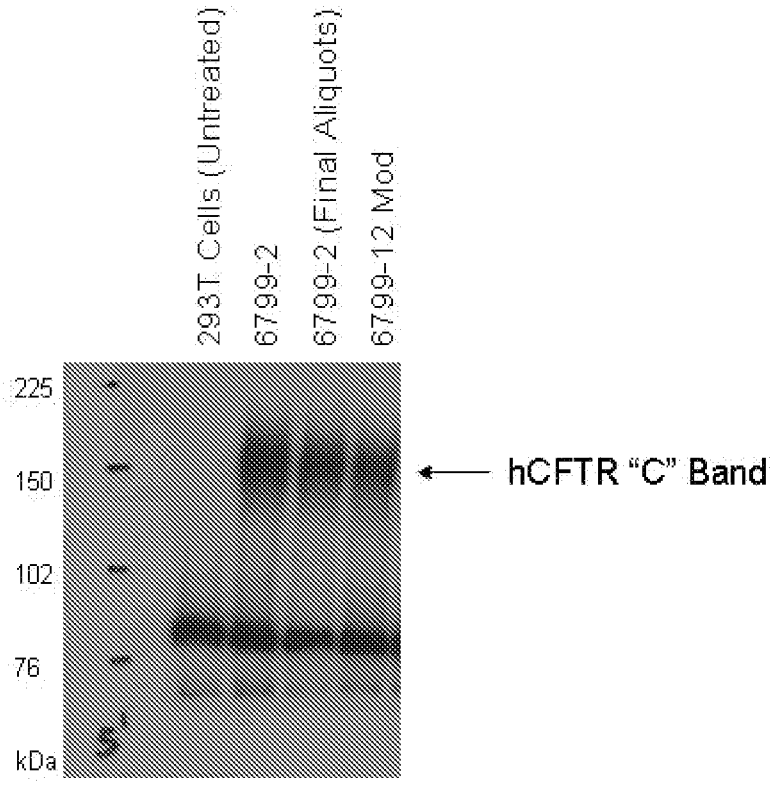

293T Cells (Untreated)
6799-2
6799-2 (Final Aliquots)
6799-12 Mod
225
150
102
76
kDa
hCFTR "C" Band

Figure 1A

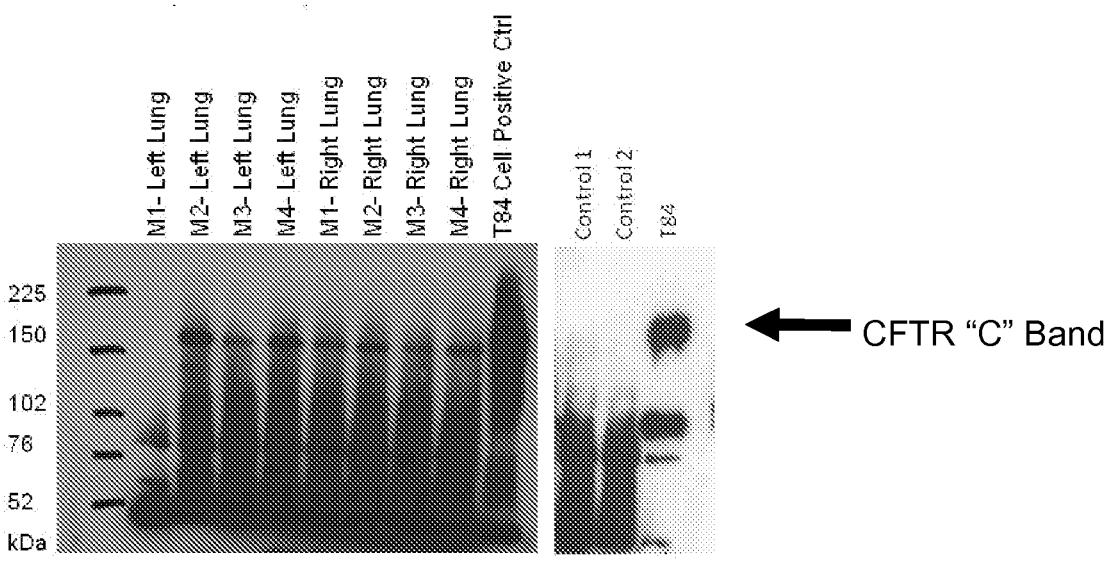

M1- Left Lung
M2- Left Lung
M3- Left Lung
M4- Left Lung
M1- Right Lung
M2- Right Lung
M3- Right Lung
M4- Right Lung
T84 Cell Positive Ctrl
Control 1
Control 2
T84
225
150
102
76
52
kDa
CFTR "C" Band

Figure 1B

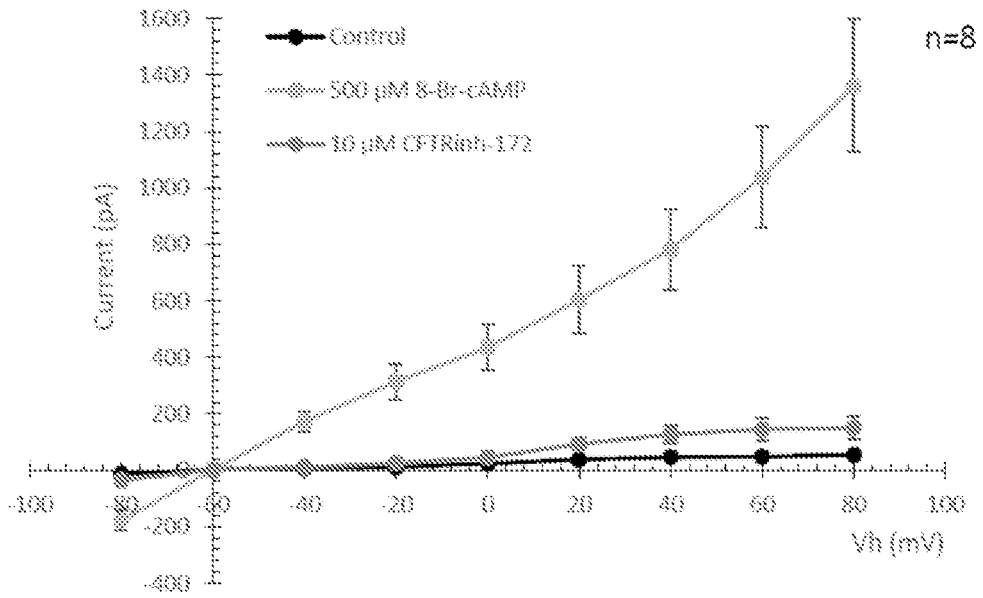

Control
500 µM 8-Br-cAMP
10 µM CFTRinh-172
n=8
Current (pA)
Vh (mV)
1600
1400
1200
1000
800
600
400
200
0
-200
-400
-100
-80
-60
-40
-20
0
20
40
60
80
100

Figure 2

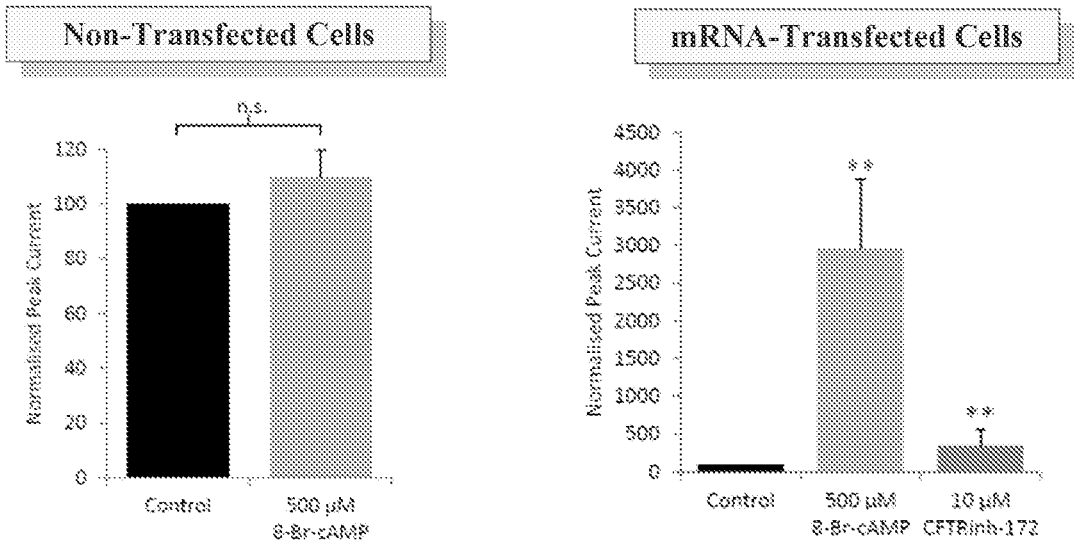

Non-Transfected Cells
n.s.
Normalized Peak Current
120
100
80
60
40
20
0
Control
500 μM
8-Br-cAMP
mRNA-Transfected Cells
Normalised Peak Current
4500
4000
3500
3000
2500
2000
1500
1000
500
0
**
**
Control
500 μM
8-Br-cAMP
10 μM
CFTRinh-172

Figure 3

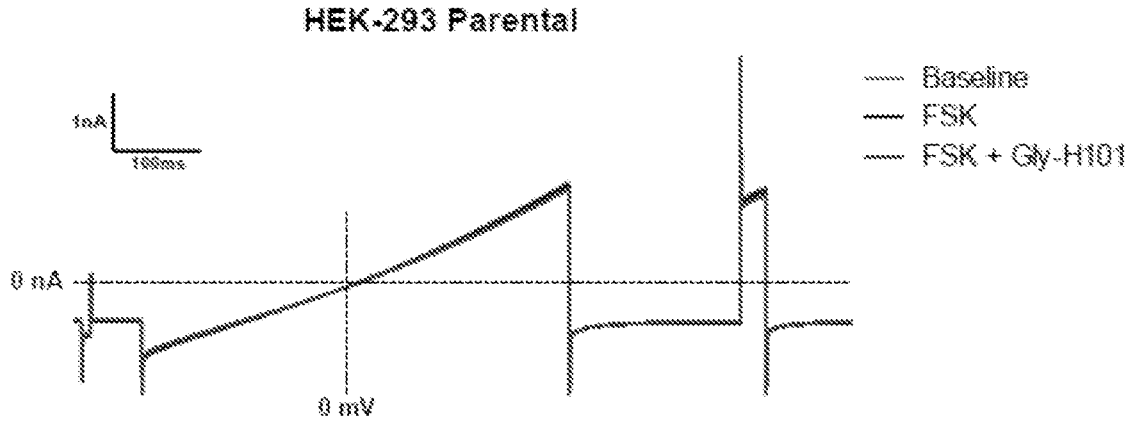


Figure 4

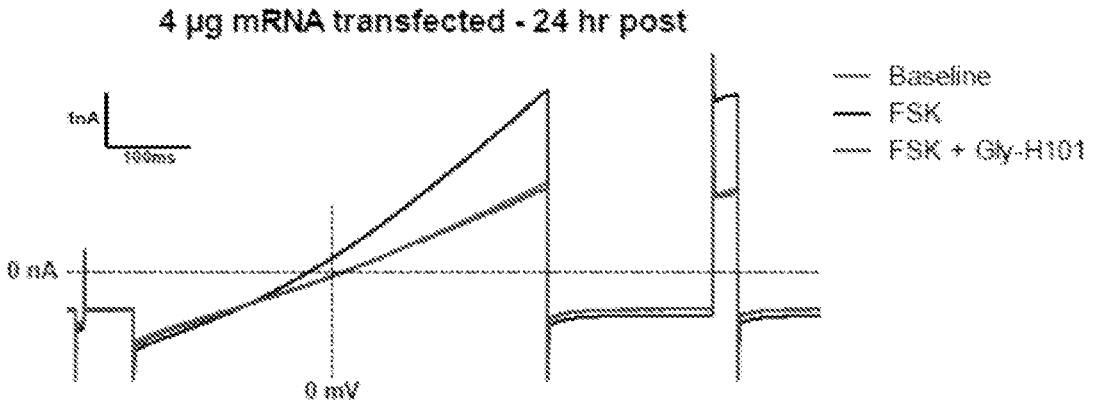

4 µg mRNA transfected - 24 hr post
Baseline
FSK
FSK + Gly-H101
nA
100ms
0 nA
0 mV

