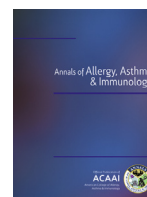




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Mouse allergen exposure and decreased risk of allergic rhinitis in school-aged children

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ABSTRACT

Background: Little is known about exposure to mouse allergen (Mus m 1) and allergic rhinitis (AR).

Objective: To evaluate the association between mouse allergen exposure and AR in children.

Methods: We examined the relation between mouse allergen level in house dust and AR in 511 children aged 6 to 14 years in San Juan, Puerto Rico. Study participants were chosen from randomly selected households using a multistage probability sample design. The study protocol included questionnaires, allergy skin testing, and collection of blood and dust samples. AR was defined as current rhinitis symptoms and skin test reactivity to at least one allergen.

Results: In the multivariate analyses, mouse allergen level was associated with a 25% decreased odds of AR in participating children (95% confidence interval, 0.62–0.92). Although endotoxin and mouse allergen levels were significantly correlated ($r = 0.184$, $P < .001$), the observed inverse association between Mus m 1 and AR was not explained by levels of endotoxin or other markers of microbial or fungal exposure (peptidoglycan and glucan).

Conclusion: Mouse allergen exposure is associated with decreased odds of AR in Puerto Rican school-aged children.

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Introduction

Allergic rhinitis (AR) affects up to approximately 14% of adults¹ and approximately 22% of children² in the United States, and its prevalence can be as high as 60% to 80% among children with asthma.^{3,4} In Europe, a large multicenter study that combined survey and physical examination data reported that AR affects approximately 13% to 23% of the population⁵; that study reported up to approximately 45% underdiagnosis. We recently reported up to approximately 75% AR underdiagnosis among

Puerto Rican children,⁶ who bear a disproportionate burden of asthma.⁷

The presence and severity of AR have been associated with several comorbidities in children, including asthma, otitis media, and adenoid hypertrophy.⁸ It has also been associated with a higher risk of chronic sinusitis in adults.⁹ AR may worsen asthma severity and control by enhancing lower airway inflammation¹⁰ and may delay recovery of lung function after asthma exacerbations.¹¹ Adequate treatment with nasal corticosteroids may improve lung function in children with asthma,¹² although some studies have found no improvement on asthma-related airway inflammation.¹³

Exposure to higher levels of mouse urinary protein (Mus m 1, hereafter called mouse allergen) has been previously linked with mouse sensitization and indicators of asthma severity or control in some studies^{14,15} but not in others.^{16,17} To date, little is known about the association between mouse allergen exposure and AR. We hypothesized that mouse allergen exposure would be associated with decreased prevalence of AR in Puerto Rican children and explored potential mechanisms by analyzing possible correlated microbe-associated molecular patterns (MAMPs).

Drs Jacobs and Forno contributed equally to the manuscript.

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Methods

Study Population

The details of the study recruitment and protocol have been previously described.^{6,18,19} In brief, from March 2009 to June 2010, children in San Juan, Puerto Rico, were chosen from randomly selected households using a multistage probability sample design scheme similar to that of a prior study.²⁰ Primary sampling units (PSUs) were randomly selected neighborhood clusters based on the 2000 US Census, and secondary sampling units were randomly selected households within each PSU. A household was eligible if one or more residents were children aged 6 to 14 years. In households with more than one eligible child, one child was randomly selected for screening.²⁰ After selection and screening, we attempted to enroll a total of 783 children. Parents of 105 of these 783 eligible households refused to participate or could not be reached; there were no significant differences in age, sex, or area of residence between eligible children who did ($n = 678$ [87%]) and did not ($n = 105$ [13%]) agree to participate. For the current study, which was focused on AR and mouse allergen exposure, only those with nonmissing data on allergy skin testing and Mus m 1 levels ($n = 511$) were included; no significant differences were found between those included and those excluded from analysis ($n = 167$) (eTable 1). Written parental consent was obtained for participating children, from whom written assent was also obtained. The study was approved by the institutional review boards of the University of Puerto Rico (San Juan, Puerto Rico), Brigham and Women's Hospital (Boston, Massachusetts), and the University of Pittsburgh (Pittsburgh, Pennsylvania).

