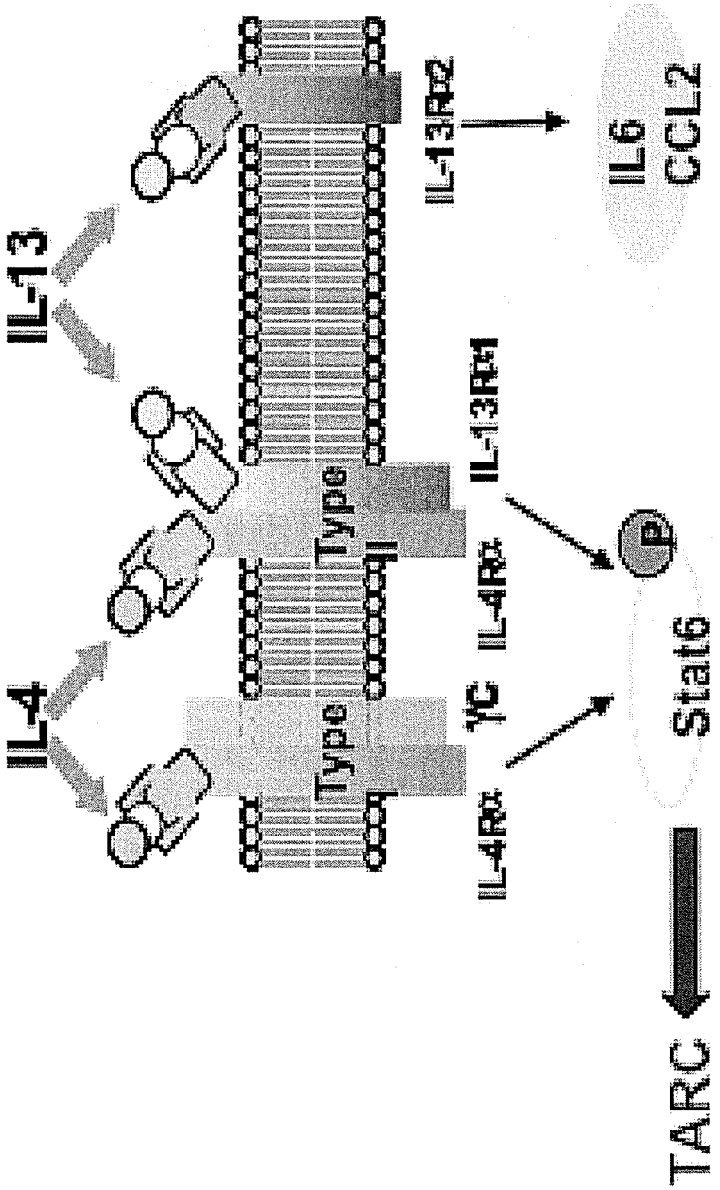

IL-13
IL-4
Type II
Type I
IL-13Rα2
IL-13Rα1
IL-4Rα
γC
IL-4Rα
P
Stat6
IL6
CCL2
TARC

FIGURE 1

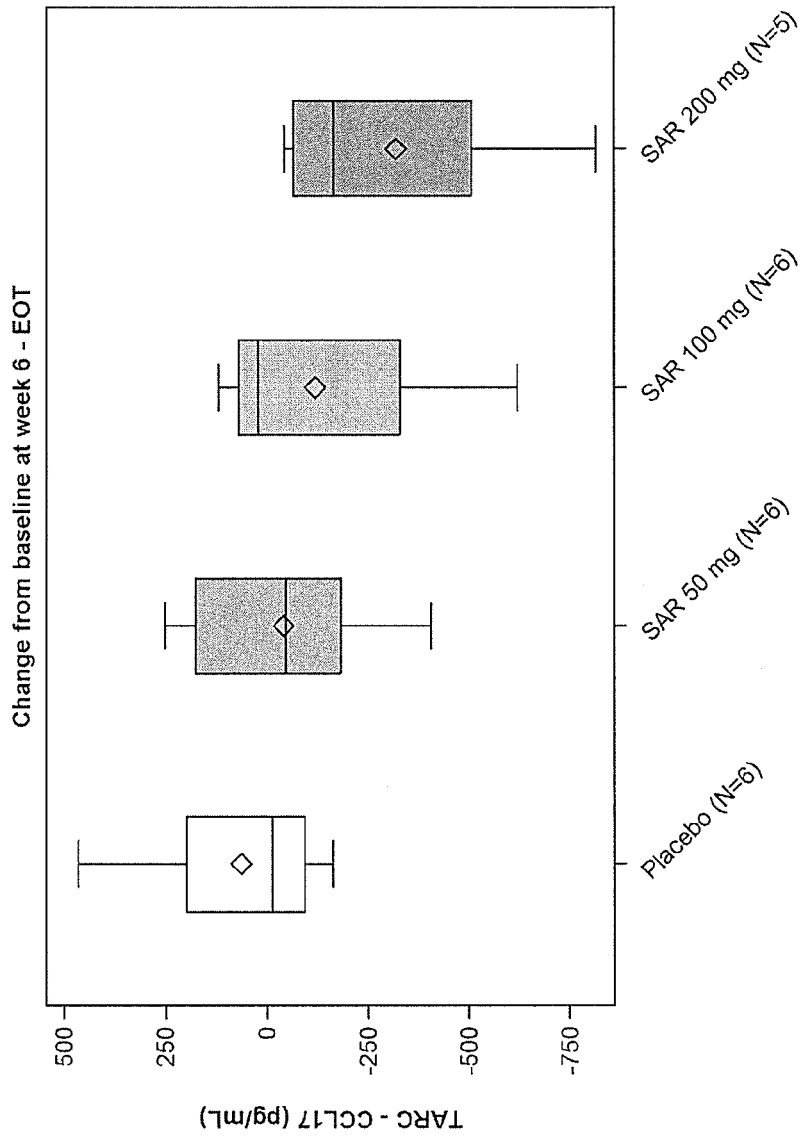

Change from baseline at week 6 - EOT
TARC - CCL17 (pg/mL)
500
250
0
-250
-500
-750
Placebo (N=6)
SAR 50 mg (N=6)
SAR 100 mg (N=6)
SAR 200 mg (N=5)
Treatment group

