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Human mononuclear phagocyte molecules and the use of monoclonal antibodies in their detection

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INTRODUCTION

Monoclonal antibodies (MoAb) have provided a powerful means of analysing molecular function. As will be described, many MoAb have already been successfully used to unravel the functions of myeloid molecules, most notably the receptors involved in phagocytosis. These types of antibodies and many others were investigated and compared in the Third International Workshop on Human Leucocyte Differentiation Antigens (Oxford, 1986) (McMichael *et al.*, 1987; reviewed by Shaw, 1987; Franklin, Hogg & Mason, 1987). Table 1 lists 16 groups or clusters of differentiation (CD) of myeloid MoAb which were defined by the Workshop (Hogg & Horton, 1987). Mononuclear phagocytes (Mph) are reported to make more than 60 products which indicates a biosynthetic capacity greater than that recorded for any other single cell type (Cohn, 1983). These products are not all made simultaneously but at different stages of the Mph life cycle indicating that they perform a different spectrum of functions at each stage of their maturational sequence. The present challenge is to link up the phenomena detected with MoAb to those Mph molecules about which much is already known. Very few of the anti-Mph MoAb are completely lineage specific. For example, CD14, 31, w32 and 34 MoAb react with Mph, endothelium and variably with other types of cells; for the molecules recognized by these MoAb there are no known functions. However, it is hoped that defining the full cell distribution of various molecules will give some clues as to their role in the functional repertoire of the Mph. Much of the detailed information, outlined in the next few sections, about the functioning of the receptors for complement (CR) and immunoglobulin (FcR) has been obtained with the use of specific MoAb.

Keywords human mononuclear phagocyte molecules monoclonal antibodies

HUMAN MONONUCLEAR PHAGOCYTE MOLECULES

LFA-1/CR3/p150,95 family (CD11a,b,c and CD18)

The LFA-1/CR3/p150,95 family is a trio of related leucocyte differentiation molecules which have distinct α chains but share a common β chain (Sanchez-Madrid *et al.*, 1983; reviewed by Martz, 1987). LFA-1 is expressed on essentially all cells of haematopoietic origin but CR3 and p150,95 are relatively myeloid specific. CR3 is present on monocytes, granulocytes and large granular lymphocytes, i.e. natural killer cells, and p150,95 is expressed on monocytes and to an even greater degree on most tissue macrophages (Hogg *et al.*, 1985). Granulocytes when activated can express p150,95. It is very highly expressed on hairy leukaemia cells (Schwarting, Stein & Wang, 1985), some B cell lines and some cloned cytotoxic T cells (Miller, Schwarting & Springer, 1986).

Several of the first described 'macrophage specific' antibodies such as Mac-1, OKM1 and Mo1 are directed against the CR3 α chain which appears to be very immunogenic in the mouse. Monoclonal antibodies of this type have been instrumental in proving that the CR3 molecule which serves as a receptor for the complement component iC3b, is an important receptor for particle phagocytosis and subsequent respiratory burst response in Mph (Beller, Springer & Schreiber,

Table 1. Monoclonal antibodies which recognize mononuclear phagocyte molecules

CD group	Molecule	kD	Typical MoAb	Distribution on haemopoietic cells
CD11a	LFA-1 α chain	180	MHM24, CIMT	Most leucocytes
CD11b	CR3 α chain	165	Mol, OKM1, 44	Monocytes, granulocytes, LGL
CD11c	p150,95 α chain	150	KB23, 3.9, Ki-M1, Bu-15	Monocytes, grans (wk), macrophages
CD18	common β chain	95	MHM23, 60.3	Most leucocytes
CDw12		?	M67, MG14	Monocytes, granulocytes, platelets
CD13		150	MY7, WM-15	Monocytes, granulocytes
CD14		55	UCHM1, Mo2	Monocytes, DRC
CD15	anti X	CHO	IG10, VIMD5	Granulocytes (monocytes)
CD16	FcR_{low}	50–60	3G8, CLB/FcRgran1	Granulocytes
CDw17	anti lactoceramide	Lipid	T5A7, (G)035	Monocytes, granulocytes, platelets
CD31	gpIIa?	130–140	SG134, TM3	Monocytes, granulocytes, platelets
CDw32	FcRII?	40	IV3, CIKM5, 2E1	Monocytes, granulocytes, platelets, B cells (T cells), (bone marrow)
CD33		67	L4F3, L1B2, My9	Myelogenous leukaemia
CD34		115	BI-3C5, My10	Myeloid and lymphoblastic leukaemia
CD35	CR1	220	E11, J3B11, J3D3, To5	Monocytes, granulocytes, DRC, red cells
CD36	platelet gpIV?	85	5F1, CIMeg1	Monocytes, platelets

?, Further confirmation needed.

