MEMBRANE AND SOLUBLE LOW AFFINITY IgE RECEPTOR CD23 EXPRESSION, CYTOKINE PROFILES AND SERUM IgE IN BOTH ALLERGIC RHINITIS AND ATOPIC DERMATITIS.

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The membrane low affinity IgE receptor (CD23), its soluble fragment (sCD23 or IgE binding factor), Interleukin 4 (IL-4) and Interferon γ (IFN-γ) are considered to be immunomodulators of the IgE synthesis.The degree of CD23 expression seems related to a probable dysregulation of the IgE synthesis and with the type of allergic disease. We have investigated the membrane CD23 expression on peripheral blood mononuclear cells and its relationship with serum levels of sCD23, IL-4, IgE and IFN-γ. Forty three atopic patients, 27 with perennial allergic rhinitis (PAR) and 16 with atopic dermatitis (AD) were selected. Twenty healthy non-atopic subjects were used as age matched controls. Expression of membrane CD23 on CD3, CD4 and CD8 T cell subsets, B cells and NK cells were analyzed by two color flow cytometry, while sCD23, IL-4, IgE and IFN-γ were measured by ELISA or RIA techniques. We found in children patients increased values of CD19 + cells, being this increase highly significant in the PAR group. A relevant group of patients also showed a significant increase in CD19+/CD23+ cells and serum levels of IgE, with the highest values of IgE in the AD group. The cytokines were comparable to controls. However, children (controls and patients) exhibited higher values of sCD23 than adults. Thus, membrane and sCD23 may play important roles in the immunopathology of IgE synthesis in both PAR and AD.

Key words: Low affinity IgE receptors. Soluble CD23. Perennial allergic rhinitis. Atopic dermatitis

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NIVELES DEL RECEPTOR DE IgE DE BAJA AFINIDAD CD23, SU FRACCION SOLUBE, CITOCINAS E IgE SERICA, EN PACIENTES CON RINITIS ALERGICA PERENNE Y DERMATITIS ATOPICA.

El receptor deIgE de baja afinidad CD23, su fragmento soluble (sCD23 o factor de unión de IgE), interleucina 4 (IL-4) e interferón γ (IFN-γ), son considerados como los inmunomoduladores de la síntesis de IgE. El grado de expresión de CD23 parece estar relacionado con una alteración en la síntesis de IgE y con el tipo de enfermedad alérgica. Nosotros hemos investigado la expresión de CD23 de membrana en células mononucleares de sangre periférica y su relación con los niveles séricos de sCD23, IL-4, IgE e IFN-γ. Seleccionamos 43 pacientes atópicos, 27 con rinitis alérgicas perenne (PAR) y 16 con dermatitis atópica (AD). Escogimos como grupo control 20 indivíduos sanos no atópicos, con edades similares a los pacientes. La expresión de CD23 de membrana en linfocitos T CD3 y sus subpoblaciones CD4 y CD8, así como en linfocitos B y células NK, fue analizado por citometría de flujo utilizando la técnica de marcaje doble con anticuerpos monoclonales específicos conjugados con dos fluorocromos independientes, mientras que los niveles séricos de sCD23, IL-4, IgE e IFN-γ fueron determinados por técnicas de ELISA y RIA. Encontramos valores aumentados de linfocitos B CD19+ en el grupo de niños, siendo dicho aumento significativo con los niños con PAR. En un número relevante de pacientes, observamos un aumento importante de los linfocitos CD19+/CD23+ y de los niveles séricos de IgE, con los valores más altos de IgE en AD. Los niveles de las citocinas evaluadas fueron similares entre pacientes y controles. Sin embargo, los niños (controles y pacientes) exhibieron niveles de sCD23 más elevados que los adultos, sugiriendo que la expresión del CD23 en la membrana del linfocito B o en forma soluble parece tener un papel importante en la inmunopatología de la síntesis de IgE, tanto en PAR como en AD.

Palabras Claves: Receptor de baja afinidad de IgE. CD23 soluble. Rinitis alérgica perenne. Dermatitis atópica.