FIGURE 2

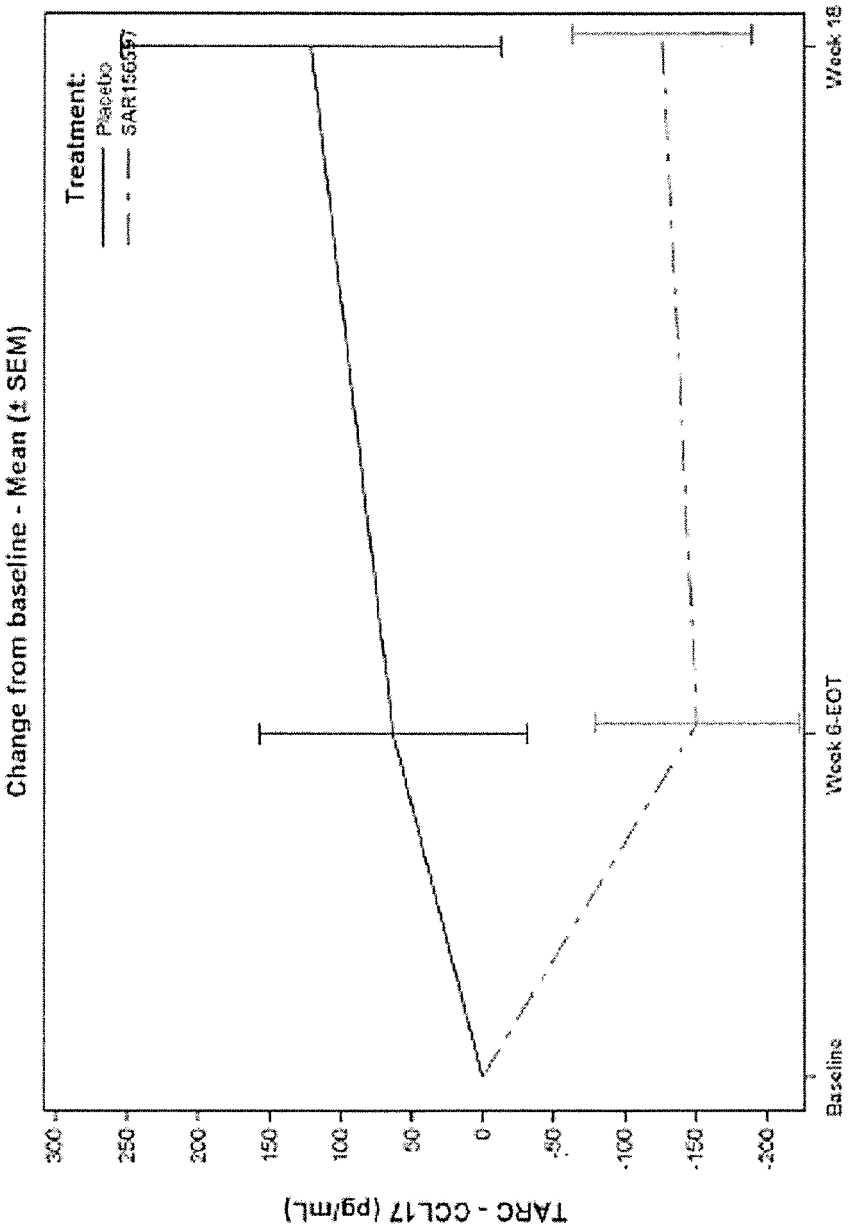

Change from baseline - Mean (± SEM)
Treatment:
Placebo
SAR156597
TARC - CCL17 (pg/mL)
300
250
200
150
100
50
0
-50
-100
-150
-200
Baseline
Week 6-EOT
Week 18

FIGURE 3

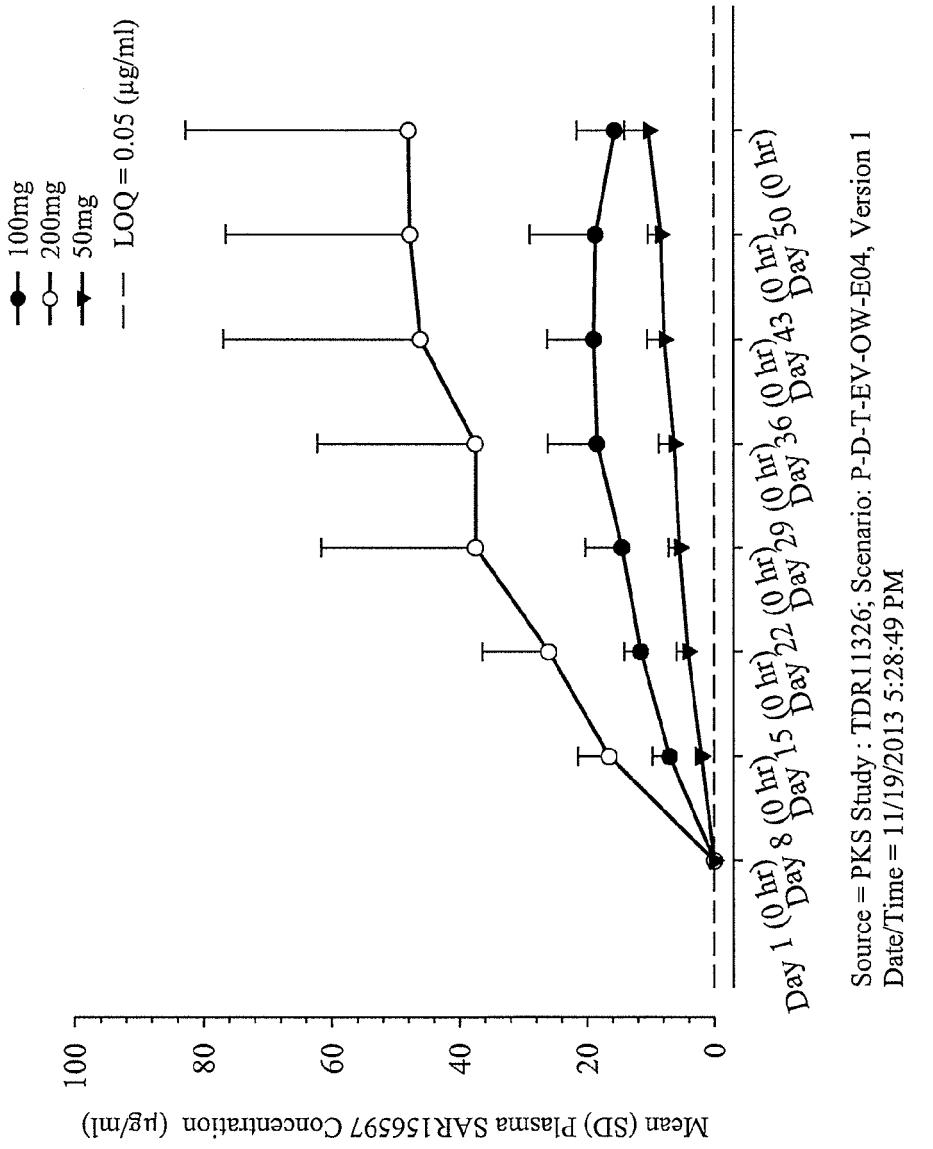

Mean (SD) Plasma SAR156597 Concentration (µg/ml)
100
80
60
40
20
0
100mg
200mg
50mg
LOQ = 0.05 (µg/ml)
Day 1 (0 hr)
Day 8 (0 hr)
Day 15 (0 hr)
Day 22 (0 hr)
Day 29 (0 hr)
Day 36 (0 hr)
Day 43 (0 hr)
Day 50 (0 hr)
Source = PKS Study : TDR11326; Scenario: P-D-T-EV-OW-E04, Version 1
Date/Time = 11/19/2013 5:28:49 PM