1982). Furthermore, MoAb blocking studies show that there are two distinct ligand binding sites on CR3, one for iC3b and another detected by the binding of zymosan, the β glucan component of bakers' yeast (Ross, Cain & Lachmann, 1985a). The second site must be engaged before particle ingestion occurs. Because some anti-CR3 MoAb block both kinds of binding, the two sites are thought to be close together on the CR3 α chain.

This type of CR3 binding requires the pathogen to be opsonized, but there is mounting evidence that unoponized bacteria may bind and be phagocytosed by this family of molecules. Thus, phagocytosis of unopsonized *Staphylococcus epidermidis* by neutrophils is blocked by anti-CR3 and anti-LFA-1 MoAb (Ross *et al.*, 1985b) and binding of *E. coli* by cultured monocytes is blocked by MoAb to LFA-1, CR3 and p150,95 (Wright & Jong, 1986). This suggests that different binding sites recognize these pathogens and that there may be multiple binding sites with different ligand requirements for unopsonized bacteria on the LFA-1/CR3/p150,95 family. Whether some of this binding is mediated via complement components synthesized by macrophages has not been fully explored (Ezekowitz *et al.*, 1983).

What has been unexpected is the finding that p150,95 also has specificity for iC3b (Malhotra, Hogg & Sim, 1986). As CR3 is chiefly confined to circulating monocytes and granulocytes, whereas p150,95 is expressed in large amounts on tissue macrophages, it can be speculated that the two receptors satisfy different requirements for iC3b-mediated phagocytosis in these two different microenvironments. However, as discussed below, both molecules may have other functions.

The relationship between members of the LFA-1/CR3/p150,95 family was initially discovered through investigation of an extremely rare type of patient suffering from severe bacterial and fungal infections (Springer *et al.*, 1984; Anderson *et al.*, 1985; Ross *et al.*, 1985b; reviewed in Martz, 1987). These patients have a defect in the synthesis of the LFA β chain subunit which results in a lack of expression of all three members of the LFA-1 family. As well as obvious problems with phagocytosis the patients are deficient in a variety of functions which depend on cell adherence. Specifically, patients neutrophils and probably also their monocytes are unable to respond to tissue injury chemotactic signals by adhering to endothelium (marginating) and moving through endothelium (diapedsis) to the site of tissue injury (Springer & Anderson, 1986). This problem is due

to a lack of CR3 and apparently p150,95 which in normal cells are present on the membrane and in secondary granules (Todd *et al.*, 1984), the latter being shed as a myeloid cell undergoes oriented migration under the influence of a chemotactic signal (Wright & Gallin, 1979). Although this role of CR3 and p150,95 has been well described for neutrophil migration, rather less is known about whether monocytes perform in the same manner. In addition, this adherence related role of CR3 and p150,95 has been stated not to involve iC3b (yet another ligand?).

Monocytes also express the third member of this family, the LFA-1 molecule. However, in relatively few studies has the role of monocyte LFA-1 been investigated. It is well known that the LFA-1 molecule participates in adhesive interactions between T cells, B cells and their targets and in various kinds of lymphocyte homotypic reactions (see Martz, 1987). Not surprisingly, it appears that monocytes also use LFA-1 in homotypic adhesion reactions (Mentzer, Faller & Burakoff, 1986). In a second study, LFA-1 positive activated murine Mph were shown to use the LFA-1 molecule to strengthen weak tumour target cell binding which lead on to cytolysis (Strassmann *et al.*, 1986). Most recently both monocyte LFA-1 as well as T cell LFA-1 have been shown to be essential for the initial interaction between monocytes and T cells in an immune response (Dougherty & Hogg, 1987). Preliminary evidence indicates that the 90 kD protein, ICAM-1 (Rothlein *et al.*, 1986) which serves as the ligand for LFA-1-mediated homotypic adhesion acts also as a ligand for monocyte LFA-1 (G. Dougherty, pers. comm.). It is not known whether LFA-1 serves as an 'adhesive glue' in these homotypic and heterotypic cell interactions or whether it plays some more active role.

