG3
SERPINH1
MMP2
DCN
COL10A1
COL3A1*
FBN1
MMP12
OSM
TNC
COL1A2
COL1A1
TGFB1
IGH-3
IGH-1A*
TPSAB1
IGHG1
IGH-8
IGKC*
IGK@
CRLF1
Plasma Membrane
NPTXR
IGHM
Cytoplasm
PAHA1
CTSS
KRT19
Nucleus
PLAG1
IGL@
IGK-V28
C
Extracellular Space
Unknown
IGH-8
IGHG1
IGH-1A
IGKC*
IGK-V28
CRLF1
LYZ*
SERPINH1
COL3A1*
TPSAB1
COL1A2
COL1A1
TGFB1
LCN2
Plasma Membrane
NPTXR
FCGR1A
ABCB1B
Cytoplasm
KRT19
PAHA1
PLOD2
ARG1
SBP2
RRIC
CYP4A10
CYP24A1
Nucleus
PLAG1
EGR1
CEBPB
CEBPA
PPARG
CTPS
RXRA
EDF1
MYF5
EPPB9

Figure 38

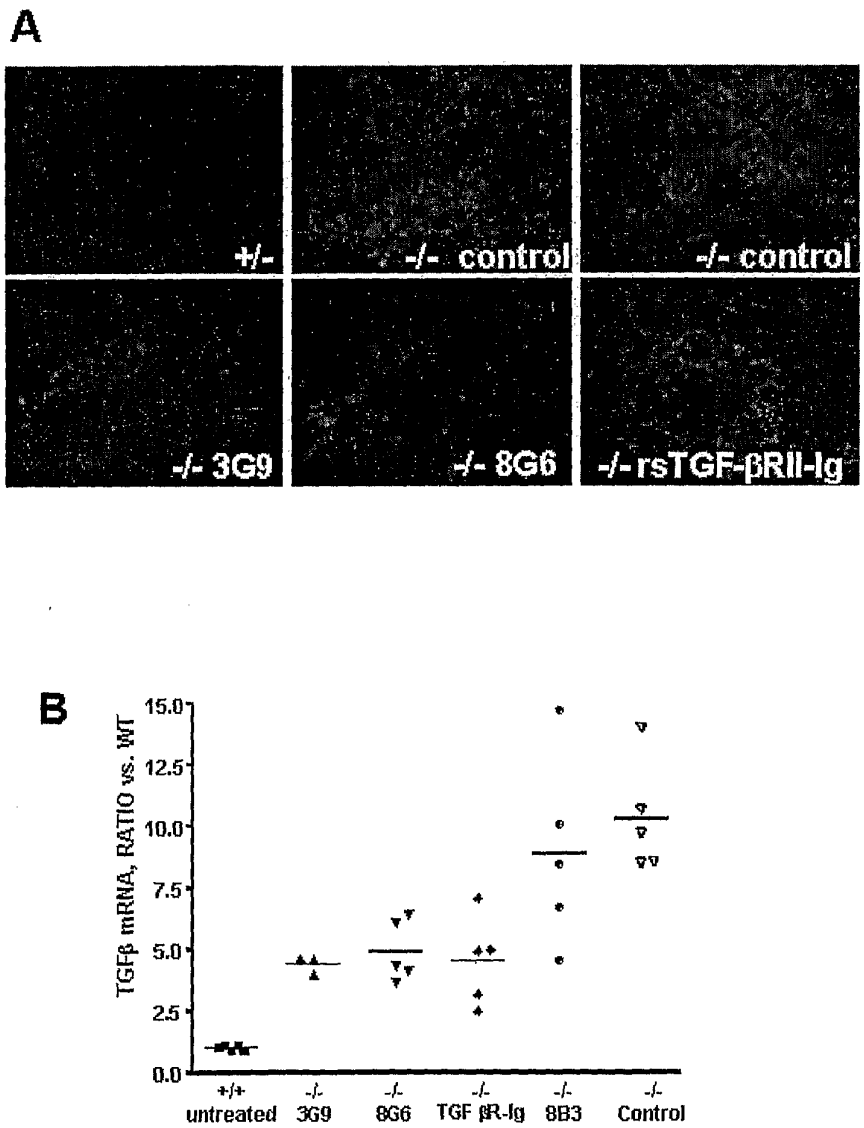

A
+/-
-/- control
-/- control
-/- 3G9
-/- 8G6
-/- rsTGF-βRII-Ig
B
TGFβ mRNA, RATIO vs. WT
15.0
12.5
10.0
7.5
5.0
2.5
0.0
+/+ untreated
-/- 3G9
-/- 8G6
-/- TGF βR-Ig
-/- 8B3
-/- Control

Figure 39

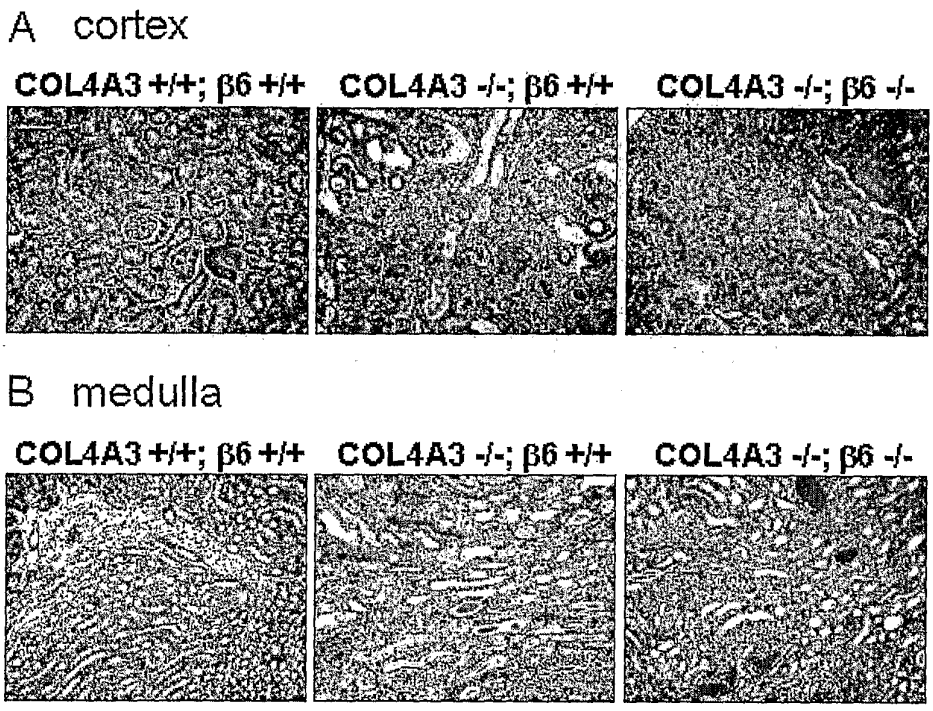

A cortex
COL4A3 +/+; β6 +/+
COL4A3 -/-; β6 +/+
COL4A3 -/-; β6 -/-
B medulla
COL4A3 +/+; β6 +/+
COL4A3 -/-; β6 +/+
COL4A3 -/-; β6 -/-