Figure 5

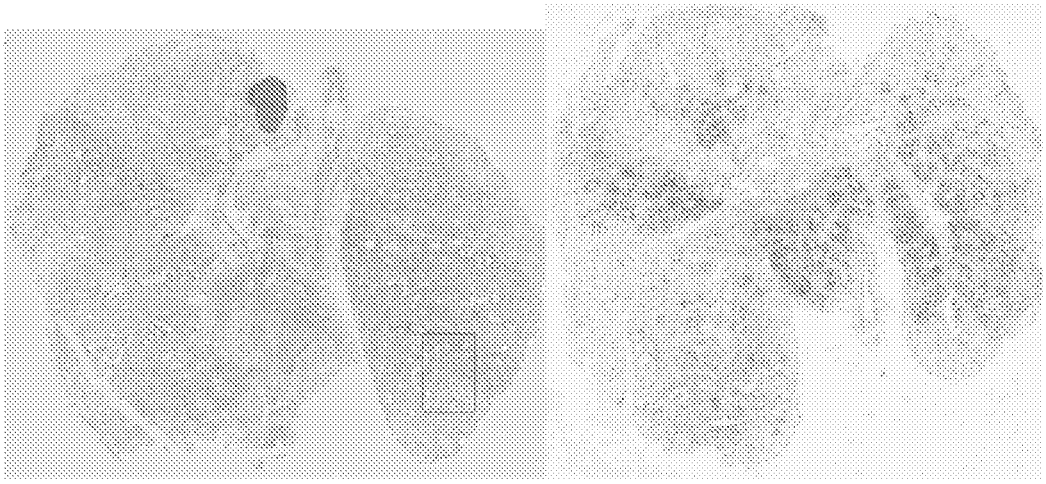


Figure 6

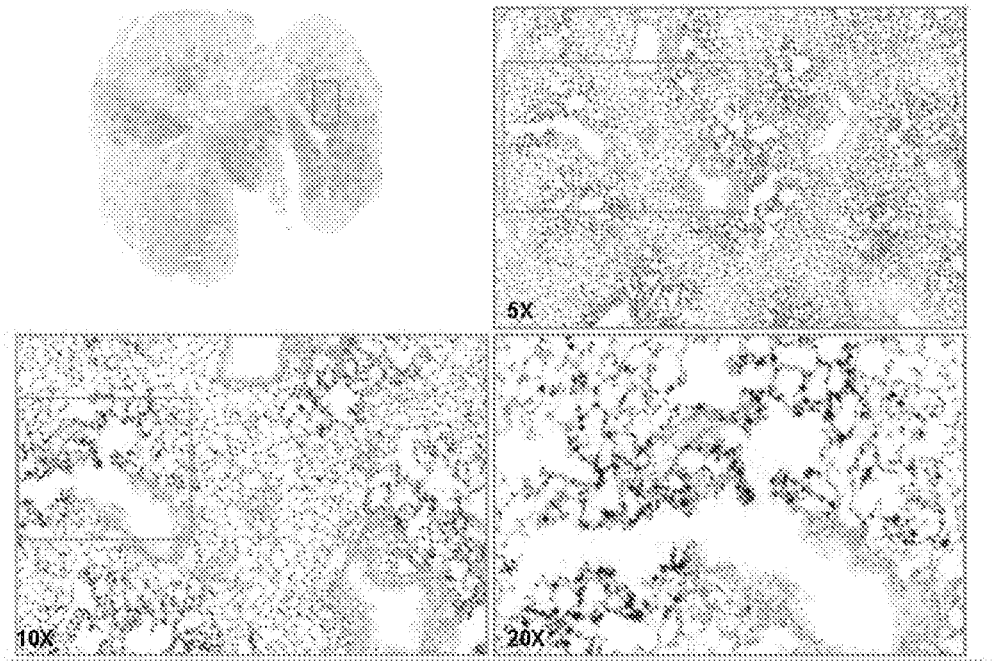


Figure 7

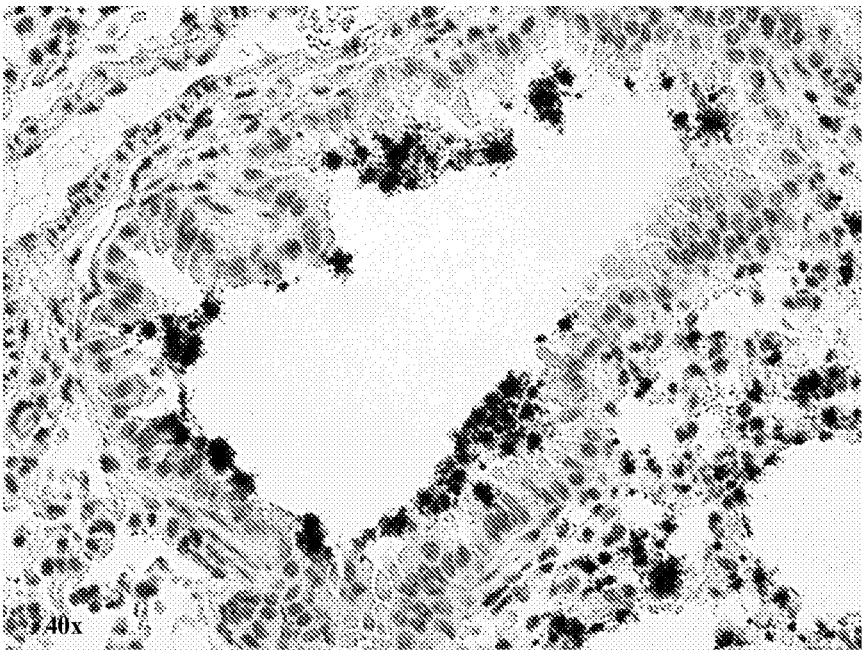


Figure 8

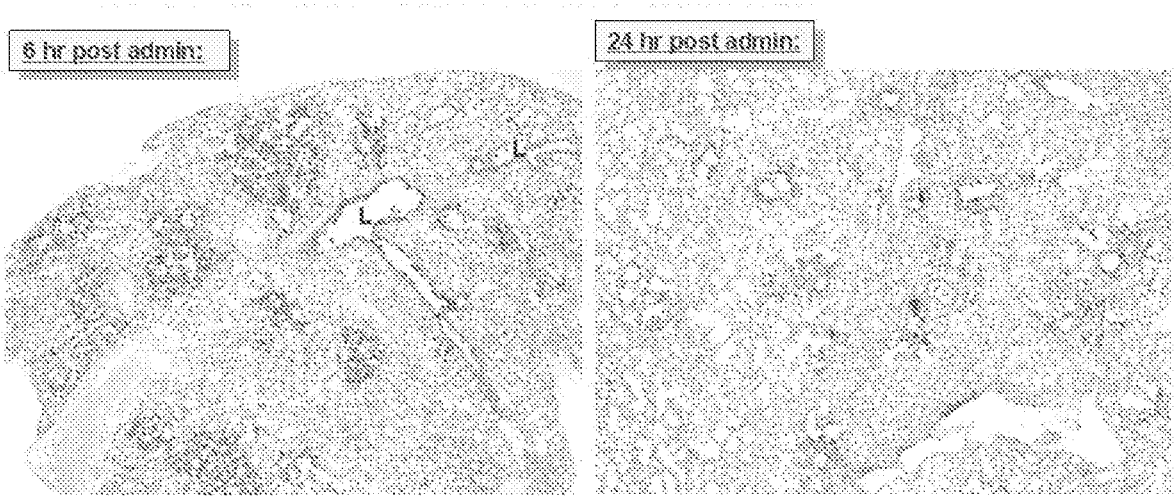


Figure 9

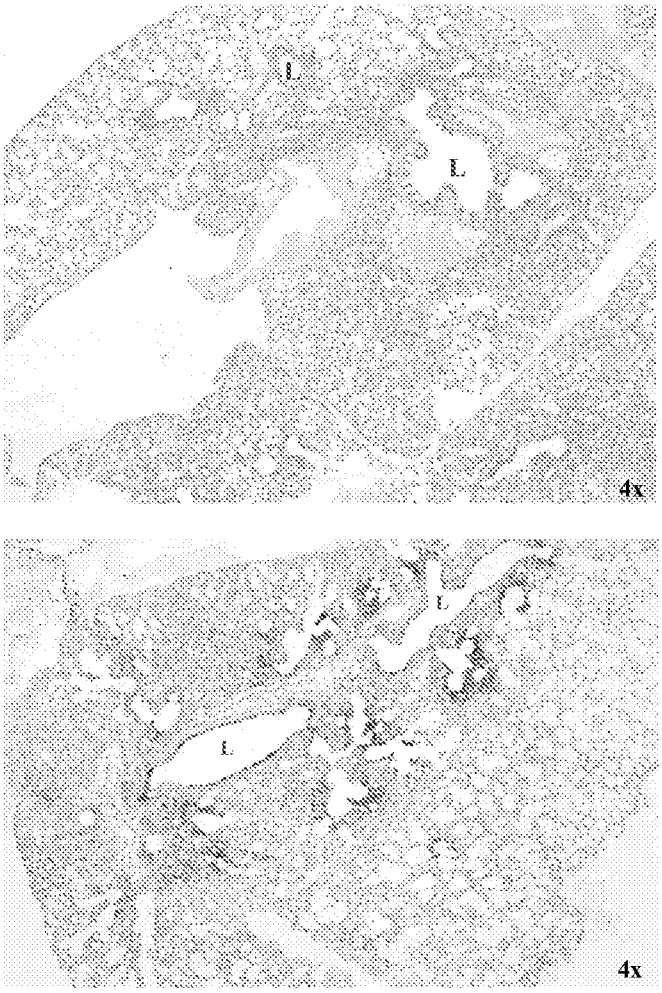


Figure 10

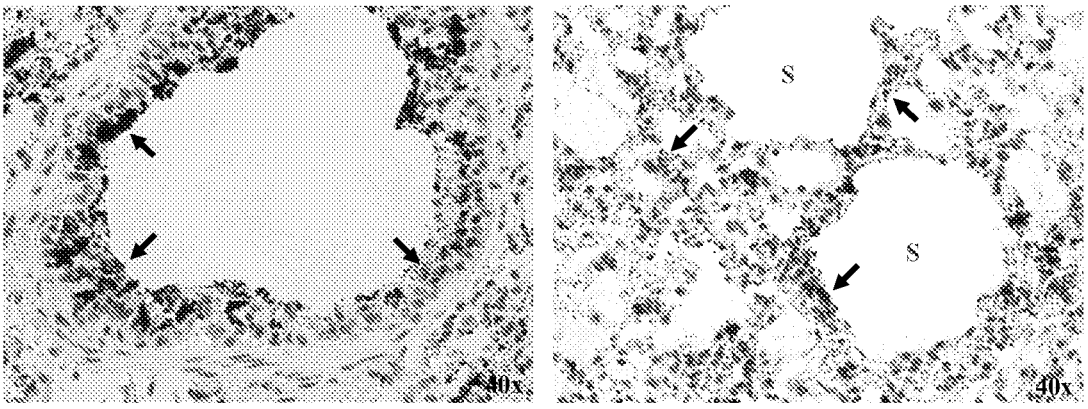
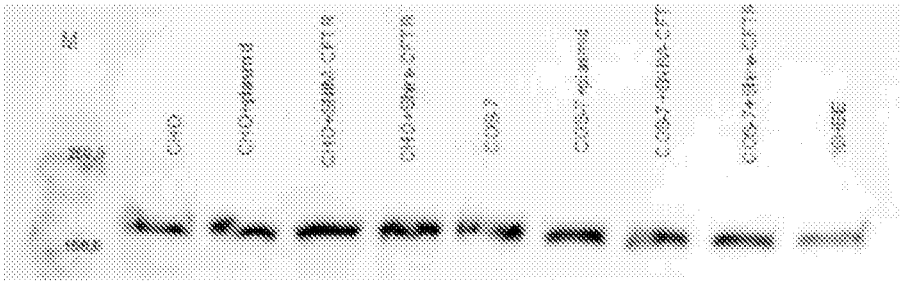
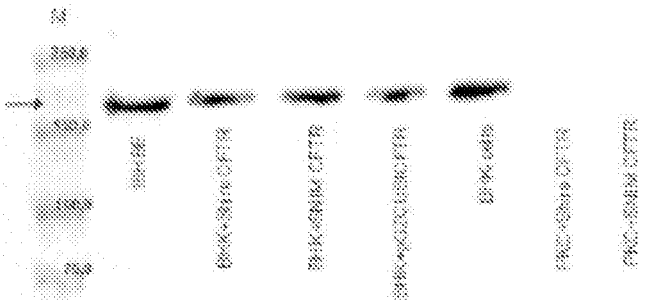


Figure 11

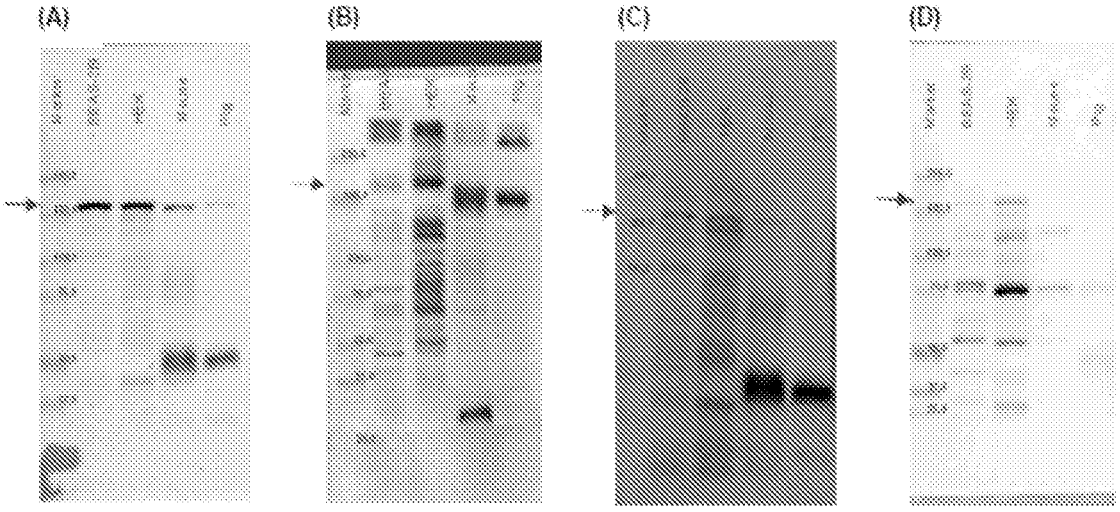
A



B



Figures 12 A & B



Figures 13 A-D

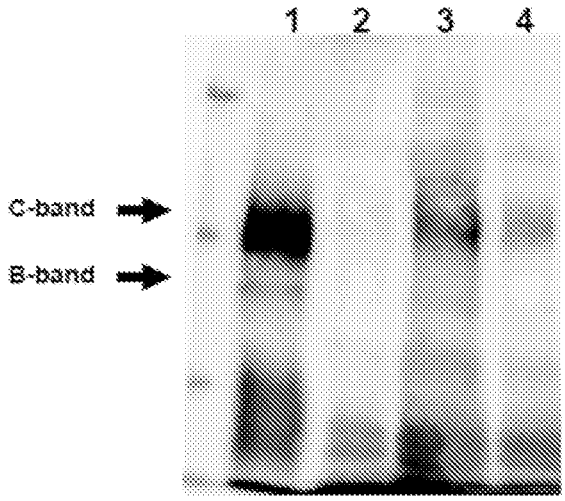


Figure 14

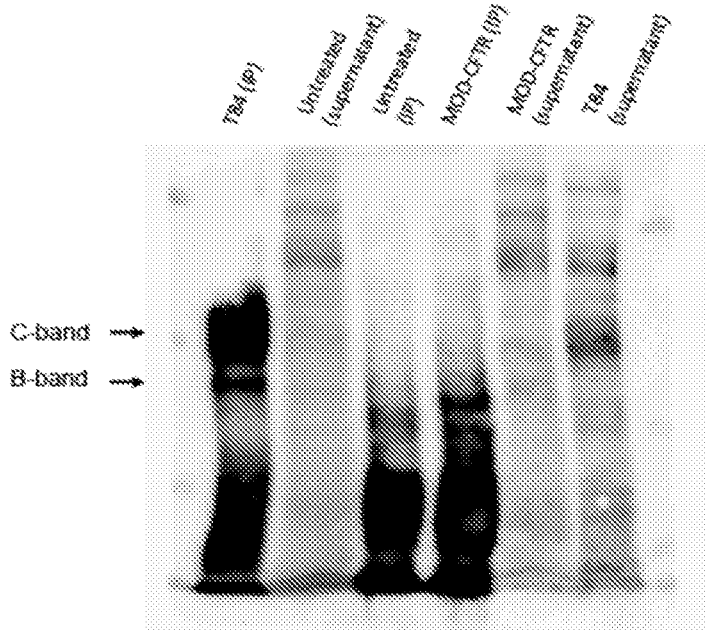

TBA (IP)
Untreated (supernatant)
Untreated (IP)
MDD-CFTR (IP)
MDD-CFTR (supernatant)
TBA (supernatant)
C-band
B-band

Figure 15

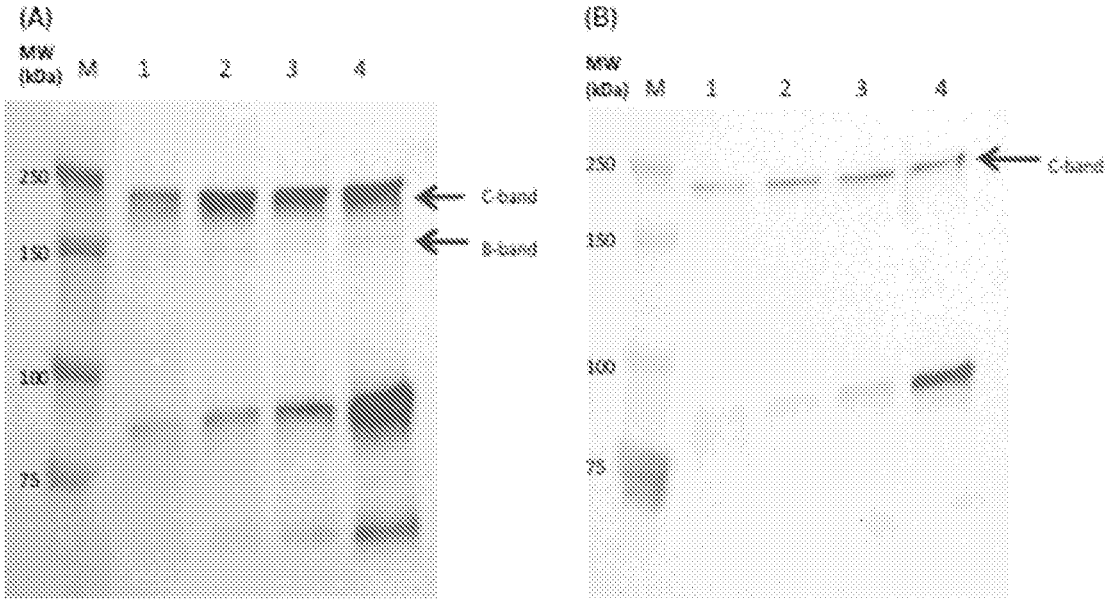

(A)
MW (kDa)
M
1
2
3
4
250
150
100
75
C-band
B-band
(B)
MW (kDa)
M
1
2
3
4
250
150
100
75
C-band

Figure 16 A&B

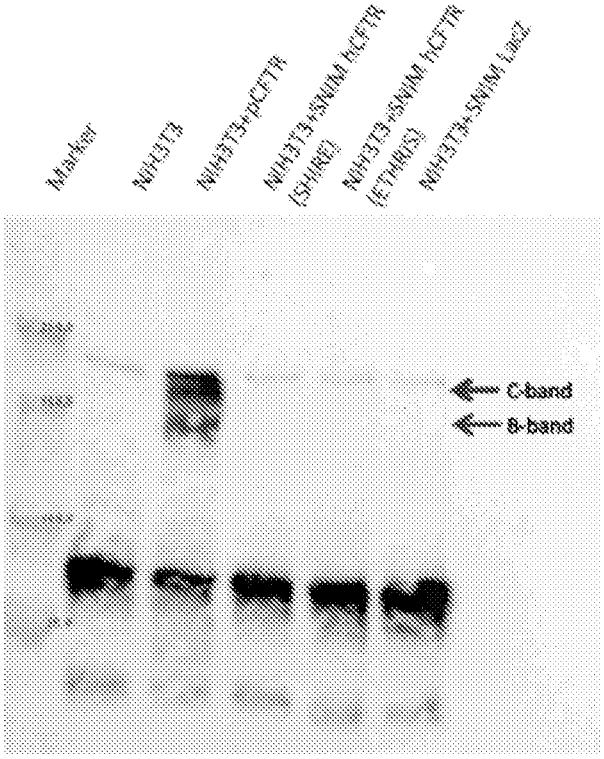

Marker
NIH3T3
NIH3T3+pCFTR
NIH3T3+SNIM hCFTR (SHIRE)
NIH3T3+SNIM hCFTR (ETHRIS)
NIH3T3+SNIM Lacz
C-band
B-band

