

Function and expression of adhesion molecules on human basophils

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Although the human basophil is predominantly a circulating cell, it is known to participate in a variety of inflammatory responses. For example, basophils have clearly been identified in skin at sites of contact hypersensitivity, erythema multiforme, bullous pemphigoid, and cutaneous basophil hypersensitivity reactions and in the airways of subjects with allergic rhinitis and asthma.^{1, 2} In addition, an influx of basophils accompanies the allergic late phase response that occurs after antigen challenge of the skin and airways.³⁻⁵ Thus basophils, like other granulocytes, can emigrate from the intravascular compartment into specific tissues. The observation that increased numbers of basophils accumulate at certain inflammatory sites suggests that they are activated and recruited to these locations. During this process it is necessary for these cells to interact with endothelial cells, parenchymal cells, and extracellular matrix proteins as they undergo margination, transendothelial migration, and enter the tissue space. Essentially all of the steps in this process involve the interaction of basophil cell surface adhesion molecules with specific adhesion molecule counter-receptors. Several extensive reviews have recently been written on cell adhesion molecule biology⁶⁻⁸ and the potential role of these molecules in allergic diseases.⁹⁻¹¹ This article will focus on the expression and function of adhesion molecules on human basophils.

Abbreviations used

ICAM:	Intercellular adhesion molecule
IL:	Interleukin
LFA:	Leukocyte function-associated antigen
MCP:	Monocyte chemotactic protein
MIP:	Macrophage inflammatory protein
VCAM:	Vascular cell adhesion molecule
VLA:	Very late activation antigen

BASOPHIL ADHESION MOLECULE PHENOTYPE

Basophils have recently been subjected to extensive phenotypic analysis. Techniques such as immunofluorescence and flow cytometry have been used to detect and quantify a wide variety of cell surface structures.^{12, 13} With respect to the expression of cell adhesion molecules, basophils have on their surfaces several molecules belonging to the integrin, selectin, and immunoglobulin gene superfamilies, as well as carbohydrate molecules that are ligands for selectins (Table I). These molecules are primarily constitutively expressed and expression is not altered by cell activation. A major exception to this is the finding that activation by certain secretagogues, cytokines, or chemoattractants is associated with a rapid increase in the cell surface expression of $\beta 2$ integrins (e.g., CD11b but not CD11a) and CD35 (CR1) (Fig. 1). Associated with these changes is a more gradual decline in surface expression of L-selectin¹⁴⁻¹⁶ (see Table II). Identical phenotypic changes in expression of CD11b and L-selectin appear to have occurred in basophils that have been recruited into the lower airways after segmental allergen challenge *in vivo*.¹⁷

During the process of migration a series of events occurs in which cell adhesion is coordinated with deadhesion, which enables the leukocyte to move into tissues.⁷ Whereas changes in the

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TABLE I. Expression of adhesion molecules on human basophils

Type	Name (CD designation)	Ligands	Expressed on basophils
Integrins			
$\beta 1$ (VLA) family	VLA-1, $\alpha 1\beta 1$ (CD49a/CD29)*	Collagen, laminin	No
	VLA-2, $\alpha 2\beta 1$ (CD49b/CD29)*	Collagen, laminin	No
	VLA-3, $\alpha 3\beta 1$ (CD49c/CD29)*	Collagen, laminin, others	Yes
	VLA-4, $\alpha 4\beta 1$ (CD49d/CD29)*	VCAM-1, fibronectin	Yes
	VLA-5, $\alpha 5\beta 1$ (CD49e/CD29)*	Fibronectin	Yes
	VLA-6, $\alpha 6\beta 1$ (CD49f/CD29)*	Laminin	No
$\beta 2$ family	LFA-1, $\alpha L\beta 2$ (CD11a/CD18)	ICAM-1, ICAM-2, ICAM-3	Yes
	Mac-1, $\alpha M\beta 2$ (CD11b/CD18)	C3bi, ICAM-1, others	Yes
	p150,95, $\alpha X\beta 2$ (CD11c/CD18)	C3bi, fibrinogen, others	Yes
$\beta 3$ family	$\alpha IIb\beta 3$ (CD41/CD61)	Fibrinogen, fibronectin, others	No
	$\alpha v\beta 3$ (CD51/CD61)*	Vitronectin, others	No
Others	$\alpha 6\beta 4$ (CD49f/CD104)*	Laminin	No
	Act-1,* $\alpha 4\beta 7$	MAAdCAM-1, VCAM-1, fibronectin	Yes
	HML-1,* $\alpha E\beta 7$ †	Unknown epithelial antigen	No
	L-selectin (CD62L)	GlyCAM-1, CD34, MAAdCAM-1	Yes
Selectins	E-selectin (CD62E)	Sialyl-Lewis ^x , others	No
	P-selectin (CD62P)	Sialyl-Lewis ^x , others	No
Immunoglobulin gene superfamily	PECAM-1 (CD31)	CD31, others	Yes
	ICAM-1 (CD54)	LFA-1	Yes
	ICAM-2 (CD102)*	LFA-1	Yes
	ICAM-3 (CD50)*	LFA-1	Yes
Carbohydrates	Lewis ^x (CD15)	P-selectin	No‡
	Sialyl-Lewis ^x (CD15s)	E- and P-selectin	Yes
	Sialyl-dimeric Lewis ^x	E-selectin	Yes

