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## Genetic variation in small proline rich protein 2B as a predictor for asthma among children with eczema

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### Abstract

**Background**—Small proline rich protein 2B (SPRR2B) is a skin and lung epithelial protein associated with allergic inflammation in mice that has not been evaluated in human atopic diseases.

**Objective**—To determine whether single-nucleotide polymorphisms (SNPs) in *SPRR2B* are associated with childhood eczema and with the phenotype of childhood eczema combined with asthma.

**Methods**—Genotyping for *SPRR2B* and filaggrin (*FLG*) was performed in 2 independent populations: the Cincinnati Childhood Allergy & Air Pollution Study (CCAAPS; N = 762; birth-age, 4 years) and the Greater Cincinnati Pediatric Clinical Repository (GCPCR; N = 1152; ages 5–10 years). Eczema and eczema plus asthma were clinical outcomes based on parental report and clinician's diagnosis. Genetic analyses were restricted to whites and adjusted for sex in both cohorts and adjusted for environmental covariates in CCAAPS.

**Results**—Variants in *SPRR2B* were not significantly associated with eczema in either cohort after Bonferroni adjustment. Children from both cohorts with the CC genotype of the *SPRR2B* rs6693927 SNP were at 4 times the risk for eczema plus asthma (adjusted odds ratio, 4.1; 95% confidence interval, 1.5– 10.9; *P* = .005 in CCAAPS; and adjusted odds ratio, 4.0; 95% confidence

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### Supplementary data

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interval, 1.8–9.1;  $P < .001$  in the GCPCR), however. SNPs in *SPRR2B* were not in strong linkage disequilibrium with the R501X and del2282 *FLG* mutations, and these findings were independent of *FLG*.

**Conclusions**—An SNP in *SPRR2B* was predictive of asthma among white children with eczema from 2 independent populations. *SPRR2B* polymorphisms may serve as important predictive markers for the combined eczema plus asthma phenotype.

Eczema is a chronic inflammatory skin condition commonly associated with other atopic diseases, such as asthma.<sup>1,2</sup> Genetic variants in epidermal proteins, such as filaggrin (*FLG*), are thought to play a critical role in the development of eczema and have been associated with the combination of eczema plus asthma.<sup>2–6</sup> The *FLG* gene is located within the epidermal differentiation complex, a region on chromosome 1q21 that also encodes for numerous other proteins involved in maintaining the skin barrier.<sup>7–10</sup>

Linkage and expression studies indicate that *FLG* alone does not account for the strong association between region 1q21 and eczema nor for the possible association between this region and the combined phenotype of eczema plus asthma.<sup>4,11,12</sup> Small proline rich proteins (SPRRs) are cross-linking components of the keratinocyte-cornified envelope encoded on 1q21 that may be critically important to the formation of the skin barrier.<sup>13,14</sup> *SPRR2B* in particular has been shown to be induced by allergens and the T<sub>H</sub>2 cytokine, interleukin 13, in mouse models of asthma and allergic gastrointestinal disease.<sup>15,16</sup> Moreover, *SPRR2B* messenger RNA expression is increased during asthma exacerbations, and large allele frequency differences exist between human populations with high rates of asthma vs those with a lower prevalence of the disease.<sup>17,18</sup> Together, these findings suggest that *SPRR2B* may play a role in both eczema and asthma.

We hypothesized that polymorphisms in *SPRR2B* would be significantly associated with childhood eczema and with the eczema plus asthma phenotype. To test this hypothesis, we examined differences in the frequency of single-nucleotide polymorphisms (SNPs) in *SPRR2B* between children with and without eczema, and eczema plus asthma who were participating in the Cincinnati Childhood Allergy & Air Pollution Study (CCAAPS) and the Greater Cincinnati Pediatric Clinic Repository (GCPCR) at Cincinnati Children’s Hospital Medical Center.<sup>18,19</sup>

## Methods

CCAAPS is a longitudinal birth cohort at high risk for atopy.<sup>19</sup> Newborns in the Cincinnati metropolitan area were identified by public birth records from 2001 to 2003. All 762 infants had a parent with symptoms of asthma, allergic rhinitis, or eczema and with at least one positive skin prick test result to a panel of 15 aeroallergens. Parents signed an informed consent approved by the institutional review board of the University of Cincinnati. The GCPCR (N = 1152) includes children 5 to 17 years of age from subspecialty clinics at Cincinnati Children’s Hospital and control subjects from the general population.<sup>18</sup> Parents signed an informed consent approved by the Cincinnati Children’s Hospital institutional review board. (Further details are provided in Table 1 and in the eMethods.)

## Outcome measures

**Eczema**—The definition of eczema in CCAAPS was adapted from a validated questionnaire (International Study of Asthma and Allergies in Childhood) and included a parental report of the child’s scratching *and* redness, “raised bumps,” or dry skin/scaling for *at least 6 of the last 12 months*.<sup>20</sup> Children who tested positive for eczema at any point from 1 through 4 years of age were considered cases. This definition was established a priori and

was previously used in CCAAPS.<sup>21</sup> For the GCPCR, cases with eczema included children with a physician's diagnosis or a parental report of eczema. A separate analysis with eczema based on the clinician's diagnosis at 1, 2, 3, or 4 years of age was performed in CCAAPS. Physical examination findings considered to be consistent with eczema included erythema, papulation, excoriations, and/or lichenification.