FIGURE 4

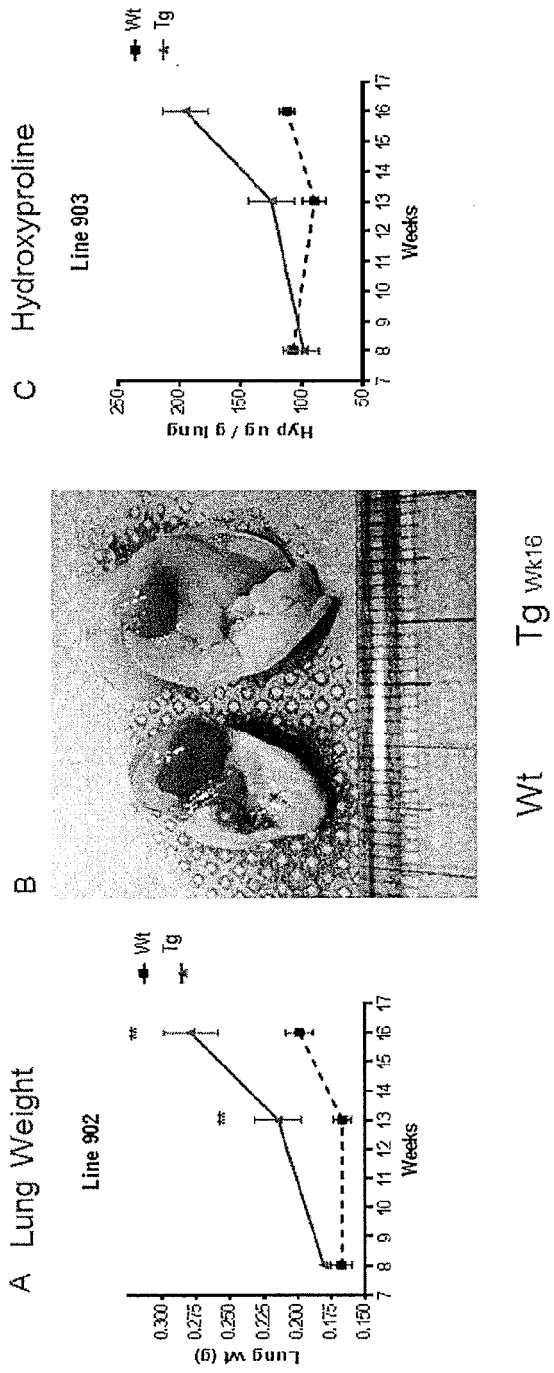

A Lung Weight
Line 902
Wt
Tg
Lung wt (g)
Weeks
B
Wt
Tg Wk16
C Hydroxyproline
Line 903
Wt
Tg
Hyp ug / g lung
Weeks

FIGURE 5

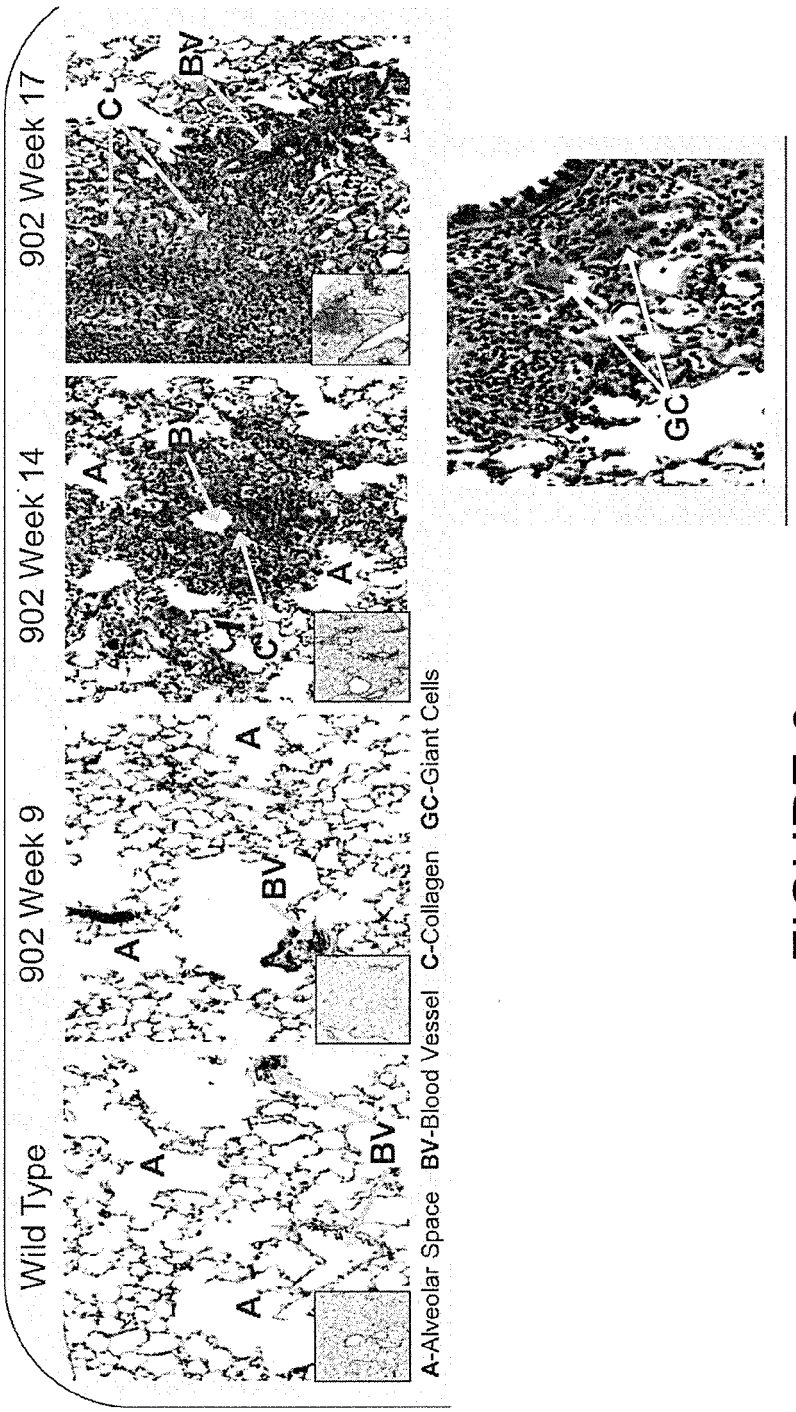

Wild Type
902 Week 9
902 Week 14
902 Week 17
A
BV
C
B
GC
A-Alveolar Space BV-Blood Vessel C-Collagen GC-Giant Cells

