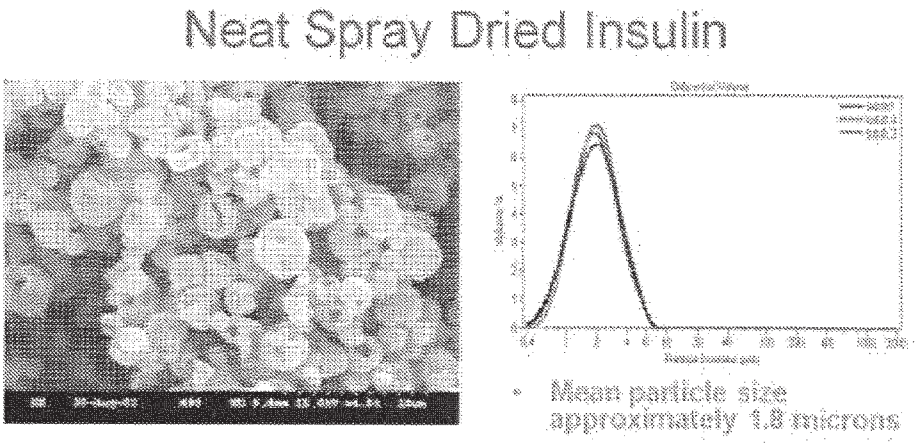

Neat Spray Dried Insulin
• Mean particle size approximately 1.8 microns

FIGURE 1

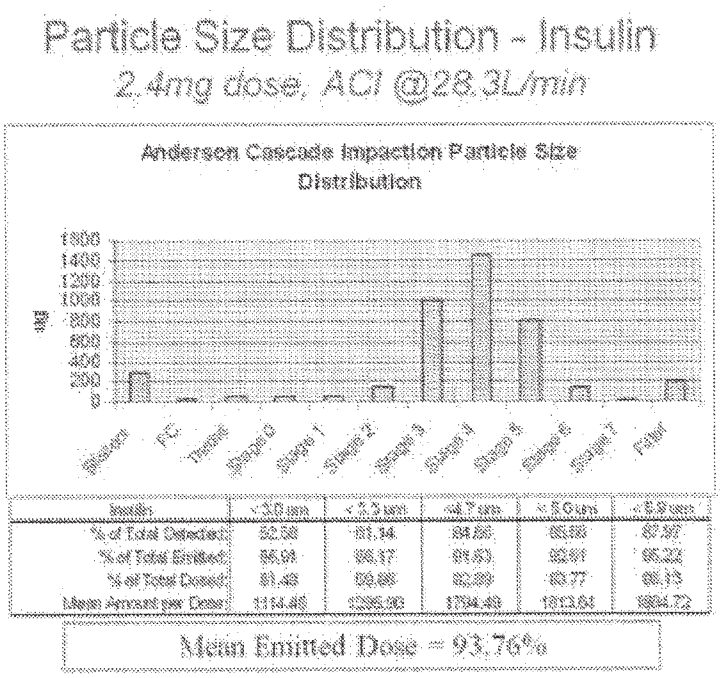
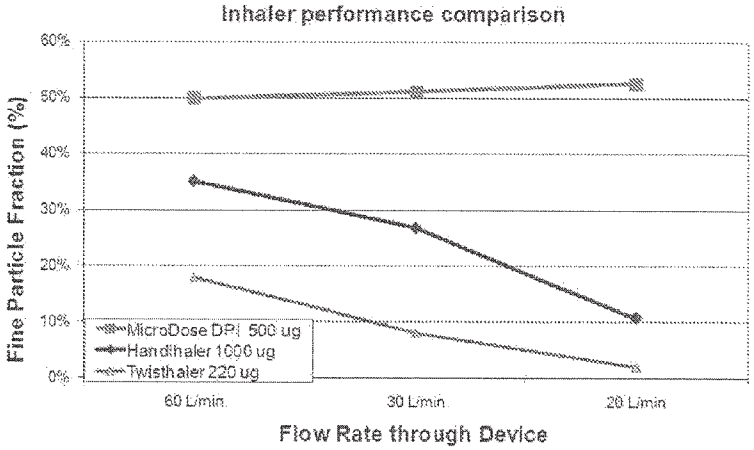

Particle Size Distribution - Insulin
2.4mg dose, ACI @28.3L/min
Andersen Cascade Impaction Particle Size Distribution
Mean Emitted Dose = 93.76%