**Eczema with asthma**—Having eczema at any point from 1 through 4 years of age combined with asthma at the age of 4 years served as a secondary outcome measure for CCAAPS.<sup>2</sup> Given that objective testing for asthma could not be performed in CCAAPS due to the age of the children, a case definition for asthma at the age of 4 years was developed; this case definition included a parental report of persistent wheezing (≥ 2 wheezing episodes not associated with a cold or upper respiratory tract infection) at both 3 and 4 years of age or a diagnosis of asthma by a child's physician by 4 years of age.<sup>22</sup> Although this case definition is not asthma per se, for the sake of simplicity it will be referred to as *asthma* for the remainder of the article. The reference group for the eczema plus asthma outcome included children with neither condition or just eczema or asthma alone (but not both). For the GCPCR, cases included children with both eczema and asthma, whereas the reference group had neither condition or just eczema or asthma alone. In both CCAAPS and the GCPCR, a separate analysis was performed in which only children with neither eczema nor asthma were included in the reference group. (Additional details are provided in the eMethods.)

### Selection of SNPs

A priori, we decided to use the GCPCR as a replication cohort. Therefore, SNPs evaluated in CCAAPS were the same as those analyzed concurrently in the GCPCR. The *SPRR2B* SNPs chosen included 1 intronic tagging SNP (rs6693927), 2 SNPs in the 5' and 3' untranslated regions (rs7525198 and rs6673356, respectively), and a missense mutation (rs404408).<sup>18</sup> Tagging SNPs and SNPs in regulatory regions with minor allele frequency greater than 5% across the *SPRR2B* gene were chosen to adequately represent the gene, as previously described.<sup>23</sup>

### Genotyping

*SPRR2B* genotyping for CCAAPS and the GCPCR was accomplished using a LightTyper platform and a custom Illumina Golden Assay, respectively.<sup>18,24,25</sup> The rs6693927 and rs7525198 SNPs were genotyped with error rates of less than 2% and were in Hardy Weinberg equilibrium (eTable 1). The rs6673356 and rs404408 SNPs were not included in further analyses because genotyping results did not meet quality controls. Genotyping of *FLGR501X* was accomplished by polymerase chain reaction and restriction fragment length polymorphism in CCAAPS and the GCPCR as previously described (eMethods).<sup>6,26</sup> Primer sequences and genotyping methods for *FLG* 2282del4 in the GCPCR, as well as further information regarding genotyping of *SPRR2B*, are provided in the online supplement.

### Statistical analysis

SAS statistical software (SAS Institute Inc, Cary, North Carolina) was used to perform multivariate logistic regression to adjust findings in CCAAPS for host and environmental covariates, including income under \$50,000, breastfeeding (yes/no), dog and/or cat ownership (yes/no based on home visit), and house dust endotoxin exposure at 1 year of age (based on home visit). All potential covariates listed in eTable 2 were initially included in the maximum likelihood estimated model and removed if  $P > .15$ . Analyses in the GCPCR were adjusted for sex. Environmental covariates from the GCPCR were not available at the time of this analysis. Analyses in both cohorts were restricted to whites given the small

sample size of African Americans. A priori, children older than 10 years were excluded from the analysis in the GCPCR to improve comparability with CCAAPS and to decrease recall bias related to transient eczema occurring at younger ages.<sup>27</sup>

A genotypic analysis for *SPRR2B* was performed. This model was chosen given that the mode of inheritance is not known and an additive model may be less likely to detect an association with relevant outcomes in the case of recessive traits.<sup>28</sup> To perform a genotypic analysis, we used logistic regression to calculate adjusted odds ratios (aORs), 95% confidence intervals (CIs), and *P* values that represented the relationship between genotypes of rs6693927 and rs7525198 (eg, TT vs all others; CC vs all others; CT vs all others) and the outcomes of eczema and eczema plus asthma. For rs6693927, TT represents a homozygous recessive with 2 TT alleles, CT represents a heterozygote, and CC represents a homozygous recessive with 2 CC alleles. A haplotype analysis using PLINK software was also conducted to determine whether there were additional effects from combined genotypes of rs6693927 and rs7525198.<sup>29</sup> Linkage disequilibrium (LD) ( $D'$  and  $r_2$ ) between *SPRR2B* and *FLG* variants was estimated using Haploview.<sup>30</sup> A LD-adjusted Bonferroni calculation (0.03) was applied to genetic findings to account for multiple comparisons.

## Results

### Study population characteristics

In the CCAAPS cohort, 161 of 396 whites (41%) had eczema for at least 1 year from 1 through 4 years of age, whereas 59 of 328 whites (18%) ages 5 to 10 years in the GCPCR had the disease (Table 2). Among whites with eczema from CCAAPS, 144 of 161 (89%) were atopic based on 1 positive skin prick test result to a panel of 15 aeroallergens at any point from 1 through 4 years of age; skin prick test results were not available for the GCPCR. Findings related to host and environmental covariates in CCAAPS are presented in eTable 3.