FIGURE 6

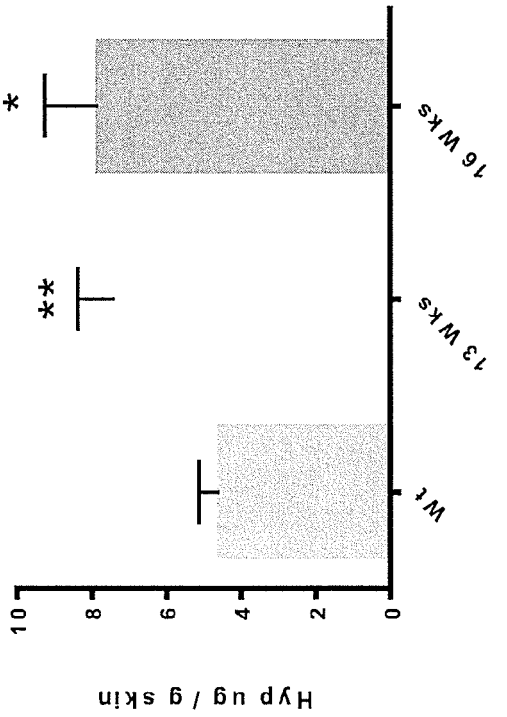


FIGURE 7

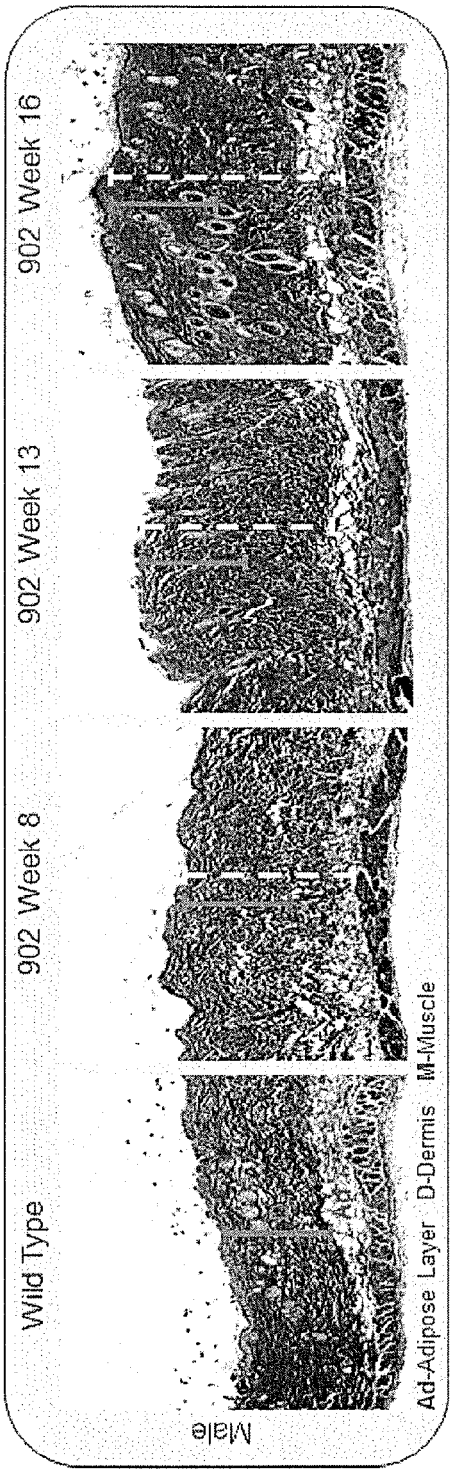

Male
Wild Type
902 Week 8
902 Week 13
902 Week 16
Ad-Adipose Layer D-Dermis M-Muscle