Figure 17

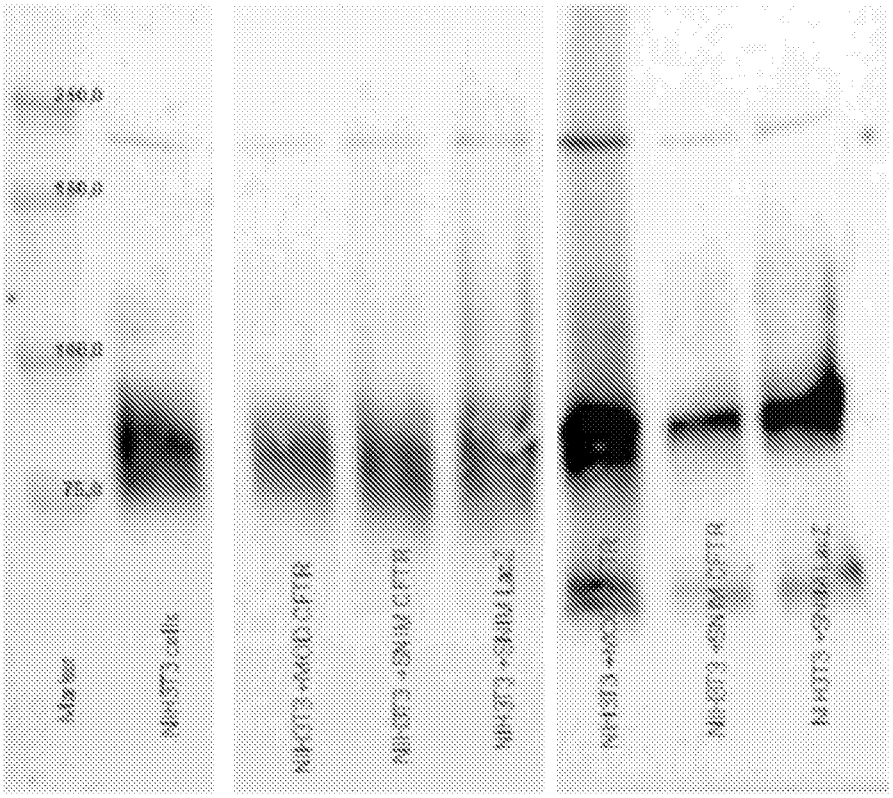


Figure 18

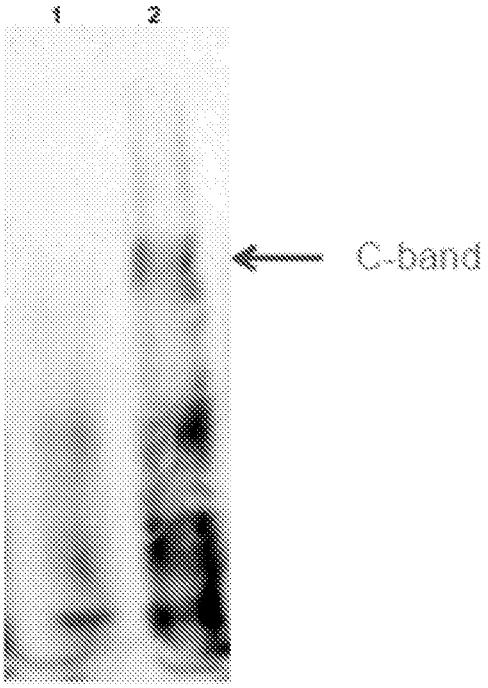


Figure 19

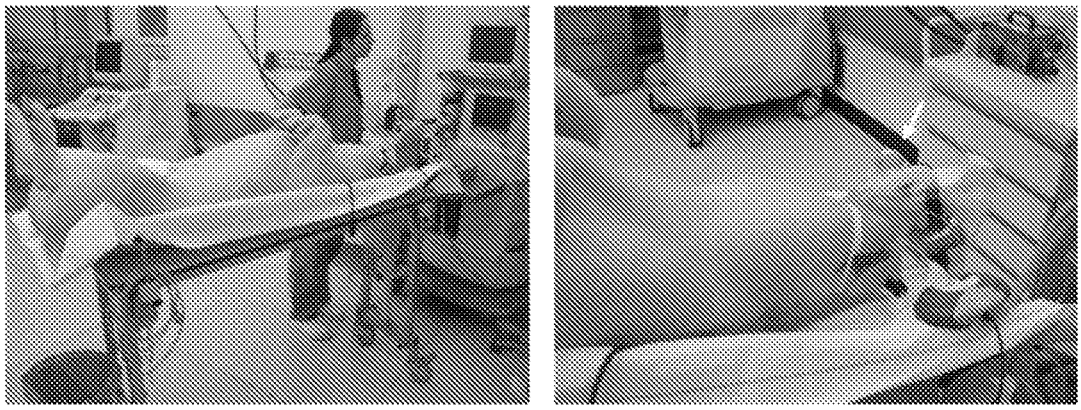


Figure 20

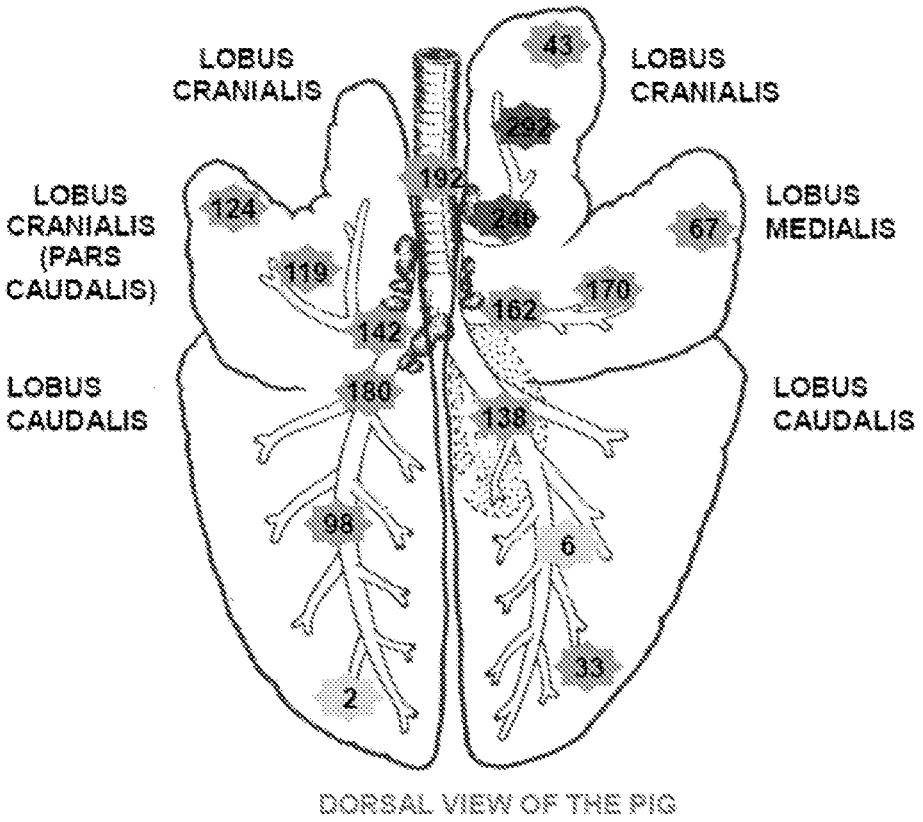

LOBUS CRANIALIS
LOBUS CRANIALIS
LOBUS CRANIALIS (PARS CAUDALIS)
LOBUS MEDIALIS
LOBUS CAUDALIS
LOBUS CAUDALIS
43
292
192
240
124
67
119
170
162
142
180
138
98
6
33
2
DORSAL VIEW OF THE PIG