### Genetic predictors of eczema

Among whites from CCAAPS, the TT genotype of the rs6693927 SNP (TT\_rs6693927) in *SPRR2B* was protective against eczema after adjustment for sex (aOR, 0.5; 95% CI, 0.2–0.9; *P* = .03); however, this finding did not meet criteria for significance based on LD-adjusted Bonferroni correction (*P* < .03 was significant). There was a trend toward an association with eczema after adjustment for environmental covariates (aOR, 0.5; 95% CI, 0.3–1.1; *P* = .09; Fig 1). Findings for TT\_rs6693927 in the GCPCR study population were not statistically significant (Fig 1 and eTable 4). The *SPRR2B* rs7525198 SNP was not associated with eczema in either CCAAPS or the GCPCR. In addition, the combination of rs7525198 and rs6693927 was not more predictive of eczema than rs6693927 alone, based on findings from combined genotype (diplotype) and haplotype analyses (data not shown).<sup>29</sup>

### Genetic predictors of the eczema plus asthma phenotype

We next evaluated the association between polymorphisms in *SPRR2B* and the presence of both eczema and asthma.<sup>2</sup> As indicated in Table 2, 25 whites (7%) from CCAAPS and 28 whites (9%) from the GCPCR had both conditions. An odds ratio for TT\_rs6693927 could not be calculated for CCAAPS because none of the children with this genotype had the phenotype of eczema plus asthma; the odds ratio for the CC genotype of the rs6693927 SNP (CC\_rs6693927) was therefore calculated instead. Among whites from both CCAAPS and the GCPCR, CC\_rs6693927 conferred a 4-fold increased risk for the eczema plus asthma phenotype (aOR, 4.1; 95% CI, 1.5–10.9; *P* = .005 after adjustment for host and environmental covariates from the logistic regression model in CCAAPS; and aOR, 4.0; 95% CI, 1.8–9.1; *P* < .001 after adjustment for sex in the GCPCR; Fig 2 and eTable 5).

These findings met the LD-adjusted Bonferroni criteria for significance ( $P < .03$ ). As was the case with eczema, rs7525198 did not confer significant effects for eczema plus asthma by itself, and the combination of rs7525198 and rs6693927 was not more predictive of eczema plus asthma than the latter SNP alone (data not shown).<sup>29</sup>

### Additional analyses based on different definitions of eczema and eczema plus asthma

As a secondary analysis, we also evaluated eczema defined solely by clinician's diagnosis at 1, 2, 3, or 4 years of age in CCAAPS. Findings were similar to those seen with the survey definition of eczema in CCAAPS. Among whites ages 1 to 4 years, 117 (44%) had clinician-diagnosed eczema and 149 (56%) did not. There was a possible protective effect from clinician-diagnosed eczema conferred by the TT\_6693927 genotype after adjustment for host and environmental covariates (aOR, 0.6; 95% CI, 0.4–1.1;  $P = .10$ ; Fig 3); however, this finding was not statistically significant.

We also evaluated the relationship between the eczema plus asthma phenotype using the clinician's diagnosis of eczema definition in CCAAPS. Findings were strikingly similar to those seen with the survey definition of eczema. There were 16 children (7%) with the clinician's diagnosis of eczema plus asthma and 217 children (93%) in the reference group. A strong association was found between the CC\_6693927 genotype and the combination of clinician-diagnosed eczema plus asthma (aOR, 5.3; 95% CI, 1.6–17.4;  $P = .005$  after adjustment for host and environmental covariates from the logistic regression model; Fig 4). These findings met the LD-adjusted Bonferroni criteria for significance ( $P < .03$ ).

To further clarify the relationship between polymorphisms in *SPRR2B* and the eczema plus asthma phenotype, an additional analysis was conducted in which the reference group included only children with neither eczema nor asthma ( $n = 195$  in CCAAPS and  $n = 100$  in the GCPCR). Findings from this analysis were nearly identical to those previously reported. That is, CC\_rs6693927 conferred increased risk for eczema plus asthma (aOR, 4.5; 95% CI, 1.6–13.1;  $P = .005$  after adjustment for host and environmental covariates from the logistic regression model in CCAAPS; and aOR, 4.6; 95% CI, 1.9–11.3;  $P < .001$  in the GCPCR). These findings met the LD-adjusted Bonferroni criteria for significance ( $P < .03$ ).

### Association between rs6693927 and asthma

To better understand the relationship between the rs6693927 SNP and the eczema plus asthma phenotype, we also evaluated the relationship between this SNP and asthma alone (without eczema). Among whites from CCAAPS, there was a trend toward a protective effect from asthma conferred by the TT\_6693927 genotype after adjustment for host and environmental covariates (aOR, 0.3; 95% CI, 0.09–1.1;  $P = .06$ ; Fig 5). Among whites 5 to 10 years of age from the GCPCR, there was also a trend toward increased risk for asthma alone conferred by the CC\_6693927 genotype (aOR, 1.6; 95% CI, 1.0–2.7;  $P = .06$ ).

### Determination of the relationship to FLG polymorphisms

Given the previously reported association between *FLG* null mutations and the eczema plus asthma phenotype and that both *FLG* and *SPRR2B* are located on chromosome 1q21, we next determined whether the effects of *SPRR2B* were related to LD with *FLG*. *FLG* null mutations were not in strong LD with *SPRR2B* polymorphisms ( $r_2 < .05$ ,  $D' < .68$  for R501X and 2282del4 in the GCPCR, with similar findings for R501X in CCAAPS).

