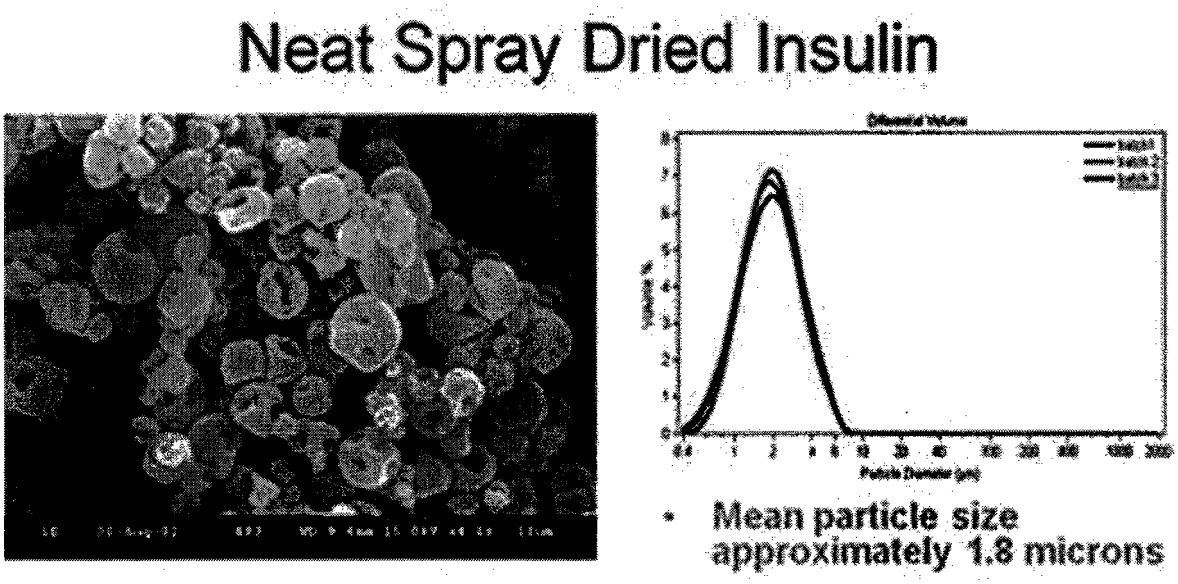
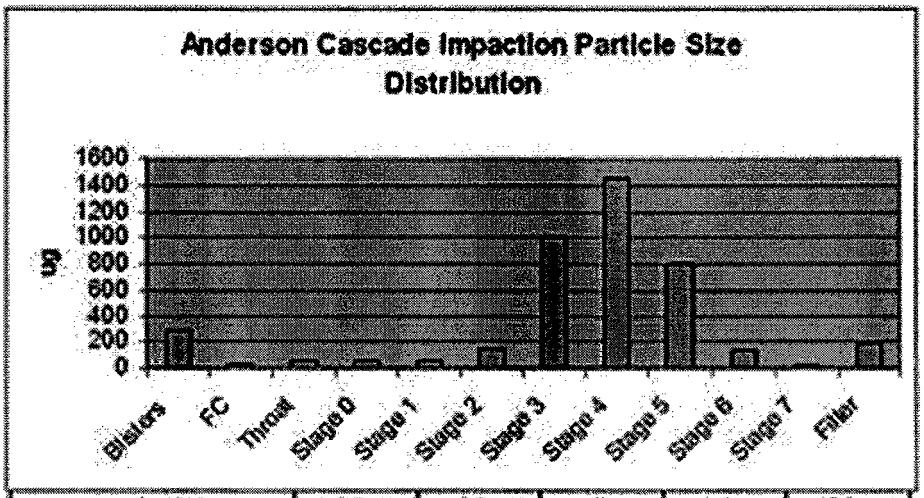

Neat Spray Dried Insulin
• Mean particle size approximately 1.8 microns

FIGURE 1

Particle Size Distribution - Insulin

2.4mg dose, ACI @28.3L/min

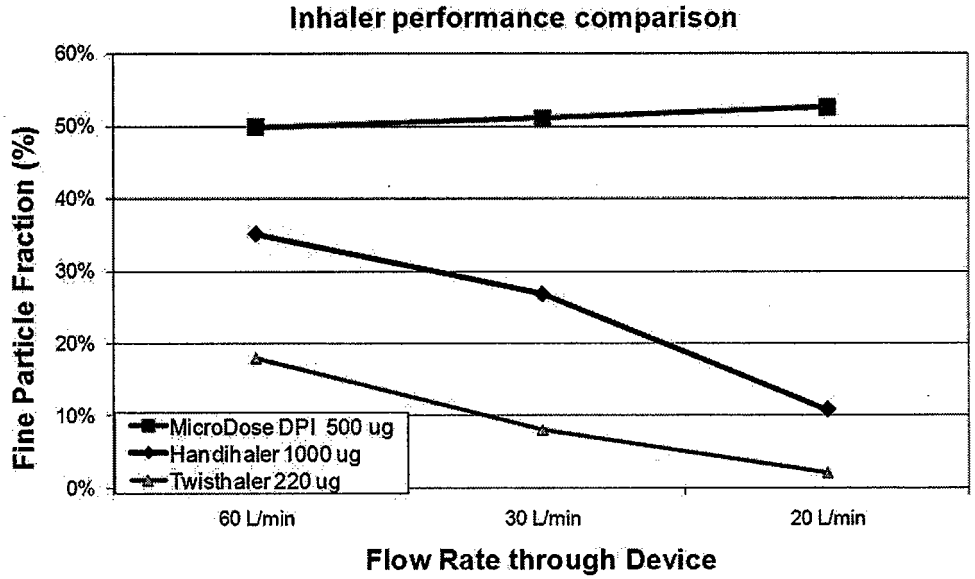


Insulin	< 3.0 um	< 3.3 um	< 4.7 um	< 5.0 um	< 5.8 um
% of Total Detected:	52.58	61.14	84.66	85.56	87.97
% of Total Emitted:	56.91	66.17	91.63	92.61	95.22
% of Total Dosed:	51.48	59.86	82.89	83.77	86.13
Mean Amount per Dose:	1114.45	1295.90	1794.49	1813.64	1864.72

Mean Emitted Dose = 93.76%

FIGURE 2

Efficiency & flow rate comparison of MicroDose DPI vs. two marketed 'passive' DPIs



Jet milled (micronized) corticosteroid w/lactose

FIGURE 3

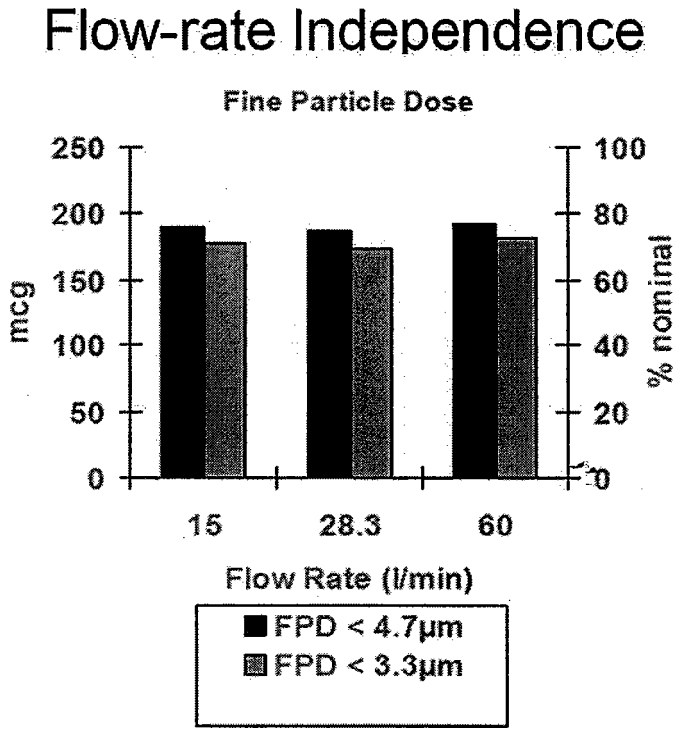

Flow-rate Independence
Fine Particle Dose
250
200
150
100
50
0
mcg
100
80
60
40
20
0
% nominal
15
28.3
60
Flow Rate (l/min)
FPD < 4.7µm
FPD < 3.3µm
Spray-dried neat peptide 250 mcg

FIGURE 4

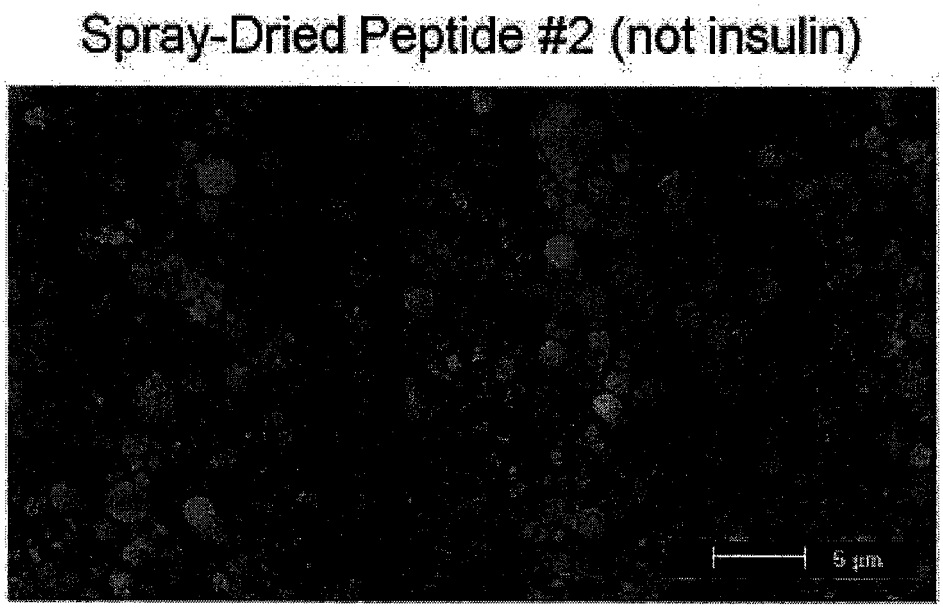


FIGURE 5

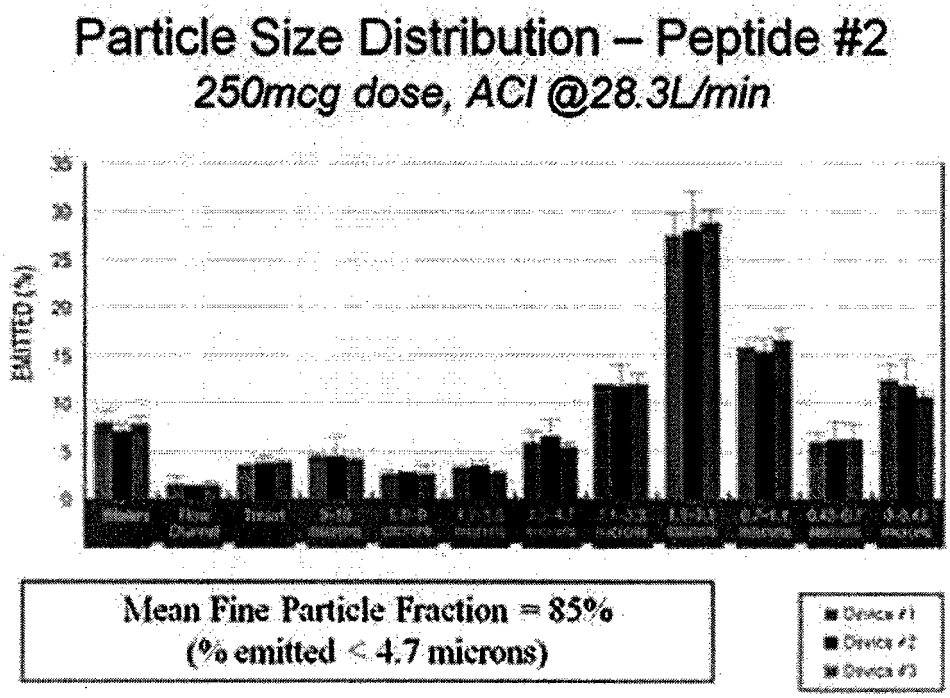

Particle Size Distribution – Peptide #2
250mcg dose, ACI @28.3L/min
Emitted (%)
Mean Fine Particle Fraction = 85%
(% emitted < 4.7 microns)