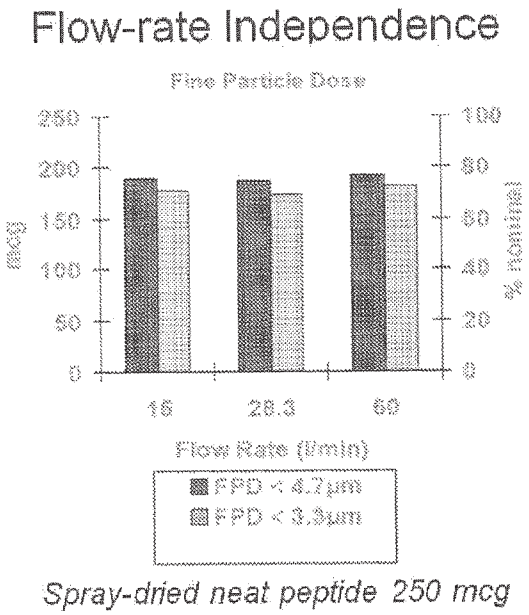
FIGURE 2

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



Jet milled (micronized) corticosteroid w/lactose

FIGURE 3



Spray-dried neat peptide 250 mcg

FIGURE 4

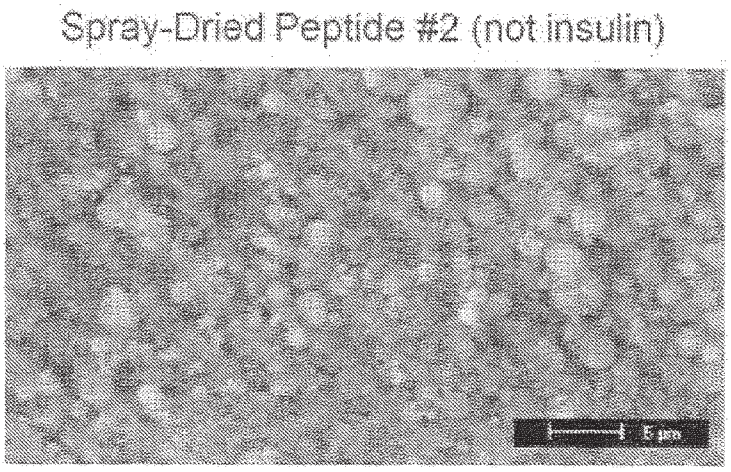


FIGURE 5

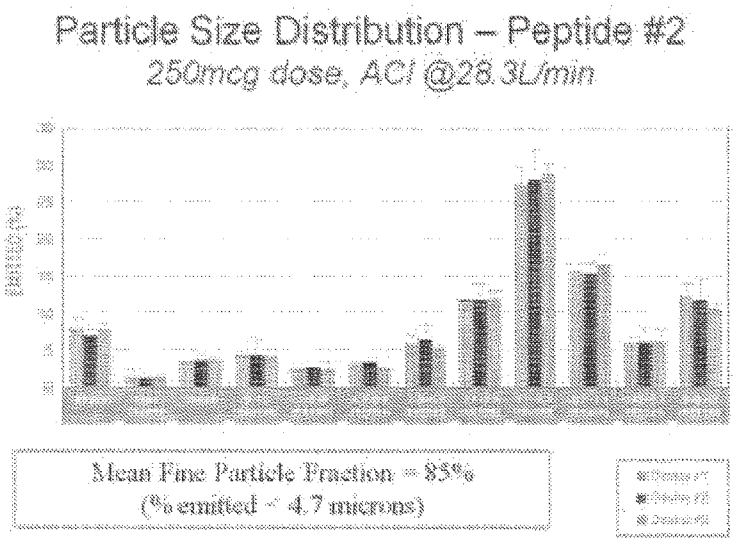

Particle Size Distribution – Peptide #2
250mcg dose, ACI @28.3L/min
Mean Fine Particle Fraction = 85%
(% emitted < 4.7 microns)

FIGURE 6

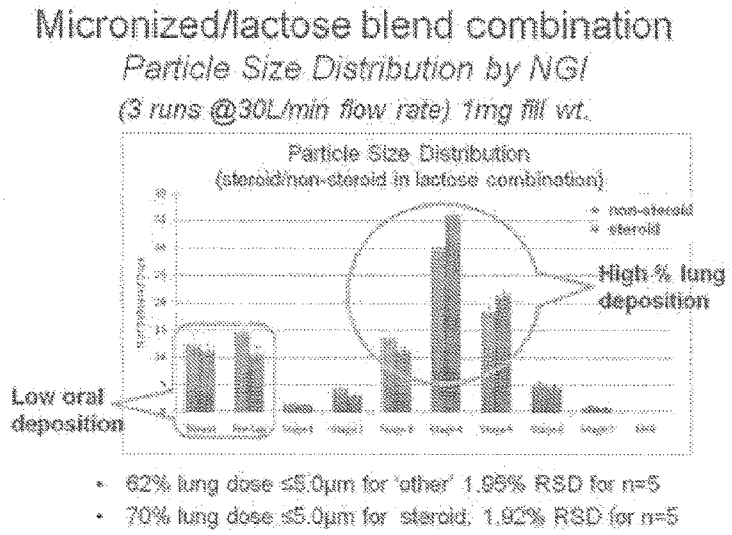

Micronized/lactose blend combination
Particle Size Distribution by NGI
(3 runs @30L/min flow rate) 1mg fill wt.
Particle Size Distribution
(steroid/non-steroid in lactose combination)
non-steroid
steroid
High % lung deposition
Low oral deposition
62% lung dose ≤5.0µm for 'other' 1.95% RSD for n=5
70%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

