Interferon Gamma Gene Polymorphism
As a Marker of Atopy In Egyptian Asthmatic Patients
Research Article

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Summary

Background and Objectives: Interferon gamma (IFN-γ) is one of the most important endogenous mediators of immunity and inflammation, produced by Th1 cell lineage. Aberrant production of IFN-γ has been described in a multitude of autoimmune and chronic inflammatory diseases. IFN-γ plays an important anti-inflammatory role in asthma by suppressing tumour necrosis factor (TNFα) signaling, and expression of IL-6, IL-8, and eotaxin induced by exposure to TNF-α. It also induces inflammatory genes such as vascular endothelial growth factor (VEGF) and expression of IL-17 receptors. The current study aimed to clarify the association between IFN-γ gene polymorphism, total IgE level and absolute eosinophilic count in patients suffering from bronchial asthma, and to evaluate the correlation of various IFN-γ gene genotypes with the occurrence of acute status asthmaticus.

Patients and Methods: The study included 30 patients suffering from bronchial asthma, and 10 normal volunteers as a control group. For all patients and controls total IgE was measured by Enzyme Linked Immunosorbent Assay (ELISA), the IFN-γ gene polymorphism at position +874 was determined by Amplification Refractory Mutation System (ARMS) Polymerase Chain Reaction, and absolute eosinophilic count was recorded.

Results: There was a significant association between genotypes & the frequency of the A allele of the +874 T/A polymorphism in asthmatic patient when compared with controls.
while there was no significant difference between the genotypes IFN-γ regarding IgE level and eosinophilic count.

Conclusion: The presence of AA gene polymorphism of IFN-γ gene is an indicator of the inflammation in asthmatic patients and is therefore a good target for therapeutic strategies.

I. Introduction:
Asthma is a chronic disease of airways which is recognized as a highly prevalent health problem in the developed and developing world. Asthma is characterized by bronchial inflammation, airway hyper-responsiveness induced by specific and nonspecific stimuli, and reversible bronchial obstruction with the appearance of respiratory symptoms such as dyspnea, chest tightness, wheezing, and cough. Airway inflammation plays a central role in the pathogenesis of bronchial asthma and is associated with an increase in airway responsiveness to several trigger factors such as aeroallergens which induce bronchoconstriction in atopic asthma patients. The pathogenesis of bronchial asthma is not completely understood and it is well known that this clinical condition has a multifactorial etiology (Amato et al., 2007).

Asthma is a complex genetic disorder with several overlapping phenotypes. There is strong evidence of a genetic component in asthma. Multiple environmental factors are also known to modulate the clinical expression of asthma as well as the asthma associated phenotypes: bronchial hyperresponsiveness, atopy, and elevated IgE. It is a commonly held view that asthma is caused by multiple interacting genes, some having a protective effect and others contributing to the disease pathogenesis, with each gene having its own tendency to be influenced by the environment (Ober C., 2005).

For a long time, the production of IFN-γ has been considered to be restricted to activated natural killer (NK) cells, CD4+ T helper-1 (Th1) cells, and CD8+ T cytotoxic cells. However, we now know that these cells are the most potent, but not the only sources of IFN-γ. Several studies have identified additional IFN-γ-secreting cell types, including γδ T cells, NKT cells, macrophages, dendritic cells, naive CD4+ T cells, and even B cells (Szabo et al., 2003).

IFN-γ gene is located on chromosome 12q14, the functional SNP at position +874 (T/A) is located at the 5'-end of the first intron of human IFN-γ gene. The T allele correlates with high IFN-γ expression. Transcriptional factor and Nuclear Factor Kappa Beta (NF-kB) binds preferably to DNA containing IFN-γ +874 T allele and increases the expression IFN-γ gene. Association studies have shown variable results in different ethnic populations with AA phenotype associated with pulmonary disease (Hashemi et al., 2011).