Study Procedures

Study participants completed a protocol that included questionnaires, allergy skin testing, and collection of dust samples. The child's parents completed 2 questionnaires used in the Genetics of Asthma in Costa Rica Study.²¹ These questionnaires were used to obtain information about the child's general and respiratory health, family history, sociodemographic characteristics, in utero smoke exposure, family history, and household characteristics.

Skin test reactivity (STR) to aeroallergens, histamine, and saline diluent was assessed using a multitest device (Lincoln Diagnostics, Decatur, Illinois) on the skin of the forearm (in a site free of eczema). Aeroallergens tested included house dust mites (*Dermaphagoides pteronyssinus* and *Dermatophagoides farinae*), *Blomia tropicalis*, German cockroach (*Blattella germanica*), mouse pelt, dog dander, cat dander, mold mix, *Alternaria tenuis*, mixed tree pollen, mixed grass pollen, mugwort sage, and ragweed (Alk-Abello, Round Rock, Texas). A skin test result was considered positive if the maximum wheal diameter exceeded the diluent wheal diameter by 3 mm or more.

Dust samples were obtained from 3 areas in the home: the one in which the child sleeps (usually his/her bedroom), the living room or television room, and the kitchen. The dust was sifted through a 50-mesh metal sieve, and the fine dust was reweighed, extracted, and aliquoted for analysis of allergens from mouse (mouse urinary protein [Mus m 1]), dust mite (*D pteronyssinus* [Der p 1]), cockroach (*B germanica* [Bla g 2]), dog dander (Can f 1), and cat dander (Fel d 1), as well as MAMPs of glucan, peptidoglycan, and endotoxin (eAppendix). Levels of allergens and MAMPs were transformed to a log₁₀ scale for analysis and are reported as geometric means for clarity.

Outcome Definition

AR was defined as both current symptoms suggestive of AR and STR to 1 allergen or more; this definition is consistent with Allergic Rhinitis and Its Impact on Asthma 2008 guidelines.²² A child was

Table 1

Characteristics of the study participants^a

Characteristic	No AR (n = 264 [51.7%])	AR (n = 247 [48.3%])
Baseline characteristics		
Age, mean (range), y	10.2 (9.9–10.5)	10.5 (10.1–10.8)
Female sex	126 (47.7)	113 (45.8)
Parental educational level greater than high school	205 (77.7)	204 (82.6)
Higher household income >\$15,000 per year	80 (31.6)	89 (36.8)
Private or employer-based health insurance	77 (29.2)	94 (38.1) ^b
Asthma		
Leukotriene inhibitor use in prior 6 months	92 (34.9)	176 (71.3) ^c
Inhaled corticosteroid use in prior 6 months	19 (7.2)	49 (19.8) ^c
Atopic history		
History of eczematous rash ever	24 (9.1)	64 (25.9) ^c
Family history		
Parental history of AR	59 (22.4)	104 (42.1) ^c
Parental history of asthma	40 (15.2)	57 (23.2) ^b
Parental history of eczema	111 (42.2)	145 (58.7) ^c
Home environment		
No. of older siblings, mean (range)	4 (1.5)	8 (3.3)
Shared bedroom	1.8 (1.6–2.0)	1.6 (1.4–1.8)
History of daycare	155 (58.7)	121 (49.0) ^b
Signs of mold or mildew	48 (18.3)	63 (25.9) ^b
Dog at home	88 (33.5)	119 (48.2) ^c
Cat at home	132 (50.4)	131 (53.0)
Seeing rats or mice	32 (12.3)	21 (8.5)
Skin test reactivity		
≥1 Allergen	81 (30.7)	57 (23.1)
Total No. of positive skin test results (range)	143 (54.2)	247 (100.0) ^c
Dust mite mix	2.8 (2.3–3.3)	5.6 (5.1–6.0) ^c
<i>Blomia tropicalis</i>	47 (17.9)	108 (43.9) ^c
Cockroach	81 (31.5)	179 (73.7) ^c
Mouse	47 (18.0)	106 (43.6) ^c
Dog	39 (14.8)	72 (29.2) ^c
Cat	42 (15.9)	82 (33.2) ^c
Mold mix	68 (25.8)	103 (41.7) ^c
<i>Alternaria</i>	25 (9.5)	37 (15.0)
Mixed trees	44 (16.7)	75 (30.4) ^c
Mixed grasses	59 (22.4)	83 (33.6) ^b
Mugwort sage	28 (12.2)	49 (21.9) ^b
Ragweed	22 (9.6)	43 (19.8) ^c
Home allergen levels, geometric mean (95% CI)		
Log Der p, μg/g	73 (27.7)	131 (53.0) ^c
Log Bla g 2, U/g	4.2 (3.7–4.9)	4.8 (4.1–5.5)
Log Mus m 1, ng/g	1.9 (1.6–2.3)	1.8 (1.5–2.2)
Log Can f 1, μg/g	12.7 (9.7–16.6)	8.5 (6.3–11.4) ^b
Log Fel d 1, μg/g	0.19 (0.15–0.25)	0.16 (0.12–0.21)
Microbial associated molecular patterns, geometric mean (95% CI)		
Log glucan, μg/mg	0.04 (0.03–0.06)	0.03 (0.02–0.04)
Log peptidoglycan, μg/mg	0.14 (0.11–0.17)	0.15 (0.12–0.19)
Log endotoxin, EU/mg	0.014 (0.009–0.02)	0.015 (0.01–0.02)