FIGURE 7

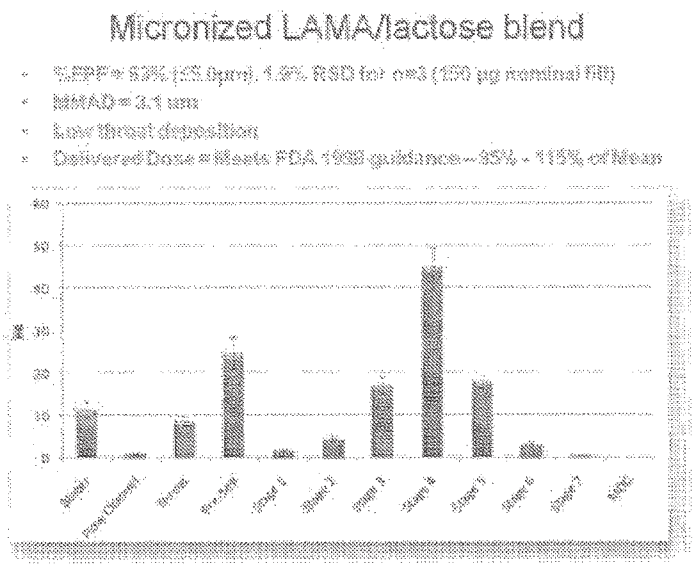

Micronized LAMA/lactose blend
Model
Throat
Stage 1
Stage 2
Stage 3
Stage 4
Stage 5
Stage 6
Stage 7
MOC

