Role of IL-17 on Nasal Airway Remodeling in a Murine Model of Allergic Rhinitis

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INTRODUCTION

In allergic rhinitis (AR) and asthma, chronic inflammatory reactions caused by repetitive allergen challenges make structural changes to the airway wall—namely pathologic airway remodeling. It might contribute to the airway remodeling process either through the accumulation of neutrophils or the release of matrix metalloproteinases (MMPs) as well as cytokines, IL-6, TNF-α, and IL-11 by resident cells.1 Moreover, the overexpression of IL-17 can lead to significant airway inflammation, mucus production and subepithelial collagen deposit in genetically manipulated mice.2 However, these studies provided little evidence for the role of IL-17 in the progression of airway remodeling, much less is known about the role of IL-17 in the development of nasal airway remodeling.

In this study, the role of IL-17 in nasal airway remodeling was investigated by using a polyclonal ovum (OVA)-challenged mouse model (BALB/c mice and IL-17-deficient mice).

METHODS AND MATERIALS

Forty-four female BALB/c mice (6 weeks of age, weighted 20 to 30 g) were divided into 4 groups: (1) BALB/c negative control group (WT-PBS group, n=10) challenged with PBS, (2) BALB/c allergy group (WT-OVA group, n=10) challenged with OVA, (3) IL-17 KO control group (KO-PBS group, n=10) challenged with PBS and (4) IL-17 KO allergy group (KO-OVA group, n=10) challenged with OVA.

The procedure for allergen sensitization and challenge was carried out as published previously with some modification (Figure 1).3 At each time of sacrifice, the frequencies of sneezing and nasal rubbing were counted for 10 minutes after intranasal provocation with 1% OVA.

Serum levels of OVA-specific IgE were measured by solid-phase ELISA. Serum samples collected from mice at each sacrifice were serially diluted and added to 96 well plates coated with purified anti-mouse IgE mAb. Non-specific reactions were blocked with 3% bovine serum albumin. To detect OVA-specific IgE, biotin-labeled OVA was added, followed by horseradish peroxidase-conjugated anti-biotin. Then, 3,3’,5,5’-tetramethylbenzidine was added. The optical density (OD) was measured using a microplate reader at 450 nm. The OVA-specific IgE titer was expressed as reciprocal log2 of the last dilution that resulted in an OD value 0.1 higher than background.

The spleen was removed and pooled from 5 mice per group. The final concentration of the airway was 24-well plates coated with purified anti-mouse IgE mAb. Non-specific reactions were blocked with 3% bovine serum albumin. To detect OVA-specific IgE, biotin-labeled OVA was added, followed by horseradish peroxidase-conjugated anti-biotin. Then, 3,3’,5,5’-tetramethylbenzidine was added. The optical density (OD) was measured using a microplate reader at 450 nm. The OVA-specific IgE titer was expressed as reciprocal log2 of the last dilution that resulted in an OD value 0.1 higher than background.

The heads were fixed in 10% formaldehyde, decalcified in 10% EDTA-°C with the monoclonal anti-mouse antibody anti-IFN-γ, IL-4 and IL-10 were determined using the ELISA kit (Endogen, Woburn, MA).

The production of MMP-9 and TIMP-1 in splenocyte supernatant after IL-17 deficiency was confirmed by Western blot analysis. IL-11 by resident cells.1 Moreover, the overexpression of IL-17 can lead to significant airway inflammation, mucus production and subepithelial fibrosis at the nasal mucosa. In addition, airway remodeling patterns in the histology were compared between lung and nasal mucosa.

RESULTS

IL-17-deficient mice showed significant decrease in allergic symptom scores, mean levels of OVA-specific IgE, interleukin-4, and subepithelial fibrosis at the nasal mucosa. Additionally, airway remodeling in the nasal tissue was identified later than in the lung tissue. Immunofluorescence staining against MMP-9 revealed stronger intensity in the BALB/c mice. Furthermore, MMP-9 and TIMP-1 expression at the nasal mucosa was also down-regulated in the IL-17-deficient mice.

Conclusion: Our results, which demonstrate that IL-17-deficient mice have less subepithelial fibrosis, and lower MMP-9 and TIMP-1 levels at the nasal tissues, suggest that IL-17 might have a potential role in the airway remodeling of allergic rhinitis.

REFERENCES