FIGURE 6

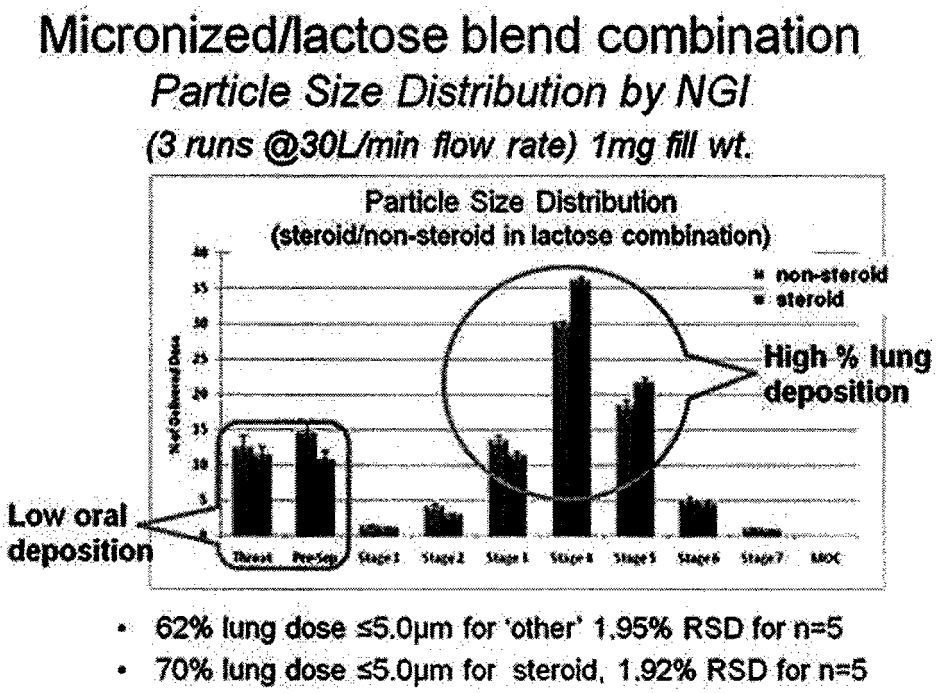

Micronized/lactose blend combination
Particle Size Distribution by NGI
(3 runs @30L/min flow rate) 1mg fill wt.
Particle Size Distribution
(steroid/non-steroid in lactose combination)
non-steroid
steroid
High % lung deposition
Low oral deposition
Throat
PreSep
Stage 3
Stage 2
Stage 1
Stage 0
Stage 5
Stage 6
Stage 7
MOC
62% lung dose ≤5.0µm for 'other' 1.95% RSD for n=5
70% lung dose ≤5.0µm for steroid, 1.92% RSD for n=5

FIGURE 7

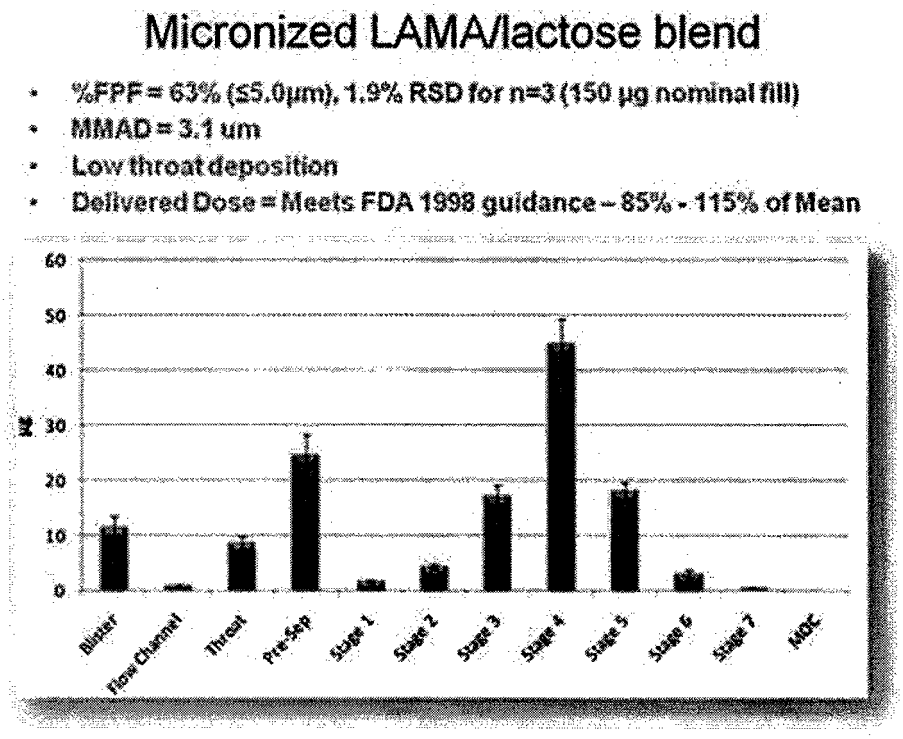

Micronized LAMA/lactose blend
%FPF = 63% (≤5.0µm), 1.9% RSD for n=3 (150 µg nominal fill)
MMAD = 3.1 um
Low throat deposition
Delivered Dose = Meets FDA 1998 guidance – 85% - 115% of Mean
60
50
40
30
20
10
0
Blister
Flow Channel
Throat
Pre-Sep
Stage 1
Stage 2
Stage 3
Stage 4
Stage 5
Stage 6
Stage 7
MOC

FIGURE 8

Activated MK2 Differentially Expressed in Human IPF vs. Normal Lung

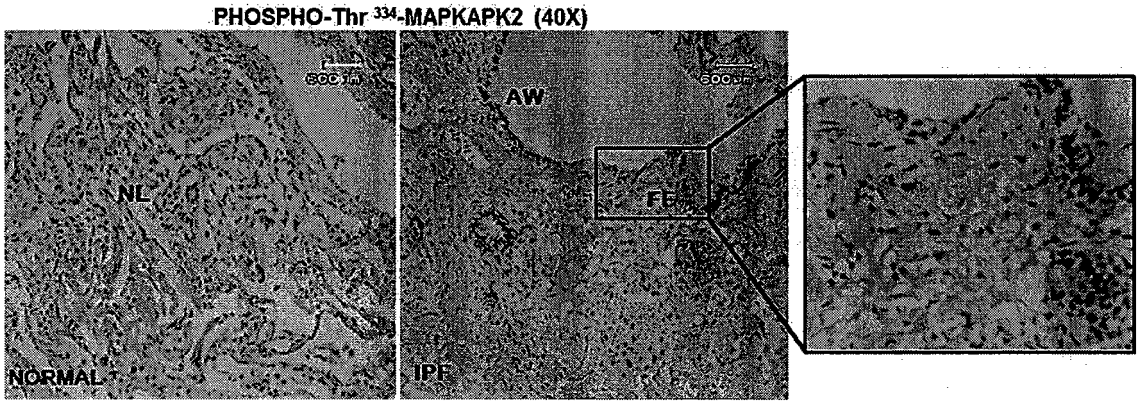


FIGURE 9

Bleomycin Model of Idiopathic Pulmonary Fibrosis: Prevention Model

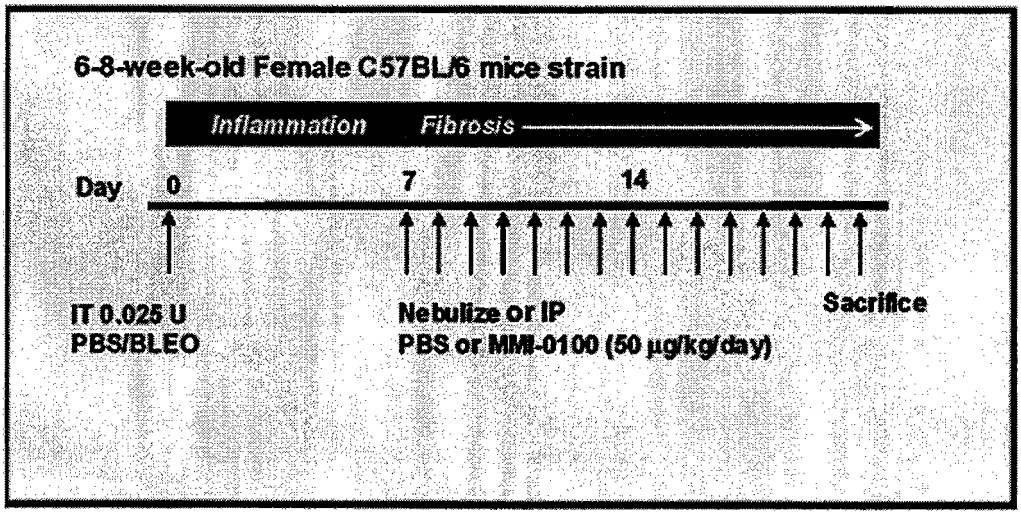


FIGURE 10

MMI-0100 Inhibits Development of Fibrosis in Idiopathic Pulmonary Fibrosis Prevention Model

