Innate immune responses to rhinovirus are reduced by the high-affinity IgE receptor in allergic asthmatic children

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Background: Children with allergic asthma have more frequent and severe human rhinovirus (HRV)–induced wheezing and asthma exacerbations through unclear mechanisms.
Objective: We sought to determine whether increased high-affinity IgE receptor (FcεRI) expression and cross-linking impairs innate immune responses to HRV, particularly in allergic asthmatic children.
Methods: PBMCs were obtained from 44 children, and surface expression of FcεRI on plasmacytoid dendritic cells (pDCs), myeloid dendritic cells, monocytes, and basophils was assessed by using flow cytometry. Cells were also incubated with rabbit anti-human IgE to cross-link FcεRI, followed by stimulation with HRV-16, and IFN-α and IFN-λ1 production was measured by Luminex. The relationships among FcεRI expression and cross-linking, HRV-induced IFN-α and IFN-λ1 production, and childhood allergy and asthma were subsequently analyzed.
Results: FcεRIα expression on pDCs was inversely associated with HRV-induced IFN-α and IFN-λ1 production. Cross-linking FcεRI before HRV stimulation further reduced PBMC IFN-α (47% relative reduction; 95% CI, 32% to 62%; $P < .0001$) and IFN-λ1 (81% relative reduction; 95% CI, 69% to 93%; $P < .0001$) secretion. Allergic asthmatic children had higher surface expression of FcεRIα on pDCs and myeloid dendritic cells when compared with that seen in nonallergic nonasthmatic children. Furthermore, after FcεRI cross-linking, allergic asthmatic children had significantly lower HRV-induced IFN responses than allergic nonasthmatic children (IFN-α, $P = .004$; IFN-λ1, $P = .02$) and nonallergic nonasthmatic children (IFN-α, $P = .002$; IFN-λ1, $P = .01$).
Conclusions: Allergic asthmatic children have impaired innate immune responses to HRV that correlate with increased FcεRI expression on pDCs and are reduced by FcεRI cross-linking. These effects likely increase susceptibility to HRV-induced wheezing and asthma exacerbations. (J Allergy Clin Immunol 2012;130:489-95.)

Key words: *Asthma, allergic, rhinovirus, interferon, FcεRI, IgE receptor, plasmacytoid dendritic cells*

Aeroallergen sensitization is a pivotal risk factor for the development of human rhinovirus (HRV)–induced wheezing illnesses.[1] Children who wheeze with HRV infections during early life are at increased risk for school-age asthma,[2,3] and children with concomitant aeroallergen sensitization have the greatest risk of subsequent asthma development.[2,4] Once asthma is established, HRV is the most common cause of exacerbations, having been identified as a causative agent in 50% to 90% of asthma exacerbations in children and adults.[5-8] In a cohort of school-aged children with asthma, sensitization to aeroallergens was associated with similar numbers of viral infections but more frequent and severe upper and lower virus-induced respiratory illnesses.[9] Furthermore, Heymann et al[10] have demonstrated that school-aged children with asthma exacerbations severe enough to require hospitalization are likely to be both allergic and infected with HRV. However, the mechanisms underlying allergy-virus interactions in asthma inception and exacerbation are incompletely understood and represent an important area for further study.

Interferons contribute significantly to the host response to viral infections, and impaired interferon production from mononuclear cells has been associated with both asthma and allergic sensitization.[11-13] Insufficient production of IFN-λ1 by airway