## Discussion

Evidence from the literature has established that epidermal barrier function plays a critical role in eczema and possibly in the phenotype of eczema plus asthma.<sup>1,2,5</sup> The combination

of eczema plus asthma may represent a distinct endophenotype with unique pathogenic and prognostic implications.<sup>5,31</sup> Identification of risk factors that may modify the risk of asthma among children with eczema is important.<sup>31,32</sup> In addition, improved understanding of the relationship between eczema and asthma may provide mechanistic insights into the pathogenesis of asthma.<sup>5,32</sup> *FLG* mutations alone are unlikely to account for the strong genetic linkage between the epidermal differentiation complex on chromosome 1q21 and the eczema plus asthma phenotype.<sup>1,2</sup> Given this premise and based on preliminary data from RNA expression studies and allele frequency differences in asthmatic populations, we explored the relationship among childhood eczema, the combination of eczema plus asthma, and *SPRR2B*, an epithelial protein encoded on 1q21.<sup>17,18</sup> We demonstrated a possible association between an SNP in *SPRR2B* and eczema among whites 4 years and younger from the CCAAPS cohort; however, this finding was not statistically significant after Bonferroni correction. A nonsignificant trend toward an association between this SNP and asthma was also seen in both CCAAPS and the GCPCR. Interestingly, in both cohorts, the CC genotype of the rs6693927 SNP conferred strong, statistically significant effects among children who had the eczema plus asthma phenotype. That is, the rs6693927 CC genotype conferred an approximately 4-fold increased risk for eczema plus asthma in both CCAAPS and the GCPCR. Findings for this SNP did not appear to be related to *FLG* polymorphisms. Thus, polymorphisms in *SPRR2B* may independently serve as useful markers to predict the development of asthma among children with eczema.

Mechanistic studies to explain the reasons for an association between *SPRR2B* polymorphisms and the eczema plus asthma phenotype have yet to be conducted. Alterations in *SPRR2B* may potentially result in a defective skin barrier. Small proline rich proteins, including *SPRR2B*, play an important role in the formation of the keratinocyte-cornified envelope.<sup>33</sup> After cross-linking by transglutaminases, they serve as the scaffold on which other epithelial proteins are added.<sup>34</sup> It is not clear, however, whether the link between *SPRR2B* and asthma is entirely mediated by effects on the skin barrier. In contrast to *FLG*, which is not expressed in the lungs, *SPRRs* are expressed in multiple tissues throughout the body. *SPRR2B* in particular is expressed in the lungs of mice, and its expression is specifically altered in the nasal epithelium of asthmatic patients.<sup>15,17,34</sup> It has also been speculated that the altered expression of *SPRR* genes as part of a stress response to UV light, infection, or allergic inflammatory signals may reflect a role in tissue repair.<sup>34-36</sup> This implies that quantitative or functional abnormalities involving *SPRRs* might lead to a dysfunctional repair response with the potential for pathologically adverse outcomes. Alternatively, up-regulation of *SPRR2B* during asthma exacerbations may reflect another undiscovered role of this protein in allergic inflammation.<sup>17,34</sup>

Although there is a possible association between the rs6693927 polymorphism in *SPRR2B* and eczema and a strong relationship with the combination of eczema and asthma, there are limitations to what may be concluded from these findings. It is possible that this association reflects genetic linkage with other epidermal barrier proteins encoded on region 1q21, besides *FLG*, and/or that *SPRR2B* is coexpressed with other *SPRRs* that are responsible for clinically meaningful responses. The rs6693927 SNP has not been clearly related to changes in *SPRR2B* protein function or expression, and the possibility exists that this SNP may be a *marker* of disease causing mutations rather than disease causing itself. Another possible limitation is that there were relatively small numbers of children with the eczema plus asthma phenotype from both cohorts. There were also differences in the cohorts studied, including that they enrolled children of different ages and that CCAAPS is a high-risk birth cohort, whereas the GCPCR includes both atopic and control children. Differences in the prevalence of eczema between the cohorts are reflective of these factors. Findings related to asthma in the CCAAPS cohort will be validated once the children are old enough to undergo objective testing. Despite these differences, the prevalence of the eczema plus asthma

phenotype was similar between cohorts; further, odds ratios for the effects of *SPRR2B* polymorphisms were almost identical. In addition, findings were similar despite different outcome definitions between cohorts and were comparable in CCAAPS regardless of the outcome definition used.

In conclusion, the rs6693927 SNP in *SPRR2B* was significantly associated with the eczema plus asthma phenotype among whites from both cohorts. It was not significantly associated with eczema in CCAAPs or in the GCPCR. Findings were independent of *FLG* polymorphisms and were robust despite potential differences in the cohorts.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