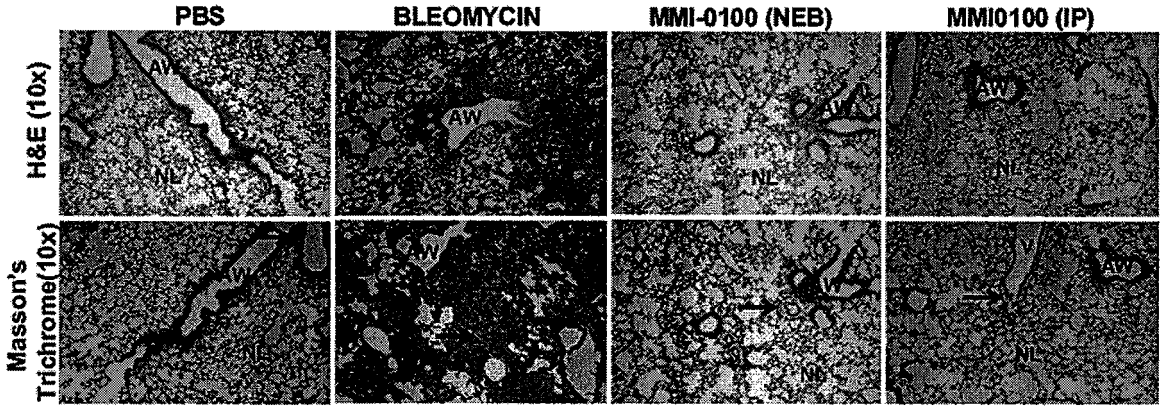


FIGURE 11

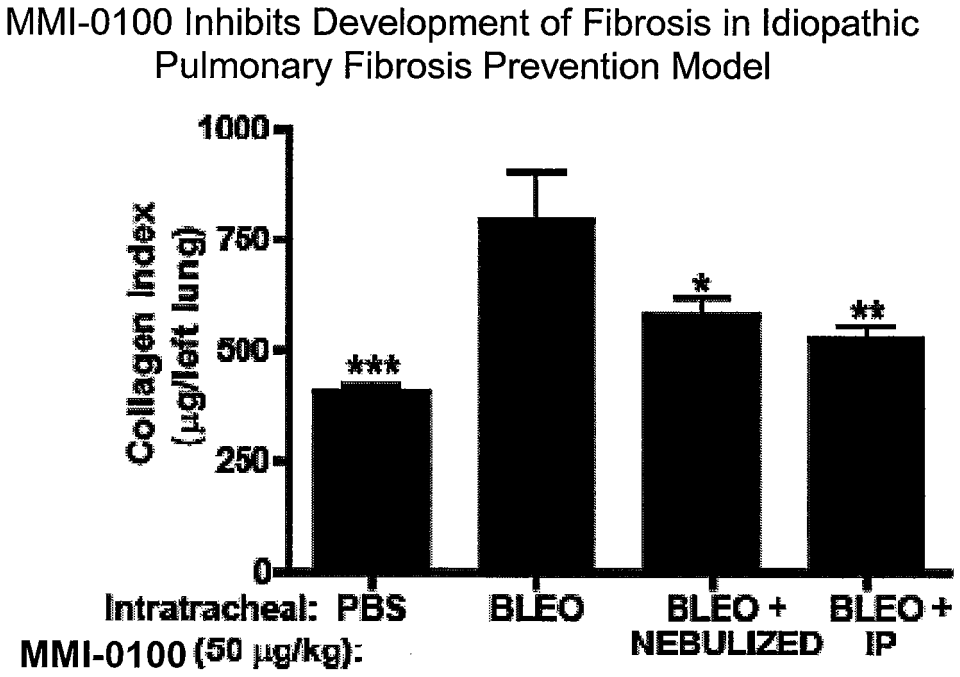

MMI-0100 Inhibits Development of Fibrosis in Idiopathic Pulmonary Fibrosis Prevention Model
Collagen Index (µg/left lung)
1000
750
500
250
0
***
*
**
Intratracheal: PBS
BLEO
BLEO + NEBULIZED
BLEO + IP
MMI-0100 (50 µg/kg):

FIGURE 12

MMI-0100 Dose-Response Data in Idiopathic Pulmonary Fibrosis Prevention Model

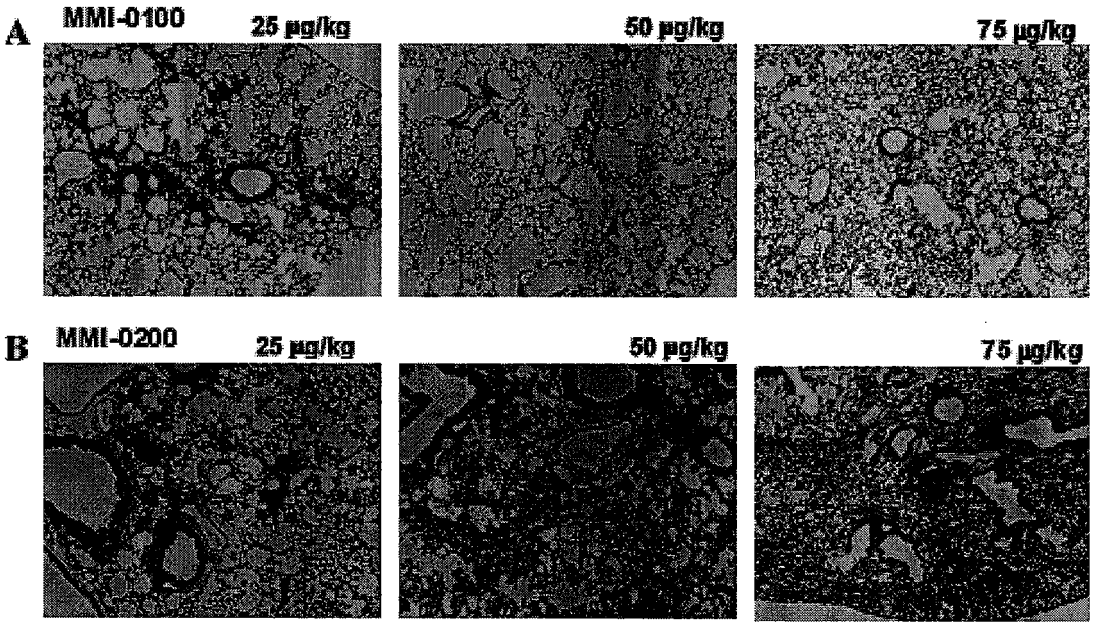


FIGURE 13

MMI-0100 Reduces Systemic T-cell Activation in Idiopathic Pulmonary Fibrosis Prevention Model

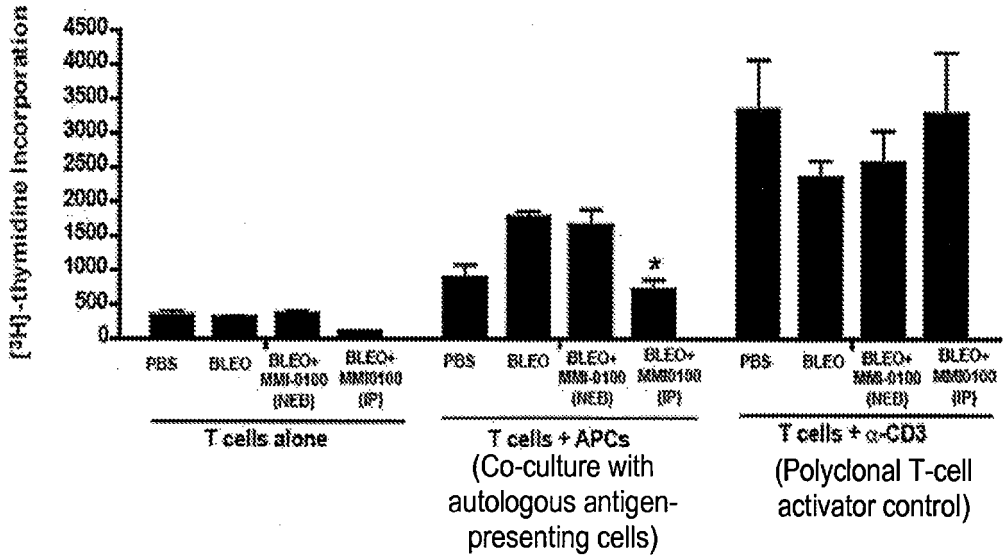


FIGURE 14

Bleomycin Model of Idiopathic Pulmonary Fibrosis: Treatment Model

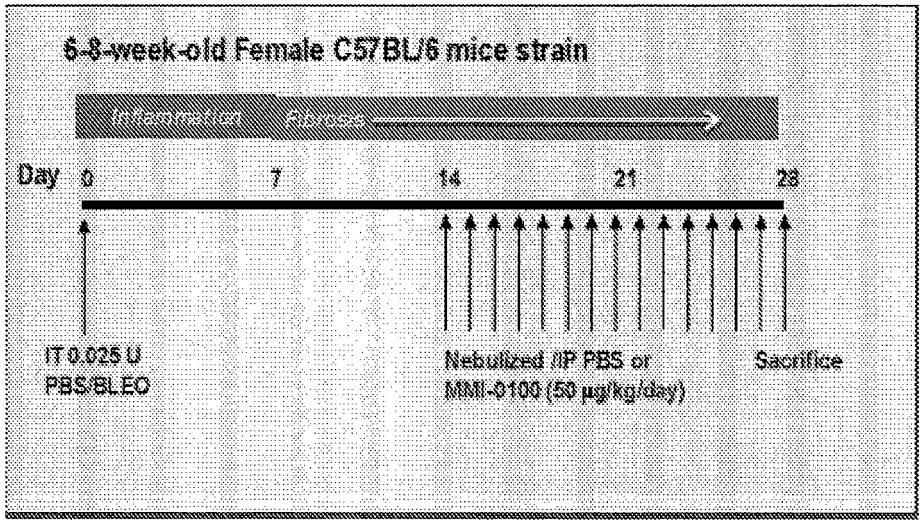


FIGURE 15

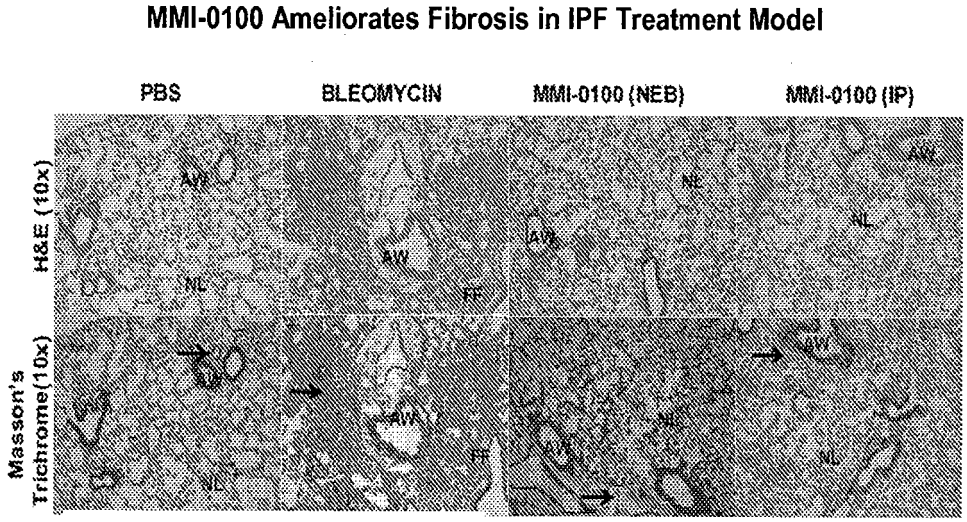

MMI-0100 Ameliorates Fibrosis in IPF Treatment Model
PBS
BLEOMYCIN
MMI-0100 (NEB)
MMI-0100 (IP)
H&E (10x)
Masson's Trichrome(10x)
AW
NL
FF