Figure 40A

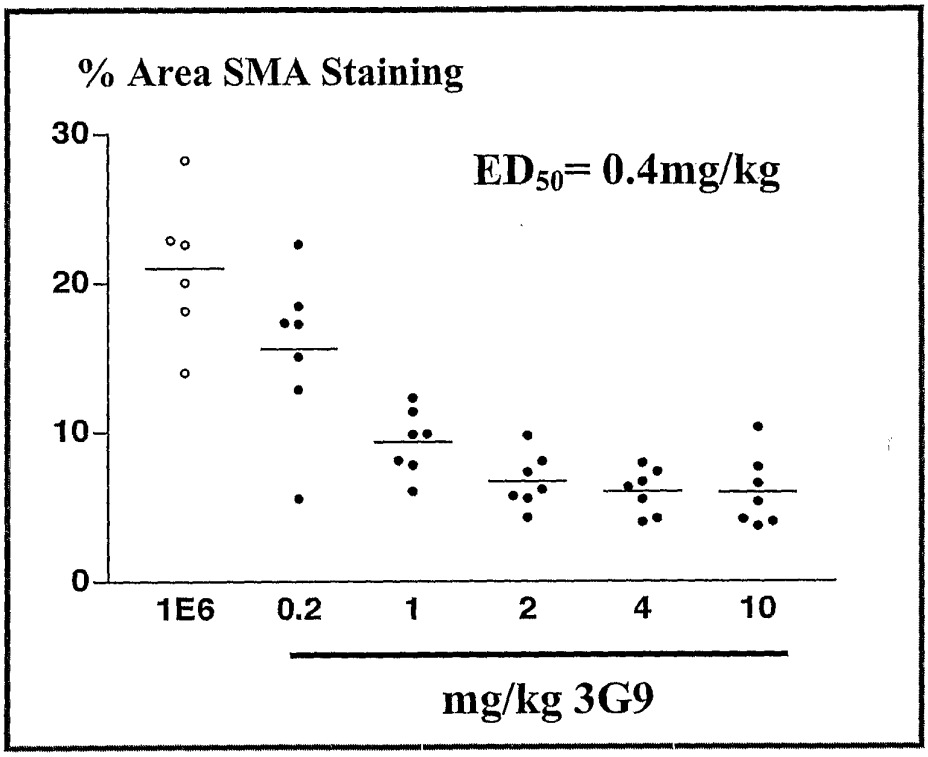

Cortex
% Area SMA Staining
30
20
10
0
ED50= 0.4mg/kg
1E6
0.2
1
2
4
10
mg/kg 3G9

Figure 40B

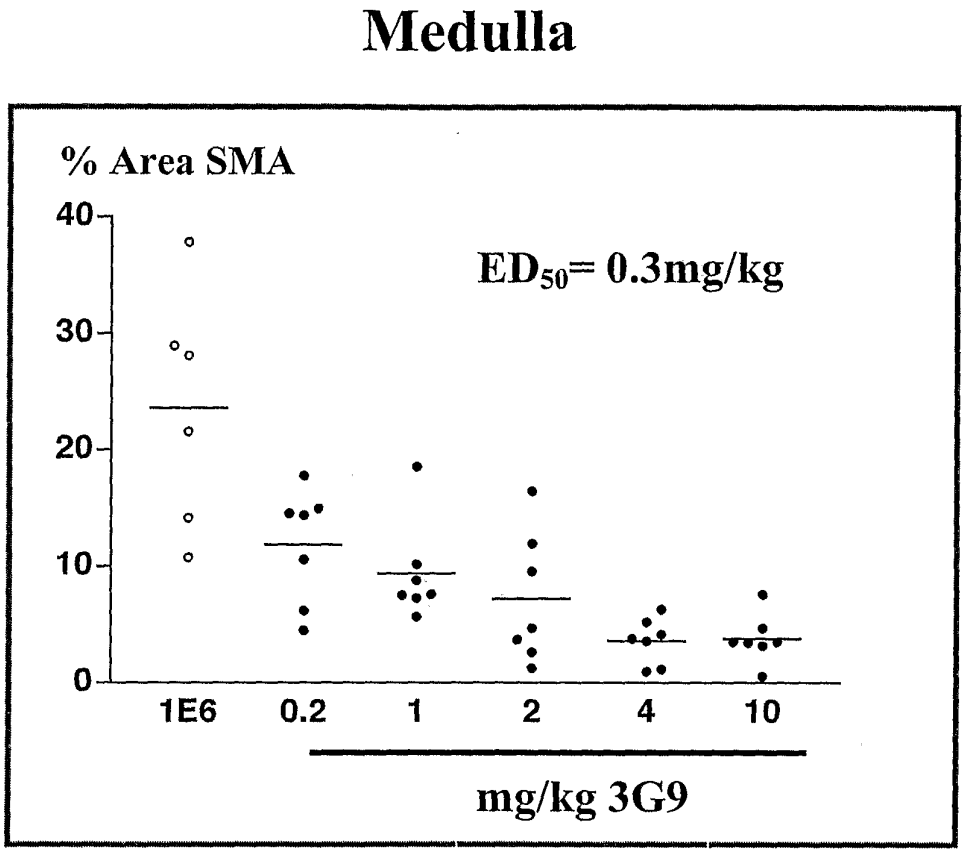

Medulla
% Area SMA
40
30
20
10
0
ED50= 0.3mg/kg
1E6
0.2
1
2
4
10
mg/kg 3G9

Figure 41

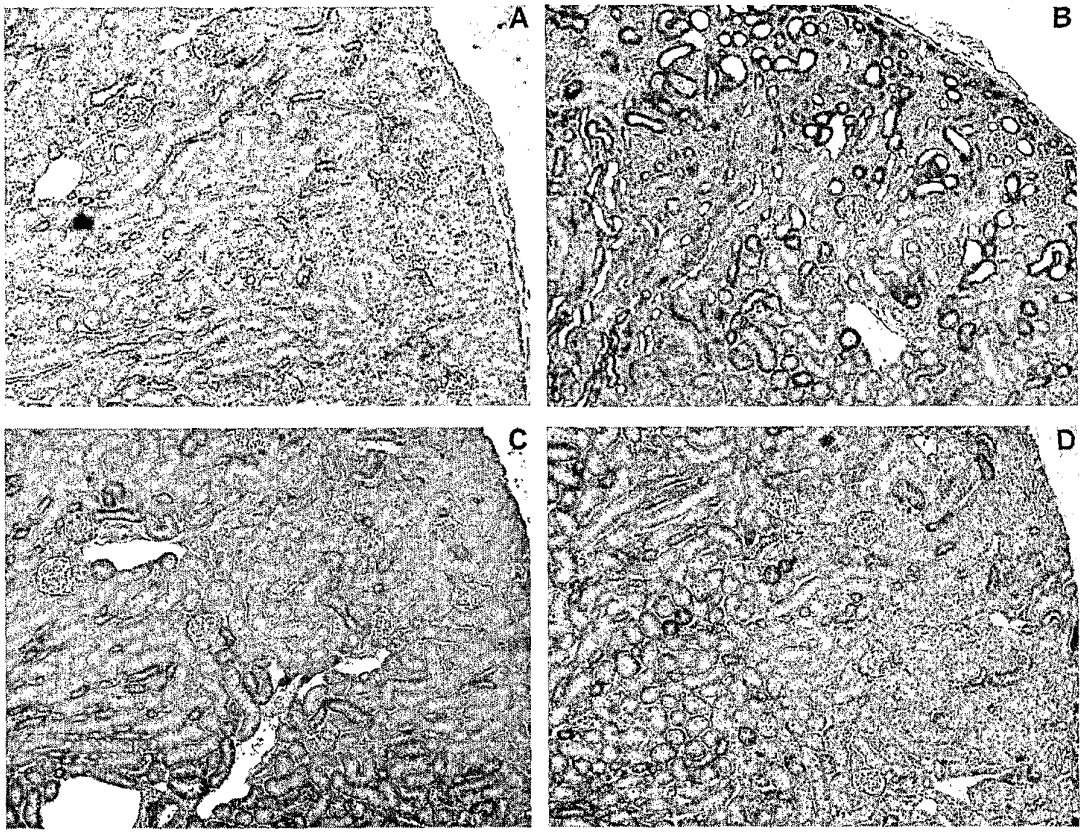


Figure 42

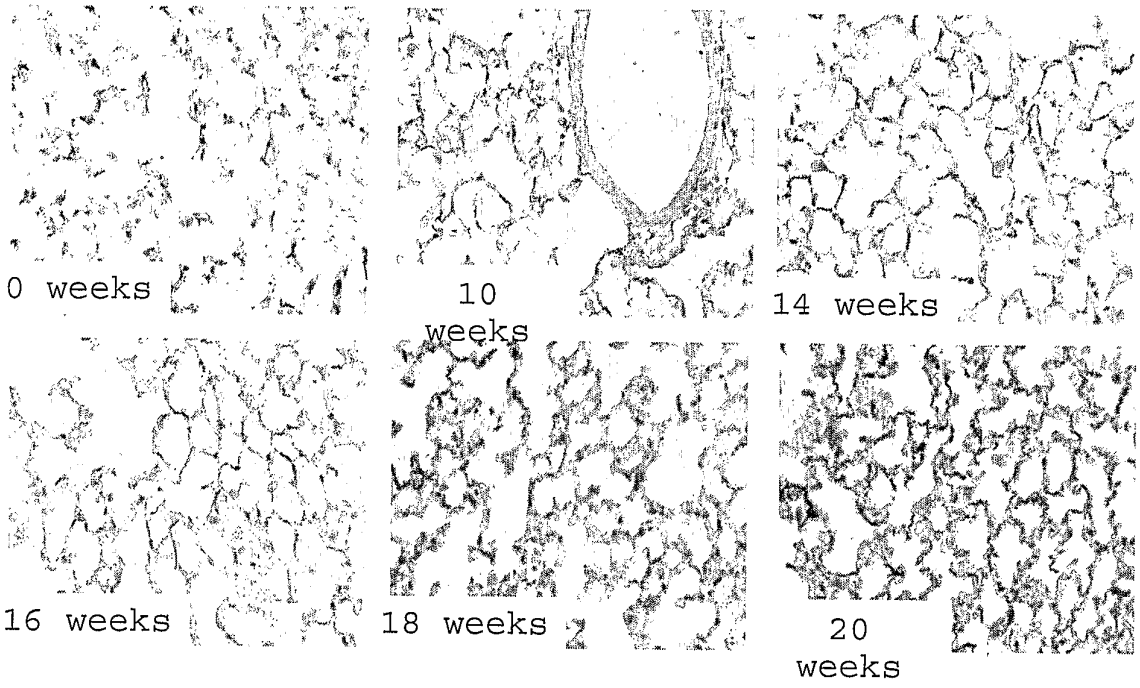
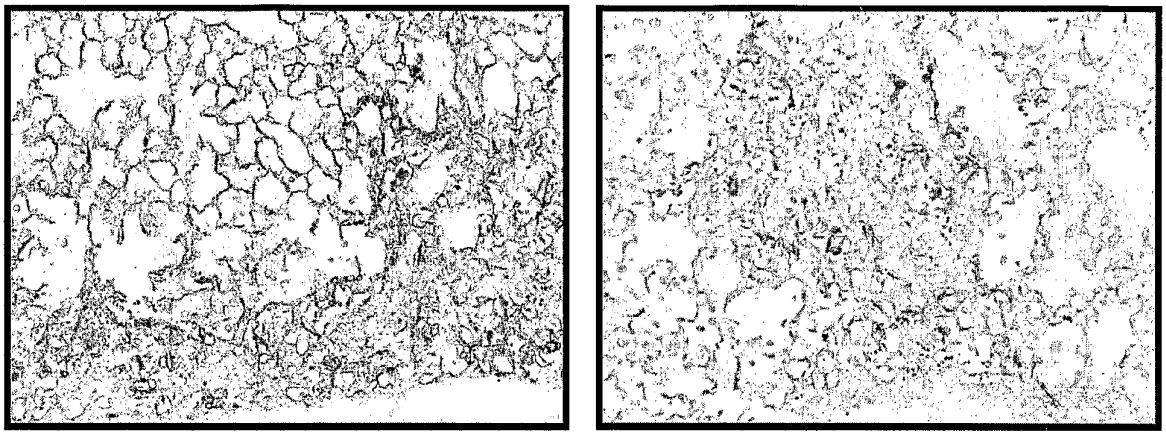


Figure 43



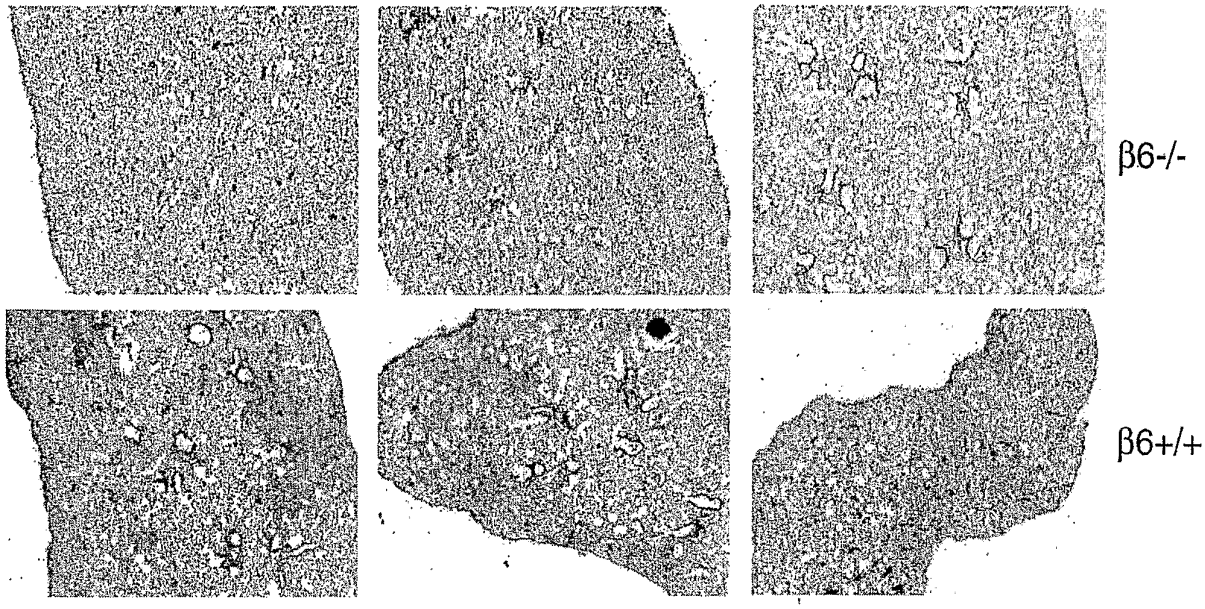


FIGURE 44

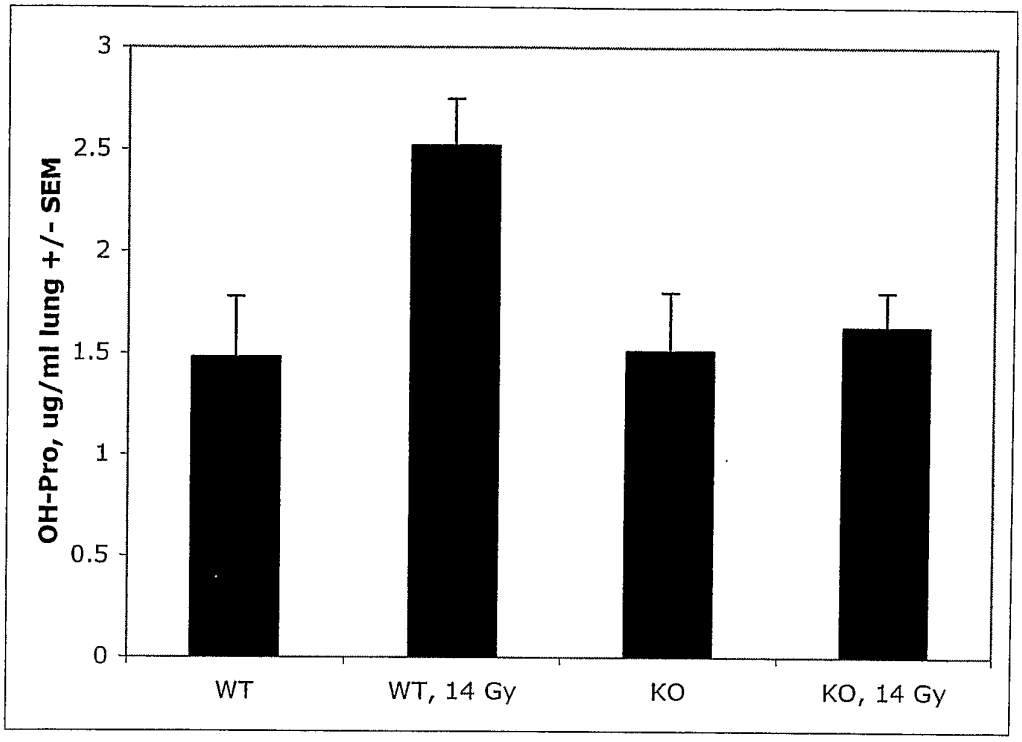


FIGURE 45

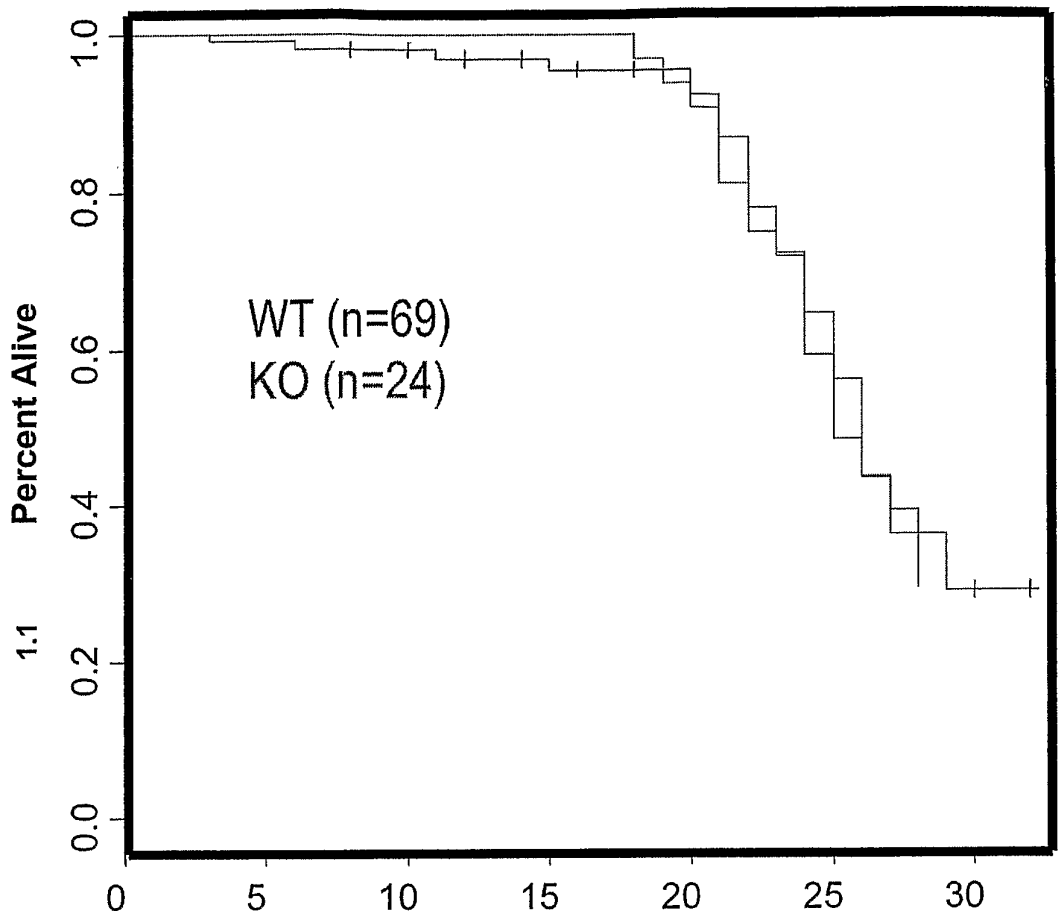


FIGURE 46

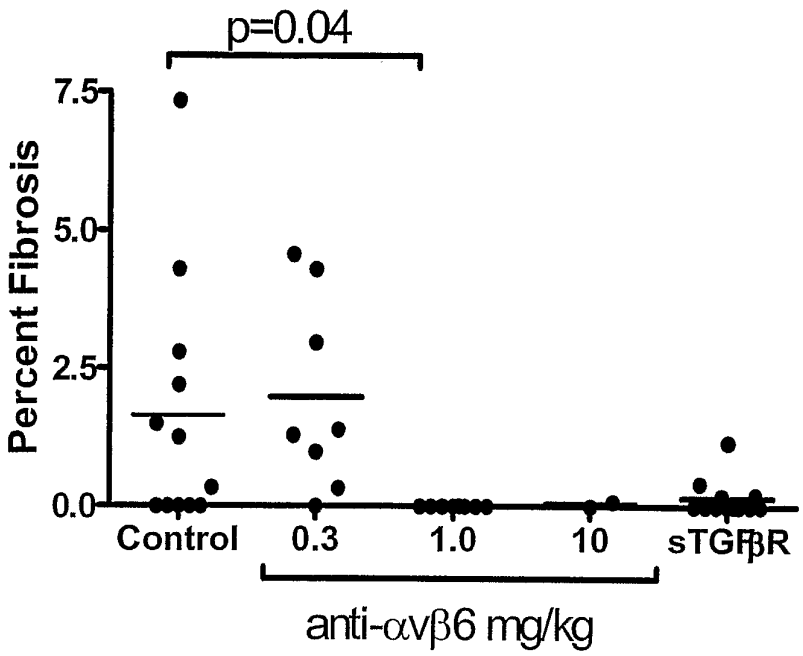

p=0.04
7.5
5.0
2.5
0.0
Percent Fibrosis
Control
0.3
1.0
10
sTGFβR
anti-αvβ6 mg/kg