FIGURE 8

Activated MK2 Differentially Expressed in Human IPF vs. Normal Lung

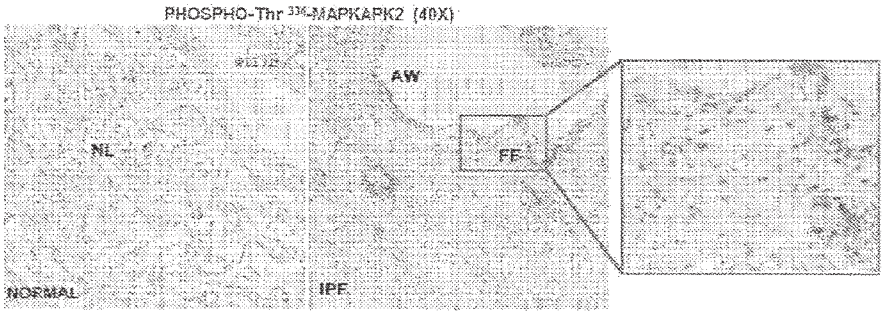


FIGURE 9

Bleomycin Model of Idiopathic Pulmonary Fibrosis: Prevention Model

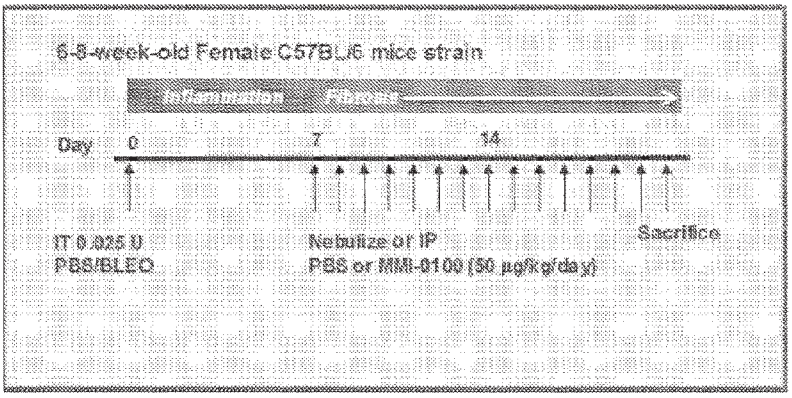


FIGURE 10

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

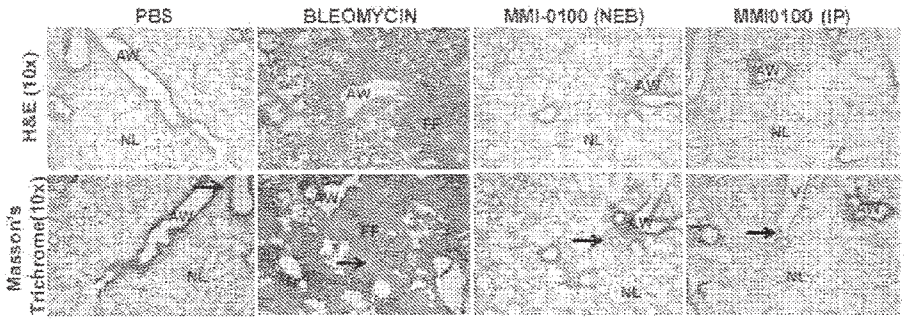


FIGURE 11

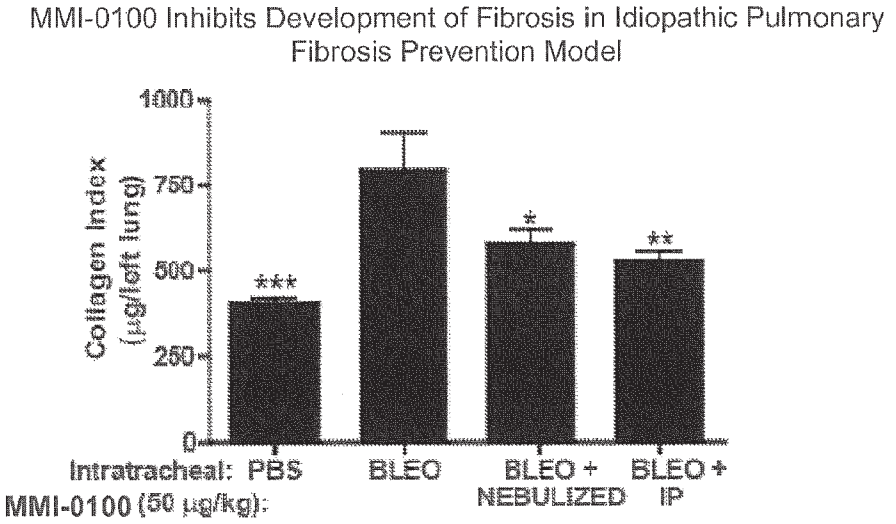

MMI-0100 Inhibits Development of Fibrosis in Idiopathic Pulmonary Fibrosis Prevention Model
Collagen Index (µg/left lung)
1000
750
500
250
0
***
*
**
Intratracheal: PBS
BLEO
BLEO + NEBULIZED
BLEO + IP
MMI-0100 (50 µg/kg):

FIGURE 12

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

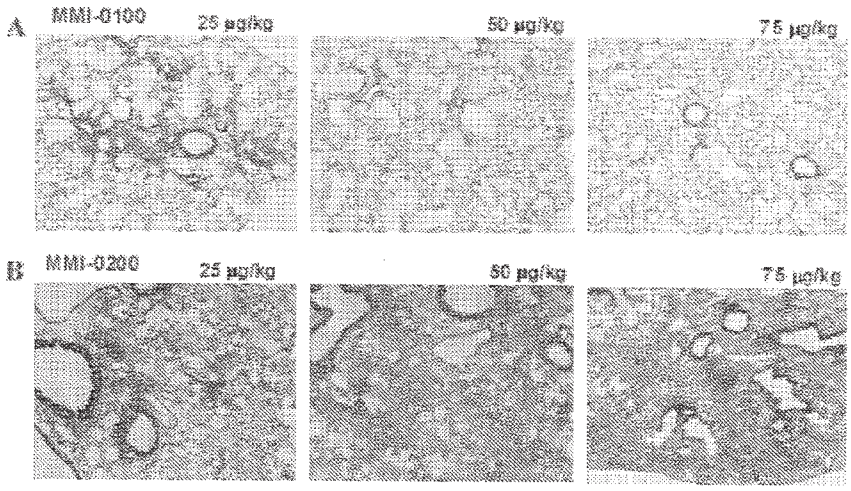


FIGURE 13

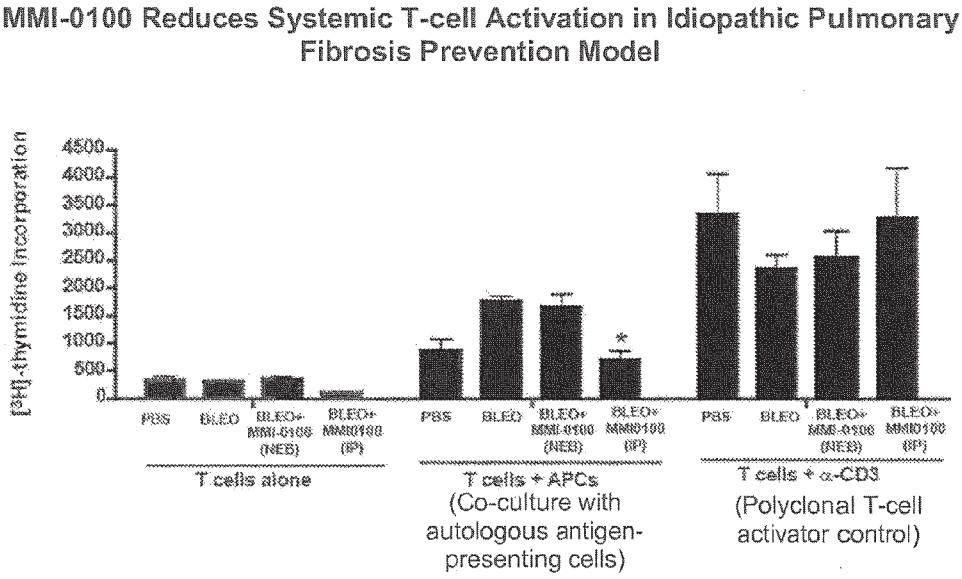

MMI-0100 Reduces Systemic T-cell Activation in Idiopathic Pulmonary Fibrosis Prevention Model
[3H]-thymidine incorporation
4500
4000
3500
3000
2500
2000
1500
1000
500
0
PBS
BLEO
BLEO+ MMI-0100 (NEB)
BLEO+ MMI0100 (IP)
*
T cells alone
T cells + APCs
(Co-culture with autologous antigen-presenting cells)
T cells + α-CD3
(Polyclonal T-cell activator control)

