Research Article

Association of FcεRIβ polymorphisms with risk of asthma and allergic rhinitis: evidence based on 29 case–control studies

Huanhuan Guo1, Tao Peng1, Ping Luo2, Huabin Li3, Shuo Huang1, Shuang Li1, Weidong Zhao3 and Xuhong Zhou1

1Department of Otorhinolaryngology, Head and Neck Surgery, Zhongnan Hospital of Wuhan University, Wuhan, China; 2Department of Clinical Laboratory Medicine and Center for Gene Diagnosis, Zhongnan Hospital of Wuhan University, Wuhan, China; 3Department of Otolaryngology, Head and Neck Surgery, Affiliated Eye, Ear, Nose and Throat Hospital, Fudan University, Shanghai, China

Correspondence: Xuhong Zhou (zhouxuhong62@126.com) or Weidong Zhao (zhaowda@sina.com)

Purpose: Accumulating evidence has shown that allergic diseases are caused by a complex interaction of genetic and environmental factors, some single nucleotide polymorphisms (SNPs) existing in high-affinity IgE receptor β chain (FcεRIβ) are potential risk factors for allergic diseases. However, the results have been inconsistent and inconclusive due to the limited statistical power in individual study. Thus, we conducted a meta-analysis to systematically evaluate the association between FcεRIβ SNPs and allergic diseases risk.

Methods: Eligible studies were collected from PubMed, Embase, Web of Science, Chinese National Knowledge Infrastructure, and WanFang databases. Pooled odd ratios (ORs) and corresponding 95% confidence intervals (95% CIs) were calculated to assess the strength of the relationships between five polymorphisms (E237G, -109 C/T, RsaI ex7, and I181L) and the risk of allergic diseases by using five genetic models. In addition, the stability of our analysis was evaluated by publication bias, sensitivity, and heterogeneity analysis.

Results: Overall, a total of 29 case–control studies were included in this meta-analysis. We found that E237G (B vs. A: OR = 1.28, 95% CI = 1.06–1.53, P < 0.001, I² = 63.1%) and -109 C/T (BB vs. AA + AB: OR = 1.58, 95% CI = 1.26–1.98, P < 0.001, I² = 66.4%) were risk factors for allergic diseases.

Conclusion: Our meta-analysis suggests that polymorphisms in FcεRIβ may be associated with the development of allergic diseases.

Introduction

Allergic rhinitis (AR) is a common nasal mucosal inflammation, approximately 10–20% of the global population suffers from AR, and the classic symptoms of AR are nasal congestion, nasal itching, sneezing, and rhinorrhea. Allergic conjunctivitis presents as itchy, watery eyes resulting from the same pathophysiology as AR and is not surprisingly a common comorbid condition.

As an allergen-mediated disorder of the nasal passage, AR shares several similarities with another allergic disease of the lower respiratory tract: asthma. Not surprisingly, the two conditions are often comorbid; 85% of patients with asthma have AR whereas 40% of patients suffering from AR have or will develop asthma [1]. As a type 1 immunoglobulin (Ig)E-mediated hypersensitivity process, symptoms of them are triggered by allergens. The reported prevalence of allergic diseases has been steadily increasing. The true incidence probably remains underestimated. Asthma, one of the most common chronic respiratory diseases of childhood, is characterized by recurrent respiratory symptoms, reversible variable airway obstruction, airway inflammation, and increased bronchial hyper-responsiveness [2–4]. Its incidence is on the rise among children, which brings heavy burden to the whole society and results in huge medical
Figure 1. Flow chart of selection process in this meta-analysis

Figure 2. ORs and 95% CIs for the associations between E237G polymorphism and allergic diseases risk in allelic genetic model for overall populations
expenditure around the world. It is thought to be caused by a combination of genetic and environmental factors [5,6].

AR and asthma are complex multifactorial disorders, with both genetic and environmental components determining disease expression, show strong familial aggregation and heritability [7,8], thus suggesting that genetic risk factors may underlie the risk of developing, or the clinical presentation of, allergic diseases [9-11]. Allergic diseases are also associated with elevated serum IgE levels and increased mediator release from activated inflammatory cells. Allergens cross-link IgE bound to FcεRIα that causes FcεRI clustering and activates the receptor complexes (FcεRIα, FcεRIβ, and FcεRIγ–γ homodimer) on the surface of mast cells or basophils, releasing vasoactive mediators, such as histamine. Although the search for genetic susceptibility factors related to allergic diseases is a promising field, gene variations related to FcεRI as potential risk factors for allergic diseases have not been comprehensively analyzed, and the results available are in some cases contradictory, some studies showed the variant of Glu237Gly of FcεRIβ gene showed association with atopic diseases and the variant is also associated with very high total serum IgE levels [12-19], but others were showed no association with atopic asthma [20-22].

FcεRI has a tetrameric structure consisting of three distinct polypeptides including the IgE-binding α chain, 4-fold membrane-spanning β chain, and disulfide-linked γ–γ homodimer [23]. The β chain of the FcεRI is found on mast cells and basophils, and acts as a signal amplifier in mast cell activation [24-26]. Cross-linking of this receptor leads to increased IL-4 production by these cells. The aggregation of FcεRI by the binding of IgE with multivalent antigens has been shown to induce the release of histamine, leukotrienes, and inflammatory cytokines, and plays an important role in allergic inflammation [27,28]. Furthermore, the β chain was previously reported to amplify early activation signals 5–7-fold through FcεRI in humans [25]. The β chain has also been suggested to function as a stabilizer of the FcεRI complex [29]. It contains an immunoreceptor tyrosine-based activation motif, a conserved feature of many antigen receptors that imparts signaling competence. The FcεRI β chain acts as a signal amplifier through the immunoreceptor tyrosine-based activation motif in its C-terminal intracellular region. Mutations in the FCER1B gene could alter IL-4 production and thus modify IgE levels.

Several studies on the genetic background of atopy likely to contribute to the pathogenesis of allergies [30-33], of these, a significant role for polymorphisms in the FcεRI β chain in the manifestation of the phenotype has been suggested. Genetic linkage studies demonstrated that a locus in chromosome 11q13 [34] encompassing the β chain gene was linked to various allergic disorders and high levels of serum IgE [35-37]. Polymorphisms in FcεRIβ have been linked to atopy, asthma, and allergies. This meta-analysis comprehensively discussed the association between the FcεRIβ polymorphisms and allergic diseases risk.

Materials and methods
Strategy for literature search
The electronic databases of PubMed, Embase, Web of science, Chinese National Knowledge Infrastructure (CNKI), and WanFang database were comprehensively searched to retrieve relevant articles published between January 2000 and August 2017. Databases were searched using the search term: “bronchial asthma, asthma, allergic rhinitis, nasal allergy, allergic diseases,” “Fc epsilon RI beta, FcεRIβ, high-affinity IgE receptor beta chain, beta-subunit of the high-affinity receptor for IgE,” “single nucleotide polymorphism, SNP, polymorphism, polymorphisms” as well as their combinations were employed as the searching keywords. The corresponding Chinese version was used in the Chinese databases. To obtain more data, we manually searched the references of related articles. Our analysis only focused on the studies that were written in English and Chinese. When the same authors or laboratories reported this issue on the same population, only the latest published full-text article was included.