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Abbreviations used
COAST: Childhood Origins of Asthma
HRV: Human rhinovirus
mDC: Myeloid dendritic cell
pDC: Plasmacytoid dendritic cell

mononuclear cells has been linked to more severe HRV-induced illness and obstructive patterns on pulmonary function testing in allergic asthmatic patients compared with nonallergic control subjects.[11] Additionally, plasmacytoid dendritic cells (pDCs) from allergic patients produce less IFN-α on Toll-like receptor 9 stimulation,[12] and pDCs from allergic asthmatic patients produce less IFN-α after stimulation with influenza virus.[13] Interestingly, this impaired IFN-α production in pDCs has been linked to surface expression of the high-affinity IgE receptor FcεRI. Although FcεRI on mast cells and basophils is classically known to mediate the effector phase of the allergic response through type I hypersensitivity reactions, a trimeric form of FcεRI is also expressed on pDCs, myeloid dendritic cells (mDCs), and monocytes.[14] Increased expression and cross-linking of FcεRI on pDCs has been associated with diminished IFN-α production to influenza viruses.[13] Therefore we hypothesized that increased FcεRI expression on PBMCs would reduce HRV-induced IFN-α and IFN-λ1 production. Furthermore, HRV-induced IFN-α and IFN-λ1 production would be further reduced by cross-linking FcεRI and would be lowest in allergic asthmatic children. To test these hypotheses, we examined PBMC responses to HRV in a subset of children enrolled in the Childhood Origins of Asthma (COAST) study.

METHODS

Study population

Participants in this mechanistic study were 10- to 12-year-old children enrolled in the COAST study, a birth cohort including children at high risk for asthma and allergic disease based on having at least 1 parent with asthma or allergic sensitization. Details regarding the study design and characteristics of its subjects have been previously published.[2,15] Additional children with asthma were enrolled in the COAST study between 9 and 11 years of age to increase the study population. These subjects were born during the same time frame and met the same inclusion criteria as the children in the original cohort. For this mechanistic study, we obtained peripheral blood samples from 44 subjects as part of their annual COAST study visit. The Human Subjects Committee of the University of Wisconsin approved the study, informed consent was obtained from the parents, and assent was obtained from the children.

Definitions of allergy and asthma

Total IgE and allergen-specific IgE levels to dog, cat, cockroach, ragweed, birch, timothy grass, *Alternaria alternata*, *Dermatophagoides farinae*, and *Dermatophagoides pteronyssinus* were measured with an automated fluoroenzyme immunoassay (Unicap 100; Pharmacia and Upjohn Diagnostics, Kalamazoo, Mich), as previously described.[1] Allergen-specific IgE levels of 0.35 kU/L or greater (class I) were considered positive, and the sensitivity for detection of total IgE was 2 kU/L. The presence of allergic sensitization was defined as having 1 or more positive values for allergen-specific IgE.

Current asthma was diagnosed based on previously published criteria[2] of at least 1 of the following characteristics in the previous year: (1) a physician's diagnosis of asthma, (2) use of albuterol for coughing or wheezing episodes (prescribed by physician), (3) use of a daily controller medication, (4) a step-up plan including use of albuterol or short-term use of inhaled corticosteroids during illness, and (5) use of prednisone for asthma exacerbation.

Immunologic studies

Specimens of peripheral blood were collected, and PBMCs were isolated with Ficoll density gradient centrifugation, as previously described.[16] PBMCs were incubated with either rabbit IgG isotype control (1 μg/mL; Bethyl Laboratories, Montgomery, Tex), rabbit anti-human IgE (0.1 or 1 μg/mL), or media alone for 2 hours. PBMCs were then incubated with either HRV-16 (2.5×10^6 plaque-forming units/mL) or media alone for 24 hours. Supernatants were subsequently collected and analyzed for IFN-α and IFN-λ1 production by using a multiplex assay (Millipore, Billerica, Mass).