FIGURE 14

Bleomycin Model of Idiopathic Pulmonary Fibrosis: Treatment Model

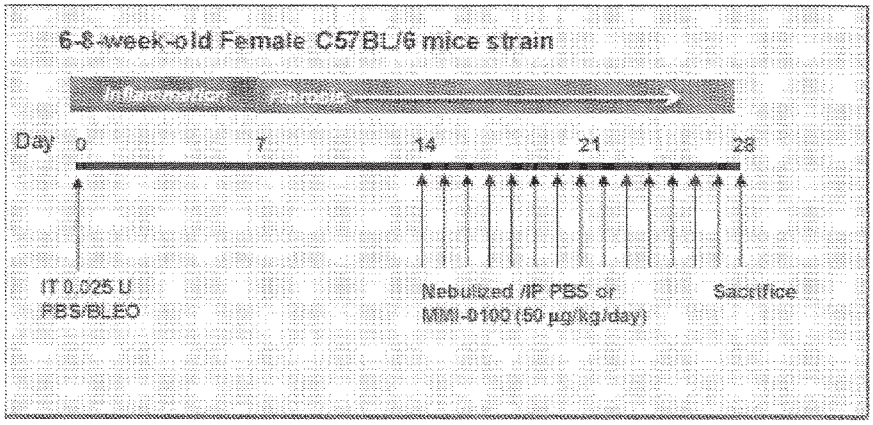


FIGURE 15

DRAWING SHEET 16/25

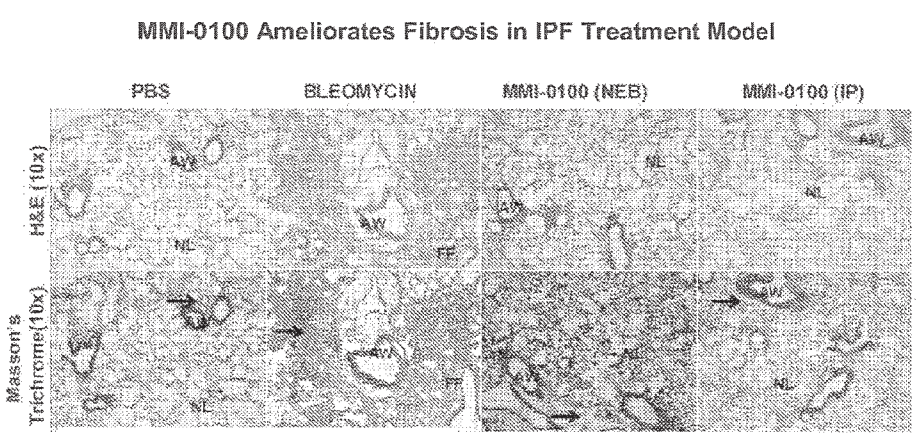


FIGURE 16

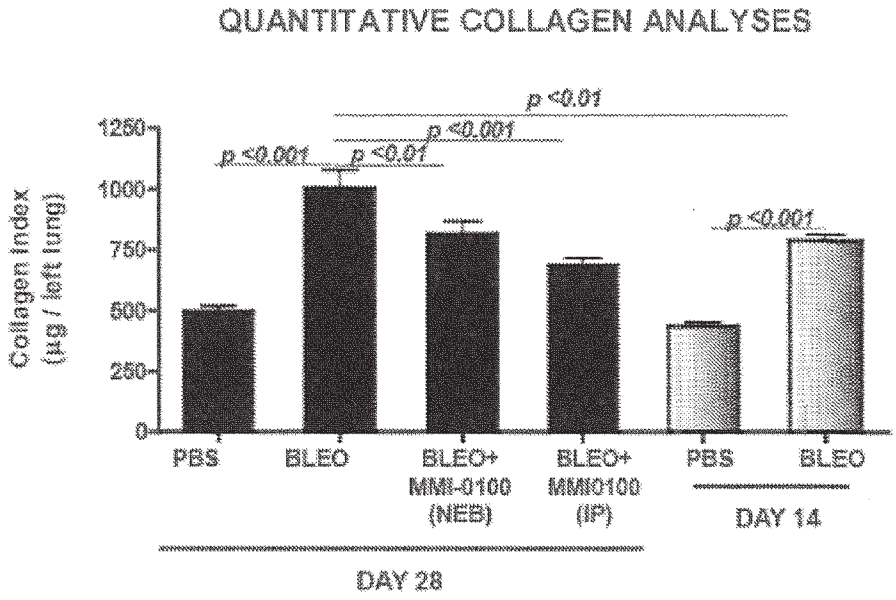

QUANTITATIVE COLLAGEN ANALYSES
Collagen Index (µg / left lung)
1250
1000
750
500
250
0
p <0.01
p <0.001
p <0.001
p <0.01
p <0.001
PBS
BLEO
BLEO+ MMI-0100 (NEB)
BLEO+ MMI0100 (IP)
PBS
BLEO
DAY 14
DAY 28

