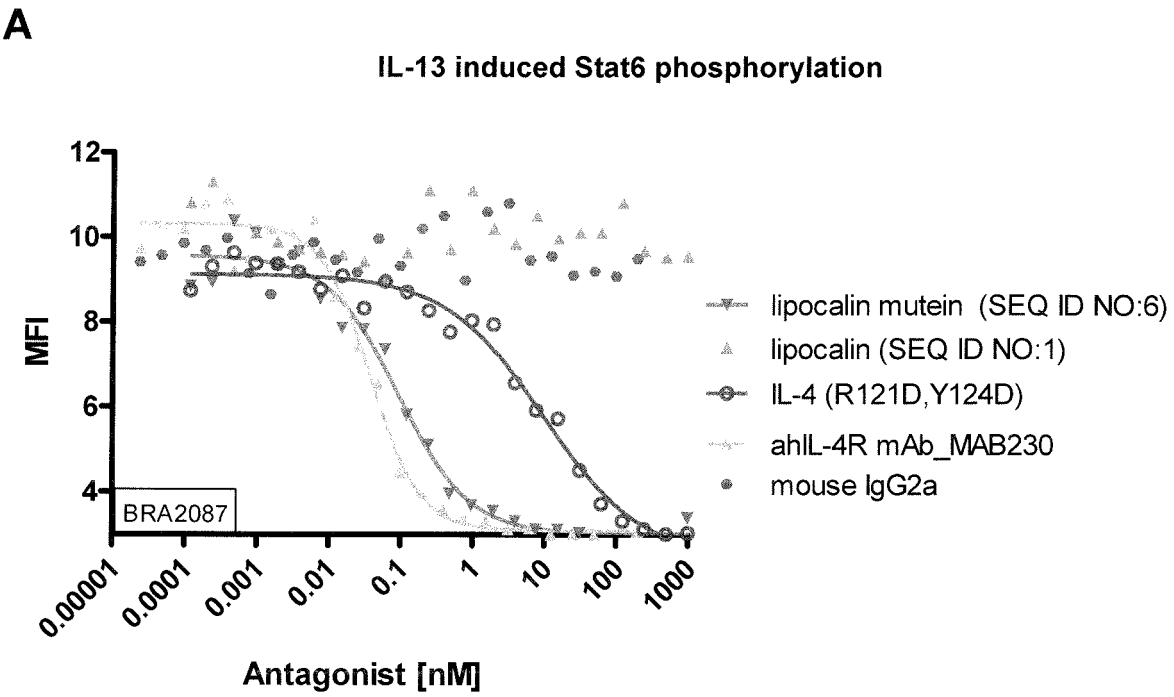
Figure 1

A


IL-13 induced Stat6 phosphorylation
MFI
12
10
8
6
4
BRA2087
0.00001
0.0001
0.001
0.01
0.1
1
10
100
1000
Antagonist [nM]
lipocalin mutein (SEQ ID NO:6)
lipocalin (SEQ ID NO:1)
IL-4 (R121D,Y124D)
ahIL-4R mAb_MAB230
mouse IgG2a