These LFA-1 family proteins are now thought to form part of a new supergene family of 'adhesion' molecules all of which have a high molecular weight α chain and nonrelated β chain of lower molecular weight (reviewed by Hynes, 1987). Many members of this group were identified by testing the ability of MoAb to block the binding of various cell types to fibronectin and by using the fibronectin 'cell recognition' hexapeptide, Gly-*Arg-Gly-Asp*-Ser-Pro (RGD) to isolate further family members (reviewed by Leptin, 1986). The N-terminal amino acid sequences of LFA-1 and CR3 α chains are homologous (Springer, Teplow & Dreyer, 1985). The platelet IIb glycoprotein (of the gpIIbIIIa molecule—see below) also has significant sequence homology to LFA-1 and CR3 α chains (Charo *et al.*, 1986). A cell transfectant containing a genomic clone coding for these three molecules has been described by Cosgrove *et al.* (1986). Very recently the β subunit of the LFA-1/CR3/p150,95 family has been cloned and found to have 45% homology to band III of integrin, which forms part of the receptor for fibronectin and integrin on chicken fibroblasts (Kishimoto *et al.*, 1987; Law *et al.*, 1987). In addition the LFA-1 family β chain has a 47% homology to platelet gpIIIa (see Hynes, 1987). A speculation is that the α subunits i.e. LFA-1, gpIIb confer ligand binding specificity and the β subunits i.e. LFA-1 family β chain, band III and gpIIIa are responsible for intracytoplasmic, possibly cytoskeletal interactions.

CR1

Another receptor involved in complement-mediated phagocytosis is CR1, the ligand for the complement component C3b/C4b (reviewed in Ross, 1987). CD35 MoAb recognize four allotypic variants of CR1 which, in order of frequency, are molecules of 190, 220, 160 and 250 kD, with the last two being very rare (Dykman *et al.*, 1985). No functional differences have been detected among the CR1 alleles. This receptor is expressed on many cell types: 550–700 receptors on red cells, 3000 receptors on unstimulated myeloid cells and even greater numbers on kidney podocytes and dendritic reticulum cells in B cell germinal centres. CR1 binds immune complexes and in this way red cells, which as a population account for most of the CR1, deliver immune complexes to Kupffer cells in the liver. It has been estimated that the half-life of fixed C3b on red cells in whole human serum is approximately 90 s. However, this is sufficient time for CR1-associated immune complexes to be stripped from red cells in the liver (Cornacoff *et al.*, 1983). Macrophages also bind antigen-antibody complexes directly but require activation before ingesting them. This second signal is provided by interaction of Mph fibronectin or laminin receptors with ligand (Wright, Craigmyle & Silverstein, 1983; Bohnsack *et al.*, 1985).

The number of CR1 per cell is an inherited trait and persons with low CR1 numbers are thought to have a decreased ability to clear immune complexes (Wilson *et al.*, 1982; Walport *et al.*, 1985). In

addition CR1 numbers are low in several autoimmune conditions such as SLE and autoimmune haemalytic anaemia and other disorders such as AIDS and lepromatous leprosy. There has been controversy as to whether such low CR1 levels are an inherited or acquired trait. Persons suffering from autoimmune disorders tend to have lower numbers of CR1 than the general population but in two studies their close relatives resemble the normal population (Walport *et al.*, 1985; M. Walport pers. comm.). Thus, the answer seems to be that it is an acquired phenomenon. In contrast to this data is a Boston study in which relatives of SLE patients were shown to have CR1 numbers significantly lower than unrelated normal persons (Wilson *et al.*, 1982). The reason for the differences in the findings of these various studies is not at all clear.

Both CR1 and CR3 have many similarities in expression and function on Mph. For both receptors, the level of expression is normally low; however when the cells are stimulated via a chemotactic signal the expression of both receptors dramatically and rapidly increases. This increase comes from the release of the contents of cytoplasmic secondary granules to the membrane (Berger, O'Shea & Cross, 1984). There are a number of functions that only CR3 can perform: (1) CR3 performs adherence functions (Springer & Anderson, 1986), (2) CR3 can bind unopsonized bacteria (Ross *et al.*, 1985b; Wright & Jong, 1986). (3) CR3 can trigger the respiratory burst in neutrophils and leukotriene release from monocytes (Austen & Czop, 1985).

