Content is available at: CRDEEP Journals
Journal homepage: http://www.crdeepjournal.org/category/journals/ijls/

International Journal of Life Sciences
(ISSN: 2277-193x) (Scientific Journal Impact Factor: 6.106)

UGC Approved-A Peer Reviewed Quarterly Journal

Research Paper

An Association Study of STAT6 Gene Polymorphism with Asthma

Parwat Raj Pandey[1] and Rashmi Arnold[2]

[1:] Centre for Biotechnology Studies, APS University, Rewa (M.P.)
[2:] Department of Zoology, Govt. Model Science College Rewa (M.P.)

ARTICLE DETAILS

Corresponding Author:
Parwat Raj Pandey

Key words:
STAT6 gene, Allele frequency, PCR, Restriction Enzyme, Asthma.

ABSTRACT

The human signal transducer and activator of transcription 6 (STAT6) gene represents one of the most promising candidate genes for asthma and other inflammatory diseases on the chromosomal region 12q13–q24. Therefore, Bronchial asthma is a common disease with multiple determinants that include genetic variation. Signal transducer and activator of transcription 6 (STAT6) is a central molecule in the signal transduction pathway used by interleukin-4 (IL-4) in immunoglobulin E (IgE) isotype switching. Signal transducer and activator of transcription 6 (STAT6) is a key transcription factor involved in both interleukin-4 (IL-4) and IL-13-mediated biological responses, such as allergies. Recently, we reported that the polymorphism of the STAT6 gene exon 1 was associated with allergic diseases, while another group studied the G2964A variant of the STAT6 gene's association with atopic asthma. Genotype frequency between Asthma patient and healthy control groups were slightly different and but not significantly associated with Asthma ($\chi 2$=2.025,P=0.3633). Thus allele frequency ($\chi 2$=0.8091, P=0.3684) and carriage rate ($\chi 2$=0.4590, P=0.4981) were also not significantly different between both case and control groups.An odds ratio of 0.7860 in Asthma group respectively for '*CC*' genotype indicated a no role in protective effect of this wild type genotype.

1. INTRODUCTION:

Asthma has become the most common chronic childhood disease in developed nations, affecting more than 155 million individuals. Both, gene–gene as well as gene–environment interactions contribute to its overall phenotype. Total serum IgE levels, eosinophil cell count, bronchial hyper-responsiveness (BHR), to the chromosomal region 12q13–q24 in different ethnic populations worldwide [3]. The human *STAT6* gene, which belongs to the STAT-family of transcription factors, maps to chromosome 12q13.3–q14.1, encompasses over 19 kb and contains 23 exons. The first two exons of the *STAT6* gene are non-coding [5′untranslated region (5′UTR). STAT6 is involved in the interleukin 4 (IL-4) and interleukin 13 (IL-13) signaling pathway, two cytokines that are related to allergic asthma and other inflammatory and allergic diseases. IL-4 induces the proliferation of T-lymphocytes and is important for the differentiation of Th2-cells. Furthermore, IL-4 activation of B lymphocytes (B-cells) triggers class-switching to the IgE isotype. IL-13, which is secreted by activated T-cells, shares many biological functions with IL-4 [1-4].

Asthma is one of the most common respiratory diseases caused by acute and chronic bronchial inflammation that result in variable airway obstruction. The inflammatory response of asthma is tightly associated with an immune disorder characterized by IgE production and an imbalance between T helper cell 1 (Th1) and T helper cell 2 (Th2), both of which have a strong genetic component [6]. The signal transducer and activator of transcription 6 (STAT-6) is critical for effects mediated by IL-4, including induction of Th2 and IgE responses, and antigen-induced airway inflammation and hyperresponsiveness. A few groups have already studied the association between the polymorphisms in the 30 untranslated region of the STAT-6 gene and asthma. However, the results of these studies are not consistent [5]. The signal transducer and activator of transcription 4 (STAT-4) is known to be essential for mediating responses of IL-12 in

[1]Corresponding Author can be contacted at: Centre for Biotechnology Studies, APS University, Rewa (M.P.)
Received: 10-01-2026; Sent for Review on: 12-01-2026; Draft sent to Author for corrections: 25-01-2026; Accepted on: 30-01-2026; Online Available from 03-02-2026
DOI: 10.5281/zenodo.18465145.

lymphocytes and for regulating the differentiation of T helper cells. IFN-g, a representative TH1 cytokine, also plays an important role in the induction of immune-mediated inflammatory responses of asthma. However, thus far, little is known about the associations of the STAT-4 and IFN-g gene polymorphisms with asthma [5-7].