FIGURE 47

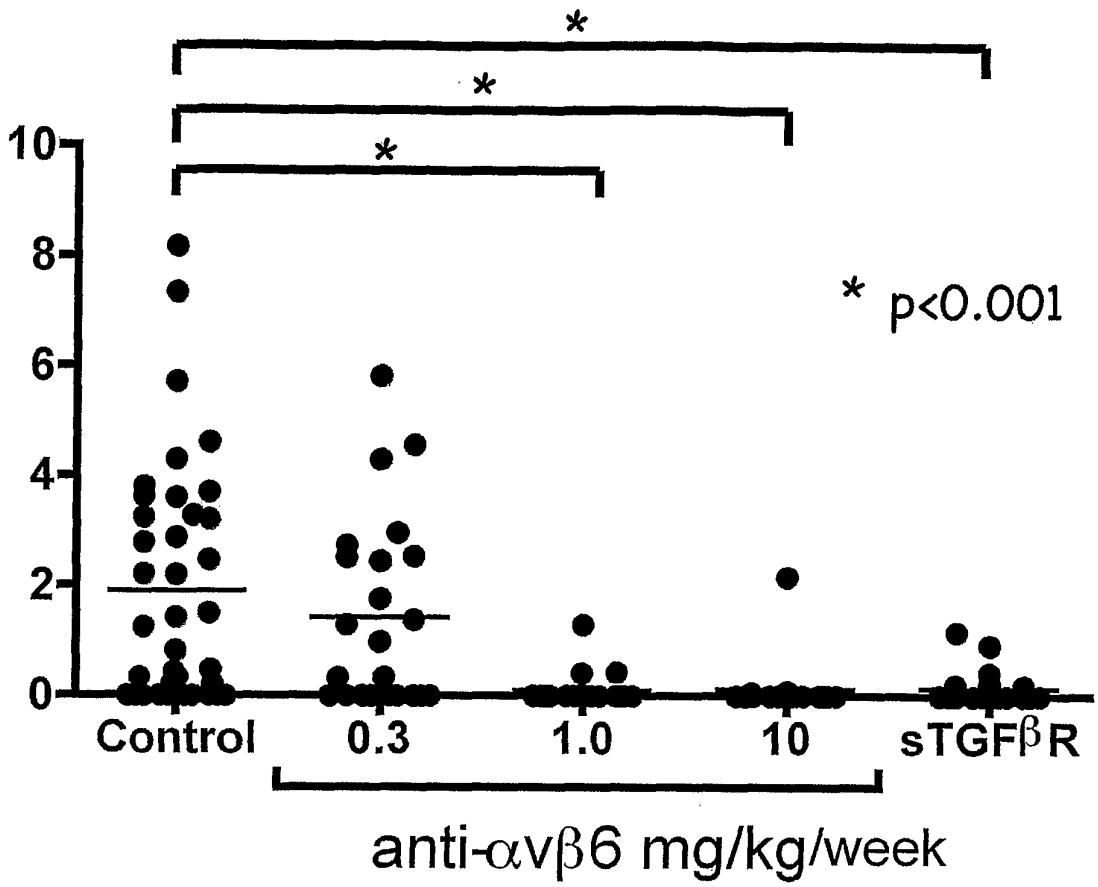


FIGURE 48

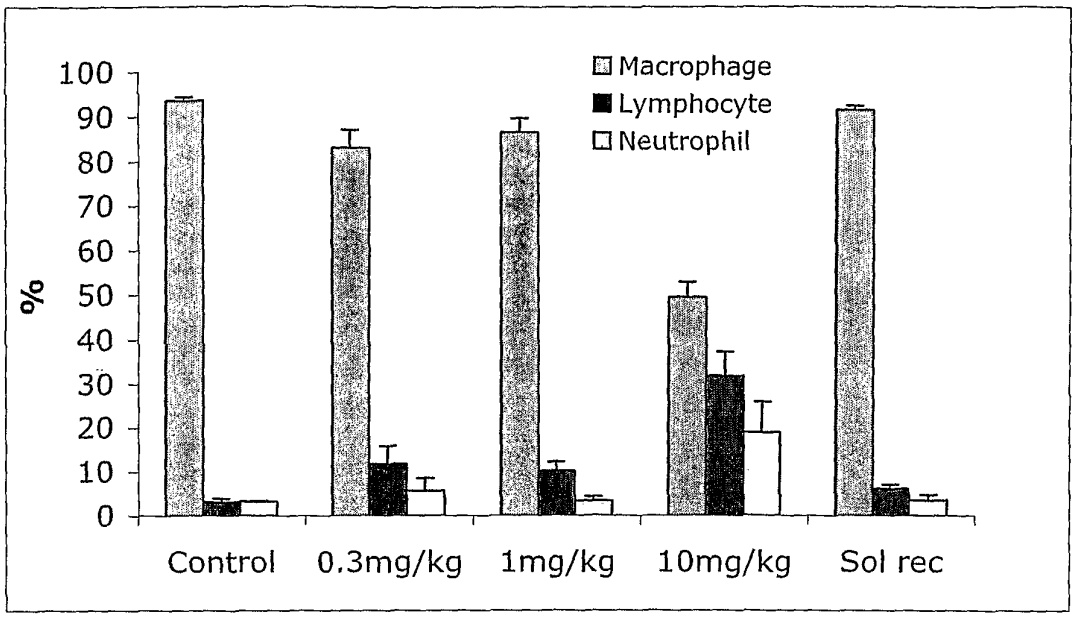

Macrophage
Lymphocyte
Neutrophil
%
100
90
80
70
60
50
40
30
20
10
0
Control
0.3mg/kg
1mg/kg
10mg/kg
Sol rec

FIGURE 49

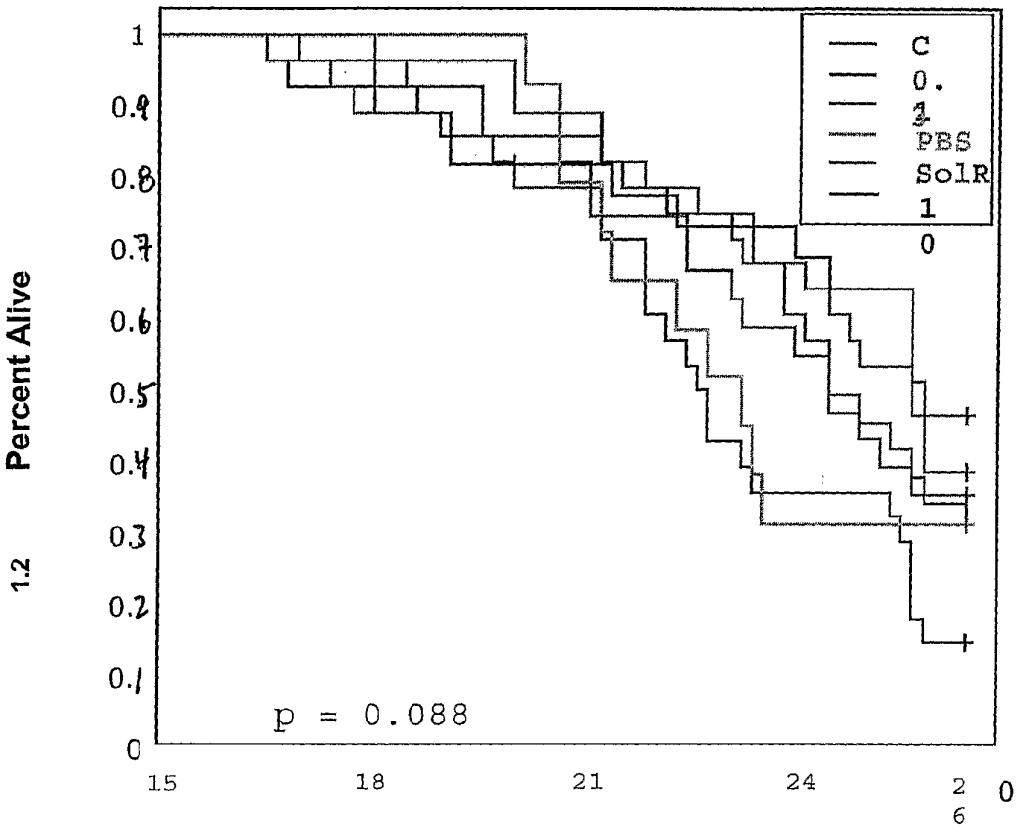

Percent Alive
1.2
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
15
18
21
24
26
0
C
0.
1
PBS
SolR
1
0
p = 0.088

FIGURE 5D

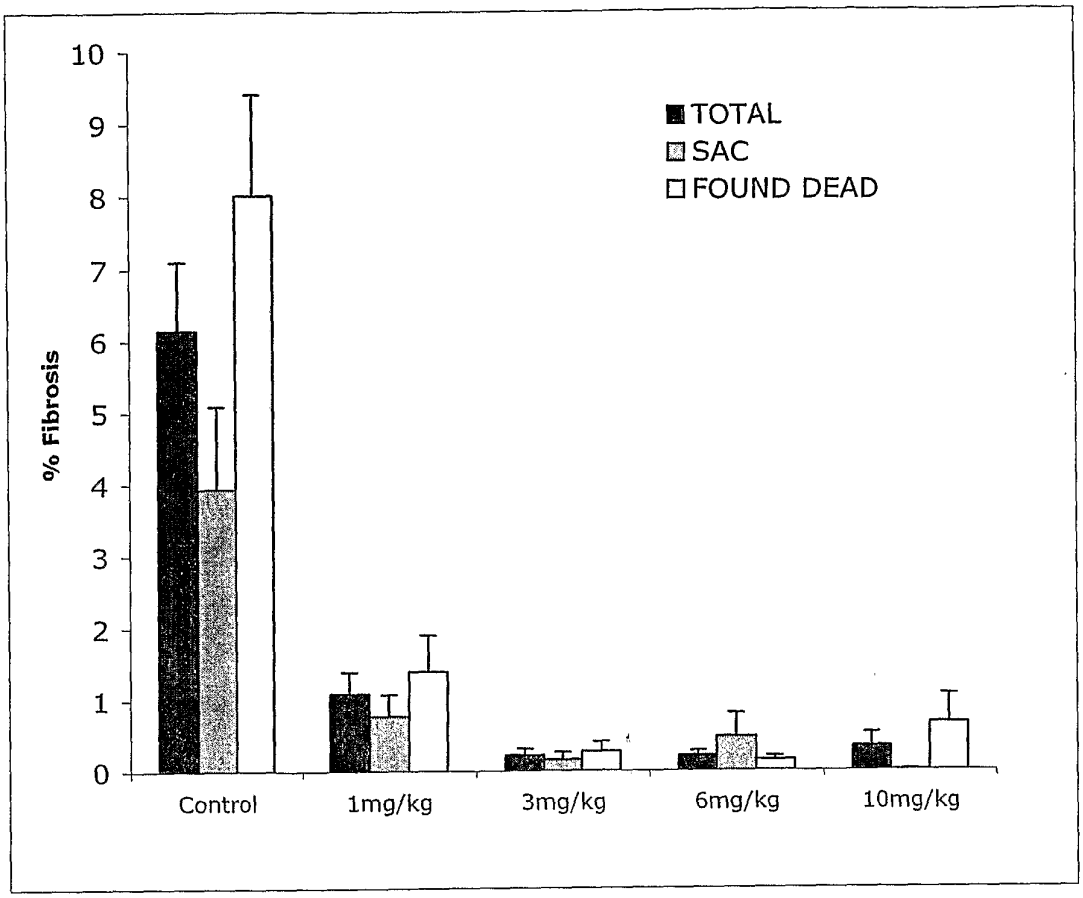

10
9
8
7
6
5
4
3
2
1
0
% Fibrosis
TOTAL
SAC
FOUND DEAD
Control
1mg/kg
3mg/kg
6mg/kg
10mg/kg

FIGURE 51

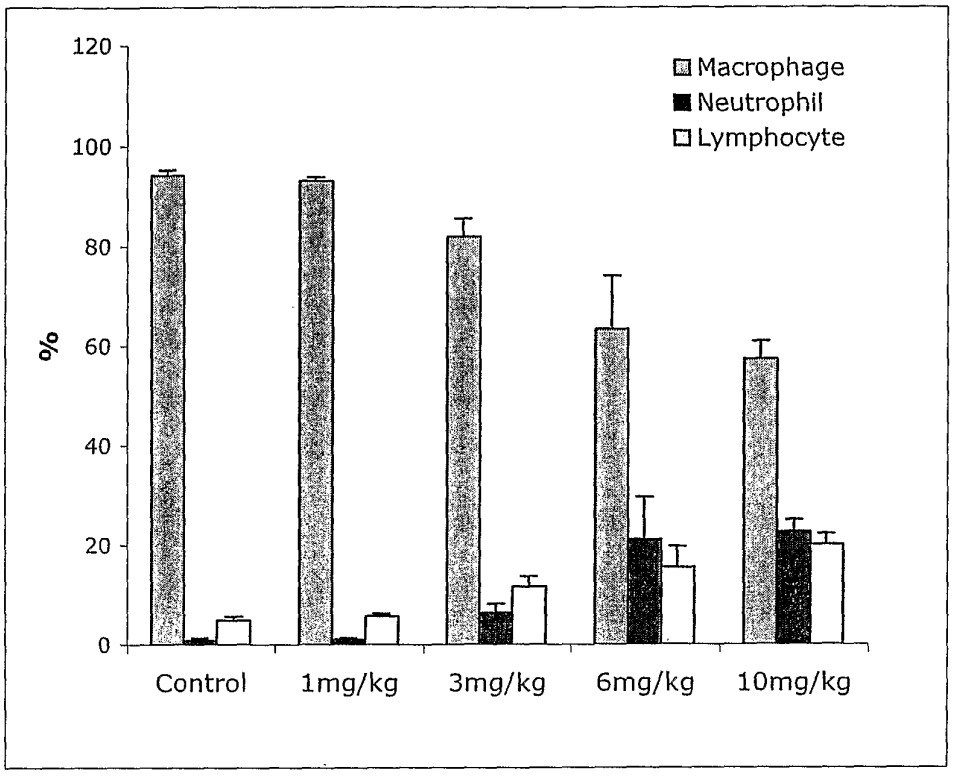

120
100
80
60
40
20
0
%
Macrophage
Neutrophil
Lymphocyte
Control
1mg/kg
3mg/kg
6mg/kg
10mg/kg