Inclusion and exclusion criteria
The following criteria were set to choose the studies included in the current meta-analysis: (1) case–control design; (2) the study must offer the sample size, distribution of alleles, genotypes, or other information that can help us infer the results; and (3) the publication on the association between polymorphisms of FcεRIβ and risk of asthma and/or allergic rhinitis. The exclusion criteria were as follows: (1) review articles, case reports, and meta-analysis; (2) the studies were conducted on animals; (3) genotype distribution data were unavailable; and (4) when multiple publications reported on the same or overlapping data, we used the most recent or largest population.

Data extraction
Data were carefully extracted independently by two authors (Huan-huan Guo and Ping Luo) according to the inclusion and exclusion criteria. Disagreements were resolved through discussion and arbitration by a third author if
Quality assessment

The quality of studies was independently assessed by the two reviewers using the Newcastle–Ottawa scale (NOS) [38] based on three aspects: selection, comparability, and exposure of cases and controls. NOS scores ranged from 0 to 9, and articles with a score equal to or higher than six were regarded as high quality.

Statistical analysis

Hardy–Weinberg equilibrium (HWE) for the genotype distribution of FcεRIβ in controls was tested by χ² analysis with exact probability. The pooled odd ratio (OR) with 95% confidence interval (CI) was used to assess the strength of the associations between the genetic variants and allergic diseases risk. For the FcεRIβ polymorphism, “A” stands for wild-type gene, and “B” for mutant gene, the allelic (B vs. A), heterozygous (AB vs. AA), dominant (AB+BB vs. AA), and recessive (BB vs. AA+AB) genetic models were used to obtain pooled ORs. The evaluated genetic models for each study were based mostly on those used in primary studies. Heterogeneity assumption was evaluated by a X² based Q test and I² test [39]. A significant Q test (P<0.10) indicated heterogeneity across studies. I² was used to measure the percentage of variability in point estimated that due to heterogeneity rather than sampling error. When there was no statistical heterogeneity, we used a fixed effects model (the Mantel–Haenszel method) [40], otherwise, a random effects model (DerSimonian and Laird method) was used [41]. The subgroup analysis was performed according to ethnicity, allergic status, and HWE status of controls. Begg rank correlation method and the Egger linear regression method were used to assess potential publication bias [42,43]. The meta-analysis was necessary. For each study, the following data were recorded: first author, year of publication, country, age, allergic status, number of cases and controls, and genotype distributions in cases and controls.
Figure 4. ORs and 95% CIs for the associations between E237G polymorphism and allergic diseases risk in allelic genetic model by allergic status

performed using STATA Version 12.0 (Stata Corp, College Station, TX, U.S.A.) software. P value less than 0.05 was considered statistically significant. All P values presented are two-tailed.

Results
Main characteristics of the selected studies
Figure 1 outlined the study process of selection. Briefly, we first identified 234 articles. After applying the inclusion and exclusion criteria, a total of 29 articles including 6496 allergic diseases patients and 5828 controls were screened out. Of the 29 articles, 9 were written in Chinese [22,44-51] and 20 in English [13-21,52-62]. Among them, 22 were conducted in Asian populations and 7 in Caucasian populations. The FccRIβ polymorphism was measured by seven different methods (ARMS-PCR, PCR-SSCP, PCR-RFLP, SNP-IT™, ABI, MALDI-TOF, and TaqMan). Within the genotype distribution in the controls, the value of HWE was either extracted in the articles directly or calculated using the data of controls. Only three studies deviated from HWE [52,60,49]. Table 1 listed the main characteristics of included studies. Table 2 exhibited the distribution information of alleles and genotypes of FccRIβ polymorphism.

Association of E237G and -109C/T polymorphisms in asthma and/or allergic rhinitis risk
Twenty-five case–control studies involving the E237G polymorphism with 10,084 individuals (5081 cases and 5003 controls) were included in this meta-analysis. The overall results suggested that the allelic model of E237G polymorphism had an increased the risk of the allergic diseases (B vs. A: OR = 1.28, 95% CI = 1.06–1.53, P<0.001, I² = 63.1%, Figure 2). No significant association was revealed in the pooled results under other genetic model statistically. For subgroup analysis based on the ethnicity, significantly increased risk were observed in Asian population for allelic model (B vs. A: OR = 1.23, 95% CI = 1.05–1.45, P=0.004, I² = 53.6%, Figure 3) and recessive genetic model (BB
Table 1 Main characteristics of included studies in this meta-analysis