FIGURE 8

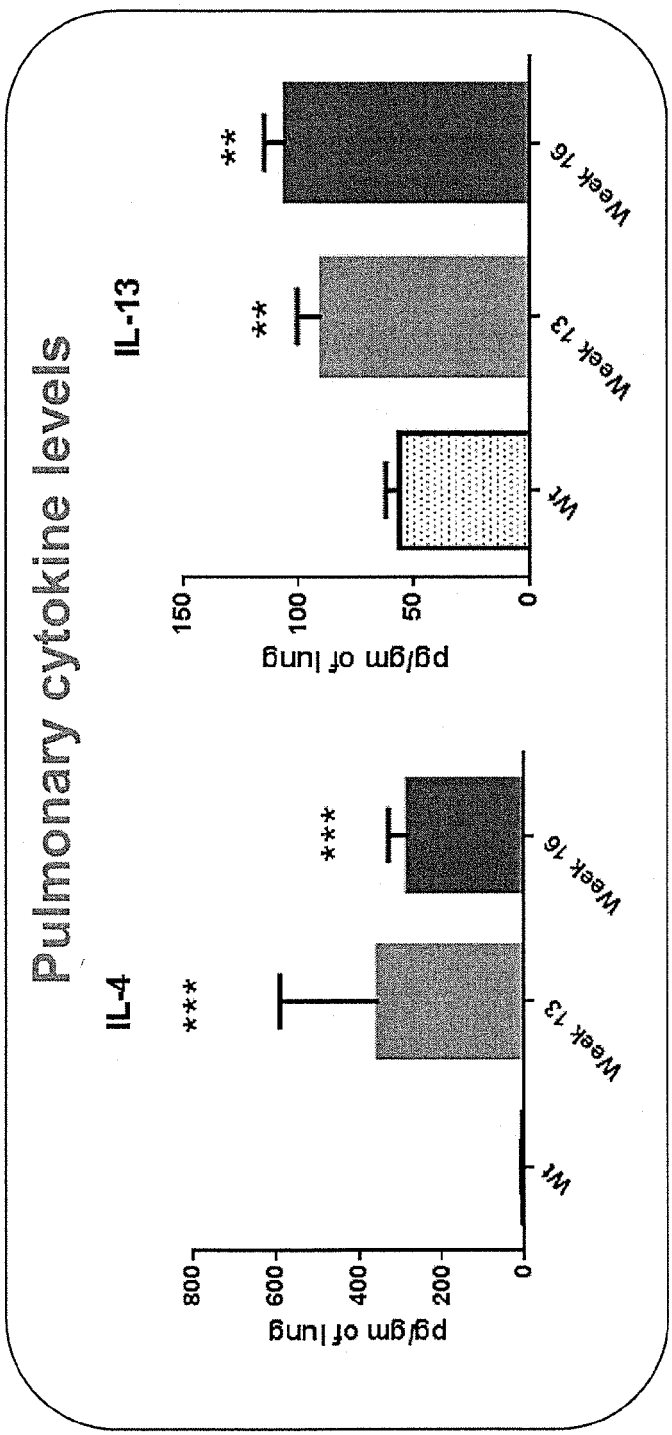

Pulmonary cytokine levels
IL-4
pg/gm of lung
800
600
400
200
0
***
***
Wt
Week 13
Week 16
IL-13
pg/gm of lung
150
100
50
0
**
**
Wt
Week 13
Week 16

FIGURE 9

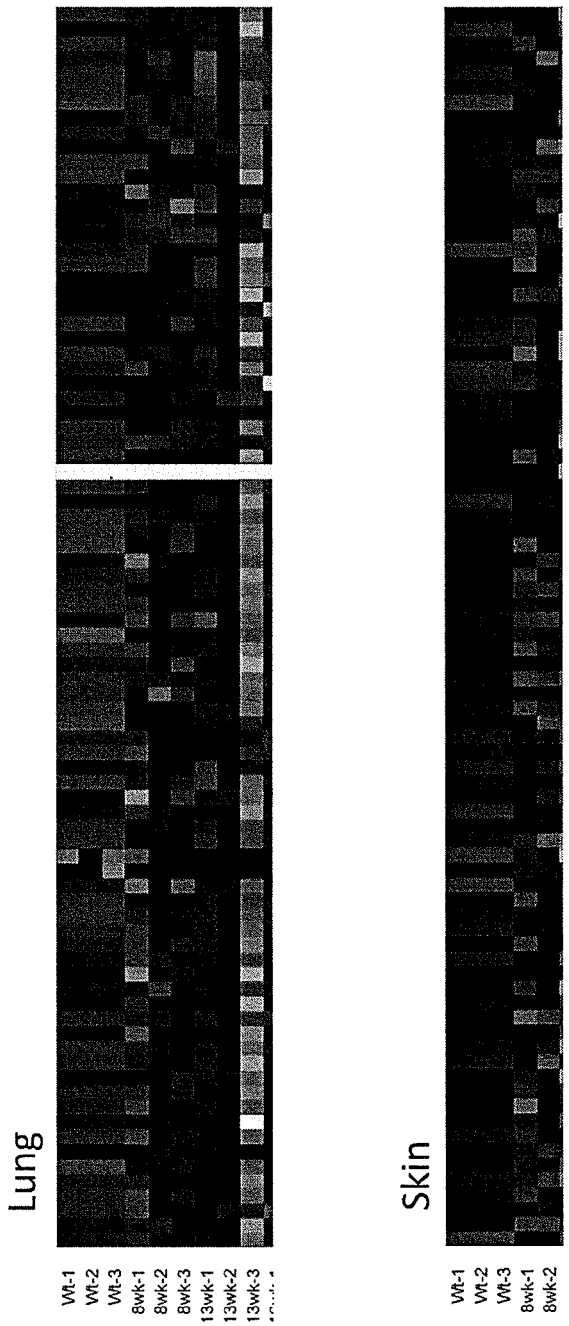

Lung
Wt-1
Wt-2
Wt-3
8wk-1
8wk-2
8wk-3
13wk-1
13wk-2
13wk-3
Skin
Wt-1
Wt-2
Wt-3
8wk-1
8wk-2

FIGURE 10

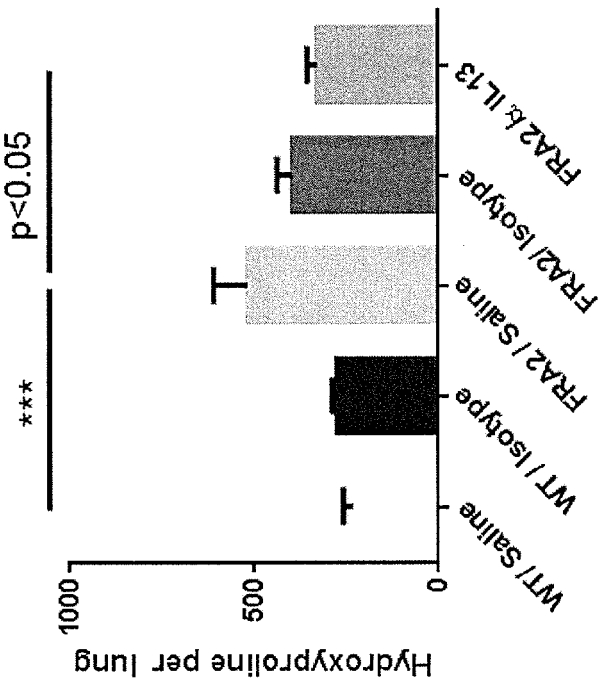

Hydroxyproline per lung
1000
500
0
WT/ Saline
WT / Isotype
FRA2 / Saline
FRA2/ Isotype
FRA2 & IL13
***
p<0.05