B

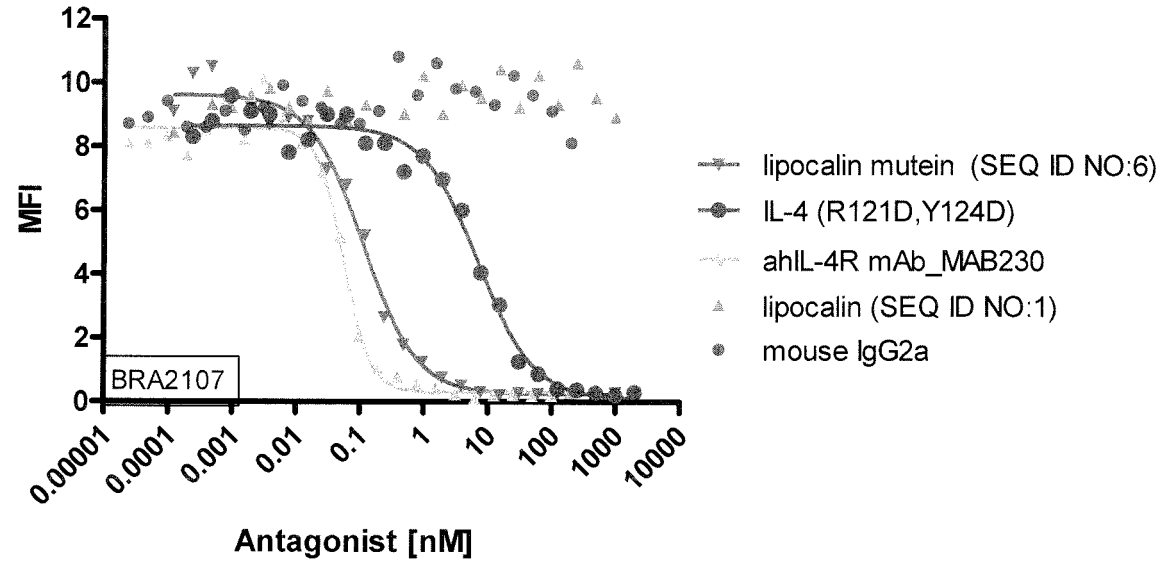

IL-4 induced Stat6 phosphorylation
MFI
12
10
8
6
4
2
0
BRA2107
0.00001
0.0001
0.001
0.01
0.1
1
10
100
1000
10000
Antagonist [nM]
lipocalin mutein (SEQ ID NO:6)
IL-4 (R121D,Y124D)
ahIL-4R mAb_MAB230
lipocalin (SEQ ID NO:1)
mouse IgG2a

Figure 2

Inhibition of human IL-4 induced Stat6 prophorylation in splenocytes isolated from hIL-4RA/hIL-13RA1 knock-in mice

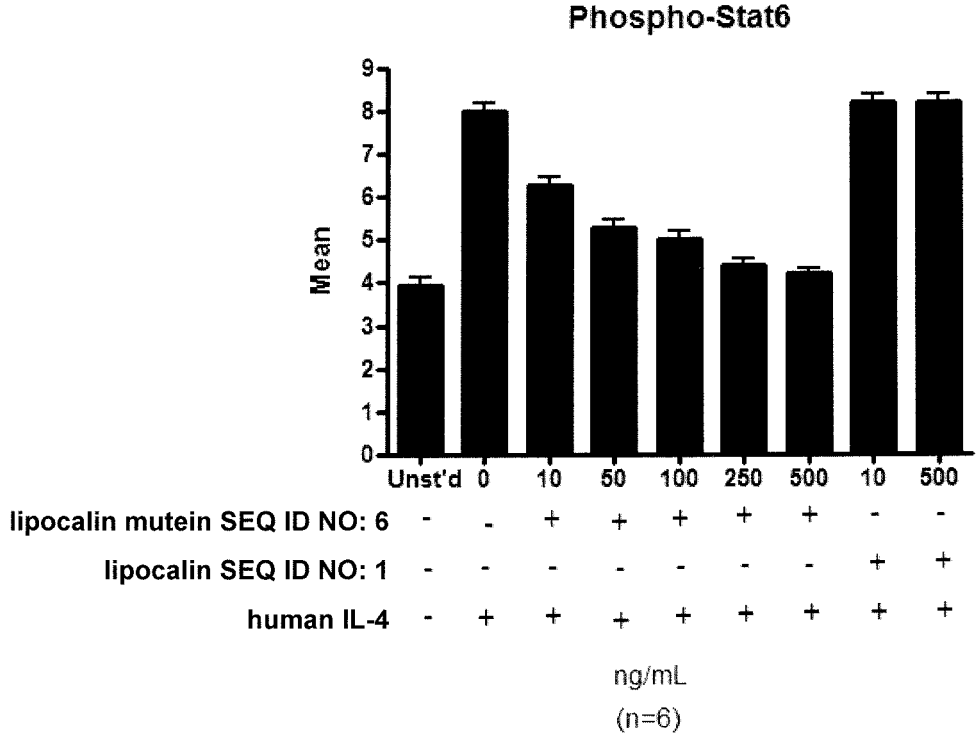


Figure 3

Inhibition of Human IL-13 induced eotaxin expression in hIL-4RA/hIL-13RA1 knock-in mice

