Abstract

Asthma remains a heavy burden on health-care systems, despite significant advances in our understanding of the disease pathophysiology and the availability of more effective therapies. The cost related to hospital admissions during exacerbations is a substantial proportion of the cost associated with the disease.

Epithelial studies suggest that exposure to urban particulate matter can promote the development of asthma and is associated with asthma exacerbations [1-3]. Many studies have demonstrated that increases in air pollution result in a greater use of asthma medication, more consultations with general practitioners and increased hospital admissions for asthma [4].

Similarly, viral respiratory tract infections particularly with respiratory syncytial virus (RSV) or macaque (MV)- Env is most commonly associated with bronchiolitis, childhood wheeze and induction of asthma exacerbations [5,6] in children, 50-76% in adults [7].

Within the airway, the epithelium is a major target for RSV infection and these cells are also critically important in processing inhaled airborne particles. Accordingly, it is important to understand how environmental stresses such as virus infection and ambient particulate matter exacerbate the pathophysiology of asthma.

Methods

Inflammatory response of asthmatic epithelial air-liquid-interface cultures to mechanical wounding, respiratory syncytial virus and particulate matter

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Introduction

Specific Aim

The objectives of this study were to characterize the responses of asthmatic and non-asthmatic-derived ALI epithelial cultures to the following environmental insults: mechanical wounding, respiratory syncytial virus, asthmatic aerosol and non-asthmatic/asthmatic airway epithelial cells and their response to common environmental insults such as mechanical wounding, respiratory syncytial virus (RSV) and particulate matter (EHC-93).

Methods

ALI-AEC cultures were differentiated into ALI cultures on a fee-for-service basis by MatTek Corporation, Ashland, MA, using differentiated air-liquid interface (ALI) epithelial cultures derived from asthmatic and non-asthmatic (n=6) airway epithelial cells. Tracheal tissues and ALI cultures were embedded for immunohistochemical analysis (see below) and supernatant was stored at -80°C or embedded for immunohistochemical analysis.

Results

Figure 2. The asthmatic epithelium is composed of an altered epithelial phenotype

Figure 3. Wound closure is delayed in asthmatic derived ALI cultures

Figure 4. Viral screening in epithelial cultures

Figure 5. RSV stimulates an enhanced inflammatory response in asthmatic ALI cultures

Figure 6. Inflammatory profiles following exposure to EHC-03

Summary

Our study characterizes the use of an air liquid interface (ALI) epithelial cultures derived from asthmatic and non-asthmatic donors and their response to common environmental insults such as mechanical wounding, respiratory syncytial virus (RSV) and particulate matter (EHC-93).

We demonstrate for the first time that the tracheal tissue and ALI cultures generated from the above donors display an altered epithelial phenotype. In particular asthmatic epithelial cells have increased expression of baseline cell surface markers (CD44, CD142) and decreased expression of adhesive junction protein E-cadherin.

Importantly we demonstrate that asthmatic ALI cultures exhibit enhanced expression of QAM-103. E-kinin, and IL-4 compared to non-asthmatic ALI cultures in response to RSV infection. In contrast this inflammatory response was not observed for all environmental insults as both asthmatic and non-asthmatic ALI cultures released similar concentrations of IL-4, IL-6, and QAM-103 in response to mechanical wounding and to EHC-93 exposure.

This study highlights the use of air liquid interface culture systems to evaluate the response of differentiated epithelial cells to extreme environmental insults.

References


Figure 1. Phenotype of ALI cultures from asthmatic and non-asthmatic airways

Figure 2. The asthmatic epithelium is composed of an altered epithelial phenotype

Figure 3. Wound closure is delayed in asthmatic derived ALI cultures

Figure 4. Viral screening in epithelial cultures

Figure 5. RSV stimulates an enhanced inflammatory response in asthmatic ALI cultures

Figure 6. Inflammatory profiles following exposure to EHC-03

Figure 7. Generation of ALI cultures from asthmatic and non-asthmatic airways

Figure 8. The asthmatic epithelium is composed of an altered epithelial phenotype

Figure 9. Wound closure is delayed in asthmatic derived ALI cultures

Figure 10. Viral screening in epithelial cultures

Figure 11. RSV stimulates an enhanced inflammatory response in asthmatic ALI cultures