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Intestinal epithelial cells express the CD23/FcεRII molecule: enhanced expression in enteropathies

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SUMMARY

Immunohistochemical analysis of normal human intestine revealed that two anti-CD23 monoclonal antibodies (mAb), EBVCS 1 and EBVCS 2, reacted with human intestinal epithelial cells. Both mAb exhibited an exclusive reactivity with epithelial cells of the small and large bowels. Staining with both EBVCS 1 and EBVCS 2 was localized on the apical and basal sides of enterocytes. Enhanced expression of CD23 on gut epithelial cells was found in inflammatory bowel diseases, in children with food intolerance to cows' milk proteins and in a young infant with severe autoimmune enteropathy. Western blot analysis of anti-CD23 mAb reactivity with gut epithelial cell extracts showed the presence of a non-reducible 42,000–45,000 M_r polypeptide compatible with the membrane form of the intact CD23 molecule. These data show that CD23 is constitutively expressed by intestinal epithelial cells and that its expression is enhanced in enteropathies.

INTRODUCTION

Expression of major histocompatibility complex (MHC) class II antigens is a prerequisite for antigen presentation and a mandatory recognition element in accessory cell/T-cell interactions defining self and non-self. Expression of class II antigens in the normal intestine is unique, since the bowel is in a chronic state of controlled inflammation, and normal enterocytes constitutively express MHC class II molecules. It has been previously reported that enterocytes of various species exhibit accessory cell functions and are able to process and present soluble antigen to specific T cells.[1,3] However, MHC class II-dependent antigen presentation by normal human enterocytes can result in selective expansion of $CD8^+$ T cells.[2] Conversely, $CD4^+$ memory T cells proliferate in response to exogenous antigen presented by enterocytes from patients with inflammatory bowel disease (IBD).[4] Normal enterocytes express HLA-DR, weak levels of DP and no detectable DQ molecules,[5] whereas enterocytes from IBD patients expressed DR, DP[5] and sometimes DQ. It has been proposed that differences in expression of MHC class II and other surface antigens may help to explain the unusual function of these cells.

The human CD23 molecule, the low-affinity receptor for the Fc portion of IgE,[6,7] is a 45,000 MW molecule expressed on the cell surface of haematopoietic cells, including B lymphocytes, follicular dendritic cells of lymph nodes, macrophages and epidermal Langerhans' cells (reviewed in ref. 8). CD23 has been described to be implicated in a number of IgE-dependent functions such as IgE production,[9] antigen focusing[10] and cytotoxicity against parasites.[11] In addition, CD23 has been reported to be implicated in IgE-independent functions, including B-cell growth,[12] germinal centre B-cell survival,[13] prothymocyte maturation,[14] myeloid precursor proliferation[15] and T/B lymphocyte conjugate formation.[16] Several lines of evidence indicated that CD23 may be implicated in antigen presentation. CD23 and HLA-DR are spacially associated on B cells[17] and converge at a single pole of the cell under interleukin-4 (IL-4) stimulation.[18] Both CD23 and HLA-DR molecules are up-regulated together by the same cytokine on a given cell type [i.e. granulocyte–macrophage colony-stimulating factor (GM-CSF) for monocytes, IL-4 for B cells].[19] Finally, ligands binding within the lectin homology region of CD23 prevent B cells from stimulating allogeneic mixed lymphocyte responses.[18] It has been proposed that CD23 could serve as a co-stimulatory adhesion molecule in antigen presentation with special reference to a potential role in the regulation of IgE synthesis. The aim of the present study was to examine expression of the CD23 molecule by intestinal epithelial cells (IEC) in normal conditions, and to determine whether enhanced expression could be found in various enteropathies.

Abbreviations: CMPI, cows' milk protein intolerance; CD, Crohn's disease; FcεRII, type II receptor for the Fc portion of IgE; IBD, inflammatory bowel disease; IFN-γ, interferon-γ; IEC, intestinal epithelial cells; mAb, monoclonal antibodies; NPC, nasopharyngeal carcinoma; TEC, thymic epithelial cells; UC, ulcerative colitis.