IFN-γ plays a key role in macrophage activation, inflammation, host defense against intracellular pathogens, Th1 responses, and tumor control. In parallel, IFN-γ exerts regulatory functions to limit tissue damage associated with inflammation and to modulate Th (T-helper) and Treg (T-regulator) differentiation. IFN-γ can either augment or suppress autoimmunity and associated pathology in a context-and disease-specific manner (Stark GR., 2007).
Th1 cytokines such as interferon (IFN) γ, IL-12, and IL-2 are thought to have an inhibitory effect on Th2 cells and decrease the amount of IL-4, IL-5, IL-13 and IgE production (Renaud, 2001) IFN-γ producing Th1 cells have been reported to protect against allergic responses by attenuating the activity of Th2 effector cells (Marsh et al., 1994)

We analyzed the allelic distribution of the +874 T/A polymorphism of the IFN-γ gene in bronchial asthma, its relationship with IgE level and absolute eosinophilic count as atopic markers, and the relationship between the allele and disease severity.

II. Patients and Methods:

The current study included 30 patients suffering from bronchial asthma who were recruited from the outpatient chest clinic, beni suef University Hospital, beni suef, Egypt between January and June 2012. Among the 30 patients, 19 were females and 11 were males, 20 patients suffered from chronic asthma while 10 were in acute status asthmaticus. Ten normal age and sex matched volunteers were included as control group.

All cases and controls were subjected to detailed history taking, complete clinical examination, and lab investigations including: complete blood count, absolute eosinophilic count, total serum IgE by ELISA and genotyping of IFN-γ gene to detect genetic polymorphism at position +874 by ARMS-PCR.

II.A. Blood Sample Collection

Eight ml blood was withdrawn under complete aseptic conditions, and divided into 3 portions: 3 ml of whole blood was collected in sterile EDTA-containing tubes for DNA extraction and PCR, and 2 ml was collected in another sterile EDTA-containing tube for complete hemogram and absolute eosinophil counts that were determined according to Burrows et al (Burrows et al., 1980) The remainder was left for 30 to 60 minutes for spontaneous clotting at room temperature before being centrifuged at 3000 rpm for 10 minutes to obtain serum. Serum samples were kept frozen at –20°C for determination of total IgE that was measured by ELISA using AccuBind IgE Quantitative Kits, (Lake Forest, California, USA).

II.B. Detection of IFNγ gene polymorphism by ARMS-PCR

Genomic DNA was isolated using the Genomic DNA Purification Kit (GeneJET Genomic DNA Purification Kit, #K0721).

Genotyping for the polymorphisms in IFN-γ was performed according to Pravica et al (Pravica et al., 2000) and genes were typed using the Amplification Refractory Mutation System Polymerase Chain Reaction (ARMS-PCR). To assess the success of PCR amplification in both reactions, an internal control was amplified using a pair of primers designed from the nucleotide sequence of the human growth hormone (HGH).

The primer sequences used for amplification were as follows: allele-specific sense primer T 5'-TTC TTA CAA CAC AAA ATC AAA TCT-3'; allele-specific sense primer A 5'-TTT TTA CAA CAC AAA ATC AAA TCA-3'; antisense common primer of IFN-γ 5'-TCA ACA AAG CTG ATA CTC CA-3'; control primer (HGH) (sense), 5'-CCTTCCAAC CAT TCC CTT A-3'; control primer (HGH) (antisense), 5'-TCA CGG ATTTCT GTG GTG TTTC-3'. The reaction mix of the total volume of 25 µL included 12.5 µL Taq PCR Master Mix, 5 µL of the extracted DNA, 1µL of the allele specific sense T or A, 1 µL of anti-sense common primer for interferon gamma, 1 µL of control primer sense, 1 µL of control primer of anti-sense and 3.5 µL of deionized water.

Amplification was performed using a DNA thermal cycler (Perkin Elmer 9700 Gene
amplification PCR system) according to the 10 cycles of 95°C for 15 seconds, 62°C for 50 seconds, and 72°C for 40 seconds, then 20 cycles of 95°C for 20 seconds, 56°C for 50 seconds and 72°C for 50 seconds. The amplified products were separated by electrophoresis on a 3% agarose gel stained with ethidium bromide. The gel was visualized under a UV transilluminator with a 100–1000 base pair (bp) DNA ladder ready to use (gene ladder™) and photographed.