FIGURE 11

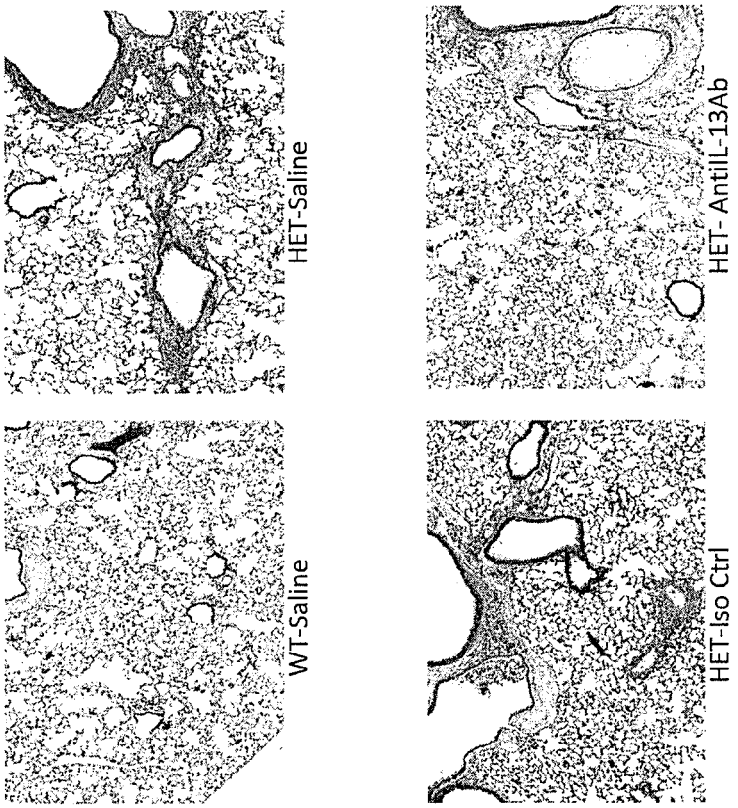


FIGURE 12

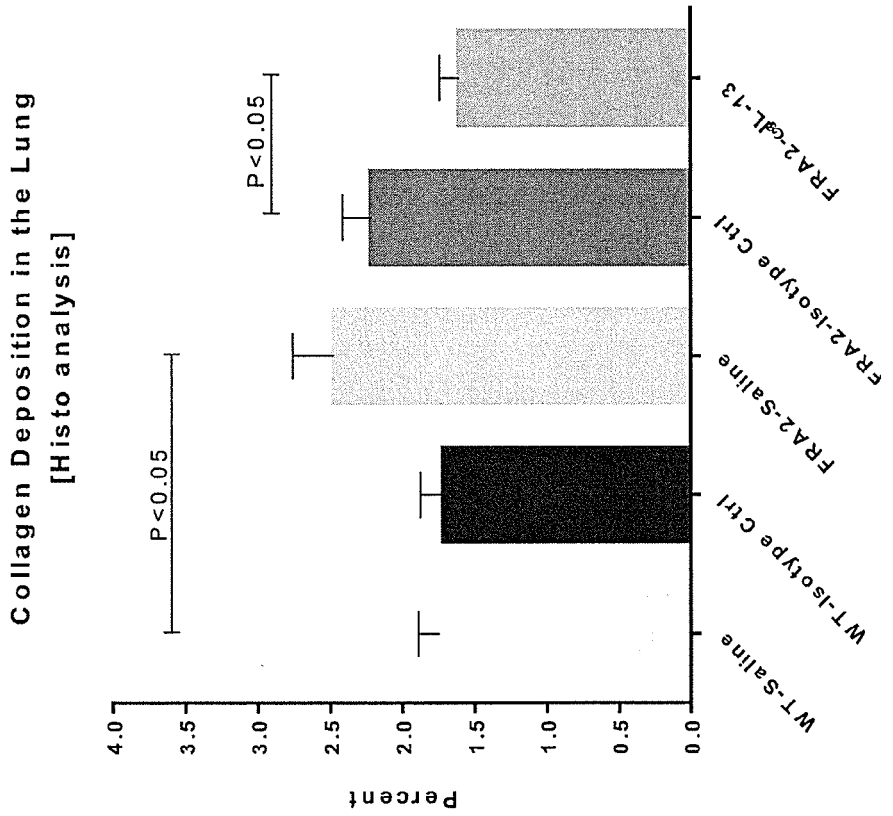

Collagen Deposition in the Lung
[Histo analysis]
Percent
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
P<0.05
P<0.05
WT-Saline
WT-Isotype Ctrl
FRA2-Saline
ERA2-Isotype Ctrl
FRA2-αIL-13

FIGURE 13

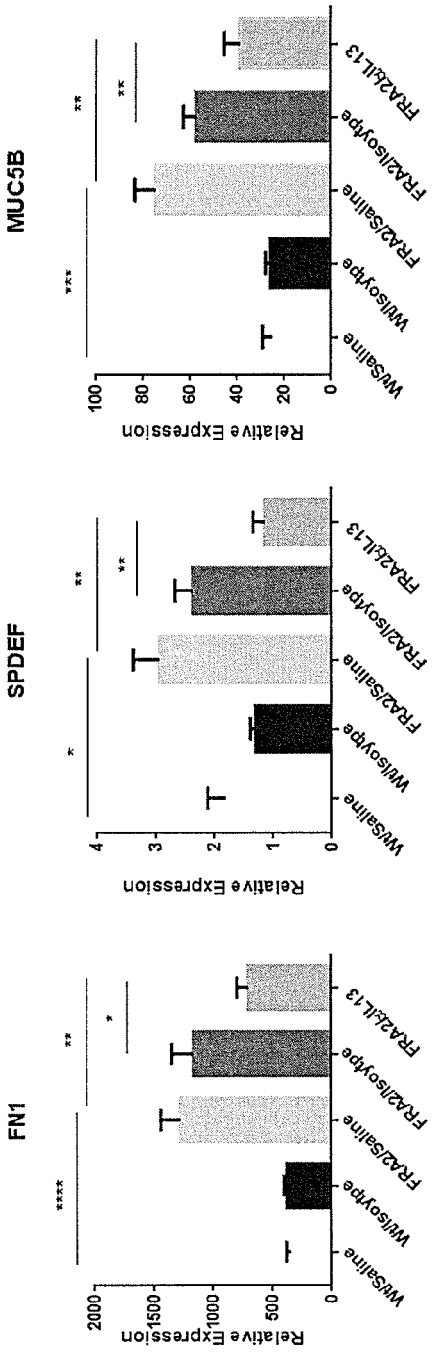

MUC5B
SPDEF
FN1
Relative Expression
WtSaline
WtIsotype
FRA2/Saline
FRA2/Isotype
FRA2&IL13