Flow cytometry

The following fluorochrome-conjugated anti-human antibodies were used for identification of pDCs, mDCs, monocytes, and basophils and assessment of FcεRIα expression in peripheral blood: lineage fluorescence isothiocyanate cocktail (containing CD3, CD14, CD16, CD19, CD20, and CD56), CD123–phycoerythrin-Cy5, HLA-DR–PerCP, CD11c–allophycoyanain, CD14–Pacific Blue (BD Biosciences, San Jose, Calif) and FcεRIα-phycoerythrin (eBioscience, San Diego, Calif). Data were acquired by using a BD LSRII Flow Cytometer. Immune cell populations were identified as follows: pDCs—lineage-negative, HLA-$DR^+CD11c^-CD123^+$ cells; mDCs—lineage-negative, HLA-$DR^+CD11c^+CD123^-$ cells; monocytes—$CD14^+$ cells; and basophils—lineage-negative, HLA-DR^-CD123^+ cells. FcεRI expression, reported as the percentage of $FcεRI^+$ cells, was determined on pDCs, mDCs, monocytes, and basophils. Sample compensation was performed by using unstained and single-stained anti-mouse IgG, κ polystyrene microparticle beads (BD Biosciences) as controls. Compensation was calculated in FACS DiVa software (version 6.0, BD Biosciences) during acquisition and calculated again in FlowJo software (version 9.3.2; TreeStar, Ashland, Ore) for final data analysis.

Statistical analysis

Repeated-measures ANOVA models were used to assess the effects of cross-linking FcεRI on HRV-induced interferon production in PBMCs incubated with isotype control IgG, anti-IgE (0.1 or 1 μg/mL), or media alone. Linear models were constructed to incorporate allergic sensitization and asthma as covariates for interferon responses and possible effect modifiers for FcεRI cross-linking. Global tests for main effects and interactions were performed, and pairwise comparisons between the asthma/allergy groups were evaluated according to the Fisher protected least significant difference. Pairwise relationships between total IgE levels, HRV-induced interferon production, and percentage of pDCs, mDCs, monocytes, and basophils positive for surface FcεRIα expression were assessed by using the Pearson correlation coefficient after log transformation. A 2-sided P value of .05 was considered statistically significant. Analyses were performed with SAS version 9.2 software (SAS Institute, Cary, NC).

RESULTS

Study population

Of the 44 children included in this study, 14 had aeroallergen sensitization and current asthma (allergic asthma), 3 were not sensitized to aeroallergens but had current asthma (nonallergic asthma), 13 had aeroallergen sensitization but did not have asthma (allergic nonasthmatic), and 14 had neither aeroallergen sensitization nor asthma (nonallergic nonasthmatic, Table I).

Increased FcεRI expression and cross-linking inhibits HRV-induced interferon production

The percentage of $FcεRIα^+$ pDCs was inversely associated with HRV-induced IFN-α and IFN-λ1 production (Table II).

TABLE I. Baseline characteristics of the 4 groups

	Allergic asthmatic children	Nonallergic asthmatic children	Allergic nonasthmatic children	Nonallergic nonasthmatic children
No.	14	3	13	14
Age (y)	11.6	11.8	11.3	11.3
Sex (male/female)	10/4	1/2	4/9	6/8
Total IgE (kU/L)	533 (218-884)	21 (12-109)	60 (37-333)	20 (7-66)
No. of positive allergen-specific *in vitro* IgEs	6 (3-7)	0	2 (1-5)	0
FEV_1 (% predicted)	100 (92-110)	107 (95-107)	104 (95-111)	102 (95-120)

All values are expressed as medians, with 25th and 75th percentile ranges where indicated. Prebronchodilator percent predicted FEV_1 values are expressed.

TABLE II. Relationships between percentages of $Fc\varepsilon RI^+$ pDCs, mDCs, monocytes, and basophils and production of HRV-induced IFN-α and IFN-λ1

	pDCs	mDCs	Monocytes	Basophils
IFN-α	$R = -0.37$, $P = .01$	$R = -0.29$, $P = .05$	$R = -0.12$, $P = .42$	$R = -0.20$, $P = .18$
IFN-λ1	$R = -0.42$, $P = .005$	$R = -0.24$, $P = .11$	$R = -0.18$, $P = .24$	$R = -0.28$, $P = .07$

All values are expressed as Pearson Rho *(R)* estimates.