| First author     | Year  | Country          | Ethnicity         | Allergic status | Sample size | Genotype distribution | Genotyping methods | P for HWE | Quality score |
|------------------|-------|------------------|-------------------|-----------------|-------------|-----------------------|-------------------|----------|--------------|
|                   |       |                  |                   |                 |             | Case/Control          |                   |          |              |
|                   |       |                  |                   |                 |             | Case                  | Control           |          |              |
|                   |       |                  |                   |                 |             | Wild                  | Heterozygous      | Homozygous | Alleles      | Wild         | Heterozygous | Homozygous | Alleles      |          |          |
|                   |       |                  |                   |                 |             | EE                    | EG                | GG         | E            | G            | EE           | EG         | GG         | E            | G            |          |
| Laprise, C. [14]  | 2000  | France and Canada| Caucasian         | Asthma          | 100/100     | 80 19 1 179 21       | 98 2 0 198 2      | ARMS-PCR | 0.92         | 7            |
| Soriano, J.B. [52]| 2000  | Spain             | Caucasian         | Asthma          | 146/50      | 134 11 1 280 12      | 43 4 3 90 7       | ARMS-PCR | <0.05        | 6            |
| Takabayashi, A. [20]| 2000| Japan            | Asian             | Asthma          | 100/100     | 69 27 4 166 34       | 65 33 2 162 38    | PCR-SSCP | 0.35         | 7            |
| Chen, H. [44]     | 2000  | China             | Asian             | Asthma          | 101/60      | 59 39 3 157 45       | 30 16 1 76 18     | PCR-RFLP | 0.50         | 8            |
| Nagata, H. [15]   | 2001  | Japan             | Asian             | Allergic rhinitis| 233/100    | 155 76 7 373 93      | 77 18 5 172 28    | PCR-RFLP | 0.01         | 6            |
| Zeng, L.X. [45]   | 2001  | China             | Asian             | Asthma          | 69/28       | 61 5 3 127 11       | 27 1 0 55 1       | ARMS-PCR | 0.92         | 8            |
| Cui, T.P. [17]    | 2003  | China             | Asian             | Asthma          | 216/198     | 125 11 165 51       | 148 46 4 171 27   | PCR-RFLP | 0.85         | 8            |
| Tang, Y. [46]     | 2003  | China             | Asian             | Asthma          | 60/65       | 49 11 0 109 11      | 61 4 0 126 4     | ARMS-PCR | 0.80         | 7            |
| Korzycka-Zaborowska, B. [21] | 2004 | Poland            | Caucasian         | Asthma          | 98/87       | 92 6 0 190 6       | 83 4 0 170 4     | ARMS-PCR | 0.83         | 8            |
| Rigoli, L. [18]   | 2004  | Italy             | Caucasian         | Asthma          | 100/103     | 79 16 5 178 22      | 102 1 0 205 1     | PCR-SSCP | 0.96         | 7            |
| Zhang, X.Z. [53]  | 2004  | China             | Asian             | Asthma          | 141/157     | 81 57 3 219 63      | 108 42 7 258 56   | ARMS-PCR | 0.27         | 8            |
| Zhang, X.Z. [53]  | 2004  | Malaysia          | Asian             | Asthma          | 69/100      | 49 19 0 117 19      | 77 23 0 177 23   | ARMS-PCR | 0.19         | 8            |
| Zhang, X.Z. [53]  | 2004  | India             | Asian             | Asthma          | 82/98       | 71 10 1 152 12      | 80 18 0 178 18   | ARMS-PCR | 0.32         | 8            |
| Cui, T.P. [47]    | 2004  | China             | Asian             | Asthma          | 106/106     | 60 40 6 160 52      | 78 26 2 182 30   | PCR-RFLP | 0.92         | 8            |
| Zhao, K.S. [40]   | 2004  | China             | Asian             | Asthma          | 151/105     | 126 23 2 275 27     | 92 13 0 197 13   | ARMS-PCR | 0.50         | 6            |
| Liu, T. [22]      | 2006  | China             | Asian             | Asthma          | 60/50       | 45 14 1 48 11       | 39 10 1 88 12    | PCR-RFLP | 0.71         | 8            |
| Kim, E.S. [55]    | 2009  | Korea             | Asian             | Asthma          | 347/127     | 224 9 4 582 112    | 99 28 0 224 30   | SNP-IT TM | 0.16        | 7            |
| Wang, J.Y. [19]   | 2009  | China             | Asian             | Asthma          | 449/512     | 309 121 16 739 153  | 314 165 27 793 219 | ABI      | 0.39        | 7            |
| Dmitrieva-Zdorova, E.V. [59] | 2012 | Russia            | Caucasian         | Asthma          | 224/172     | 221 3 0 441 7       | 170 2 0 342 2     | MALDI-TOF | 0.94        | 7            |
| Zheng, B.Q. [51]  | 2012  | China             | Asian             | Asthma          | 198/110     | 126 61 11 313 83    | 76 29 5 181 39    | PCR-RFLP | 0.31         | 7            |
| Ramphuli, K. [60] | 2014  | India             | Asian             | Asthma          | 192/188     | 170 21 1 361 23     | 163 24 1 350 26   | TaqMan    | 0.91         | 8            |
| Ramphuli, K. [60] | 2014  | China             | Asian             | Asthma          | 192/192     | 139 45 8 327 57     | 136 38 18 323 61  | PCR-RFLP | <0.05        | 7            |
| Amo, G. [61]      | 2016  | Spain             | Caucasian         | Allergic rhinitis| 149/526     | 146 3 0 295 3       | 144 277 105 1013 39 | TaqMan    | 0.18        | 7            |

Continued over
Table 1 Main characteristics of included studies in this meta-analysis (Continued)

| First author       | Year | Country | Ethnicity          | Allergic status | Sample size | Genotype distribution | Genotyping methods | P for HWE | Quality score |
|--------------------|------|---------|--------------------|-----------------|-------------|-----------------------|-------------------|-----------|---------------|
|                    |      |         |                    |                 |             | Case/Control | Case |
|                    |      |         |                    |                 |             | Genotype | Alleles | Control |
|                    |      |         |                    |                 |             | Alleles | Alleles | Alleles |
|                   |      |         |                    |                 |             | Wild | Heterozygous | Homozygous | Alleles | Wild | Heterozygous | Homozygous | Alleles | Alleles | Alleles |
| E237G              |      |         |                    |                 |             |        |        |        |        |        |        |        |
| Amo, G. [61]       | 2016 | Spain   | Caucasian          | Asthma and allergic rhinitis | 366/526 | 330 | 33 | 0 | 695 | 37 | 144 | 277 | 105 | 1013 | 39 | TaqMan | 0.18 | 7 |
| Hua, L. [62]       | 2016 | China   | Asian              | Asthma          | 1000/1000 | 65 | 276 | 659 | 1594 | 406 | 23 | 289 | 688 | 1605 | 335 | TaqMan | 0.25 | 7 |
|                    |      |         |                    |                 |             |        |        |        |        |        |        |        |        |        |        |        |        |        |        |
|                    |      |         |                    |                 |             |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |
| -109C/T            |      |         |                    |                 |             |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |        |
| Hizawa, N. [13]    | 2000 | Japan   | Asian              | Asthma          | 226/226 | 85 | 123 | 18 | 277 | 175 | 108 | 99 | 19 | 312 | 140 | PCR-RFLP | 0.58 | 8 |
| Cui, T.P. [17]     | 2004 | China   | Asian              | Asthma          | 106/106 | 44 | 52 | 10 | 140 | 72 | 41 | 57 | 8 | 139 | 73 | PCR-RFLP | 0.05 | 7 |
| Gan, X. [49]       | 2004 | China   | Asian              | Asthma          | 45/45 | 23 | 12 | 10 | 58 | 32 | 19 | 14 | 12 | 53 | 38 | PCR-RFLP | 0.02 | 7 |
| Zhao, K.S. [50]    | 2004 | China   | Asian              | Asthma          | 120/87 | 46 | 69 | 11 | 161 | 91 | 40 | 38 | 9 | 118 | 56 | PCR-RFLP | 0.995 | 8 |
| Hizawa, N. [54]    | 2006 | Japan   | Asian              | Asthma          | 374/374 | 157 | 178 | 39 | 485 | 203 | 156 | 169 | 49 | 483 | 265 | TaqMan | 0.76 | 8 |
| Kim, E.S. [55]     | 2016 | Korea   | Asian              | Asthma          | 347/127 | 159 | 167 | 20 | 470 | 224 | 69 | 54 | 3 | 187 | 67 | SNP-IT | 0.04 | 6 |
| Li, H. [56]        | 2009 | China   | Asian              | Asthma          | 192/192 | 110 | 58 | 24 | 291 | 93 | 78 | 90 | 24 | 245 | 139 | PCR-RFLP | 0.04 | 7 |
| Sharma, S. [57]    | 2009 | India   | Asian              | Asthma          | 237/221 | 37 | 113 | 87 | 189 | 286 | 74 | 108 | 39 | 256 | 187 | TaqMan | 0.97 | 8 |
| Tikhonova, V. [58] | 2010 | Russia  | Caucasian          | Asthma          | 140/136 | 53 | 69 | 18 | 175 | 105 | 48 | 70 | 18 | 167 | 105 | PCR-RFLP | 0.34 | 7 |
| Ramphul, K. [60]   | 2014 | India   | Asian              | Asthma          | 189/188 | 35 | 99 | 55 | 163 | 215 | 35 | 87 | 66 | 162 | 214 | TaqMan | 0.51 | 8 |
| Amo, G. [61]       | 2016 | Spain   | Caucasian          | Asthma and allergic rhinitis | 149/526 | 47 | 67 | 35 | 161 | 137 | 144 | 277 | 105 | 565 | 487 | TaqMan | 0.18 | 7 |
| Amo, G. [61]       | 2016 | Spain   | Caucasian          | Asthma and allergic rhinitis | 366/526 | 100 | 188 | 78 | 388 | 344 | 144 | 277 | 105 | 565 | 487 | TaqMan | 0.18 | 7 |

Abbreviations: ARMS-PCR, primer amplification refractory mutation system polymerase chain reaction; HWE, Hardy–Weinberg equilibrium; MALDI-TOF, matrix-assisted laser desorption/ionization-time of flight mass spectrometry; NA, not available or applicable; PCR-RFLP, polymerase chain reaction-restriction fragment length polymorphism; PCR-SSCP, polymerase chain reaction-single strand conformation polymorphism; SNP, single nucleotide polymorphism.