FcγR

A third family of receptors which engage in phagocytosis and endocytosis are the Fc receptors (FcR). To date, three different FcR for IgG (FcγR) have been identified (reviewed by Burton, 1985; Unkeless, 1986; Anderson & Looney, 1986) on human Mph. These are named FcRI, FcRII and FcR_{low}. In addition, there is an FcR for IgE, but uncertainty about receptors for IgA and no identified receptor for IgM. The FcγR bind the human IgG isotypes in the order of IgG1≡IgG3 > IgG4 and are reported not to bind IgG2. Although these FcγR are thought to assist the Mph in its scavenger role, their widespread presence on many haemopoietic cell types suggests further unknown functions for this family. The CD16 MoAb react with the 50–70 kD FcR_{low} which is chiefly present on neutrophils and NK cells but also on some tissue macrophages. No mouse homologue of this receptor has been identified. FcRII is a 40 kD molecule in man (Looney, Abraham & Anderson, 1986) which is present on many haemopoietic cells (Anderson & Looney, 1986) and endothelium (Hogg & Horton, 1987). It can be distinguished from FcR_{low} and the third receptor FcRI by reactivity with CDw32 MoAb. In addition, it has been named FcRII because it is similar to murine FcRII in its selective binding of murine IgG1/IgG2b. Murine FcRII is however, a molecule of 47–60 kD, so whether they are homologues remains to be proven. The 72 kD FcRI is the most mononuclear phagocyte specific of these three FcγR. Two specific MoAb for FcRI have been identified, named MoAb 32 and 10.1, the latter being specific for an epitope near the binding site (Anderson *et al.*, 1986; G. J. Dougherty *et al.*, unpublished). FcRI can also be identified by its ability to bind murine IgG2a.

The individual roles of these receptors are not yet clearly identified. Of the three FcγR, FcRI alone binds monomeric Ig with an affinity of 5×10^8/M. Such a high binding affinity would suggest that any available receptor would be immediately occupied by soluble serum Ig. However, the expression of FcRI is inducible by γ-IFN (Perussia *et al.*, 1983) so one could imagine a scenario in which FcRI was expressed 'on the spot' in circumstances of a tissue immune response. In assays *in vitro* FcRI is active in ADCC (Steplewski, Lubeck & Koprowski, 1983) and can activate the respiratory burst cycle when crosslinked (Anderson *et al.*, 1986). Both FcRII and FcR_{low} preferentially bind complexed immunoglobulin. In an experiment carried out with chimpanzees, a CD16 FcR_{low} MoAb named 3G8 was able to block the clearance of antibody-sensitized chimpanzee RBC but not soluble complexes (Clarkson *et al.*, 1986). This was an unexpected result as experiments *in vitro* would have lead to the prediction that such clearance should have taken place via the CR3 receptor. The fact that these different receptors appear to do much the same job may not be accidental. Perhaps the factors which determine which receptor is to be engaged depend upon the nature of the virus, bacterium or other particle, the extent of antibody response and mixture of isotypes produced or the state of complement activation. To work out the individual capabilities of the CR and FcR each will have to be tested in isolation either by blocking the others with MoAb or

by individual testing of transfected cloned receptor genes. Blocking antibodies are now available for all the recognized CR and FcγR and clones for at least some of them have also been isolated.

The analysis of several FcR genes suggests that this will be a complex family of molecules. The cloning of murine FcRII has yielded three genes which are highly homologous in their extracellular domains but with great differences in the cytoplasmic domains (Ravetch *et al.*, 1986; Lewis *et al.*, 1986). Two of these genes are expressed by Mph, and one by Mph and lymphocytes. The relationship of the three genes to FcRII has not yet been determined but this finding may account for some of the diversity in FcRII seen in different cell types (Ravetch *et al.*, 1986). It seems clear that the proteins coded for by these genes would have similar Ig binding properties but the potential for very different intracellular signalling mechanisms, which is an unprecedented situation. FcRII belongs to the immunoglobulin supergene family as does the rabbit polyIg FcR which functions in the transport of IgA across epithelial cells (Mostov, Friedlander & Blobel, 1984). In contrast to FcRII and the polyIg FcR, is the human FcR for IgE which has striking homology to several lectin binding proteins (Ikuta *et al.*, 1987). One might have expected these receptors, all of which bind to the Fc of various Ig isotypes, to have had substantial sequence homology. However, perhaps they do not have as much functional homology as has been assumed. The binding site of FcRI has been localized to the hinge region of the Cγ2 domain of IgG (reviewed in Burton, 1985). There is no information about where other FcR bind. At this stage, similarities between the various FcR may be more apparent than real. The FcR, attached to the 'business' end of the various Ig isotypes, may individually deliver very different signals to the cells on which they are located. As mentioned above, even the same class of FcR may have a choice of signalling pathways.