FIGURE 52

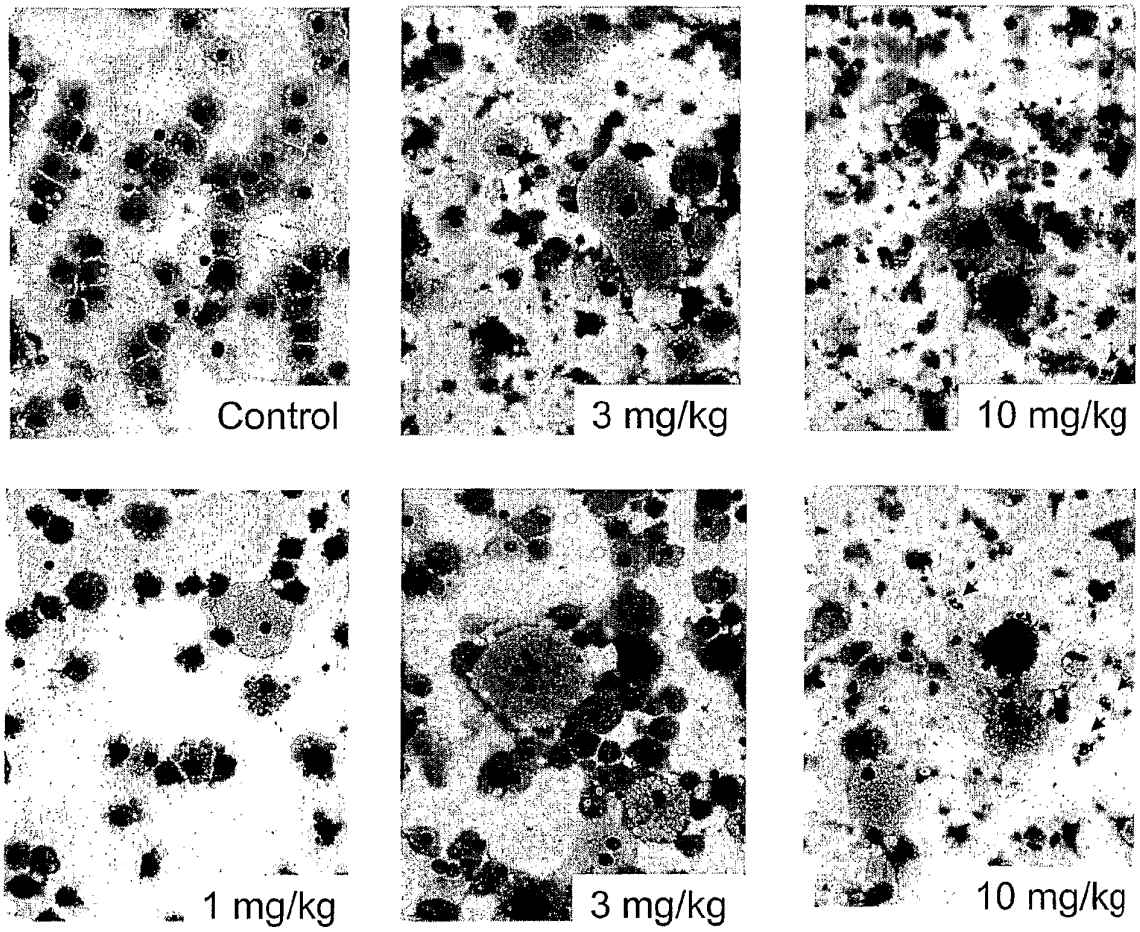


FIGURE 53

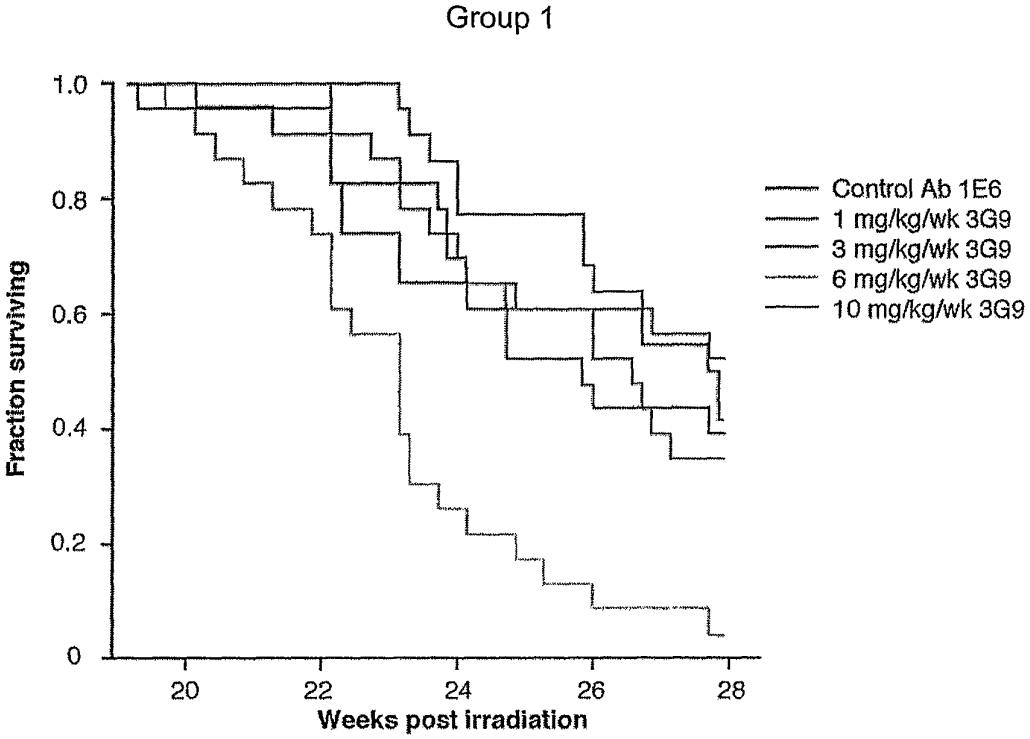

Group 1
1.0
0.8
0.6
0.4
0.2
0
Fraction surviving
20
22
24
26
28
Weeks post irradiation
Control Ab 1E6
1 mg/kg/wk 3G9
3 mg/kg/wk 3G9
6 mg/kg/wk 3G9
10 mg/kg/wk 3G9

FIGURE 54

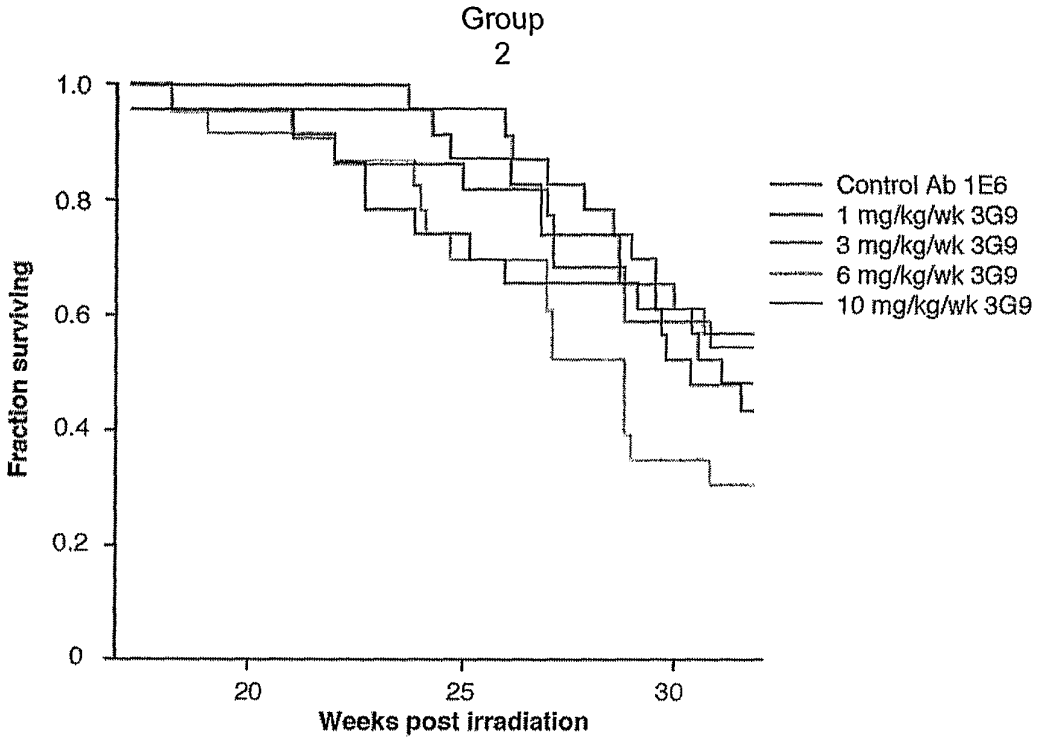

Group
2
1.0
0.8
0.6
0.4
0.2
0
Fraction surviving
20
25
30
Weeks post irradiation
Control Ab 1E6
1 mg/kg/wk 3G9
3 mg/kg/wk 3G9
6 mg/kg/wk 3G9
10 mg/kg/wk 3G9

FIGURE 17

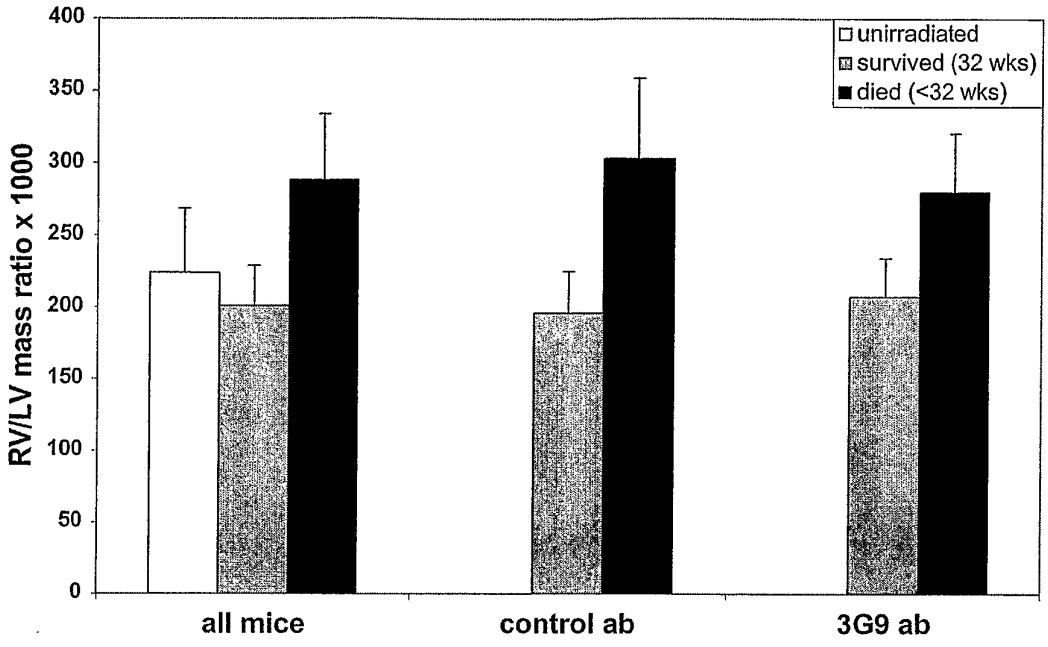

400
350
300
250
200
150
100
50
0
RV/LV mass ratio x 1000
unirradiated
survived (32 wks)
died (<32 wks)
all mice
control ab
3G9 ab

