***Title:*** **Food allergy genetics and epigenetics: a review of genome-wide association studies** **(Online repository)**

**Table S1.** Primary immunodeficiencies that have food allergy as a symptom

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Condition** | **Clinical presentation** | **Identified genes** | **Inheritance** | **Estimated prevalence of FA** |
| ADA-Severe combined immunodeficiency (SCID) | Erythroderma, opportunistic infections (bacterial, viral, fungal), dermatitis, elevated IgE | *ADA* | Autosomal recessive | 11%5 |
| CD40 ligand deficiency | Recurrent fever, sinopulmonary infection, neutropenia, opportunistic infections | *CD40LG* | X-linked recessive | 8% 6 |
| Common variable immunodeficiency (CVID) | Bacterial and viral infections, diarrhea, autoimmunity, lymphoproliferation | Unidentified (heterogenous) | Unidentified (heterogenous) | 11-33% 6-8 |
| Combined immunodeficiency (CID) | Severe atopy, recurrent infections, autoimmunity, mild thrombocytopenia, poor growth | *ARPC1B* | Autosomal recessive | 33-50%6,9,10 |
| Atopic dermatitis, allergy, asthma, respiratory tract infections and viral infections, elevated IgE | *CARD11*(complete LoF mutation can lead to SCID) | Autosomal dominant | 32%11 |
| Atopic dermatitis, allergy, asthma, recurrent pyogenic and viral skin infections and respiratory tract infections | *CARD14* (LoF)12 | Autosomal dominant | n/a |
| Severe atopy, cold urticaria, recurrent infections, EBV lymphoproliferation and other malignancy | *CARMIL2* (RLTPR deficiency) | Autosomal recessive | 13%13 |
| DOCK8 immunodeficiency syndrome (DIDS) | Severe atopic dermatitis and allergies, bacterial and viral infections, autoimmunity | *DOCK8* | Autosomal recessive | 55-100%14,15 |
| Hyper-IgE syndrome (HIES) | Atopic dermatitis, skin abscesses, skeletal and connective tissue abnormalities, eosinophilia | *STAT3* (LoF) (Job’s Syndrome) | Autosomal dominant | 20-29%6,14 |
| Atopic diseases, bronchiectasis, skin abscesses, neurodevelopmental delay; renal, intestinal and heart defects | *PGM3* (PGM3 deficiency) | Autosomal recessive | 63%16 |
| Atopic disease, Marfan-like syndrome, skeletal and connective tissue abnormalities, vascular abnormalities | *TGFBR*/*SMAD* (Loeys-Dietz Syndrome) | Autosomal dominant | 30-31%17,18 |
| Severe allergies, atopic dermatitis, chronic mucocutaneous candidiasis, pneumonias, skeletal and connective tissue abnormalities | *ZNF341 (ZNF341 deficiency)* | Autosomal recessive | 21%19 |
| Immune dysregulation, polyendocrinopathy, enteropathy, X-linked (IPEX)20,21 | *Severe atopy, autoimmunity, eosinophilia, recurrent severe infections, lymphoproliferation* | *FOXP3* | X-linked | n/a |
| IPEX-related21,22 | Atopic dermatitis, autoimmunity, growth failure, dysmorphic features | *CD25**STAT5b**ITCH* | Autosomal recessive | 7.16 - 74%§23 |
| Selective IgA deficiency | Frequently asymptomatic; allergy, infections, autoimmunity, serum IgA levels < (0.07 g/L) | Unknown | Unknown | 0-25%6,24 |
| Wiskott-Aldrich syndrome (WAS) | Atopic dermatitis, allergies opportunistic infections, bloody diarrhea, autoimmunity, hematological malignancies | *WAS* | X-linked recessive | 20-33%6,25 |
| X-linked thrombocytopenia (XLT) | Easy bruising, mild-severe anemia, milder phenotype than above | *WAS* | X-linked recessive | 20-30%25 |
| Comel-Netherton Syndrome† | Severe atopy, elevated IgE, cutaneous infections | *SPINK5* | Autosomal recessive | 85-100%26-28 |
| Peeling skin disease29,30† | Peeling skin, food allergies, erythroderma, pruritus, ichthyosis | *CDSN* | Autosomal recessive | n/a |
| Severe dermatitis, multiple allergies and metabolic wasting (SAM) syndrome† | Severe food allergy and atopic dermatitis, metabolic wasting | *DSG1**DSP* | Autosomal recessive | n/a |

Abbreviations used: FA, food allergy; LoF, loss of function mutation.

