

IL-13 induces periostin via MAP kinase and STAT6 phosphorylation. Inhibiting periostin decreases MUC5AC mucin secretion.

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Background

Periostin is a biomarker for severe asthma. We have shown that periostin is produced in normal human bronchial epithelial (NHBE) cells after exposure to IL-13 and that rh-periostin modestly increases MUC5AC secretion. However, the precise mechanism of periostin production and its effect on NHBE cells is not well described.

Objectives

In differentiated NHBE cells:

1. Evaluate the cell signaling pathways of IL-13-induced periostin production.
2. Investigate how periostin inhibits MUC5AC production.

Methods

Cell culture

NHBE cells were grown for 14 days at air-liquid interface (ALI) with or without IL-13 to produce a goblet or ciliated cell phenotype. Experimental conditions are shown in Figure 1.

NHBE cells were exposed to IL-13 and specific inhibitors; leflunomide (JAK/STAT6 inhibitor) or PD98059 (MEK/ERK inhibitor) for 72 hours after fully differentiated.

For OC-20 exposure, NHBE cells were cultured with IL-13 and OC-20, a periostin neutralization antibody for 14 days.

Periostin and MUC5AC secretion

Periostin in apical supernatant and basolateral medium, and MUC5AC in apical supernatant was measured by ELISA.

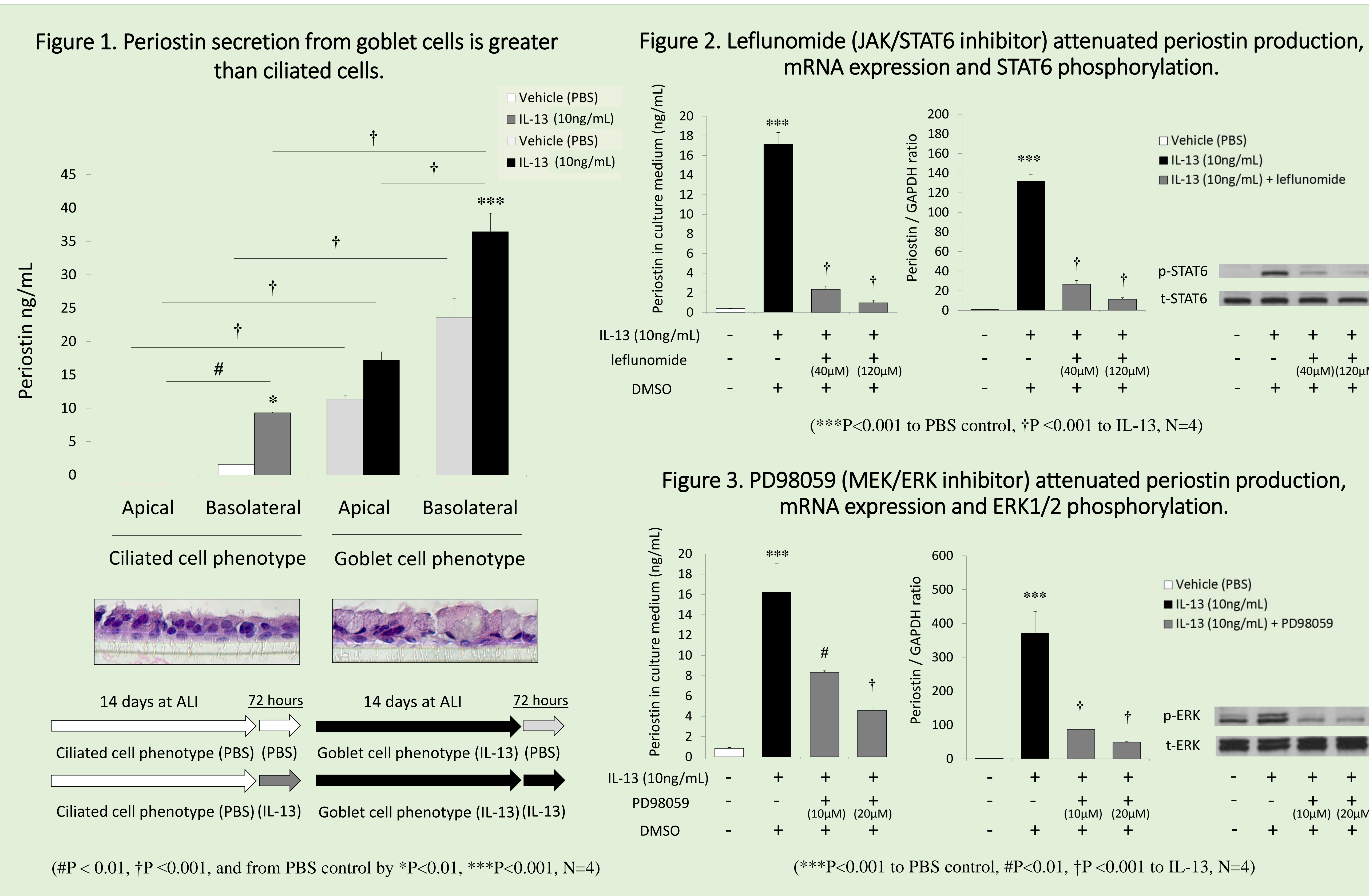
Periostin and MUC5AC mRNA expression

Periostin and MUC5AC mRNA expression was measured by RT-PCR.

STAT6 and ERK1/2 activity

Phosphorylation of STAT6 and ERK1/2 activation was evaluated by Western blotting.

Results



Discussion

IL-13-induced periostin production from ciliated cells is detected almost exclusively at the basolateral side. IL-13-transformed goblet cells secrete periostin to both the apical and basolateral sides.

Periostin secretion is predominantly directed toward the basolateral side of the cells suggesting that periostin may be involved in the remodeling process.

IL-13-induced periostin production was mediated by MAP kinase and STAT6 phosphorylation. This is consistent with reports that MAP kinase and STAT6 pathways have an important role in periostin production.

IL-13-driven mucin production is partially inhibited by OC-20, a specific periostin neutralizing antibody.

Conclusions

Airway epithelial cells, in particular goblet cells, are likely to be an important source of periostin in the serum and sputum in the airway.

Periostin production in differentiated airway cells is mediated, in part, by JAK/STAT6 and MEK/ERK.

Periostin is associated with mucus hypersecretion.

References

1. Izuhara K, et al. Periostin in allergic inflammation. *Allergy Int* 2014; 63: 143-151.
2. Bentley JK, et al. Periostin is required for maximal airways inflammation and hyperresponsiveness in mice. *J Allergy Clin Immunol* 2014; 134: 1433-42.