Monocyte and platelet molecules

The number of molecules shared between monocytes (plus frequently polymorphs) and platelets is only beginning to be appreciated. Five myeloid CD groups, CDw12, CDw17, CD31, CDw32 and CD36 recognize such molecules (Hogg & Horton, 1987). The CDw17 MoAb react with lactoceramide and the CDw32 MoAb are thought to detect FcRII (Anderson & Looney, 1986). The CD31 antibodies are specific for the gpIIa molecule which was first identified on platelets and then on endothelium (van Mourick *et al.*, 1985). CD36 antibodies detect gpIV thought to be the thrombospondin receptor (von dem Borne *et al.*, 1987). Cell transfectants which express CD31 specific proteins (Goyert & Ferrero, 1987) and CD36 specific proteins (Look *et al.*, 1987b) are available. There is still a lack of definitive proof as to whether monocytes synthesize the gpIIbIIIa molecule (CDw41 MoAb), which acts as a receptor for fibrinogen, fibronectin and von Willebrands factor (also see LFA-1/CR3 p150,95 section). This extensive sharing of molecules between Mph and platelets suggests that these two cell types may have more in common in functional terms than has previously been suspected. As well as having procoagulant activity, Mph may perform other activities thought to be the exclusive property of platelets.

Other well-defined myeloid proteins with unknown function

Four other CD groups react with Mph proteins which are now well defined but for which no function is yet known. Cell transfectants have been made for all four groups (Look *et al.*, 1987b; Goyert & Ferrero, 1987). Such transfectants are presently being used for several purposes. In practical terms, antibody screening of transfectants provides a rapid means of defining specificities of unknown selections of MoAb. Transfectants can also be used to immunize mice of the same haplotype strain with the hope that the ensuing immune response will be directed solely against the transfected molecule. On the other hand, the use of MoAb to select transfected gene products provides a means of cloning genomic sequences coding for a particular protein. Finally, transfection of cloned cDNA and subsequent synthesis of a desired MoAb-reactive protein provides a means of 'joining up' the circle of identification between isolated cDNA and protein.

CD13

The first of these groups is the CD13 cluster of MoAb which are specific for a 150 kD protein on monocytes and granulocytes. These MoAb also react with various types of tissue Mph which bear processes having a rather distinctive fibrous or 'lacy' appearance. As CD13 MoAb stain other

structures such as vascular tissue, sweat glands and bile canaliculi with the same fibrous pattern, one could be tempted to investigate basement membrane proteins in the search for candidate target molecules. As the molecular cloning of the gene encoding gp150 has now been reported, the nature of this protein may soon be revealed (Look *et al.*, 1987a).

CD14

More is known about the 55 kD protein with which the CD14 MoAb react. Although very few of the anti Mph MoAb have exclusive Mph specificity, the CD14 cluster of MoAb is amongst the most specific, although in tissue sections these MoAb react with dendritic reticulum cells (DRC) and some endothelium. By a variety of tests the 20 CD14 MoAb analysed in the Third Workshop were shown to react with a number of epitopes on this molecule. This heterogeneity was reflected in the immunohistochemical staining patterns of the individual MoAb, some of which labelled only monocytes, DRC and some endothelium, while others were more broadly reactive, labelling in addition to the aforementioned, also tonsil Langerhan's cells, interdigitating cells, some granulocytes and even basophils. The N terminus of the gp55 protein has been sequenced (Bazil *et al.*, 1986) and the cloning of the gene was announced at the Third Workshop by S. Goyert (New York) but, to date, there is no hint as to what the function of this rather exclusively monocyte protein might be.