Cross-linking FcεRI on PBMCs before HRV stimulation significantly reduced HRV-induced IFN-α production. This effect was observed at both the 0.1 and 1 μg/mL concentrations of anti-IgE when compared with no pretreatment (0.1 μg/mL [mean ± SE]: 1192 ± 126 vs 1410 ± 150 pg/mL, $P = .002$; 1 μg/mL: 750 ± 108 vs 1410 ± 150 pg/mL, $P < .0001$; Fig 1, *A*). Cross-linking FcεRI also reduced HRV-induced IFN-λ1 secretion (0.1 μg/mL: 125 ± 20 vs 206 ± 36 pg/mL, $P < .0001$; 1 μg/mL: 39 ± 9 vs 206 ± 36 pg/mL, $P < .0001$; Fig 1, *B*). Similar inhibition of HRV-induced interferon production was obtained by means of preincubation with an mAb specific for FcεRIα (data not shown).

Allergic sensitization, asthma, and interferon responses

We next examined whether the observed relationships between FcεRI and HRV-induced interferon secretion from PBMCs were associated with asthma, allergic sensitization, or both clinical phenotypes. In the absence of FcεRI cross-linking, HRV-induced IFN-α and IFN-λ1 responses tended to be lower in allergic asthmatic children compared with those seen in other children, but these differences were not statistically significant. After FcεRI cross-linking, however, HRV-induced IFN-α production was significantly lower in allergic asthmatic children (mean ± SE, 366 ± 126 pg/mL) than in both allergic nonasthmatic (1085 ± 261 pg/mL, $P = .004$) and nonallergic nonasthmatic (878 ± 159 pg/mL, $P = .002$) children (Fig 2, *A*). Similarly, IFN-λ1 production after FcεRI cross-linking was significantly lower in allergic asthmatic children (16 ± 5 pg/mL) than in both allergic nonasthmatic (62 ± 28 pg/mL, $P = .02$) and nonallergic nonasthmatic (42 ± 8 pg/mL, $P = .01$) children (Fig 2, *B*). There were no significant differences between the interferon production of the allergic nonasthmatic and nonallergic nonasthmatic children (Fig 2). The group of nonallergic asthmatic children was too small (n = 3) to provide adequate power to compare these children with the other 3 groups.

FcεRI expression, allergy, and asthma

We next compared FcεRIα expression on PBMCs in children based on allergic and asthmatic phenotypes. Children with allergic asthma had a higher percentage of $Fc\varepsilon RI\alpha^+$ pDCs (mean ± SE: 74.3 ± 5.9 vs 44.8 ± 7.2, adjusted $P = .009$) and mDCs (83.1 ± 2.1 vs 66.8 ± 4.8, $P = .04$) when compared with nonallergic nonasthmatic children (Table III). Allergic nonasthmatic children had significantly greater percentages of $Fc\varepsilon RI\alpha^+$ mDCs compared with those seen in nonallergic nonasthmatic children (Table III).

Relationships among total IgE level, FcεRI expression, and HRV-induced interferon production

Finally, we examined total IgE level as a potential biomarker for FcεRI expression and the cross-linking relationships observed above. There was a significant positive correlation between total IgE levels and percentages of $Fc\varepsilon RI\alpha^+$ pDCs ($R = 0.60$, $P < .0001$), mDCs ($R = 0.48$, $P = .001$), and basophils ($R = 0.47$, $P < .001$). A similar trend was observed for $Fc\varepsilon RI\alpha^+$ monocytes ($R = 0.28$, $P = .07$). Moreover, the percentage of $Fc\varepsilon RI^+$ pDCs correlated with the percentage of $Fc\varepsilon RI\alpha^+$ mDCs ($R = 0.70$, $P < .0001$) and basophils ($R = 0.73$, $P < .0001$). However, HRV-induced interferon production was not significantly associated with total IgE levels in the absence of FcεRI cross-linking (IFN-α: $R = -0.18$, $P = .24$; IFN-λ1: $R = -0.12$, $P = .44$). When FcεRI was cross-linked before HRV stimulation, total IgE levels were inversely associated with HRV-induced IFN-α (1 μg/mL: $R = -0.42$, $P = .004$) and IFN-λ1 (0.1 μg/mL: $R = -0.38$, $P = .01$; 1 μg/mL: $R = -0.39$, $P = .009$) production.