Abbreviations: PAR: perennial allergic rhinitis. AD: atopic dermatitis. PBMC: peripheral blood mononuclear cells. sCD23: soluble CD23

INTRODUCTION

Allergic rhinitis and atopic dermatitis are characterized by a high and sustained synthesis of IgE following stimulation by environmental antigens (allergens) [1]. Perennial allergic rhinitis (PAR) is considered a classical immediate hypersensitivity reaction [2], while atopic dermatitis (AD) is a chronic eczematous reaction characterized by pruritus and lichenification, onset during childhood and an association with other forms of atopy in the patient or in the patient's family [3]. Several reports have suggested that the etiology of both entities involves alterations in the regulation of immunoglobulin E (IgE) production [4-6].

A complex network has been implicated in the regulation of IgE synthesis including several cell types and lymphokines. One factor considered as a major regulator of IgE is the membrane low affinity receptor for IgE, FcεRII, also designated as CD23. Therefore, alterations in CD23 production may play a role in the pathogenesis of allergic diseases [5]. CD23 exists in two forms, FcεRIIa and FcεRIIb. These forms differs only in six amino acids [6]. This membrane bound structure may be cleaved to produce soluble products (sCD23) with molecular weights between 25-23 and 37 kD [6].

CD23 is a multifunctional molecule, which may exert different functions according to the cell type on which it is expressed. For instance, on eosinophils, platelets and monocytes, CD23 mediates IgE dependent cellular cytotoxicity against parasites [7] as well as IgE-dependent release of inflammatory mediators [8].

On antigen presenting cells (Langerhans and B cells), CD23 focuses on the IgE-dependent presentation of antigen to T cells [9]. On the other hand, sCD23 has a number of biological functions. Its main activity appears to be the competitive binding of IgE, thus preventing binding of IgE by membrane bound CD23 [10]. Biological effects include stimulation of primed or ongoing IgE production [11] and inhibition of spontaneous migration by monocytes [12].

We report herein the universal presence and the significative increase of the expression of membrane CD23 on B cells of both PAR and AD patients.

Table 1. Phenotypic analysis of PBMC in children (Patients vs controls)

	Controls (n=10)		PAR (n=14)		AD (n=13)	
	mm^3	%	mm^3	%	mm^3	%
Leucocytes	6380±546		7117±576		8919±540 [1]	
Lymphocytes	2769±386	43±4	3877±469	54±4	4227±501	48±5
CD3+	2102±362	74±3	2517±299	66±3	3009±363	71±2
CD4+	1096±196	40±3	1372±181	36±2	1614±248	36±3
CD8+	771±162	27±2	935±166	24±3	1056±202	24±3
CD19+	246±37	10±2	687±149 [1]	16±2	476±83	13±2
CD56+	324±83	11±2	652±149	16±3	593±79 [1]	14±1

Results are expressed as the arithmetic mean ± standard error of absolute (cells/mm^3) and percentage (%) values of cells with positive fluorescence by flow cytometry.
[1] $p<0.05$ when compared to controls.

Table 2. Phenotypic analysis of PBMC in adults (Patients vs controls).

	Controls (n=10)		PAR (n=13)		AD (n=3)	
	mm^3	%	mm^3	%	mm^3	%
Leucocytes	5980±433		6844±695		6463±288[c]	
Lymphocytes	2033±150	34±2	2292±258[b]	34±3[b, l]	2361±130	37±2
CD3+	1469±102	73±2	1613±156[b]	73±2	1379±38[c]	58±2[c, l]
CD4+	871±76	43±2	1194±242	41±3	738±23	31±1*
CD8+	535±47	27±2	569±78[b]	25±2	645±103[c]	27±2
CD19+	207±27	10±1	265±50[b]	11±1[b]	184±56	8±2
CD56+	420±65	20±3[a]	430±75	18±2	621±174	26±7

Results are expressed as the arithmetic mean ± standard error of absolute (cells/mm^3) and percentage (%) values of cells with positive fluorescence by flow cytometry.
[l]p<0.05 when compared to controls.[a] p<0.05 when compared to control children. [b] p<0.05when compared to PAR children. [c] p<0.05 when compared to AD children