Bold text indicates five different polymorphisms of FcεRIβ.
Table 2 Summary ORs and 95% CIs of FcεRIβ polymorphisms and allergic diseases risk

| Variables                     | $N$ | B vs. A | AB + BB vs. AA | BB vs. AA + AB | AB vs. AA |
|-------------------------------|-----|---------|----------------|----------------|----------|
| E237G                         |     | OR (95% CI) | $P$ | $P^2$ (%) | OR (95% CI) | $P$ | $P^2$ (%) | OR (95% CI) | $P$ | $P^2$ (%) |
| Overall                       | 25  | 1.28 (1.06, 1.53) | <0.001 | 63.1 | 1.00 (0.60, 1.67) | <0.001 | 94.1 | 1.62 (0.85, 3.11) | <0.001 | 80.2 |
| Ethnicity                     |     |          |     |       |          |     |       |          |     |       |
| Caucasian                     | 7   | 1.80 (0.72, 4.53) | <0.001 | 79 | 0.64 (0.08, 4.99) | <0.001 | 96 | 0.40 (0.02, 6.79) | <0.001 | 81 |
| Asian                         | 18  | **1.23 (1.05, 1.45)** | 0.004 | 53.6 | 1.19 (0.92, 1.54) | <0.001 | 73.2 | **2.10 (1.22, 3.62)** | <0.001 | 68.8 |
| Allergic status               |     |          |     |       |          |     |       |          |     |       |
| Asthma                        | 20  | 1.25 (1.04, 1.51) | <0.001 | 63 | 1.19 (0.91, 1.57) | <0.001 | 73.7 | **2.09 (1.19, 3.56)** | <0.001 | 67.7 |
| Allergic rhinitis             | 2   | 0.69 (0.12, 3.97) | 0.006 | 86.9 | 0.12 (0.00, 55.88) | <0.001 | 98.9 | 0.21 (0.00, 18.15) | 0.003 | 88.6 |
| Allergic rhinitis and/or Asthma | 3  | 2.74 (0.65, 11.43) | 0.012 | 77.3 | 1.02 (0.02, 60.58) | <0.001 | 97.3 | 0.55 (0.00, 1117.47) | <0.001 | 93.1 |
| HWE ≥0.05                     | 22  | 1.33 (1.08, 1.63) | <0.001 | 65 | 1.01 (0.56, 1.81) | <0.001 | 94.7 | 1.99 (0.98, 4.08) | <0.001 | 78.2 |
| <0.05                         | 3   | 1.03 (0.64, 1.66) | 0.103 | 56 | 1.06 (0.58, 1.92) | 0.06 | 64.5 | 0.77 (0.40, 1.48) | 0.477 | 0 |
| -109C/T                       |     |          |     |       |          |     |       |          |     |       |
| Overall                       | 15  | 1.10 (0.95, 1.28) | <0.001 | 76 | 1.08 (0.88, 1.30) | 0.06 | 73.8 | **1.58 (1.26, 1.98)** | <0.001 | 66.4 |
| Ethnicity                     | 3   | 1.00 (0.87, 1.15) | 0.922 | 0 | 0.92 (0.75, 1.15) | 0.716 | 0 | **1.50 (1.18, 1.92)** | 0.866 | 0 |
| Caucasian                     | 12  | 1.13 (0.93, 1.36) | <0.001 | 81 | 1.13 (0.88, 1.47) | <0.001 | 78.4 | **1.60 (1.19, 2.14)** | <0.001 | 71.6 |
| Allergic status               |     |          |     |       |          |     |       |          |     |       |
| Asthma                        | 13  | 1.11 (0.93, 1.33) | <0.001 | 79 | 1.11 (0.87, 1.42) | <0.001 | 76.8 | **1.58 (1.20, 2.08)** | <0.001 | 69.6 |
| Allergic rhinitis             | 1   | 0.99 (0.76, 1.28) | – | – | 0.82 (0.55, 1.21) | – | – | **1.65 (1.07, 2.55)** | – | – |
| Allergic rhinitis and/or Asthma | 1  | 1.03 (0.85, 1.24) | – | – | 1.00 (0.74, 1.35) | – | – | **1.46 (1.05, 2.02)** | – | – |
| HWE ≥0.05                     | 12  | 1.06 (0.91, 1.24) | <0.001 | 76 | 1.02 (0.82, 1.27) | <0.001 | 72.7 | **1.54 (1.19, 1.99)** | <0.001 | 72.2 |
| <0.05                         | 3   | 1.30 (0.87, 1.94) | 0.042 | 68.5 | 1.40 (0.88, 2.23) | 0.084 | 59.7 | **1.80 (1.10, 2.92)** | 0.049 | 5.1 |
| RsaI_in2                      |     |          |     |       |          |     |       |          |     |       |
| Overall                       | 3   | 1.14 (0.45, 2.88) | 0.005 | 81.3 | 1.01 (0.21, 4.78) | 0.049 | 66.7 | 0.84 (0.33, 2.17) | 0.045 | 75 |
| RsaI_ex7                      |     |          |     |       |          |     |       |          |     |       |
| Overall                       | 2   | 0.91 (0.41, 2.04) | 0.659 | 0 | 0.90 (0.40, 2.07) | 0.651 | 0 | – | – | – |
| I181L                         |     |          |     |       |          |     |       |          |     |       |
| Overall                       | 2   | 2.00 (1.35, 2.97) | – | – | **4.19 (2.35, 7.47)** | – | – | **3.11 (1.03, 7.84)** | – | – |

Bold values indicate statistically significant results.
Association of Rsal_in2, Rsal_ex7, and I181L polymorphisms in asthma and/or allergic rhinitis risk

For these three polymorphisms, three studies that focused on the association of Rsal_in2 polymorphisms and allergic diseases risk involving 274 cases and 217 controls, two studies that focused on the association between Rsal_ex7 polymorphisms and allergic diseases risk involving 177 cases and 130 controls, and two studies that focused on the association of I181L polymorphisms and allergic diseases risk involving 290 cases and 150 controls were pooled into the meta-analysis. No significant association was found for Rsal_in2 and Rsal_ex7 polymorphisms in all genetic models. For I181L polymorphism, significant association with increased allergic diseases risk was also observed in B vs. A (OR = 2.00, 95%CI = 1.35-2.97), AB+BB vs. AA (OR = 4.19, 95%CI = 2.35-7.47) and AB vs. AA (OR = 4.15, 95%CI = 2.33-7.41) genetic models.