Includes data from references 12, 13, 25, 40, and Bochner et al. unpublished observations.

*Expression of these markers was examined using monoclonal antibodies provided by the Fifth International Conference on Human Leukocyte Differentiation Antigens.⁴³

†The αE subunit has been designated CD103.

‡Expression can be detected after treatment of basophils with neuraminidase.^{25, 44}

total amount of cell adhesion molecules or their localization on the cell surface may be occurring during these processes, it appears likely that swift alterations in the affinity of cell adhesion molecules is involved in many of these events. For example, leukocyte interaction with endothelial adhesion molecules can lead to cell activation, a process called "inside-out signaling."¹⁸ In addition, studies from several laboratories have demonstrated that rapid changes in the avidity of $\beta 1$ and $\beta 2$ integrins on leukocytes can occur as a result of cell activation or by manipulating the extracellular concentration of divalent cations.¹⁹ For example, specific monoclonal antibodies can be used to detect neopeptides that become exposed when conformational changes occur in association with augmented integrin adhesiveness. One such antibody, NKI-L16, recognizes a calcium-sensitive epitope on CD11a, the α chain of leukocyte function-associated antigen 1 (LFA-1);

expression of this epitope is necessary for LFA-1-mediated adhesion.²⁰ We have recently used this antibody to examine the divalent cation sensitivity of CD11a on human basophils. As shown in Fig. 2, this epitope was most effectively displayed in the presence of 1 mmol/L calcium or strontium, whereas manganese and magnesium are less effective; this finding is similar to results obtained with lymphocytes.²¹ In Fig. 3 it can be seen that calcium concentrations as low as 100 nmol/L are capable of inducing some expression of the NKI-L16 epitope, expression of which is optimal at 1 mmol/L calcium. In contrast, immunofluorescent signals using another CD11a antibody, which can block LFA-1-mediated adhesion, were unaffected by divalent cations (Figs. 2 and 3). Studies are in progress to determine whether there is a correlation between cation conditions for NKI-L16 binding and LFA-1-mediated adhesion of basophils to substrates such as intercellu-

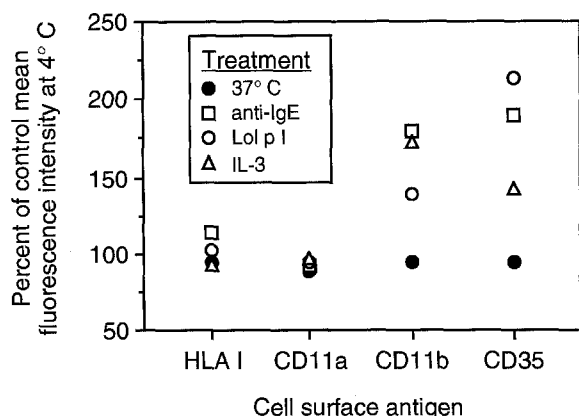


FIG. 1. Effect of various stimuli on basophil expression of selected surface markers. Aliquots of basophils were kept at 4° C or incubated at 37° C for 30 minutes in the presence or absence of polyclonal goat antihuman IgE (100 ng/ml), *Lol p 1* (100 ng/ml), or IL-3 (10 ng/ml). Cells were then analyzed for expression of CD11a, CD11b, CD35, or human leukocyte antigen class I (as a control) as previously described.⁴⁰

lar adhesion molecule-1 (ICAM-1) and whether basophil priming or stimulation will alter the cation requirements for LFA-1 activation.