Abbreviation: AR, allergic rhinitis.

^aData are presented as number (percentage) of patients unless otherwise indicated.

^b $P < .05$ for the difference between patients with and without AR on univariate analysis.

^c $P < .005$ for the difference between patients with and without AR on univariate analysis.

considered to have current symptoms suggestive of AR if there were affirmative answers to 2 questions (taken from the International Study of Asthma and Allergies in Childhood questionnaire²³): (1) “Has your child ever had hay fever or a runny or stuffy nose accompanied by sneezing and itching at a time when he/she did not have a cold or flu?” and (2) “Has your child had these symptoms in the last 12 months?” Asthma was defined as physician-diagnosed asthma and wheeze in the previous year.

Table 2Multivariate analysis of mouse allergen level and AR by mouse sensitization status^a

All Patients	Unadjusted (n = 511)		Adjusted model 1A (n = 511)		Adjusted model 2A (n = 328)	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Mus m 1, ng/g ^b	0.84 (0.70–1.00)	.049	0.75 (0.62–0.92)	.005	0.72 (0.57–0.92)	.009
Endotoxin ^b	1.11 (0.64–1.92)	.70	...	...	1.22 (0.66–2.24)	.53
Health insurance type	1.49 (1.03–2.16)	.03	1.66 (1.10–2.52)	.02	1.61 (0.91–2.83)	.10
Asthma	4.63 (3.19–6.74)	<.001	6.40 (4.20–9.73)	<.001	5.08 (3.01–8.59)	<.001
Shared bedroom	0.68 (0.48, 0.96)	.03	0.50 (0.33–0.76)	.001	0.44 (0.26–0.73)	.002
Sensitized to mouse	Unadjusted (n = 111)		Adjusted model 1B (n = 111)		Adjusted model 2B (n = 76)	
Mus m 1, ng/g ^b	0.78 (0.52–1.19)	.26	0.71 (0.44–1.13)	.15	0.79 (0.41–1.51)	.47
Endotoxin ^b	0.83 (0.28–2.52)	.75	...	...	0.89 (0.26–3.05)	.86
Health insurance type	0.94 (0.41–2.15)	.88	0.99 (0.39–2.50)	.98	0.86 (0.24–3.12)	.82
Asthma	4.79 (2.07–11.12)	<.001	6.56 (2.48–17.37)	<.001	4.62 (1.48–14.47)	.009
Shared bedroom	0.78 (0.35–1.71)	.53	0.61 (0.24–1.52)	.29	0.63 (0.21–1.96)	.43
Not sensitized to mouse	Unadjusted (n = 400)		Adjusted model 1C (n = 400)		Adjusted model 2C (n = 252)	
Mus m 1, ng/g ^b	0.88 (0.72–1.07)	.20	0.79 (0.63–0.99)	.04	0.74 (0.56–0.98)	.03
Endotoxin ^b	1.27 (0.66–2.44)	.48	...	...	1.42 (0.68–2.95)	.34
Health insurance type	1.72 (1.13–2.61)	.01	1.97 (1.22–3.17)	.005	2.10 (1.10–4.02)	.02
Asthma	4.80 (3.12–7.37)	<.001	6.84 (4.21–11.14)	<.001	5.54 (2.96–10.38)	<.001
Shared bedroom	0.64 (0.43–0.95)	.03	0.44 (0.27–0.72)	.001	0.35 (0.19–0.65)	.001

Abbreviations: AR, allergic rhinitis; CI, confidence interval; OR, odds ratio.

