

Background

We have previously reported that transformed airway goblet cells act as immune effector cells to secrete inflammatory mediators including IL-8 in response to lipopolysaccharide (LPS) exposure. LPS is the canonical ligand for TLR4 signaling.

IL-13 transforms airway cells into a goblet cell phenotype; thus we hypothesized that IL-13 would increase TLR4 expression in cultured normal human bronchial epithelial (NHBE) cells.

Methods

Cell culture and IL-8 ELISA

NHBE cells were grown at air-liquid interface for 14 days with rhIL-13 or PBS to transform to a goblet or ciliated phenotype.

At day 14, cells were exposed to PBS, LPS, IL-13 or a combination of each in basal media for 24 hours. Apical and basal IL-8 protein was measured by ELISA at day 15.

Toll Like Receptor gene expression

TLR3, 4, 7 and 8 mRNA expression was measured by RT-PCR.

Western blot analysis

Western blot identifies two TLR4 bands; glycosylated TLR4 which is expressed on the cell surface, and non-glycosylated TLR4 (sc-10741, Santa Cruz).

Results

Figure 1 IL-13 increased *only* TLR4 mRNA expression in NHBE cells

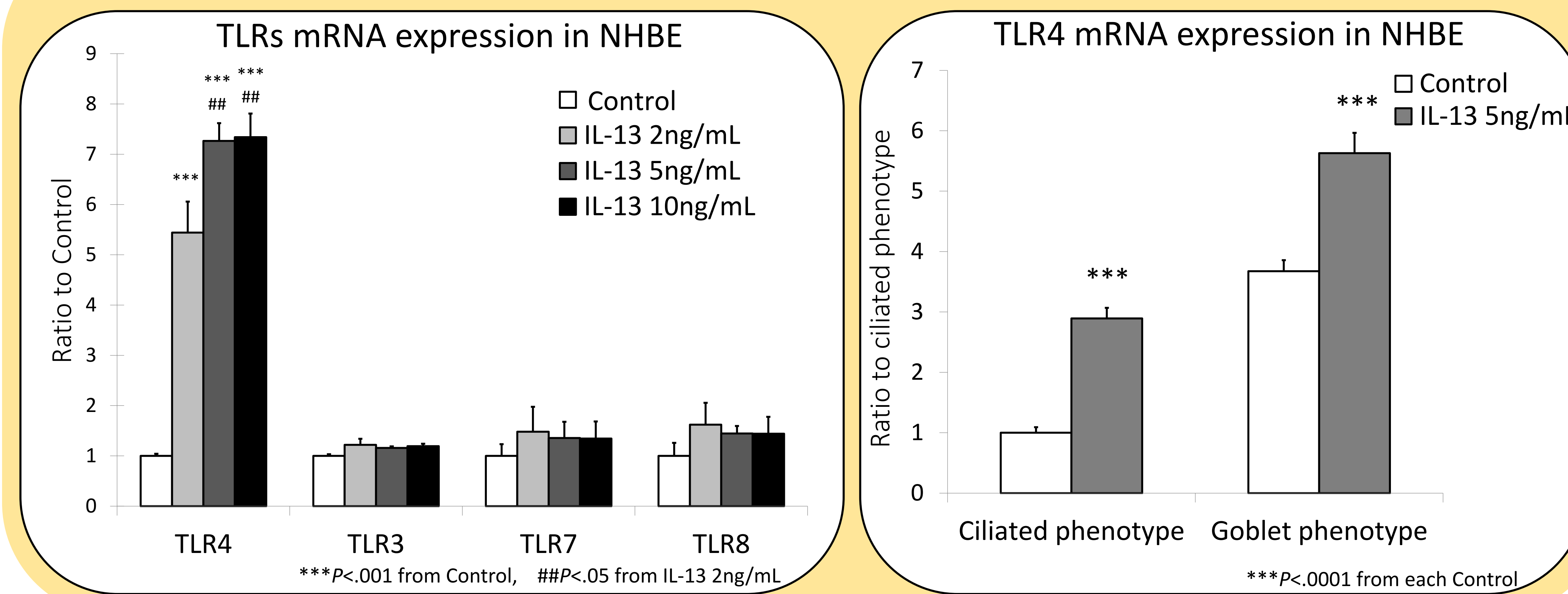


Figure 2 IL-13 increased glycosylated (surface expressed) TLR4 in NHBE cells

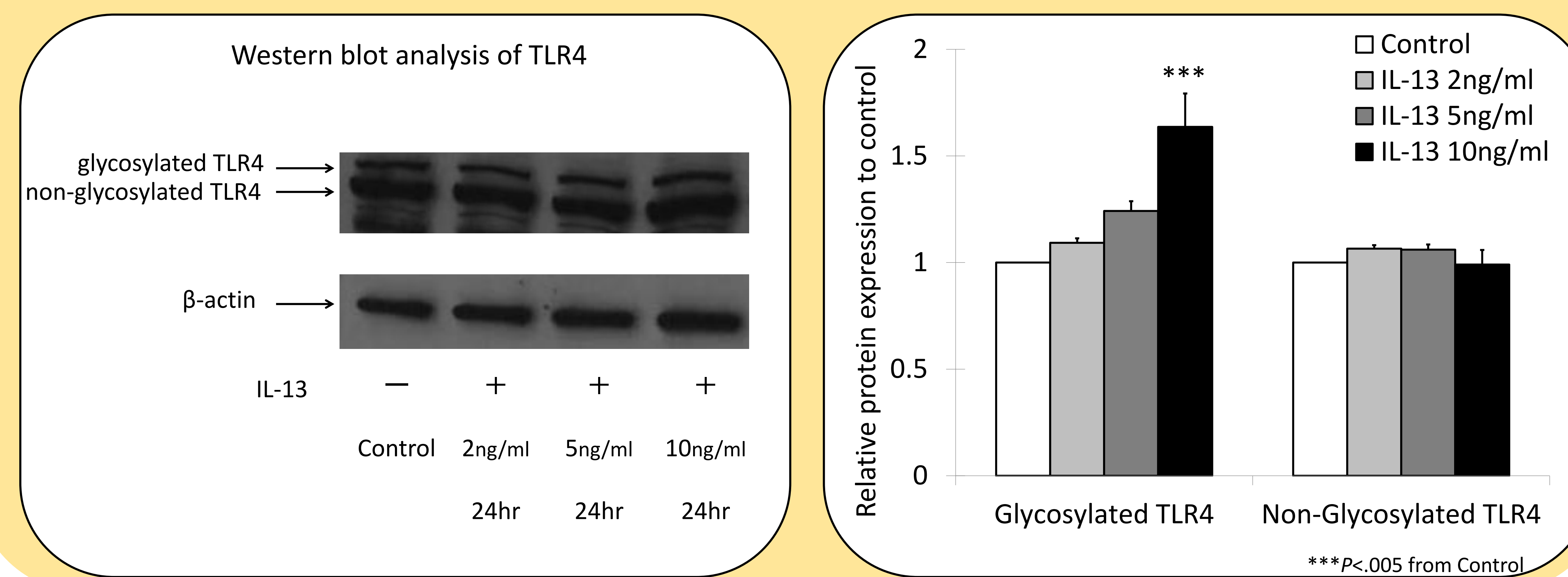
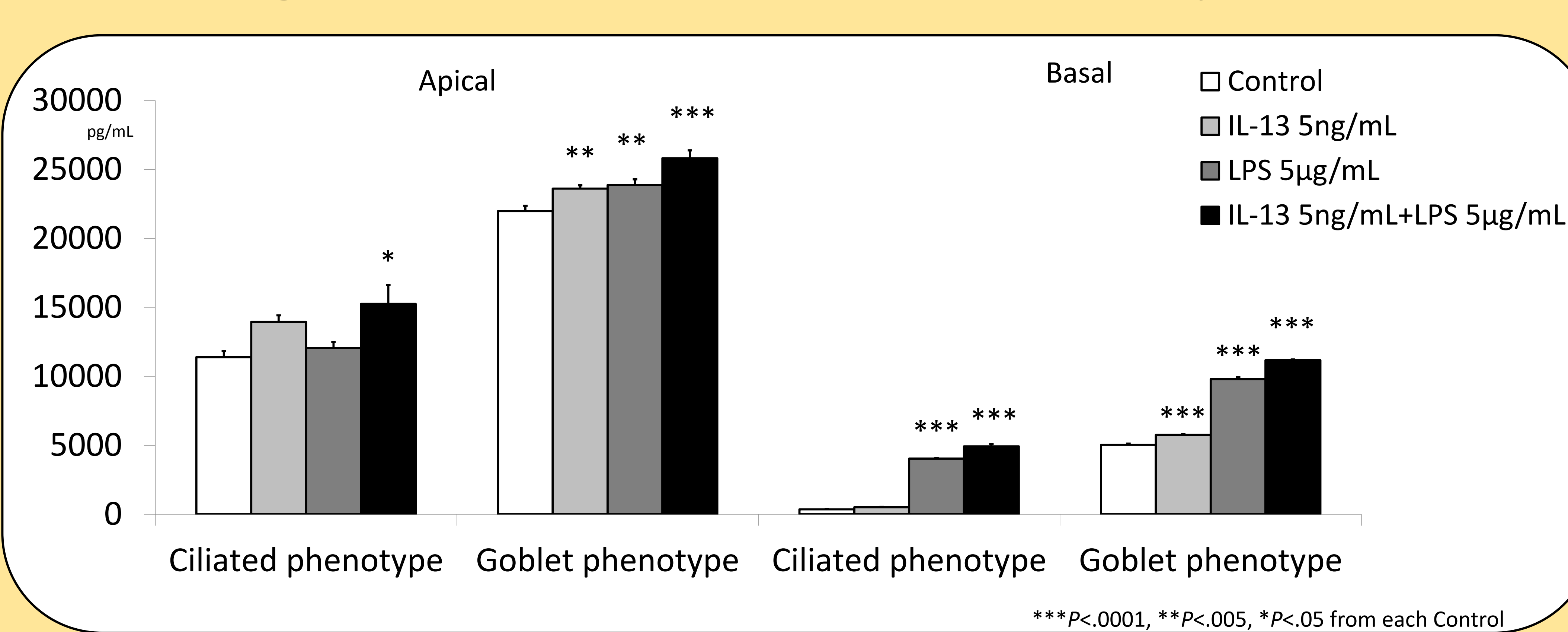


Figure 3 LPS increased IL-8 in NHBE cells stimulated by IL-13



Discussion

IL-13 increased TLR4 but not TLR 3, 7, or 8 mRNA expression after 14 days exposure in both ciliated and goblet phenotypes. Glycosylated (surface protein) TLR4 expression was increased but non-glycosylated TLR4 was not. LPS increased IL-8 in IL-13 stimulated NHBE cells.

These data suggest that IL-13 not only increases goblet cell metaplasia and mucus secretion, but also that IL-13 can enhance TLR4 receptor expression on airway goblet cells and responsiveness to LPS.

Conclusion

IL-13 increases TLR4 surface receptor expression in NHBE (goblet) cells. High IL-13 levels may increase the susceptibility to endotoxin and dust mite related exacerbations of airway diseases like asthma.

References

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