Figure 21

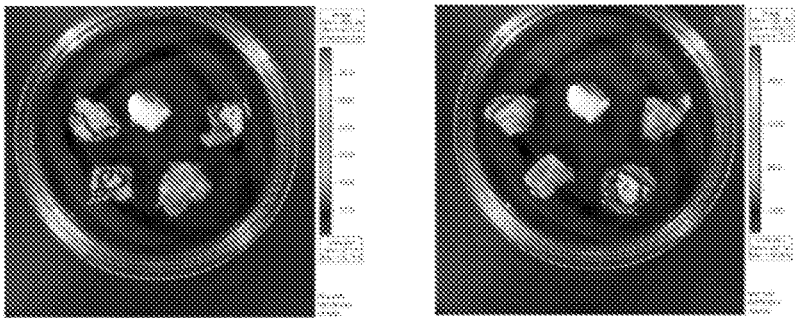


Figure 22

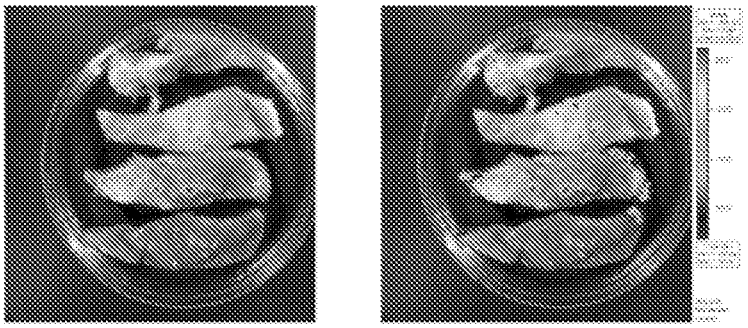


Figure 23

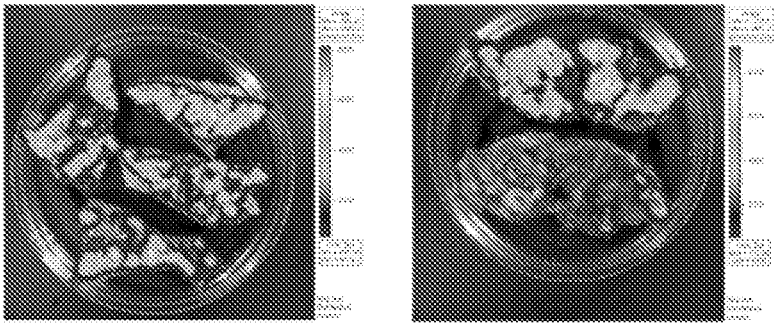


Figure 24

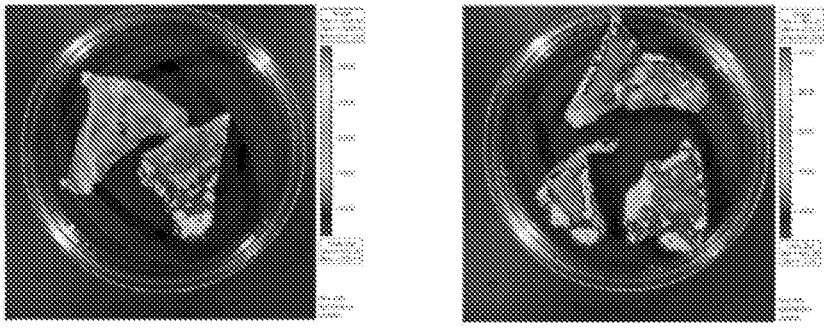


Figure 25

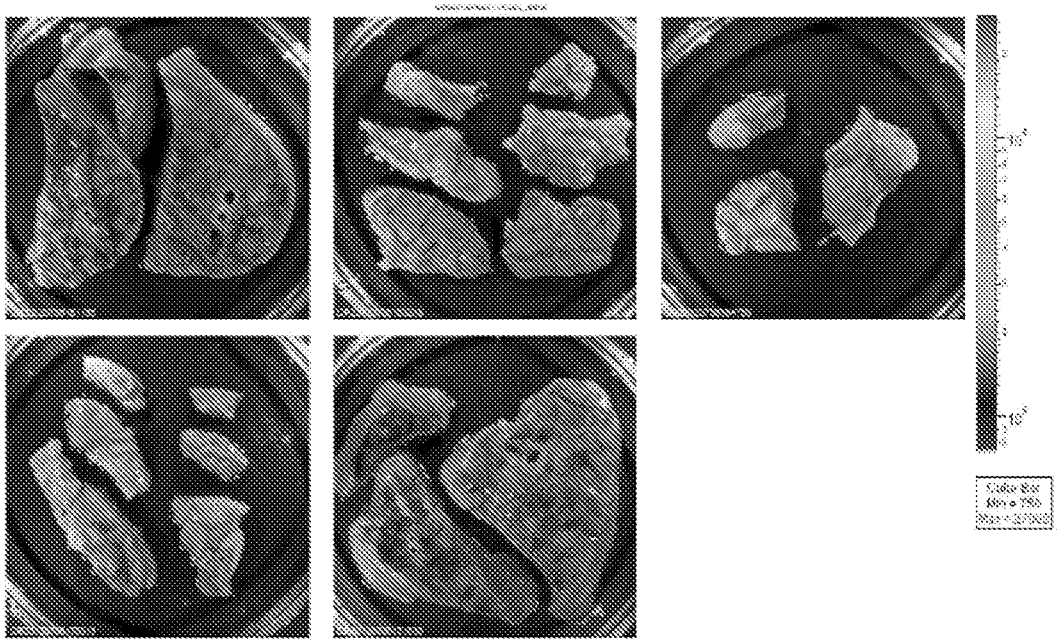


Figure 26

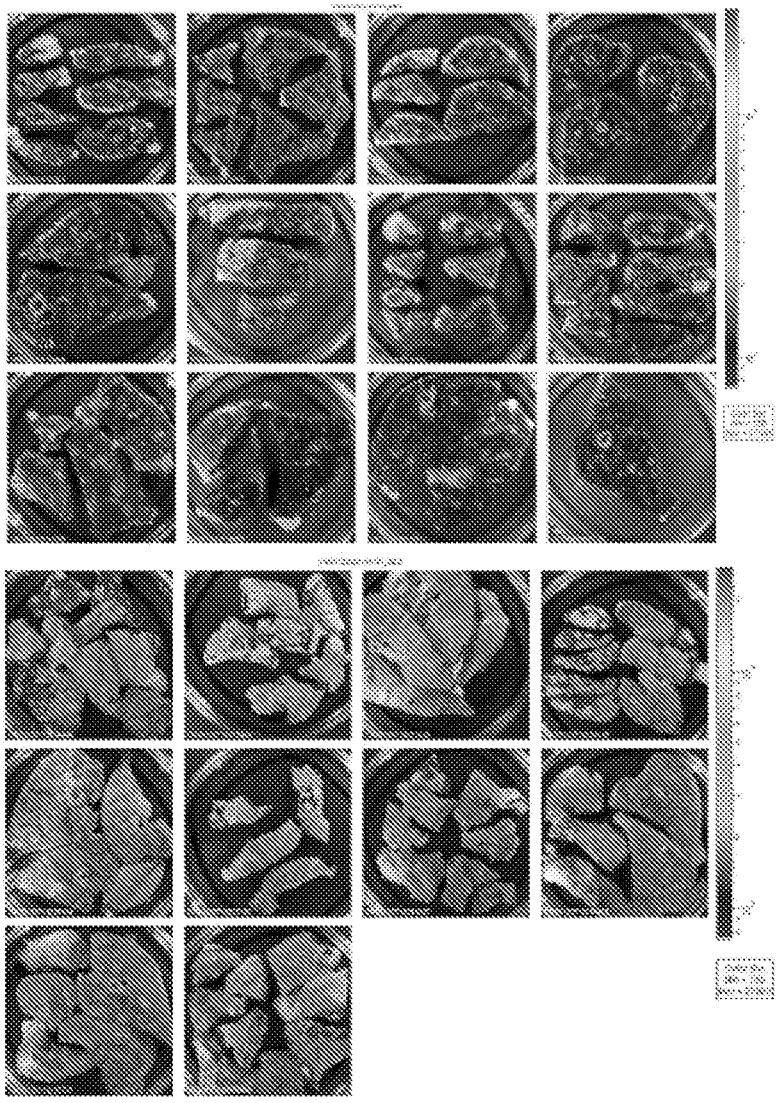


Figure 27

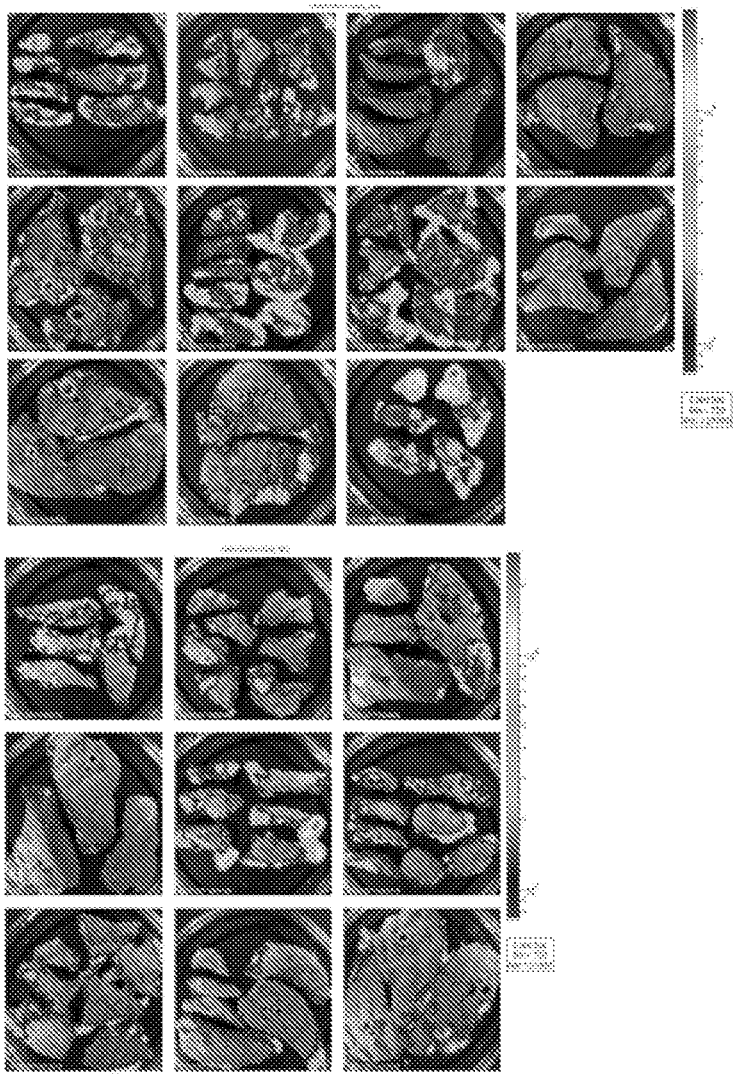


Figure 28

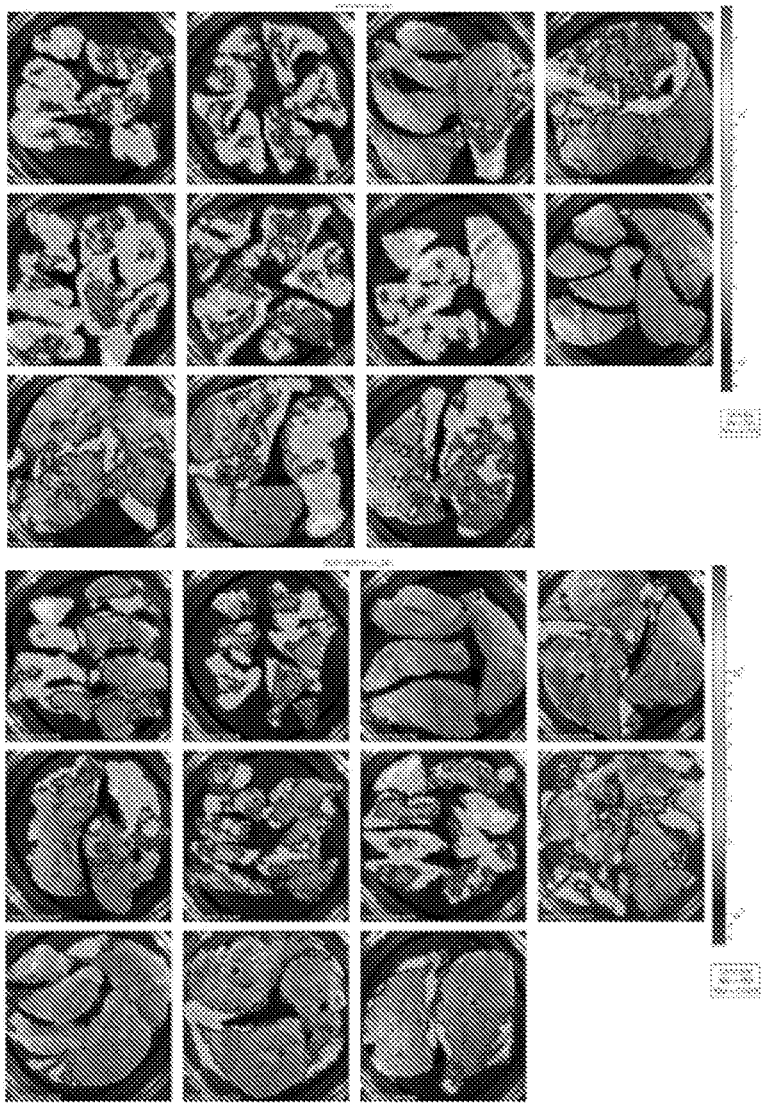


Figure 29

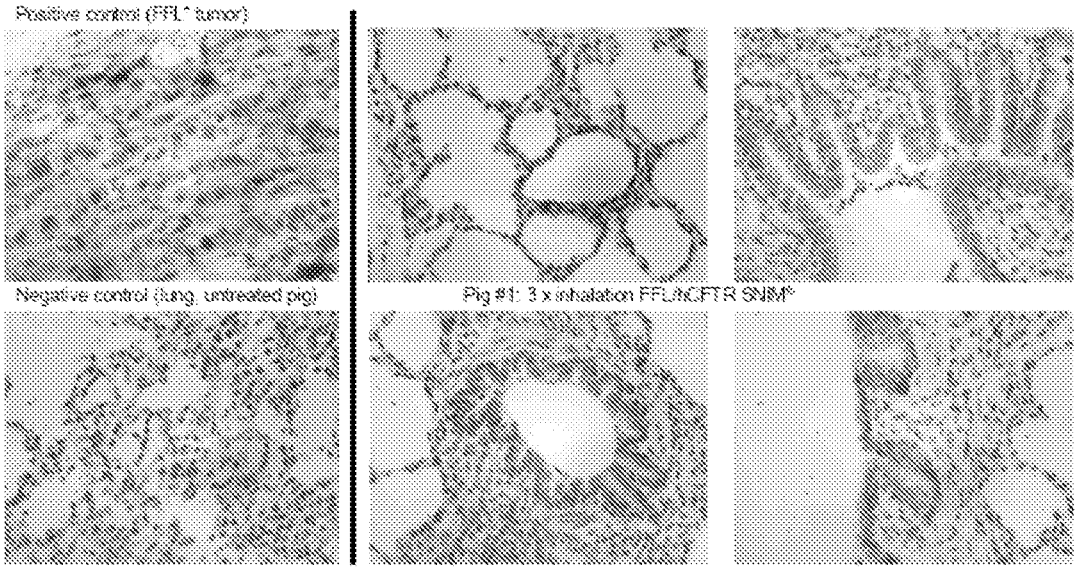

Positive control (FFL+ tumor)
Negative control (lung, untreated pig)
Pig #1: 3 x inhalation FFL/hCFTR SNIM®

Figure 30

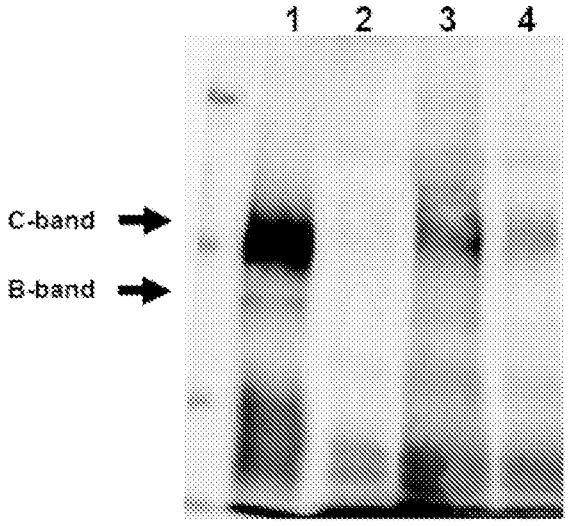


Figure 31

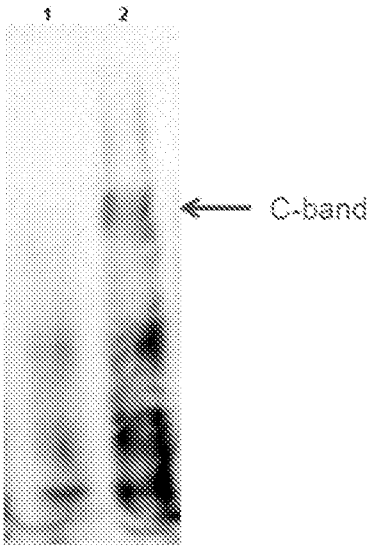


Figure 32

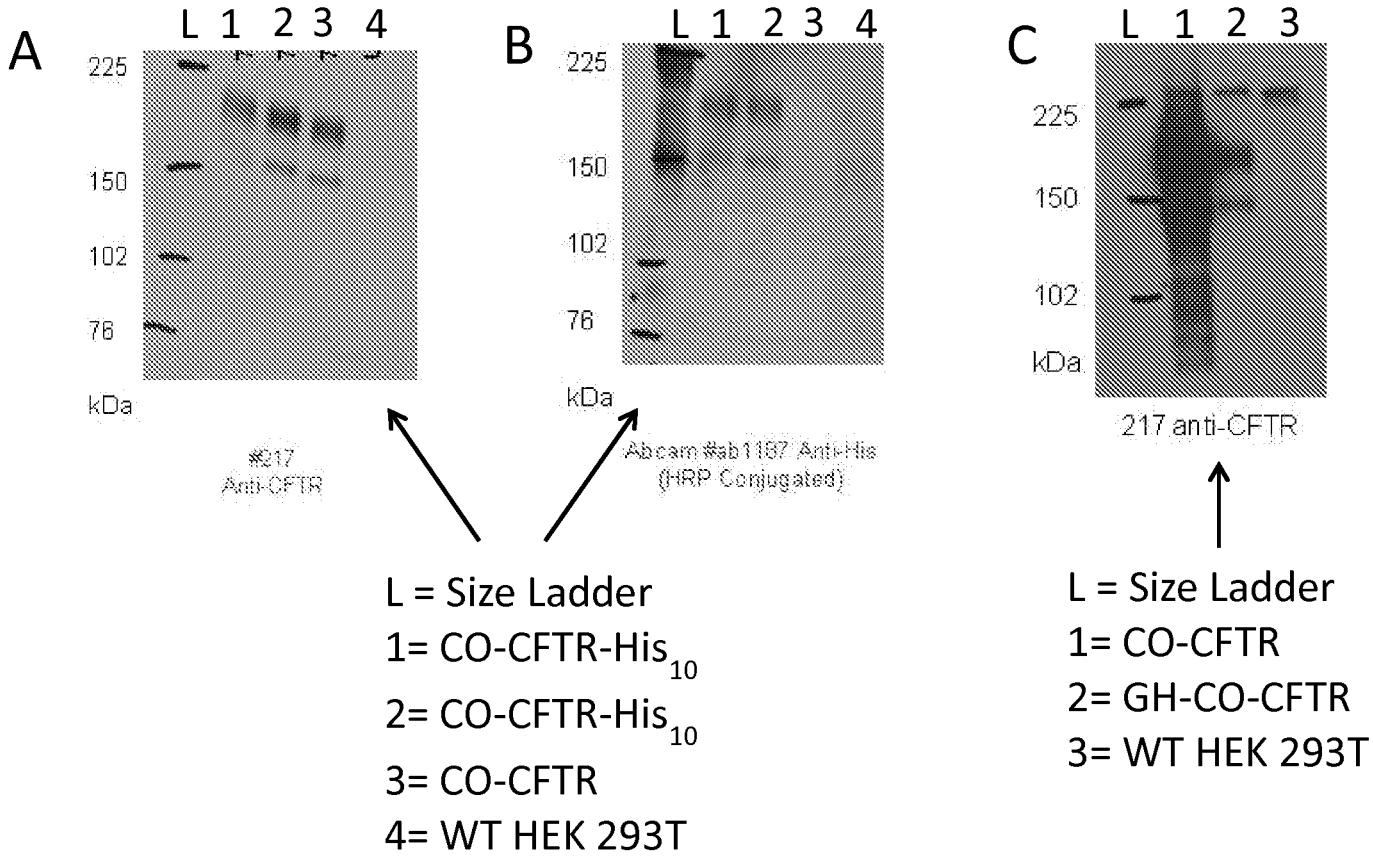

A
L 1 2 3 4
225
150
102
76
kDa
#217
Anti-CFTR
B
L 1 2 3 4
225
150
102
76
kDa
Abcam #ab1187 Anti-His
(HRP Conjugated)
C
L 1 2 3
225
150
102
kDa
217 anti-CFTR
L = Size Ladder
1= CO-CFTR-His10
2= CO-CFTR-His10
3= CO-CFTR
4= WT HEK 293T
L = Size Ladder
1= CO-CFTR
2= GH-CO-CFTR
3= WT HEK 293T

Figure 33

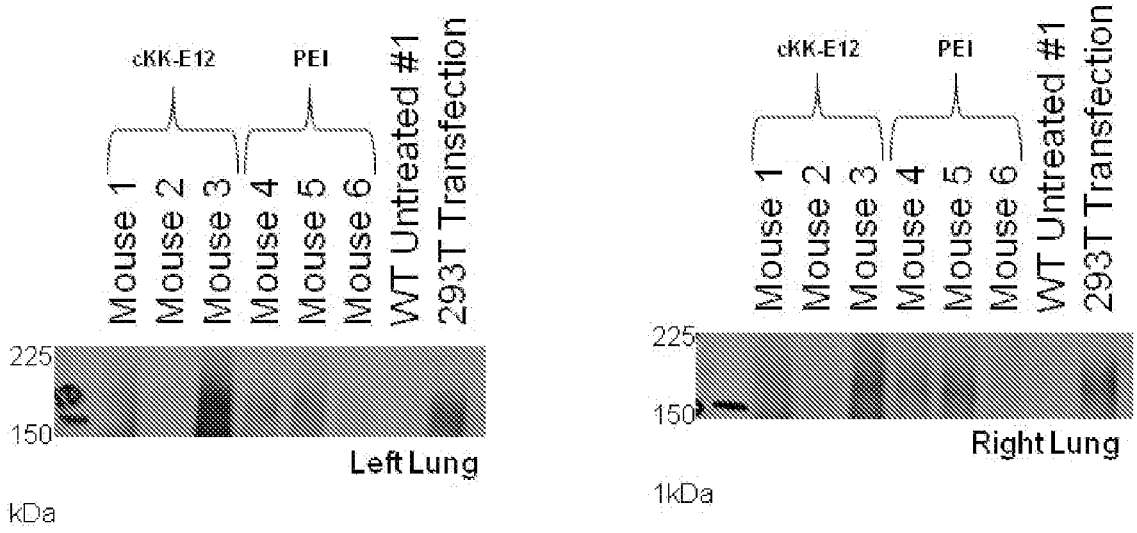

cKK-E12
PEI
Mouse 1
Mouse 2
Mouse 3
Mouse 4
Mouse 5
Mouse 6
WT Untreated #1
293T Transfection
225
150
Left Lung
kDa
cKK-E12
PEI
Mouse 1
Mouse 2
Mouse 3
Mouse 4
Mouse 5
Mouse 6
WT Untreated #1
293T Transfection
225
150
Right Lung
1kDa