^aAll models are adjusted for age, sex, and variables listed; model 2 I additionally adjusted for endotoxin level.^bPer each log₁₀-unit increment.

Statistical Analysis

Bivariate analyses were conducted using the Fisher exact tests for categorical variables and 2-sample 2-sided *t* tests for continuous variables. Logistic regression was used for the multivariable analyses. Because of their known relation to AR, all models included age, sex, and type of health insurance (private or employer based vs others). Other covariates (Table 1) were also included in the initial multivariate models if $P \leq .20$ in bivariate analyses; these additional covariates remained in the final models if they were associated with AR at $P < .05$ or if they changed the parameter estimates by 10% or more. The Pearson correlation coefficient was used to assess the associations between levels of MAMPs and mouse allergen. Parental educational level was dichotomized into at least one parent completed high school vs none. Household income was dichotomized into above or below \$15,000 per year because that was the approximate median income in Puerto Rico during the study. Eczematous rash referred to ever having a prolonged, itchy, scaly, or weepy rash. All analyses were performed using STATA/SE statistical software, version 12.1 (StataCorp, College Station, Texas).

Results

The characteristics of participants ($n = 511$) who did and did not have AR are given in Table 1. AR was present in 247 (48.3%) of participating children. Variables significantly and positively associated with AR included asthma, an eczematous rash, parental AR, parental asthma, history of daycare, reported signs of mold or mildew in the home, STR to 1 allergen or more, total number of positive skin test results, and STR to dust mite, *B tropicalis*, cockroach, mouse, dog, cat, *Alternaria*, mixed trees, mixed grasses, mugwort sage, and ragweed. Mus m 1 and shared bedroom were significantly and inversely associated with AR.

Table 2 gives the multivariate analysis of mouse allergen exposure and AR. After adjustment for age and sex (model 1A in Table 2), private and employer-based health insurance and asthma were significantly associated with increased odds of AR, whereas Mus m 1 level and shared bedroom were significantly associated with decreased odds of AR: each log₁₀-unit increment in Mus m 1 level decreased the odds of AR by 25% (95 CI, 8%–38%). Among children

sensitized to mouse (model 1B in Table 2), there was a similar trend for a reduction in the odds of AR with increasing Mus m 1 level, although it did not reach statistical significance ($P = .15$), and asthma was still associated with increased odds of AR. Among children not sensitized to mouse (model 1C in Table 2), Mus m 1 level was significantly associated with decreased odds of AR after adjustment for relevant covariates: each log₁₀-unit increase in Mus m 1 level decreased the odds of AR by approximately 21% (95 CI, 1%–37%). Because asthma was such a strong predictor of AR in our sample, we then explored whether there was an interaction between mouse allergen and asthma on AR, without significant results (data not shown).

Given that prior studies have found an inverse association among exposure to microbial components and asthma or allergic sensitization,²⁴ we then investigated whether findings for mouse allergen and AR were due to correlated microbial components detected in house dust (endotoxin, peptidoglycan, and glucan). Figure 1 shows scatterplots for glucan, peptidoglycan, and endotoxin vs Mus m 1. Of the 3, only endotoxin was significantly correlated with Mus m 1 ($r = 0.184$, $P < .001$).

In light of this correlation, we added (log₁₀-transformed) endotoxin levels to the multivariable models of mouse allergen and AR (see models 2A–2C in Table 2). In these models, endotoxin was not significantly associated with AR among all patients (model 2A) or in the subgroups of children sensitized (model 2B) or not sensitized (model 2C) to mouse. Adding endotoxin to the models also did not affect the inverse association between Mus m 1 level and AR, although interestingly it decreased the parameter estimates for asthma by more than 10%.

Discussion

To the best of our knowledge, this is the first study to examine the association between mouse allergen level and AR in children. We report that exposure to higher levels of mouse allergen are associated with decreased odds of AR and that these results are driven by children who are not sensitized to mouse.