§ pediatric population and symptoms of food allergy wider than typical, include eczema, reflux, abdominal cramping, diarrhea

† primary immunodeficiency with skin barrier

**Table S2: Food allergy loci investigated in candidate genes studies (adapted from Suaini et al 2018 and Kanchan et al 2021)39,40**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **SNP ID** | **Chr** | **Gene** | **Food allergy phenotype** | **OR** | **p-value** | **Reference** | **Study population** | **Diagnostic criteria** |
| Not given | 1 | *FCGR2A* | food allergy | No ORs given, only frequencies | None significant *(p‐*values not given) | Pawlik 200446 | 77 pediatric patientsAge and sex NR\* | diagnostic criteria NR\* |
| Combined null genotype R501X and 2282del4 | 1 | *FLG* | peanut allergy | English: 3.2 (1.4‐7.2) English, Dutch, Irish: 5.3 (2.8‐10.2) | 0.02513.0 × 10−6 | Brown 201147 | English: 3.2 (1.4‐7.2) English, Dutch, Irish: 5.3 (2.8‐10.2)Dutch: 3.5 (1.1‐11.4)Irish: 3.3 (1.0‐11.7) | 71 pediatric patientsEnglish cohort (n=35); recruited at birth and followed for ≥7 y; M/F: 19/16Dutch cohort (n=20); Age (mean (range)): 7.5 (3-14); M/F: 14/6Irish cohort (n=16); Age (mean (range)): 10.5 (1-18); M/F: 7/9 |
| Combined null genotype R501X, 2282del4, R2447X and S3247X | 1 | ***FLG*** | peanut allergy | Dutch: 3.5 (1.1‐11.4)Irish: 3.3 (1.0‐11.7) | 0.03350.0640 | Brown 201147 |
| rs6696556 | 1 | ***FLG*** | food allergy | 1.05 (0.84‐1.31) | 0.68 | Hirota 201741 | **(I)**Age (mean ± s.d): primary set 5.2yrs±3.; validation set 5.8yrs±3.3Male/Female (M/F): primary set 419/174; validation set 188/91  | **(I)**positive OFC OR definitive clinical history after food intake |
| p.S2889\* | 1 | ***FLG*** | food allergy | 2.32 (1.37‐3.98) | 0.001 | Hirota 201741 |
| 6 FLG null variants, c.3321delA, p.Q1701\*, p.S2554\*, p.S2889\*, p.S3296\* and p.K4022\* | 1 | ***FLG*** | food allergy | 1.42 (1.04‐1.92) | 0.024 | Hirota 201741 |
| 5 filaggrin null mutations (del22824, 501‐C/T, R2447X, S3247 and 3702delG) | 1 | ***FLG*** | cow’s milk allergy | No ORs given, only frequencies | None significant *(p>*0.003) | Savilahti 201048 | **(II)**87 patients age range: 8.0–9.3 yrs | **(II)**diagnostic criteria NR |
| 5 polymorphisms (R501X, 2282del4, S3247X, 3702delG and R2447X) | 1 | ***FLG*** | food allergy | 10 y: 2.9 (1.2‐7.0)18 y: 2.5 (1.2‐ 5.3) | 0.0220.032 | Venkataraman 201449 | 1150 pediatric patientsM/F: 569/581 (49.5)Genotype determined in 79% of children at 18yrs | 1) a reaction to a recognized food allergen as defined by the European Union AND2) a report of recognized allergic symptoms AND3) temporal relationship: symptoms developing within 4 hours of food ingestion |
| R501X, 2282del4, R2447X, S3247X and 3702delG | 1 | ***FLG*** | food allergy | 3.2 (1.2‐8.5) | 0.016 (0.055 after adjusting for eczema | Tan 201250 | 283 infants, mean age and sex NR | positive OFC or SPT (wheal diameter >8mm) |