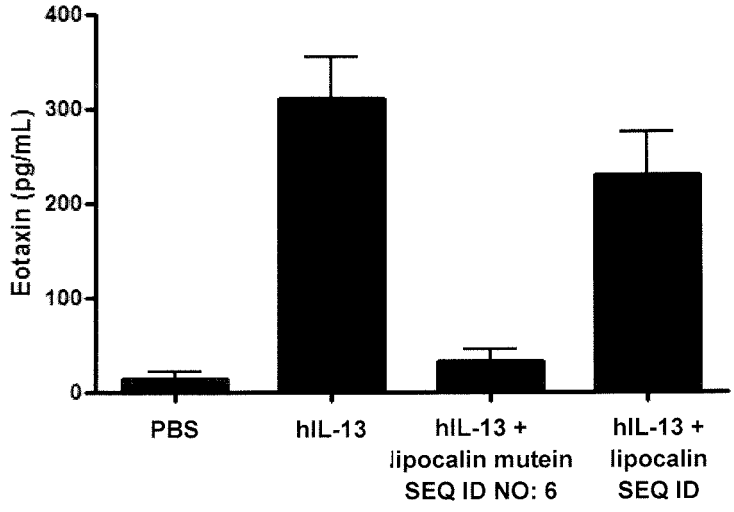
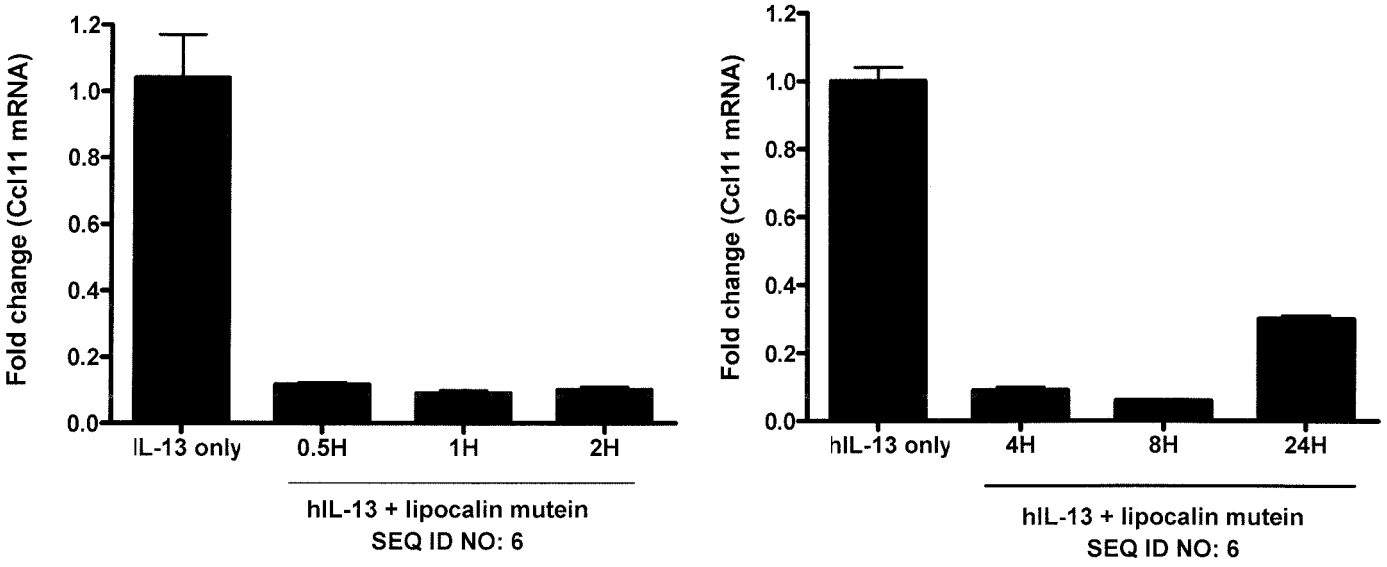