Exposure to mouse allergen has been linked to increased odds of atopic sensitization, predominantly in inner-city or urban environments.^{16,25} In a cohort of children with parental history of

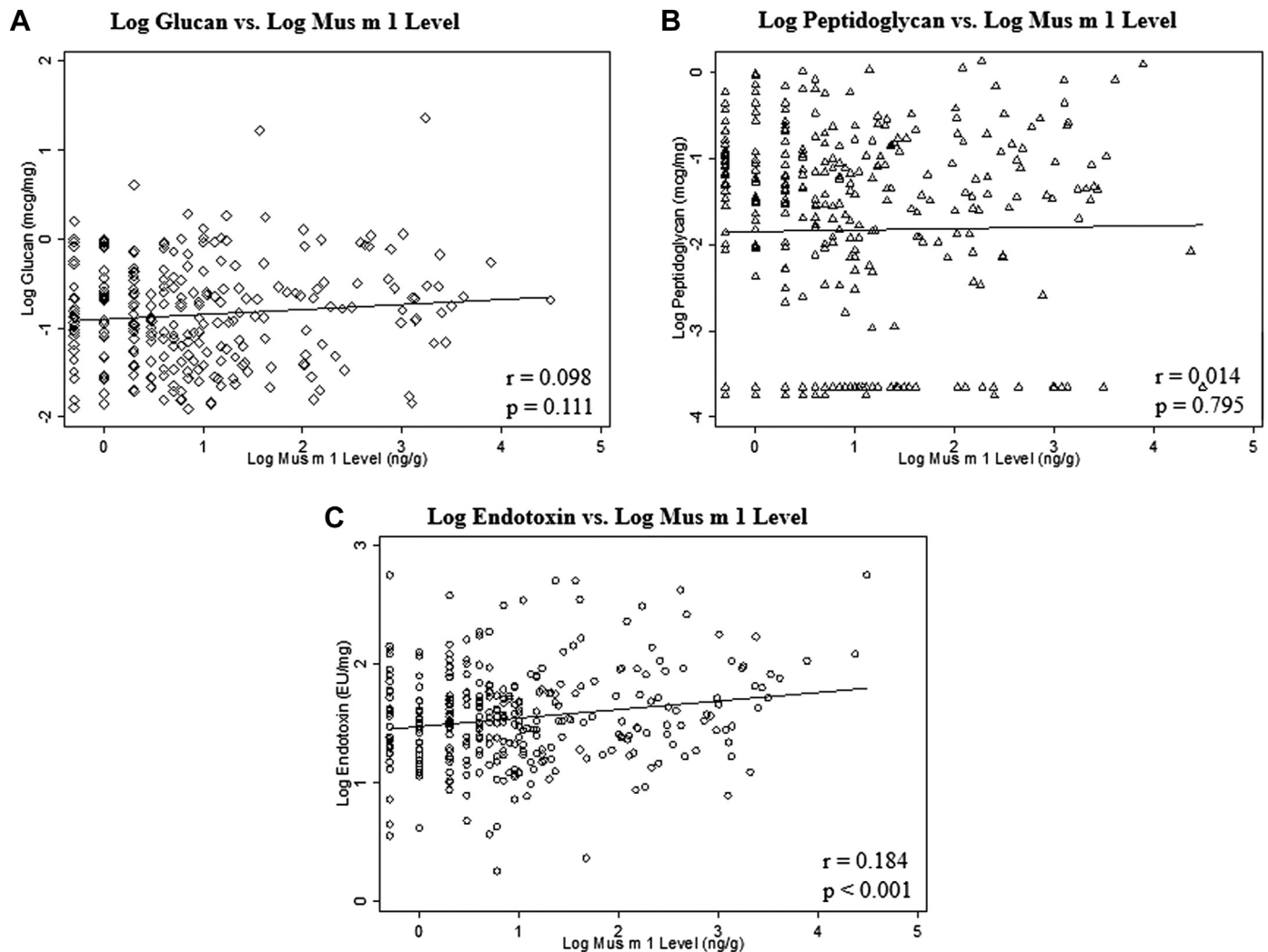


Figure 1. Scatterplots of microbe-associated molecular patterns (MAMPs) vs Mus m 1. Log₁₀ MAMPs and log₁₀ Mus m 1 levels are plotted with regression lines. Pearson correlation coefficient (r) and associated P values are shown for each plot.

