Introduction

Asthma is the most common chronic condition in children worldwide, and despite advances in our understanding of the disease, there is still no cure for the disease. In addition to asthma, airway remodeling has also been shown to play a critical role in the chronic obstructive disease observed in asthmatic individuals, characterized by a loss of epithelial barrier function and mucus cell metaplasia.

Methods

To determine the ability of airway epithelial cells during the process of epithelial-mesenchymal transition (EMT) to remodel collagen in the presence of cytokines, 16HBEo- cells cultured for 48 h in type I collagen gel were polymerized at 37°C for 8 h. The A549 and 16HBEo- cells were trypsinized and seeded at 100,000 cells/well on 24-well plates coated with BSA (0.4 mg/ml), collagen type I (10 µg/ml), or玻璃质α胶原(10 ng/ml), or IL-13 (20 ng/ml). Cells were incubated with the drugs Fluticasone (10 µM) or Salbutamol, in the presence of TNF-α (10 ng/ml), or IL-13 (20 ng/ml) or TNF-α + IL-13. After the 48 h treatment incubation, cell lysates were collected for examining protein expression of TGFβ1-induced EMT proteins in airway epithelial cells. The aim of this study was to investigate the extent of TGFβ1-induced EMT on epithelial cells using TGFβ1-treated alveolar and bronchial airway cell lines and measuring aspects of EMT function. Additionally, as acute exacerbations of asthma are associated with inflammation requiring the use of anti-inflammatory medications, we will evaluate the effect of TGFβ1 and Th1/Th2 cytokine combinations. Fluticasone and Salbutamol on TGFβ1-induced EMT.

Results

Fig. 1. Th1 and Th2 inflammatory cytokines modulate TGFβ1-induced EMT

A. Airway Epithelial Cells

E-cadherin

Fibronectin-E3A

Collagen 1α1

Plasma Fibronectin

B. Alveolar Epithelial Cells

E-cadherin

Fibronectin-E3A

Collagen 1α1

Plasma Fibronectin

Fig. 2. IL-13 enhances TGFβ1-induced collagen gel contraction by airway epithelial cells

A. Airway Epithelial Cells

E-cadherin

Fibronectin-E3A

Collagen 1α1

Plasma Fibronectin

B. Alveolar Epithelial Cells

E-cadherin

Fibronectin-E3A

Collagen 1α1

Plasma Fibronectin

Fig. 3. TGFβ1-induced airway epithelial cell collagen remodeling is not enhanced by the presence of Th1 or Th2 inflammation

A. Airway Epithelial Cells

E-cadherin

Fibronectin-E3A

Collagen 1α1

Plasma Fibronectin

B. Alveolar Epithelial Cells

E-cadherin

Fibronectin-E3A

Collagen 1α1

Plasma Fibronectin

Fig. 4. Fluticasone and Salbutamol can enhance TGFβ1-induced EMT

A. Airway Epithelial Cells

E-cadherin

Fibronectin-E3A

Collagen 1α1

Plasma Fibronectin

B. Alveolar Epithelial Cells

E-cadherin

Fibronectin-E3A

Collagen 1α1

Plasma Fibronectin

Fig. 5. The presence of collagen 1 enhances TGFβ1-induced expression of ECM proteins in airway epithelial cells

A. Collagen 1α1

B. Fibronectin

Fig. 6. TGFβ1-induced epithelial cell collagen remodeling is not enhanced by the presence of Th1 or Th2 inflammation

A. Airway Epithelial Cells

E-cadherin

Fibronectin-E3A

Collagen 1α1

Plasma Fibronectin

B. Alveolar Epithelial Cells

E-cadherin

Fibronectin-E3A

Collagen 1α1

Plasma Fibronectin

Fig. 7. The presence of collagen 1 enhances TGFβ1-induced expression of ECM proteins in airway epithelial cells

A. Collagen 1α1

B. Fibronectin

Summary

Our data indicate that Th1 and Th2 inflammation can influence the control and function of both alveolar and airway epithelial cells that have been performed together. The data suggest that a novel role for IL-13 signaling in the induction of TGFβ1-mediated EMT in the airway may have implications for the understanding of the role of EMT in asthma and other chronic lung diseases.