CD33 and CD34

Two other clusters of MoAb CD33 and CD34, detect proteins on promyelocytic and stem cell leukaemias respectively and have been of use in classifying myeloid leukaemias. The CD33 MoAb react with multipotential progenitor cells (CFU-GEMM), with CFU-C and some BFU-E as well as myeloid precursors up to the promyelocyte stage (Griffin *et al.*, 1984). The reactivity of CD34 MoAb is restricted to the very immature progenitor cells, both myeloid and lymphoid. Curiously it appears that endothelial cells also express the same 115 kD molecule as is present on the progenitor cells (R. Sutherland, pers. comm.).

CONCLUDING REMARKS

The LFA-1/CR3/p150,95 family provides an excellent example of the insight which can be gained into the structure and functioning of a family of molecules through the use of monoclonal antibodies. It seems clear that the next group of molecules to yield their secrets in a similar way will be the Fc receptors. For some of the other well-characterized Mph molecules, one awaits the chance or intuitive experiment which points towards a function which can then be dissected with the appropriate collection of monoclonal antibodies.

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REFERENCES

ANDERSON, D.C., SMALSTIEG, F.C., FINEGOLD, M.J., HUGHES, B.J., ROTHLEIN, R., MILLER, L.J., KOHL, S., TOSI, M.F., JACOBS, R.L., WALDROP, T.C., GOLDMAN, A.S., SHEARER, W.T. & SPRINGER, T.A. (1985) The severe and moderate phenotypes of heritable Mac-1, LFA-1 deficiency: their quantitative definition and relation to leucocyte dysfunction and clinical features. *J. infect. Dis.* **152,** 668.

ANDERSON, C.L., GUYRE, P.M., WHITIN, J.C., RYAN, D.H., LOONEY, R.J. & FANGER, M.W. (1986) Monoclonal antibodies to Fc receptors for IgG on human mononuclear phagocytes: antibody characterization and induction of superoxide production in a monocyte cell line. *J. biol. Chem.* **261,** 12856.

ANDERSON, C.L. & LOONEY, R.J. (1986) Human leukocyte IgG Fc receptors. *Immunol. Today* **7,** 264.

AUSTEN, K.F. & CZOP, J.K. (1985) Release of leukotrienes by human monocytes on stimulation of their phagocytic receptor for β-glucan and other particulate activators of complement. *Fec. Proc.* **44,** 736.

BAZIL, V., HOREJSI, V., BAUDYS, M., KRISTOFOVA, H., STROMINGER, J.L., KOSTKA, W. & HILGERT, I. (1986) Biochemical characterization of a soluble form of the 53-kDa monocyte surface antigen. *Eur.*

J. Immunol. **16,** 1583.

BELLER, D.I., SPRINGER, T.A. & SCHREIBER, R.D. (1982) Anti-Mac-1 selectively inhibits the mouse and human type three complement receptor. *J. exp. Med.* **156,** 1000.

BERGER, M., O'SHEA, J. & CROSS, A.S. (1984) Human neutrophils increase expression of C3bi as well as C3b receptors upon activation. *J. clin. Invest.* **74,** 1566.

BOHNSACK, J.F., KLEINMAN, H.K., TAKAHASHI, T., O'SHEA, J.J. & BROWN, E.J. (1985) Connective tissue proteins and phagocytic cell function. *J. exp. Med.* **161,** 912.

VON DEM BORNE, A.E.G., RISSEEUW-BOGAERT, M.J., BOS, M.J.E., GITTAY, J., VISSER, F.J., V.D. SCHOOT, E. & TETTEROO, P.A.T. (1987) Biochemical and serological studies with monoclonal antibodies against platelets. In: *Leucocyte Typing III. White Cell Differentiation Antigens.* (Eds A.J. McMichael *et al.*) (in press) Oxford University Press, Oxford.

BURTON, D.R. (1985) Immunoglobulin G: functional sites. *Molecular Immunol.* **22,** 161.

CHARO, I.F., FITZGERALD, L.A., STEINER, B., RALL, S.C., BEKEART, L.S. & PHILLIPS, D.R. (1986) Platelet glycoproteins IIb and IIIa: Evidence for a family of immunologically and structurally related glycoproteins in mammalian cells. *Proc. natl. Acad. Sci.* **83,** 8351.