Bronchial asthma is the most common chronic disease among children in the world. It affects up to 300 million people worldwide. The prevalence among Egyptian hildren aged 3–15 years was 8.2% [2]. Bronchial asthma is influenced by genetic and environmental factors. The disease is defined by the presence of airway hyperreactivity, mucus overproduction, and chronic eosinophilic inflammation [8]. Asthma is often characterized by enhanced total serum IgE level upon the exposure to allergens, which is known as an atopy. Many family studies, through genome-wide linkage studies, confirmed the involvement of genetic predisposition in the development of atopy in asthmatic patients [9]. The elevated IgE production in asthmatic patients results in promotion of acute hypersensitivity responses, chronic eosinophil-predominant allergic inflammation with T helper-2 (Th2) cells cytokine production [10]. IL-4 serves as an essential proinflammatory cytokine in immune regulation mediated by activated T helper cells (Th) and facilitates immunoglobulin E isotype switching in B cells, growth, and differentiation of B cells and monocytes. As an important signal molecule, IL-4 can exacerbate airway inflammation through modulating eosinophils, lymphocytes, and air epithelial cells that play an important role in the pathogenesis of asthma. Moreover, IL-4 plays a pivotal role in phenotypic changes of bronchial asthma, such as airway hyperresponsiveness, eosinophil infiltration, and mucus overproduction [11]. Also STAT6, the signaling molecule from JAK/STAT pathway, activated by IL-4 and IL-13 cytokines, plays an important role in IgE production and allergic airway inflammation. Signal transducer and activator of transcription (STAT) is a family of latent cytoplasmic transcription factors activated by specific cytokine receptor-mediated signal transducers. Selective activation of *STAT6* by IL-4 or IL-13 involves phosphorylation, dimerization and then translocation into the nucleus, where it binds to specific DNA elements TTC (N3/4) GAA within the promoter region, activating gene transcription [8-12].

2. MATERIALS AND METHODS:

2.1 Study population:

The study population consisted of 208 unrelated subjects comprising of 96Asthma patients and 112 ethnically matched controls of central Indian population were included in this study. In this region Hindu, Muslim and some Sikh peoples are mainly living but most people's belong to Hindu religion in this region.

2.2 Blood collection and plasma/serum separation:

Venous blood samples were obtained from the subjects after 12 hours of overnight fasting in vacutainers with and without appropriate anti-coagulants. Immediately, plasma and serum from the respective vacutainers were separated by centrifuging the tubes at 1000 rpm for 10 min. at 4˚C

2.3 Method for DNA isolation:

Genomic DNA was extracted from whole blood by the modification of salting out procedure described by Miller and coworkers (Miller *et al*. 1988). Frozen blood sample was thawed at room temperature. 0.5 ml. of whole blood sample was suspended in 1.0 ml. of lysis buffer (0.32 M Sucrose, 1 mM Mgcl2, 12 mM Tris and 1% Triton-X-100) in a 1.5 ml. microcentrifuge tubes. The supernatant was discarded carefully in a jar containing disinfectant, as pellet formed is loosely adhered to the bottom of centrifuge tube. The pellet was resuspended in 0.2 ml. of lysis buffer and recentrifuge at 11,000 rpm for 5 min. The pellet was than dissolved in 0.2 ml. of deionized autoclaved water and mixed thoroughly on vortexer. The mixture was centrifuged at 14,000 rpm for 1 min. at 4˚C. Supernatant was discarded to gain an intact pellet. To the above pellet, 80 µl. of proteinase K buffer (0.375 M Nacl, 0.12 M EDTA, pH 8.0) and 10 µl. of 10% SDS (10% w/v SDS, pH 7.2) was added. Mixture was well frothed with the help of micro tip to allow proper lysis of pelleted nuclei. After digestion was complete, 100 µl. of saturated cold 5M Nacl was added and shaken vigorously for 15 sec. To the above mixture 0.2 ml. of deionized, autoclaved water and 0.4 ml. of phenol-chloroform (4:1 v/v) was added to remove most of the non nucleic acid organic molecules. Supernatant was discarded. The pellet was washed twice with 1 ml. of 70% alcohol. The mixture was again centrifuged at 14,000 rpm for 1 min. 4˚C. Supernatant was discarded and pellet was air dried for 10-20 min. The pelleted DNA was rehydrated in 100-200 µl. of TE buffer pH 7.4 (10 mM Tris-HCL pH 7.4, 1mM EDTA, pH 8.0). DNA was allowed to dissolve overnight at 37˚C before quantization.