Figure 4

A

Inhibition of IL-13 induced Eotaxin RNA in the lung tissue of human IL-4RA/human IL-13 double knock-in mice (time course)



B

Inhibition of IL-13 induced Eotaxin RNA in the lung tissue of human IL-4RA/human IL-13 double knock-in mice (dose response)

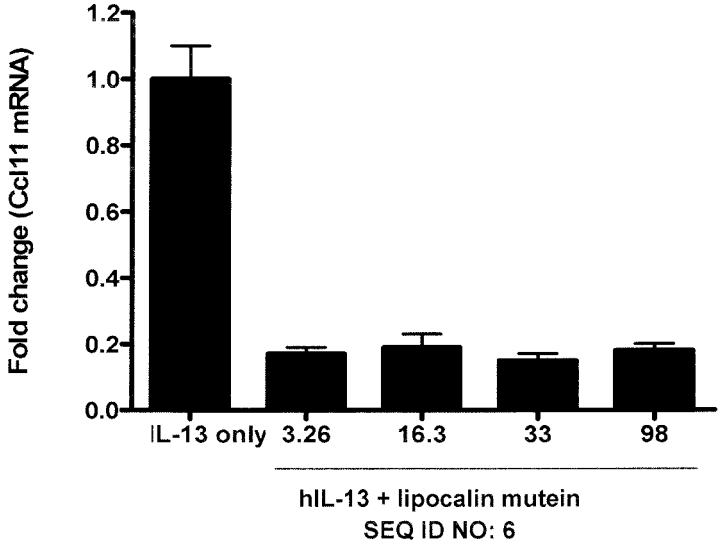


Figure 4 (cont'd)

C

Inhibition of IL-13 induced Eotaxin RNA in the lung tissue of human IL-4RA/human IL-13 double knock-in mice (comparison with IL-4 (R121D, Y124D))