II.C. Statistical Analysis
The SPSS 10.0 for windows was used for data management and analysis and the Microsoft power point for charts. Parametric quantitative data were presented as mean±SD. For comparison of the group means, the Student's t-test was used. Non parametric quantitative data were expressed as median (percentiles), and Mann-Whitney test was used for comparison of medians. Qualitative data was expressed as frequency and percentage. Association between qualitative data was done using Chi-square test. Spearman correlation coefficient was used to correlate between qualitative variables. Risk estimate was done by odds ratio. P value was considered significant <0.05 (Knapp RG., 1992).

III. Results:
The current study was carried out on 30 patients with bronchial asthma, clinical data of which were presented in Table 1. Ten normal age and sex matched normal volunteers were included in the study as a control group.

Assessment of the genotyping of patients for IFN-γ gene by ARM-PCR showed that 14 (46.7%) patients had AA genotype, 9 (30%) had TA genotype and 7(23.3%) had TT. Four (40%) of control had TA genotype, 6 (60%) had TT and none had AA genotype. In regards to acute asthmatic patients it was found that 8 (80%) had AA genotype, 2 (20%) had TT and none had TA following protocol; 95°C for 1 minute followed by

Two sample products were available for each participant (1 for each specific T or A allele of the IFN-γ alleles).

ARMS-PCR for the polymorphisms in IFN-γ (+874T/A) revealed a 500-bp product for HGH as a control gene, and a 300-bp product for T874 (homozygous for allele T; TT), or A874 (homozygous for allele A; AA), or both alleles T and A (heterozygous; TA) (Figure 1).

On comparing the control group to all patents group in regards to their clinical data (Table 1): There was no statistically significant difference found between studied and control group in regards to Age (P-value > 0.05) and Sex (P-value > 0.05). While comparing control group to all patients group in regards to their laboratory data (Table 1): There was a statistically significant difference between all patients group and control group in regards to Absolute Eosinophilic Count (P-value 0.001) and Total Serum IgE (P-value 0.005).

Comparing chronic asthmatic patients to patients with acute status asthmaticus in regards their clinical data (Table 1): There was no statistically significant difference found between chronic asthmatic patients and patients with acute status asthmaticus in regards to Age (P-value > 0.05) and Sex (P-value > 0.05), while comparing chronic asthmatic patients to patients with acute status asthmaticus in regards to their laboratory data (Table 1): There was a statistically significant difference between chronic asthmatic patients and patients with acute status asthmaticus in regards to Absolute Eosinophilic Count (P-value 0.001) and Total Serum IgE (P-value 0.001).

Comparing control group to all patients group as regards IFN-γ genotypes (Table 2) there was a high statistically significant difference in IFN-γ genotypes frequencies between all patients group.
and control group (P-value 0.006).

Also comparing control group to different patients group as regards IFN-γ genotypes (Table 2 & Figure 2) there was a high significant difference in IFN-γ genotypes frequencies between chronic asthmatic patients, acute asthmatic patients and control groups.

Also there is increased frequency of IFN-γ genotype AA among asthmatic patients especially acute asthmatic patients compared to the control group (P-value 0.005).

Table 1. Comparison between asthmatic patients, and control group for age, sex, blood eosinophilic count and serum total IgE