2.4 Polymorphism screening:

In general, the genomic DNA extracted from peripheral blood of healthy individuals and diseased individuals was subjected to PCR followed by restriction digestion and electrophoresis to genotype both the groups for relevant gene of interest. All the PCRs were carried out in a PTC 200 thermal cycler (MJ Research Inc. USA). PCR is a rapid, inexpensive and simple mean of producing relatively large copy number of DNA molecules from the small amounts of source DNA material, even when the source DNA is of relatively poor quality. When DNA is digested with certain restriction enzymes under non-standard conditions, cleavage can occur at sites different from the normal recognition sequence. Such aberrant cutting is called "star activity" which can be due to high pH (>8.0) or low ionic strength, extremely high concentration of enzyme (>100 U/µgof DNA) and presence of organic solvents in the reaction (e.g. ethanol, DMSO).The PCR and restriction digestion conditions were optimized for specific locus of relevant segment of the gene to be studied. The PCR products as well as the digested products were separated on either agarose gel or polyacrylamide gel depending on their size. Gels were stained with ethidium bromide solution (0.5 µg/ml) and subsequently visualized and photographed under UV transilluminator.

2.5 Detection of STAT6 (rs324011) Polymorphism:
The STAT6 gene, including the rs324011 (2892C/T) polymorphism, is located on chromosome 12, specifically at the region 12q13.3-q14.1. Genotyping pattern of the wild-type genotype (CC) was not digested and give 132bp whereas the mutated homozygous genotype (TT) was cut as 107 and 25bp (runout from the gel).

2.6 Primer sequences:
The oligonucleotides sequences (primers) used were those described by RM El-Gohary ***(El-Gohary RM,, et al., 2020).***
Forward primer - 5'- CTCTTCCCACCCCTGTGTCTATC-3'
Reverse primer - 5'-TCCCATAGATAGCCCTCCTAGGTAC-3'

2.7 PCR Mix:
For each DNA sample 25 µl of PCR reaction mixture was prepared containing 5 µl template DNA (final concentration 100-200 ng/ µl), 2.5 µl of 10X *Taq* polymerase buffer (10 mM Tris HCl pH 8.8, 50 mM KCl, 1.5 mM MgCl2, 0.01% gelatin, 0.005% Tween-20, 0.005% NP-40; final concentration 1X; Genetix Biotech Asia Pvt. Ltd., India), 1 µl of 10 mM dNTPs (Banglore Genei, Bangalore, India), 1 µl of 25 pmol/µl of forward and reverse primers specific for IL1- β gene, 0.2 µl of 5U/ µl of *Taq* DNA polymerase (final concentration 1U; Genetix Biotech Asia Pvt. Ltd. India) and sterile water to set up the volume of reaction mixture to 25 µl.

2.8 Thermal profile:
Thermal profile used for the amplification of desired segment of gene was as follows: Initial denaturation at 95˚C for 2 min and 35 cycles of denaturation at 95˚C for 1 min, annealing at 54˚C for 1 min and extension at 74˚C for 1 min, followed by final extension at 74˚C for 10 min. PCR products were separated on 2% agarose gel (2% w/v, Sigma) using a 100 bp molecular weight (MW) marker to confirm the PCR product size of 132 bp.

2.9 Genotyping:
The PCR products were analyzed by electrophoresis on 3% agarose gel then visualized under a UV transilluminator with 100-bp ladder. The amplification products were132 bp for C whereas the 107bp and 25bp of the T allele occurred.