FIGURE 17

Reduced Activated MK2 with MMI-0100 in IPF Treatment Model

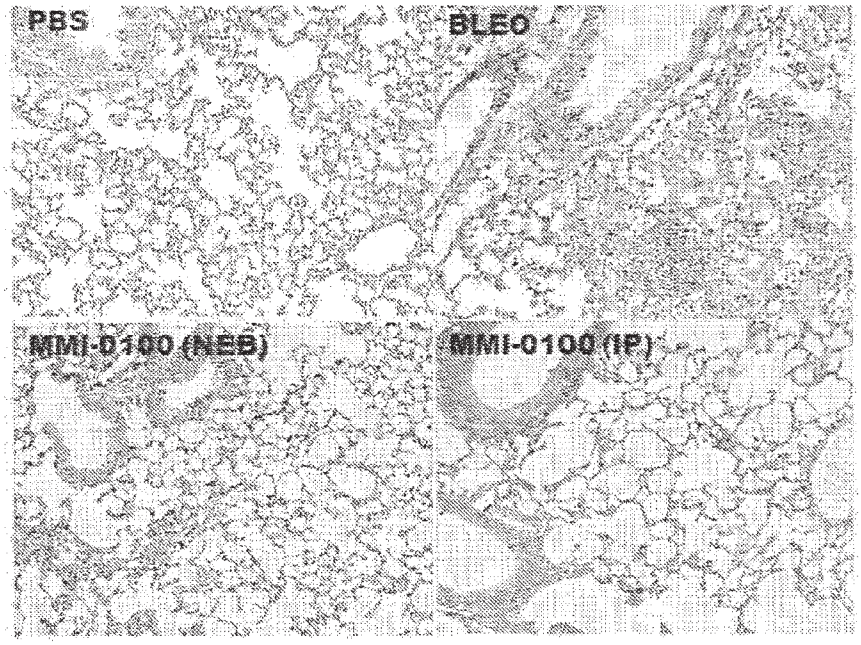


FIGURE 18

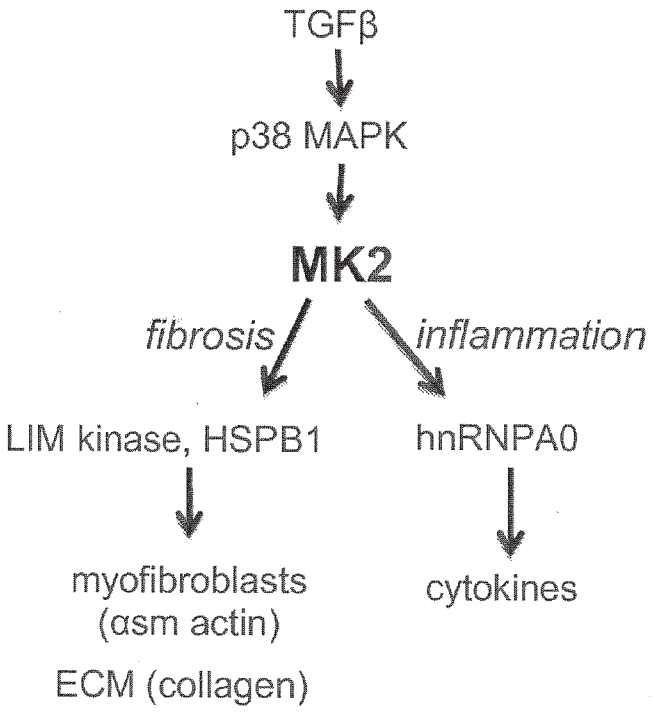

TGFβ
p38 MAPK
MK2
fibrosis
inflammation
LIM kinase, HSPB1
hnRNPA0
myofibroblasts
(αsm actin)
ECM (collagen)
cytokines