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Table 1. Description of the patients

Group	Patients	No. of patients	Clinical status	Age	Serum IgE*	CD23†
A	Control	8	Normal‡	Adult	—	+
B	Control	5	Normal§	< 24 months	—	+
C	UC	4	Active¶	Adult	NT	+++
	CD	4	Active¶	Adult	NT	+++
D	Reaginic CMPI	4	Active**	< 1 year	+++	+++
E	Non-reaginic CMPI	9	Active††	< 1 year	+++	+++
F	AIE	1	Active‡‡	4 months	+++	+++

* Serum IgE level: (−) < 0·35 IU/ml; (+++) > 200 IU/ml.

† Intensity of immunofluorescence staining on gut cryostat section: (+) moderate (mostly membrane); (+++) high (membrane and intracytoplasmic).

‡ Control endoscopy following polypectomy.

§ Check-up endoscopy in hypotrophic children, without diarrhoea.

¶ Untreated patient.

** Reaginic CMPI patients before cows' milk protein-free diet.

†† Non-reaginic CMPI patients before cows' milk protein-free diet.

‡‡ Only parenteral feeding, and before therapy.

MATERIAL AND METHODS

Antibodies

The following mouse monoclonal antibodies (mAb) were used in this study: EBVCS 1 and EBVCS 2 (IgG1) mAb specific for human CD23[20] (kindly provided by B. Sugden, McArdle Institute, Madison, WI); EBVCS 2, recognizes the lectin domain of the CD23 molecule where IgE binds, whereas EBVCS 1 binds outside this lectin domain;[21] BER-EP4 mAb specific for epithelial cell antigen (Dako, Traffes, France); anti-HLA-DR mAb (Dako), anti-CD3 and anti-CD19 mAb (Becton Dickinson, Traffes, France); an irrelevant [keyhole limpet haemocyanin (KLH) specific] mouse IgG1 mAb was used as a negative control.

Biopsy specimens

Bowel endoscopy biopsy specimens, obtained from patients described in Table 1, were immediately snap frozen in Tissue Tek (Miles Labs, Kankakee, IL) and stored in liquid nitrogen.

Immunohistochemical analysis on cryostat sections

Acetone-fixed cryostat sections (4 μ) were stained with specific antibodies (1:10 dilution of hybridoma supernatant), followed by a fluorescein isothiocyanate (FITC)-conjugated-F(ab')$_2$ fragment of rabbit anti-mouse IgG(H + L) (dilution 1/30) (Zymed, Biosoft, France). Specificity controls included slides incubated with an irrelevant mouse IgG1 mAb or with the FITC conjugate alone. All stained sections were reviewed independently by at least two investigators including a trained pathologist. Slides were read with the investigator blinded to the source of the tissue as well as the antibody used. Each section was compared to its corresponding control consisting of an irrelevant isotype-matched antibody or no added antibody.

Isolation of IEC

IEC were isolated from the stools of patient E presenting with autoimmune enteropathy (AIE)[22] with severe diarrhoea, total villus atrophy and desquamation of the epithelium (see Table 1). This patient also exhibited very intense labelling of the intestinal epithelium with the anti-CD23 mAb (Table 1). The stools of this patient represented an enriched source of almost pure epithelial cells. Stools recovered over a 2-hr period preceding the experiment, were washed three times with ice-cold phosphate-buffered saline (PBS) pH 7·4 containing 4 mM EDTA. The cells of the pellet consisted almost exclusively (90%) of viable enterocytes. Staining of cell smears with the peroxidase substrate AEC in the presence of H_2O_2 did not reveal any peroxidase-containing cells, thus ruling out the presence of eosinophils in our epithelial cell preparation. Epithelial cells were immediately lysed at +4° in lysis buffer containing 0·5% NP-40 in 30 mM Tris pH 7·5, 150 mM NaCl, 2 mM EDTA, 1 mM $MgCl_2$, and supplemented with 1 mM phenylmethylsulphonfluoride (PMSF) and 2 mM tosyl lysine chloromethyl (TLCK) as protease inhibitors. Aliquots of IEC lysate were frozen at −80° until use in Western blot analyses.