3. RESULTS:

3.1 Detection of STAT6 (rs324011) polymorphism:
The STAT6 gene, including the rs324011 polymorphism, is located on chromosome 12, specifically at the region 12q13.3-q14.1. STAT6 rs324011 (2892C/T) SNP is found in the second intron; interestingly the C→T substitution creates an additional putative binding site for Nuclear Factor κB (NF-κB), therefore, enhancing NF-κB mediated STAT6 gene transcription with concomitant elevated STAT6-mediated IgE production. Genotyping pattern of the wild-type genotype (CC) was not digested and give 132bp whereas the mutated homozygous genotype (TT) was cut as 107 and 25bp (runout from the gel). The heterozygous genotype (TC) was represented as fragments of 132, and 107bp whereas 25bp runout from the gel due to small size of DNA fragments **(Depicted in figure no. 4.2.)**

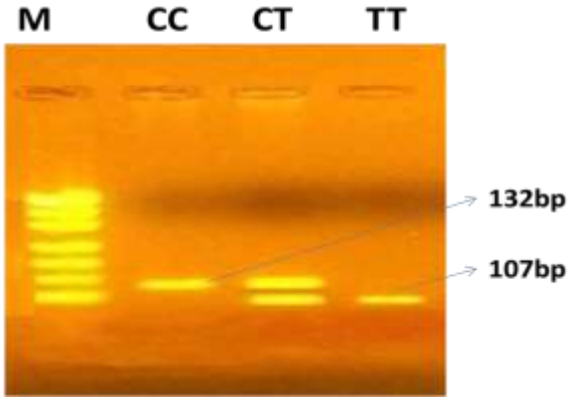


Fig 1: Representative gel picture of STAT6 (rs324011)polymorphism. Lane M represents 50 bp molecular marker, Lane CC Wild type genotype, Lane CT heterozygous genotype and Lane TT variant genotype.

Genotype frequency between Asthma patient and healthy control groups were slightly different and but not significantly associated with Asthma ($\chi 2$=2.025,P=0.3633). Thus allele frequency ($\chi 2$=0.8091, P=0.3684) and carriage rate ($\chi 2$=0.4590, P=0.4981) were also not significantly different between both case and control groups.An odds ratio of 0.7860 in Asthma group respectively for '*CC*' genotype indicated a no role in protective effect of this wild type genotype. In addition, all genotype CT and TT was also not showing protective effects. Data from allele frequency of allele '*C*' was found in large in the population. Here, allele frequency was not showing differences between healthy and disease population. Carriage rate of allele '*C*' was slightly high in CT group whereas carriage rate of allele '*C*' was also high in disease group but no significant association showing in carriage rate. The pattern of genotype and allele distribution in disease and control group suggested no significant association of ***STAT6*** **(rs324011)** gene with Asthma disease

Table 1. Frequency distribution and association of Genotype, allele frequency and carriage rate of *STAT6*gene polymorphism in population of Vindhyan region using Chi Square Test

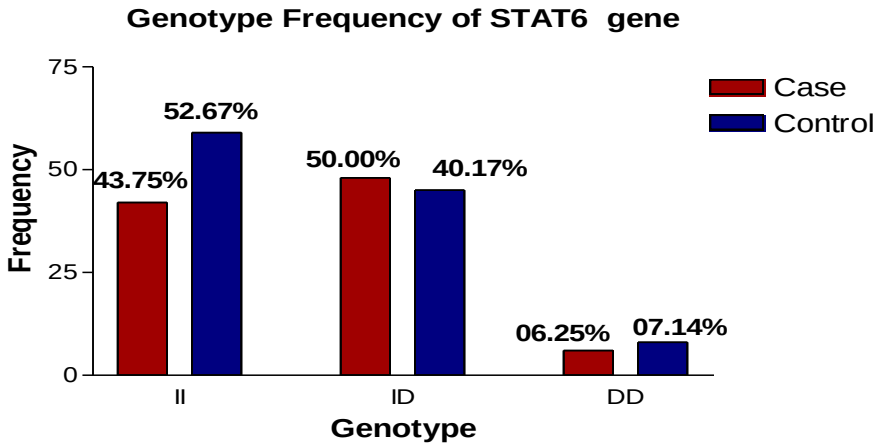
STAT6 **GENE**	**CASE N= 96**		**CONTROL N=112**		**CHI SQUARE VALUE χ^2 (P Value)**
	N	**%**	**N**	**%**	
Genotype					
CC	42	43.75	59	52.67	
CT	48	50.00	45	40.17	2.025 (0.3633ns)
TT	06	06.25	08	07.14	
Allele					
C	132	68.75	163	72.76	0.8091 (0.3684ns)
T	60	31.25	61	27.23	
Carriage Rate					
C	90	62.50	104	66.24	0.4590 (0.4981ns)
T	54	37.50	53	33.75	

(- denotes the level of significant association between case and control.)*
(N – Number of individuals in study group.)
(% - Genotype allele frequency and carriage rate expressed in percentage.