FIGURE 14

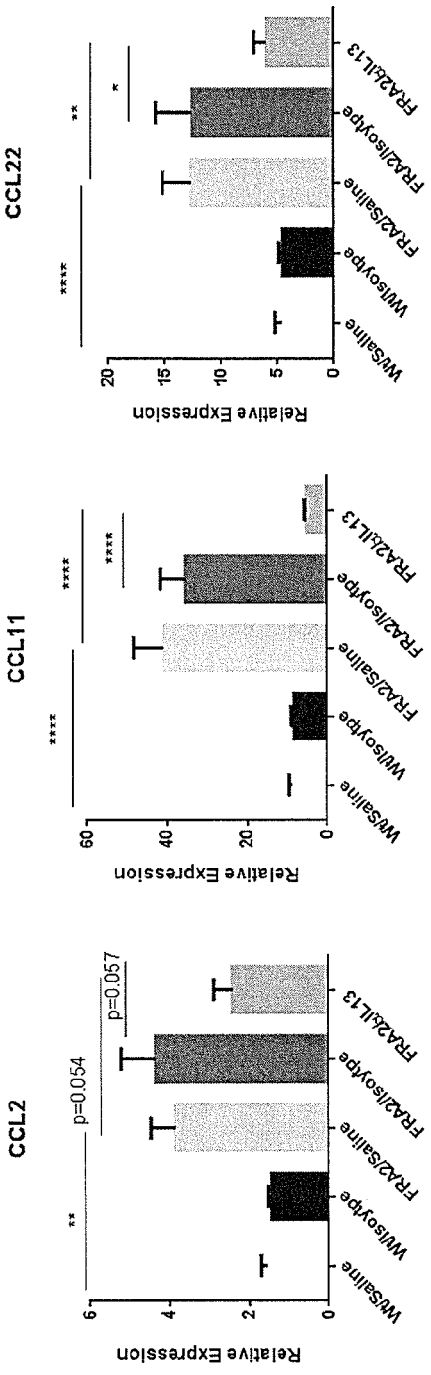

CCL2
CCL11
CCL22
Relative Expression
WtSaline
WtIsotype
FRA2Saline
FRA2Isotype
FRA2&IL13
p=0.054
p=0.057

FIGURE 15

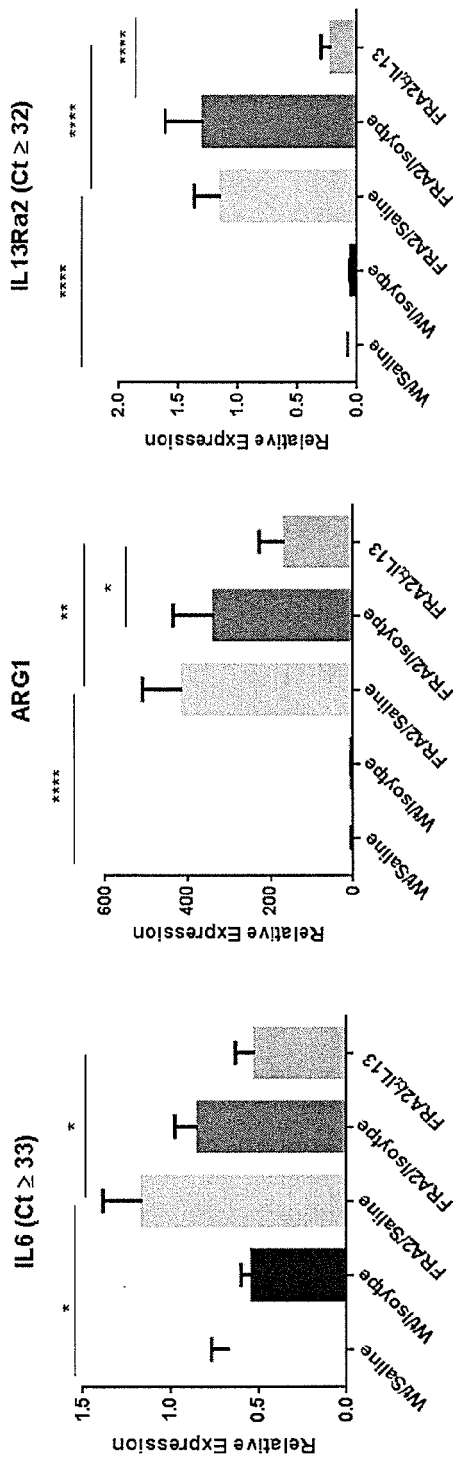

IL13Ra2 (Ct ≥ 32)
Relative Expression
0.0
0.5
1.0
1.5
2.0
****
****
****
Wt/Saline
Wt/Isotype
FRA2/Saline
FRA2/Isotype
FRA2&IL13
ARG1
Relative Expression
0
200
400
600
****
**
*
Wt/Saline
Wt/Isotype
FRA2/Saline
FRA2/Isotype
FRA2&IL13
IL6 (Ct ≥ 33)
Relative Expression
0.0
0.5
1.0
1.5
*
*
Wt/Saline
Wt/Isotype
FRA2/Saline
FRA2/Isotype
FRA2&IL13

FIGURE 16

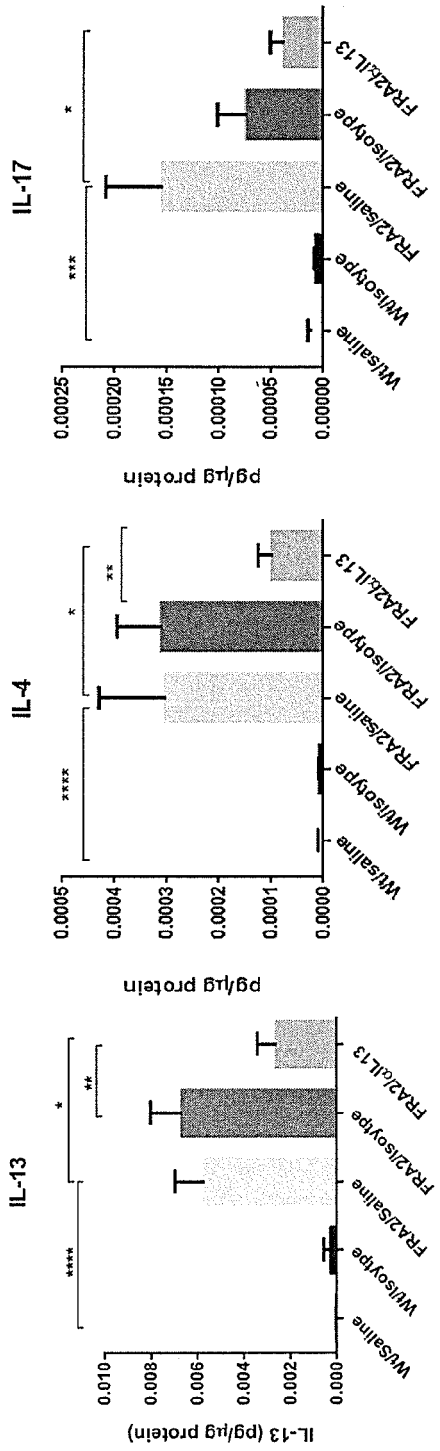

IL-17
pg/µg protein
0.00025
0.00020
0.00015
0.00010
0.00005
0.00000
***
*
Wt/saline
Wt/isotype
FRA2/saline
FRA2/isotype
FRA2/IL-13
IL-4
pg/µg protein
0.0005
0.0004
0.0003
0.0002
0.0001
0.0000
****
*
**
Wt/saline
Wt/isotype
FRA2/saline
FRA2/isotype
FRA2/IL-13
IL-13
IL-13 (pg/µg protein)
0.010
0.008
0.006
0.004
0.002
0.000
****
*
**
Wt/saline
Wt/isotype
FRA2/Saline
FRA2/isotype
FRA2/IL-13