| Combined rs61816761, rs41370446, rs138726443 and rs150597413 | 1 | ***FLG*** | peanut allergy | 1.96 (1.49‐2.58) | 5.12 × 10−7 | Asai 201351 | 679 Caucasian pediatric patients, mean age and sex NR | peanut-specific IgE ≥ 0.35 kU/lAND SPT (wheal diameter >3mm) (with or without anaphylaxis)peanut-specific IgE ≥ 0.35 kU/lORSPT (with or without anaphylaxis) |
| ‐1082 | 1 | ***IL10*** | cow’s milk allergy | No ORs given, only frequencies | 0.027 (*p*c = 0.054) | Jacob 201358 | **(III)**50 pediatric patientsMean age NR; M/F: 6/8 | **(III)**double-blind, placebo-controlled food challenge |
| rs1800896, rs1800872 | 1 | ***IL10*** | food allergy | No ORs given, only frequencies | 0.9940.770 | Chen 201259 | 37 pediatric patients Mean ± s.d):8.06 ± 6.25M/F: 23/14 | food-specific IgE level of 0.7 kU/L  |
| rs12079994 | 1 | *NLRP3* | food-induced anaphylaxis | 1.81 (1.09‐2.99) | 0.021 | Hitomi 200964 | 320 pediatric patientsAge (mean ± s.d): 4.2 ± 3.3; Male/Female 233/87 | OFC OR definitive episode AND confirmation of antigen specific IgE levels (level not specified) |
| rs4925650 | 1 | *NLRP3* | food-induced anaphylaxis | 1.77 (1.26‐2.49) | 9.1 x 10-4 | Hitomi 200964 |
| rs3806265 | 1 | *NLRP3* | food-induced anaphylaxis | 1.71 (1.20‐2.43) | 0.0029 | Hitomi 200964 |
| rs4612666 | 1 | *NLRP3* | food‐induced anaphylaxis | 1.81 (1.27‐2.56) | 8.6 x 10-4 | Hitomi 200964 |
| rs10925026 | 1 | *NLRP3* | food‐induced anaphylaxis | 1.53 (1.09‐2.16) | 0.013 | Hitomi 200964 |
| rs10754558 | 1 | *NLRP3* | food‐induced anaphylaxis | 1.80 (1.28‐2.54) | 6.8 x 10-4 | Hitomi 200964 |
| rs10733112 | 1 | *NLRP3* | food‐induced anaphylaxis | 1.71 (1.21‐2.40) | 0.0021 | Hitomi 200964 |
| rs2027432, rs4925648, rs12048215, rs10754555, rs10925019, rs4925654, rs12565738 and rs4378247 | 1 | *NLRP3* | food allergy | No ORs given | None significant *(p* >0.05) | Hitomi 200964 |
| rs2476601 | 1 | *PTPN22* | cow’s milk allergy | No ORs given, only frequencies | None significant *(p* > 0.003) | Savilahti 201048 | **(II)** | **(II)** |
| rs11236809 | 11 | ***C11orf3*/*LRRC32*** | food allergy | 1.34 (1.14-1.59) | 0.00056 | Hirota 201741 | **(I)** | **(I)** |
| +7883G/T (GG+ GT/TT) | 2 | CREL | cow’s milk allergy | 4.1 (1.82-9.29) | 0.0004 | Rahmoun 201845 | 30 pediatric patientsAge (mean): 15.2mo; M/F: 21/9 | OFC and clinical history |
| rs6780220 | 3 | *GLB1* | food allergy | 1.40 (1.21‐1.62) | 8.2 × 10−6 | Hirota 201741 | **(I)** | **(I)** |
| rs878860 | 3 | *OR10A3*/*NLRP10* | food allergy | 1.10 (0.95‐1.27) | 0.21 | Hirota 201741 |
| rs5743708 | 4 | *TLR2* | cow’s milk allergy | No ORs given, only frequencies | None significant *(p>*0.05) | Galli 201068 | **(IV)**57 pediatric patientsAge (median (range)): 58mo (6-198); M/F: 29/28 | **(IV)**SPT (wheal > 3mm) |