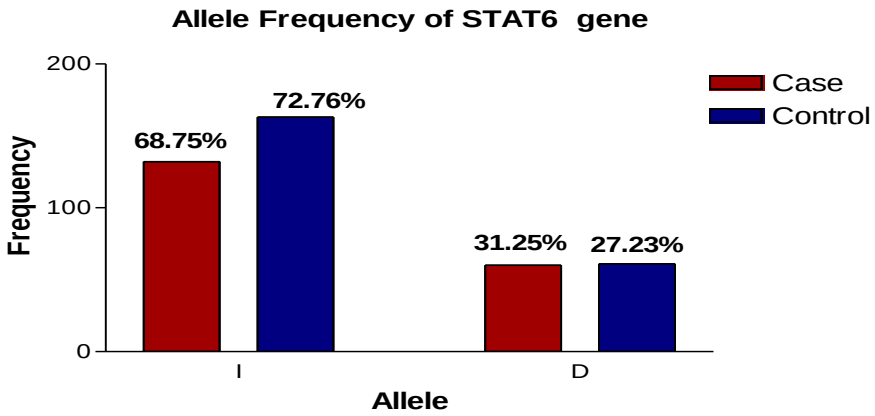
Table 2. Fisher Exact Test values of STAT 6 gene polymorphism

STAT6 **GENE**	**CASE N= 96**		**CONTROL N=112**		**P Value**	**Odds Ratio (95% confidence interval)**
	N	**%**	**N**	**%**		
Genotype						
CC	42	43.75	59	52.67	0.4792	0.7860 (0.4507 to 1.371)
CT	48	50.00	45	40.17	0.1646	1.489 (0.8587 to 2.582)
TT	06	06.25	08	07.14	1.0000ns	0.8667 (0.2897 to 2.593)
Allele						
C	132	68.75	163	72.76		0.8233 (0.5388 to 1.258)
T	60	31.25	61	27.23	0.3877	1.215 (0.7949 to 1.856)
Carriage Rate	90	62.50	104	66.24		0.8494 (0.5295 to 1.363)
C	54	37.50	53	33.75	0.5472	1.177 (0.7339 to 1.889)
T						

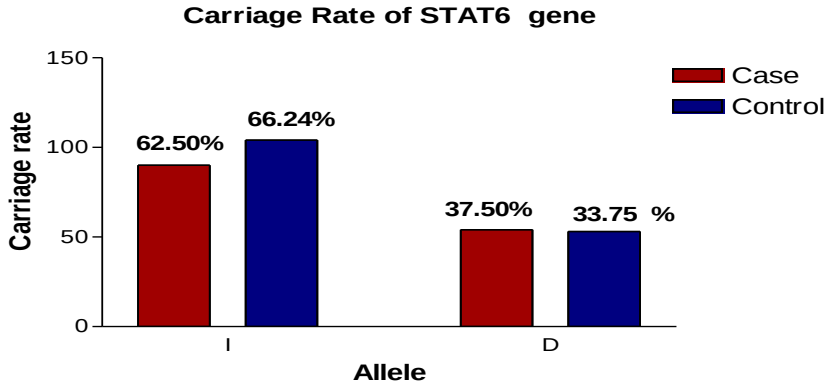
(- denotes the level of significant association between case and control.)*
(N – Number of individuals in study group.)
(% - Genotype allele frequency and carriage rate expressed in percentage.)



Graph 1: Genotype Frequency of *STAT6* gene



Graph 2. Allele Frequency of *STAT6*gene



Graph 3: Carriage rate of *STAT6*gene

4. DISCUSSION:

The polymorphic study Fediv A and Melnik E were also suggested association STAT6 gene polymorphism with Asthma.The distribution of FTO and STAT6 genes polymorphism in patients with bronchial asthma (BA), associated with obesity (Ob) depending on the main disease severity degree [14]. The detection of deletions in FTO and STAT 6 genes was realized by the method of polymerase chain reaction (PCR) using specific primers. In the main group, among patients with BA and Ob, carriers of T/T genotype were 36,84 %, T/A – 45,61 %, A/A – 17,55 % against 40 %, 60 % and 0 % respectively in PHP group by FTO gene. Carriers of C/C genotype in the main group were 38,6 %, C/T – 35,09 %, T/T – 26,31 % against 40 %, 55 % and 5 % respectively in PHP group by STAT6 gene. In the main group the light persisting BA was diagnosed in 20,0 % of cases, middle severity – in 60,0 % and severe – in 20,0 % of patients. In the group of comparison this disease severity was observed in 17,7 %, 66,5 % and 15,8 % of observations, respectively asthma [14].