Sensitivity analysis and publication bias

We omitted each particular study to verify whether our results were influenced by each individual study or not. The pooled ORs were not materially altered, indicating the robustness and stable of the results in this meta-analysis (Figure 6). The Begg’s funnel plot and Egger’s test were used to evaluate the publication bias (Table 4). All the plots were found to be roughly symmetrical, indicating no publication bias presented as shown in Figure 7.

Discussion

In the last decade, analysis of SNPs has become the newest approach for detection and localization of the genetic determinants of asthma [63-66]. Genetic factors are important in defining total serum IgE levels. Linkage analyses have localized a gene or genes that influence atopic phenotype at chromosome 11q13 [34-36]. In this meta-analysis, we discussed five polymorphisms in FcεRIβ (E237G, -109 C/T, Rsal_in2, Rsal_ex7, and I181L) which were considered to have certain correlation to allergic diseases by pooled results from 29 eligible case-control studies. Only two extensively investigated SNPs (E237G and -109 C/T) were involving large sample of studies included this meta-analysis. Other SNPs (Rsal_in2, Rsal_ex7, and I181L) had limited number of studies, especially for V183L, we failed to collect enough studies and data to comprehensively analyze the risk for allergic diseases.

The results demonstrated that FcεRIβ E237G polymorphism in allelic model acts as significant increased risk for asthma, especially in Asians, which is consistent with previous results [66,67]. The stratification on allergic status and ethnicity did reveal a statistically significant association for E237G and the risk of allergic diseases. With respect to FcεRIβ -109 C/T polymorphism, a significantly association was observed in recessive genetic model, it has been demonstrated that -109 C/T polymorphism may play an important role in pathophysologic mechanisms and the subgroup analysis by allergic status and ethnicity also showed the increased risk for allergic diseases, which validated the previous speculation [67]. For I181L polymorphism, significant association with increased allergic diseases risk was also observed in three genetic models, given the limited number of studies, more data are required to validate these associations.
Table 3 Clinical characteristics of E237G and -109 C/T polymorphisms

| Study                | Sex (F/M) | Age (years) | Positive RAST (≥0.35 UA/ml) | Total IgE | Case Control | Case Control |
|----------------------|-----------|-------------|-----------------------------|-----------|--------------|--------------|
|                      | Case      | Control     | Case                        | Control   | Case          | Control      |
| E237G                | 41/59     | NA          | 27 ± 2 (18–35)              | NA        | –            | –            |
| Laprise, C. [14]     | 92/54     | NA          | 58 ± 16 (23–90)             | NA        | –            | –            |
| Soriano, J.B. [52]   | 92/54     | NA          | 27 ± 2 (18–35)              | NA        | –            | –            |
| Takabayashi, A. [20] | 92/54     | NA          | 27 ± 2 (18–35)              | NA        | –            | –            |
| Nagata, H. [15]      | 92/54     | NA          | 27 ± 2 (18–35)              | NA        | –            | –            |
| Zeng, L.X. [45]      | 101/115   | 93/105      | 27 ± 2 (18–35)              | NA        | –            | –            |
| Cui, T.P. [17]       | 92/54     | NA          | 27 ± 2 (18–35)              | NA        | –            | –            |
| Tang, Y. [46]        | 92/54     | NA          | 27 ± 2 (18–35)              | NA        | –            | –            |
| Zhang, X.Z., China   | 58/42     | 50/53       | Children 5–13               | Children 6–14 | –            | –            |
|                      | 77/64     | 53/104      | 52 ± 16 (23–90)             | 32 ± 9    | 70 ± 12 (23–90) | NA (IU/ml) |
| Zhang, X.Z., Malaysia| 43/25     | 45/55       | 45 ± 14 (23–90)             | 34 ± 9    | 63 ± 9 (23–90) | NA (IU/ml) |
| Zhang, X.Z., India   | 50/32     | 39/59       | 50 ± 17 (23–90)             | 34 ± 10   | 63 ± 9 (23–90) | NA (IU/ml) |
| Cui, T.P. [47]       | 47/59     | 48/54       | 40.37 ± 15.09 (18–69)       | 37.12 ± 12.63 (20–60) | –            | –            |
| Zhao, K.S. [49]      | 60/91     | 42/63       | 1.5–14                      | 2–14      | EE 91 ± 0.35 (23–90) | NA (IU/ml) |
| Liu, T. [22]         | 36.5      | 38.5        | EE 91 ± 0.35 (23–90)        | EE 91 ± 0.35 (23–90) | –            | –            |
| Kim, E.S. [55]       | 107/240   | NA          | 11.11 ± 4.05                | NA        | –            | –            |
| Li, H. [56]          | 96/96     | 96/96       | 3–12                        | 18–22     | –            | –            |
| Wang, J.Y. [19]      | 148/301   | 266/246     | 7.82 ± 3.81                 | 8.37 ± 2.45 | –            | –            |

Continued over
Table 3 Clinical characteristics of E237G and -109 C/T polymorphisms (Continued)

| Study               | Sex (F/M)     | Age (years)                  | Positive RAST (≥ 0.35 UA/ml) | Total IgE | Case Control | Case Control |
|---------------------|---------------|------------------------------|------------------------------|-----------|--------------|--------------|
| Dmitrieva-Zdorova, E.V. [59] | 119/105       | Mid 32.7 ± 10.5, Moderate/severe 38.3 ± 12.6 | 36.9 ± 10.1 | – – | IgE level (IU/ml) Mild 210 (53–535) Moderate/severe 252 (128–648) | 45 (23–89) |
| Zheng, B.Q. [51]    | 94/104        | 3.5                          | 3.8                          | – – | – – | – – |
| Ramphul, K. [60]    | – –           | 3–12                         | 18–22                        | – – | – – | – – |
| Amo, G. [61]        | 294/221       | 32.2 ± 15.1 (14–79)          | 28.4 ± 12.1 (18–84)          | – – | IgE level (IU/ml) 254.1 ± 401.5 (0–4800) | NA |
| Hua, L. [62]        | 497/503       | 4.90 (3–12)                  | 23.32 (18–25)                | 807     | NA           | – – |
| Hizawa, N. [13]     | 119/107       | TT 45.8 ± 16.5               | EE 68                        | TT 2.63 ± 0.56 | TT 2.649 ± 0.9241 | TT 1.73 ± 0.57 |
| Cui, T.P. [17]      | 47/59         | 40.37 ± 15.09 (18–69)        | EE 30                        | EE 2.37 ± 0.56 | CC 2.44 ± 0.56 | CC 1.75 ± 0.57 |
| Cui, T.P. [47]      | 101/115       | 19.6 ± 21.9 (3–65)           | CC 2.5 ± 0.8660              | 1.23 ± 0.66 | 1.3 ± 0.47 | 2.32 ± 0.33 |
| Gan, X. [48]        | 24/21         | 6–65                         | – –                          | 2.26 ± 0.56 | 2.32 ± 0.83 | 2.32 ± 0.83 |
| Zhao, K.S. [50]     | 50/76         | 35/52                        | – –                          | 2.26 ± 0.56 | 2.32 ± 0.56 | 2.32 ± 0.56 |
| Hizawa, N. [54]     | 209/165       | 128/246                      | 45 (16–81)                   | 269     | 210          | 2.4 ± 0.64 |
| Kim, E.S. [55]      | 107/240       | NA                           | 2.4 ± 0.86                   | 5.17 ± 1.76 | 1.86 ± 0.64 | NA |
| Li, H. [56]         | 96/96         | 96/96                        | 269                          | 210     | 2.4 ± 0.64 | 1.86 ± 0.64 |
| Sharma, S. [57]     | 123/114       | 117/104                      | 34.4 ± 12.5                  | 35.0 ± 10.6 | 2.85 ± 0.47 | 2.32 ± 0.33 |
| Tikhonova, V. [58]  | 26/114        | 65/71                        | 3–17                         | 4–17    | – – | – – |
| Ramphul, K. [60]    | – –           | 3–12                         | 18–22                        | – – | – – | – – |
| Amo, G. [61]        | 294/221       | 265/261                      | 32.2 ± 15.1 (14–79)          | – – | IgE level (IU/ml) 254.1 ± 401.5 (0–4800) | NA |
| Hua, L. [62]        | 497/503       | 497/503                      | 4.90 (3–12)                  | 23.32 (18–25) | 807 | NA |