DISCUSSION

In this study we identified a mechanism that may underlie the important clinical observation that children with allergic sensitization, particularly those both sensitized and exposed, have more clinically significant lower respiratory tract illnesses and asthma exacerbations caused by HRVs.[9,10,17] We have demonstrated that the frequency of pDCs expressing the high-affinity IgE receptor FcεRI is inversely associated with HRV-induced IFN-α and IFN-λ1 secretion. Moreover, cross-linking of this receptor before HRV stimulation by using antibodies to either IgE or the receptor itself significantly inhibited IFN-α and

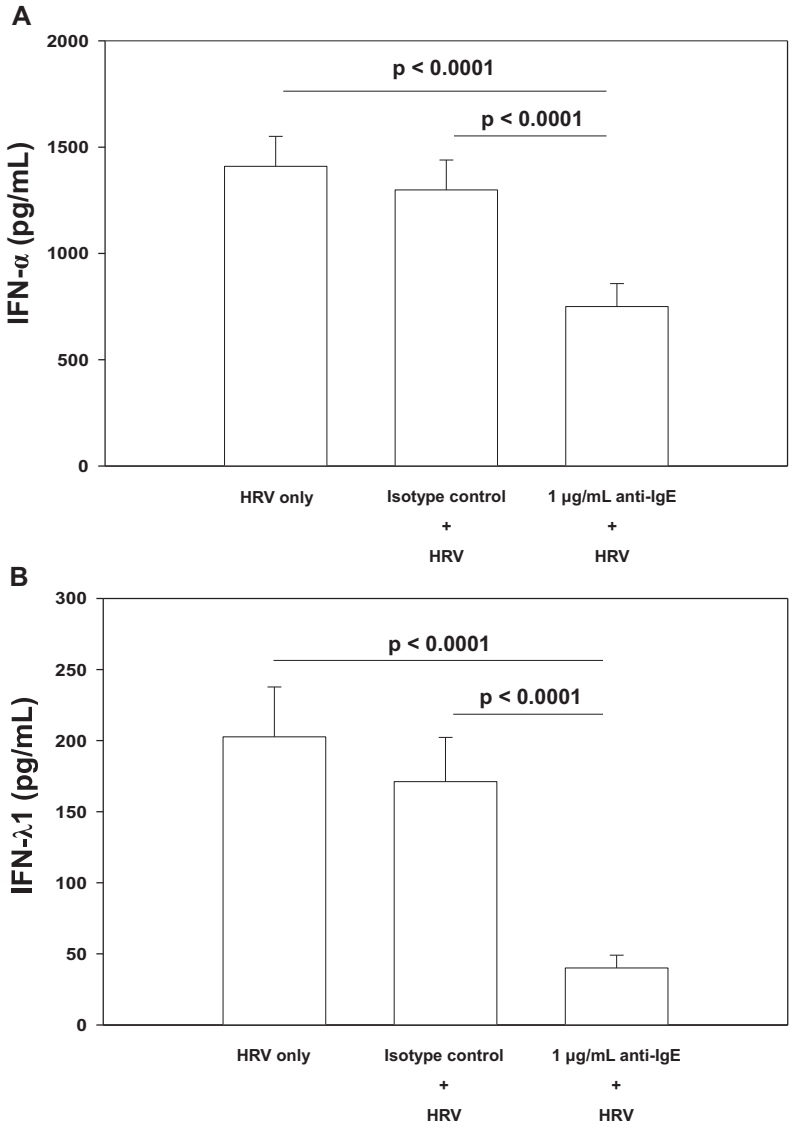

FIG 1. A, Comparison of PBMC HRV-induced mean IFN-α production when pretreated with media (no pretreatment), 1 μg/mL rabbit IgG isotype control antibody, or 1 μg/mL anti-IgE for 2 hours. Pretreatment of PBMCs with 1 μg/mL anti-IgE to cross-link FcεRI resulted in significantly lower HRV-induced IFN-α production (mean ± SE: 750 ± 108 pg/mL) compared with pretreatment with 1 μg/mL rabbit IgG isotype control (1299 ± 141 pg/mL, $P < .0001$) or no pretreatment (1410 ± 150 pg/mL, $P < .0001$) n = 44. **B,** Comparison of PBMC HRV-induced mean IFN-λ1 production (in picograms per milliliter) when pretreated with media (no pretreatment), 1 μg/mL rabbit IgG isotype control antibody, or 1 μg/mL anti-IgE for 2 hours. Pretreatment of PBMCs with 1 μg/mL anti-IgE to cross-link FcεRI resulted in significantly decreased HRV-induced IFN-λ1 production (mean ± SE: 39 ± 9 pg/mL) compared with pretreatment with 1 μg/mL rabbit IgG isotype control (171 ± 31 pg/mL, $P < .0001$) or no pretreatment (206 ± 36 pg/mL, $P < .0001$) n = 44.

IFN-λ1 production by half or more, and these effects were especially pronounced in children with allergic asthma. These findings are of particular clinical relevance because up to 90% of asthma exacerbations in children are related to HRV infection,[8] they most often occur in children with concomitant aeroallergen sensitization,[10] and current therapies are only partially effective in preventing exacerbations.[18]

Notably, the inverse relationships between total IgE levels and diminished interferon secretion were only apparent after FcεRI cross-linking. An argument could be made that the observed lack of correlation with total IgE levels was due to culturing the PBMCs in IgE-free media; however, the half-life of the IgE-FcεRI complex has been found to be approximately 16 hours in suspension,[19] and our experiments were initiated within a few hours of blood sample collection. The significant correlations between total IgE levels and percentages of $FcεRI^+$ PBMCs identified in our patient population suggest that FcεRI cross-linking might represent a key event leading to impairment of virus-induced interferon production. More importantly, the significant inverse correlations between total IgE levels and HRV-induced interferon secretion in the presence of FcεRI cross-linking provide direct evidence for the potential biologic relevance of this pathway *in vivo*, where cross-linking of allergen-specific IgE in the scenario of sensitization and