MATERIALS AND METHODS

Patients

The patients consisted of 43 individuals from the Allergic Diseases outpatient clinic of the Institute of Immunology of Central University Medical School. Twenty seven were children (< 12 years): 14 had PAR (6 males and 8 females, mean age 7 + 1 years) and 13 had AD (4 males and 9 females, mean age 6 + 1 years). Sixteen patients were adults: 13 had PAR (5 males and 8 females, mean age 22 + 4 years) and 3 had AD (1 males and 2 females, mean age 22 + 4 years). All patients had eosinophilia (>350 eosinophils/mm^3). Parasitic infection was ruled out by serial stool tests as previously reported [13]. Increased eosinophils in the nasal cytology smears (>25% of total cells) were universally present in PAR patients; in addition, positive Prick test for aeroallergens (*Dermatophagoides pteronyssinus and farinae*, tobacco, dust, mold, grass, weed, tree and feather mix) and/or food antigens (chocolate, corn, rice, potato, chicken, pork, cow's milk, tomato, egg, shellfish, fish and citrus mix) (Hollister Stier Laboratories, Spokane, USA) were elicited in both groups.

The control group consisted of 10 children (4 males and 6 females, mean age 7 + 1 years) and 10 adults (5 males and 5 females, mean age 29 + 2 years); none had history of allergic diseases. Hematology and stool tests were normal. Prick tests employing the same set of allergens, were negative.

Measurement of serum IgE

Serum IgE levels were analyzed by Quanticlone IgE RIA kit (Kallestead Diagnostic, Chaska MN, USA) with a normal range from 0 to 180 U.I./ml as previously established [13].

Cell phenotype analysis

Cell surface molecules were determined by single and dual color flow cytometry (EPICS-753 Coulter Corporation, Hialech FI USA). FITC or RD1 tagged monoclonal antibodies against CD3, CD4, CD8, CD19, CD56 and CD23 (Coulter Corporation) were added to peripheral blood mononuclear cells (PBMC) obtained by centrifugation over Ficoll-Hypaque gradients [14]; total leukocyte and differential counts were assessed in the same blood sample, following a standarized protocol [14].

sCD23 and serum cytokine levels

Serum sCD23 was measured by a commercial immunoassay (Cell free CD23 test kit, T Cell Diagnostic, Inc Cambridge USA); normal values were between 15 to 250 U.I./ml. Serum IL-4 was measured by ELISA (Human IL-4 ELISA Test kit, Intertest-4 Genzyme Corporation, Cambridge, USA); values are expressed in pg/ml.

Serum IFN-γ was measured by a solid phase sandwich ELISA method (Intertest-γ Human IFN-γ kit,

Table 3. Phenotypic analysis of PBMC/ CD23 in children (Patients vs controls)

	Controls (n=10)		PAR (n=14)		AD (n=13)	
	mm^3	%	mm^3	%	mm^3	%
PBMC/CD23+	27±7	1.1+0.3	212±54 [1]	5±1 [1]	129±35 [1]	4 [1]
CD3+/CD23+	0	0	14±6	0.4+0.2 [1]	8±3	0.3±0.1
CD4+/CD23+	0	0	5±4	0.2±0.1	5±3	0.2±0.1
CD8+/CD23+	0	0	2±2	0.1±0.1	2±2	0.1±0.1
CD19+/CD23+	1±1	0.1±0.1	144±56 [1]	4±1 [1]	133±36 [1]	2.8±0.5 [1]
CD56+/CD23+	0	0	2±2	0.1±0.1	2±2	0.3±0.3

Results are expressed as the arithmetic mean ± standard error of absolute (cells/mm^3) and percentage (%) values of cells with positive fluorescence by flow cytometry.
[1] $p<0.005$ when compared to controls.

Genzyme Corporation, Cambridge, USA); values are expressed in pg/ml.

Statistical analysis

The statistical significance of the difference in lymphocyte subpopulations and serum cytokines were evaluated by an unpaired nonparametric test (Mann-Whitney test). Values of total IgE were log transformed. The possible correlation of CD23+ lymphocytes and serum cytokines was evaluated by the Pearson test.