FIGURE 5b

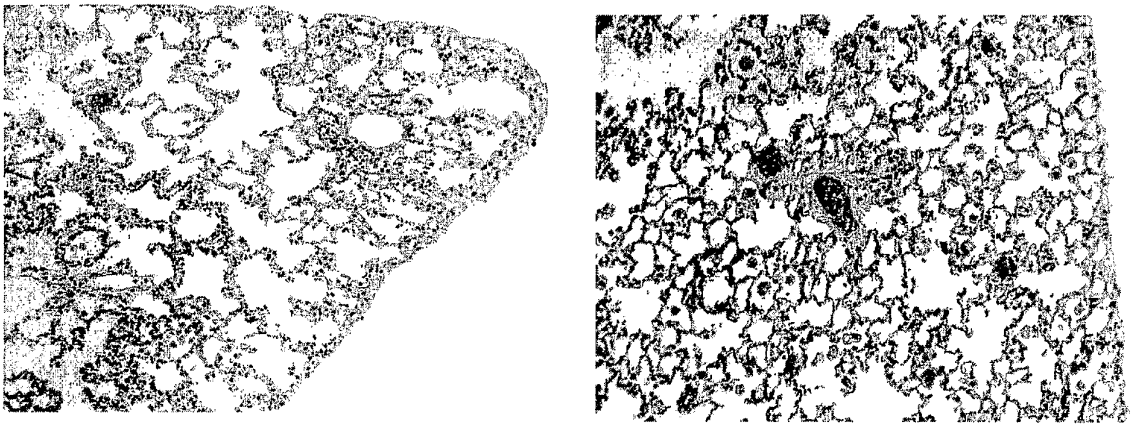


FIGURE 57

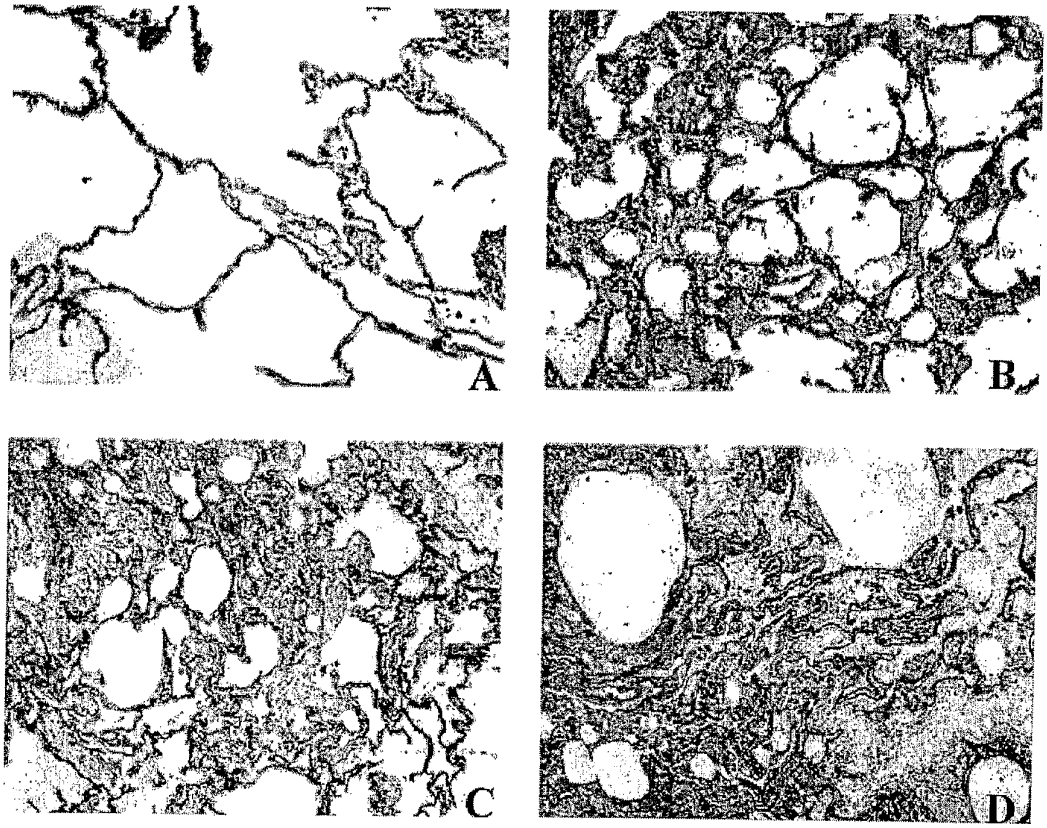


FIGURE 5B

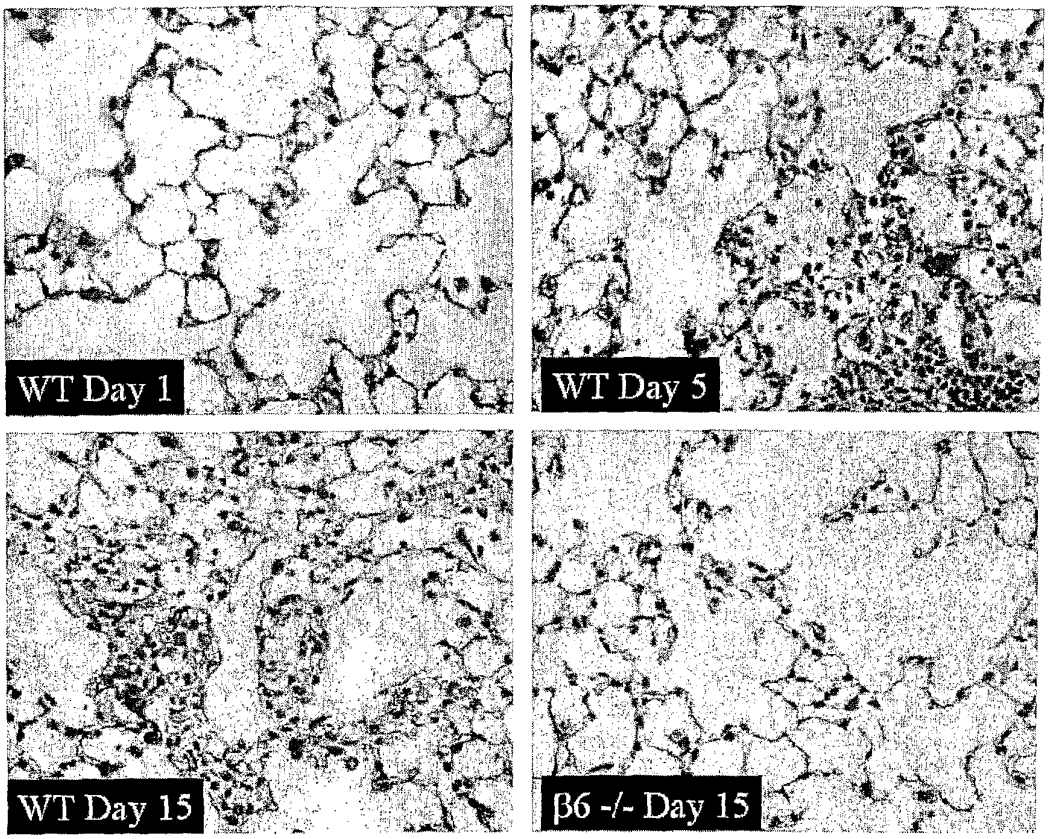


FIGURE 59

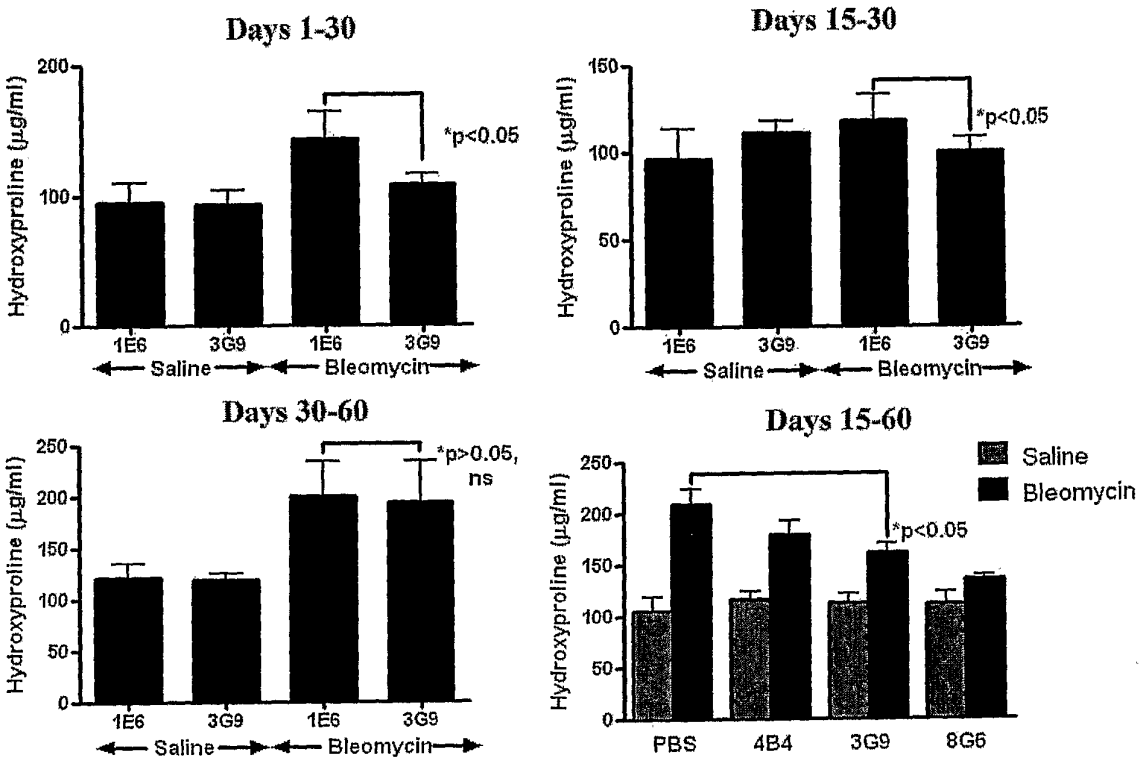

Days 1-30
Hydroxyproline (µg/ml)
200
100
0
*p<0.05
1E6
3G9
1E6
3G9
Saline
Bleomycin
Days 15-30
Hydroxyproline (µg/ml)
150
100
50
0
*p<0.05
1E6
3G9
1E6
3G9
Saline
Bleomycin
Days 30-60
Hydroxyproline (µg/ml)
250
200
150
100
50
0
*p>0.05, ns
1E6
3G9
1E6
3G9
Saline
Bleomycin
Days 15-60
Hydroxyproline (µg/ml)
250
200
150
100
50
0
*p<0.05
Saline
Bleomycin
PBS
4B4
3G9
8G6

FIGURE 60

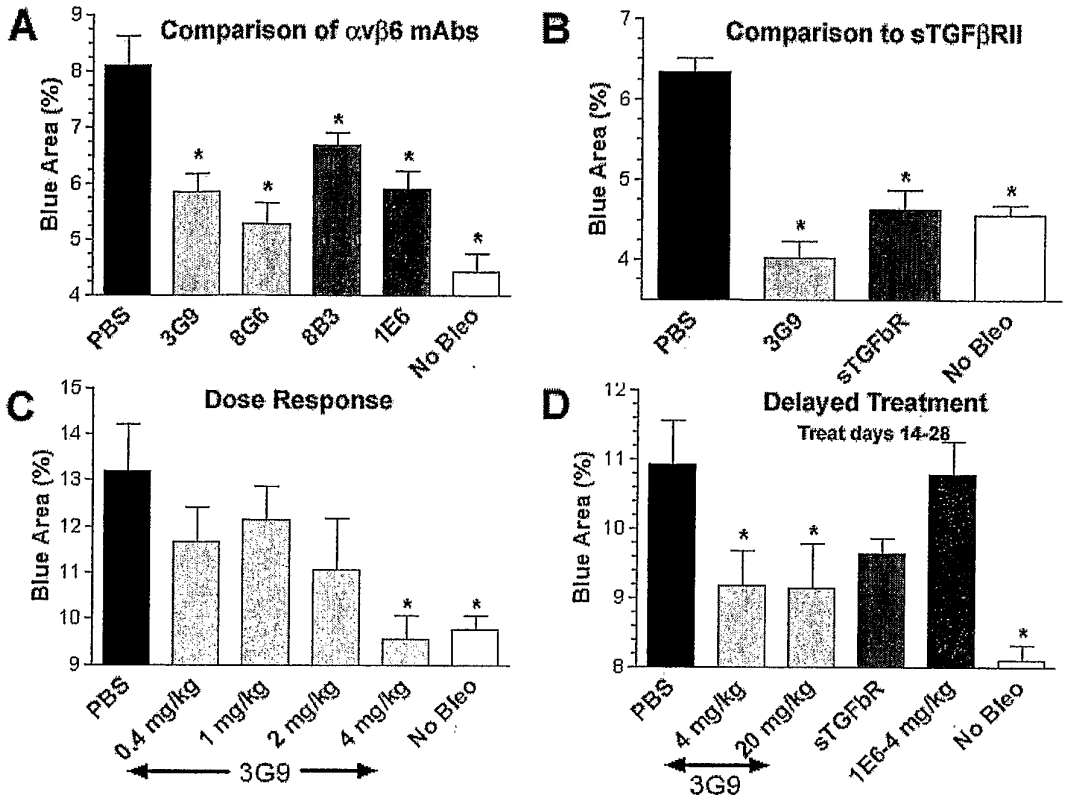

A
Comparison of αvβ6 mAbs
Blue Area (%)
PBS
3G9
8G6
8B3
1E6
No Bleo
B
Comparison to sTGFβRII
Blue Area (%)
PBS
3G9
sTGFbR
No Bleo
C
Dose Response
Blue Area (%)
PBS
0.4 mg/kg
1 mg/kg
2 mg/kg
4 mg/kg
No Bleo
3G9
D
Delayed Treatment
Treat days 14-28
Blue Area (%)
PBS
4 mg/kg
20 mg/kg
sTGFbR
1E6-4 mg/kg
No Bleo
3G9

FIGURE 61

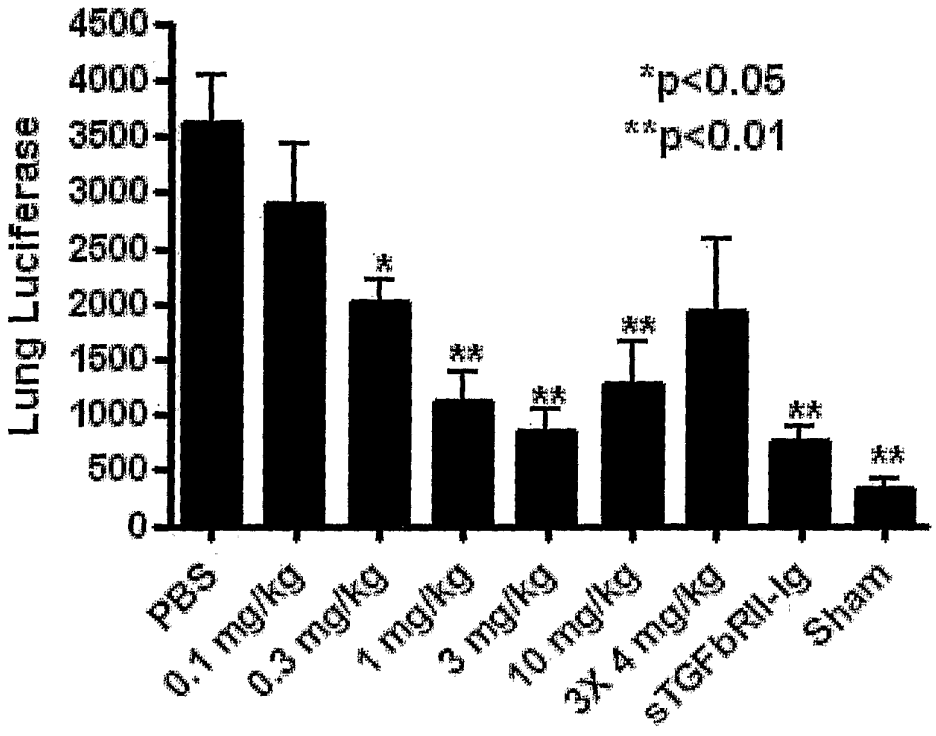

Lung Luciferase
4500
4000
3500
3000
2500
2000
1500
1000
500
0
*p<0.05
**p<0.01
*
**
**
**
**
**
PBS
0.1 mg/kg
0.3 mg/kg
1 mg/kg
3 mg/kg
10 mg/kg
3X 4 mg/kg
sTGFbRII-Ig
Sham