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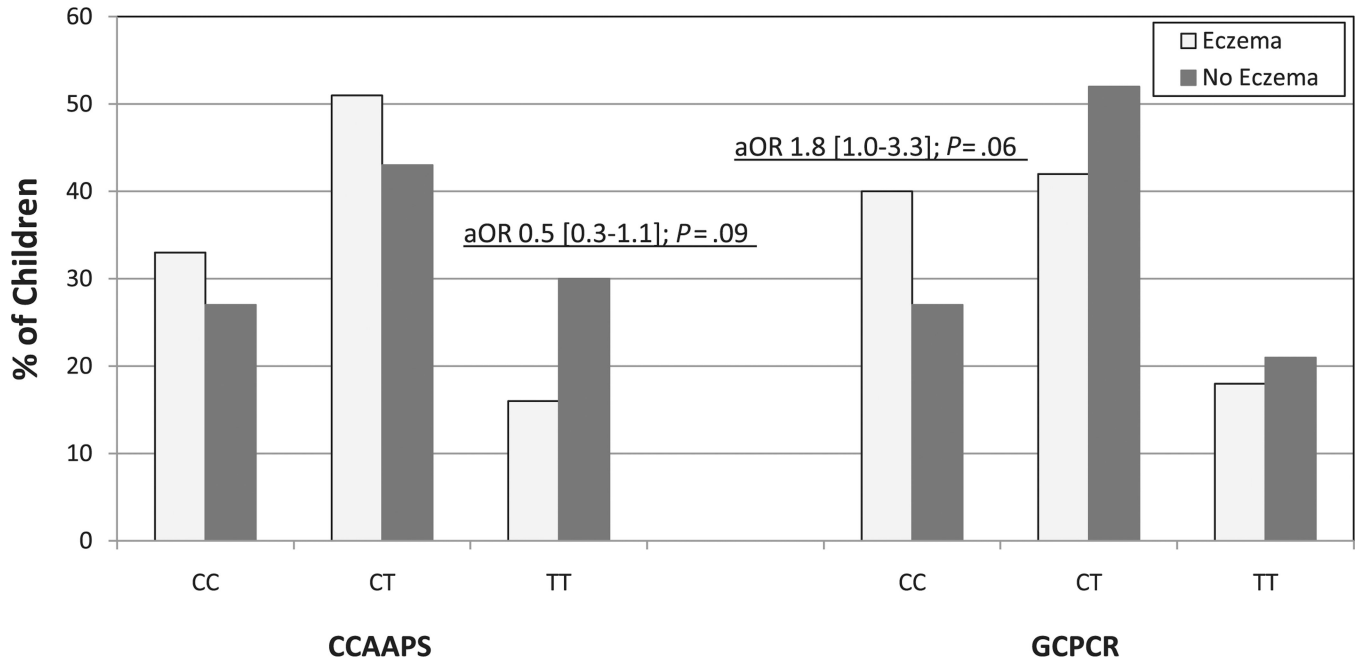
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