Figure 34

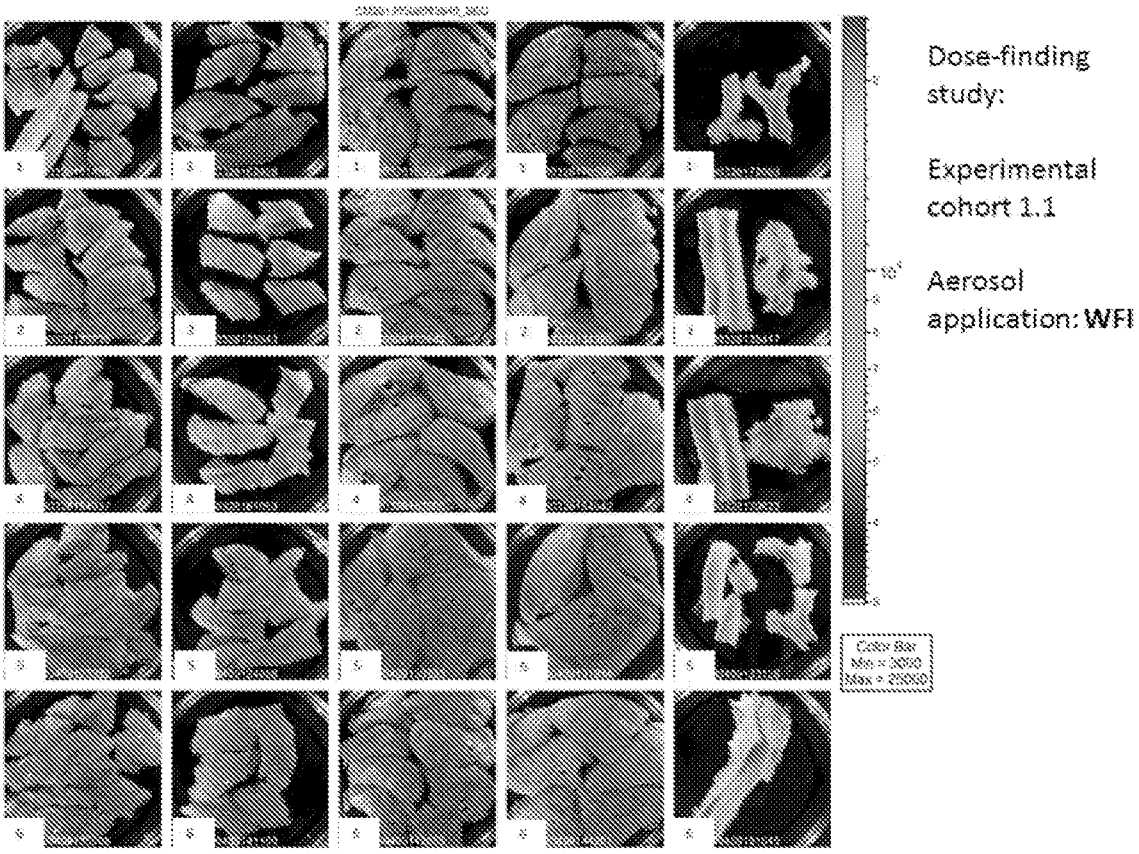

Dose-finding study:
Experimental cohort 1.1
Aerosol application: WFI

Figure 35

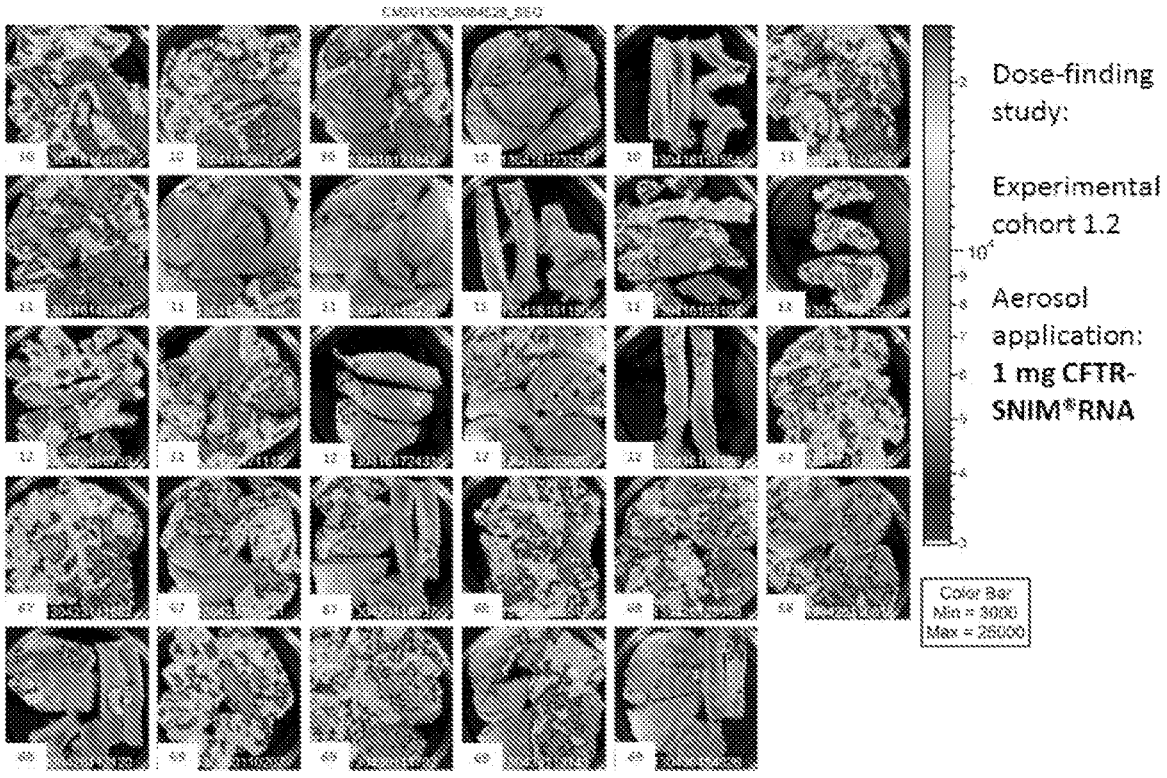

Dose-finding study:
Experimental cohort 1.2
Aerosol application:
1 mg CFTR-SNIM®RNA
Color Bar
Min = 3000
Max = 25000

Figure 36

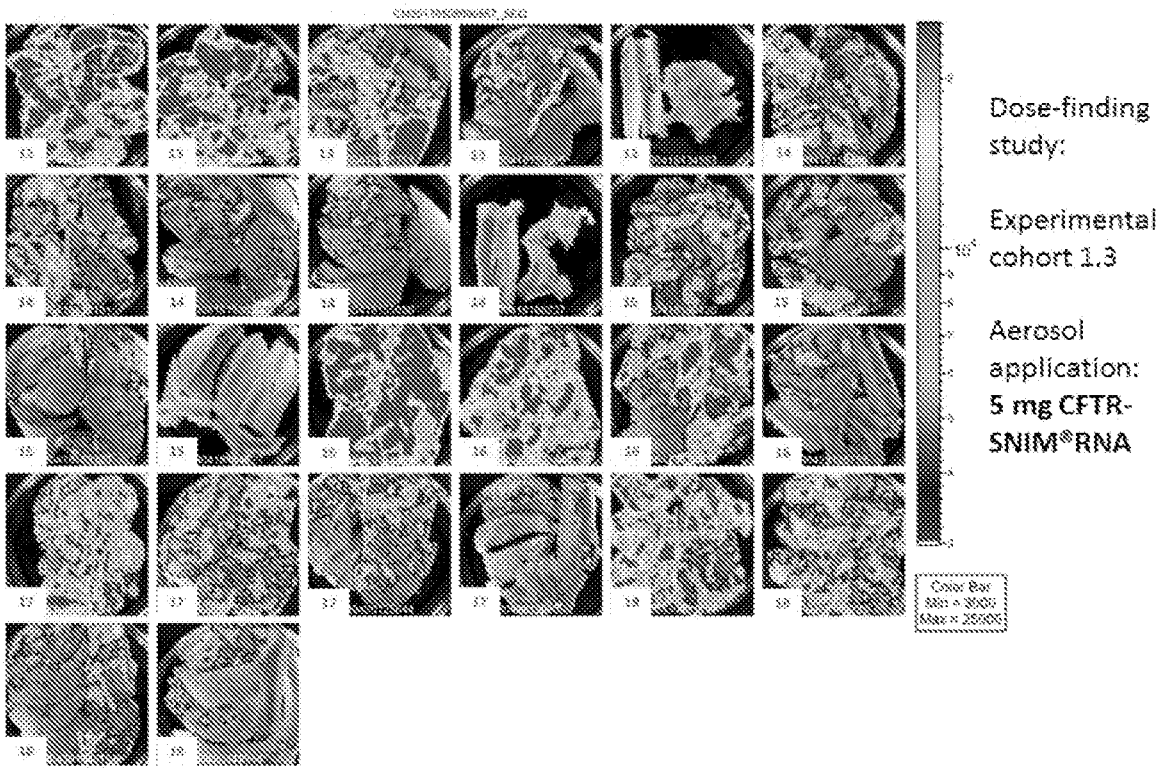

Dose-finding study:
Experimental cohort 1.3
Aerosol application:
5 mg CFTR-SNIM®RNA

Figure 37

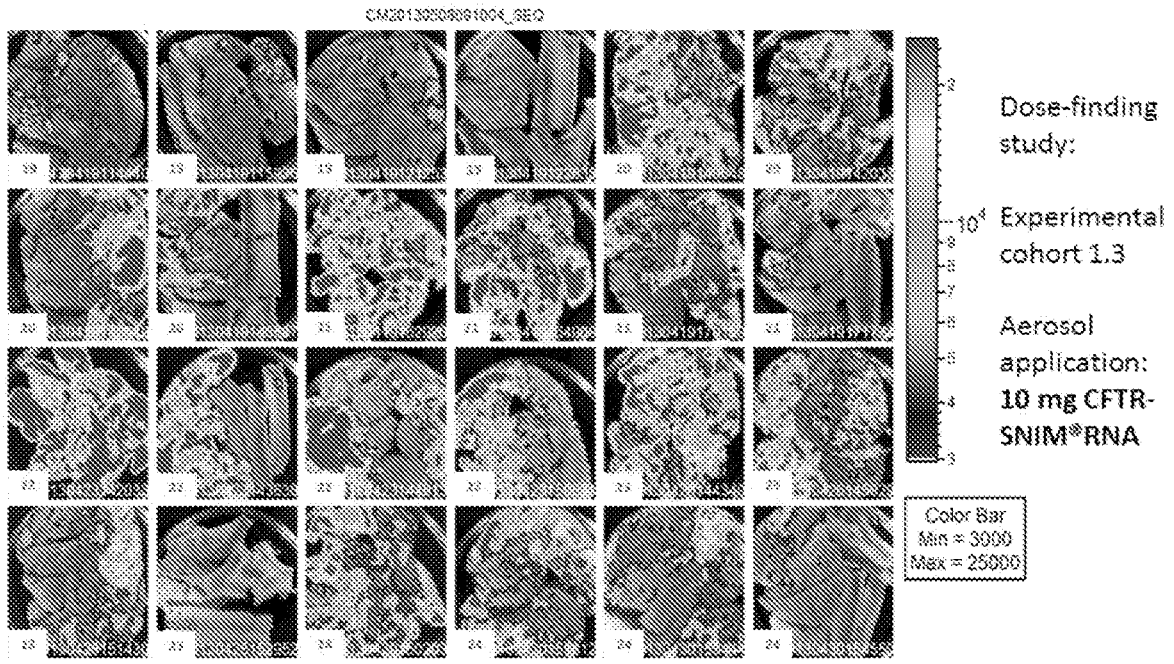

Dose-finding study:
Experimental cohort 1.3
Aerosol application:
10 mg CFTR-SNIM®RNA
Color Bar
Min = 3000
Max = 25000

Figure 38

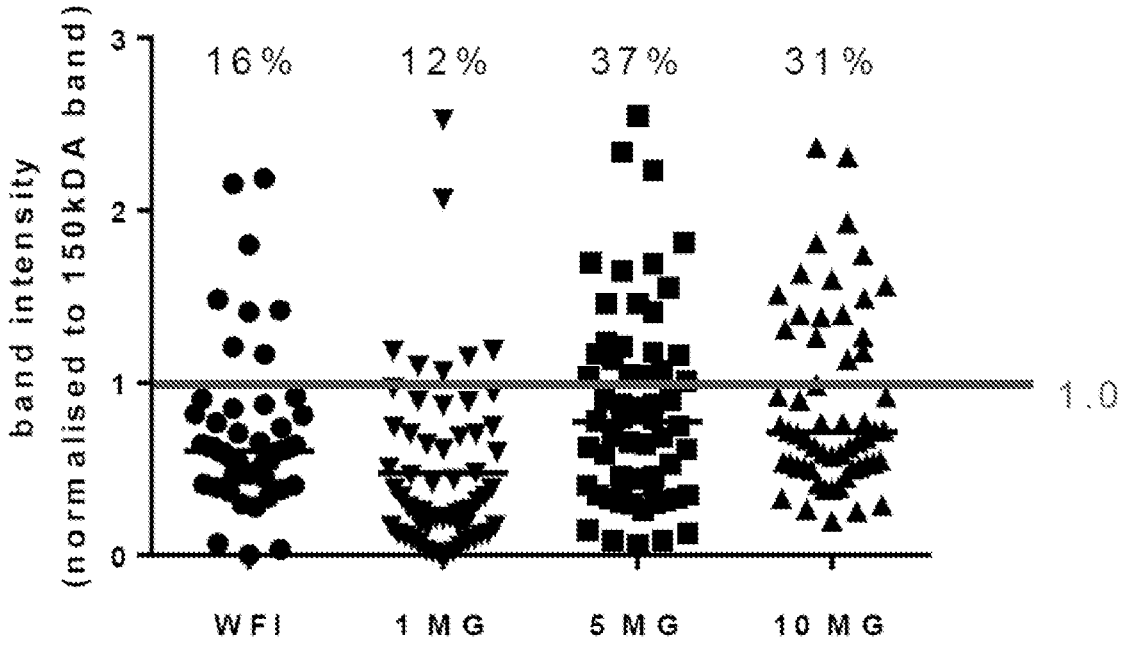

band intensity
(normalised to 150kDA band)
3
2
1
0
16%
12%
37%
31%
1.0
WFI
1 MG
5 MG
10 MG