CLARKSON, S.B., KIMBERLY, R.P., VALINSKY, J.E., WITMER, M.D., BUSSEL, J.B., NACHMAN, R.L. & UNKELESS, J.C. (1986) Blockade of clearance of immune complexes by an anti-Fcγ receptor monoclonal antibody. *J. exp. Med.* **164,** 474.

COHN, Z.A. (1983) *The Macrophage-Versatile Element of Inflammation.* In The harvey Lectures Series 77. Academic Press, New York, London.

CORNACOFF, J.B., HEBERT, L.A., SMEAD, W.L., VAN AMAN, M.E., BIRMINGHAM, D.J. & WAXMAN, F.J. (1983) Primate erythrocyte-immune complex-clearing mechanism. *J. clin. Invest.* **71,** 236.

COSGROVE, L.J., SANDRIN, M.S., RAJASEKARIAH, D. & MCKENZIE, I.F.C. (1986) A genomic clone encoding the α chain of the OKM1, LFA-1 and platelet IIb-IIIa molecules. *Proc. natn. Acad. Sci.* **83,** 752.

DOUGHERTY, G.J. & HOGG, N. (1987) The role of monocyte LFA-1 in accessory cell function. *Eur. J. Immunol.* (in press).

DYKMAN, T.R., HATCH, J.A., AQUA, M.S. & ATKINSON, J.P. (1985) Polymorphism of the C3b/C4b receptor (CR1) characterization of a fourth allele. *J. Immunol.* **134,** 1787.

EZEKOWITZ, R.A.B., SIM, R.B., HILL, M. & GORDON, S. (1983) Local opsonization by secreted macrophage complement components. Role of receptors for complement in uptake of zymosan. *J. exp. Med.* **159,** 244.

FRANKLIN, W.A., HOGG, N. & MASON, D.Y. (1987) Human leukocyte differentiation antigens. Review of the third international workship. *Mol. & Cell. Probes* (in press).

GOYERT, S.M. & FERRERO, E. (1987) Isolation and characterization of a cDNA clone encoding gp55, the Mo2/My4/LeuM3 monocyte antigen. In: *Leucocyte Typing III. White Cell Differentiation Antigens.* (Eds A.J. McMichael, *et al.*) (in press) Oxford University Press, Oxford.

GRIFFIN, J.D., LINCH, D., SABBATH, K., LARCOM, P. & SCHLOSSMAN, S.F. (1984) A monoclonal antibody reactive with normal and leukemic human myeloid progenitor cells. *Leuk. Res.* **8,** 521.

HOGG, N., TAKACS, L., PALMER, D.G., SELVENDRAN, Y. & ALLEN, C. (1985) The p150,95 molecule is a marker of human mononuclear phagocytes: comparison with expression of class II molecules. *Eur. J. Immunol.* **16,** 240.

HOGG, N. & HORTON, M.A. (1987) Joint report of the myeloid section of the third international workshop on human leucocyte differentiation antigens. In: *Leucocyte Typing III. White Cell Differentiation Antigens.* (Eds A.J. McMichael, *et al.*) (in press) Oxford University Press, Oxford.

HYNES, R.O. (1987) Integrins: A family of cell surface receptors. *Cell* **48,** 549.

IKUTA, K., TAKAMI, M., KIM, C.W., HONJO, T., MIYOSHI, T., TAGAYA, Y., KAWABE, T. & YODOI, J. (1987) Human leucocyte Fc receptor for IgE: sequence homology of its cloned cDNA with animal lectins. *Proc. natn. Acad. Sci. USA.* **84,** 819.

KISHIMOTO, T.K., O'CONNOR, K., LEE, A., ROBERTS, T.M. & SPRINGER, T.A. (1987) Cloning the β subunit of the leukocyte adhesion proteins: homology to an extracellular receptor defines a novel supergene family. *Cell* **48,** 681.

LAW, S.K.A., GAGNON, J., HILDRETH, J.E.K., WELLS, C.E., WILLIS, A.C. & WONG, A.J. (1987) The primary structure of the β-subunit of the cell surface adhesion glycoproteins LFA-1, CR3 and p150,95 and its relationship to the fibronectin receptor. *EMBO J.* **6,** 915.

LEPTIN, M. (1986) The fibronectin receptor family. *Nature* **321,** 728.

LEWIS, V.A., KOCH, T., PLUTNER, H. & MELLMAN, I. (1986) A complementary DNA clone for a macrophage-lymphocyte Fc receptor. *Nature* **324,** 372.