Flow cytometry analysis

Epithelial cells (10^6) were stained with specific mouse IgG mAb followed by FITC-conjugated-F(ab')$_2$ fragments of rabbit anti-mouse IgG(H + L) antibodies (Zymed). Dead cells were gated by forward scatter and side scatter analysis. Flow cytometry analysis was performed on a FACScan (Becton Dickinson) cell analyser using logarithmic scale for data evaluation.

Western blot analysis

Cells (100 μl) from 10×10^6 IEC and 2 μg of recombinant human CD23 purified from Sf9 cell lysate,[23] were migrated on a 12%

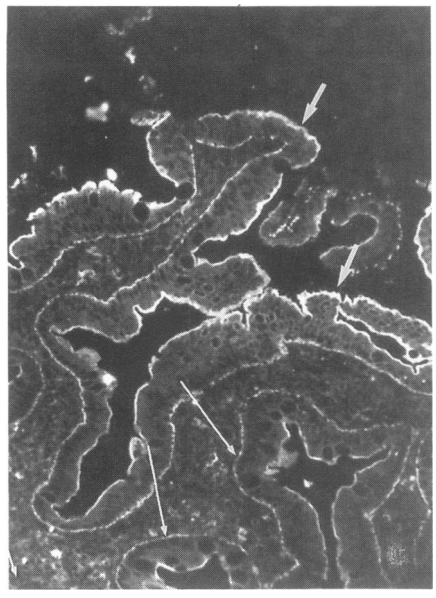

Figure 1. Immunohistochemical staining of normal human intestine with anti-CD23 antibodies. In control infants' duodenum (group B), EBVCS 2 mAb stained the apical and basal sides of enterocyte membranes in the crypts (thin arrow) and in the villi (thick arrow). Magnification × 112.

acrylamide gel and analysed by SDS–PAGE. The proteins were electrophoretically transferred onto a nitocellulose membrane. The non-specific binding sites on the membrane were blocked in PBS, 0·1% (w/v) Triton X-100, 1% (w/v) casein, 1% (w/v) gelatin and then labelled according to the method of Towbin *et al.*[24] with pooled EBVCS 1 and EBVCS 2 mAb (1/10 dilution of supernatant). The binding of the specific Ab was revealed with 4 μg/ml of peroxidase-labelled goat anti-mouse IgG(H+L) antibody (Sigma, La Verfillère, France) and developed with 0·5% (w/v) AEC in acetate buffer, 0·014% (v/v) hydrogen peroxide.

RESULTS

Indirect immunofluorescence analyses of CD23 expression by human intestinal epithelial cells

Immunohistochemical studies of CD23 expression on normal intestine (groups A and B, Table 1) was carried out using two specific mAb, EBVCS 1 and EBVCS 2. These two anti-CD23 mAb strongly stain follicular dendritic cells and mantle zone B cells in germinal centres of tonsils. In the normal intestine, both anti-CD23 mAb reacted with IEC, and stained both villus and crypt epithelial cells (Fig. 1). In the small and large bowels the pattern of CD23 reactivity appeared as a cell-surface staining of the apical and the basal sides of enterocytes. Control slides where the specific mAb was replaced by an irrelevant isotype-matched mAb gave no detectable background staining (not shown). These data indicated that normal human IEC constitutively expressed a CD23-like molecule.