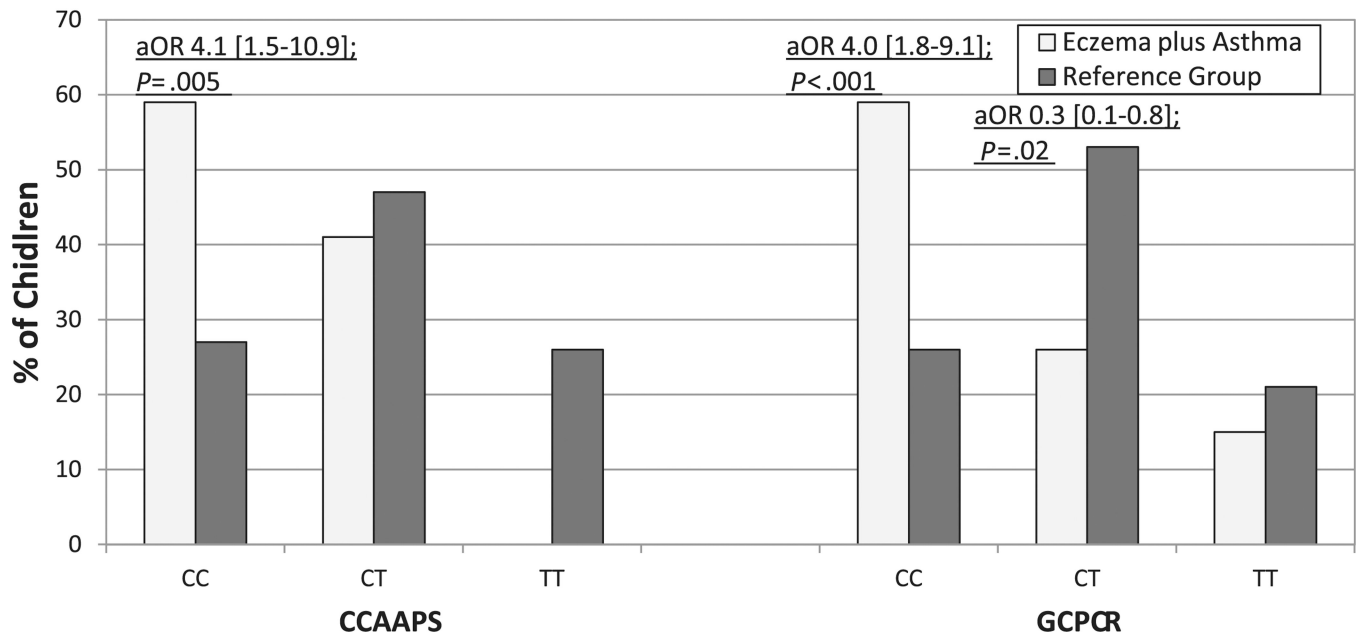
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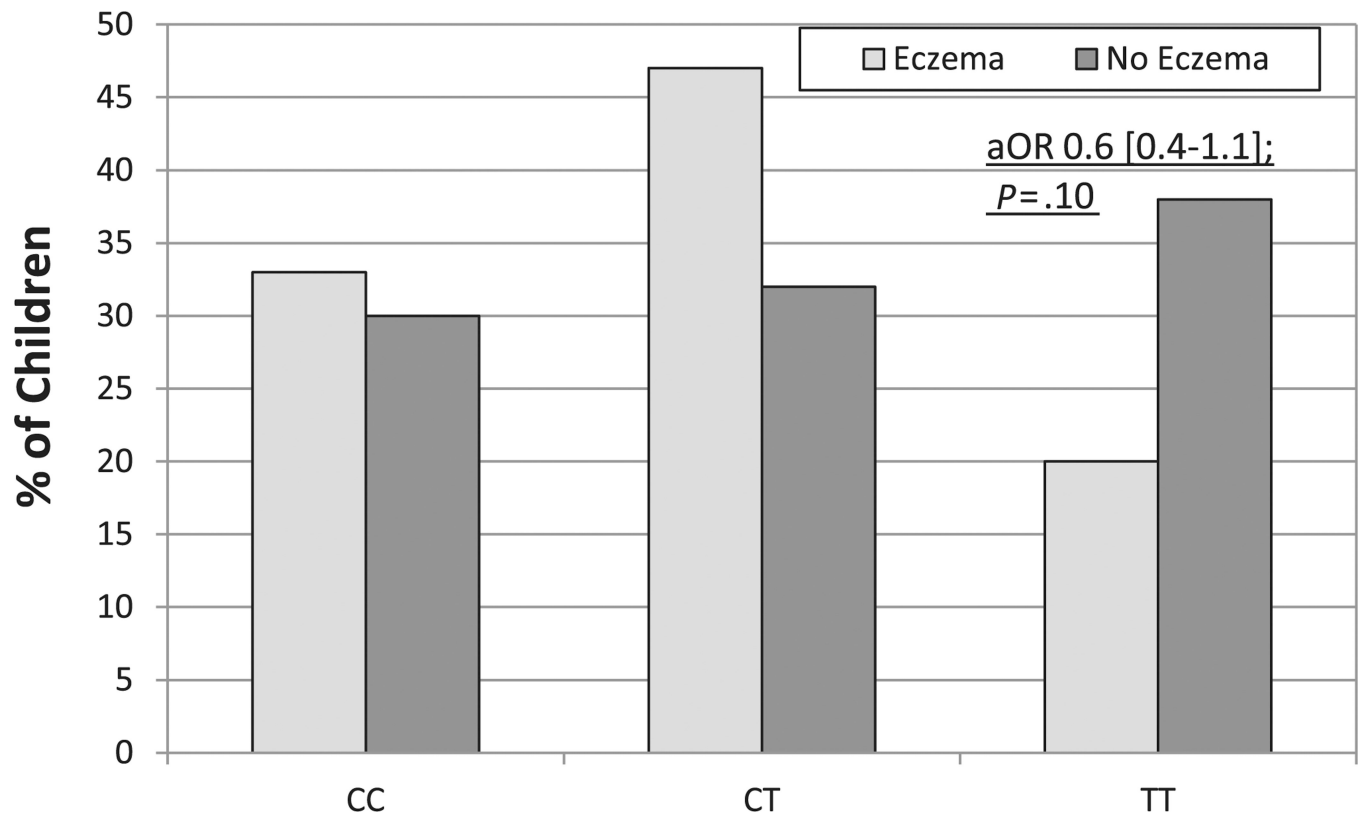