FUNCTION OF ADHESION MOLECULES ON HUMAN BASOPHILS

It is now generally accepted that a series of steps is necessary for leukocyte migration into tissues.⁷ Circulating cells undergo a process termed "rolling" during which they attach loosely to the endothelium. This "tethering" step probably involves selectins and their carbohydrate counterligands. For tight leukocyte adhesion to occur, leukocyte activation, or "triggering," is required, presumably under the influence of chemoattractants. Subsequently, transendothelial migration (diapedesis) occurs, during which time the leukocytes move through the endothelial barrier and into the extravascular space. These latter adhesion and migration events can be mediated by $\beta 1$ and $\beta 2$ integrins and adhesion molecules belonging to the immunoglobulin family (e.g., ICAM-1, vascular cell adhesion molecule-1 [VCAM-1], and platelet-endothelial cell adhesion molecule-1). During firm adhesion and transendothelial migration, changes occur in both avidity and expression of integrins on the leukocyte surface. Therefore the preferential recruitment of a given cell type, such as a basophil, is likely to be the net result of many adhesion-dependent events, not the result of any one single cell-specific chemoattractant or adhesion molecule pathway.

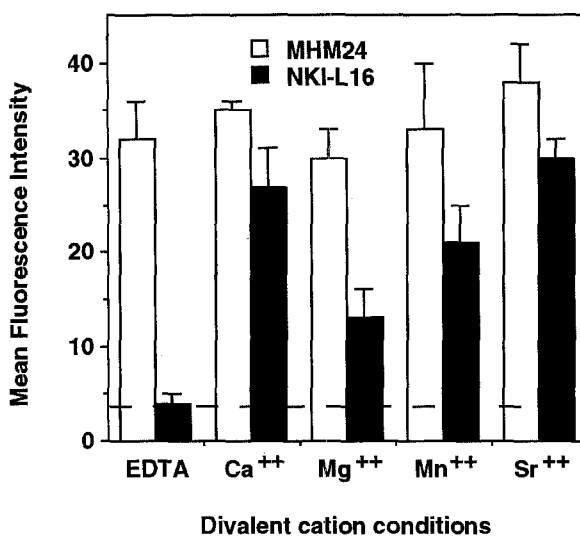


FIG. 2. Effect of divalent cations on basophil CD11a activation. Basophils were preincubated in buffers that contained the indicated divalent cations (1 mmol/L) or ethylene diamine tetraacetic acid (5 mmol/L) for 30 minutes at 37° C, then labeled for indirect immunofluorescence as previously described⁴⁰ using two mouse antihuman CD11a monoclonal antibodies: NKI-L16 (IgG2a, provided by Y. van Kooyk and C. Figdor, The Netherlands Cancer Institute, Amsterdam), recognizing an activation-dependent epitope⁴¹ or MHM24 (IgG1, provided by J.E.K. Hildreth, Johns Hopkins University, Baltimore, Md.), recognizing a non-activation-dependent epitope.⁴² The average mean fluorescence intensity using an irrelevant, isotype-matched control IgG1 antibody (background negative control) is shown as a dotted line. Values represent mean $\pm$ SEM from three separate experiments.

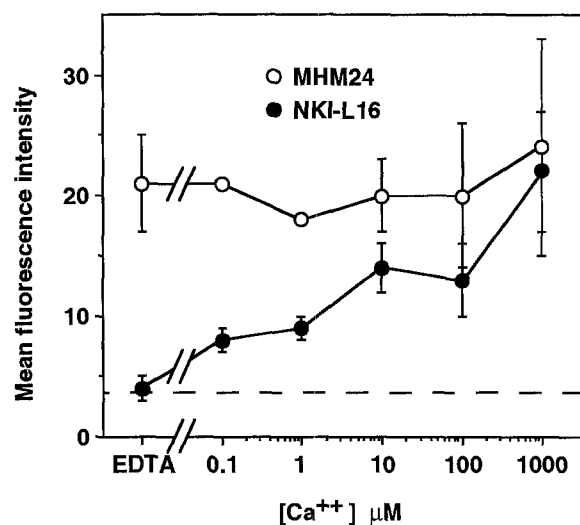


FIG. 3. Concentration-dependent activation of basophil LFA-1 by calcium. The protocol was identical to that outlined for Fig. 1. Values represent mean $\pm$ SEM from two to three separate experiments.