In IBD patients (group C, Table 1) the CD23 reactivity with the gut epithelium was strikingly enhanced both in ulcerative colitis (UC) (not shown) and in Crohn's disease (CD). In both diseases, anti-CD23 mAb gave a strong cytoplasmic staining of villus epithelial cells and reacted with crypt enterocytes as well

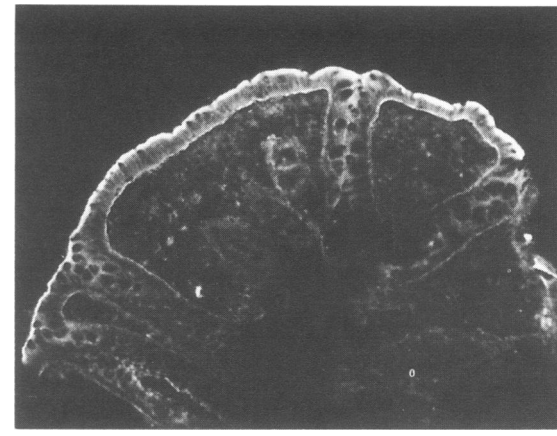

Figure 2. Increased CD23 staining of epithelial cells in gut enteropathies. EBVCS 2 exhibited a strong cytoplasmic reactivity with colon epithelial cells in CD (group C). Magnification × 112.

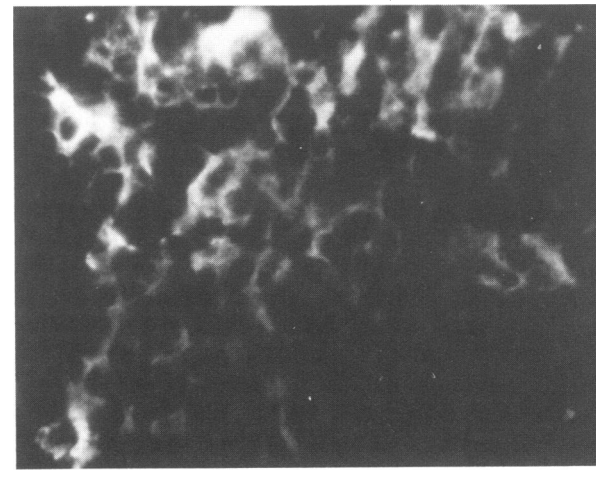

Figure 3. Clusters of $CD23^+$ dendritic-like cells in IBD. EBVCS 2 reacted with clusters of cells with dendritic morphology in the lamina propria of the colon in a CD patient. Magnification × 400.

(Fig. 2). A similar observation was found in the inflamed appendix (data not shown). Interestingly, clusters of $CD23^+$ dendritic-like cells were found in the lamina propria of the large bowel in IBD patients, but not in control intestines (Fig. 3). Patients with a reaginic form of cows' milk protein intolerance (CMPI) associated with high titres of specific IgE in the serum (group D, Table 1), presented an intense cytoplasmic and membrane staining of IEC with anti-CD23 mAb comparable to that obtained with IBD patients. Interestingly, aged-matched non-reaginic CMPI patients exhibited a similar increase in anti-CD23 mAb reactivity (group E, Table 1). Likewise, IEC of both the small and large bowels of the AIE patient exhibited an intense cytoplasmic staining for CD23 in the cytoplasm and at the apical and basal membranes of enterocytes (group F, Table 1).

Western blot analyses

In order to confirm that enterocytes expressed the CD23 polypeptide with a biochemical approach, we used epithelial