**Fig. 1.** Genotypes of rs6693927 and eczema among whites in the Cincinnati Childhood Allergy & Air Pollution Study (CCAAPS) (1–4 years of age) and Greater Cincinnati Pediatric Clinical Repository (GCPCR) (5–10 years of age) cohorts. The figure shows the percentage of children with genotypes of the rs6693927 SNP based on whether they had eczema. Adjusted odds ratios (aORs) for statistically significant or borderline effects are given. Data from CCAAPS were adjusted for sex, income, breastfeeding, cat ownership, dog ownership, and endotoxin (eTable 3). Data from the GCPCR were adjusted for sex.

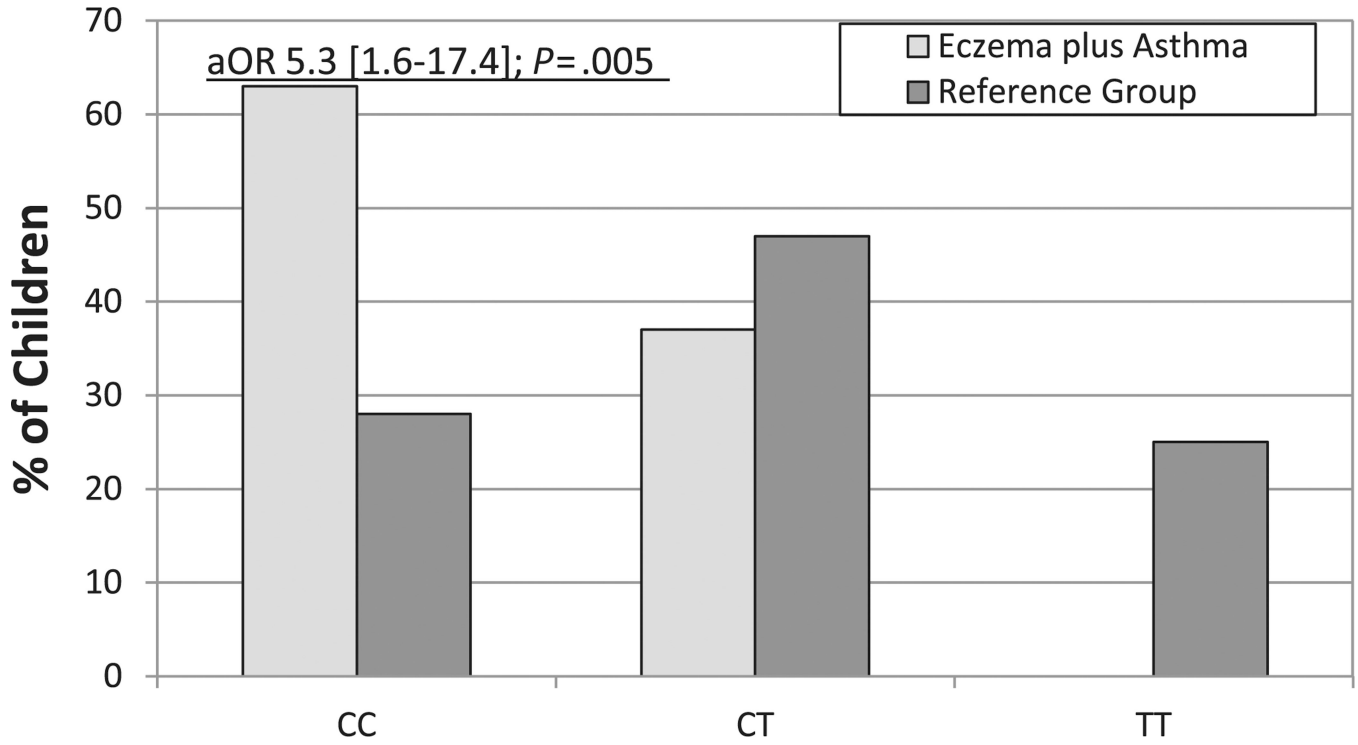


**Fig. 2.**

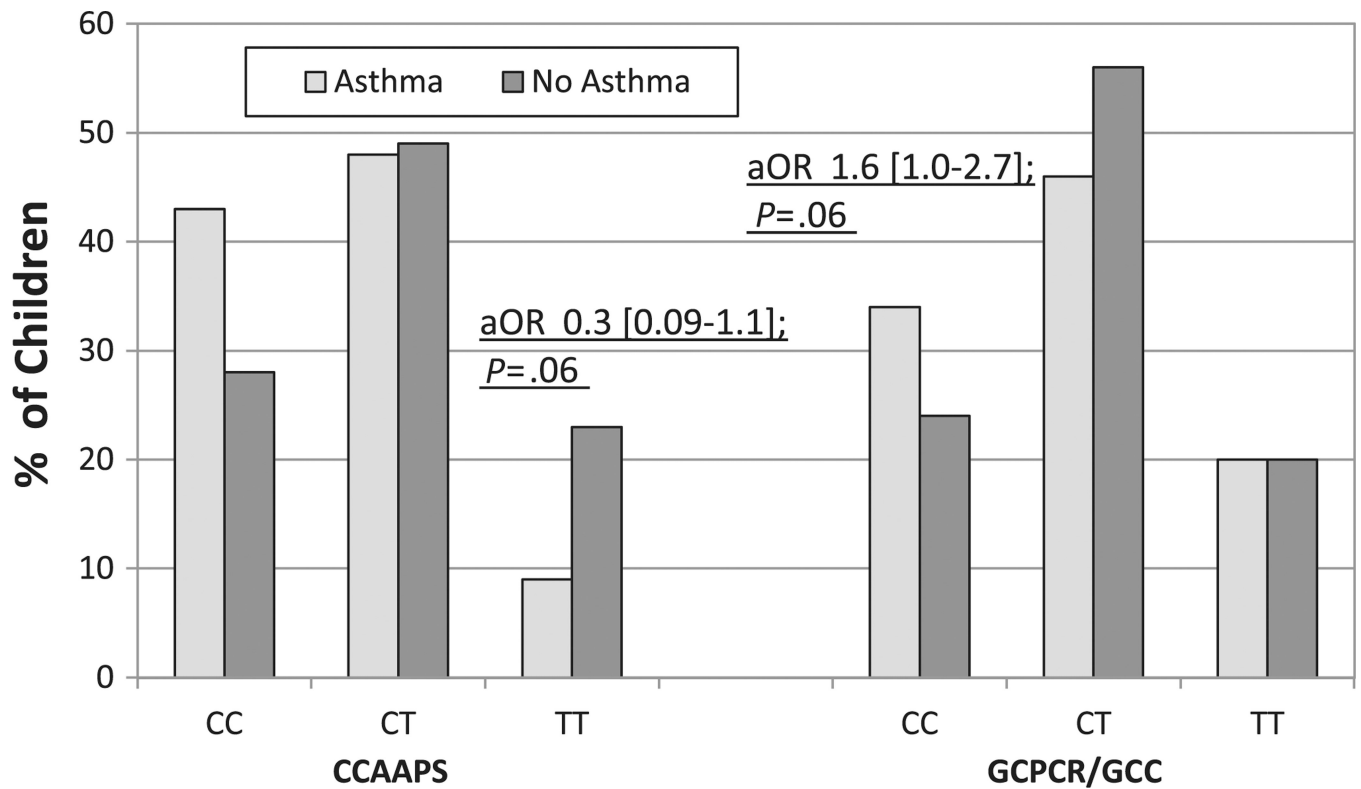
Genotypes of rs6693927 and the eczema plus asthma phenotype among whites in the Cincinnati Childhood Allergy & Air Pollution Study (CCAAPS) (1–4 years of age) and Greater Cincinnati Pediatric Clinical Repository (GCPCR) (5–10 years of age) cohorts. The figure shows the percentage of children with genotypes of the rs6693927 single-nucleotide polymorphism based on whether they had the combination of eczema and asthma. The reference group for this analysis included children with neither condition or just with eczema or asthma (but not both). Adjusted odds ratios (aORs) are displayed for statistically significant effects. Data from CCAAPS were adjusted for sex, income, breastfeeding, cat ownership, dog ownership, and endotoxin (eTable 3). Data from the GCPCR were adjusted for sex.