So, among patients with BA, associated with Ob with the middle and severe course of asthma the percent of heterozygous (T/A) and mutant carriers (A/A) rs9939609 polymorphism of FTO gene is higher than at the light course. The analogous situation is observed at the study of rs324011 polymorphism of STAT6 (C2892T) gene among this category of patients. So, the determination of FTO and STAT6 genes polymorphism in patients with BA, associated with Ob, can be considered as a marker of the more severe course of asthma [13-16].

Signal transducer and activator of transcription 6 (STAT6) is central to type 2 (T2) inflammation, and common noncoding variants at the STAT6 locus associate with various T2 inflammatory traits, including diseases, and its pathway is widely targeted in asthma treatment. asthma [18]. The association of p.L406P with plasma protein levels, white blood cell counts, and the risk of asthma and allergic phenotypes was tested. Significant associations in other cohorts were also tested using a burden test. The effects of p.L406P on STAT6 protein function were examined in cell lines and by comparing $CD4^+$ T-cell responses from carriers and noncarriers of the variant.p.L406P associated with reduced plasma levels of STAT6 and IgE as well as with lower eosinophil and basophil counts in blood. It also protected against asthma, mostly driven by severe T2-high asthma [19].

p.L406P led to lower IL-4–induced activation in luciferase reporter assays and lower levels of STAT6 in $CD4^+$ T cells. We identified multiple genes with expression that was affected by the p.L406P genotype on IL-4 treatment of $CD4^+$ T cells; the effect was consistent with a weaker IL-4 response in carriers than in noncarriers of p.L406P asthma [19]. A partial loss-of-function variant in STAT6 resulted in dampened IL-4 responses and protection from T2-high asthma, implicating STAT6 as an attractive therapeutic target asthma [17-20].

Our study of Genotype frequencies, allele frequencies and carriage rates of *STAT6* (rs324011) alleles are depicted in table no. 4.6. Genotype frequency between Asthma patient and healthy control groups were slightly different and but not significantly associated with Asthma ($\chi 2$=2.025,P=0.3633). Thus, allele frequency ($\chi 2$=0.8091, P=0.3684) and carriage rate ($\chi 2$=0.4590, P=0.4981) were also not significantly different between both case and control groups. An odds ratio of 0.7860 in Asthma group respectively for '*CC*' genotype indicated a no role in protective effect of this wild type genotype. In addition, all genotype CT and TT was also not showing protective effects. Data from allele frequency of allele '*C*' was found in large in the population. Here, allele frequency was not showing differences between healthy and disease population. Carriage rate of allele '*C*' was slightly high in CT group whereas carriage rate of allele '*C*' was also high in disease group but no significant association showing in carriage rate. The pattern of genotype and allele distribution in disease and control group suggested no significant association of *STAT6* (rs324011) gene with Asthma disease.

A murine asthmatic model was used to analyze the in vivo regulatory function of Treg-of-B (P) cells. The data demonstrated that STAT6 played a critical role in the generation of Treg-of-B (P) cells, which confirmed with STAT6-deficient T cells and the STAT6 inhibitor AS1517499 asthma [15,22]. When STAT6 was lacking, Treg-of-B (P) cells exerted impaired suppressive ability with decreased LAG3 expression. Furthermore, Peyer's patch B cells played an essential role in regulatory T cell generation. In the absence of Peyer's patch B cells, T cells expressed decreased phosphorylated STAT6, which was followed by decreased LAG3 expression and impaired suppressive ability, suggesting that Peyer's patch B cells provided the critical signal to activate STAT6 phosphorylation in T cells asthma [6,23].

