Impaired ciliary differentiation of airway epithelial cells from asthmatics with and without exercise-induced bronchoconstriction

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Abstract

Asthma is a respiratory syndrome characterized by periods of reversible airflow obstruction, often in response to inhaled stimuli such as pollutants or allergens.

Introduction

Asthma is a chronic inflammatory disease of the airways characterized by periodic exacerbations leading to airflow obstruction. Exercise-induced bronchoconstriction (EIB) is a common asthma phenotype that affects up to 50% of asthmatics.

Materials & Methods

EXPERIMENTAL OVERVIEW

Differential expression of air-liquid interface cell lineages

Diffusion of inflammatory mediators IL-6 and IL-8

Hypothesis

We hypothesized that the differentiation process is altered in airway epithelial cultures both EIB(-) and EIB(+) asthmatic donors compared to healthy control donors.

Specific Aim

The aim of this study was to phenotype the in vitro differentiation process of human airway epithelial cells from non-asthmatic control donors and asthmatic donors with and without EIB.

Results

Figure 1. Differentiation of ciliated cells is impaired in airway epithelial cells from asthmatic donors

Figure 2. Cilia are significantly shorter in EIB(-) cultures

Figure 3. EIB(-) asthmatic air-liquid interface cultures have significantly more basal cells

Figure 4. Expression of ciliogenesis genes is correlated with histology findings

Results

Figure 5. Release of inflammatory mediators IL-6 and IL-8 differs between disease states and during differentiation

Summary

Ciliary differentiation is impaired in ALI cultures of airway epithelial cells from EIB(-) and EIB(+) asthmatics.

EIB(+) cultures have shorter cilia and an expanded eif5-expressing basal population.

Expression of ciliogenesis-related genes FOXI1, DAXA1, SPAG8 are significantly correlated with the percentage of ciliated cells at the apical surface of ALI cultures.

Asthmatic cultures release less IL-6 but more IL-8 than control cultures.

Future work will aim to elucidate the mechanisms underlying aberrant mucociliary differentiation in asthma through mRNA and miRNA sequencing.

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References