Abbreviations: NA, not available; RAST, allergy skin prick test result.
Figure 5. ORs and 95% CIs for the associations between E237G polymorphism and allergic diseases risk in allelic genetic model by HWE.

Figure 6. Sensitivity analysis through the deletion of each study to reflect the individual influence on the calculated ORs in allelic genetic model of E237G polymorphism.
Table 4 Evaluation of the publication bias of E237G and -109 C/T polymorphisms of the included studies

| Genotype | B vs. A | AB + BB vs. AA | BB vs. AA + AB | BB vs. AA | AB vs. AA |
|----------|---------|---------------|----------------|-----------|-----------|
| E237G    |         |               |                |           |           |
| P(Begg's)| 0.168   | 0.797         | 0.085          | 0.487     | 0.907     |
| P(Egger) | 0.102   | 0.358         | 0.012          | 0.307     | 0.333     |
| -109 C/T |         |               |                |           |           |
| P(Begg's)| 0.656   | 0.656         | 0.921          | 0.235     | 0.882     |
| P(Egger) | 0.894   | 0.555         | 0.128          | 0.411     | 0.589     |

Figure 7. Funnel plot analysis to detect publication bias for allelic genetic model of E237G polymorphism

The weight of studies is presented by the size of circles.

Heterogeneity is one of the most important problems when performing the meta-analysis. The results should be interpreted with caution when heterogeneity exists. There was high heterogeneity in this meta-analysis. Considering that differences in allergic status, ethnicity and WHE may affect the results, we conducted subgroup analysis by allergic status, ethnicities and WHE, the heterogeneity was decreased or removed after subgroup analysis; however, there still existed or increased in some groups, perhaps, the source of heterogeneity may be from different ages or other clinical characteristics such as sex and environmental exposures, unfortunately, there were no enough data to extract to analyze.

Although this is not the first meta-analysis focused on the association between FcεRIβ polymorphisms and allergic diseases, there were some strengths of our study: first, most of the genotype distributions in controls were consistent with HWE. Second, the relationship was analyzed by using five kinds of genetic models, and the results were statistically significant. Third, the methodological issues for meta-analysis, such as Egger’s test, Begg’s funnel plots, and subgroup analysis were performed to ensure the stability of the results. On the other hand, the limitations could not be ignored: first, the interaction of gene–gene and gene–environment should be considered. Second, most of the included studies were conducted in Asian and Caucasian populations, although other ethnicities should be considered. Third, different genotyping methods were used in the respective studies, which might partly influence the result.

Conclusions

In conclusions, it is believed that subjects with FcεRIβ polymorphisms tend to develop allergic diseases, severity of symptoms caused by genetic variation could independently modify predisposition to allergic diseases. A greater understanding of the genetic basis of asthma and allergic rhinitis holds great promise for the identification of novel
therapeutic targets. Further multicentric investigations still need to confirm the relationship of these polymorphisms of FceRIβ and allergic diseases susceptibility.

**Author Contribution**

H.H.G. and X.H.Z. conceived and designed the study, H.H.G. and P.L. searched the databases and extracted the data, T.P. and H.B.L. analyzed the data. H.H.G., S.H., and S.L. wrote the draft of the paper. X.H.Z. and W.D.Z. reviewed and revised the manuscript. All the authors approved the final manuscript.

**Funding**

The authors declare that there are no sources of funding to be acknowledged.

**Competing Interests**

The authors declare that there are no competing interests associated with the manuscript.

**Abbreviations**

AR, allergic rhinitis; CI, confidence interval; HWE, hardy–weinberg equilibrium; NOS, newcastle–ottawa scale; OR, odd ratio; SNP, single nucleotide polymorphism.

**References**

1. Kakli, H.A. and Riley, T.D. (2016) Allergic rhinitis. *Prim. Care* **43**, 465–475, [https://doi.org/10.1016/j.pop.2016.04.009](https://doi.org/10.1016/j.pop.2016.04.009)
2. Accordini, S., Corsico, A., Cerveri, I., Gislason, D., Gusvik, A., Janson, C. et al. (2008) The socio-economic burden of asthma is substantial in Europe. *Allergy* **63**, 116–124, [https://doi.org/10.1111/j.1398-9995.2007.01523.x](https://doi.org/10.1111/j.1398-9995.2007.01523.x)
3. Tattersfield, A.E., Knox, A.J., Britton, J.R. and Hall, I.P. (2002) Asthma. *Lancet* **360**, 1313–1322, [https://doi.org/10.1016/S0140-6736(02)11312-2](https://doi.org/10.1016/S0140-6736(02)11312-2)
4. Bochner, B.S. and Busse, W.W. (2000) Allergy and asthma. *J. Allergy Clin. Immunol.* **105**, 51–70, [https://doi.org/10.1053/jaci.2000.65706](https://doi.org/10.1053/jaci.2000.65706)
5. Kauffmann, F. and Demenais, F. (2012) Gene-environment interactions in asthma and allergic diseases: challenges and perspectives. *J. Allergy Clin. Immunol.* **130**, 1229–1240, quiz 1241–1222, [https://doi.org/10.1016/j.jaci.2012.10.038](https://doi.org/10.1016/j.jaci.2012.10.038)
6. Leung, T.F., Tang, N.L., Chan, I.H., Li, A.M., Ha, G., Lam, C.W. et al. (2002) Distribution in allele frequencies of predisposition-to-atopy genotypes in Chinese children. *Pediatr. Allerinol.** **34**, 419–424, [https://doi.org/10.1002/pupl.10210](https://doi.org/10.1002/pupl.10210)
7. Cui, T., Wang, L., Wu, J. and Xie, J. (2003) The association analysis of FcεRIβ with allergic asthma in a Chinese population. *Chin. Med. J.* **116**, 1875–1878
8. Rigoli, L., Di Bella, C., Procopio, V., Barberio, G., Barberi, I., Caminiti, L. et al. (2004) Molecular analysis of sequence variants in the Fc epsilon receptor I beta gene and 114 gene promoter in Italian families. *Allergy* **59**, 213–218, [https://doi.org/10.1111/j.1398-9995.2003.00385.x](https://doi.org/10.1111/j.1398-9995.2003.00385.x)
9. Wang, J.Y., Lou, Y.H., Wu, Y.J., Hsiao, Y.H. and Wu, L.S. (2009) An association study of 13 SNPs from seven candidate genes with pediatric asthma and a preliminary study for genetic testing by multiple variants in Taiwanese population. *J. Clin. Immunol.* **29**, 205–209, [https://doi.org/10.1007/s10875-008-9256-6](https://doi.org/10.1007/s10875-008-9256-6)
20 Takabayashi, A., Ihara, K., Sasaki, Y., Suzuki, Y., Nishima, S., Izhura, K. et al. (2000) Childhood atopic asthma: positive association with a polymorphism of IL-4 receptor alpha gene but not with that of IL-4 promoter or Fc epsilon receptor I beta gene. Exp. Clin. Immunogenet. 17, 63–70, https://doi.org/10.1159/000019125