TABLE II. Effect of various stimuli on basophil adhesion to endothelial cells in vitro

Stimulus	Concentrations tested	Enhancement of adhesion	Target of effect
Cytokines			
IL-1	0.25-8 units/ml	Yes	Endothelium
IL-2	1-100 units/ml	No	
IL-3	0.1-3 ng/ml*	Yes	Basophil
IL-4	1-1000 units/ml	Yes	Endothelium
IL-5	0.1-100 units/ml	No	
IL-6	0.1-10 ng/ml	No	
GM-CSF	0.1-10 units/ml	No	
IFN- γ	0.1-100 units/ml	No	
TNF- α	0.01-10 ng/ml	Yes	Endothelium
	10-1000 ng/ml*	Yes	Basophil
Chemokines			
IL-8	0.2-200 ng/ml	No	
Platelet factor 4	1-100 ng/ml	No	
β -thromboglobulin	1-100 ng/ml	No	
IP 10	1-100 ng/ml	No	
GRO	1-100 ng/ml	No	
MCP-1 (MCAF)	1-100 ng/ml	No	
RANTES	1-100 ng/ml	No	
MIP-1 α	1-100 ng/ml	No	
MIP-1 β	1-100 ng/ml	No	
Secretagogues and other stimuli			
Anti-IgE	0.1-100 ng/ml*	Yes	Basophil
Allergen	0.1-100 ng/ml*	Yes	Basophil
FMLP	0.01-1 μ mol/L*	Yes	Basophil
Platelet-activating factor	0.01-1 μ mol/L*	Yes	Basophil
A23187	0.04-1 μ g/ml*	Yes	Basophil
C5a	100 nmol/L*	Yes	Basophil
Phorbol diesters	0.3-30 ng/ml*	Yes	Basophil
	0.3-30 ng/ml	Yes	Endothelium

Includes data from references 14, 22-24, 26, and Bochner et al. unpublished observations.

FMLP, N-formyl-methionyl-leucyl-phenylalanine; *GM-CSF*, granulocyte-macrophage colony-stimulating factor; *IFN- γ* , interferon- γ ; *TNF- α* , tumor necrosis factor- α .

*Treatment of basophils leads to a rapid increase in surface expression of CD11b and a decrease in L-selectin expression; other stimuli listed have no such effect.

Results of studies examining the adhesion of basophils to cultured human vascular endothelial cells have shown that adhesiveness of basophils can be enhanced by a variety of stimuli. Several chemotactic factors, the cytokine interleukin 3 (IL-3), and IgE-dependent secretagogues can directly stimulate divalent cation-dependent attachment of basophils to endothelial monolayers in vitro.^{14, 22, 23} For both IL-3 and IgE-dependent secretagogues, these effects are not seen with neutrophils, and they occur at concentrations of stimulus below the threshold required to induce histamine release. Therefore exposure of circulating basophils to low levels of these agents in vivo may contribute to their selective adhesion and re-

cruitment during certain inflammatory responses.

The endothelium also plays an active role during the process of leukocyte adherence by expressing new or enhanced levels of adhesion molecules on its surface after being activated by specific stimuli. For example, the cytokines IL-1 and tumor necrosis factor, as well as phorbol diesters and bacterial endotoxin, will stimulate cultured endothelial cells to express ICAM-1, E-selectin, and VCAM-1, each of which are ligands for basophils.^{22, 24, 25} Like other granulocytes, human basophils use sialylated surface molecules to interact with endothelial E-selectin, but the expression of these sialylated Lewis^x structures is unusual in that it is bimodal, which