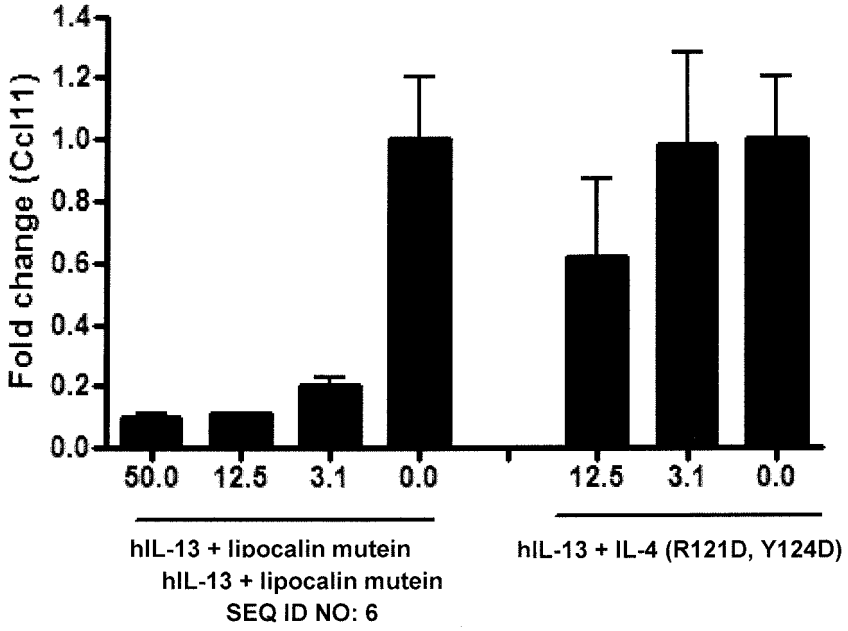
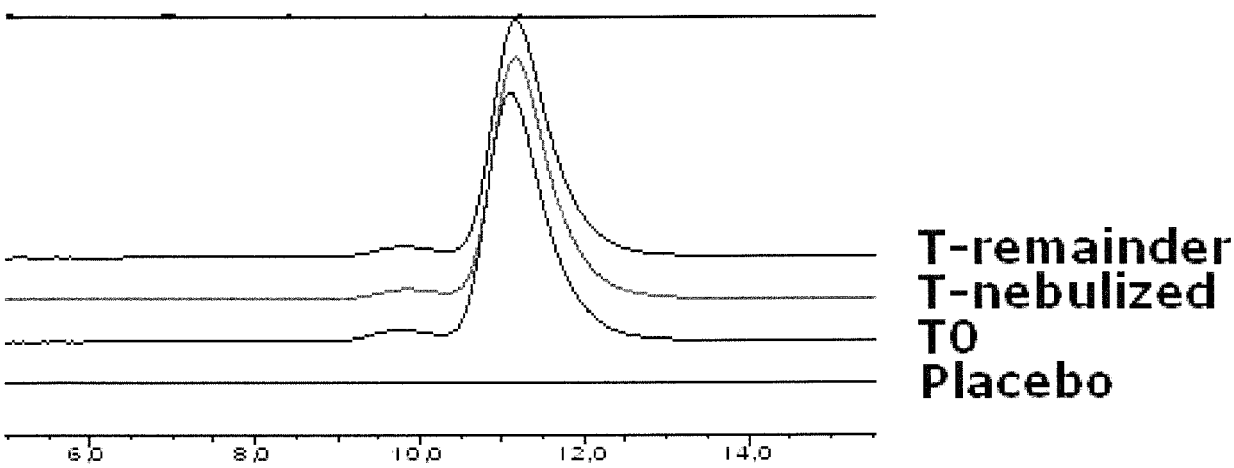


Figure 5

A

HP-SEC analysis of starting material, nebulized and material remaining in reservoir