FIGURE 16

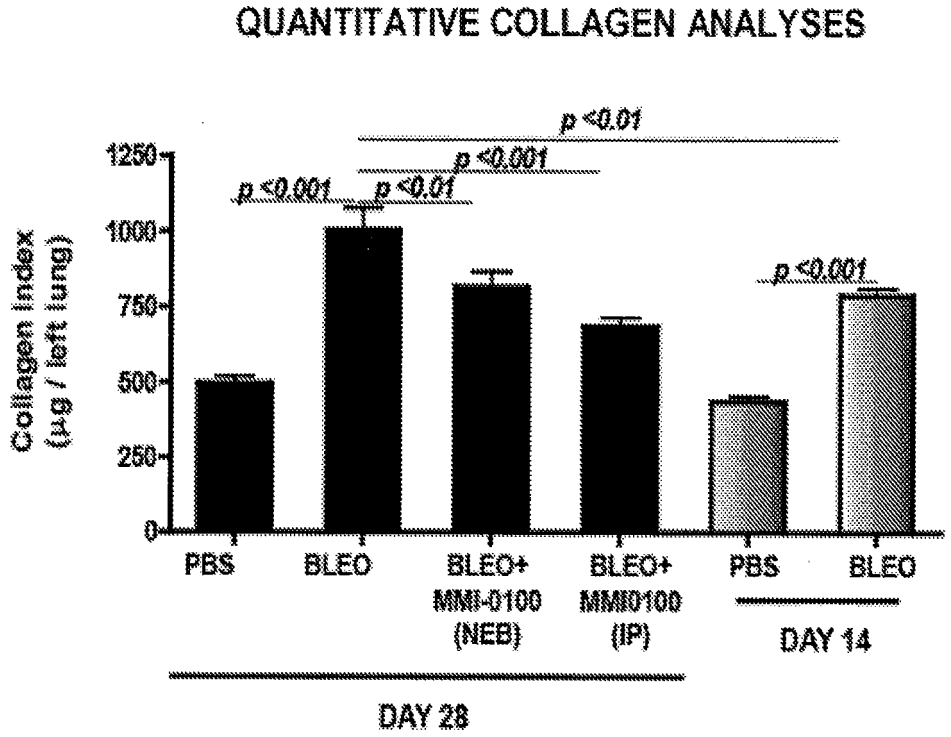

QUANTITATIVE COLLAGEN ANALYSES
Collagen index (µg / left lung)
1250
1000
750
500
250
0
p <0.01
p <0.001
p <0.001
p <0.01
p <0.001
PBS
BLEO
BLEO+ MMI-0100 (NEB)
BLEO+ MMI0100 (IP)
PBS
BLEO
DAY 14
DAY 28

FIGURE 17

Reduced Activated MK2 with MMI-0100 in IPF Treatment Model

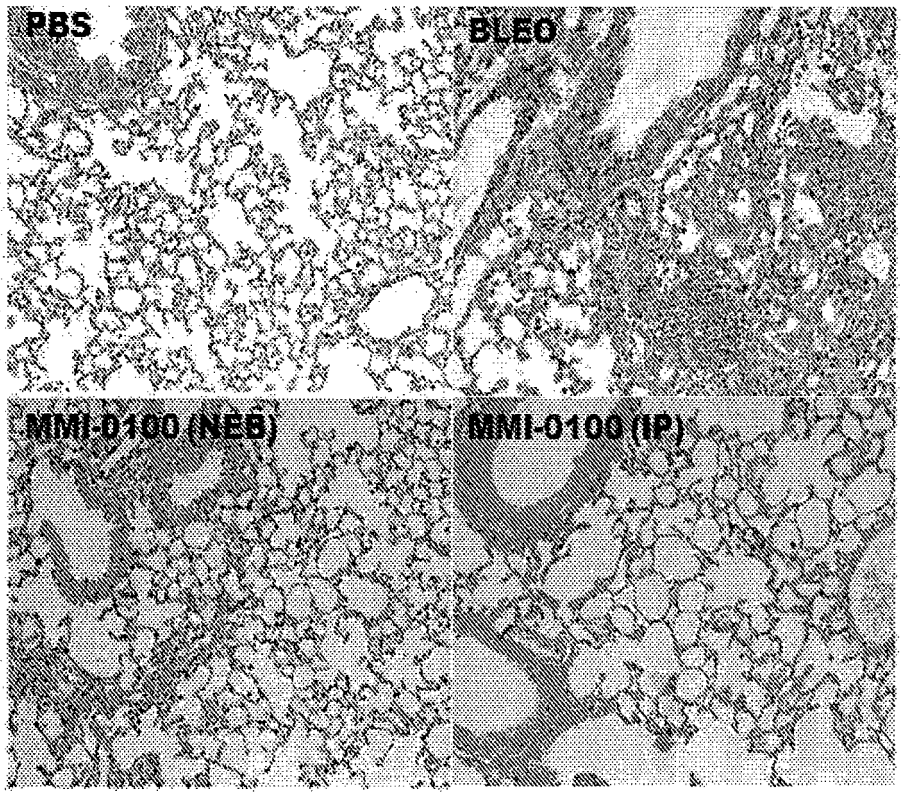


FIGURE 18

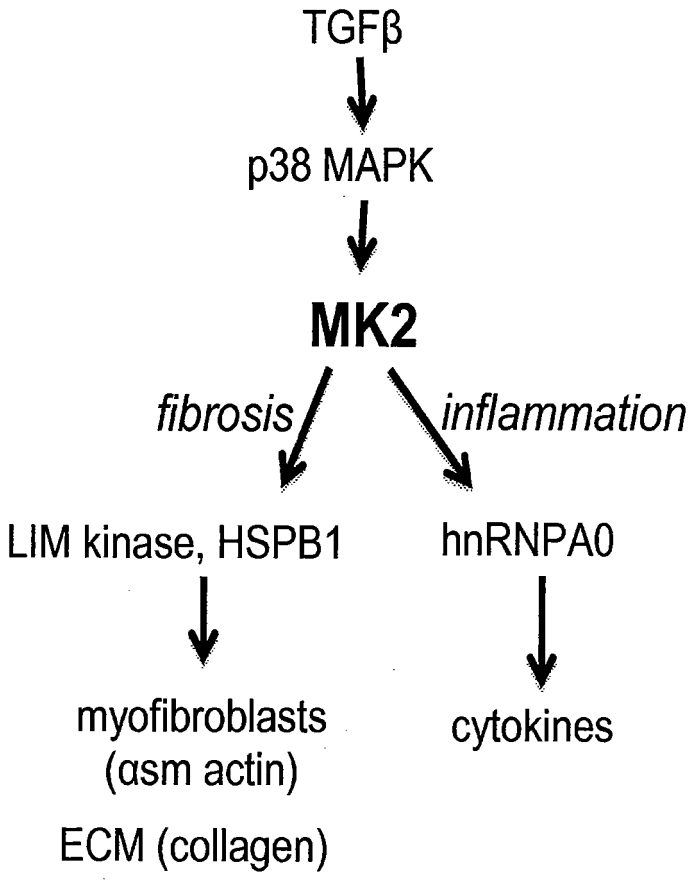

TGFβ
p38 MAPK
MK2
fibrosis
inflammation
LIM kinase, HSPB1
hnRNPA0
myofibroblasts
(αsm actin)
ECM (collagen)
cytokines

FIGURE 19

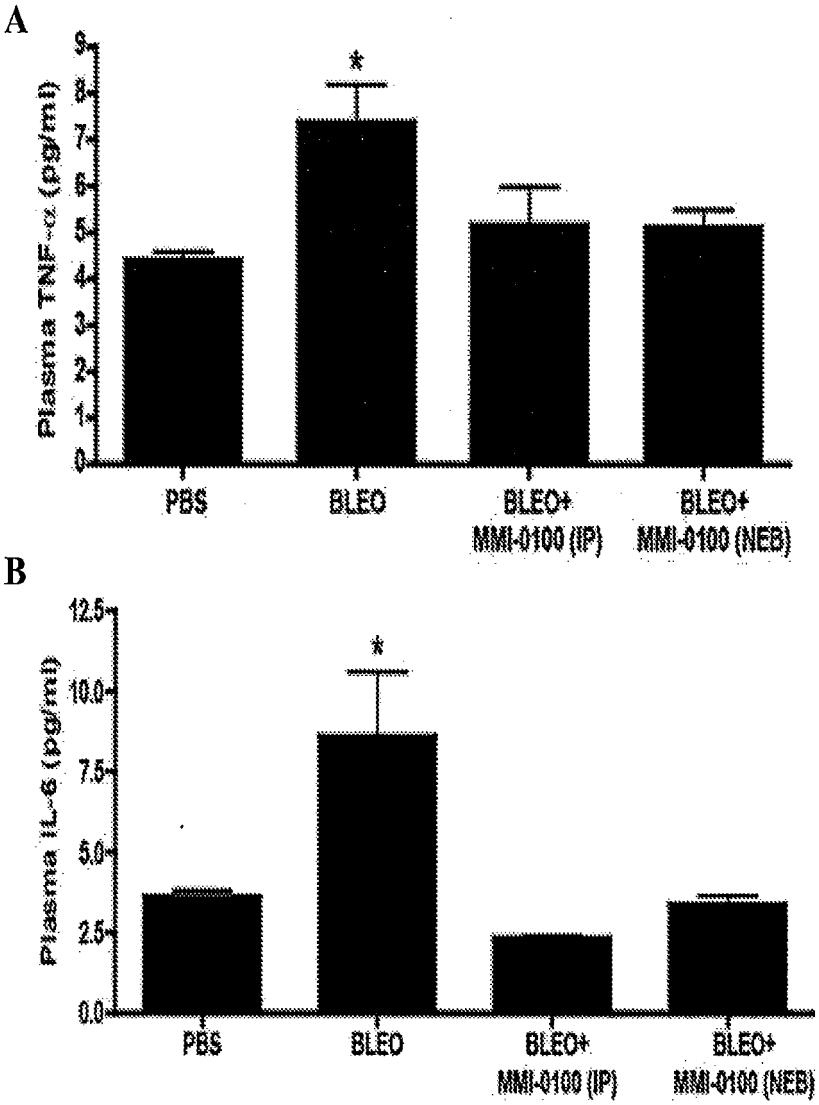

A
Plasma TNF-α (pg/ml)
9
8
7
6
5
4
3
2
1
0
*
PBS
BLEO
BLEO+ MMI-0100 (IP)
BLEO+ MMI-0100 (NEB)
B
Plasma IL-6 (pg/ml)
12.5
10.0
7.5
5.0
2.5
0.0
*
PBS
BLEO
BLEO+ MMI-0100 (IP)
BLEO+ MMI-0100 (NEB)