suggests that only a subset of basophils are capable of interacting with E-selectin.²⁵ Whether this distinct distribution of Sialyl-Lewis^x-containing structures influences basophil adhesion to P-selectin has not yet been determined. ICAM-1 and E-selectin are ligands for all granulocytes, and therefore no differences have been found among granulocytes for binding to these molecules. In contrast, neutrophils, unlike basophils and eosinophils, cannot adhere to the cytokine-inducible endothelial cell adhesion molecule VCAM-1 because they lack the counterreceptor for VCAM-1, the integrin very late activation antigen-4 (VLA-4) ($\alpha 4\beta 1$, CD49d/CD29).²⁴⁻²⁶ It is not yet known whether these adhesion molecules or others are responsible for basophil transendothelial migration. Besides its interaction with VCAM-1, VLA-4 can also be a ligand for the cell attachment region (CS-1) of fibronectin²⁷; it appears likely that basophils are therefore capable of attaching to this extracellular matrix protein. In addition, we have recently determined that basophils express $\alpha 4\beta 7$ (Act-1),²⁵ an alternative ligand for VCAM-1 and fibronectin,^{28, 29} as well as a newly characterized molecule termed mucosal addressin cell adhesion molecule-1 (MAdCAM-1) that has structural homology to both VCAM-1 and ICAM-1 and appears to be involved in lymphocyte homing to the gut mucosa.^{30, 31} This is intriguing in light of the longstanding interest in the role of basophils in Crohn's disease and parasite immunity in various animal models,^{1, 32} and suggests a possible role for the interaction of $\alpha 4\beta 7$ with MAdCAM-1 in trafficking of basophils to the gut during certain immune responses in vivo.

With respect to possible basophil-selective "triggers" that may play a role in stimulating transendothelial migration and chemotaxis, previous studies of basophil recruitment have identified a variety of stimuli that are chemotactic for human basophils, including C5a,³³ cytokines such as interferon- γ , IL-3, and granulocyte-macrophage colony-stimulating factor,^{34, 35} and chemokines such as RANTES, macrophage inflammatory protein 1 α (MIP-1 α), monocyte chemoattractant protein-1 (MCP-1), and MCP-3.^{36, 37} With the exception of IL-3¹⁴ and possibly MCP-3, which has not been tested, none of the cytokines or chemokines have any direct effect on basophil adhesion molecule expression or adhesion to endothelium in vitro (Table II). These observations are similar to those made with eosinophils, where RANTES was found to have potent chemotactic activity and stimulate transendothelial migration without having any di-

rect effect on eosinophil adhesion molecule expression or adhesion to endothelium.^{38, 39} Future studies of the effect of chemokines and other stimuli on basophil transendothelial migration should help to clarify the role of chemoattractants in basophil recruitment responses.

CONCLUSIONS

Human basophils express a typical pattern of cell adhesion molecules on their surface, including certain selectins, integrins, Sialyl-Lewis^x-containing carbohydrates, and those belonging to the immunoglobulin adhesion molecule family. The function of many of these molecules has now been established in a variety of static in vitro adhesion assays, yet their function under conditions of shear stress, during transendothelial migration, during interaction with extracellular matrix proteins, or in vivo remain unexplored. Defining the role(s) of known adhesion molecules on both basophils and endothelial cells is imperative if we are to learn how these leukocytes are recruited to the skin and airways of persons with allergic diseases. With this information, it may be possible to selectively block basophil influx and allergic inflammation in vivo.

REFERENCES

1. Mitchell EB, Askenase PW. Basophils in human disease. *Clin Rev Allergy* 1983;1:427-48.
2. Lichtenstein LM, Bochner BS. The role of basophils in asthma. *Ann NY Acad Sci* 1991;629:48-61.
3. Charlesworth EN, Hood AF, Soter NA, Kagey-Sobotka A, Norman PS, Lichtenstein LM. Cutaneous late-phase response to allergen: mediator release and inflammatory cell infiltration. *J Clin Invest* 1989;83:1519-26.
4. Iliopoulos O, Baroody FM, Naclerio RM, Bochner BS, Kagey-Sobotka A, Lichtenstein LM. Histamine containing cells obtained from the nose hours after antigen challenge have functional and phenotypic characteristics of basophils. *J Immunol* 1992;148:2223-8.
5. Guo C-B, Liu MC, Galli SJ, Bochner BS, Kagey-Sobotka A, Lichtenstein LM. The histamine containing cells in the late phase response to antigen in the lung are basophils. *Am J Respir Cell Molec Biol* 1994;10:384-90.
6. Springer TA. Adhesion receptors of the immune system. *Nature* 1990;346:425-34.
7. Springer TA. Traffic signals for lymphocyte recirculation and leukocyte emigration: the multistep paradigm. *Cell* 1994;76:301-14.
8. Harlan J, Liu D. Adhesion: its role in inflammatory disease. New York: W.H. Freeman and Co., 1992.
9. Montefort S, Holgate ST, Howarth PH. Leucocyte-endothelial adhesion molecules and their role in bronchial asthma and allergic rhinitis. *Eur Respir J* 1993;6:1044-54.
10. Baroody FM, Lee B-J, Lim MC, Bochner BS. Implicating adhesion molecules in nasal allergic inflammation. *Eur Arch Oto-Rhino-Laryngol* 1994 (in press).