B

Laser diffraction of nebulized formulation

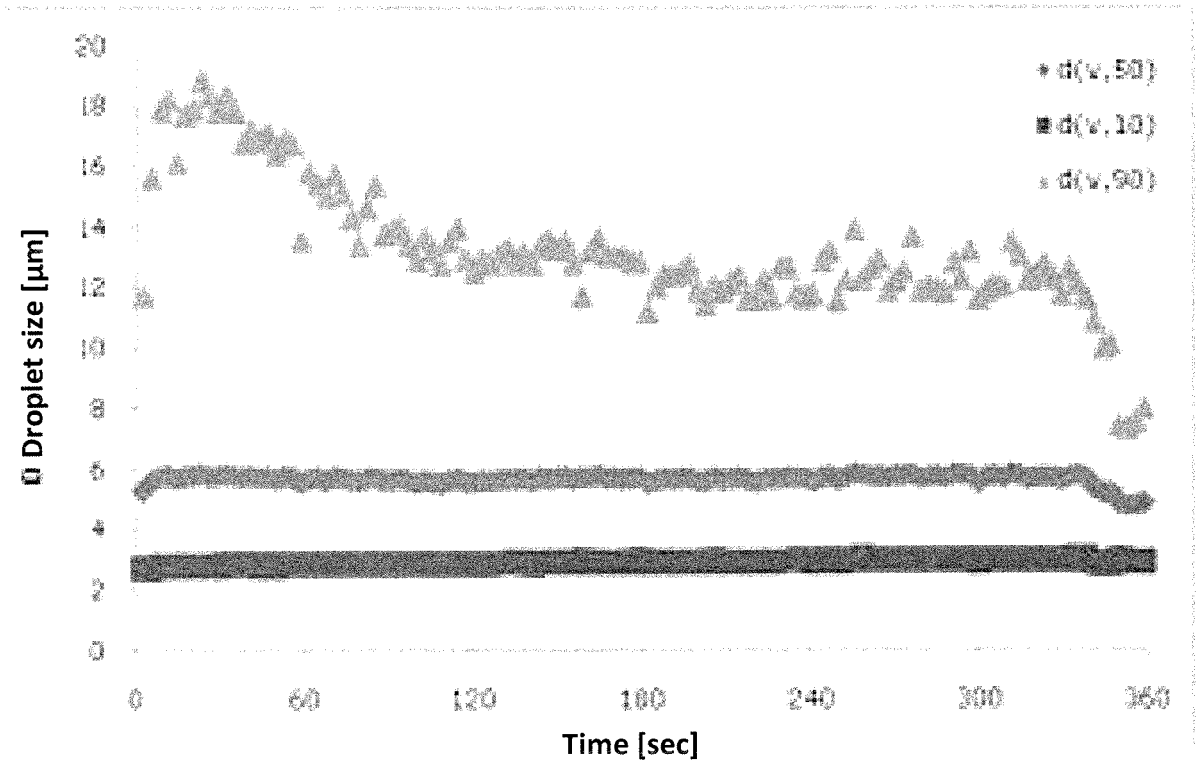
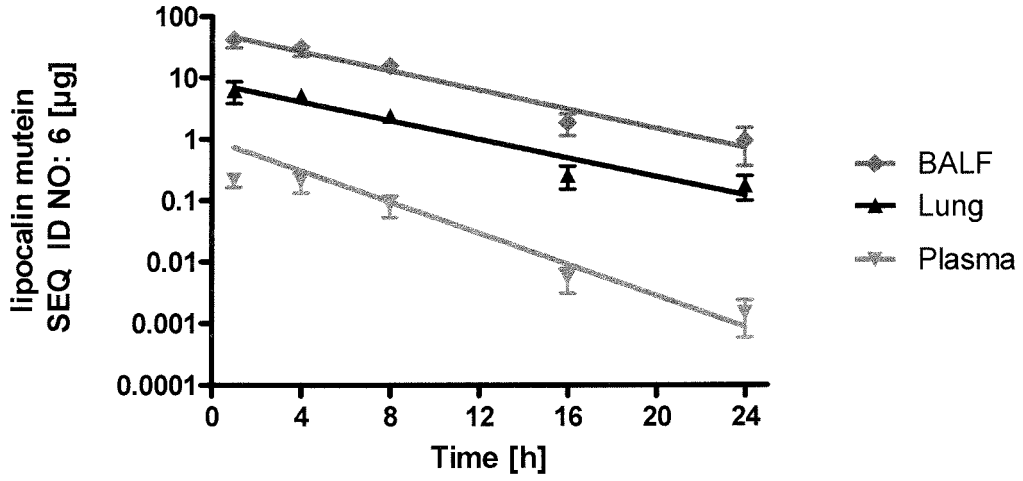


Figure 6

Pharmacokinetic properties and biodistribution of a lipocalin mutein in human IL-4RA/human IL-13 double knock-in mice after intratracheal instillation

A

Calculated total amounts of the mutein in plasma, BALF and lung tissue



B

Measured plasma and lung tissue concentrations of the mutein in relation to an estimated EC_{90} of 0,7µg/ml (dashed line)