Figure 39

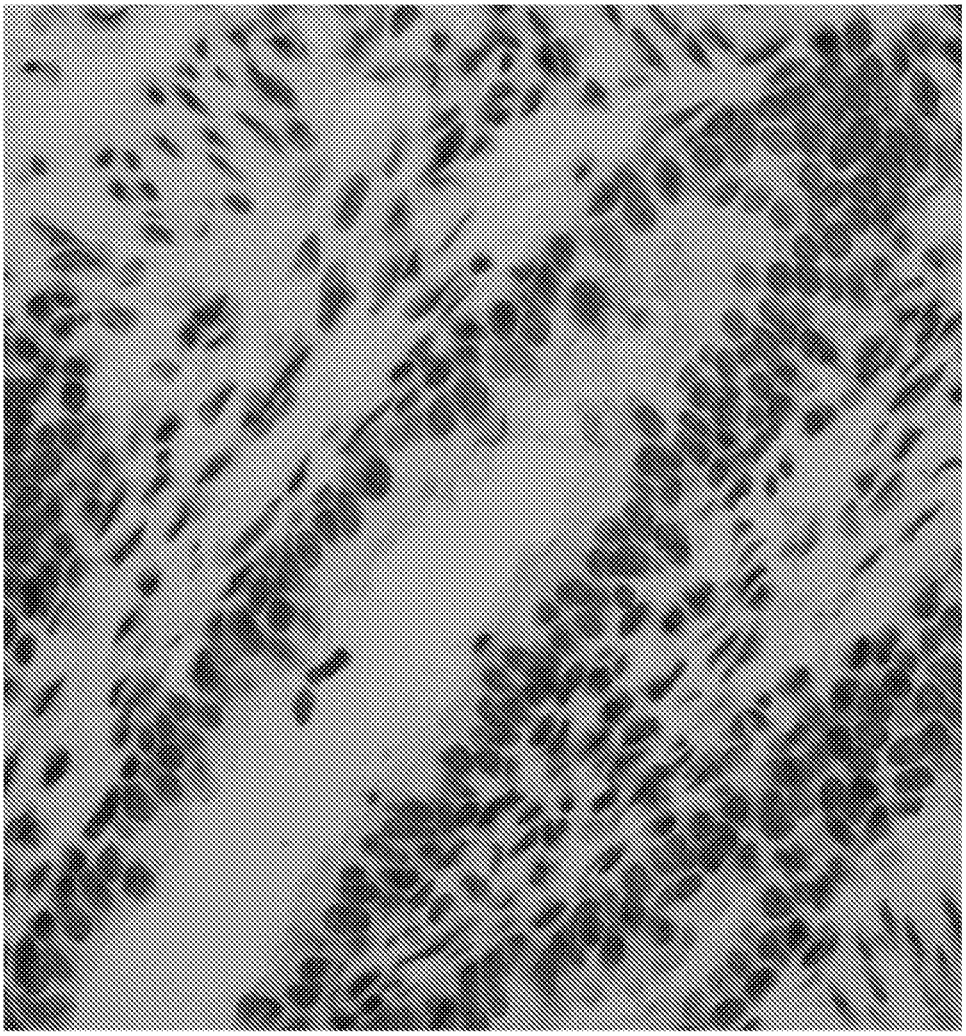


Figure 40

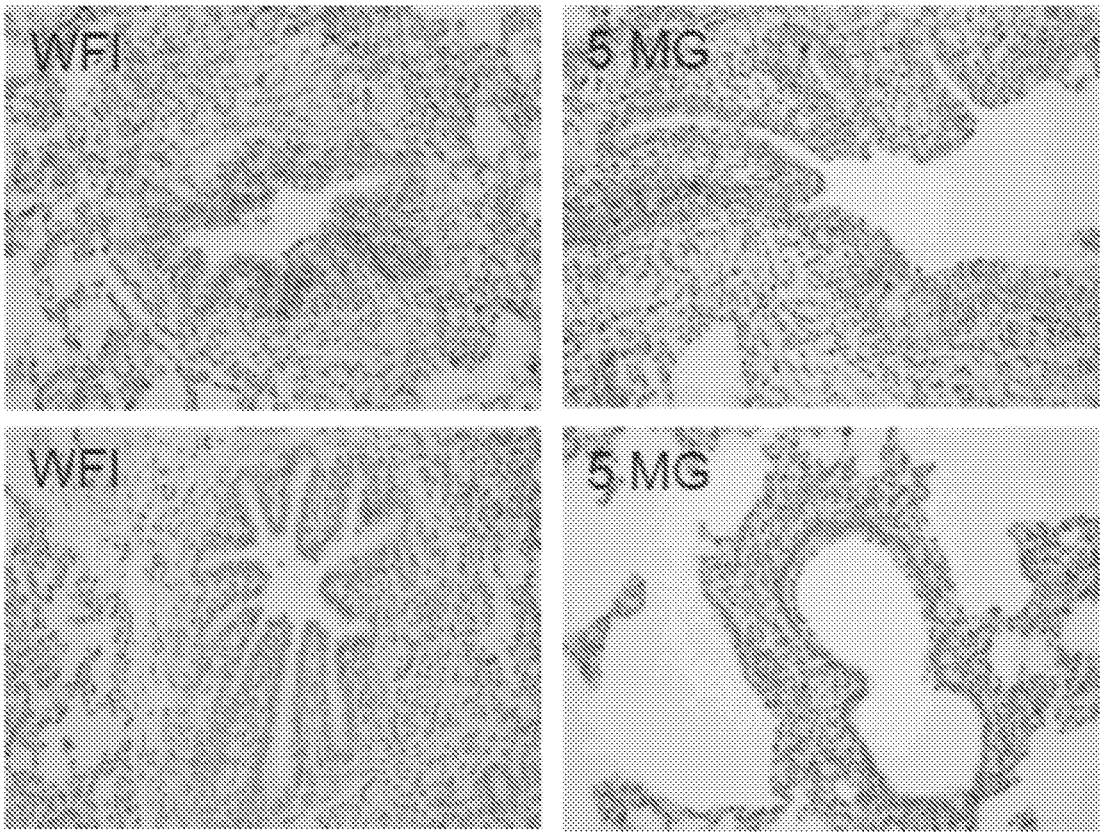


Figure 41

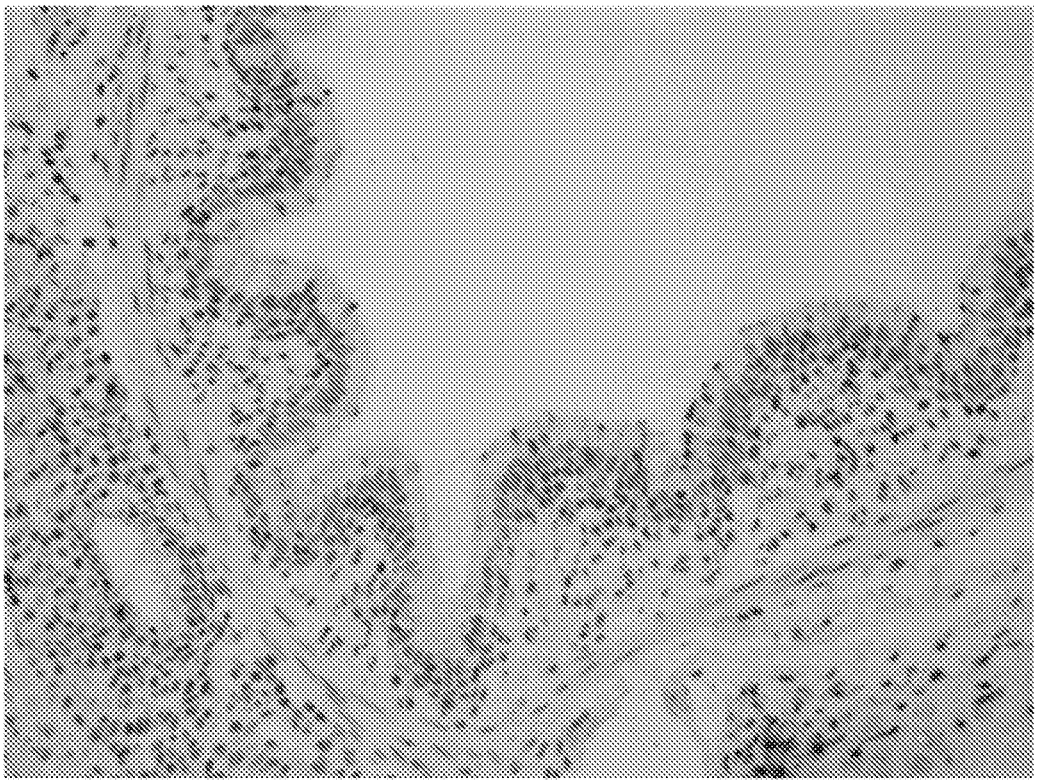


Figure 42

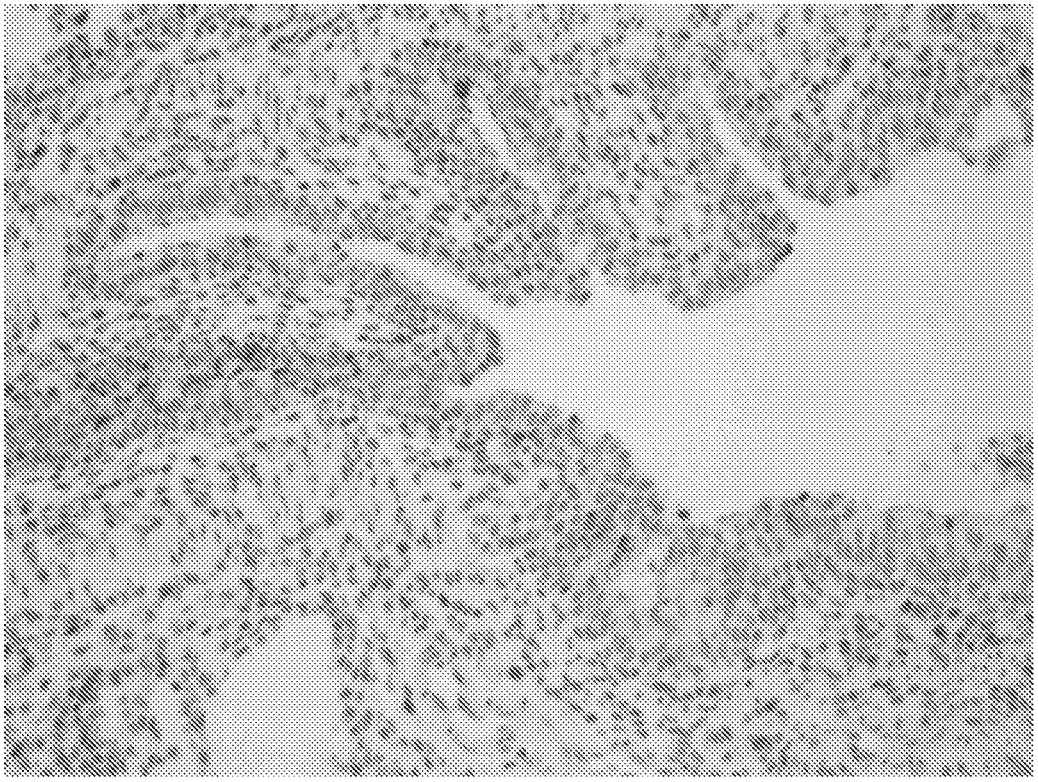


Figure 43

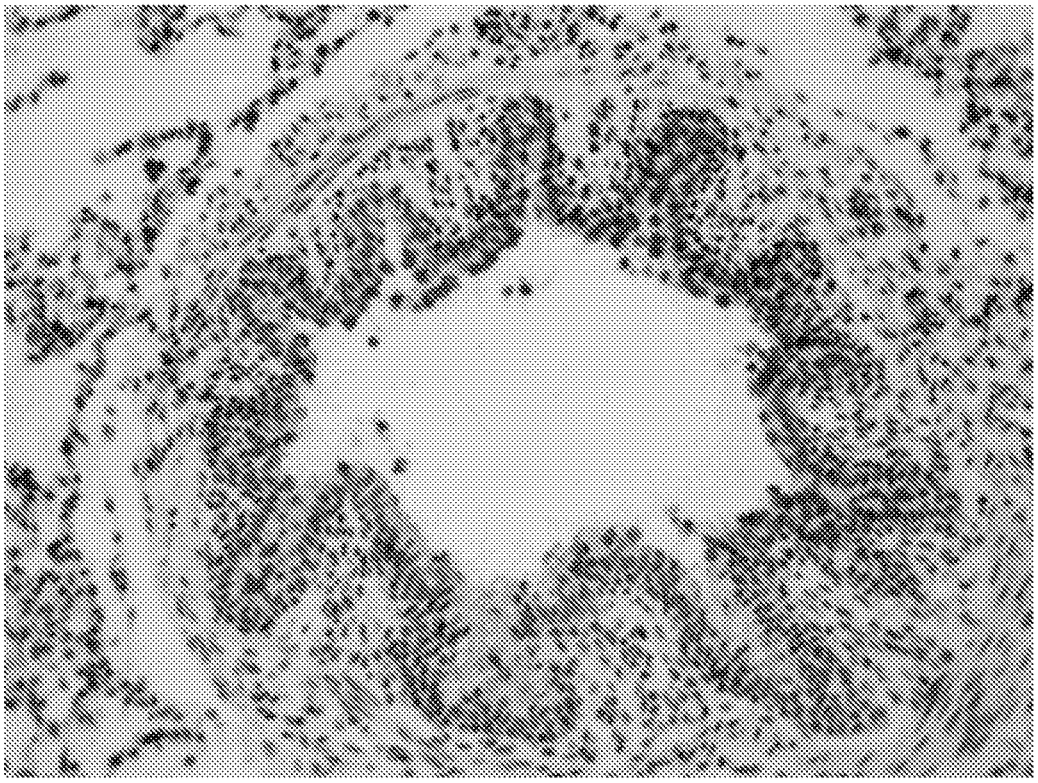


Figure 44

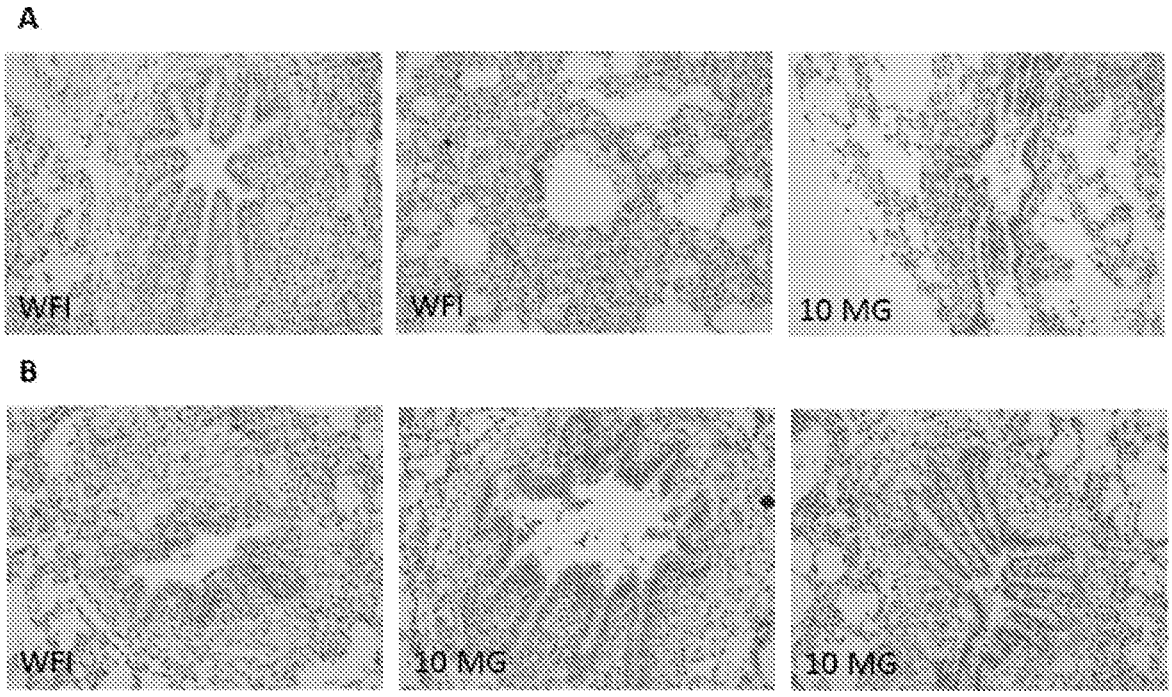


Figure 45

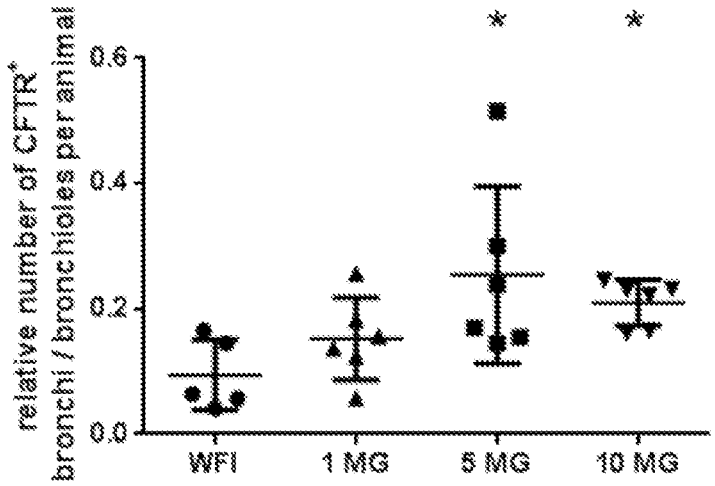
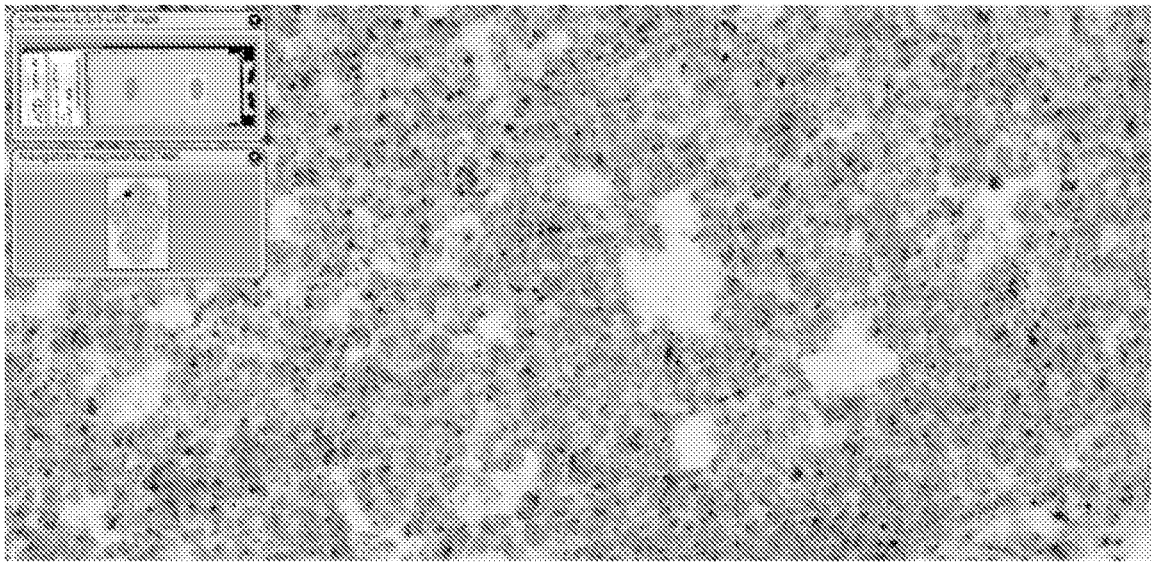

relative number of CFTR+ bronchi / bronchioles per animal
0.6
0.4
0.2
0.0
WFI
1 MG
5 MG
10 MG
*
*

Figure 46

A



B

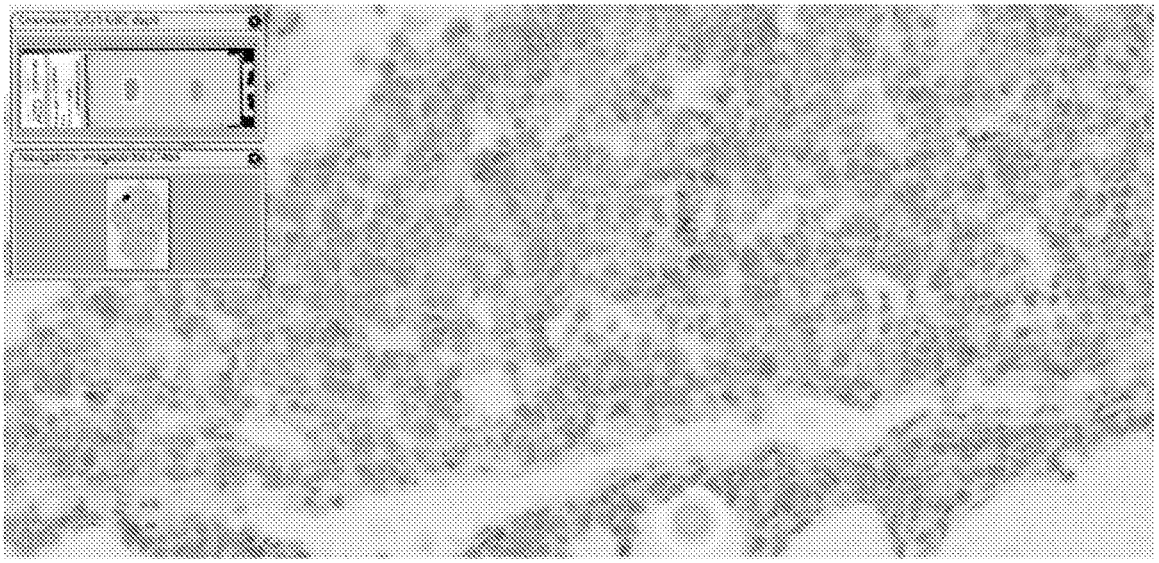
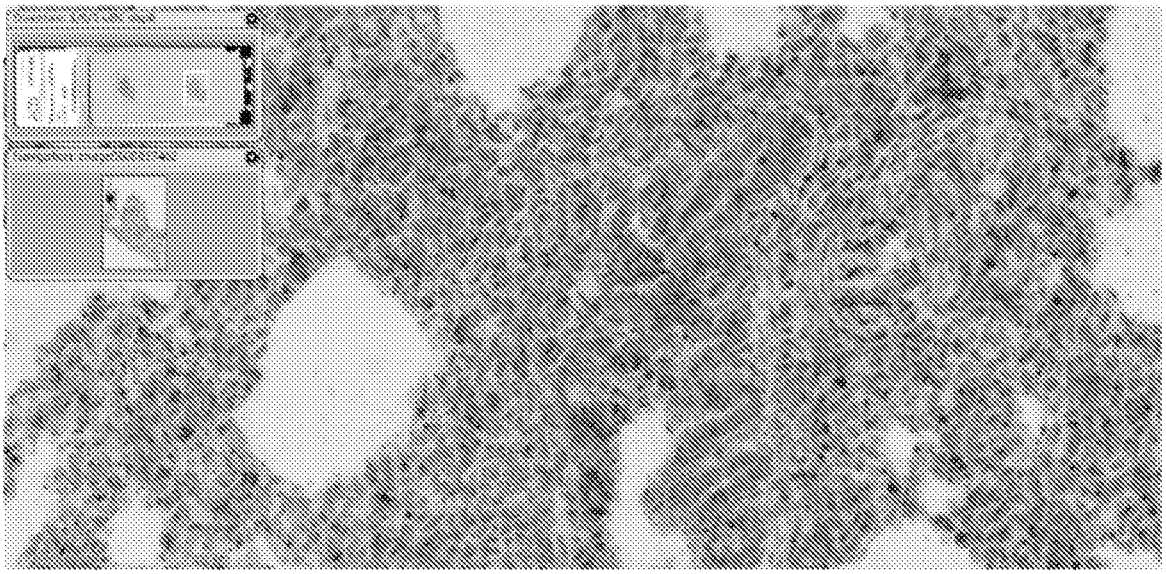