FIGURE 17

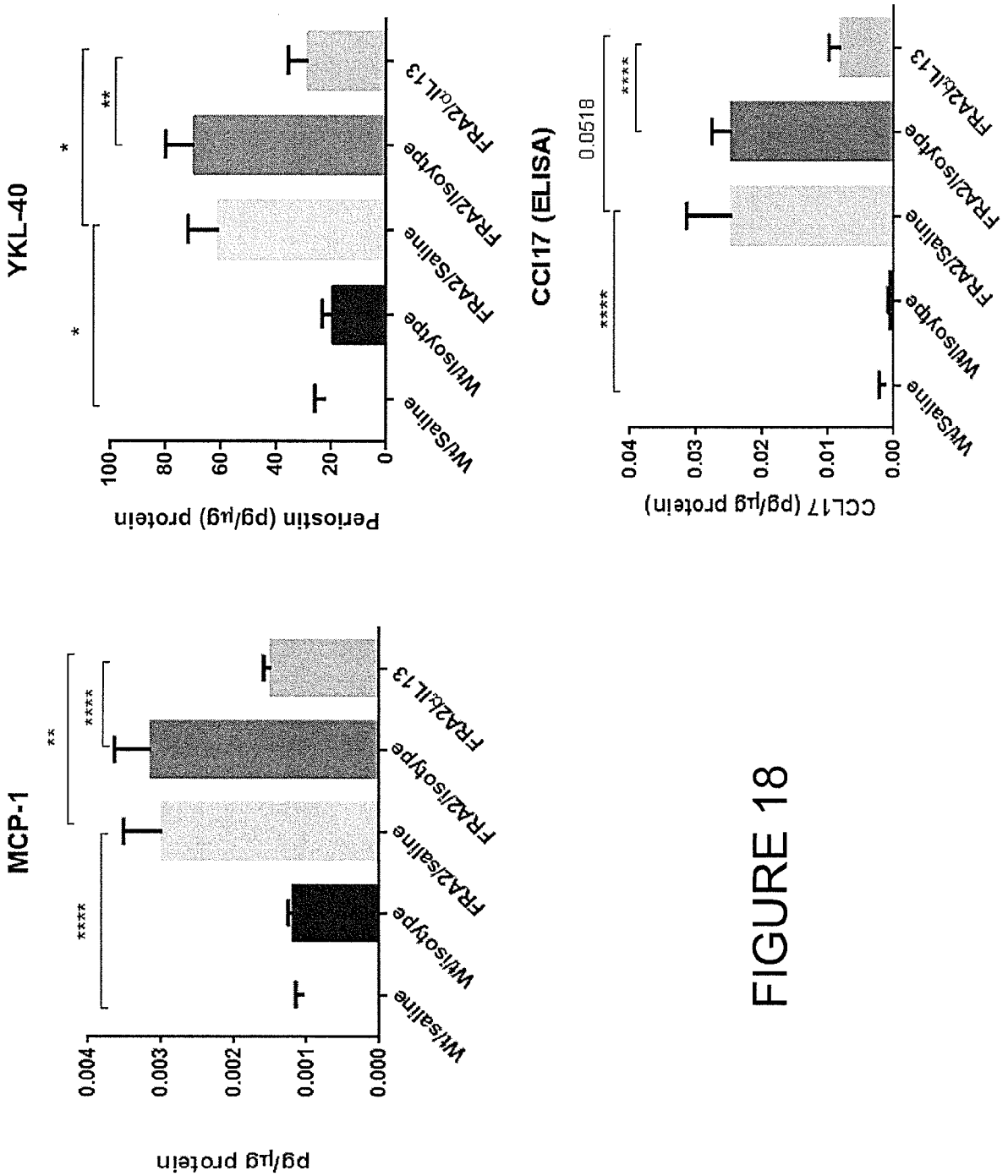

YKL-40
Periostin (pg/µg) protein
100
80
60
40
20
0
*
*
**
Wt/saline
Wt/isotype
FRA2/saline
FRA2/isotype
FRA2/αIL-13
CCl17 (ELISA)
CCL17 (pg/µg protein)
0.04
0.03
0.02
0.01
0.00
0.0518
****
****
Wt/saline
Wt/isotype
FRA2/saline
FRA2/isotype
FRA2/βIL-13
MCP-1
pg/µg protein
0.004
0.003
0.002
0.001
0.000
****
**
****
Wt/saline
Wt/isotype
FRA2/saline
FRA2/isotype
FRA2/βIL-13

FIGURE 18

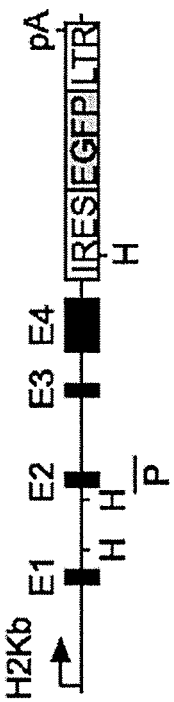


FIGURE 19A

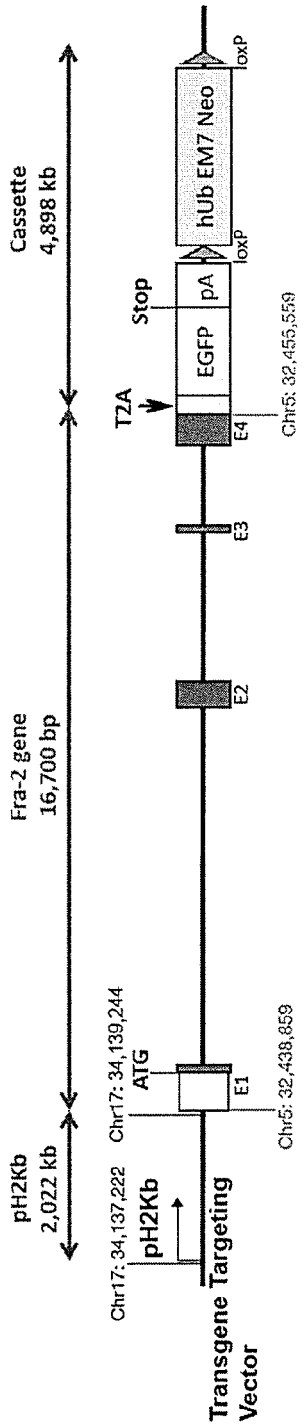


FIGURE 19B