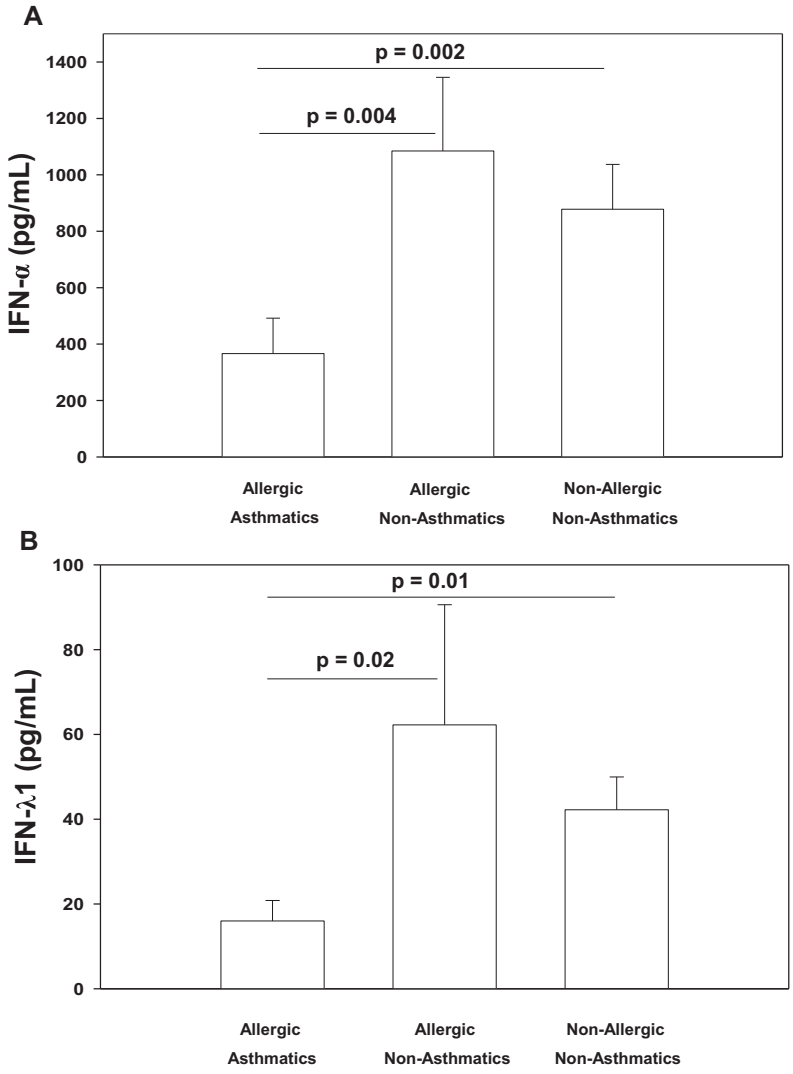

FIG 2. A, Comparison of allergic asthmatic (n = 14), allergic nonasthmatic (n = 13), and nonallergic nonasthmatic (n = 14) children's PBMC HRV-induced IFN-α production (in picograms per milliliter) after cross-linking FcεRI with 1 μg/mL anti-IgE for 2 hours before HRV stimulation. Allergic asthmatic children had significantly lower HRV-induced IFN-α production (mean ± SE: 366 ± 126 pg/mL) than both allergic nonasthmatic (1085 ± 261 pg/mL, *P* = .004) and nonallergic nonasthmatic (878 ± 159 pg/mL, *P* = .002) children. **B,** Comparison of allergic asthmatic (n = 14), allergic nonasthmatic (n = 13), and nonallergic nonasthmatic (n = 14) children's PBMC HRV-induced mean IFN-λ1 production (in picograms per milliliter) after cross-linking FcεRI with 1 μg/mL anti-IgE for 2 hours before HRV stimulation. Allergic asthmatic children had significantly lower HRV-induced IFN-λ1 production (mean ± SE: 16 ± 5 pg/mL) than both allergic nonasthmatic (62 ± 28 pg/mL, *P* = .02) and nonallergic nonasthmatic (42 ± 8 pg/mL, *P* = .01) children.

exposure could also result in significant impairment of interferon responses to HRV.

pDCs produce up to 95% of the IFN-α[20] in peripheral blood on stimulation with viruses, despite making up only 0.2% to 0.8% of the PBMC population.[21] In our study HRV-induced interferon secretion was most significantly inversely associated with pDC FcεRI expression, suggesting that these cells are principally involved in this effect. The mechanism by which increased FcεRI expression on pDCs, even in the absence of FcεRI cross-linking, leads to impaired interferon production is unclear. One possibility might be related to signaling through the FcεRIγ subunit, an immunoreceptor tyrosine-based activation motif that recruits and regulates tyrosine kinases, such as the Src and Syc families.[22] Interestingly, immunoglobulin-like transcript 7 and blood dendritic cell antigen 2 are regulatory surface receptors specific to pDCs that both signal through FcεRIγ, and cross-linking either immunoglobulin-like transcript 7 or blood dendritic cell antigen 2 inhibits interferon synthesis in response to viruses.[22,23] Thus, it is possible that cross-linking FcεRI directly inhibits HRV-induced IFN-α and IFN-λ1 production, but additional mechanisms may contribute to impaired interferon production in allergic asthmatic children as well.