**Fig. 3.** Genotypes of rs6693927 and clinician-diagnosed eczema among whites in the Cincinnati Childhood Allergy & Air Pollution Study (CCAAPS) cohort (1–4 years of age). The figure shows the percentage of whites from CCAAPS with genotypes of the rs6693927 single-nucleotide polymorphism based on whether they had clinician-diagnosed eczema. Data were adjusted for sex, income, breastfeeding, cat ownership, dog ownership, and endotoxin.



**Fig. 4.** Genotypes of rs6693928 and the clinician-diagnosed eczema plus asthma phenotype among whites from Cincinnati Childhood Allergy & Air Pollution Study (CCAAPS) (1–4 years of age). The figure shows the percentage of whites from CCAAPS (ages 1–4) with genotypes of the rs6693927 single-nucleotide based on whether they had the combination of clinician-diagnosed eczema and asthma. The reference group for this analysis included children with neither condition or just with eczema or asthma (but not both). Odds ratios adjusted for sex, income, breastfeeding, cat ownership, dog ownership, and endotoxin are displayed for statistically significant effects.



**Fig. 5.** Genotypes of rs6693928 and asthma among whites in the Cincinnati Childhood Allergy & Air Pollution Study (CCAAPS) (1–4 years of age) and the Greater Cincinnati Pediatric Clinical Repository (GCPCR) (5–10 years of age). The figure shows the percentage of whites from CCAAPS and the GCPCR with genotypes of the rs6693927 SNP based on whether they had asthma. Data from CCAAPS were adjusted for sex, income, breastfeeding, cat ownership, dog ownership, and endotoxin. Data from the GCPCR were adjusted for sex.

**Table 1**

Description of the Cincinnati Childhood Allergy and Air Pollution Study (CCAAPS) and the Greater Cincinnati Pediatric Clinic Repository (GCPCR)

Variable	CCAAPS	GCPCR
Type of cohort	Longitudinal birth cohort study of children from atopic parents	Children from subspecialty clinics at an academic, pediatric medical center and control children from the general population
Total No. of children	762	1,152
Age of children at time of data collection, y	1–4	5–17 (5- to 10-year-olds analyzed)
Study population	Identified from birth records (2001–2003) in Cincinnati and Northern Kentucky and (a) had at least 1 parent with symptoms of asthma, allergic rhinitis, or eczema and positive skin prick test results to 1/15 aeroallergens and (b) lived <400 m or > 1,500 m from a major road	Cases recruited from allergy/immunology, pulmonary, and dermatology clinics. Some controls recruited from headache, plastics, and orthopedics clinics; some controls recruited from the general population in Cincinnati.
Definition of eczema	Primary: a parental report of the child's scratching and redness, "raised bumps," or dry skin/scaling for at least 6 of the last 12 months; Secondary clinician's diagnosis	A physician's diagnosis or a parental report of eczema
Definition of asthma	A parental report of persistent wheezing ( 2 episodes not associated with a cold or upper respiratory tract infection) at both 3 and 4 years of age or a physician's diagnosis of asthma by 4 years of age	A physician's diagnosis of asthma

**Table 2**

White children meeting criteria for eczema with and without asthma in the Cincinnati Childhood Allergy and Air Pollution Study (CCAAPS) (1–4 years of age) and Greater Cincinnati Pediatric Clinic Repository (GCPCR) (5–10 years of age) Cohorts

Characteristic	No. (%) of children	
	CCAAPS	GCPCR
Any eczema	161 (41) <sup>a</sup>	59 (18) <sup>b</sup>
No eczema	235	269
Eczema plus asthma	25 (7)	28 (9)
No eczema or asthma	195 (56)	111 (34)
Eczema but no asthma	114 (33)	31 (10)
No eczema with asthma	16 (5)	158 (48)

<sup>a</sup>Sufficient information to determine whether white children met criteria for eczema (1–4 years of age) was available for 396 children from CCAAPS; information for both eczema (1–4 years of age) and asthma (4 years of age) was available for 350 children. Because of this, the denominator used to determine the percentage of children with eczema is 396, whereas the denominator used for other percentages for CCAAPS is 350.

<sup>b</sup>Sufficient information to determine whether white children met criteria for eczema and/or asthma was available for 328 children from the GCPCR. The denominator was 328 for all percentage calculations for the GCPCR.