RESULTS

PBMC phenotypic analysis

Controls

The phenotypic analysis of PBMC in controls showed that both children and adults exhibited similar cell subpopulations values (*Table 1, 2 and 3*). In relation to CD23, adults had a significantly higher value of CD19+/CD23+ cells than children ($p<0.005$) (*Table 4*). There were no differences between both groups when serum levels of IgE, sCD23, IL-4 and IFN (were assessed (*Table 5*).

Patients

When evaluating the PBMC phenotypic profiles, we found that children with PAR showed a significantly increase of total CD19+ B cells ($p<0.05$) when compared to controls (*Table 1*). Children with AD exhibited leukocytosis and increased values of total CD56+ cells ($p<0.05$) when compared to controls (*Table 1*). In adults with PAR, no differences were found when compared to controls. However, adults with AD exhibited a significant diminution of the percentage of CD3+ cells ($p<0.05$) and CD4+ cells ($p<0.05$) (*Table 2*).

PAR adults had increased values of lymphocytes and total CD19+ B cells when compared to PAR children. AD adults showed leukocytosis and increase in CD3+ cells and CD8+ cells when compared to AD children ($p<0.05$).

CD23+ cells

When CD23+ cells were investigated we found a significantly augmented value of PBMC/CD23+ ($p<0.005$) and particularly of CD19+/CD23+ cells ($p<0.001$) in both PAR and AD children when compared to controls (*Table 3*). PAR and AD adults showed an increase in CD19+/CD23+ cells when compared to controls (*Table 4*), being this difference significant only for AD adults. PAR adults exhibited lower values of PBMC/CD23+ cells ($p<0.05$) when compared to PAR children (*Table 4*). Finally, when compared the expression of CD23 in relation to IgE levels in children and adults. It was significant increased in children independents of the IgE levels (*Table 6*). While in adults this increase was observed only in patients with levels of IgE higher than 1.000 U.I./ml (*Table 7*).

sCD23 and cytokine serum levels

All patients exhibited a significant increase in the values of IgE ($p<0.005$) when compared to controls. Although AD patients had higher values of IgE than PAR patients, only in AD adults this difference was significant when compared to PAR adults. There were no differences in serum levels of sCD23, IL-4 and IFN-γ between patients and controls. However, adults had significantly lower values of sCD23 than children (*Table 5*).

DISCUSSION

The low affinity receptor for IgE, FcεRII/CD23, was described for the first time by Spielberg, Lawrence and collaborators [15] and currently is considered as one of the basic structures in the regulation of IgE synthesis. The CD23 molecule is a type II integral membrane glycoprotein which is continuously cleaved by autoproteolysis into soluble fragments released to the extracellular fluid and referred to as soluble CD23 [16,17]. On normal B lymphocytes, CD23 is selectively expressed on surface IgM/IgD bearing cells and is lost after isotype switching [18].

The very few available reports estimated the value of CD23 in lymphocytes of normal subjects ranging from 1 to 4% and constant for all ages [19, 20]. Following previously reported standarized clinical protocols for normal subjects [13, 21], we studied 20 control individuals (10 children and 10 adults) without history of either allergic disease or parasitic infection and found significantly higher values of CD19+/CD23+ cells (1% vs 0%) in control adults when compared to children. Thus, further efforts should be made to establish the standard normal values of this molecule.

The specific aim of the present investigation was to explore in PAR and AD patients the expression of CD23 among the different PBMC cell populations and to gain further insight in relation to serum levels of both sCD23 and certain cytokines. While PAR adults showed comparable values of CD3+, CD4+ and CD8+ to controls, we found similar to Leung et al. [19] a significant diminution in the percentage values of both CD3+ and CD4+ cells with normal values of CD8+ cells in AD adults. As a contrast, PAR children group exhibited an elevation in CD19+ B cells being the other subsets comparable to controls.