| rs17616434 | 4 | *TLR1*/*6*\*/*FAM114A1* | cow’s milk allergy | No ORs given | 0.002 | Henneman 201557 | **(V)**20 pediatric patientsMean age (± SD): 11.8yrs±4.9; M/F: 12/8 | **(V)**double blind placebo-controlled food challenge |
| rs12634229 | 5 | *CCDC80* | food allergy | 1.26 (1.08‐1.46) | 0.0039 | Hirota 201741 | **(I)** | **(I)** |
| rs2569190 | 5 | ***CD14*** | food allergy | No ORs given, only frequencies | 0.8 | Campos 200742 | 88 pediatric patientsAge (mean ± s.d): 7.1yrs±5 | immediate adverse reactions upon ingestion confirmed by OFC (unless participants were anaphylactic) |
| rs5744455 | 5 | ***CD14*** | food allergy | No ORs given, only frequencies | 0.8 | Campos 200742 |
| rs2569193 | 5 | ***CD14*** | peanut allergy | 1.33 (0.53‐3.34) | 0.54 | Dreskin 201143 | 53 highly allergic patients (adults and children); Age and sex NR | SPT (wheal > 5mm) and specific IgE >14 IU/mL OR a positive double-blind placebo-controlled food challenge |
| rs2569190 | 5 | ***CD14*** | peanut allergy | 1.97 (1.02‐3.79) | 0.04 | Dreskin 201143 |
| rs2569190 | 5 | ***CD14*** | food allergy | 1.7 (1.1‐2.8) | 0.03 | Woo 200344 | 77 pediatric patientsAge (mean ± s.d): 5.2 ± 5.3; 74% M | immediate reaction to a food AND positive antigen test responses (SPT or radio allergo-sorbent test (RAST)) confirmed by OFC |
| rs1295686 | 5 | ***IL13*** | food allergy | 1.75 (1.20‐2.53) | 0.003 | Ashley 201760 | **(VI)**367 pediatric patientsMean age (± SD): 12.7 mo ± 0.75; 58.9% M | **(VI)**SPT (wheal ≥1 mm) followed AND OFC |
| rs1295686 | 5 | ***KIF3A*/*IL13*** | food allergy | 1.44 (1.23‐1.68) | 3.1 × 10−6 | Hirota 201741 | **(I)** | **(I)** |
| rs17389644 | 5 | ***IL2*/*IL21*** | food allergy | 1.14 (0.90‐1.44) | 0.28 | Hirota 201741 |
| 77 tag‐SNPs within a region of ~263 kb capturing 387 alleles with LD of r2 ≥ 0.8 | 5 | ***SPINK5*** | food allergy | 2.95 (1.49‐5.83) | 0.001 | Ashley 201760 | **(VI)** | **(VI)** |
| G1258A | 5 | ***SPINK5*** | food allergy | No ORs given | 0.03 | Kusunoki 200565 | 136 pediatric patientsAge range: 1.5-17yrs; M/F: 65/71 | positive OFC (performed 2 -3 times) AND positive SPT AND specific IgE (≥0.7kIU/L) |
| rs9326801 | 5 | *TMEM232*/*SLC25A46* | food allergy | 1.33 (1.09‐1.61) | 0.0037 | Hirota 201741 | **(I)** | **(I)** |
| rs3806932 | 5 | *TSLP*/*WDR36* | food allergy | 1.19 (1.02‐1.40) | 0.032 | Hirota 201741 |
| HLA class II haplotypes (DQB1, DRB1 and DQA1) | 6 | ***HLA*** | cow’s milk allergy | No ORs given, only frequencies | None significant *(p* >0.003) | Savilahti 201048 | **(II)** | **(II)** |
| DRB1\*08 | 6 | ***HLA-DRB1*** | peanut allergy | No ORs given, only frequencies | 0.0021(*p*c = 0.027) | Howell 199852 | 161 Caucasian patients, mean age and sex NR | history of an allergic reaction was convincing AND positive SPT (wheal diameter >3mm) |