FIGURE 20

MMI-0100 Inhibits Myofibroblast (a-SMA) Activation in IPF Treatment Model

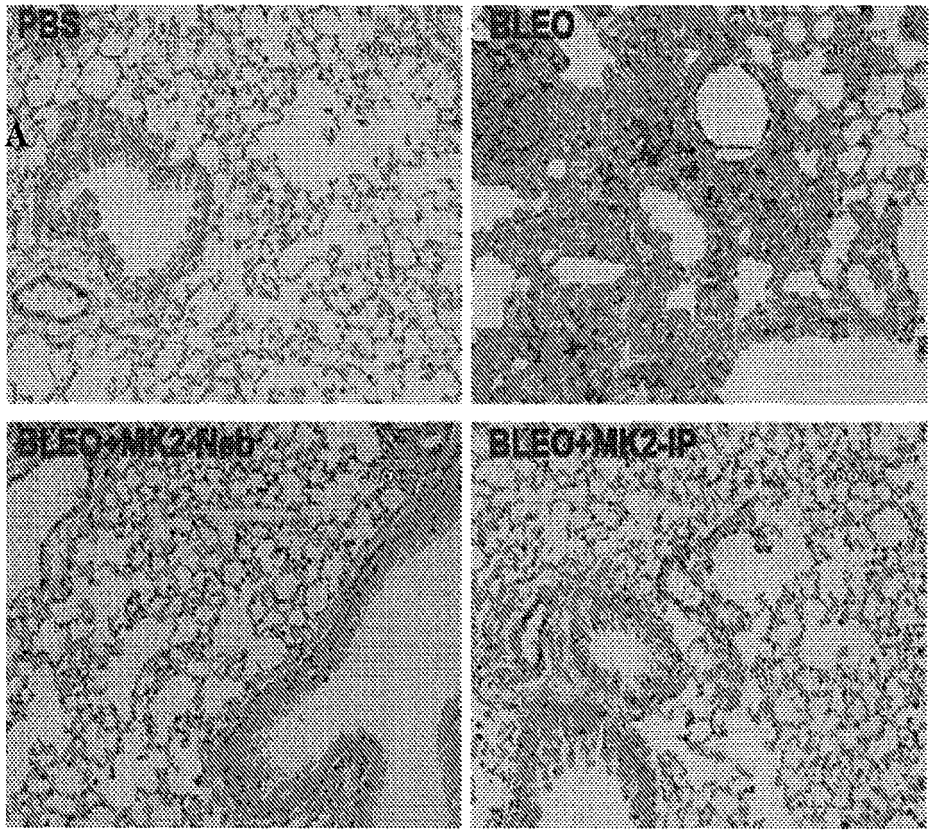


FIGURE 21

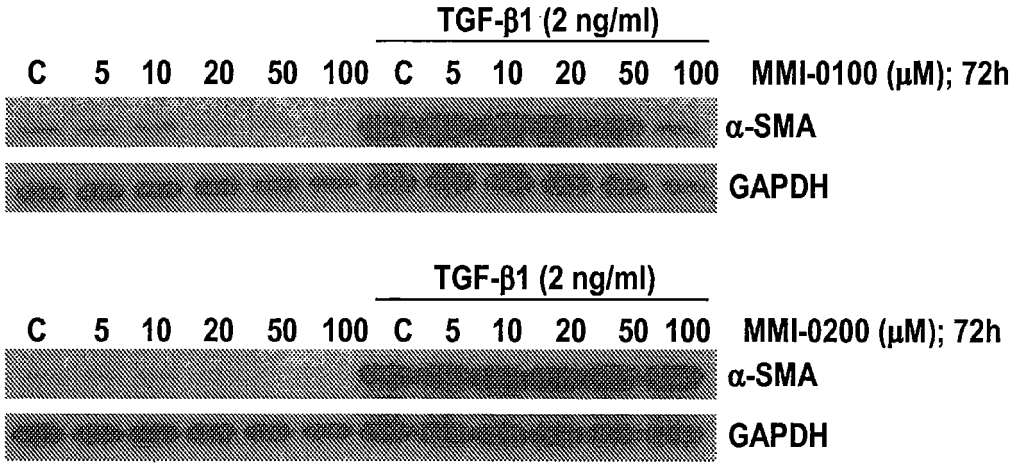

TGF-β1 (2 ng/ml)
C 5 10 20 50 100 C 5 10 20 50 100 MMI-0100 (μM); 72h
α-SMA
GAPDH
TGF-β1 (2 ng/ml)
C 5 10 20 50 100 C 5 10 20 50 100 MMI-0200 (μM); 72h
α-SMA
GAPDH

FIGURE 22

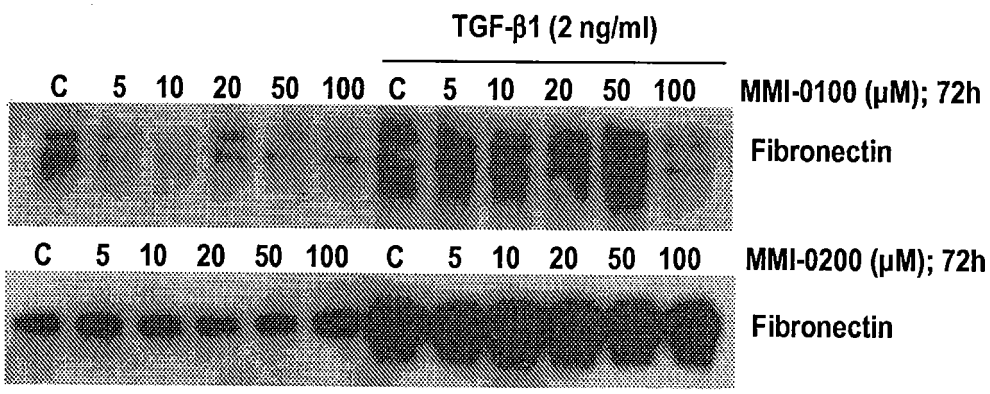

TGF-β1 (2 ng/ml)
C 5 10 20 50 100 C 5 10 20 50 100
MMI-0100 (μM); 72h
Fibronectin
C 5 10 20 50 100 C 5 10 20 50 100
MMI-0200 (μM); 72h
Fibronectin

FIGURE 23

MSC migration is regulated by fibronectin through α5β1-integrin-mediated activation of PDGFR-β

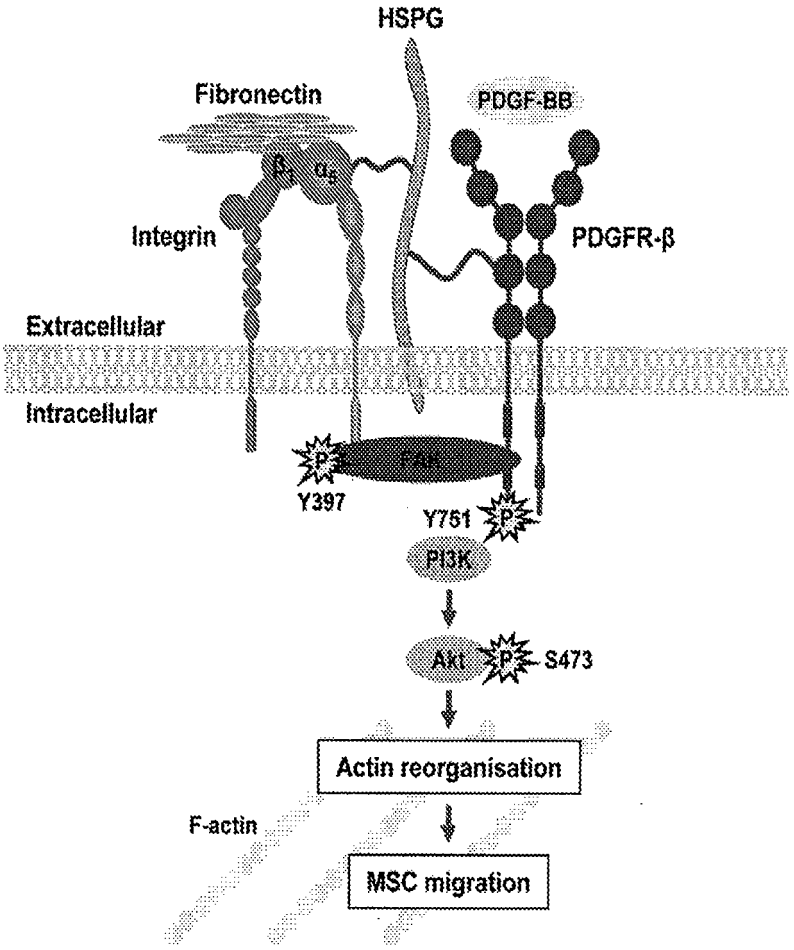
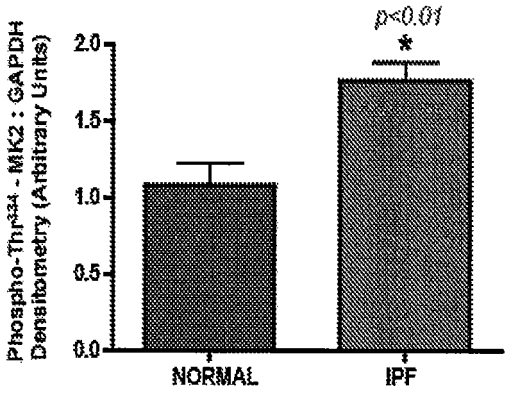