allergy or asthma, Phipatanakul et al²⁵ reported that exposure to detectable levels of Mus m 1 in home dust at 2 to 3 months of age was associated with a 2-fold increase in the odds of allergic sensitization by 7 years of age compared with those with non-detectable levels. Recently, the presence of anti-mouse IgE at 3 years of age was found to be associated with increased risk of wheeze, rhinitis, and atopic dermatitis. Thus, studies to date have reported associations between allergen level and sensitization and between sensitization and AR or asthma.²⁶ Our results suggest that exposure to mouse allergen levels in children who do not develop mouse sensitization may actually have a protective effect against the development of AR, with an approximately 21% to 25% reduction in the odds of AR per each log₁₀-unit increase in house dust Mus m 1 level. This finding is consistent with our previous report that higher levels of mouse allergen are associated with better lung function among asthmatic children who are not sensitized to mouse.¹⁷ We speculate that exposure to mouse allergen—or an associated factor—may exert protective, immunomodulatory effects among children who are not allergic to it, whereas this protective effect is lost among children who become allergic to mouse. However, given the smaller number of sensitized vs nonsensitized children, we cannot fully rule out lack of statistical power to detect an association in the sensitized group.

On the basis of all of this, we initially hypothesized that mouse allergen level might be a proxy for exposure to other microbial

exposures in these children. However, when evaluating the correlation between Mus m 1 and several MAMPs, only endotoxin was significantly (albeit weakly) correlated, and its inclusion in our models did not affect the significance or magnitude of the association between Mus m 1 and AR. Future studies will need to elucidate mechanisms by which exposure to mouse allergen may be indeed protective for AR or asthma or whether certain characteristics of these children make them less likely to develop mouse sensitization and also less prone to developing AR.

The mean level of mouse allergen in our study was 290 ng/g (0.29 μ g/g), and levels ranged from undetectable ($n = 58$) to 31,227 ng/g (or approximately 4.5 log₁₀). Although these levels are lower than those reported in similar studies performed in inner cities in the United States, particularly those from the Northeast, prior studies have found similar variability: one study in Boston reported up to 68% of households had Mus m 1 levels less than 0.25 μ g/g,²⁵ whereas other inner-city studies have reported medians of approximately 0.3 to 0.4 μ g/g.^{27,28} It will be important to determine whether differences in the level of exposure may modify the effect reported. We hypothesize that in environments with relatively low ranges of Mus m 1 levels, the beneficial effect among nonsensitized children may predominate (with no effect seen among sensitized children),¹⁷ whereas in environments with higher levels of exposure, the deleterious effect among sensitized children prevails (with no effect detected among nonsensitized children).^{29,30}

We must acknowledge several limitations. First, the cross-sectional design of the study precludes assessment of temporal associations between mouse allergen levels and the outcomes assessed. However, positive determinants of mouse allergen load, including urban neighborhoods, lower income homes, older homes, household characteristics and practices,³¹ may all be relatively stable from early life throughout childhood. This is in contrast to pet ownership, which may be more susceptible to disease-associated modification of exposure. Second, we focused on Puerto Rican children because of their disproportionate burden of asthma and atopy,⁷ and the range of mouse allergen level was lower than those reported elsewhere, as previously discussed. However, mouse allergen is ubiquitous in inner-city homes in the United States,^{16,32} and thus our findings are likely applicable to those environments and its underserved populations. Third, although we adjusted for multiple potential confounders, there may be unmeasured factors at least partly responsible for these results. Of note, additionally adjusting for dust mite (*D pteronyssinus*) allergen level and family history of AR did not change our results (data not shown).

In summary, mouse allergen level was inversely associated with AR in Puerto Rican children, independently of levels of endotoxin in house dust, and the results were driven mainly by children not sensitized to mouse. This finding could be explained by early-life induction of tolerance by mouse allergen or by microbes that are present in mouse feces but were not measured in this study.

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Supplementary Data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.anai.2014.09.007>.