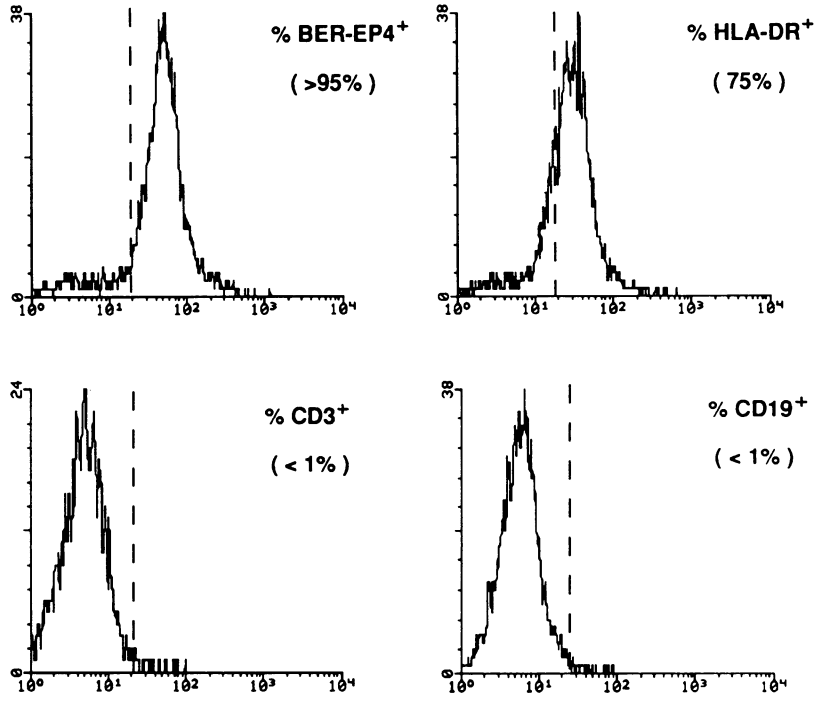

Figure 4. Flow cytometry analysis of epithelial cells isolated from the stools. Epithelial cells from the stools were stained with either BER-EP4, anti-HLA-DR, anti-CD3 or anti-CD19 mAb followed by a fluoresceinated $F(ab')_2$ fragment of rabbit anti-mouse IgG(H+L). The dotted line indicates the cut off between the positive (to the right) and the negative (to the left) population of a given staining. The percentages of cells stained are indicated in parentheses.

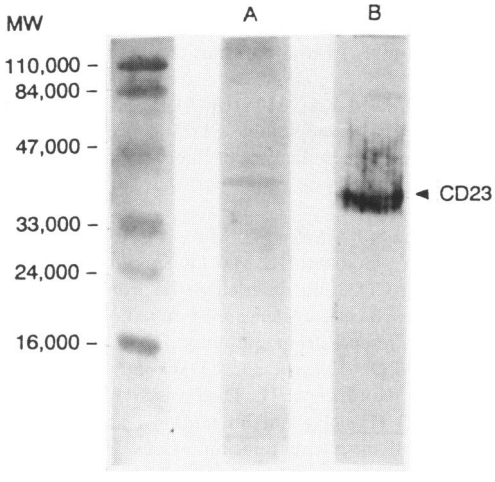

Figure 5. Western blot analysis of CD23 expression in enterocytes. Reactivity under reducing conditions of pooled EBVCS 1 and EBVCS 2 anti-CD23 mAb (1/10 dilution of supernatant) with: (A) cell lysates from 10×10^6 IEC released in the stools of the patients with AIE; (B) 2 μg of purified human recombinant CD23 from Sf9 cells.

cells from the stools of a patient with AIE, whose intestinal epithelium exhibited an intense reactivity with the anti-CD23 mAb. Flow cytometry analysis revealed that cells isolated from the stools were composed of more than 95% BER-EP4$^+$ epithelial cells, among which approximately 75% expressed HLA-DR molecules, and less than 1% CD3$^+$ T cells or CD19$^+$ B cells (Fig. 4). Although only 2% of these EC exhibited a cell-surface expression of CD23 (not shown), the high intensity of CD23 cytoplasmic staining on cryostat sections prompted us to use these EC for Western blot analysis. Lysate of these EC was tested by Western blot analysis using pooled anti-CD23 mAb. The results revealed a weak but single band corresponding to a 42,000–45,000 MW polypeptide under both reducing (Fig. 5) and non-reducing conditions (not shown), compatible with the intact form of the CD23 molecule.[8] Likewise, a non-reducible 42,000 M_r protein was obtained in a parallel Western blot analysis of purified recombinant CD23 using the same pool of anti-CD23 mAb (Fig. 5). The 'intestinal CD23' had a slightly higher M_r than the recombinant CD23. This may be due to differences in glycosylation occurring in insect cells used to express human recombinant CD23. Negative controls, performed using an irrelevant mouse IgG1 mAb instead of the anti-CD23 mAb, gave no background reactivity at all (not shown). These data confirmed that enterocyte reactivity with anti-CD23 mAb was due to the presence of the intact CD23/FcεRII molecule in these cells.