| DRB1\*08/12 (tyr16) | 6 | ***HLA-DRB1*** | peanut allergy | No ORs given, only frequencies | 0.0023(*p*c = 0.029) | Howell 199852 |
| DQB1\*04 | 6 | ***HLA-DQB1*** | peanut allergy | No ORs given, only frequencies | 0.00042 (*p*c = 0.0029) | Howell 199852 |
| DR11 | 6 | ***HLA-DR11*** | peanut allergy | No ORs given, only frequencies | 0.07 (*p*c = 1.3 | Shreffler 200653 | 73 patients, mean age 6.5yrs; 72% male | acute clinical reaction with objective symptoms to ingestion of peanut AND detectable peanut specific IgE antibody ≥ 0.35 kU/l |
| DQ7 | 6 | ***HLA-DQ7*** | peanut allergy | No ORs given, only frequencies | 0.04 (*p*c= 0.3) | Shreffler 200653 |
| 6 DQ serotypes (DQ2, DQ4, DQ5, DQ6, DQ8 and DQ9) and 17 DR allele groups (DR1, DR4, DR7, DR8, DR9, DR10, DR12, DR13, DR14, DR15, DR16, DR17, DR18, DR51, DR52, DR53 and DR103) |  | ***HLA*** | peanut allergy | No ORs given, only frequencies | None significant *(p/p*c> 0.05) | Shreffler 200653 |
| DQB1\*06:03P | 6 | ***HLA‐ DQB1*** | peanut allergy | 2.59 (1.56‐4.44) | 1.6 × 10‐4*p*c = 1.9 × 10−3 | Madore 201354 | 590 children Age (± SD): 11yrs±4; sex ratio, M:F 1:0.6 | 1) convincing clinical history OR allergic reaction OR peanut specific IgE ≥ 0.35 kU/lOR2) positive SPT (wheal diameter >3mm) AND peanut specific IgE ≥15 kU/l OR positive OFC |
| DQB1\*02 | 6 | ***HLA‐ DQB1*** | peanut allergy | 0.12 (0.07‐0.21) | 1.1 × 10‐16Pc = 1.3 × 10−15 | Madore 201354 |
| DQB1\*03:02P | 6 | ***HLA‐ DQB1*** | peanut allergy | 0.52 (0.34‐0.79) | 2.2 × 10-3*p*c = 2.6 × 10−2 | Madore 201354 |
| 8 DQB1\*05 | 6 | ***HLA‐ DQB1*** | peanut allergy | 0.21 (0.08‐0.50) | 2.5 × 10-4*p*c = 3.0 × 10−3 | Madore 201354 |
| DQB1\*05:01P | 6 | ***HLA‐ DQB1*** | peanut allergy | 0.25 (0.13‐0.47) | 7.7 × 10-6*p*c = 9.3 × 10−5 | Madore 201354 |
| B\*07, DRB1\*11 | 6 | ***HLA****‐A, B*,***DRB1***,***DQB1*** | nut allergy | No ORs given, only frequencies | None significant *(p* > 0.05) | Hand 200455 | 84 patientsAge range: 3-56 yrs; M/F: 40/44 | SPT (wheel diameter >2mm) |
| DRB1\*13 | 6 | ***HLA****‐A*, *B*,***DRB1***,***DQB1*** | nut allergy | No ORs given, only frequencies | <0.05 (*p*c=0.82) | Hand 200455 |
| DQB1\*06 | 6 | ***HLA****‐A*, *B*,***DRB1***, ***DQB1*** | nut allergy | No ORs given, only frequencies | <0.01 (*p*c= 0.37) | Hand 200455 |
| rs3808606, rs3824259, rs10089084, rs6991530, rs10504013 rs11992749, rs10109853, rs4503083, rs2955903 and rs7820268 |  | *IDO1* and *IDO2* | food allergy | No ORs given, only frequencies | None significant (P values >0.05) | Buyuktiryaki 201656 | 100 pediatric patientsMedian age (range): 3.2yrs (1.7–7.0); M/F: 74/26 | 1) Specific IgE ≥0.35 kU/l OR SPT (wheal ≥3 mm) AND2) Consistent and clear-cut history of an early reaction after ingestion AND3) Positive OFC or a clear-cut history of anaphylaxis after ingestion  |