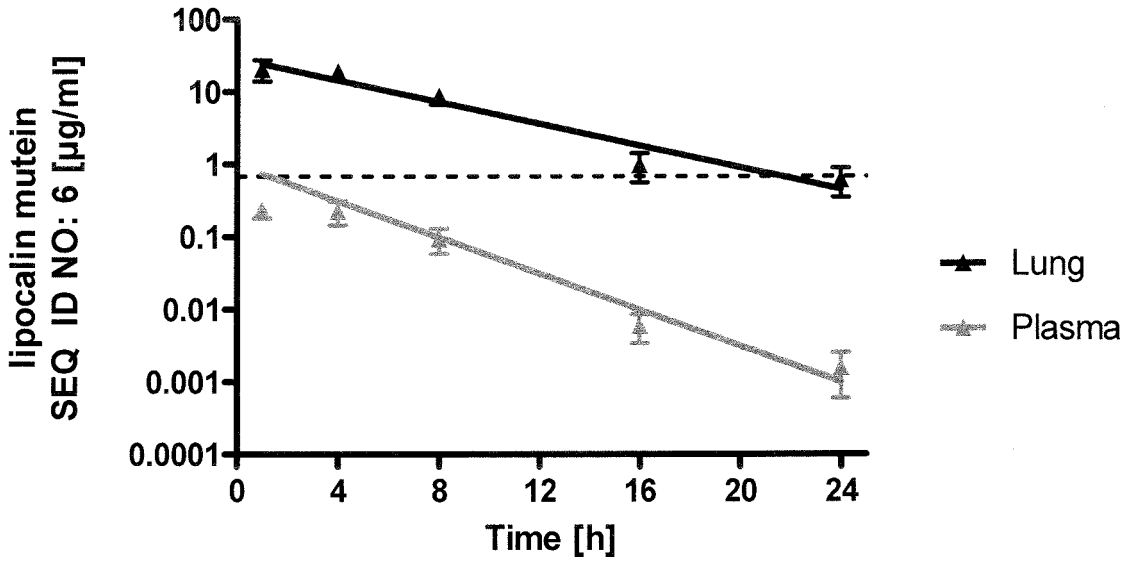
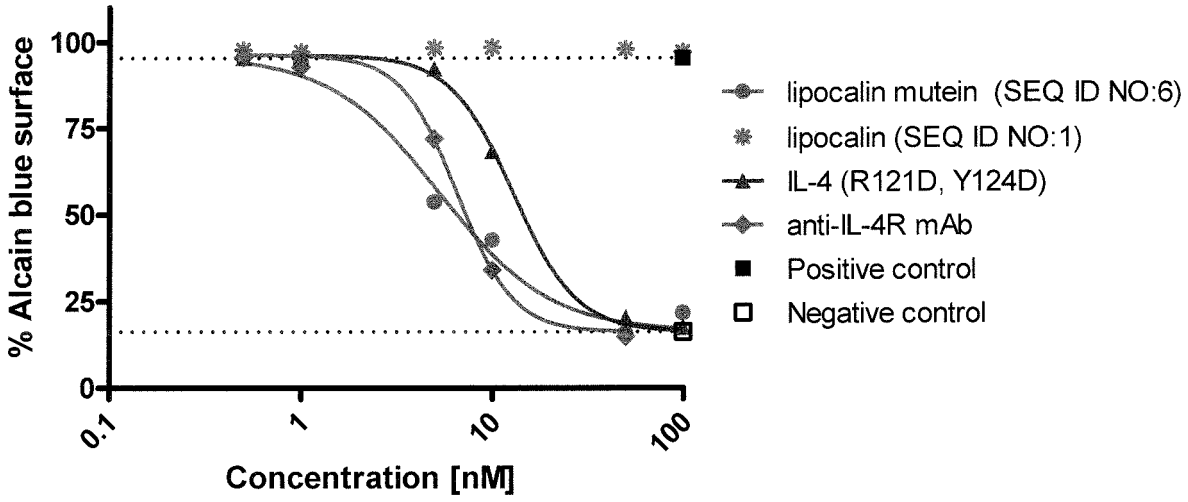


Figure 7

Inhibition of IL-13 induced goblet cell metaplasia in human airway epithelium air-liquid-interface culture system

A

Goblet cell surface area measured by Alcain blue staining (image analysis)