FIGURE 24

A



B

Correlation between Lung Function and MK2 Activation

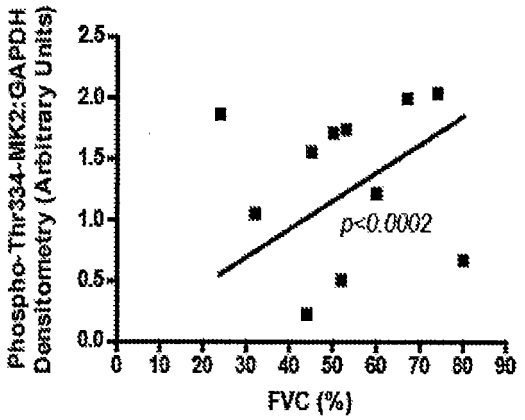


FIGURE 25

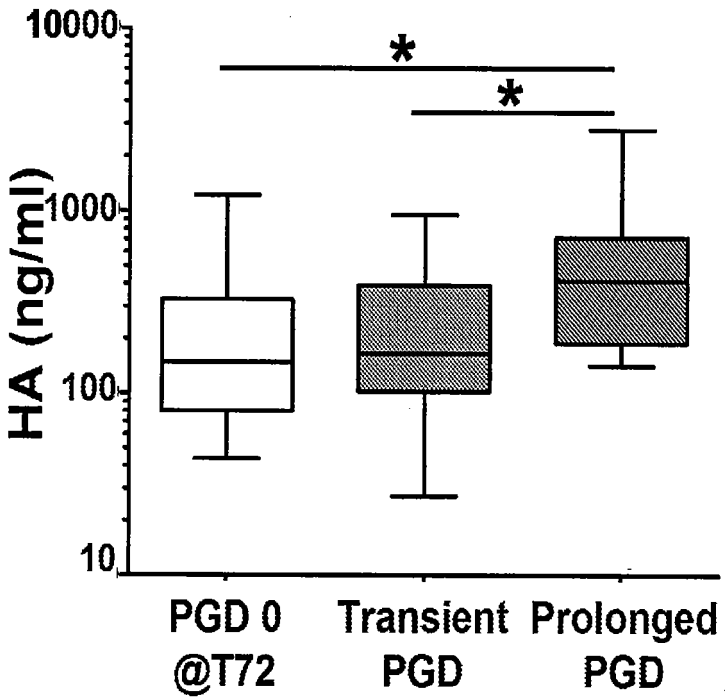

10000
1000
100
10
HA (ng/ml)
*
*
PGD 0 @T72
Transient PGD
Prolonged PGD

FIGURE 26

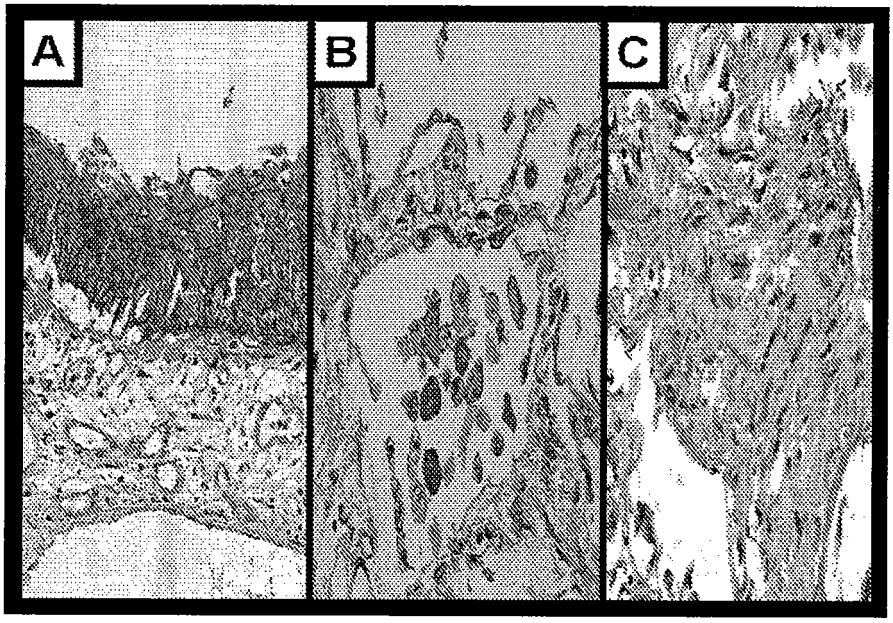


FIGURE 27

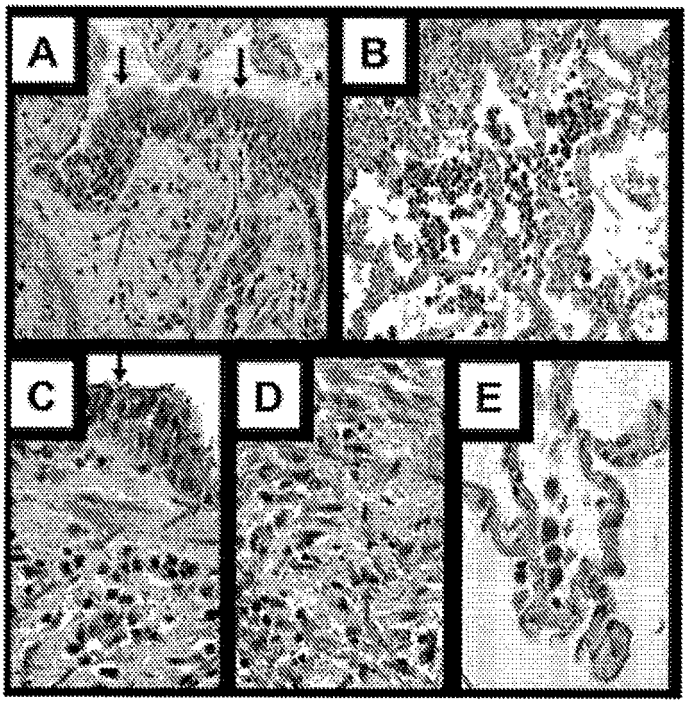


FIGURE 28

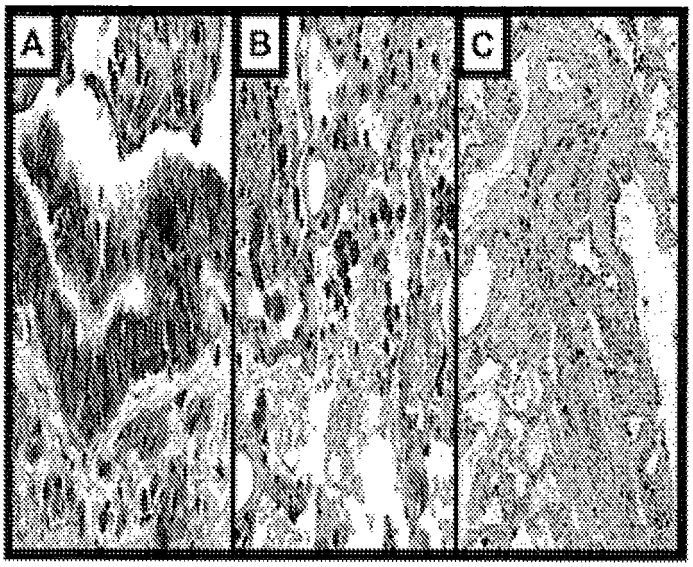


FIGURE 29

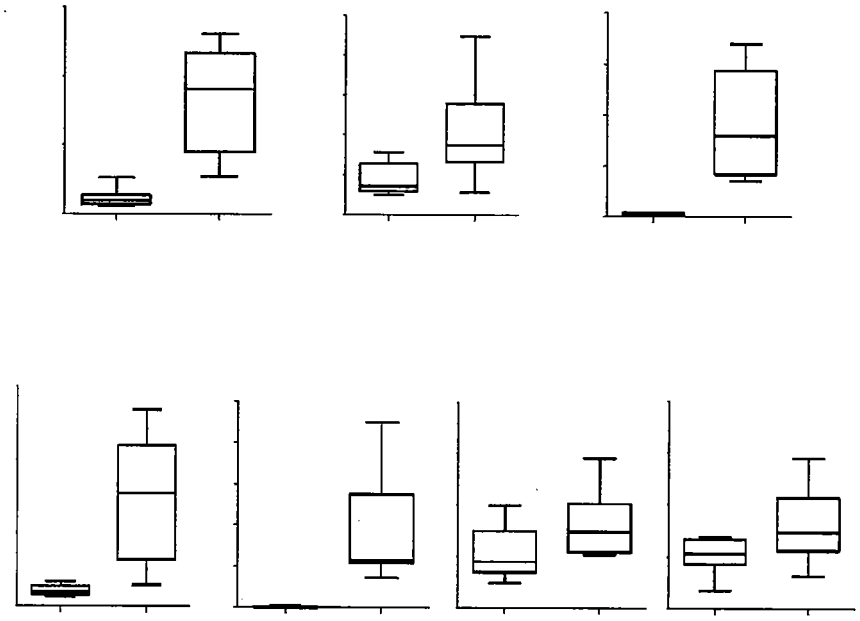


FIGURE 30

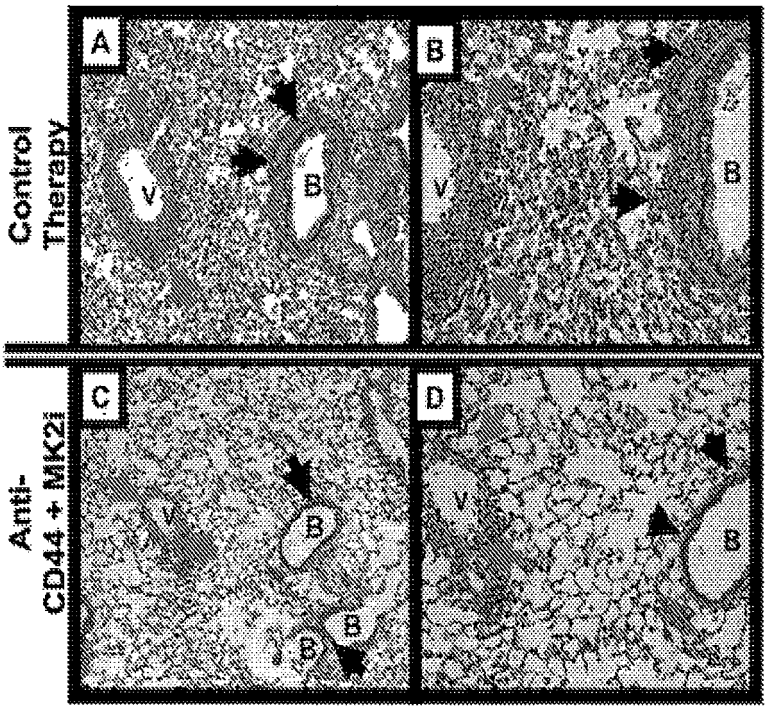


FIGURE 31

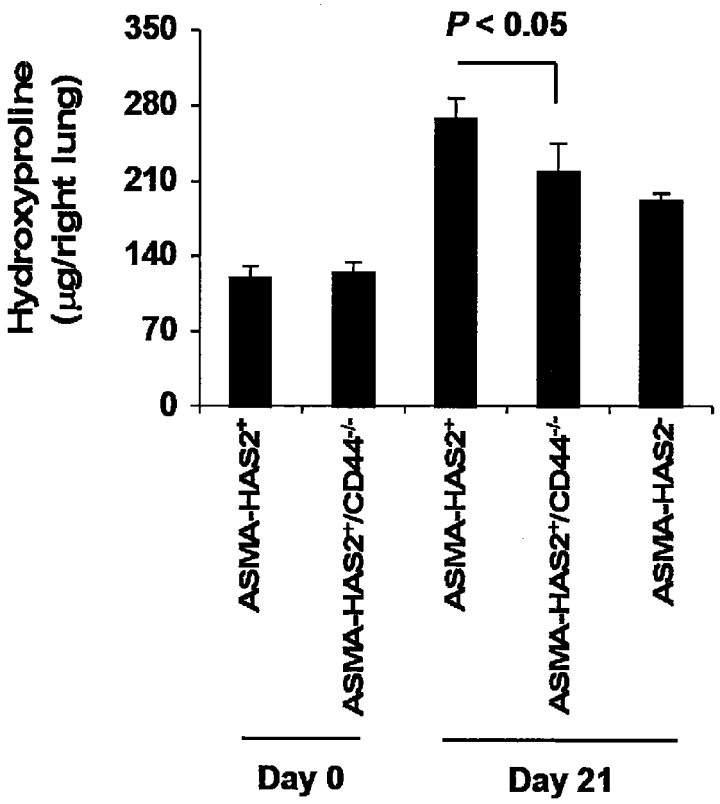

Hydroxyproline (μg/right lung)
350
280
210
140
70
0
P < 0.05
ASMA-HAS2+
ASMA-HAS2+/CD44-/-
ASMA-HAS2+
ASMA-HAS2+/CD44-/-
ASMA-HAS2-
Day 0
Day 21