11. Bochner BS, Schleimer RP. The role of adhesion molecules in human eosinophil and basophil recruitment. *J ALLERGY CLIN IMMUNOL* 1994 (in press).
12. Valent P, Bettelheim P. The human basophil. *Crit Rev Oncol Hematol* 1990;10:327-52.
13. Valent P, Bettelheim P. Cell surface structures on human basophils and mast cells. Biochemical and functional characterization. *Adv Immunol* 1992;52:333-423.
14. Bochner BS, McKelvey AA, Sterbinsky SA, et al. Interleukin-3 augments adhesiveness for endothelium and CD11b expression in human basophils but not neutrophils. *J Immunol* 1990;145:1832-37.
15. Bochner BS, Sterbinsky SA. Altered surface expression of CD11 and Leu-8 during human basophil degranulation. *J Immunol* 1991;146:2367-73.
16. Knol EF, Mul FPI, Jansen H, Calafat J, Roos D. Monitoring human basophil activation via CD63 monoclonal antibody-435. *J ALLERGY CLIN IMMUNOL* 1991;88:328-38.
17. Georas SN, Liu MC, Newman W, Beall WD, Stealey BA, Bochner BS. Altered adhesion molecule expression and endothelial activation accompanies the recruitment of human granulocytes to the lung following segmental antigen challenge. *Am J Respir Cell Mol Biol* 1992;7:261-9.
18. Lo SK, Lee S, Ramos RA, Lobb R, Rosa M, Chiroso G, Wright SD. Endothelial-leukocyte adhesion molecule-1 stimulates the adhesive activity of leukocyte integrin CR3 (CD11b/CD18, Mac-1, $\alpha_M\beta_2$) on human neutrophils. *J Exp Med* 1991;173:1493-500.
19. Smyth SS, Joneckis CC, Parise LV. Regulation of vascular integrins. *Blood* 1993;81:2827-43.
20. van Kooyk Y, Weder P, Hogervorst F, et al. Activation of LFA-1 through a Ca^{2+} dependent epitope stimulates lymphocyte adhesion. *J Cell Biol* 1991;112:345-54.
21. van Kooyk Y, Weder P, Heije K, Figdor CG. The role of extracellular Ca^{2+} in LFA-1 mediated adhesion and distribution. *J Cell Biol* 1994;124:1061-70.
22. Bochner BS, Peachell PT, Brown KE, Schleimer RP. Adherence of human basophils to cultured umbilical vein vascular endothelial cells. *J Clin Invest* 1988;81:1355-60.
23. Bochner BS, MacGlashan DW Jr., Marcotte GV, Schleimer RP. IgE-dependent regulation of human basophil adherence to vascular endothelium. *J Immunol* 1989;142:3180-6.
24. Bochner BS, Lusinskas FW, Gimbrone MA Jr., et al. Adhesion of human basophils, eosinophils, and neutrophils to IL-1-activated human vascular endothelial cells: contributions of endothelial cell adhesion molecules. *J Exp Med* 1991;173:1553-7.
25. Bochner BS, Sterbinsky SA, McKelvey AA, Newman W, Schleimer RP, MacGlashan DW Jr. Counterreceptors on human basophils for endothelial cell adhesion molecules (submitted for publication).
26. Schleimer RP, Sterbinsky SA, Kaiser J, et al. Interleukin-4 induces adherence of human eosinophils and basophils but not neutrophils to endothelium: association with expression of VCAM-1. *J Immunol* 1992;148:1086-92.
27. Wayner EA, Garcia-Pardo A, Humphries MJ, McDonald JA, Carter WG. Identification and characterization of the T lymphocyte adhesion receptor for an alternative cell attachment domain (CS-1) in plasma fibronectin. *J Cell Biol* 1989;109:1321-30.