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All asthmatic Patients</th>
<th>Chronic asthmatic</th>
<th>Acute asthmatic</th>
<th>Control</th>
<th>P-value</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of subjects</td>
<td>30</td>
<td>20</td>
<td>10</td>
<td>10</td>
<td>0.546*</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.524**</td>
<td></td>
</tr>
<tr>
<td>Age (Year)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>14-75</td>
<td>14-75</td>
<td>18-68</td>
<td>25-65</td>
<td>0.457*</td>
<td>NS</td>
</tr>
<tr>
<td>Mean±SD</td>
<td>46.4±16</td>
<td>44.2±16.5</td>
<td>50.8±14.7</td>
<td>42.2±13.04</td>
<td>0.413**</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F/M</td>
<td>19/11</td>
<td>12/8</td>
<td>7/3</td>
<td>5/5</td>
<td>0.462*</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.666**</td>
<td></td>
</tr>
<tr>
<td>Absolute eosinophilic count (cell/mm³)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>200-1521</td>
<td>200-1206</td>
<td>770-1521</td>
<td>60-204</td>
<td>0.001*</td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>708.5±390.4</td>
<td>510.3±271.6</td>
<td>1105±270.8</td>
<td>108.9±48.6</td>
<td>0.001**</td>
<td>HS</td>
</tr>
<tr>
<td>Total serum IgE (IU/ML)</td>
<td>55-918</td>
<td></td>
<td>61-99</td>
<td></td>
<td>0.005*</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>358.3±289.8</td>
<td>55-774</td>
<td>292-918</td>
<td>81.4±13.1</td>
<td>0.001**</td>
<td>HS</td>
</tr>
<tr>
<td>--------</td>
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</tr>
<tr>
<td>Mean±SD</td>
<td>507.8±178.9</td>
<td>659.5±227.8</td>
<td>659.5±227.8</td>
<td>81.4±13.1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NS: non significant
HS: highly significant

*comparing all patients group to control group
**comparing Acute to chronic patients group

Table 2. Comparison between asthmatic patients and control group for IFN-γ gene genotype

<table>
<thead>
<tr>
<th>Genotype</th>
<th>All asthmatic patients (n=30)</th>
<th>Chronic asthmatic (n=20)</th>
<th>Acute status asthmatic (n=10)</th>
<th>Control (n=10)</th>
<th>P-value</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>AA</td>
<td>14(46.7%)</td>
<td>6(30%)</td>
<td>8(80%)</td>
<td>0(0%)</td>
<td>0.006*</td>
<td>HS</td>
</tr>
<tr>
<td>TA</td>
<td>9(30%)</td>
<td>9(45%)</td>
<td>0(0%)</td>
<td>4(40%)</td>
<td>0.005**</td>
<td></td>
</tr>
<tr>
<td>TT</td>
<td>7(23.3%)</td>
<td>5(25%)</td>
<td>2(20%)</td>
<td>6(60%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NS: non significant
HS: highly significant
*comparing all patients group to control group
**comparing Acute to chronic patients group

Table 3. Comparison between different genotypes AA, TA and TT and age, sex, blood eosinophilic count and serum total IgE

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>AA (n=14)</th>
<th>TA (n=9)</th>
<th>TT (n=7)</th>
<th>P-value</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Year)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>25-72</td>
<td>14-75</td>
<td>17-60</td>
<td>0.398</td>
<td>NS</td>
</tr>
<tr>
<td>Mean±SD</td>
<td>50.2±14.6</td>
<td>45.3±17.8</td>
<td>40.1±16.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>F/M</td>
<td>5/4</td>
<td>4/3</td>
<td>0.698</td>
<td>NS</td>
</tr>
<tr>
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<td>-----</td>
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<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Blood eosinophilic count (cell/mm³)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>351-1521</td>
<td>200-1206</td>
<td>210-1359</td>
<td>0.326</td>
<td>NS</td>
</tr>
<tr>
<td>Mean±SD</td>
<td>821.6±403.8</td>
<td>581.3±34.6</td>
<td>645.7±412.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total serum IgE (IU/ML)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>113-918</td>
<td>55-774</td>
<td>96-867</td>
<td>0.467</td>
<td>NS</td>
</tr>
<tr>
<td>Mean±SD</td>
<td>415.9±308.1</td>
<td>260.3±239.8</td>
<td>369.3±318.4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NS: non significant

**Figure 1.** Amplification Refractory Mutation System-Polymerase Chain Reaction for IFN-γ polymorphism: Agarose gel electrophoresis showing ARM-PCR for polymorphism of IFN-γ gene at position (+874T/A). Every
participant was presented by 2 lanes for T and A alleles, respectively, revealed a 500-bp product for HGH as a control gene, and a 300-bp product for T874 (homozygous for allele T; TT), or A874 (homozygous for allele A; AA), or both alleles T and A (heterozygous; TA).