FIGURE 32

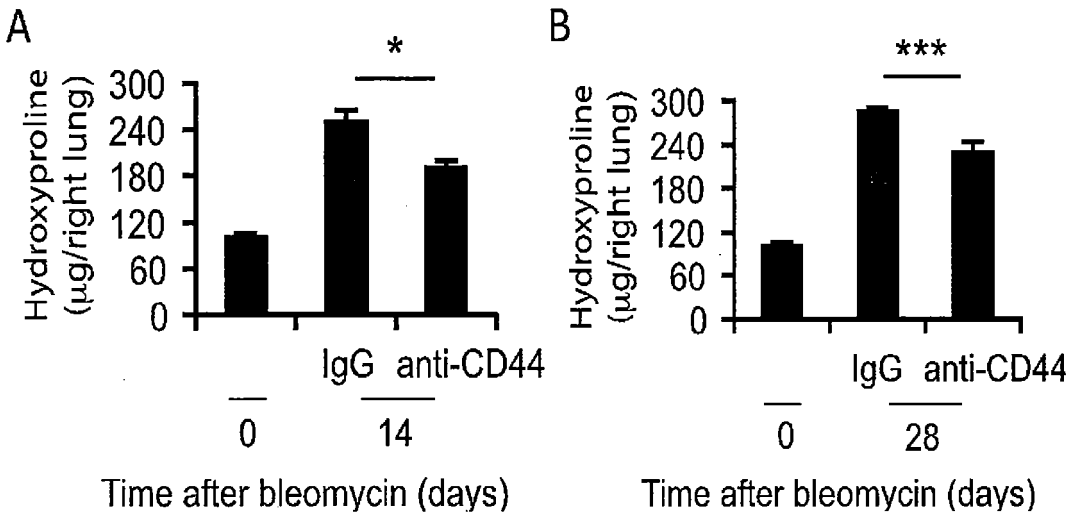

A
*
Hydroxyproline (μg/right lung)
300
240
180
120
60
0
IgG
anti-CD44
0
14
Time after bleomycin (days)
B
***
Hydroxyproline (μg/right lung)
300
240
180
120
60
0
IgG
anti-CD44
0
28
Time after bleomycin (days)

FIGURE 33

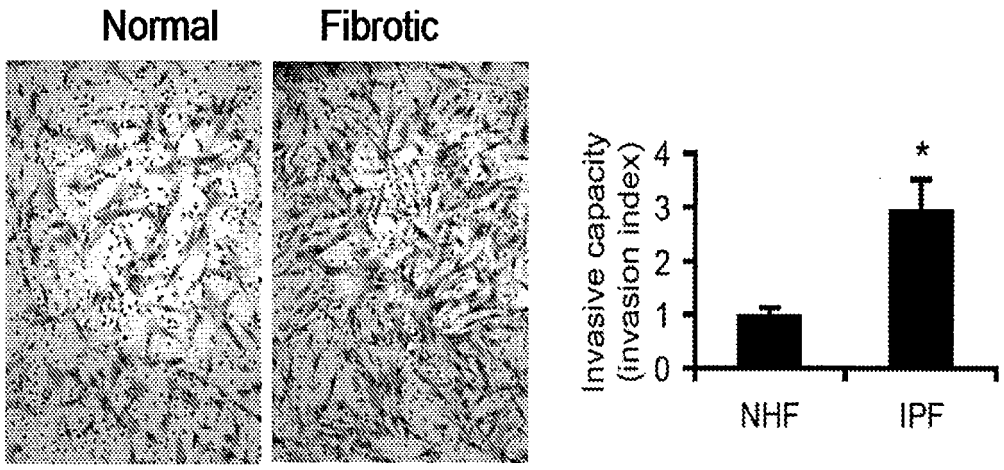

Normal
Fibrotic
Invasive capacity (invasion index)
0
1
2
3
4
*
NHF
IPF

FIGURE 34

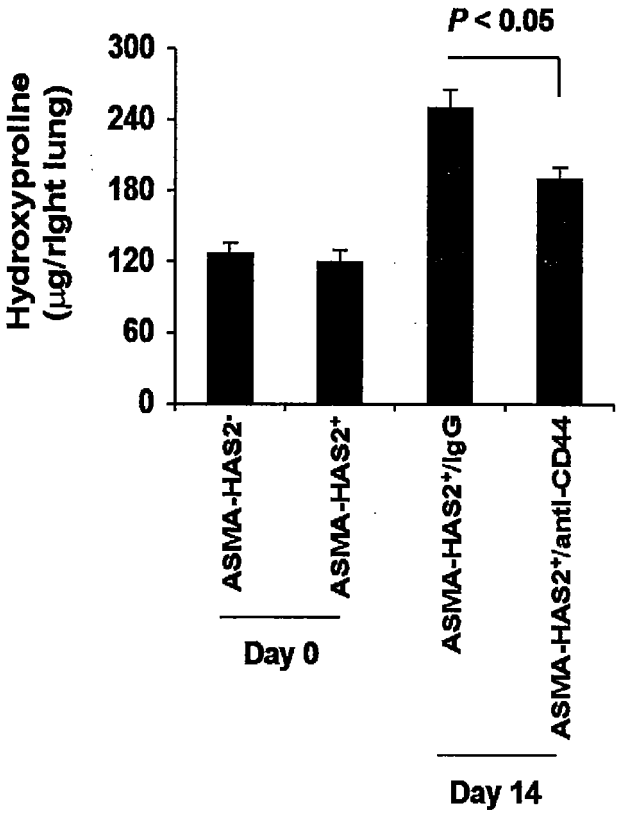

P < 0.05
Hydroxyproline (μg/right lung)
300
240
180
120
60
0
ASMA-HAS2-
ASMA-HAS2+
ASMA-HAS2+/IgG
ASMA-HAS2+/anti-CD44
Day 0
Day 14

FIGURE 35

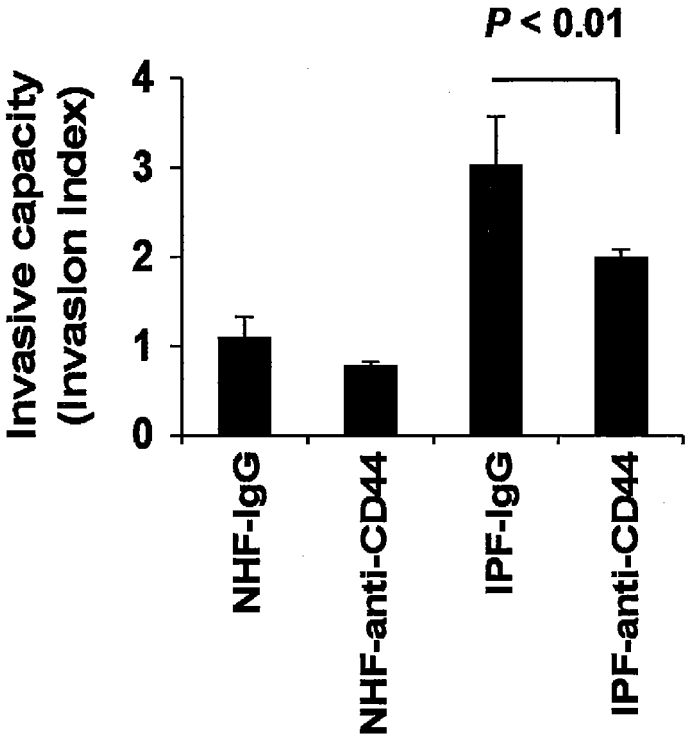

P < 0.01
Invasive capacity
(Invasion Index)
4
3
2
1
0
NHF-IgG
NHF-anti-CD44
IPF-IgG
IPF-anti-CD44

FIGURE 36

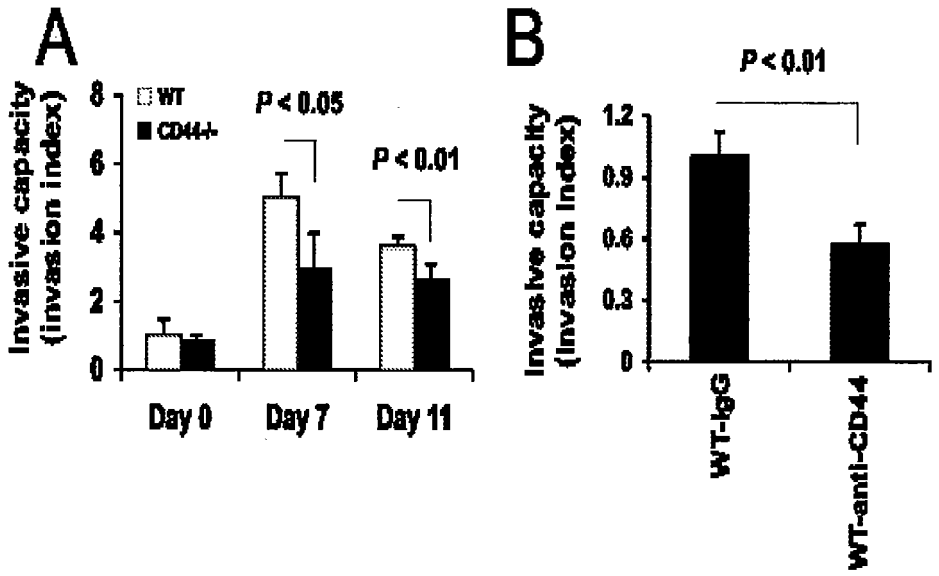

A
WT
CD44+
P < 0.05
P < 0.01
Invasive capacity (invasion index)
8
6
4
2
0
Day 0
Day 7
Day 11
B
P < 0.01
Invasive capacity (invasion index)
1.2
0.9
0.6
0.3
0
WT-IgG
WT-anti-CD44