FIGURE 62

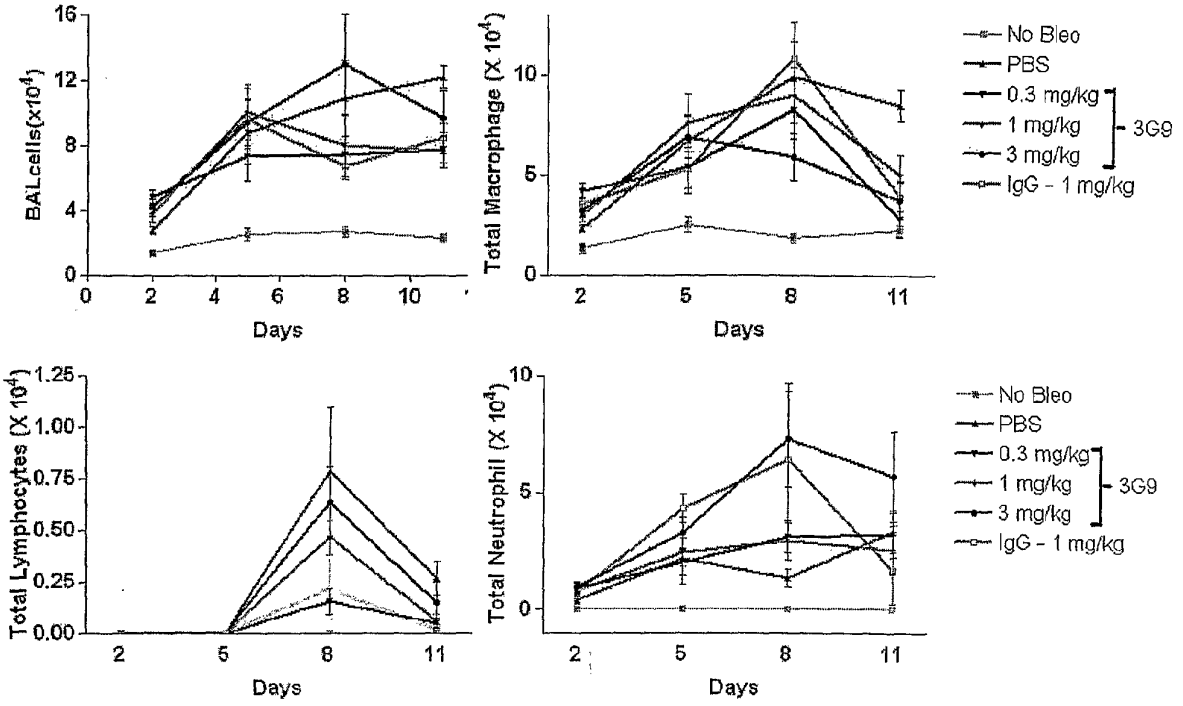

BALcells(x10⁴)
Days
Total Macrophage (X 10⁴)
Days
No Bleo
PBS
0.3 mg/kg
1 mg/kg
3 mg/kg
3G9
IgG - 1 mg/kg
Total Lymphocytes (X 10⁴)
Days
Total Neutrophil (X 10⁴)
Days
No Bleo
PBS
0.3 mg/kg
1 mg/kg
3 mg/kg
3G9
IgG - 1 mg/kg

FIGURE 63

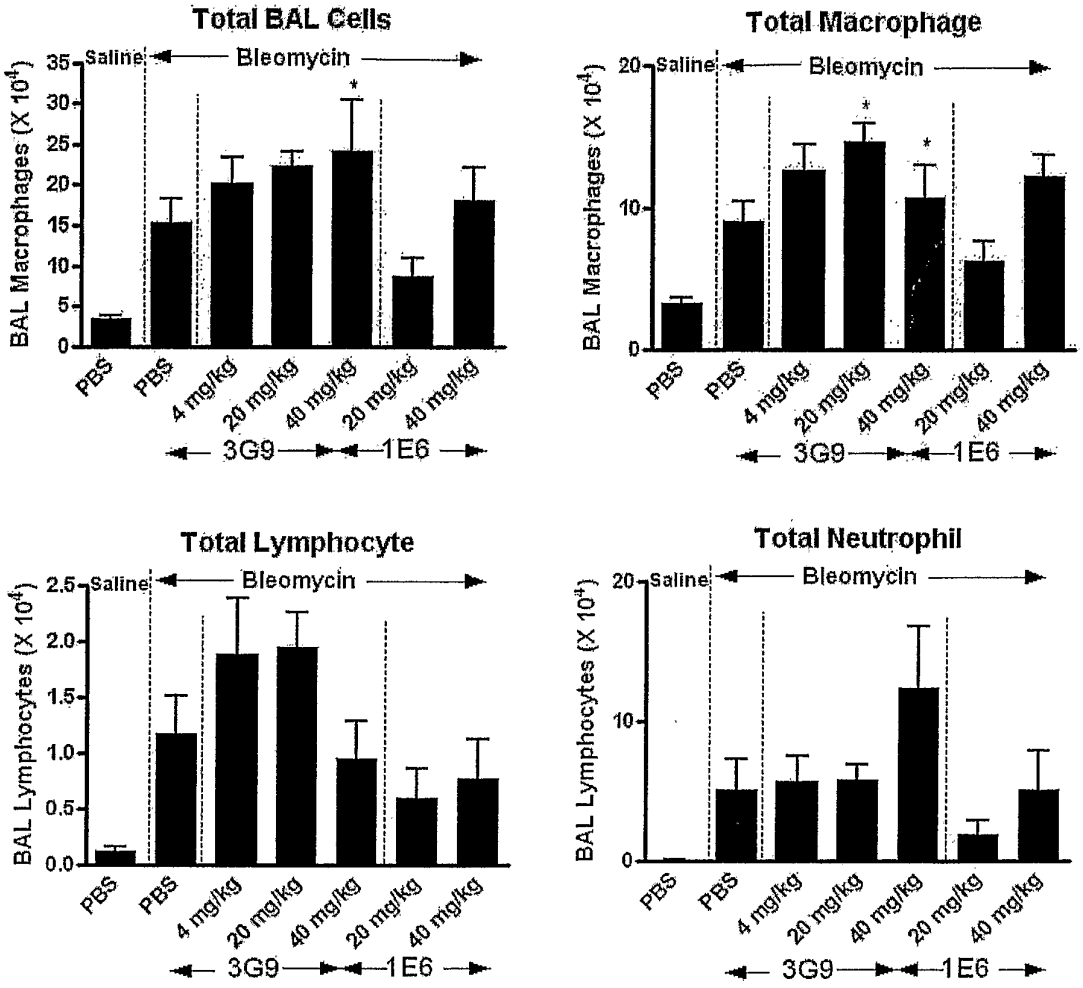
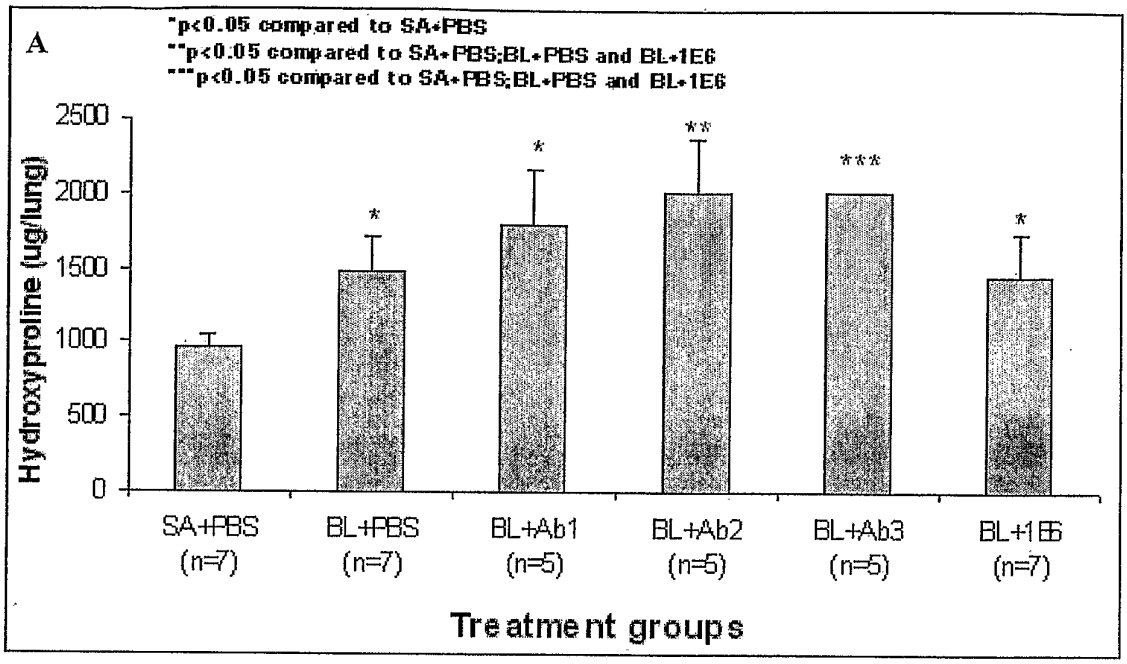

Total BAL Cells
BAL Macrophages (X 10⁴)
Saline
Bleomycin
PBS
PBS
4 mg/kg
20 mg/kg
40 mg/kg
20 mg/kg
40 mg/kg
3G9
1E6
Total Macrophage
BAL Macrophages (X 10⁴)
Total Lymphocyte
BAL Lymphocytes (X 10⁴)
Total Neutrophil
BAL Lymphocytes (X 10⁴)