DISCUSSION

The present study demonstrates that human IEC constitutively express the low-affinity receptor for IgE, i.e. the CD23 molecule. This is the first evidence of expression of the intact form of CD23 in normal human epithelial cells. CD23 expression by epithelial cells was first documented in cell lines derived from human nasopharyngeal carcinomas (NPC).[25] These malignant cells expressed the 1·7 kilobase (kb) Blast 2/CD23 mRNA and produced *in vitro* the soluble form of the CD23 molecule.[25]

However, no cell-surface expression of the intact molecule could be found in these cells. Likewise, thymic epithelial cell (TEC) cultures produced soluble CD23, which appeared to be involved in the thymocyte differentiation activity of TEC culture supernatant.[14,26] Although *in situ* hybridization revealed the presence of CD23 mRNA in epithelial cells in thymus section, there was no evidence of the intact form of the protein on TEC (P. Debré, personal communication). Interestingly, epithelial cells from tonsils or polarized epithelial cells of the renal proximal tubules did not exhibit CD23 reactivity *in situ* on cryostat section (D. Kaiserlian, unpublished data). It is possible that the lack of staining for cell-surface CD23 of TEC and NPC may be due to instability of CD23 on cells once isolated from their tissue microenvironment. Likewise, we could not detect cell-surface CD23 expression on epithelial cells isolated from the stools of the AIE patient, although EC exhibited an intense cytoplasmic CD23 reactivity *in situ*.

We found that CD23 expression was dramatically increased in several pathological diseases of the gastrointestinal tract, associated (reaginic CMPI, AIE) or not (non-reaginic CMPI, CD, UC) with elevated serum IgE levels. The common link between these diseases is the presence of a mononuclear cell inflammatory infiltrate. As CD23 expression is sensitive to regulation by IL-4 and interferon-γ (IFN-γ),[27,28] it is possible that up-regulation of CD23 by proinflammatory cytokines may explain its over-expression by enterocytes in pathoglogical situations. Constitutive expression of CD23 by normal IEC and its up-regulation in the inflamed intestine, may have functional significance in regulation of mucosal immunity. Indeed, IEC have been reported to present both exogenous protein antigens[1-3] and self-antigens (D. Kaiserlian, submitted for publication) to T cells. It is possible that the CD23 molecule expressed on enterocytes may serve as a co-stimulatory molecule, possibly involved in MHC class II-dependent antigen presentation. In this respect, it should be emphasized that like IgE, CD21 [i.e. the Epstein–Barr virus (EBV) receptor], has also been recently identified as a second ligand of CD23 expressed on the cell surface of T and B lymphocytes.[29] Because inflammatory intestinal diseases are often associated with a T-cell infiltrate, it is possible that interaction of CD23-bearing gut epithelial cells with CD21$^+$ T cells may transduce activation signals to the T cell.[30] In the inflamed intestine, up-regulation of CD23 is associated with increased MHC class II molecule expression by IEC and may strengthen lymphoepithelial interactions resulting in exaggerated antigen presentation. Alternatively, identification of CD23 as a Ca^{2+}-dependent adhesion molecule with structural homology with lectins[29,31] suggests that CD23 molecules expressed on the gut epithelium may be important in retention of inflammatory T cells in the mucosa. The functional implication of these findings in the pathophysiological mechanisms of gut enteropathies, clearly deserves further investigation.