28. Postigo AA, Sanchez-Mateos P, Lazarovits AI, Sanchez-Madrid F, de Landazuri MO. $\alpha 4\beta 7$ integrin mediates B-cell binding to fibronectin and vascular cell adhesion molecule-1 expression and function of $\alpha 4$ integrins on human B-lymphocytes. *J Immunol* 1993;151:2471-83.
29. Ruegg C, Postigo AA, Sikorski EE, Butcher EC, Pytela R, Erle DJ. Role of integrin $\alpha 4\beta 7/\alpha 4\beta P$ in lymphocyte adherence to fibronectin and VCAM-1 and in homotypic cell clustering. *J Cell Biol* 1992;117:179-89.
30. Berlin C, Berg EL, Briskin MJ, et al. $\alpha 4\beta 7$ integrin mediates lymphocyte binding to the mucosal vascular addressin MAdCAM-1. *Cell* 1993;74:185-95.
31. Briskin MJ, McEvoy LM, Butcher EC. MAdCAM-1 has homology to immunoglobulin and mucin-like adhesion receptors and to IgA1. *Nature* 1993;363:461-4.
32. Askenase PW. Role of basophils, mast cells, and vasoamines in hypersensitivity reactions with a delayed time course. *Prog Allerg* 1977;23:199-320.
33. Lett-Brown MA, Boetcher DA, Leonard EJ. Chemotactic responses of normal human basophils to C5a and to lymphocyte-derived chemotactic factor. *J Immunol* 1976;117:246-52.
34. Lett-Brown MA, Alvoet M, Hooks JJ, Georgiades JA, Thueson DO, Grant JA. Enhancement of basophil chemotaxis in vitro by virus-induced interferon. *J Clin Invest* 1981;67:547-52.
35. Tanimoto Y, Takahashi K, Kimura I. Effects of cytokines on human basophil chemotaxis. *Clin Exp Allergy* 1992;22:1020-5.
36. Bischoff SC, Krieger M, Brunner T, et al. RANTES and related chemokines activate human basophil granulocytes through different G-protein-coupled receptors. *Eur J Immunol* 1993;23:761-7.
37. Dahinden CA, Geiser T, Brunner T, et al. Monocyte chemotactic protein 3 is a most effective basophil- and eosinophil-activating chemokine. *J Exp Med* 1994;179:751-6.
38. Yamada T, Ebisawa M, MacGlashan DW Jr, et al. RANTES is a chemoattractant for human eosinophils [Abstract]. *J ALLERGY CLIN IMMUNOL* 1993;91:692.
39. Ebisawa M, Yamada T, Klunk D, et al. Regulation of eosinophil and neutrophil transendothelial migration by cytokines and chemokines [Abstract]. *J ALLERGY CLIN IMMUNOL* 1993;91:691.
40. Bochner BS, McKelvey AA, Schleimer RP, Hildreth JEK, MacGlashan DW Jr. Flow cytometric methods for analysis of human basophil surface antigens and viability. *J Immunol Methods* 1989;125:265-71.
41. Keizer GD, Visser W, Vliem M, Figdor CG. A monoclonal antibody (NKI-L16) directed against a unique epitope on the α -chain of human leukocyte function-associated antigen 1 induces homotypic cell-cell interactions. *J Immunol* 1988;140:1393-1400.
42. Hildreth JEK, August JT. The human lymphocyte function-associated (HLFA) antigen and a related macrophage differentiation antigen (HMac-1): functional effects of subunit-specific monoclonal antibodies. *J Immunol* 1985;134:3272-80.
43. Shaw S. Antibodies and molecules of the Fifth International Workshop of Leukocyte Differentiation Antigens. In: Schlossman S, Boumsell L, Gilks W, et al., eds. Leukocyte typing V: White cell differentiation antigens. Oxford: Oxford University Press, 1994 (in press).
44. Stain C, Stockinger H, Scharf M, et al. Human blood basophils display a unique phenotype including activation linked membrane structures. *Blood* 1987;70:1872-9.