Lanes 1,2 show a control case with (TA) genotype, Lanes 3,4 show a case with (TT) genotype, Lanes 5,6 show a case with (TA) genotype, Lanes 7,8 show a case with (AA) genotype, Lanes 9,10 show a case with (AA) genotype, L

Gene ladder contains (100-1000) base pairs.

Figure 2. Comparison between patients with chronic asthma, patients with acute status asthmatic and control group in regards to different genotypes.

IV. Discussion

Asthma is a clinical event caused by immune mechanisms in response to exposure to allergens. These events may or may not harm the host. These mechanism are activated by immunoglobulin E (IgE), which leads to release of mast cell mediators (Sicherer et al., 2007).

More than 20% of the world's population is thought to have IgE-mediated allergic diseases. This prevalence is rising dramatically, with its consequent effects on health care and costs (Asher and Dagli, 2004).

The development of atopic asthma depends on several genes. Disease expression is influenced by exposure to environmental factors. Several genome-wide searches have linked the development of asthma to different autosomal chromosomal regions, many of which directly or indirectly regulate IgE production and affect the activation and proliferation of cells involved in inflammatory processes associated with atopy (Wright AL., 2004).

The regions that have been most consistently reported to be in linkage or association with asthma include the cytokine gene cluster on chromosome 5 (including IL-3, IL-4, IL-5, IL-9, and IL-13), chromosome 12 (Stem Cell Factor, Interferon Gamma (IFN-γ), Insulin-Like Growth Factors, and STAT-6), and chromosome 16 (IL-4R), suggesting that these regions may harbor genes that contribute.
to the development of asthma and allergies (Hakonarson and Halapi, 2002)

IFN-γ is a dimerized soluble cytokine that is the only member of the type II class of interferons. This interferon was originally called macrophage-activating factor, a term now used to describe a larger family of proteins to which IFN-γ belongs. In humans, the IFN-γ protein is encoded by the IFN-γ gene (Zhu et al., 2010)

IFN-γ cytokine is critical for innate and adaptive immunity against viral, intracellular bacterial infections and tumor control. Aberrant IFN-γ expression is associated with a number of autoinflammatory and autoimmune diseases. The importance of IFN-γ in the immune system stems in part from its ability to inhibit viral replication directly and most importantly from its immunostimulatory and immunomodulatory effects. IFN-γ is produced predominantly by natural killer cells as part of the innate immune response, and by CD4 and CD8 T lymphocyte cells (Schoenborn and Wilson, 2007)

In the current study, the IFN-γ gene was screened to determine variations at position +874 and evaluate whether these variations are associated with clinical asthma or the severity of asthma.

Thirty asthmatic cases were included in this study, 19 female and 11 male, 20 patients with chronic asthma and 10 patients with acute status asthmaticus. The study also included 10 healthy non asthmatic individuals as controls. All asthmatic cases and controls were subjected to complete blood analyses, absolute eosinophilic count and total serum IgE level by ELISA and genotyping of the interferon gamma gene polymorphism using ARM-PCR.

On comparing asthmatic patients to control group in regards to absolute blood eosinophilic count and serum total IgE, we found that the mean blood eosinophilic count was significantly higher among the asthmatic group than control group (p-value 0.001) (Table 1).

In accordance with our results Bettiol et al., 2000, Karjalainen et al., 2003 Koh et al., 2005 Hussein., et al 2009 had found significantly higher percentages of blood and sputum eosinophils among atopic and non atopic asthmatic patients when compared to normal controls. Also we found that the mean IgE level was significantly higher among the asthmatic group compared to the control group (p-value 0.005) (Table 1) and this was in accordance with findings of Bettiol et al., 2000 and Humbert M, 2000 who suggested that the mean IgE levels obtained from asthmatic study group did not differentiate between atopic and non atopic asthmatics, but the control cases had significantly lower levels of IgE. In contrast to these findings Akpınarlı et al., 2002 reported that total IgE was significantly higher in atopic asthmatics compared to non-atopic asthmatics, and non-atopic non-asthmatics.