21 Korzycka-Zaborowska, B., Hopkin, J.M. and Gorski, P. (2004) Genetic variants of Fc epsilonRIbeta and IL-4 and atopy in a Polish population. Allergol. Immunopathol. 32, 53–58

22 Liu, T., Teng, L., Guan, L.X., Wu, L.P. and Sun, K.Y. (2006) Study on the E237G polymorphism of the Fc:RI b chain with asthma. Chin. J. Pract. Intern. Med. 26, 1520–1522

23 Blank, U., Ra, C., Miller, L., White, K., Metzger, H. and Kinet, J.P. (1999) Complete structure and expression in transfected cells of high affinity IgE receptor. Nature 337, 187–189, https://doi.org/10.1038/337187a0

24 Dombrowicz, D., Lin, S., Flaman, V., Brini, A.T., Koller, B.H. and Kinet, J.P. (1998) Allergy-associated FcRbeta is a molecular amplifier of IgE- and IgG-mediated in vivo responses. Immunity 5, 517–529, https://doi.org/10.1016/S1074-7613(00)80056-7

25 Lin, S., Cicala, C., Scharenberg, A.M. and Kinet, J.P. (1996) The Fc(epsi)onRIbeta subunit functions as an amplifier of Fc(epsi)onRigamma-mediated cell activation signals. Cell 85, 985–995, https://doi.org/10.1016/S0092-8674(00)81300-8

26 Hiraoka, S., Furumoto, Y., Koseki, H., Takagaki, Y., Taniguchi, M., Okumura, K. et al. (1999) Fc receptor beta subunit is required for full activation of mast cells through Fc receptor engagement. Int. Immunol. 11, 199–207, https://doi.org/10.1093/intimm/11.2.199

27 Galli, S.J. and Tsai, M. (2010) Mast cells in allergy and infection: versatile effector and regulatory cells in innate and adaptive immunity. Eur. J. Immunol. 40, 1843–1851, https://doi.org/10.1002/eji.201040559

28 Kim, Y.K., Oh, S.Y., Oh, H.B., Chun, S.Y., Cho, S.H., Koh, Y.Y. et al. (2002) Coding single nucleotide polymorphism in the high-affinity immunoglobulin E receptor b chain (FcepsilonRI-beta) gene is associated with immunoglobulin E receptor-mediated histamine release from basophils. Clin. Exp. Allergy: J. Br. Soc. Allergy Clin. Immunol. 32, 751–755, https://doi.org/10.1046/j.1365-2222.2002.01295.x

29 Turner, H. and Kinet, J.P. (1999) Signalling through the high-affinity IgE receptor Fc epsilonRI. Nature 402, B24–B30, https://doi.org/10.1038/35037021

30 Holgate, S.T. (1999) Genetic and environmental interaction in allergy and asthma. J. Allergy Clin. Immunol. 104, 1139–1146, https://doi.org/10.1016/S0091-6736(99)70005-9

31 Barnes, K.C. (1999) Gene-environment and gene-gene interaction studies in the molecular genetic analysis of asthma and atopy. Clin. Exp. Allergy: J. Allergy Clin. Immunol. 105, S477–S481, https://doi.org/10.1046/j.1365-2321.1999.01046.x

32 Howard, T.D., Meyers, D.A. and Bleecker, E.R. (2000) Mapping susceptibility genes for asthma and allergy. J. Allergy Clin. Immunol. 105, 47–51

33 Kraft, S., Rana, S., Jouvin, M.H. and Kinet, J.P. (2004) The role of the Fc epsilonRI beta-chain in allergic diseases. Int. Arch. Allergy Immunol. 135, 60–67, https://doi.org/10.1159/000080231

34 Simon Thomas, N., Wilkinson, J., Lonjou, C., Morton, N.E. and Holgate, S.T. (2000) Linkage analysis of markers on chromosome 11q13 with asthma and atopy in a United Kingdom population. Am. J. Respir. Crit. Care Med. 162, 1268–1272, https://doi.org/10.1164/ajrccm.162.4.9909078

35 Cookson, W.O., Sharp, P.A., Faux, J.A. and Hopkin, J.M. (1989) Linkage between immunoglobulin E responses underlying asthma and rhinitis and chromosome 11q. Lancet 1, 1292–1295, https://doi.org/10.1016/S0140-6736(89)92667-1

36 Sandford, A.J., Shirakawa, T., Moffatt, M.F., Daniels, S.E., Ra, C., Faux, J.A. et al. (1993) Localisation of atopy and beta subunit of high-affinity IgE receptor (Fc epsilonRI) on chromosome 11q. Lancet 341, 332–334, https://doi.org/10.1016/0140-6736(93)90136-5

37 Collee, J.M., ten Kate, L.P., de Vries, H.O., Klijn, J.W., Bouman, K., Scheffer, H. et al. (1993) Allele sharing on chromosome 11q13 in sibs with asthma and atopy. Lancet 342, 936, https://doi.org/10.1016/0140-6736(93)91988-X

38 Stang, A. (2010) Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur. J. Epidemiol. 25, 603–605, https://doi.org/10.1007/s10654-010-9491-z

39 Higgins, J.P. and Thompson, S.G. (2002) Quantifying heterogeneity in a meta-analysis. Stat. Med. 21, 1539–1558, https://doi.org/10.1002/sim.1186

40 Mantel, N. and Haenszel, W. (1959) Statistical aspects of the analysis of data from retrospective studies of disease. J. Natl. Cancer Inst 22, 719–748

41 Higgins, J.P., Thompson, S.G. and Spiegelhalter, D.J. (2009) A re-evaluation of random-effects meta-analysis. J. R. Stat. Soc. Series A 172, 137–159, https://doi.org/10.1111/j.1467-985X.2008.00552.x

42 Begg, C.B. and Mazumdar, M. (1994) Operating characteristics of a rank correlation test for publication bias. Biometrics 50, 1088–1101, https://doi.org/10.2307/2533446

43 Song, F. and Gilbody, S. (1998) Bias in meta-analysis detected by a simple, graphical test. Increase in studies of publication bias coincided with increasing use of meta-analysis. BMJ 316, 471