FIGURE 64



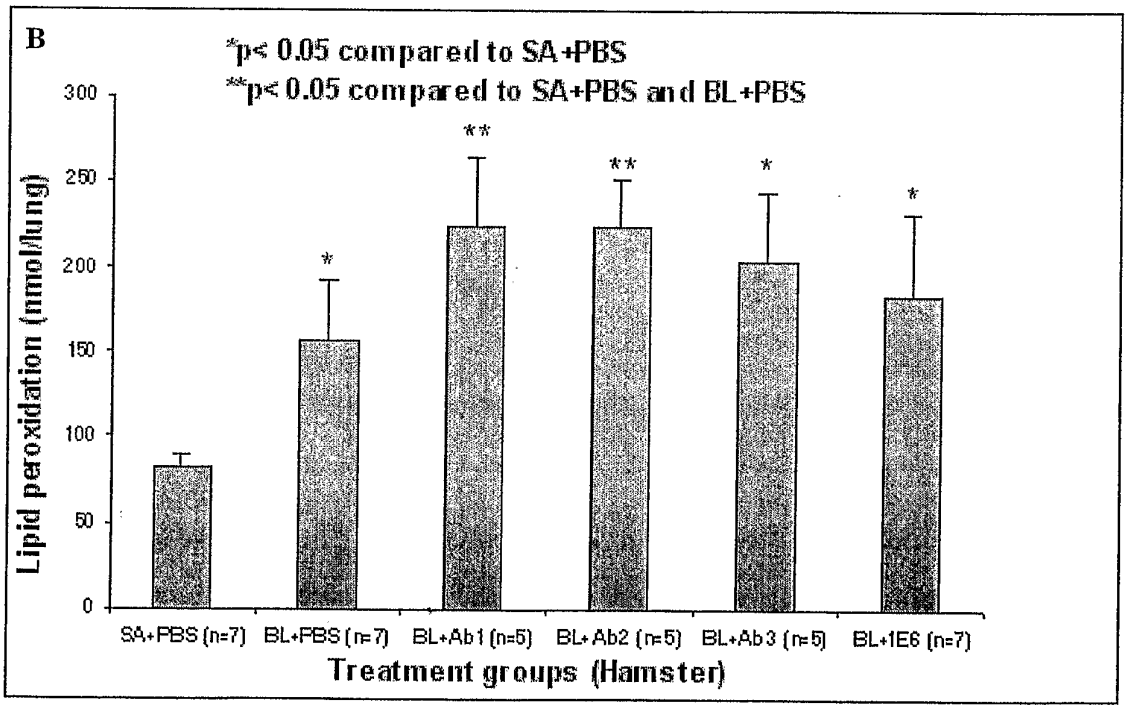


FIGURE 45A-45B

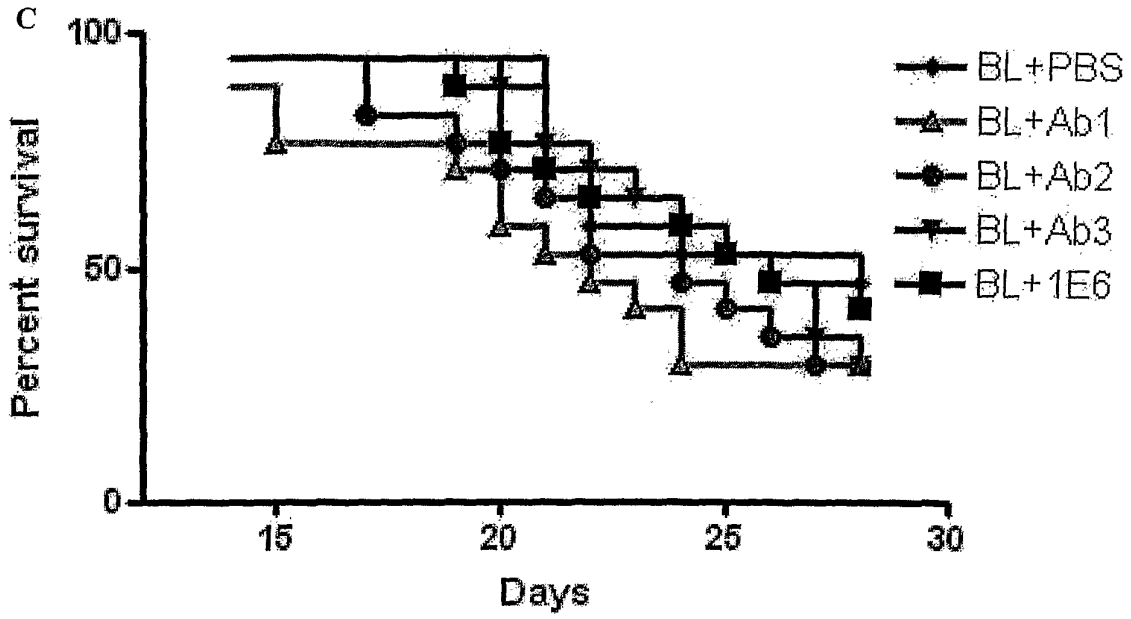

C
100
50
0
Percent survival
15
20
25
30
Days
BL+PBS
BL+Ab1
BL+Ab2
BL+Ab3
BL+1E6

FIGURE 15C

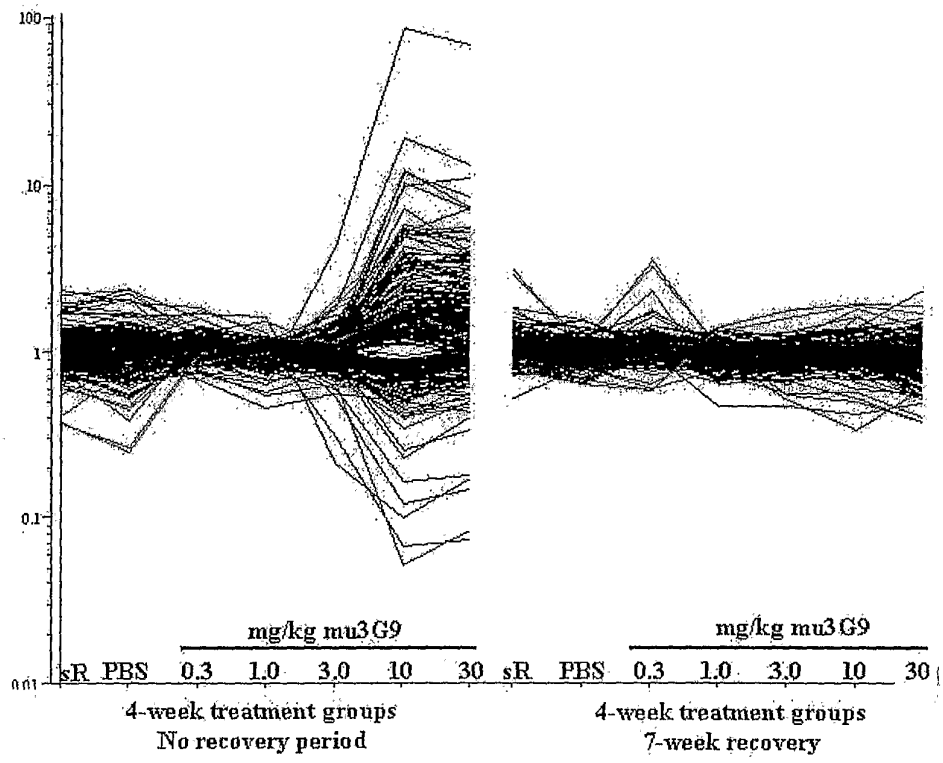

100
10
1
0.1
0.01
mg/kg mu3G9
sR PBS 0.3 1.0 3.0 10 30
4-week treatment groups
No recovery period
mg/kg mu3G9
sR PBS 0.3 1.0 3.0 10 30
4-week treatment groups
7-week recovery

FIGURE 66

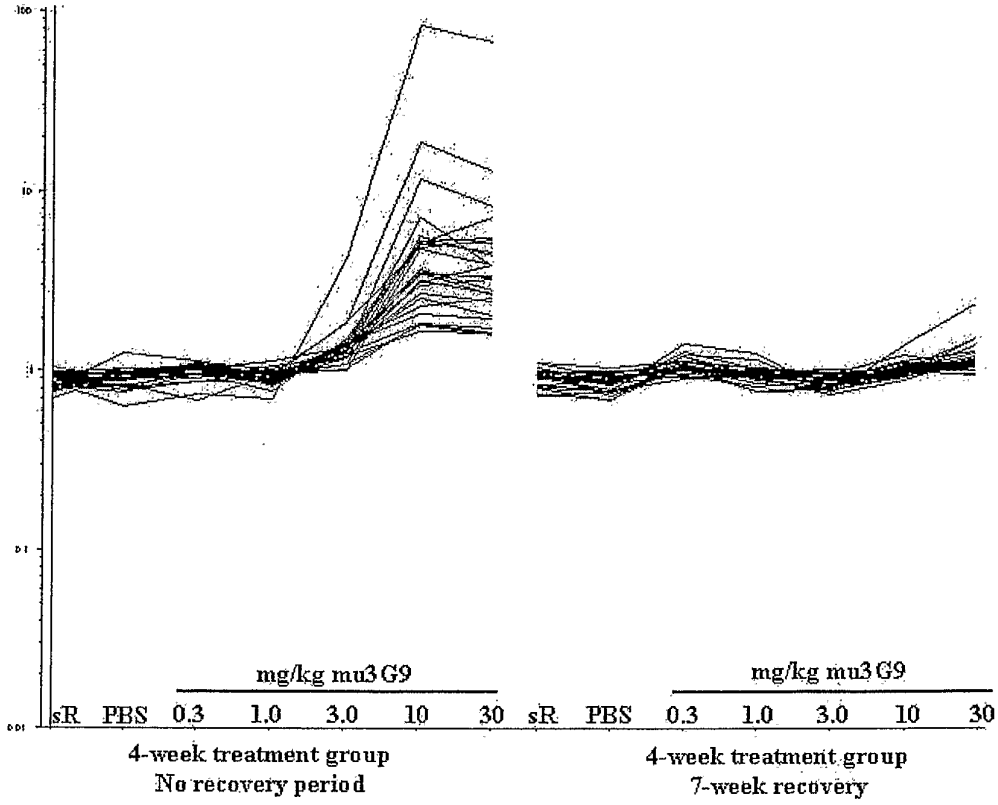

mg/kg mu3 G9
sR PBS 0.3 1.0 3.0 10 30
4-week treatment group
No recovery period
mg/kg mu3 G9
sR PBS 0.3 1.0 3.0 10 30
4-week treatment group
7-week recovery

FIGURE 67

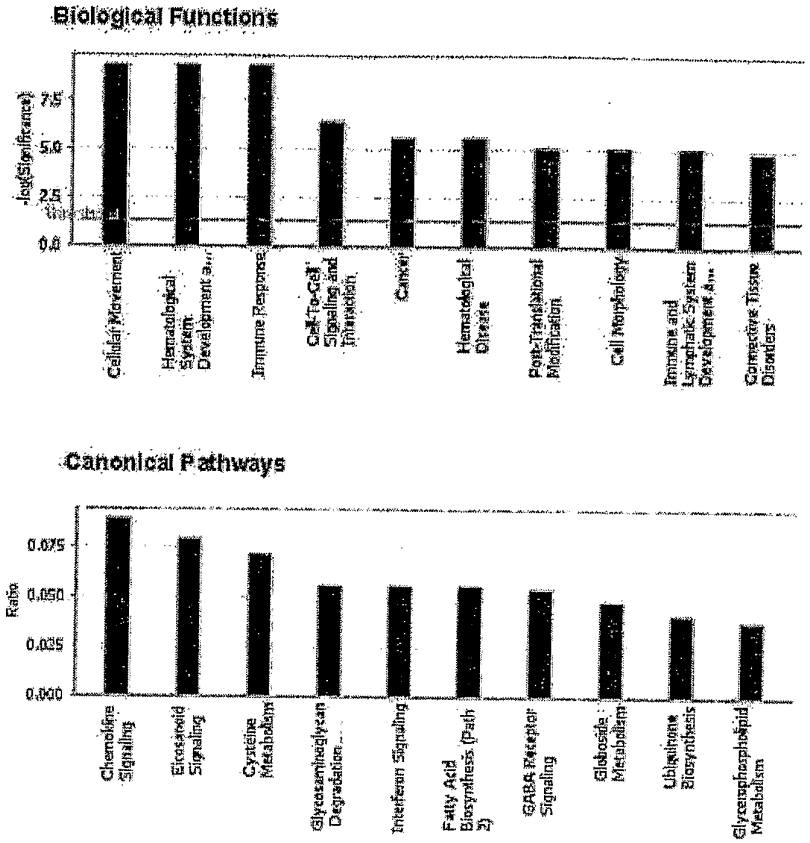

Biological Functions
-log(Significance)
7.5
5.0
2.5
0.0
Cellular Movement
Hematological System Development a...
Immune Response
Cell-To-Cell Signaling and Interaction
Cancer
Hematological Disease
Post-Translational Modification
Cell Morphology
Immune and Lymphatic System Development An...
Connective Tissue Disorders
Canonical Pathways
Ratio
0.075
0.050
0.025
0.000
Chemokine Signaling
Eicosanoid Signaling
Cysteine Metabolism
Glycosaminoglycan Degradation...
Interferon Signaling
Fatty Acid Biosynthesis (Path 2)
GABA Receptor Signaling
Globoside Metabolism
Ubiquinone Biosynthesis
Glycerophospholipid Metabolism

FIGURE 68

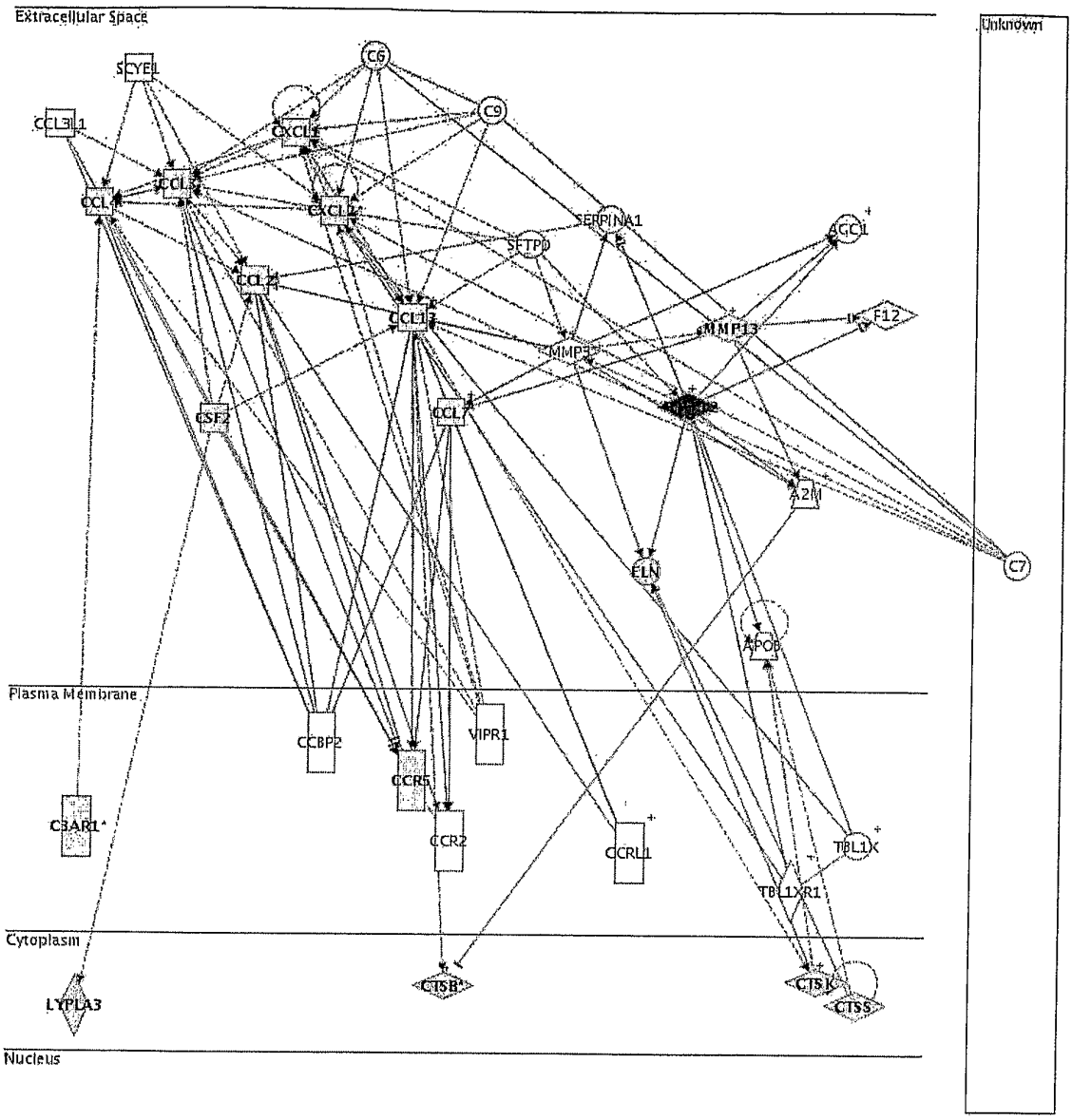

Extracellular Space
Unknown
SCYE1
C6
C9
CCL3L1
CXCL1
CCL
CCL4
CXCL2
SERPINA1
SFTPD
CCL1
CCL2
CCL13
MMP13
IK
F12
MMP3
CSF2
CCL
A2M
C7
ELN
APOB
Plasma Membrane
CCBP2
VIPR1
CCR5
C3AR1
CCR2
CCRL1
TBL1X
TBL1XR1
Cytoplasm
CTSB
CTSK
CTSS
LYPLA3
Nucleus