FIGURE 19

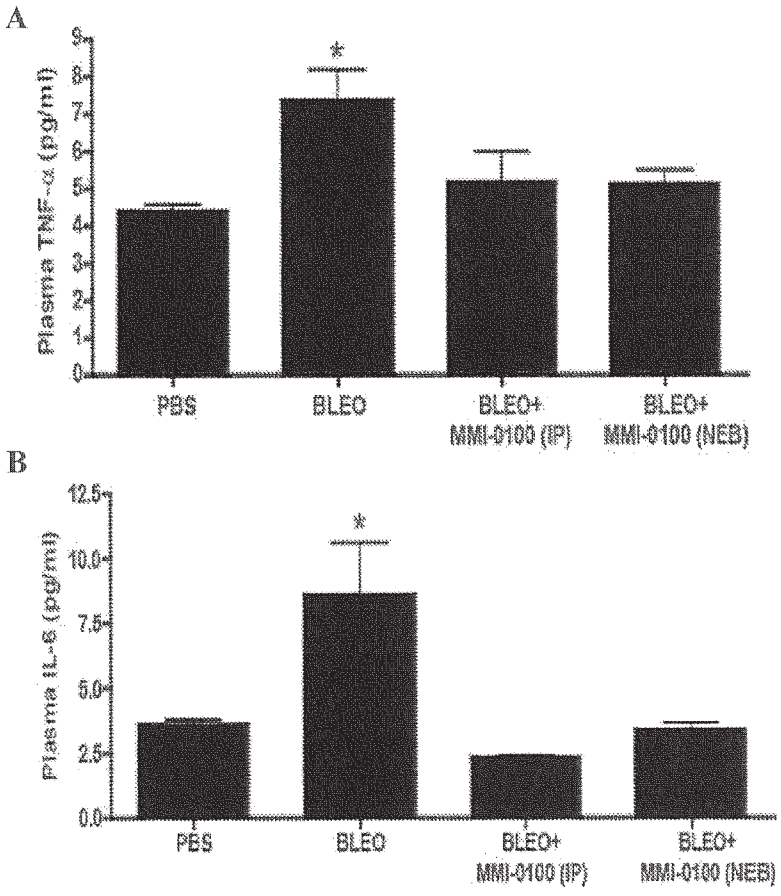

A
Plasma TNF-α (pg/ml)
0
1
2
3
4
5
6
7
8
9
*
PBS
BLEO
BLEO+ MMI-0100 (IP)
BLEO+ MMI-0100 (NEB)
B
Plasma IL-6 (pg/ml)
0.0
2.5
5.0
7.5
10.0
12.5
*
PBS
BLEO
BLEO+ MMI-0100 (IP)
BLEO+ MMI-0100 (NEB)

FIGURE 20

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

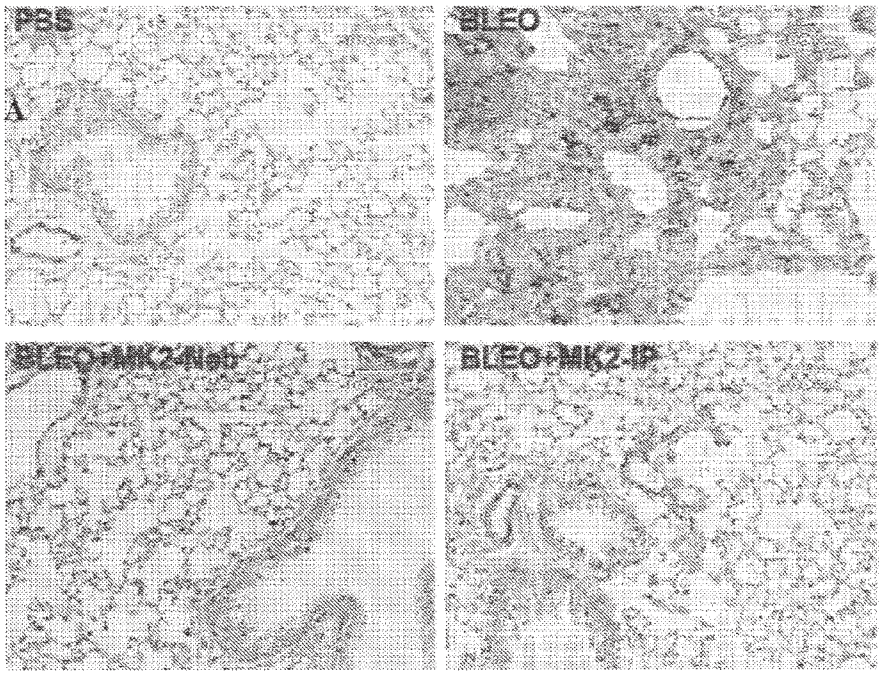


FIGURE 21

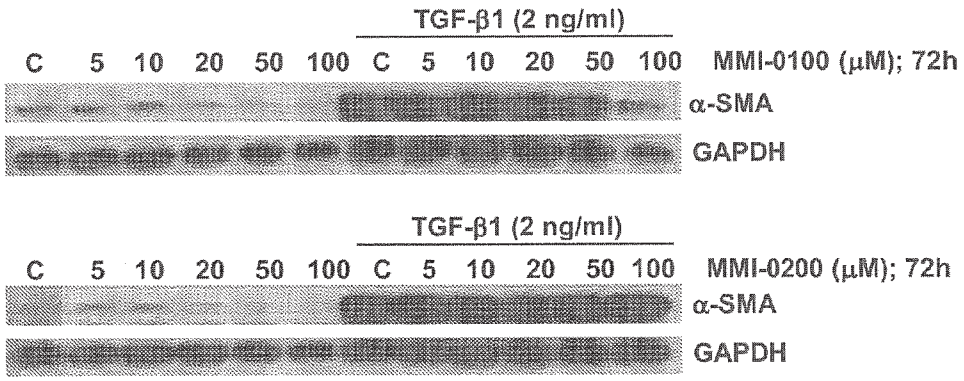

TGF-β1 (2 ng/ml)
C 5 10 20 50 100 C 5 10 20 50 100
MMI-0100 (μM); 72h
α-SMA
GAPDH
TGF-β1 (2 ng/ml)
C 5 10 20 50 100 C 5 10 20 50 100
MMI-0200 (μM); 72h
α-SMA
GAPDH