44 Chen, H., Chen, Y.Z., Hu, L.P., Fu, J., Zhang, H.O. and Ma, Y. (2000) Study on the Fcc RI-β polymorphism and susceptibility of asthma in a Chinese population. Natl. Med. J. China. 80, 664–667

45 Zeng, L.X., Zhou, S.L., Kuang, J.L. and Rao, W.H. (2001) Study of Mutation of B Chain Gene E237GA High Affinity Receptor of IgE in Asthmatics. Acta Academiae Medicinae Jiangxi 41, 43–45

46 Tang, Y., Wu, X.Q., Liu, X.Y., Zeng, Y., Li, Y.Q., Wu, Q. et al. (2003) Study on mutations of β-chain of high affinity IgE receptor gene in people of Han nationality in the south of China. Chin. J. Mod. Med. 13, 6–10

47 Cui, T.P., Jiang, W.C., Wang, L., Xie, J.G. and Wu, J.M. (2004) Association analysis of FcRRIγ gene with allergic asthma in Chinese. Chin. J. Pathophys. 20, 2049–2052

48 Gan, X., Kuang, J.L., Zou, Y.Q. and Rao, W.H. (2004) Study on the relationship between IgE high affinity receptor β-chain gene polymorphism and serum total IgE in patients with bronchial asthma. Chin. J. Tuberc. Respir. Dis. 27, 704–705

49 Zhao, K.S., Cheng, H.J., Qiao, H.M., Zhao, F.X., Sun, M.Y. and Fu, W.Y. (2004) Analysis of gene mutation for high affinity immunoglobulin E receptor chain in asthmatic children. J. Clin. Pediatr. 22, 794–797

© 2018 The Author(s). This is an open access article published by Portland Press Limited on behalf of the Biochemical Society and distributed under the Creative Commons Attribution License 4.0 (CC BY).
50 Zhao, K.S., Lu, J.R., Wang, Z.H., Guo, Y., Yu, L.Y. and Fu, W.Y. (2004) Association between FcεRI-β gene promoter polymorphism and total serum IgE levels of asthma in children. Chin. J. Prac. Pediatr. 19, 744–746
51 Zheng, B.Q., Wang, G.L., Yang, S., Lu, Y.Q., Liu, R.J. and Li, Y. (2012) Study of genetic susceptibility in 196 children with asthma. Chin. J. Contemp. Pediatr. 14, 811–814
52 Soriano, J.B., De Cid R, Estivill X, Antó, J.M., Sunyer, J., Otero, D., Roca, J. et al. (2000) Association study of proposed candidate genes/regions in a population of Spanish asthmatics. Eur. J. Epidemiol. 16, 745–750, https://doi.org/10.1023/A:1026758319621
53 Zhang, X., Zhang, W., Oiu, D., Sandford, A. and Tan, W.C. (2004) The E237G polymorphism of the high-affinity IgE receptor beta chain and asthma. Annals Allergy Asthma Immunol.: Off. Publication Am. College Allergy. Asthma, & Immunol. 93, 499–503, https://doi.org/10.1016/S1081-1206(04)61419-6
54 Hizawa, N., Maeda, Y., Konno, S., Fukui, Y., Takahashi, D. and Nishimura, M. (2006) Genetic polymorphisms at FCER1B and PAI-1 and asthma susceptibility. Clin. Exp. Allergy: J. Br. Soc. Allergy Clin. Immunol. 36, 872–876, https://doi.org/10.1111/j.1365-2222.2006.02413.x
55 Kim, E.S., Kim, S.H., Kim, K.W., Park, H.S., Shin, E.S., Lee, J.E. et al. (2009) Involvement of FcεRI > R1 beta gene polymorphisms in susceptibility to atopy in Korean children with asthma. Eur. J. Pediatr. 168, 1483–1490, https://doi.org/10.1007/s00431-009-0960-x
56 Li, H., Xiaoyan, D., Quanhua, L., Jie, L. and Yixiao, B. (2009) Single-nucleotide polymorphisms in genes predisposing to asthma in children of Chinese Han nationality. J. Investig. Allergol. Clin. Immunol. 19, 391–395
57 Sharma, S. and Ghosh, B. (2009) Promoter polymorphism in the MS4A2 gene and asthma in the Indian population. Int. Arch. Allergy Immunol. 149, 208–218, https://doi.org/10.1159/000199716
58 Tikhonova, V., Volkovich, A., Korostovsev, D. and Larionova, V. (2010) The -109C>T Polymorphism of the FcεRI Gene in Children with Asthma. Pediatr. Res. 68, 413–413, https://doi.org/10.1203/010001001-000821
59 Dmitrieva-Zdorova, E.V., Voronko, O.E., Latysheva, E.A., Storozhakov, G.I. and Archakov, A.I. (2012) Analysis of polymorphisms in T(h)2-associated genes in Russian patients with atopic bronchial asthma. J. Investig. Allergol. Clin. Immunol. 22, 126–132
60 Ramphul, K., Lv, J., Hua, L., Liu, Q.H., Fang, D.Z., Ji, R.X. et al. (2016) Single nucleotide polymorphisms predisposing to asthma in children of Mauritain Indian and Chinese Han ethnicity. Brazilian J. Med. Biological Res. = Revista brasileira de pesquisas medicas e biologicas 47, 394–397
61 Amo, G., Garcia-Menaya, J., Campo, P., Cordobes, C., Seron, M.C.P., Ayuso, P. et al. (2016) A Nonsynonymous FCER1B SNP is associated with risk of developing allergic rhinitis and with IgE levels. Sci. Rep. 6, https://doi.org/10.1038/srep19724
62 Hua, L., Zuo, X.B., Bao, X.Y., Liu, O.H., Li, J.Y., Lv, J. et al. (2016) Four-locus gene interaction between IL13, IL4, FCER1B, and ADRB2 for asthma in Chinese Han children. Pediatr. Pulmonol. 51, 364–371, https://doi.org/10.1002/ppul.23322
63 Denham, S., Koppelman, G.H., Blakely, J., Wjst, M., Ferreira, M.A., Hall, I.P. et al. (2006) Meta-analysis of genome-wide linkage studies of asthma and related traits. Respir. Res. 9, 38, https://doi.org/10.1186/1465-9921-9-38
64 Nanavaty, U., Goldstein, A.D. and Levine, S.J. (2001) Polymorphisms in candidate asthma genes. Am. J. Med. Sci. 321, 11–16, https://doi.org/10.1097/00000441-200010000-00003
65 Palmer, L.J. and Cookson, W. (2001) Using single nucleotide polymorphisms as a means to understanding the pathophysiology of asthma. Respir. Res. 2, 102–112, https://doi.org/10.1186/1186/nr45
66 Li, X., Zhang, Y., Zhang, J., Xiao, Y., Huang, J., Tian, C. et al. (2010) Asthma susceptible genes in Chinese population: a meta-analysis. Respir. Res. 11, 129, https://doi.org/10.1186/1465-9921-11-129
67 Yang, H.J., Zheng, L., Zhang, X.F., Yang, M. and Huang, X. (2014) Association of the MS4A2 gene promoter C-109T or the 7th exon E237G polymorphisms with asthma risk: a meta-analysis. Clin. Biochem. 47, 605–611, https://doi.org/10.1016/j.clinbiochem.2014.01.022