Another striking finding was a significant increase of both PBMC/CD23+ and CD19/CD23+ cells in PAR and AD children. Previous reports found these alterations only in children [5, 20]. Furthermore, Kim et al. [22] described variations only in absolute values, advancing the hypothesis of a probable relation to the physiological lymphocytosis of children. There are several reports showing an increase in PBMC/CD23+ in AD patients, being

Table 4. Phenotypic analysis of PBMC/CD23+ in adults (Patients vs controls)

	Controls (n=10)		PAR (n=13)		AD (n=3)	
	mm^3	%	mm^3	%	mm^3	%
PBMS/CD23+	35±4	1.7±0.2	58±11 [a] [1]	2.3+0.3	124±43	5±2
CD3+/CD23+	1±1	0.1±0.1	2.7±1.8	0.1±0.1	15±15	0.1±0.1
CD4+/CD23+	0	0	0	0	7±6	0.3±0.3
CD8+/CD23+	0	0	1±1	0.1±0.1	7±6	1.5±1.40
CD19+/CD23+	25±6 [b]	1.2±0.2	53±14	2±0.4	94±21 [1]	4±1 [1]
CD56+/CD23+	2±2	0.1±0.1	0	0	0	0

Results are expressed as the arithmetic mean ± standard error of absolute (cells/mm^3) and percentage (%) values of cells with positive fluorescence by flow cytometry.
[1] $p<0.05$ when compared to controls. [a] $p<0.05$ when compared to PAR children. [b] $p<0.05$ when compared to control children

different in the type of cell that express the receptor: B cells [4] or CD8+ cells [5]. We found an increase in CD19+/CD23+ cells but not in CD8+/CD23+ cells. Furthermore, PAR children also depicted significant increase of PBMC/CD23+ expression when compared to PAR adults.

Children with PAR exhibited higher values of sCD23 than adults with PAR, suggesting that sCD23 serum levels may have an age dependent variation in this disease. We did not find a correlation between serum levels of IgE and sCD23, suggesting perhaps that all serum sCD23 may not be functioning as an IgE potentiating factor. Furthermore, sCD23 may consist of multiple components with different functions, as has been shown in rodents [23].

A prolonged incubation with IL-4 is required for optimal CD23 expression in vitro and analysis of the kinetics of IL-4 receptor internalization and recycling, suggests that CD23 is mainly induced following interactions of IL-4 with recycled IL-4 receptors [24]. In contrast, IFN-γ and IFN-γ inducers inhibit IL-4 induced CD23 expression on normal B cells [25]. As in other reports [22, 20] no correlation was found between serum IgE levels and the other evaluated cytokines. When we classified patients by serum IgE level, we found increased levels of CD19+/ CD23+ cells in all children patients (*Table 6*); in adults, only those patients with IgE higher than normal, showed significant increase; this difference was evident with IgE levels higher than 1000 U.I./ml (*Table 7*). Overall, these observations may add further insight in the understanding of the IgE system and the different structures related to the IgE synthesis. Within this context, atopic children showed an increase in B cells and exhibited a significant increase of CD19+/CD23+ cells and sCD23 when compared to atopic adults. Moreover, these results suggest that atopic patients should be evaluated separately according to their clinical diagnosis.

Therefore, it is possible to suggest that the assessment of this cell population specially in children could be used as a marker of atopy, in the same way as an elevated value of serum IgE.

New investigations should be made to determine the function of T cells and the profile of cytokines in atopy, their influence on B cells and in the synthesis of IgE, probably through CD23. This in turn, should help in clarify further the differences in the immunopathology of both PAR and AD patients.

REFERENCES

1. Ishizaka K. Regulation of immunoglobulin E biosynthesis. Adv. Immunol. 1989; 47: 1-44.
2. Naclerio R. Allergic Rhinitis. N Engl. J. Med. 1991; 325: 860-869.
3. Hanifin J. Atopic dermatitis. J. Allergy. Clin. Immunol. 1984; 73: 211-220.
4. Leung D. Immunologic nature of atopic dermatitis: implications for new directions in treatment. Springer Seminars Immunopathol. 1992; 13: 427-440.
5. Yanagihara Y, Sarfati M, Marsh D, Nutman T, Delespesse G. Serum levels of IgE binding factor (soluble CD23) in disease associated with elevated IgE. Clin. Exp. Allergy 1989; 20: 395-401.
6. Delespesse G, Sarfati M, Hofstetter H. Human IgE binding factors. Immunol. Today 1989; 10: 159-165.
7. Butterworth A, Benested-Smith R, Capron A, et al. Immunity in human Schistosomiasis mansoni: Prevention by blocking antibodies of the expression of immunity in young children. Parasitology 1987; 94:

Table 5. Immunoserological evaluation of patients and controls

	CHILDREN			ADULTS		
	Controls (n=10)	PAR (n=14)	AD (n=13)	Controls (n=10)	PAR (n=13)	AD (n:3)
Log_{10} IgE (UI/ml)	1.47±0.21	2.49±0.13 [1]	2.82±0.199 [2]	1.54±0.19	2.56±0.10 [2]	3.62±0.17 [1c]
sCD23 (U/ml)	285±35	496±101	286±40	168±43	244±61 [a]	93±25 [b]
IL-4 (pg/ml)	42±4	62±10	72±17	33±2	67±16	48±17
IFN-γ (pg/ml)	41±2	49±9	87±24	44±2	40±1	38±2

Results are expressed as mean ± standard error. [1] $p<0.05$ when compared to controls. [2] $p<0.005$ when compared to controls. [a] $p<0.05$ when compared to PAR children[b]. $p<0.05$ when compared to AD children[c]. $p<0.005$ when compared to PAR patients.

Table 6. Expression of CD23 on different cell subsetsin relation to ige level in children

	PATIENTS/CHILDREN							
	Controls (n=10)		IgE=0-180 UI/ml		IgE=180-1000 UI/ml (n=10)		IgE>1000 UI/ml (n=6)	
Cell Populations	mm^3	%	mm^3	%	mm^3	%	mm^3	%
CMSP/CD23+	27±7	0	264±96 [1]	5±2 [1]	163±30 [2]	4±0 [2]	208±48 [2]	5±1 [3]
CD3/CD23+	0	0	11±11	0.3±0.3	9±3 [1]	0.35±0.1 [2]	16±6 [1]	0.5±0.2 [1]
CD4+/CD23+	0	0	6±5	0	0	0	16±6	0.5±0.2
CD8+/CD23+	0	0	0	0	0	0	10±6	0.3±0.2
CD19+/CD23+	1±1	0	129±92	3±2	134±36 [3]	3±1 [3]	160±52 [2]	4±1 [3]
CD56+/CD23+	0	0	0	0	2±1	0.1±0.1	6±5	0.2±0.2

Results are expressed as the arithmetic mean ± standard error of absolute (cells/mm^3) and percentage (%) values of cells with positive fluorescence by flow cytometry.
[1] $p<0.05$ when compared to controls. [2] $p<0.005$ when compared to controls. [3] $p<0.001$ when compared to controls

Table 7. Expression of CD23 on different cell subsets in relation to IgE level in adults

	PATIENTS/ADULTS							
	Controls (n=10)		IgE=0-180 UI/ml		IgE=180-1000 UI/ml (n=0)		IgE>1000 UI/ml (n=3)	
Cell Populations	mm^3	%	mm^3	%	mm^3	%	mm^3	%
CMSP/CD23+	35±4	2±0	45±12	2±0.3	62±14 [1]	2±0.4	124±35 [1]	35±4
CD3/CD23+	1±1	0	0	0	2±2	0.1±0.01	15±12	1±1
CD4+/CD23+	0	0	0	0	0	0	7±6	0.3±0.3
CD8+/CD23+	0	0	0	0	2±2	0.1±0.01	7±6	0.3±0.3
CD19+/CD23+	25±6	1±0	35±16	2±0.5	59±17 [1]	2±0.5	94±21 [1]	4±1
CD56+/CD23+	2±2	0	0	0	0	0	0	0

Results are expressed as the arithmetic mean ± standard error of absolute (cells/mm^3) and percentage (%) values of cells with positive fluorescence by flow cytometry.
[1] $p<0.05$ when compared to controls