Figure 47 A&B

A



B

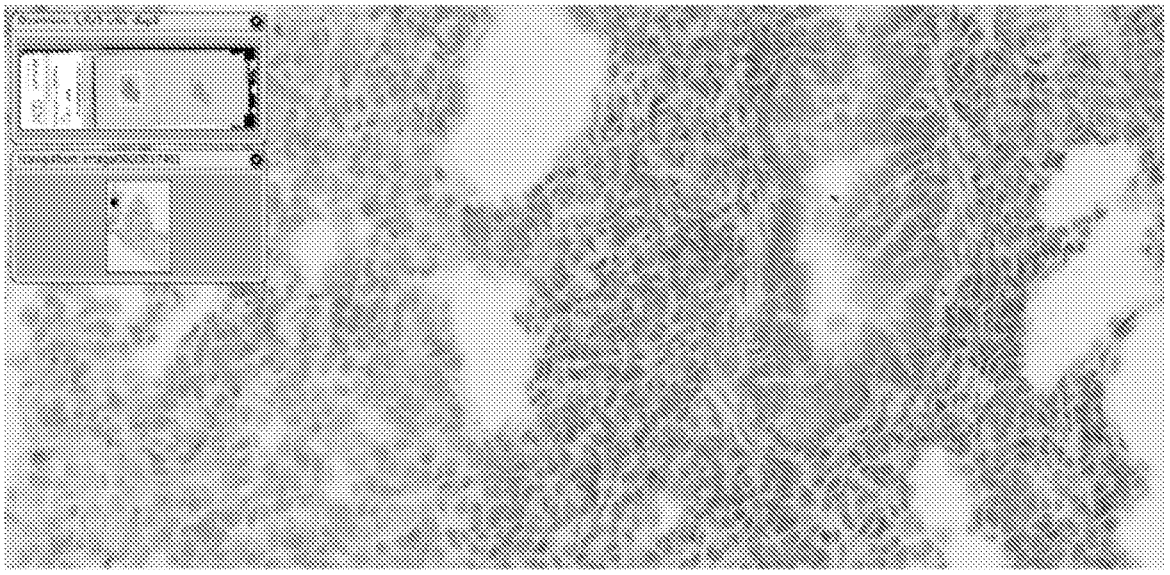
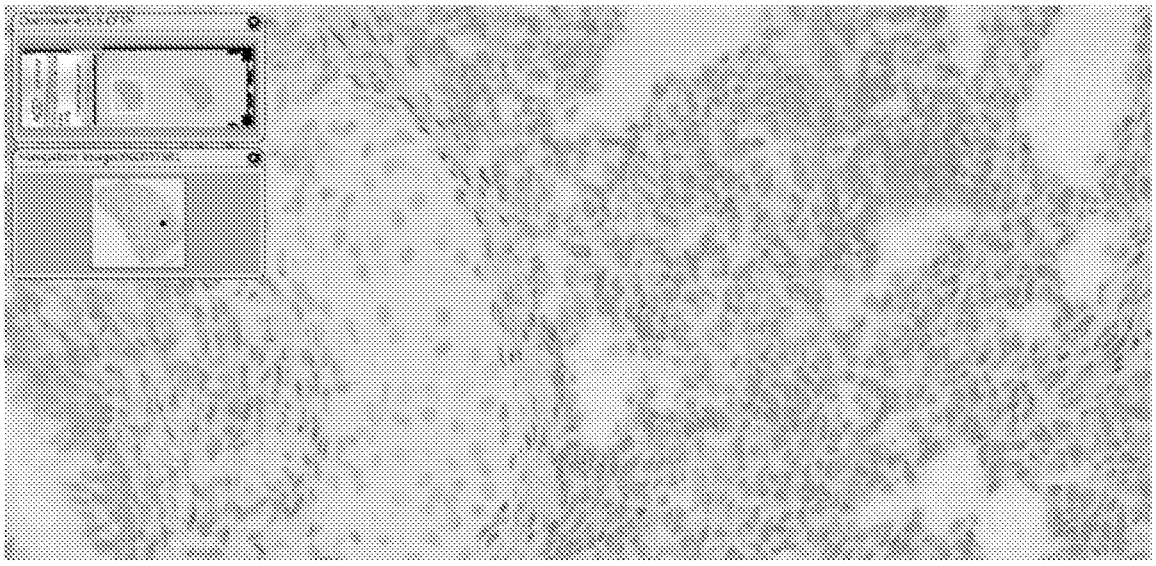


Figure 48 A&B

A



B

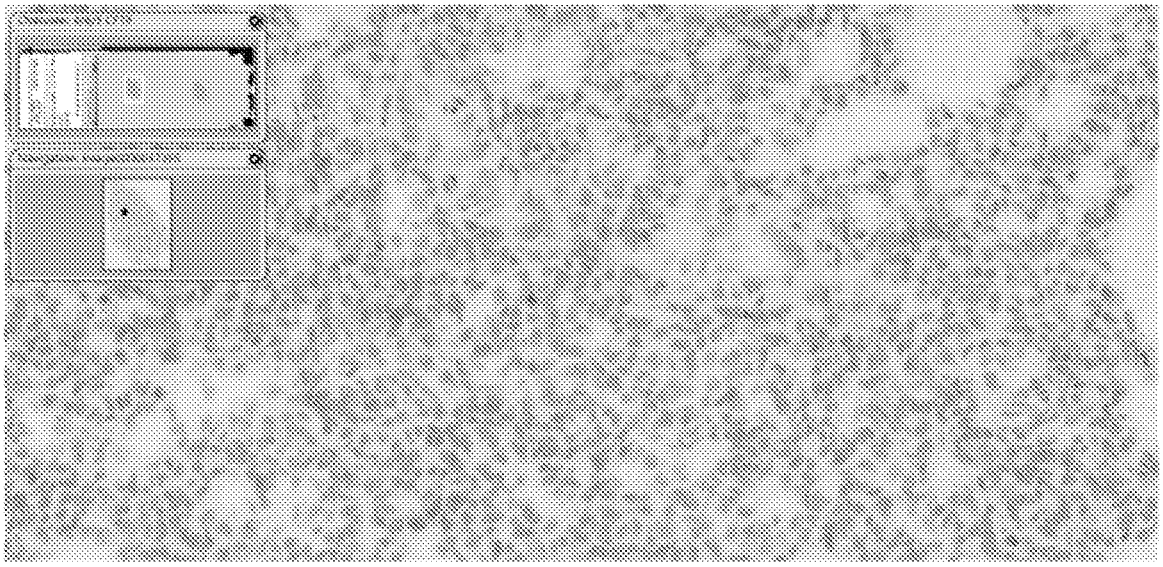
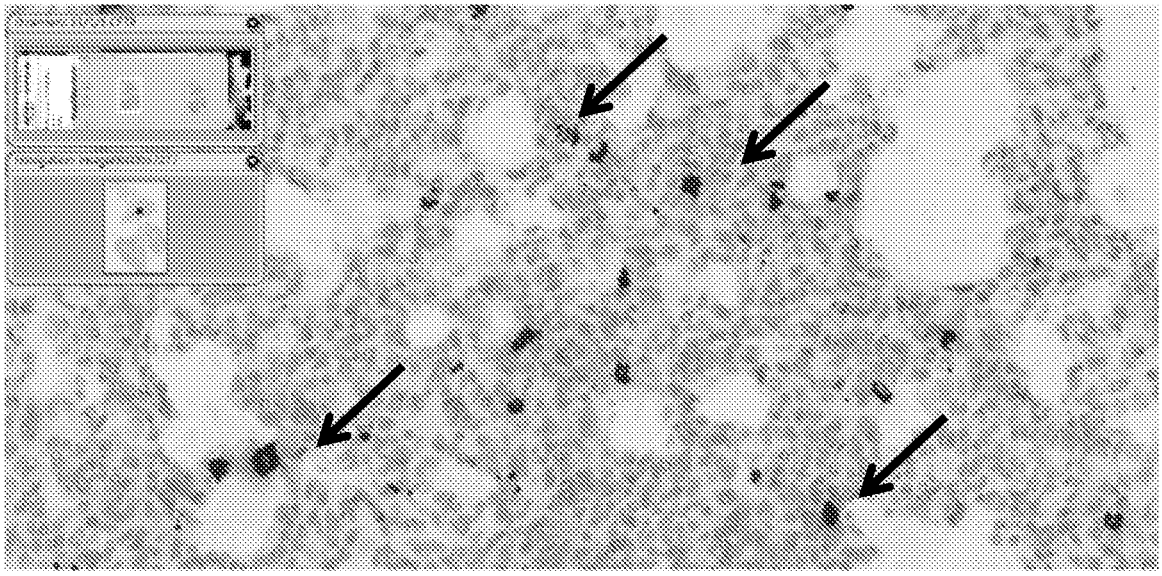


Figure 49 A&B

A



B

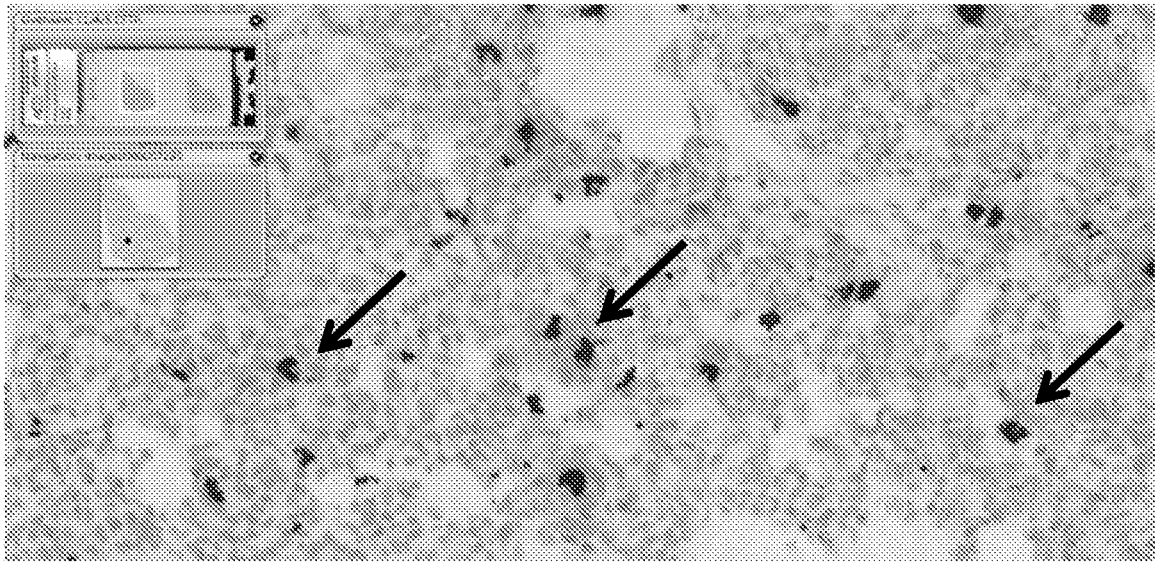
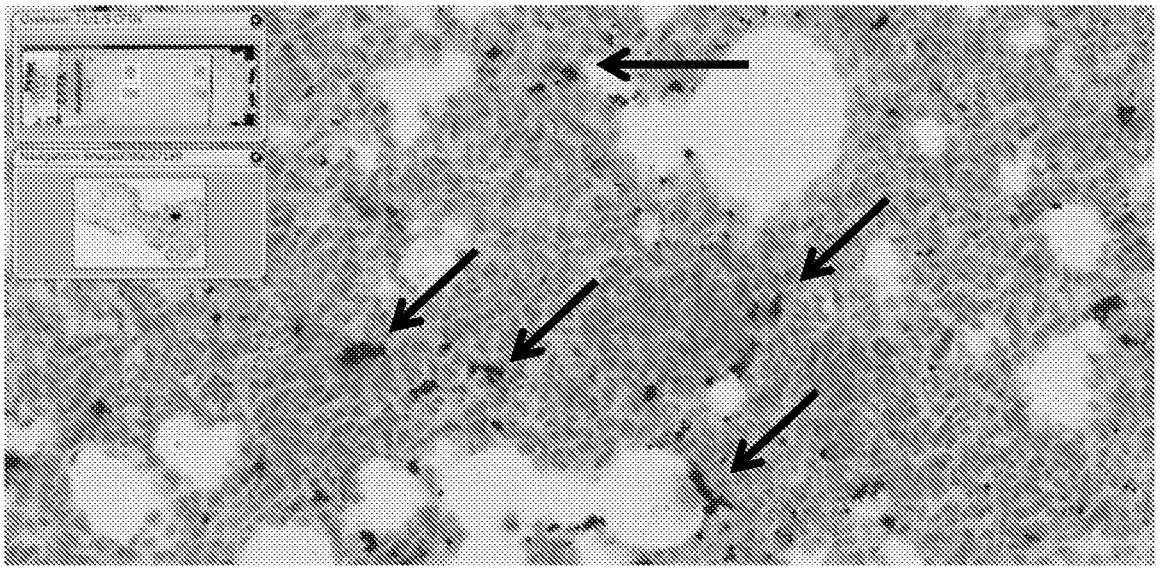


Figure 50 A&B

A



B

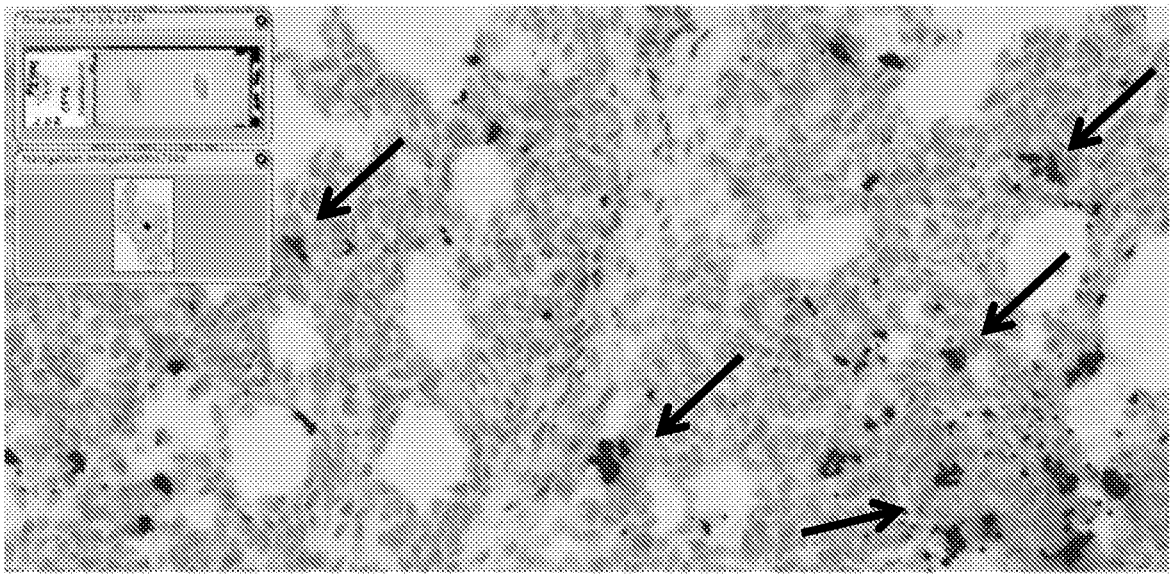
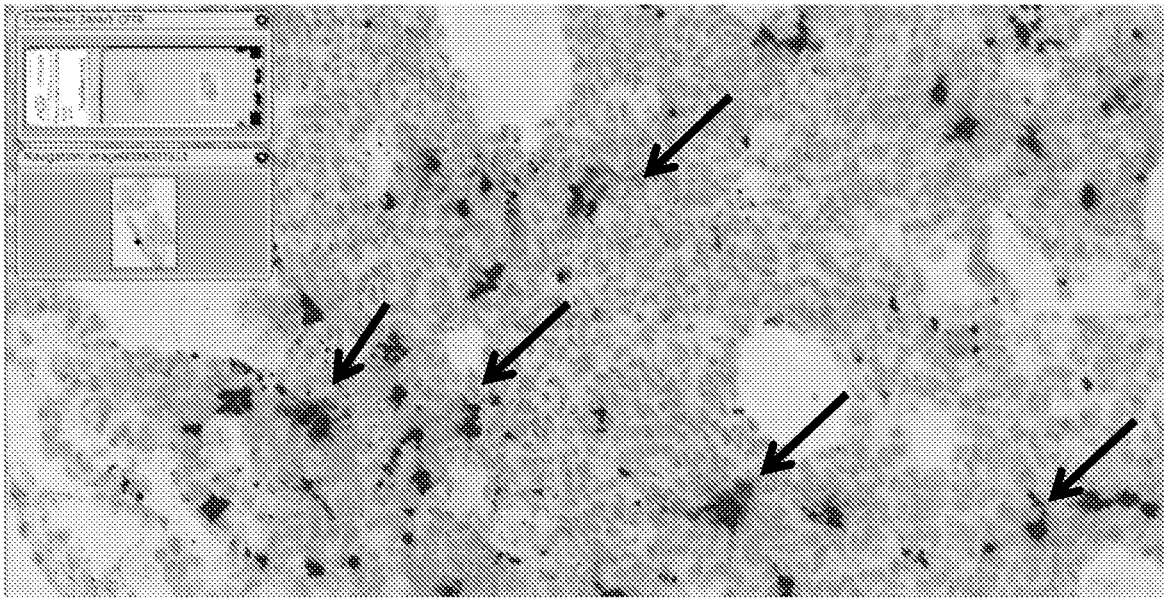