FIGURE 69A

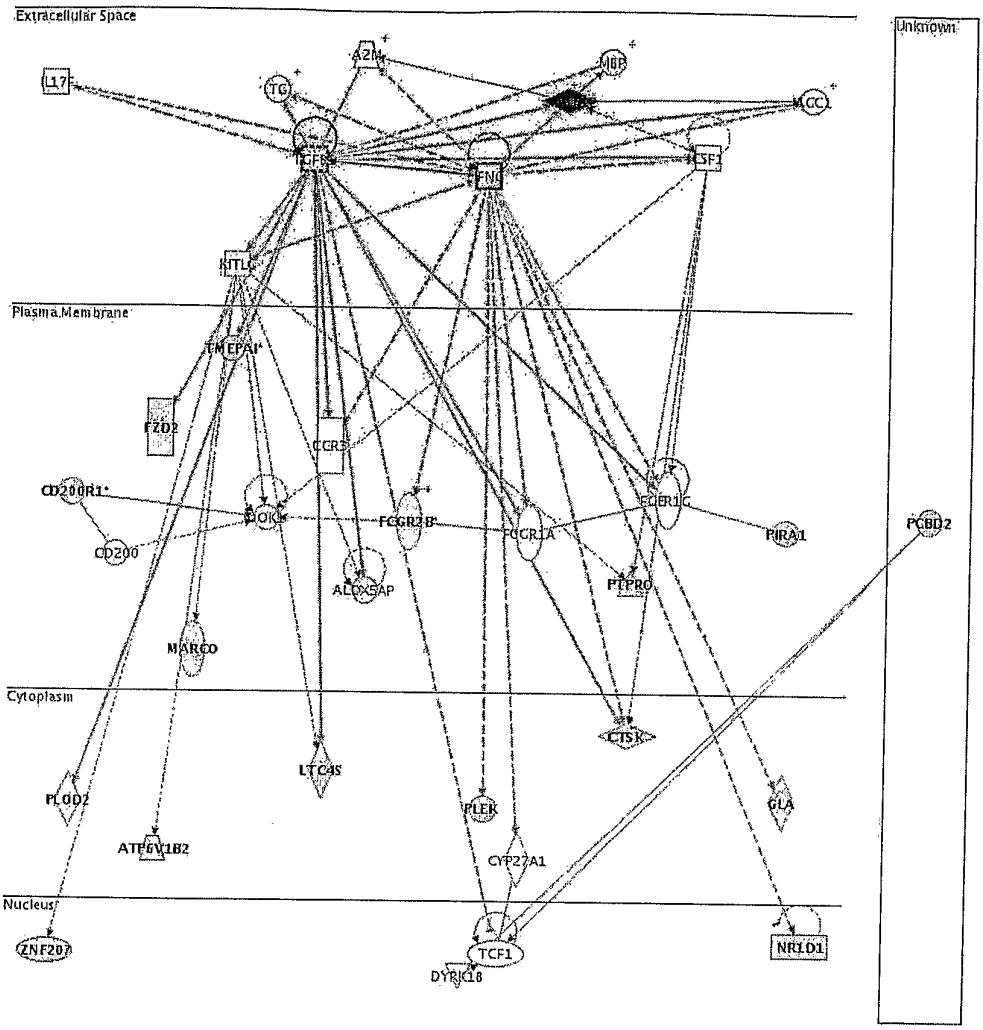

Extracellular Space
Plasma Membrane
Cytoplasm
Nucleus
Unknown
A2M
MBP
L17
TG
MCC1
CSF1
FN1
KITLG
TMEPAI
FZD2
CCR3
CD200R1
CD200
FCGR3B
FCGR1A
FCER1G
FIRA1
PCBD2
ALOX5AP
PTPRO
MARCO
CTSK
LTC4S
PLGD2
PLEK
GLA
ATP6V1B2
CYP27A1
ZNF207
TCF1
NR1D1
DYRK1B

FIGURE 69B

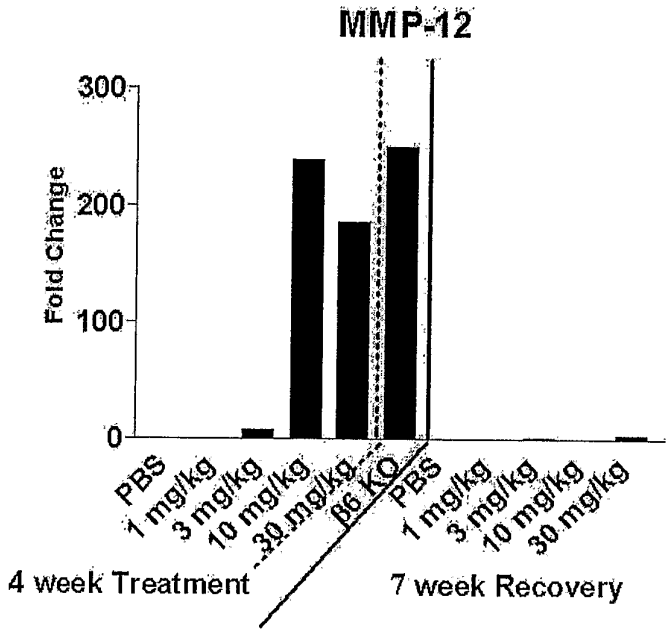

MMP-12
Fold Change
300
200
100
0
PBS
1 mg/kg
3 mg/kg
10 mg/kg
30 mg/kg
86 KO
PBS
1 mg/kg
3 mg/kg
10 mg/kg
30 mg/kg
4 week Treatment
7 week Recovery

FIGURE 7D

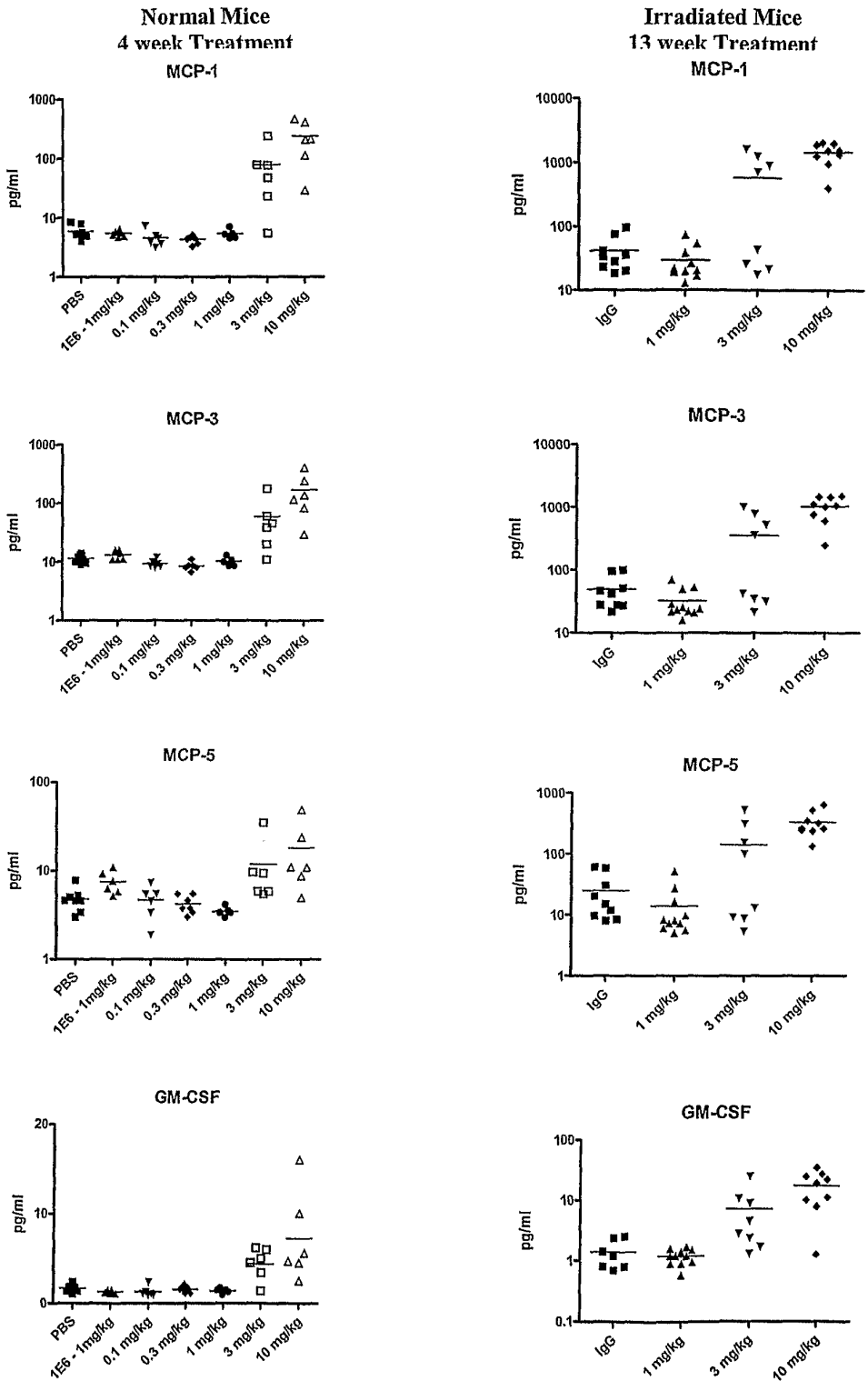

Normal Mice
4 week Treatment
MCP-1
pg/ml
1000
100
10
1
PBS
1E6 - 1mg/kg
0.1 mg/kg
0.3 mg/kg
1 mg/kg
3 mg/kg
10 mg/kg
Irradiated Mice
13 week Treatment
MCP-1
pg/ml
10000
1000
100
10
IgG
1 mg/kg
3 mg/kg
10 mg/kg
MCP-3
pg/ml
1000
100
10
1
PBS
1E6 - 1mg/kg
0.1 mg/kg
0.3 mg/kg
1 mg/kg
3 mg/kg
10 mg/kg
MCP-3
pg/ml
10000
1000
100
10
IgG
1 mg/kg
3 mg/kg
10 mg/kg
MCP-5
pg/ml
100
10
1
PBS
1E6 - 1mg/kg
0.1 mg/kg
0.3 mg/kg
1 mg/kg
3 mg/kg
10 mg/kg
MCP-5
pg/ml
1000
100
10
1
IgG
1 mg/kg
3 mg/kg
10 mg/kg
GM-CSF
pg/ml
20
10
0
PBS
1E6 - 1mg/kg
0.1 mg/kg
0.3 mg/kg
1 mg/kg
3 mg/kg
10 mg/kg
GM-CSF
pg/ml
100
10
1
0.1
IgG
1 mg/kg
3 mg/kg
10 mg/kg

FIGURE 71

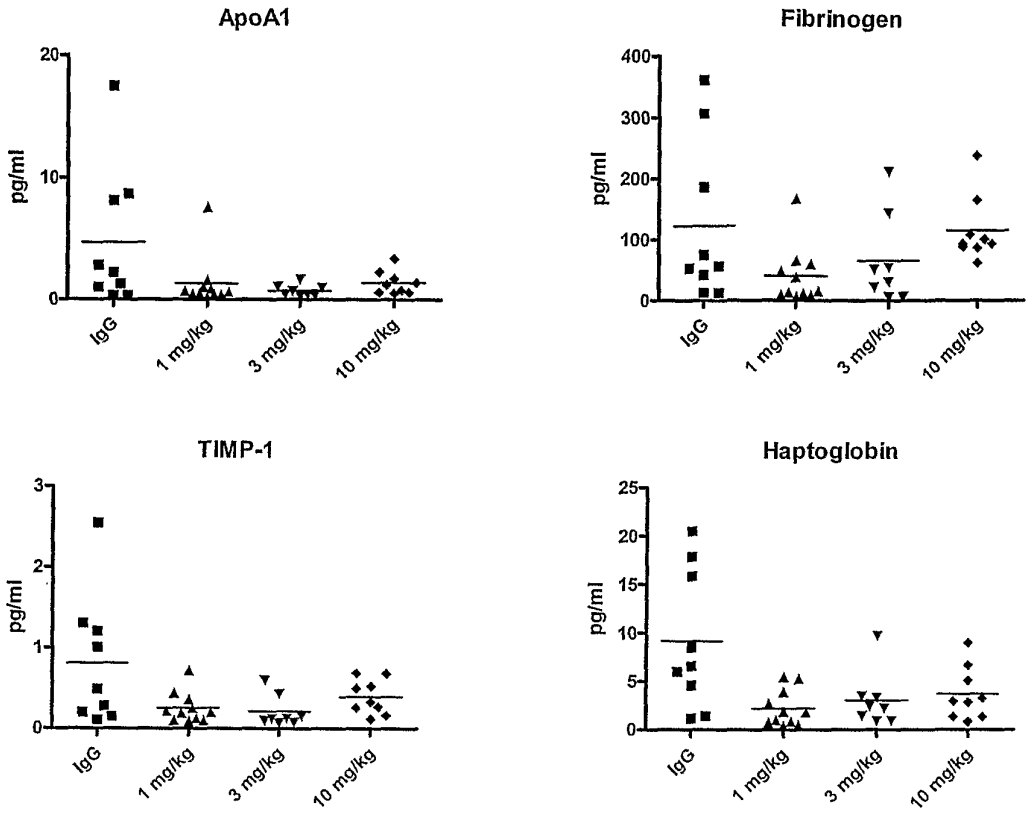

ApoA1
pg/ml
20
10
0
IgG
1 mg/kg
3 mg/kg
10 mg/kg
Fibrinogen
pg/ml
400
300
200
100
0
IgG
1 mg/kg
3 mg/kg
10 mg/kg
TIMP-1
pg/ml
3
2
1
0
IgG
1 mg/kg
3 mg/kg
10 mg/kg
Haptoglobin
pg/ml
25
20
15
10
5
0
IgG
1 mg/kg
3 mg/kg
10 mg/kg

FIGURE 72