B

Phase contrast microscopy of Alcain blue stained epithelial/goblet cells

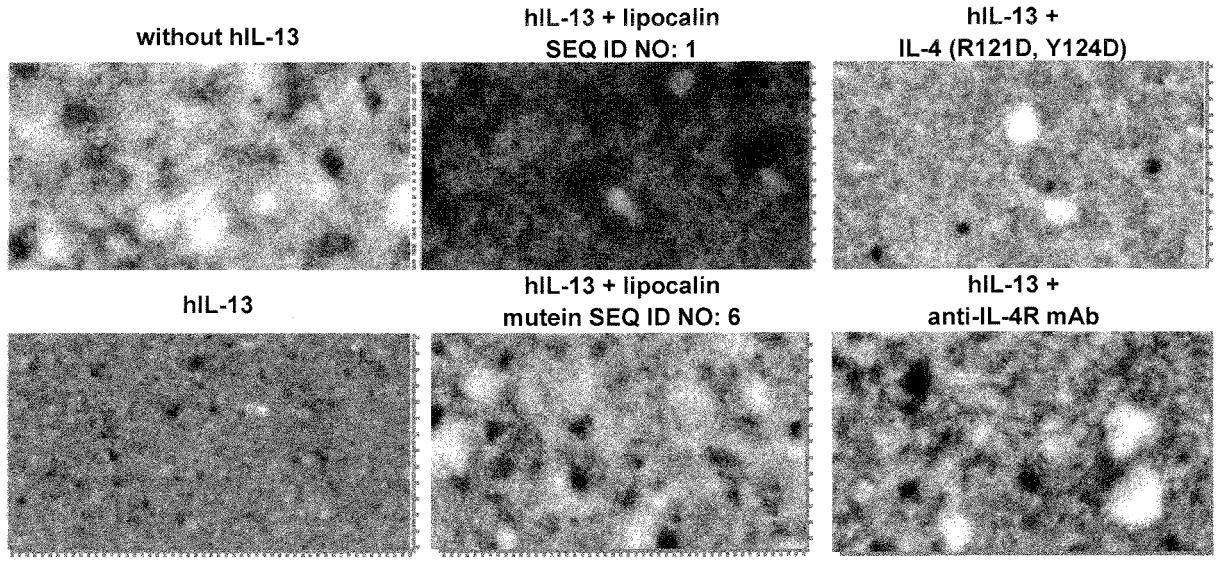
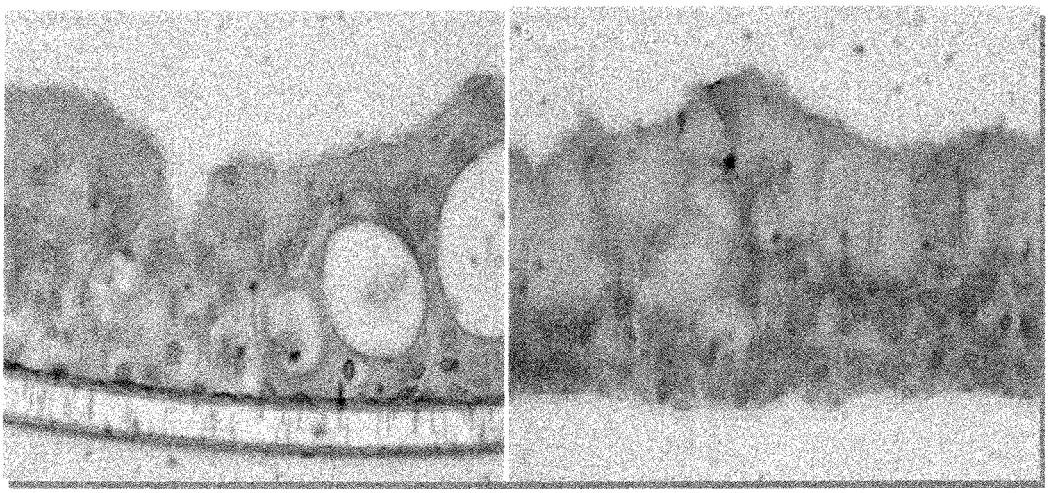


Figure 7 (cont'd)

C

Alcain blue/Neutral red stained paraffin sections without (negative) and with IL-13 (positive) on day 14



D

Eotaxin 3 in basal media of ALI culture on day 14