Figure 51 A&B

A



B

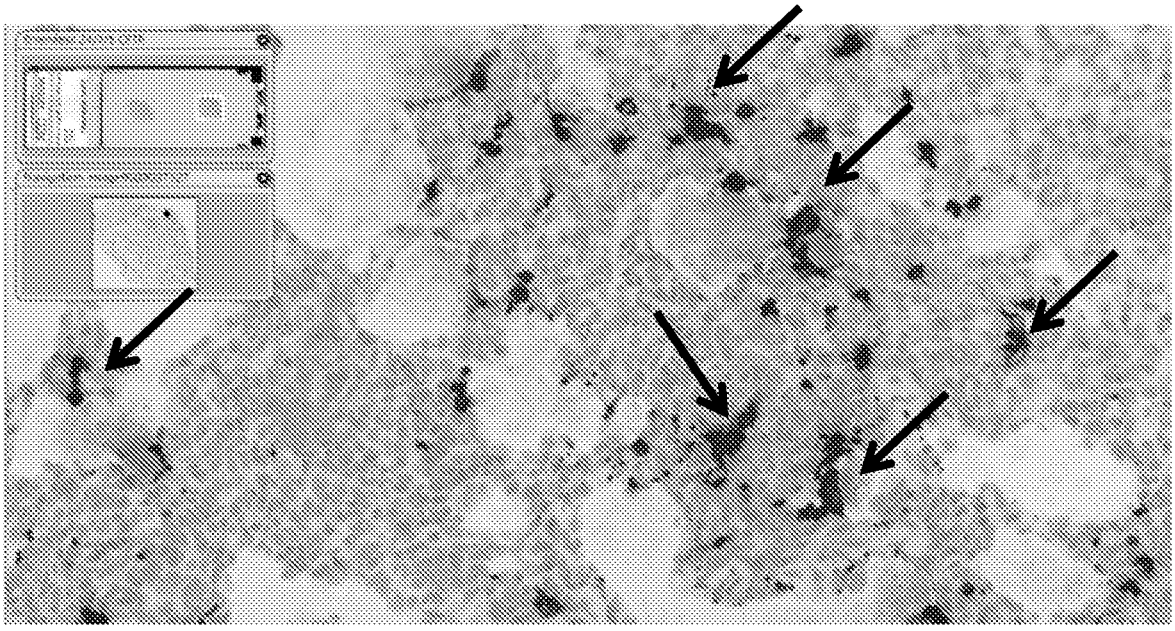
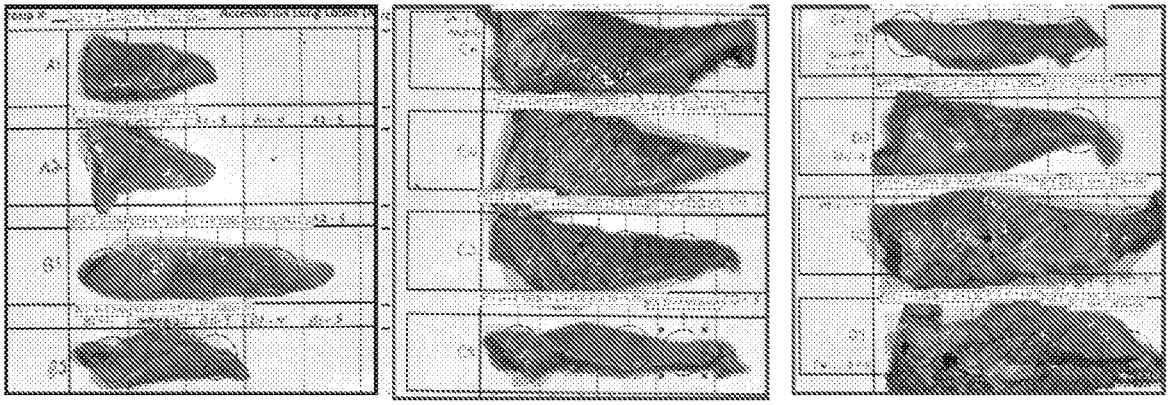


Figure 52 A&B

A

Saline



B

cKK-E12

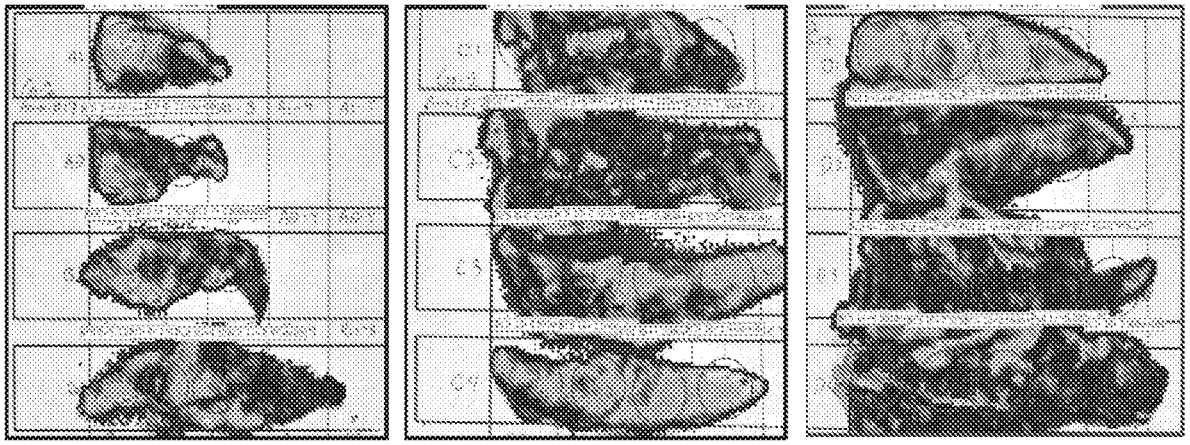


Figure 53 A&B

HEK cells transfected using complexes given to Pigs 10, 11 and 12 (1mg Dose).
HEK-UT – untransfected HEK cells

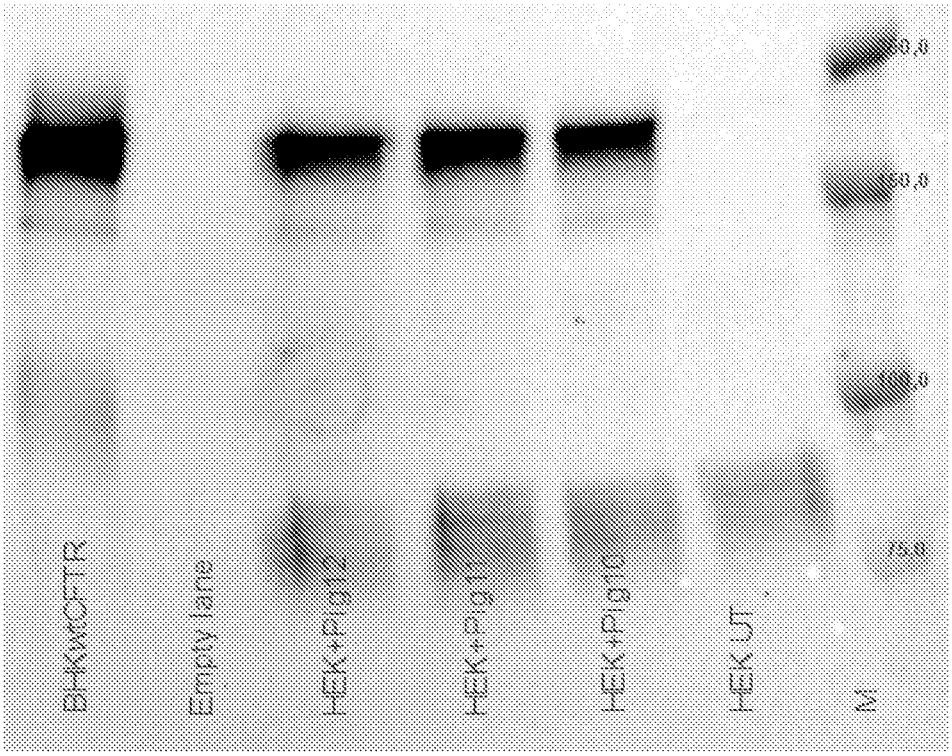


Figure 54

HEK cells transfected using complexes given to Pigs 13, 14 and 15 (5mg Dose)
HEK cells transfected using complexes given to Pigs 19, 20 and 21 (10mg Dose)

HEK-UT – untransfected HEK cells used for complexes from Pigs 19-21
HEK-UT – untransfected HEK cells used for complexes from Pigs 13-15

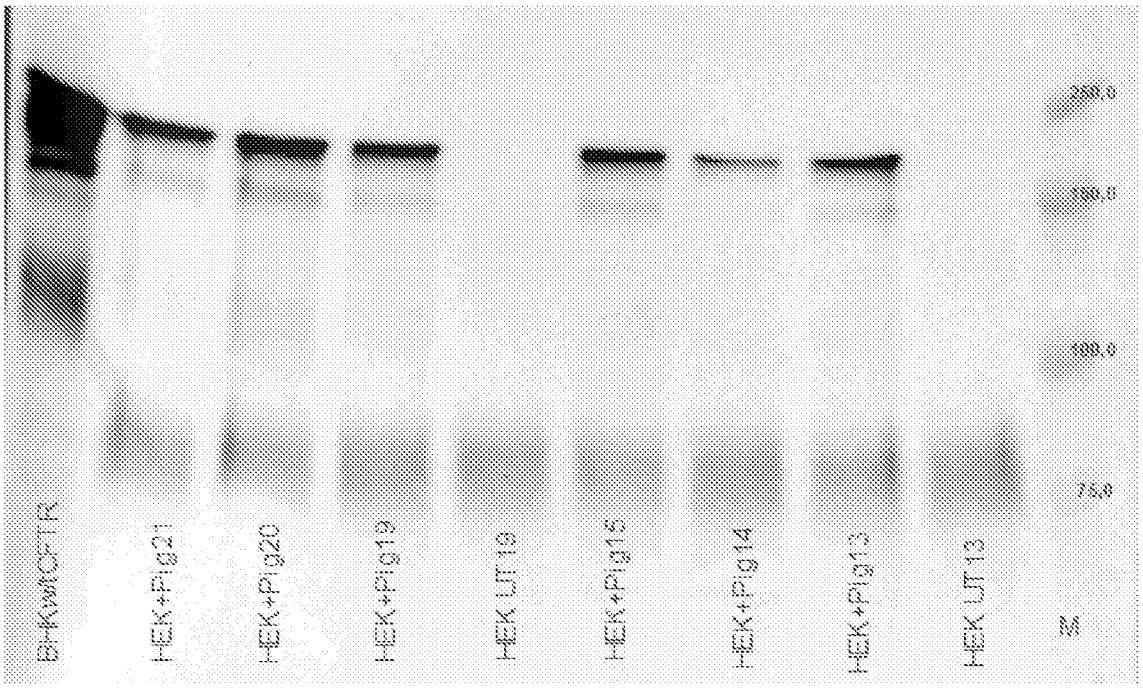


Figure 55

HEK cells transfected using complexes given to Pigs 16 (5 mg Dose), 22 (10 mg Dose) and 67 (1mg Dose)

HEK-UT 16– untransfected HEK cells used for complexes from Pigs 16, 22 and 67

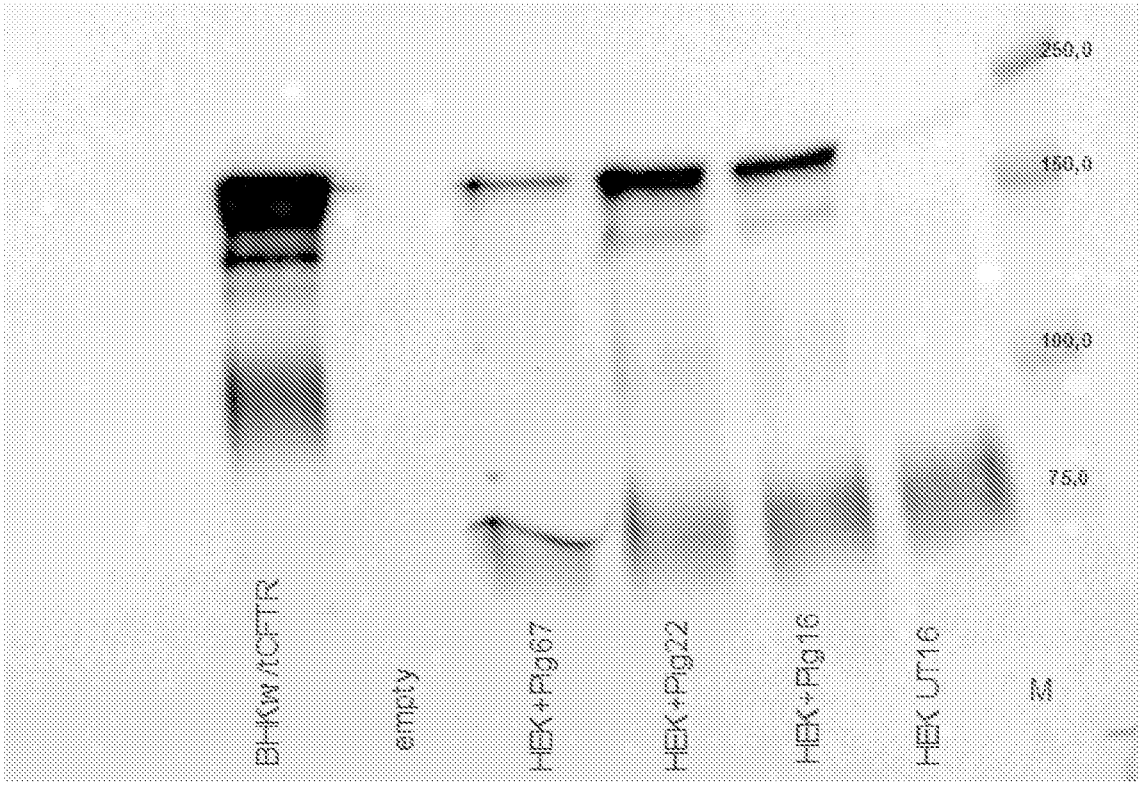


Figure 56

HEK cells transfected using complexes given to Pigs 17-18 (5 mg Doses), 23-24 (10 mg Doses) and 68-69 (1mg Doses)

HEK-UT – untransfected HEK cells

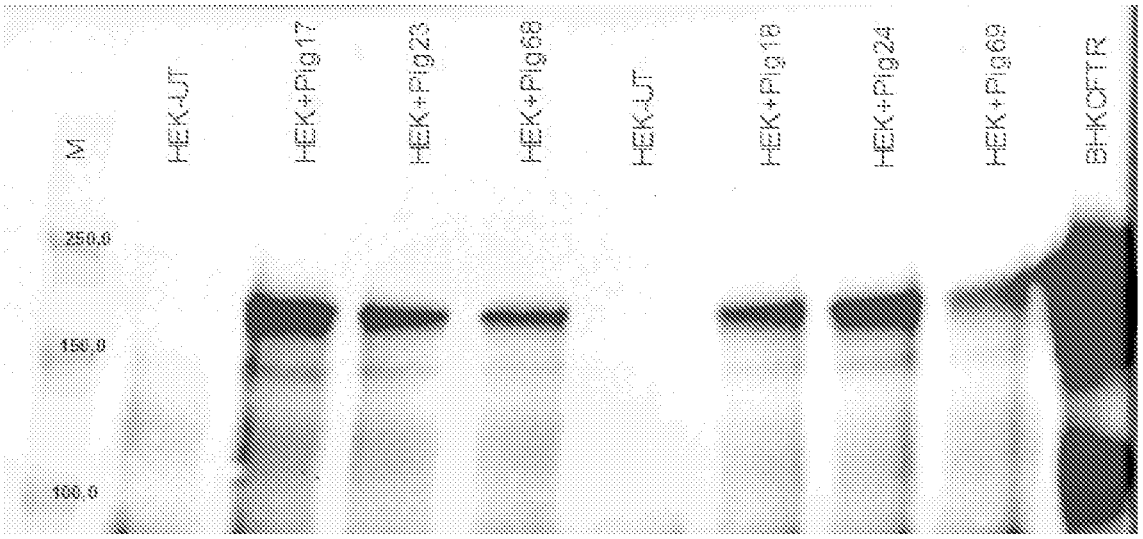


Figure 57