| rs2069772 | 8 | ***IL2*/*KIAA1109*** | cow’s milk allergy | No ORs given | 0.038 | Henneman 201557 | **(V)** | **(V)** |
| NAT2\*4 (fast acetylator), NAT2\*5, NAT2\*6 and NAT2\*7 (slow acetylators) | 8 | *NAT2* | food allergy | No ORs given, only frequencies | *p* <0.001 | Gawronska‐ Szklarz 20063 |  |  |
| rs4986790 | 9 | *TLR4* | cow’s milk allergy | No ORs given, only frequencies | None significant *(p* >0.05) | Galli 201068 | **(IV)** | **(IV)** |
| rs10995251 | 10 | *ZNF365* | food allergy | 1.32 (1.14‐1.53) | 1.7 x 10-4 | Hirota 201741 | **(I)** | **(I)** |
| rs16948048 | 10 | ***ZNF652*** | food allergy | 1.20 (0.97‐1.47) | 0.093 | Hirota 201741 |
| rs593982 | 11 | *OVOL1* | food allergy | 1.23 (1.06‐1.42) | 0.0049 | Hirota 201741 |
| rs324015 | 12 | ***STAT6*** | food-related anaphylaxis | No ORs given, only frequencies | 0.4974 | Tamura 200366 | NR\* | NR\* |
| rs324015 | 12 | ***STAT6*** | nut allergy | 2.9 (1.7‐ 4.9) | < 0.0001 | Amoli 200267 | 71 pediatric patientsAge (mean ± s.d): 9.7 ± 12.1; M/F: 35/36 | SPT and RAST |
| rs167769 | 12 | ***STAT6*** | food allergy | 1.26 (1.06‐1.50) | 0.0082 | Hirota 201741 | **(I)** | **(I)** |
| rs2041733 | 13 | *CLEC16A*/*DEXI* | food allergy | 1.15 (0.99‐1.35) | 0.074 | Hirota 201741 |
| rs57265082 | 18 | *MALT1* | peanut allergy | 10.9 | 6.49 x 10-8 | Winters 201962 | 542 pediatric patientsMean age (± SD): 7.80 mo ±1.74; M/F: 316/226 | positive OFC to peanuts at 60 months of age |
| rs12979860 | 19 | *IL28B* | food allergy | Cohort 1: 4.56 (1.7‐12.6)Cohort 2: 3.0 (1.8‐5.2) | 0.0040.04 | Gaudieri 201261 | 35 allergic pediatric patients; age and sex NR | Diagnostic criteria NR |
| -509C/T | 19 | *TGFb1* | cow’s milk allergy | No ORs given, only frequencies | 0.6419 | Jacob 201358 | **(III)** | **(III)** |
| rs6010620 | 20 | *TNFRSF6B*/*ZGPAT* | food allergy | 1.11 (0.95‐1.29) | 0.19 | Hirota 201741 | **(I)** | **(I)** |

**Abbreviations:** OFC; oral food challenge, *p*c; corrected *p* value, RAST; radioallergosorbent test, SPT; skin prick test

Genes/loci in **bold** have been replicated within the study or have evidence across multiple studies**.**

**\*** full text article not available

**Table S3: Food allergy epigenetic loci investigated in candidate genes (adapted from Safar et al 2023 and Chun et al 2024)1,2**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **CpG site** | **Chr** | **Gene** | **Food allergy phenotype** | **Cell type** | **p-value / Correction if any** | **Reference** | **Study population** | **Diagnostic criteria** |
| **Country/ Ethnicity/ Population** | **Cases / Controls (n)** |
| NA | X | ***FOXP3*** | Peanut allergy | Treg cells | *p* ˂ 0.001  | Syed *et al*. 20143 | USA/ No mention/ Pediatric and adult | 23 OIT-PA / 20 PA abstaining from peanut | DBPCFC + sIgE level + SPT |