Unchecked interferon production by pDCs has been associated with autoimmune diseases, such as lupus[24] and Sjögren syndrome[25]; therefore tight regulation of interferon responses is critical for immune homeostasis. Thus, it is possible that effects of FcεRI on interferon secretion comprise a counterregulatory pathway in place to control interferon responses. Consequently, in

TABLE III. Comparison of percentages of FcεRI$^+$ pDCs, mDCs, monocytes, and basophils of children based on allergic and asthmatic phenotypes

	Allergic asthmatic children (n = 14)	Allergic nonasthmatic children (n = 13)	Nonallergic nonasthmatic children (n = 14)
% FcεRI$^+$ cells (mean ± SE)			
pDCs	74 ± 6*	60 ± 6	45 ± 7
mDCs	83 ± 2*	83 ± 2†	67 ± 5
Monocytes	7 ± 2	7 ± 1	2 ± 0.4
Basophils	93 ± 2	93 ± 1	76 ± 7

*Significant difference between allergic asthmatic and nonallergic nonasthmatic children (pDCs: $P = .009$; mDCs: $P = .04$).
†Significant difference between allergic nonasthmatic and nonallergic nonasthmatic children (mDCs: $P = .05$). All P values are adjusted for multiple comparisons.

allergic asthmatic patients overexpression of FcεRI might lead to excessive interferon inhibition. Gill et al[13] recently demonstrated diminished pDC IFN-α production in response to influenza virus in allergic asthmatic patients compared with that seen in nonallergic control subjects. Taken together with our findings, this counterregulatory pathway might be important in the antiviral response to numerous respiratory tract viruses.

A novel aspect of our findings was the evaluation of IFN-λ1 production, especially given the recent data linking diminished IFN-λ1 responses to asthma.[11] Specifically, Contoli et al[11] have demonstrated that insufficient levels of IFN-λ1 in the asthmatic airway are associated with more severe HRV-induced illness and obstructive patterns on pulmonary function testing in allergic asthmatic adults. Interestingly, IFN-λ1 mediates its actions through a receptor distinct from the receptor for type I interferons. The results of our study suggest allergic asthmatic children have diminished type III interferon production to rhinovirus, which might represent an exciting opportunity to develop distinct antiviral therapies aimed at this pathway.

One strength of our study is the inclusion of allergic nonasthmatic children, which allows separate evaluation of effects on allergy versus asthma. Additionally, we used PBMCs, rather than isolated pDCs, to evaluate the role of FcεRI expression and cross-linking on multiple innate immune cell types and to allow for cell-cell interactions. Furthermore, the subjects studied have been well characterized, including comprehensive and repeated assessments of allergic and asthmatic phenotypes. A study limitation is that only 3 nonallergic asthmatic children were evaluated, and thus we lacked the power to compare these children with the other phenotypes; however, the vast majority of school-aged children with asthma have concomitant allergic sensitization.[18,26]

Our results might have particular clinical relevance to a recent study in inner-city children with allergic asthma by Busse et al,[27] which demonstrated the efficacy of omalizumab in preventing exacerbations during peak HRV seasons. Studying HRV-induced interferon production before/after omalizumab therapy could provide further evidence to support our hypothesis. Furthermore, it is well known that allergic sensitization is an important risk factor for asthma inception,[28] and recent evidence supports a causal role for sensitization in the development of HRV-related wheezing in preschool children.[1] It could be postulated from our study that preschool children with aeroallergen sensitization and exposure have reduced innate immune responses that could lead to greater severity of HRV-induced illnesses in early life and, consequently, lead to the development of persistent airway inflammation and asthma.

In summary, we have identified a mechanism that might link allergic asthma in childhood to deficient antiviral responses. Specifically, increased expression and cross-linking of the high-affinity IgE receptor, FcεRI, before HRV infection inhibits IFN-α and IFN-λ1 secretion from PBMCs. These findings, which were most pronounced in the context of allergic asthma, suggest that therapeutic strategies aimed at reducing FcεRI expression and cross-linking represent viable approaches to prevent HRV-induced wheezing illnesses and asthma exacerbations.

Key messages

- **Increased expression and cross-linking of the high-affinity IgE receptor, FcεRI, on pDCs is associated with reduced HRV-induced IFN-α and IFN-λ1 secretion.**
- **Allergic asthmatic children have significantly reduced HRV-induced IFN-α and IFN-λ1 production after cross-linking of FcεRI.**

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