281-300.
8. Joseph M, Tonnel A, Torpier G, Capron A, Arnoux B, Benveniste J. Involvement of immunoglobulin E in the secretory processes of alveolar macrophages from asthmatic patients. J. Clin. Invest. 1983; 221-230.
9. Pirron U, Schluch T, Prinz J, Rieber E. IgE-dependent antigen focusing by human B lymphocytes is mediated by the low affinity receptor for IgE. Eur. J. Immunol. 1990; 20: 1547-1551.
10. Uchibayashi N, Kikutani H, Barsumian E, et al. Recombinant soluble Fc epsilon receptor II (Fc epsilon RII/CD23) has IgE binding activity but no B cell growth promoting activity. J. Immunol. 1989: 142: 3901-3908.
11. Pene J, Chretien I, Rousset F, Brieve F, Bonnefoy J, De Vries J. Modulation of IL-4 induced human IgE production in vitro by IFN-gamma and IL-5: The role of soluble CD23 (s-CD23). J. Cell. Biochem. 1989; 39: 253-264.
12. Flores-Ramos L, Cairus J, Millsum M, Gordon J. Soluble fragments of the low-affinity IgE receptor (CD23) inhibit the spontaneous migration of U937 monocytic cells: Neutralization of MIF activity by a CD23 antibody. Immunology 1989; 67: 547-549.
13. Ponce D, Anderson R, Bianco N. Total serum IgE levels in Venezuelan schools children. Clin. Allergy 1983; 13: 521-530.
14. Tassinari P, Deibis L, Blanca I, Bianco N, Echeverría de Pérez G. Decreased T-cell proliferative response to common environmental antigens could be an indicator of early Human Immunodeficiency Virus-mediated lymphocyte lesions. Clin. Diagn. Lab. Immunol. 1995; 2: 404-407.
15. Spielberg H, Dainer P. Fc receptor for IgG, IgM and IgE on human leukemic lymphocytes. Clin. Exp. Immunol. 1979; 35: 286-295.
16. Letellier M, Sarfati M, Delespesse G. Mechanisms of formation of IgE binding factors (soluble CD23). I. Fc Epsilon RII bearing cells generate IgE-binding factors of different molecular weights. Mol. Immunol. 1989; 26: 1105-1112.
17. Letellier M, Nakajima T, Pulido-Cejudo G, Hofstetter H, Delespesse G. Mechanism of formation of human IgE-binding factors (soluble CD23) III. Evidence for a receptor (FcERII) associated proteolytic activity. J. Exp. Med. 1990; 172: 693-700.
18. Kikutani H, Suemura M, Owaki H et al. Fc Epsilon receptor, a specific differentiation marker transiently expressed on mature B cells before isotype switching. J. Exp. Med. 1986; 164: 1455-1469.
19. Leung D, Rhodes A, Geha R. Enumeration of T cell subsets in atopic dermatitis using monoclonal antibodies. J. Allergy. Clin. Immunol. 1981; 67: 450-455.
20. Kim K, Mayumi M, Iwai Y, et al. IgE receptors bearing lymphocytes in allergic and non allergic children. Pediatric Res. 1988; 24: 254-257.
21. Contreras C, Orozco A, Sanchez P, Ortega G, Bianco N. Physiological aspects of circulating immune complexes in the normal populations. Clin. Exp. Immunol. 1982; 48: 693-699.
22. Kim K, Nauku M, Iwai Y, et al. Soluble low affinity Fc receptors for IgE in the serum of allergic and nonallergic children. Pediatric Res. 1989; 26: 49-53.
23. Reddy M, Weissman A, Mazza D, et al. Circulating elevated levels of soluble CD23, interlerukin-4 and CD20+CD23+ lymphocytes in atopic subjects with elevated serum IgE concentrations. Ann. Allergy 1992; 69: 131-134.
24. Galizzi J, Zuber C, Cabrillat H, Djosson O, Banchereau J. Internalization of human interleukin inducible Jijoye cells. J. Biol. Chem. 1989; 264: 6984-6989.
25. De France T, Aubry J, Rousset F, et al. Human recombinant interleukin-4 induces FcE receptors (CD23) on normal human B lymphocytes. J, Exp. Med. 1987 165: 1459-1464.