| Promoter region | 1 | *FLG* | Egg allergy, Peanut allergy Sesame, allergy, Shrimp allergy, Cow’s milk allergy, Cashew allergy, Almond allergy, Hazelnut allergy, Soy allergy, Wheat allergy | Buccal samples | None significant (p ˃ 0.05) | Tan *et al*. 20144 | Australia/ No mention/ Pediatric | 34 /29 | OFC **or** clearly objective and recent history of reaction **or** SPT response > 8 mm  |
| Promoter region | 1 | *IL10* | Cow’s milk allergy | PBMCs | *p* ˂ 0.001 / Bonferroni | Berni Canani *et al.* 20155 | Italy/ No mention/ Pediatric | 10 / 10 | DBPCFC + sIgE level |
| 5 | ***IL4*** |
| 5 | *IL5* |
| 12 | *IFNG* |
| TSDR | X | ***FOXP3***  | Cow’s milk allergy | PBMCs | *p* ˂ 0.0001 / Bonferroni | Paparo *et al*. 20166 | Italy/ No mention/ Pediatric | 10 / 10 | DBPCFC + sIgE level |
| Promoter region | 1 | *IL10* | Cow’s milk allergy | CD4+ T cells | *p* ˂ 0.05 | Paparo *et al*. 20197 | Italy/ No mention/ Pediatric | 20 (after treatment) / 20 (before treatment) | DBPCFC + sIgE level + SPT |
| 5 | ***IL4*** |
| 5 | *Il5* |
| 12 | *IFNG* |
| NA | X | ***FOXP3*** |
| Promoter region | 4 | *TLR2* | Egg allergy, Peanut allergy, Nut allergy | Whole blood | None significant (*p* ˃ 0.05) | Poole *et al*. 20208 | Australia/ No mention/ Pediatric | 66 / 14 | Clinical diagnosis **and** (OFC **and/or** SPT) |
| 5 | *CD14* |
| Promoter region | 1 | *IL10* | Cow’s milk allergy, Egg allergy, Peanut allergy | PBMCs | *p* ˂ 0.01 | Paparo *et al*. 20219 | Italy/ Caucasian/ Pediatric | 12 (Stimulated cells) / 4 (Stimulated cells) | OFC |
| 5 | *IL4* | *p* ˃ 0.05 |
| 5 | *IL5* | *p* ˃ 0.05 |
| 12 | *IFNG* | *p* ˂ 0.01 |
| TSDR | X | *FOXP3* | *p* ˃ 0.05 |
| NA | 1 | *CSF1* | Peanut allergy | PBMCs | *p* ˃ 0.05 | Zhou *et al*. 202110 | USA/ Caucasian, Asian, African-American/ Pediatric | 5 discordant monozygotic twin pairs, 3 discordant dizygotic twin pairs, 2 dizygotic twin pairs (all four children having PA) | OFC + sIgE |
| NA | 1 | *FASLG* | *p* ˃ 0.05 |
| NA | 1 | *FLG* | *p* ˃ 0.05 |
| NA | 1 | *IL10* | *p* ˃ 0.05 |
| NA | 1 | *S100A6* | *p* ˃ 0.05 |
| NA | 1 | *TNFRSF25* | *p* ˃ 0.05 |
| NA | 2 | *CTLA4* | *p* ˃ 0.05 |
| NA | 2 | *ID2* | *p* ˃ 0.05 |
| NA | 2 | *IKZF2* | *p* ˃ 0.05 |
| NA | 2 | *IL1A* | *p* ˃ 0.05 |
| 5 sites | 2 | *IL1B* | 0.031 |
| NA | 2 | *IL1R1* | *p* ˃ 0.05 |
| NA | 2 | *PDCD1* | *p* ˃ 0.05 |
| NA | 3 | *CCR4* | *p* ˃ 0.05 |
| NA | 3 | *TNFSF10* | *p* ˃ 0.05 |
| NA | 4 | *CXCL1* | *p* ˃ 0.05 |
| NA | 4 | *CXCL8 (IL8)* | *p* ˃ 0.05 |
| NA | 4 | *CXCL9* | *p* ˃ 0.05 |
| 1 site | 4 | *IL2* | 0.045 |
| NA | 4 | *IL21* | *p* ˃ 0.05 |
| NA | 5 | *CD14* | *p* ˃ 0.05 |
| NA | 5 | *CSF2* | *p* ˃ 0.05 |
| 4 sites | 5 | ***IL4*** | 0.032 |
| 3 sites | 5 | *IL12B* | 0.045 |
| NA | 5 | *IL5* | *p* ˃ 0.05 |
| NA | 5 | *IL7R* | *p* ˃ 0.05 |
| NA | 5 | *IL9* | *p* ˃ 0.05 |
| NA | 6 | *CCR6* | *p* ˃ 0.05 |