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eAppendix

Methods

Study Population

From March 2009 to June 2010, children in San Juan, Puerto Rico, were chosen from randomly selected households using a scheme similar to that of a prior study.¹ In brief, households in San Juan were selected by a multistage probability sample design. Primary sampling units (PSUs) were randomly selected neighborhood clusters based on the 2000 US Census, and secondary sampling units were randomly selected households within each PSU. A household was eligible if one or more residents were children aged 6 to 14 years. In households with more than one eligible child, one child was randomly selected for screening.¹ On the basis of the sampling design, 7,073 households were selected, and 6,401 (90.5%) were contacted. Of these, 6,401 households, 1,111 had 1 or more children who were within the age range of the study and had 4 Puerto Rican grandparents. In an effort to reach a target sample size of approximately 700 children, we attempted to enroll a random sample ($n = 783$) of these 1,111 children. Parents of 105 of these 783 eligible households refused to participate or could not be reached. There were no significant differences in age, sex, or area of residence between eligible children who did ($n = 678$ [87%]) and did not ($n = 105$ [13%]) agree to participate. Because we focused on allergic rhinitis (AR) and mouse allergen exposure, only those with nonmissing data on allergy skin testing and Mus m 1 levels ($n = 511$) were included in this analysis.

Study Procedures

Study participants completed a protocol that included questionnaires, allergy skin testing, and collection of dust samples. The child's parents completed 2 questionnaires used in the Genetics of Asthma in Costa Rica Study.² These questionnaires were used to obtain information about the child's general and respiratory health, family history, sociodemographic characteristics, in utero smoke exposure, family history, and household characteristics.

Skin test reactivity (STR) to aeroallergens, histamine, and saline diluent was assessed using a multitest device (Lincoln Diagnostics, Decatur, Illinois) on the skin of the forearm (in a site free of

eczema). Aeroallergens tested included house dust mites (*Dermaphagoides pteronyssinus* and *Dermatophagoides farinae*), *Blomia tropicalis*, German cockroach (*Blattella germanica*), mouse pelt, dog dander, cat dander, mold mix, *Alternaria tenuis*, mixed tree pollen, mixed grass pollen, mugwort sage, and ragweed (Alk-Abello, Round Rock, Texas). A skin test result was considered positive if the maximum wheal diameter exceeded the diluent wheal diameter by 3 mm or more.

Dust samples were obtained from 3 areas in the home: the one in which the child sleeps (usually his/her bedroom), the living room or television room, and the kitchen. The dust was sifted through a 50-mesh metal sieve, and the fine dust was reweighed, extracted, and aliquoted for analysis of allergens from mouse (mouse urinary protein [Mus m 1]), dust mite (*D pteronyssinus* [Der p 1]), cockroach (*B germanica* [Bla g 2]), dog dander (Can f 1), and cat dander (Fel d 1), as well as measurement of microbe-associated molecular patterns (MAMPs) levels for glucan and peptidoglycan using 2-site monoclonal antibody enzyme-linked immunosorbent assays and endotoxin using a modification of the limulus amebocyte lysate assay.³ Levels of allergens and MAMPs in house dust samples were transformed to a log₁₀ scale. The highest level of each log-transformed allergen or MAMP was then used for the statistical analysis.

Written parental consent was obtained for participating children, from whom written assent was also obtained. The study was approved by the institutional review boards of the University of Puerto Rico (San Jan, Puerto Rico), Brigham and Women's Hospital (Boston, Massachusetts), and the University of Pittsburgh (Pittsburgh, Pennsylvania).

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eTable 1Characteristics of children included and excluded from analysis^a

Characteristic	Included (n = 511)	Excluded (n = 167)
Age, mean (SD), y	10.3 (0.11)	9.9 (0.21)
BMI z score, mean (SD)	0.62 (0.05)	0.43 (0.12)
Male sex, %	53.1	53.1
Private or employer-based health insurance, %	33.1	38.9
Asthma, %	52.5	49.4
Parental history of allergic rhinitis, %	19.3	17.6
Shared bedroom, %	54.1	56.2
History of daycare attendance, %	22.0	23.1
Cat reported in home, %	11.1	15.4
Visible mold reported, %	40.6	35.8
Rats or mice reported, %	26.7	29.0
Leukotriene receptor antagonist use, %	13.2	12.4

^a $P < .05$ for included vs excluded.