FIGURE 22

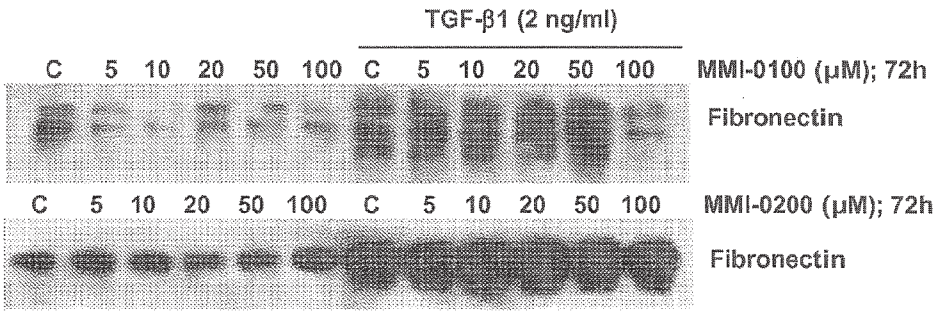

TGF-β1 (2 ng/ml)
C 5 10 20 50 100 C 5 10 20 50 100
MMI-0100 (μM); 72h
Fibronectin
C 5 10 20 50 100 C 5 10 20 50 100
MMI-0200 (μM); 72h
Fibronectin

FIGURE 23

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

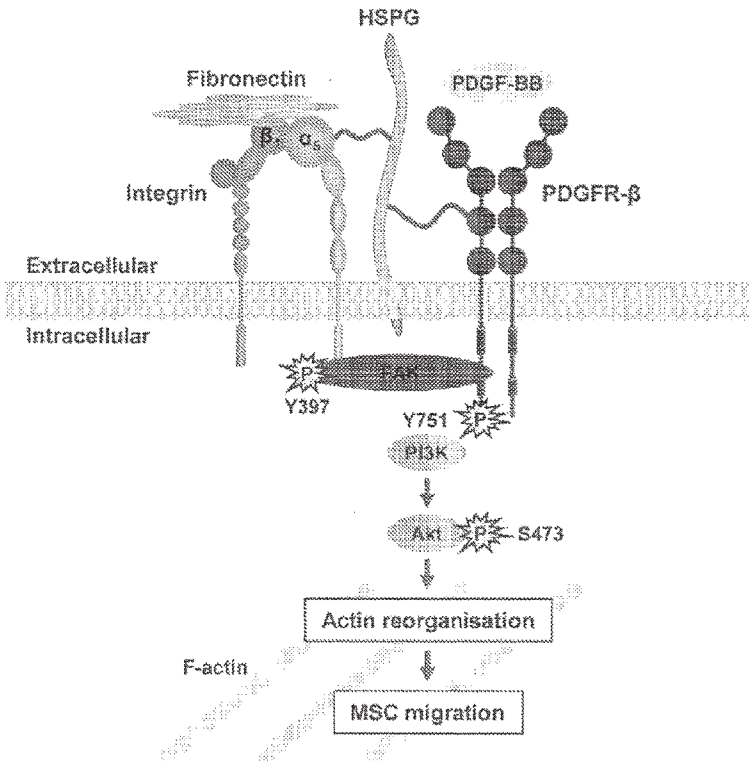
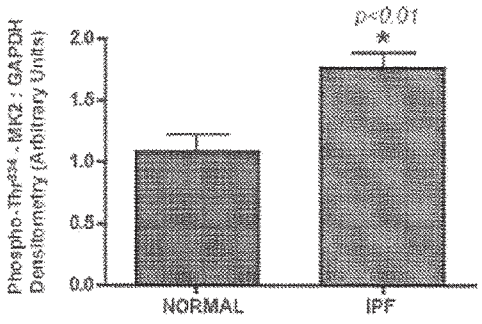


FIGURE 24

A


p<0.01
*
Phospho-Thr334 - MK2 : GAPDH
Densitometry (Arbitrary Units)
2.0
1.5
1.0
0.5
0.0
NORMAL
IPF

B

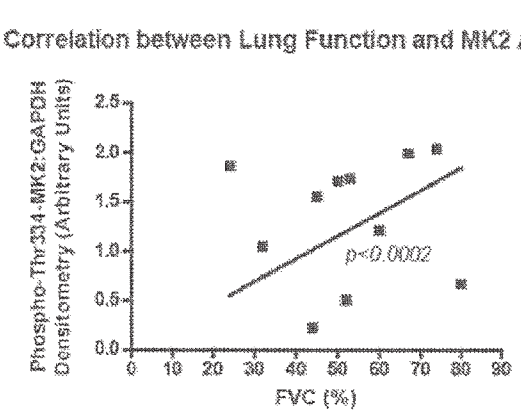

Correlation between Lung Function and MK2 Activation
Phospho-Thr334-MK2:GAPDH
Densitometry (Arbitrary Units)
2.5
2.0
1.5
1.0
0.5
0.0
p<0.0002
0
10
20
30
40
50
60
70
80
90
FVC (%)

FIGURE 25