| NA | 6 | *IL17A* | *p* ˃ 0.05 |
| 3 sites | 6 | *IL17F* | 0.034 |
| NA | 6 | *TNF (TNFA)* | *p* ˃ 0.05 |
| 7 sites | 7 | *IL6* | 0.030 |
| 5 sites | 7 | *SERPINE1* | 0.038 |
| NA | 8 | *TNFRSF10C* | *p* ˃ 0.05 |
| NA | 9 | *CD274* | *p* ˃ 0.05 |
| NA | 9 | *IFNB1* | *p* ˃ 0.05 |
| NA | 9 | *IL33* | *p* ˃ 0.05 |
| NA | 9 | *PDCD1LG2 (PDL2)* | *p* ˃ 0.05 |
| 9 sites | 10 | *CXCL12* | 0.019 |
| NA | 10 | *IL2RA* | *p* ˃ 0.05 |
| 2 sites | 11 | *BDNF* | 0.023 |
| 2 sites | 11 | *CD3E* | 0.023 |
| NA | 11 | *CD3G* | *p* ˃ 0.05 |
| NA | 11 | *CD44* | *p* ˃ 0.05 |
| NA | 11 | *CDKN1C* | *p* ˃ 0.05 |
| NA | 11 | *ETS1* | *p* ˃ 0.05 |
| NA | 11 | *MMP1* | *p* ˃ 0.05 |
| NA | 11 | *MMP3* | *p* ˃ 0.05 |
| NA | 11 | *MMP13* | *p* ˃ 0.05 |
| NA | 11 | *TOLLIP* | *p* ˃ 0.05 |
| NA | 12 | *IFNG* | *p* ˃ 0.05 |
| NA | 12 | *IL22* | *p* ˃ 0.05 |
| NA | 16 | *CREBBP* | *p* ˃ 0.05 |
| NA | 16 | *IRF8* | *p* ˃ 0.05 |
| NA | 16 | *ITGAL* | *p* ˃ 0.05 |
| NA | 17 | *CCL3* | *p* ˃ 0.05 |
| NA | 17 | *CCL4* | *p* ˃ 0.05 |
| NA | 17 | *CCL5* | *p* ˃ 0.05 |
| 9 sites | 17 | *CCR7* | 0.010 |
| NA | 17 | *CCL15 (CCL9)* | *p* ˃ 0.05 |
| NA | 18 | *MALT1* | *p* ˃ 0.05 |
| NA | 18 | *MAPRE2* | *p* ˃ 0.05 |
| NA | 19 | *TGFB1* | *p* ˃ 0.05 |
| NA | 20 | *CD40* | *p* ˃ 0.05 |
| 5 sites | 21 | *RUNX1* | 0.038 |
| NA | 22 | *EP300* | *p* ˃ 0.05 |
| NA | 22 | *LIF* | *p* ˃ 0.05 |
| NA | X | *CXCR3* | *p* ˃ 0.05 |
| NA | X | ***FOXP3*** | *p* ˃ 0.05 |
| NA | ? | *TNFSRF18* | *p* ˃ 0.05 |
| Promoter region (1 site) | 6 | *HLA-G* | Cow’s milk allergy, Egg allergy, Nut allergy, Fruit allergy | PBMCs | 0.004 / Bonferroni | Kostara *et al*. 202211 | Greece/ No mention/ Pediatric | 64 / 44 | Clinical diagnosis + OFC + sIgE level + SPT |
| Exon 2 (1 site) | 6 | *HLA-DRB1* | *p* > 0.05 |
| Exon 2 (1 site) | 6 | *HLA-DQB1* | *p* > 0.05 |
| TSDR (11 sites) | X | ***FOXP3*** | *p* ˃ 0.05 |
| 4 sites | 1 | *IL10* | Milk allergy (breastfeeding or milk formula) | PBMCs | None significant (*p* ˃ 0.05) | Gorzkiewick *et al*. 202312 | Poland / No mention / Pediatric (0-6 months old) | 38 / 89 | Clinical diagnosis + CoMiSS score ≥ 12 + sIgE + OFC  |
| 4 sites | 5 | ***IL4*** |
| 17 sites | 5 | *IL5* |
| 3 sites | 12 | *IFNG* |
| TSDR (9 sites) | X | ***FOXP3*** |

**Abbreviations:** CoMiSS; Cow’s milk-related symptom score, CMA; Cow’s milk allergy, DBPCFC; Double blind placebo-controlled food challenge, OFC; Oral food challenge, OIT; Oral immunotherapy, PA; Peanut allergy, sIgE; Specific IgE, SPT; Skin prick test, TSDR; Treg-specific demethylated region

Genes/loci in **bold** have been replicated within the study or have evidence across multiple studies**.**

Adapted from Safar *et al*. 2023 and Chun *et al*. 20241,2with search using the same keywords (PubMed, September 2024).1

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