Moreover, STAT6 deficient Treg-of-B (P) cells could not alleviate inflammation in an animal model of asthma in vivo. IL-4 was downstream of phosphorylated STAT6 and maintained Treg-of-B (P) cell survival with increased expression of Bcl-2 and BclXL. We reported a novel finding that the STAT6-LAG3 signaling axis is important for the induction and function of Treg-of-B (P) cells. Signal transducer and activator of transcription 6 (STAT6) is a key transcription factor involved in both interleukin-4 (IL-4) and IL-13-mediated biological responses, such as allergies asthma [21-24].

The 2964A variant was in significant linkage disequilibrium with the dinucleotide repeat polymorphism, the 13-GT repeat allele of STAT6 exon 1 (p =0.0000000003). There was no association between the STAT6 2964A variant and allergic subjects in a Japanese population (p = 0.2724). The genotype of 13/15-GT repeat allele heterozygosity was significantly associated with allergic subjects (p = 0.0006), as previously reported asthma [5,26]. In one major genotype of the STAT6 exon 1 (15 GT repeat homozygosity), wildtype 2964G allele homozygosity was significantly associated with allergic subjects (p = 0.0382). Genome - wide association studies have shown that particular polymorphism (SNP) or haplotype variants of *STAT6* as well as epigenetic gene modifications are associated with IgE level and asthma in childhood. There are 2 SNPs (rs71802646 and rs320411) with clinical association and proven functional effect on *STAT6* expression asthma [26,27]. The effect of *STAT6* SNPs cumulates in haplotypes and more potently during interaction with SNPs in the genes from the signalling pathway (*IL4*, *IL4Ra*, and *IL13*). Expression of *STAT6* is also influenced by DNA methylation. Atopy is traditionally believed to be maternally inherited but there is one report about paternally over transmitted *STAT6* haplotype (TCA haplotype, built from rs324011, rs3024974 and rs4559 SNPs). *STAT6* polymorphisms and their combinations have an important influence on IgE level and development of asthma. However, the interaction between SNPs in the IL-4 / IL-13 signalling pathway is of greater impact. Hypermethylation of the *STAT6* promoter is also significant in the regulation of *STAT6* expression and this fact opens possibilities for targeting therapy in asthma [25-28].

REFERENCES:

1. Tsabouri S, Mavroudi A, Feketea G, Guibas GV (2017) Subcutaneous and sublingual immunotherapy in allergic asthma in children. Front Pediatr 5: 82-97.
2. Abd El-Salam M, Hegazy AA, Adawy ZR, Hussein NR (2014) Serum level of naphthalene and 1,2benz-anthracene and their effect on the immunologic markers of asthma and asthma\ severity in children-Egypt. Public Health Res 4: 166-172.
3. Liu Y, Zhang H, Ni R, Jia WQ, Wang YY (2017) IL-4R suppresses airway inflammation in bronchial asthma by inhibiting the IL-4/ STAT6 pathway. Pulm Pharmacol Ther 43: 32-38.
4. Ober C, Yao TC (2011) The genetics of asthma and allergic disease: A 21st century perspective. Immunol Rev 242: 10-30.
5. Antczak A, Domańska-Senderowska D, Górski P, Pastuszak- Lewandoska D, Nielepkowicz-Goździńska A, et al. (2016) Analysis of changes in expression of IL-4/IL-13/STAT6 pathway and correlation with the selected clinical parameters in patients with atopic asthma. Int J Immunopathol Pharmacol 29: 195-204.
6. Wynn TA (2015) Type 2 cytokines: Mechanisms and therapeutic strategies. Nat Rev Immunol 15: 271-282.
7. Wang C, Zhu C, Wei F, Gao S, Zhang L, et al. (2017) Nuclear localization and cleavage of STAT6 is induced by kaposi's sarcoma-associated herpesvirus for viral latency. PLoS Pathog 13: e1006124.
8. Schedel M, Frei R, Bieli C, Cameron L, Adamski J, et al. (2010) An\ IgE-associated polymorphism in STAT6 alters NF-kB binding, STAT6 promoter activity, and mRNA expression. J Allergy Clin Immunol 124: 583-589.
9. Shaker OG, Sadik NA, El-Hamid NE (2013) Impact of single nucleotide polymorphism in tumor necrosis factor-α gene 308G/A in Egyptian asthmatic children and wheezing infants. Human Immunol 74: 796-802.
10. Kavalar MS, Balantic M, Silar M, Kosnik M, Korosec P et al. Association of ORMDL3, STAT6 and TBXA2R gene polymorphisms with asthma. Int J Immunogenet 39: 20-25.