Hussein et al., 2009 reported in their study that total IgE was higher in atopic asthmatic patients than in control. Johansson and Lundahl, 2001 also found that mean total serum IgE in atopic asthmatic children was higher than that of the control patients, while Kaliner, 1996 found that 40% of allergic asthmatics had normal total IgE levels.

Also on comparing acute to chronic asthmatic patients as regards their absolute blood eosinophilic count and serum total IgE, there was a high statistically significant difference in the mean blood eosinophilic
count being significantly higher among acute asthmatic patients than chronic asthmatic patients (P-value 0.001), and the mean IgE level being significantly higher among acute asthmatic patients than chronic asthma patients (P-value 0.001) (Table 1). These results were consistent with those of Hussein et al., 2009 who detected a significant association between total IgE levels, eosinophil count and disease severity in the atopic groups.

On detecting genetic polymorphisms in IFN-γ gene using ARM-PCR technique in acute asthmatic patients, chronic asthmatic patients and control subjects. Results showed high statistically significant difference in IFN-γ genotypes frequencies between chronic asthmatic patients, acute asthmatic patients and control groups, also there is increased frequency of IFN-γ genotype AA among asthmatic patients especially acute asthmatic patients compared to the control group (P-value 0.005) (Table 2).

These results agreed with those of YM Hussein et al., 2009 who demonstrated that the frequency of allele A874 was greater in atopic patients than in control patients, and that this correlates with markers of atopy (increased IgE levels and eosinophil count and decreased IFN-γ titers).

Previous studies of the IFN-γ gene variants have shown discrepant results. Pravica et al., 2000 reported that the single nucleotide polymorphism, T—A, at the 5’ end of the CA repeat of the human IFN-γ gene (+874T/A) directly affects the level of IFN-γ production and correlates with the presence of the A874 allele and low production of IFN-γ. The authors proposed that this polymorphism coincided with a nuclear factor □B (NF-□B) binding site that could have functional consequences for transcription of the human IFN-γ gene, with the result that the polymorphism could directly influence the level of IFN-γ production. However, Ohly, 2006 revealed that there was no significant association between the +874T/A polymorphism and IgE level in atopic German newborns.

This discrepancy could be due to differences in population and age groups; in other words, each analysis may identify the allele or haplotype responsible for the phenotype in that specific population.

On comparing patients with different IFN-γ gene genotypes (AA,TA and TT) as regards their age, sex, blood eosinophilic count and serum total IgE, we found that there was no statistically significant difference between different genotypes, (P-value 0.326) for blood eosinophilic count and (p-value 0.467) for mean IgE level (Table 3).

The present study revealed no significant difference between IFN-γ gene polymorphism and peripheral blood eosinophil count, and total IgE levels in all asthmatic patients. This may simply reflect the fact that IFN-γ expression is a surrogate marker of TH1 cell activation and reflects its down regulation in blood eosinophilia and serum IgE levels. This data support the hypothesis that a normal level of IFN-γ synthesis regulates disease severity in atopic diseases, as activated B-cell clones could remain active (perhaps for years) and produce IgE. Nevertheless, IgE-mediated local release of mast cells in atopic areas could lead to acute exacerbations of atopic manifestations after acute allergen exposure, although this does not imply an obligatory role for IFN-γ /IgE in the pathogenesis of chronic atopic diseases.
In conclusion, the IFN-γ gene polymorphism at position +874 AA genotype may be a good target for therapeutic strategies in asthma.

Finally, we suggest that the identification of variants of the IFN-γ gene and their role in the development of asthma may provide a focus for the development of novel diagnostic and therapeutic strategies.

References:


Bettiol J, Bartsch P and Louis R et al. (2000) Cytokine production from peripheral whole blood in atopic and non atopic asthmatic: relationship with blood and sputum eosinophilia and serum IgE levels, Allergy, 55(12), 1134-1141.