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REFERENCES

1. Bland P.W. & Warren L.G. (1986) Antigen presentation by epithelial cells of the rat small intestine. I. Kinetics, antigen specificity and blocking by anti-Ia antisera. *Immunology*, **58,** 1.
2. Mayer L. & Shlien R. (1987) Evidence for function of Ia molecules on gut epithelial cells in man. *J. exp. Med.* **166,** 1471.
3. Kaiserlian D., Vidal K. & Revillard J.P. (1989) Murine enterocytes can present soluble antigen to specific class II-restricted CD4$^+$ T cells. *Eur. J. Immunol.* **19,** 1513.
4. Mayer L. & Eisenhardt D. (1990) Lack of induction of suppressor T cells by intestinal epithelial cells from patients with inflammatory bowel disease. *J. clin. Invest.* **86,** 1.
5. Mayer L., Eisenhardt D., Salomon P., Bauer W., Plous R. & Piccinini L. (1991) Expression of class II molecules on intestinal epithelial cells in man: differences between normal and inflammatory bowel disease. *Gastroenterology*, **100,** 3.
6. Yukawa K., Kikutani H., Owaki H., Yamasaki K., Yokota A., Nakamura H., Barsumian E., Hardy R.R., Suemura M. & Kishimoto T. (1987) A B cell-specific differentiation antigen, CD23, is a receptor for IgE (FcεR) on lymphocytes. *J. Immunol.* **138,** 2576.
7. Bonnefoy J.Y., Aubry J.P., Peronne C., Wijedenes J. & Bancherau J. (1987) Production and characterization of a monoclonal antibody specific for the human lymphocyte low affinity receptor for IgE: CD23 is a low affinity receptor for IgE. *J. Immunol.* **138,** 2970.
8. Conrad D.H. (1990) FcεRII/CD23: the low affinity receptor for IgE. *Annu. Rev. Immunol.* **8,** 623.
9. Pene J., Rousset F., Briere F., Chretien I. Widemen J., Bonnefoy J.Y. & de Vries J.E. (1988) Interleukin-5 enhances interleukin-4-induced IgE production by normal human B cells. The role of soluble CD23 antigen. *Eur. J. Immunol.* **18,** 929.,
10. Kehry M.R. & Yamishita L.C. (1989) FcεRII (CD23) function on mouse B cells: role in IgE-dependent antigen focusing. *Proc. natl. Acad. Sci. U.S.A.* **86,** 7566.
11. Capron A., Dessaint J.P., Capron M., Joseph M., Ameisen J.C. & Tonnel A.B. (1986) From parasites to allergy. *Immunol. Today*, **7,** 15.
12. Gordon J., Cairns J.A., Millsum M.J., Gillis S. & Guy G.R. (1988) Interleukin-4 and soluble CD23 as progression factors for human B lymphocytes: analysis of their interactions with agonists of the phosphoinositide 'dual pathway' of signaling. *Eur. J. Immunol.* **18,** 1561.
13. Liu Y.J., Cairns J.A., Holden M.J., Abbot S.D., Jansen K.U., Bonnefoy J.Y., Gordon J. & MacLennan I.C.M. (1991) Recombinant 25kDa CD23 and interleukin-1a promote the survival of germinal center B cells: evidence for bifurcation in the devlopment of enterocytes rescued from apoptosis. *Eur. J. Immunol.* **21,** 1107.
14. Mossalayi M.D., Lecron J.C., Dalloul A.H., Sarfati M., Bertho J.M., Hofstetter H., Delespesse G. & Debre P. (1990) Soluble CD23 (FcεRII) and interleukin-1 synergistically induce early human thymocyte maturation. *J. exp. Med.* **171,** 959.
15. Mossalayi M.D., Arock M., Bertho J.M., Blanc C., Dalloul A.H., Hofstetter H., Sarfati M., Delespesse G. & Debré P. (1990) Proliferation of early human myeloid precursors induced by interleukin-1 and recombinant soluble CD23. *Blood*, **75,** 1924.
16. Aubry J.P., Shields J.G., Jansen K.U. & Bonnefoy J.Y. (1993) A multiparameter flow cytometric method to study surface molecules involved in interactions between subpopulations of cells. *J. immunol. Meth.* **159,** 161.
17. Bonnefoy J.Y., Guillot O., Spits H., Blanchard D., Ishizaka K. & Banchereau J. (1988) The low-affinity receptor for IgE (CD23) on B lymphocytes is spatially associated with HLA-DR antigens. *J. exp. Med.* **167,** 57.
18. Flores-Romo L., Johnson G.D., Ghaderi A.A., Stanworth D.R., Veronesi A. & Gordon J. (1990) Functional implication for the topographical relationship between MHC class II and the low-affinity IgE receptor: occupancy of CD23 prevents B lymphocytes

from stimulating allogeneic mixed lymphocyte reponses. *Eur. J. Immunol.* **20,** 2465.