11. Li B, Nie W, Li Q, Liu H, Liu S (2013) Signal transducer and activator of transcription 6 polymorphism and asthma risk: A meta-analysis. Int J Clin Exp Med 6: 621-631.
12. Al-Muhsen S, Vazquez-Tello A, Jamhawi A, Al-Jahdali H, Bahammam A, et al. (2014) Association of the STAT6 rs324011 (C2892T) but not rs324015 (G2964A) with atopic asthma in a Saudi Arabian population. Hum Immunol 75:791-795.
13. Godava M, Kopriva F, Bohmova J, Vodicka R, Dusek L, et al. (2012) Association of STAT6 and ADAM33 single nucleotide
14. polymorphisms with asthma bronchiale and IgE level and its possible epigenetic background. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub 156: 236-247.
15. Pykalainen M, Kinos R, Valkonen S, Rydman P, Kilpeläinen M, et al. (2005) Association analysis of common variants of STAT6, GATA3, and STAT4 to asthma and high serum IgE phenotypes. J\ Allergy Clin Immunol 115: 80-87.
16. Berenguer AG, Fernandes AT, Oliveira S, Rodrigues M, Ornelas P, et al. (2014) Genetic polymorphisms and asthma: findings from a case-control study in the Madeira island population. Biol Res 47: 40-51.
17. Kim EG, Shin HJ, Lee CG, Park HY, Kim YK, et al. (2010)DNA methylation and not allelic variation regulates STAT6 expression in human T cells. Clin Exp Med 10: 143-152.
18. Baek KJ, Cho JY, Rosenthal P, Crotty Alexander LE, Nizet V, et al. (2013) Hypoxia potentiates allergen induction of HIF-1 α, chemokines, airway inflammation, TGF- β1, and airway remodeling in a mouse model. Clin Immunol 147: 27-37.
19. Bao ZS, Hong L, Guan Y, Dong XW, Zheng HS, et al. (2011) Inhibition of airway inflammation, hyperresponsiveness and remodeling by soy isoflavone in a murine model of allergic asthma. Int Immunopharmacol 11: 899-906.
20. Shi JP, Li XN, Zhang XY, Du B, Jiang WZ, et al. (2015) Gpr97 is dispensable for inflammation in ova-induced asthmatic mice. PLoS One 10: 398-403
21. Wu YM, Xue ZW, Zhang LL, Gao NM, Du XM, et al. (2015) Comparable function of γ-tocopherols in asthma remission by affecting eotaxin and IL-4. Adv Clin Exp Med 2016; 4: 643-648.
22. Nesi RT, Kennedy-Feitosa E, Lanzetti M, Ávila MB, Magalhães CB,\ et al. (2017) Inflammatory and oxidative stress markers in experimental allergic asthma. Inflammation 40: 1166-1176.
23. Alasandagutti ML, Ansari MS, Sagurthi SR, Valluri V, Gaddam S (2017) Role of IL-13 genetic variants in signalling of asthma. Inflammation 40: 566-577.
24. Kupryś-Lipińska I, Molińska K, Kuna P (2016) The effect of omalizumab on eosinophilic inflammation of the respiratory tract in patients with allergic asthma. Pneumonol Alergol Pol 84: 232-243.
25. Malmström K, Lohi J, Sajantila A, Jahnsen FL, Kajosaari M, et al. 2017) Immunohistology and remodeling in fatal pediatric and adolescent asthma. Respir Res 18: 94-99.
26. Motomura Y, Morita H, Moro K, Nakae S, Artis D, et al. (2014) Basophil-derived interleukin-4 controls the function of natural helper cells, a member of ILC2s, in lung inflammation. Immunity 40: 758-771.
27. Cheng LE, Sullivan BM, Retana LE, Allen CD, Liang HE et al. (2015) IgE-activated basophils regulate eosinophil tissue entry by modulating endothelial function. J Exp Med 212: 513-524.
28. Li J, Lin LH, Wang J, Peng X, Dai HR, et al. (2014) Interleukin-4 and interleukin 13 pathway genetics affect disease susceptibility, serum immunoglobulin E level and gene expression in asthma. Ann Allergy Asthma Immunol 113: 173-179.