FIGURE 37

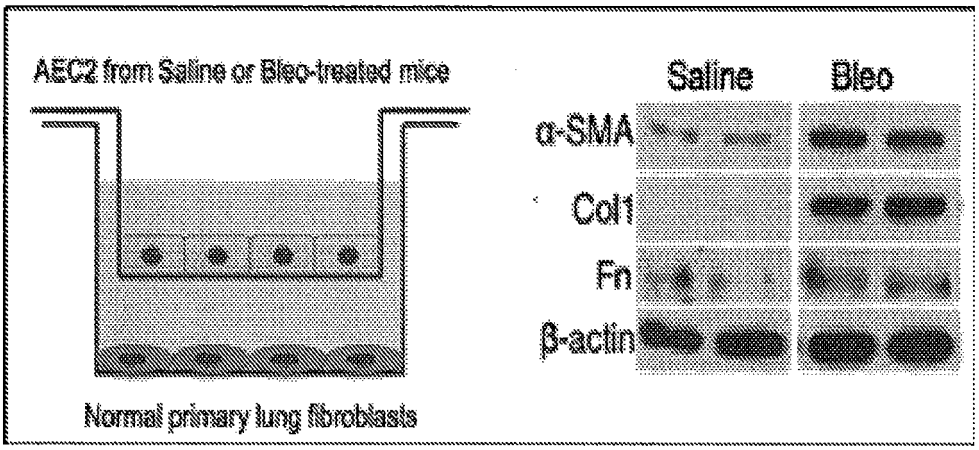

AEC2 from Saline or Bleo-treated mice
Normal primary lung fibroblasts
Saline
Bleo
α-SMA
Col1
Fn
β-actin

FIGURE 38

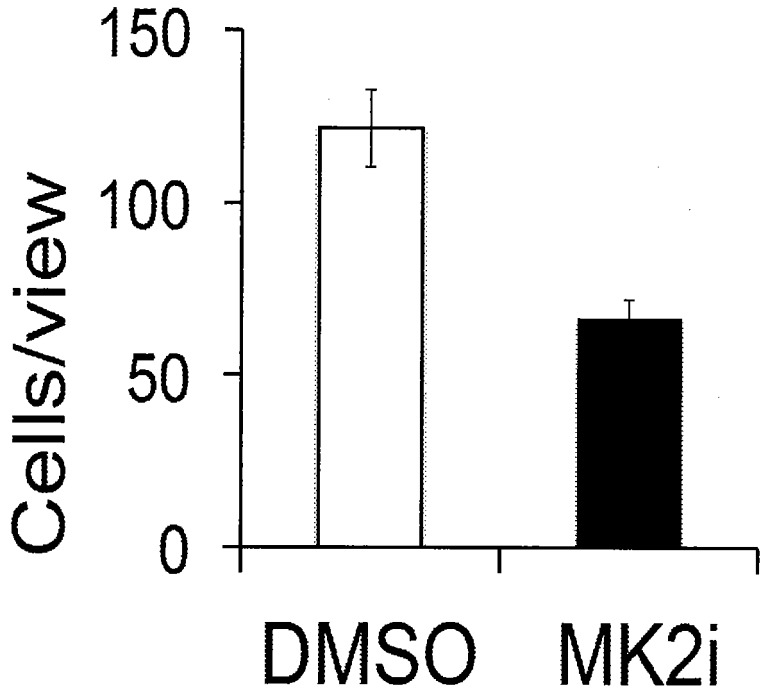


FIGURE 39

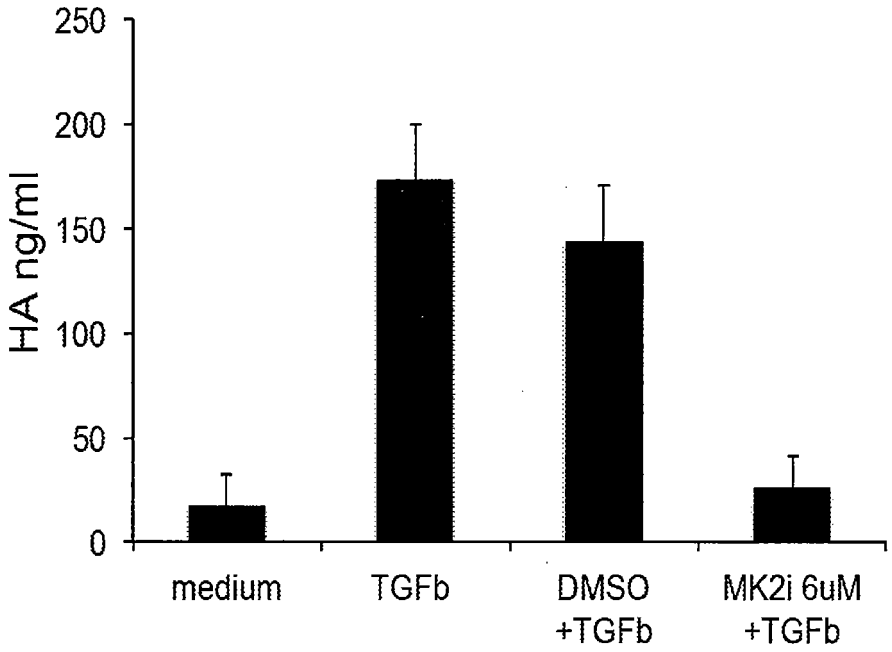

250
200
150
100
50
0
HA ng/ml
medium
TGFb
DMSO
+TGFb
MK2i 6uM
+TGFb

FIGURE 40

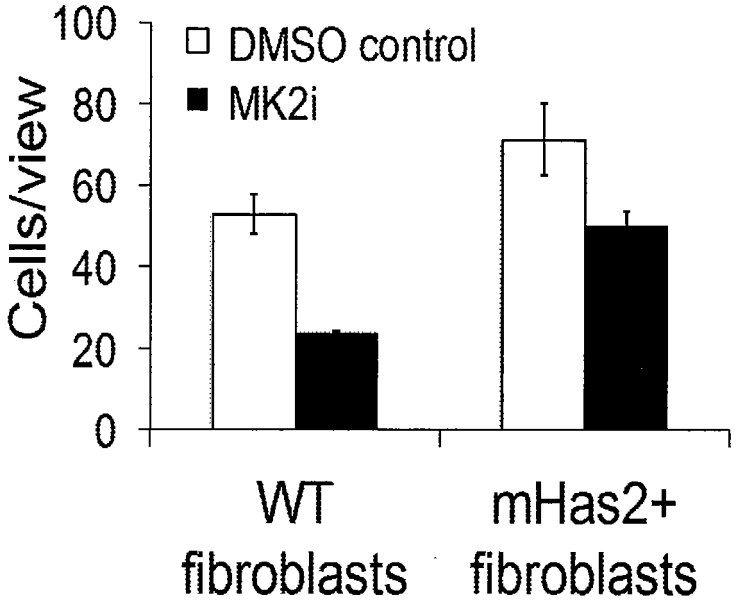

100
80
60
40
20
0
Cells/view
DMSO control
MK2i
WT fibroblasts
mHas2+ fibroblasts

FIGURE 41

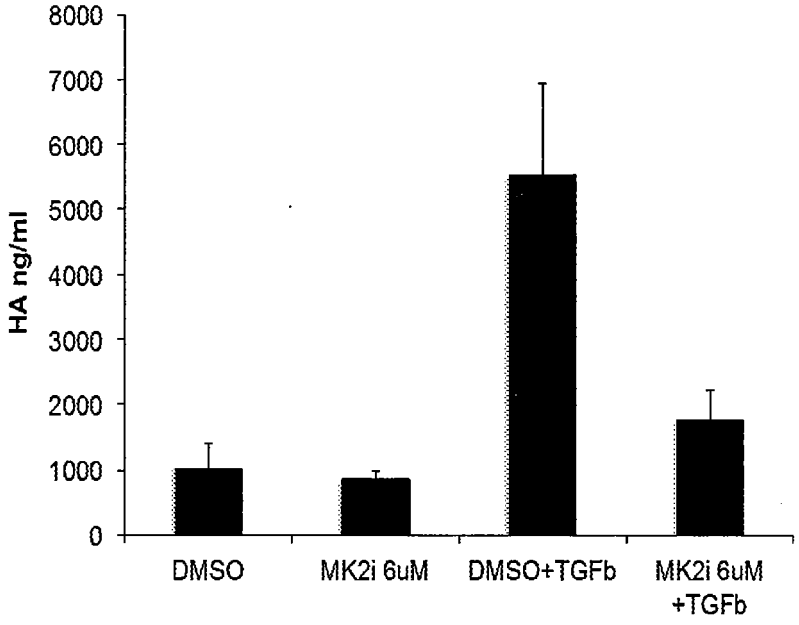

8000
7000
6000
5000
4000
3000
2000
1000
0
HA ng/ml
DMSO
MK2i 6uM
DMSO+TGFb
MK2i 6uM +TGFb

FIGURE 42

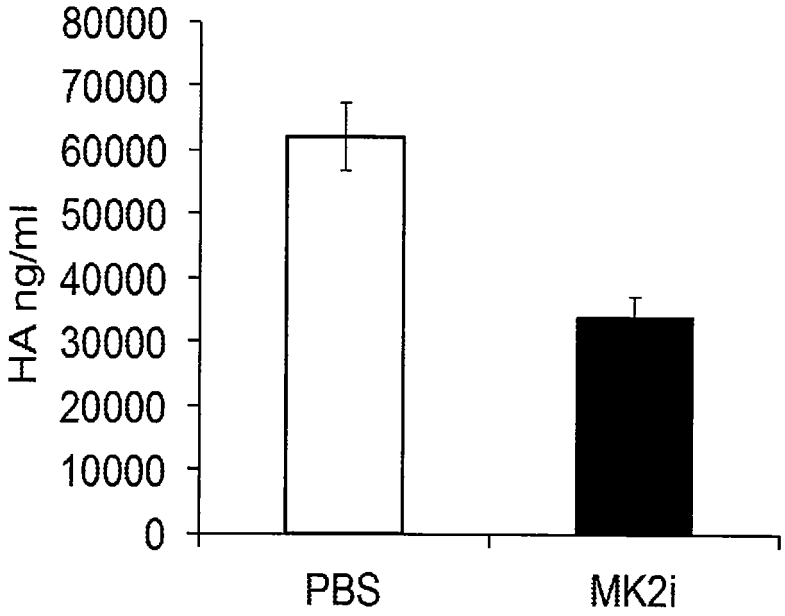

80000
70000
60000
50000
40000
30000
20000
10000
0
HA ng/ml
PBS
MK2i

FIGURE 43