19. DEFRANCE T., AUBRY J.P., ROUSSET F., VANBERVLIET B., BONNEFOY J.Y., ARAI N. *et al.* (1987) Human recombinant interleukin-4 induces Fcε receptor (CD23) on normal human B lymphocytes. *J. exp. Med.* **165,** 1459.
20. KINTNER C. & SUGDEN B. (1981) Identification of antigenic determinants unique to the surfaces of cells transformed by Epstein–Barr virus. *Nature*, **294,** 458.
21. BONNEFOY J.Y., SHIELDS J. & MERMOD J.J. (1990) Inhibition of human interleukin-4-induced IgE synthesis by a subset of anti-CD23/FcεRII monoclonal antibodies. *Eur. J. Immunol.* **20,** 139.
22. MITTON S., MIRAKION R., LARCHER V.F., DILLON M.J. & WALKER-SMITH J.A. (1989) Enteropathy and renal involvement in an infant with evidence of widespread autoimmune disturbance. *J. Pediatr. Gastroenterol. Nutr.* **8,** 39.
23. JANSEN K.U., SHIELDS J., GORDON J., CAIRNS J., GRABER P. & BONNEFOY J.Y. (1991) Expression of human recombinant CD23 in insect cells. *J. Rec. Res.* **11,** 507.
24. TOWBIN H., STAHELIN T. & GORDON J. (1979) Electrophoretic transfer of proteins from polyacrylamide gels to nitrocellulose sheets: procedure and some applications. *Proc. natl. Acad. Sci. U.S.A.* **76,** 4350.
25. BILLAUD M., BUSSON P., HUAND D., MUELLER-LANTZCH N., ROUSSELET G., PAVLISH O., WAKASUGI H., SEIGNEURIN J.M., TURSZ T. & LENOIR G.M. (1989) Epstein–Barr virus (EBV)-containing nasopharyngeal carcinoma cells express the B-cell activation antigen Blast2/CD23 and low levels of the EBV receptor CR2. *J. Virol.* **63,** 4121.
26. DALLOUL A.H., FOURCADE C., DEBRE P. & MOSSALAYI M.D. (1991) Thymic epithelial cell-derived supernatants sustain the maturation of human prothymocytes: involvement of interleukin-1 and CD23. *Eur. J. Immunol.* **21,** 2633.
27. BIEBER T., RIEGER A., NEUCHRIST C., PRINZ J.C., RIEBER E.P., BOLTZ NITULESCU G., SCHNEIDER O., KRAFT D., RING J. & STINGL G. (1989) Induction of FcεRII/CD23 on human epidermal Langerhans cells by human recombinant interleukin-4 and γ interferon. *J. exp. Med.* **170,** 309.
28. NARAY-FEJES-TOTH A. & GUYRE P.M. (1984) Recombinant human immune interferon induces increased IgE receptor expression on the human monocytic cell line U-937. *J. Immunol.* **133,** 1914.
29. AUBRY J.P., POCHON S., GRABER P., JANSEN K.U. & BONNEFOY J.Y. (1992) CD21 is a ligand for CD23 and regulates IgE production. *Nature*, **358,** 505.
30. TSOUKAS C.D.S. & LAMBRIS J.D. (1993) Expression of EBV/C3d receptors on T cells: biological significance. *Immunol. Today*, **14,** 56.
31. POCHON S., GRABER P., YEAGER M., JANSEN K., BERNARD A., AUBRY J.P. & BONNEFOY J.Y. (1992) Demonstration of a second ligand for the low affinity receptor for immunoglobulin E (CD23) using recombinant CD23 reconstituted into fluorescent liposomes. *J. exp. Med.* **176,** 389.