LOOK, A.T., PEIPER, S.C., REBENTISCH, M.B., ASHMUN, R.A., ROUSSEL, M.F., LEMONS, R.S., LE BEAU, M.M., RUBIN, C.M. & SHERR, C.J. (1987a) Molecular cloning, expression and chromosomal localization of the gene encoding a human myeloid membrane antigen (gp150). *J. clin. Invest.* **78,** 914.

LOOK, A.T., PEIPER, S.C. & ASHMUN, R.A. (1987b) Binding of independently derived monoclonal antibodies to unique myeloid differentiation antigens. In: *Leucocyte Typing III. White Cell Differentiation Antigens.* (Eds A.J. McMichael *et al.*) (in press) Oxford University Press, Oxford.

LOONEY, R.J., ABRAHAM, G.N. & ANDERSON, C.L. (1986) Human monocytes and U937 cells bear two distinct Fc receptors for IgG. *J. Immunol.* **136,** 1641.

MALHOTRA, V., HOGG, N. & SIM, R.B. (1986) Ligand binding by the p150,95 antigen of U937 monocyte cells: properties in common with complement receptor type 3 (CR3). *Eur. J. Immunol.* **16,** 1117.

MARTZ, E. (1987) LFA-1 and other accessory molecules functioning in adhesions of T and B lymphocytes. *Human Immunol.* **18,** 3.

MCMICHAEL, A. *et al.* (1987) *Leucocyte Typing III. White Cell Differentiation Antigens.* (in press) Oxford University Press, Oxford.

MENTZER, S.J., FALLER, D.V. & BURAKOFF, S.J. (1986) Interferon-γ induction of LFA-1-mediated

homotypic adhesion of human monocytes. *J. Immunol.* **137,** 108.

MILLER, L.J., SCHWARTING, R. & SPRINGER, T.A. (1986) Regulated expression of the Mac-1, LFA-1, p150,95 glycoprotein family during leucocyte differentiation. *J. Immunol.* **137,** 2891.

MOSTOV, K.E., FRIEDLANDER, M. & BLOBEL, G. (1984) The receptor for transepithelial transport of IgA and IgM contains multiple immunoglobulin-like domains. *Nature* **308,** 37.

VAN MOURIK, J.A., LEEKSMAN, O.C., REINDERS, J.H., DE GROOT, P.G. & ZANDBERGEN-SPAARGAREN, J. (1985) Vascular endothelial cells synthesize a plasma membrane protein indistinguishable from the platelet glycoprotein IIa. *J. biol. Chem.* **260,** 11300.

PERUSSIA, B., DAYTON, E.T., LAZARUS, R., FANNING, V. & TRINCHIERI, G. (1983) Immune interferon induces the receptor for monomeric IgG1 on human monocyte and myeloid cells. *J. exp. Med.* **158,** 1092.

RAVETCH, J.V., LUSTER, A.D., WEINSHANK, R., KOCHAN, J., PAVLOVEC, A., PORTNOY, D.A., HULMES, J., PAN, Y-C.E. & UNKELESS, J.C. (1986) Structural heterogeneity and functional domains of murine immunoglobulin G Fc receptors. *Science* **234,** 718.

ROSS, G.D., CAIN, J.A. & LACHMANN, P.J. (1985a) Membrane complement receptor type three (CR3) has lectin-like properties analogous to bovine conglutinin and functions as a receptor for zymosan and rabbit erythrocytes as well as a receptor for iC3b. *J. Immunol.* **134,** 3307.

ROSS, G.D., THOMPSON, R.A., WALPORT, M.J., SPRINGER, T.A., WATSON, J.V., WARD, R.H.R., LIDA, J., NEWMAN, S.L., HARRISON, R.A. & LACHMANN, P.J. (1985b) Characterization of patients with an increased susceptibility to bacterial infections and a genetic deficiency of leukocyte membrane complement receptor type 3 and the related membrane antigen LFA-1. *Blood* **66,** 582.

ROSS, G.D. (1987) Abnormalities of membrane complement receptors associated with disease. In: *Recent Advances in Clinical Immunology*, (in press).

ROTHLEIN, R., DUSTIN, M.L., MARLIN, S.D. & SPRINGER, T.A. (1986) A human intercellular adhesion molecule (ICAM-1) distinct from LFA-1. *J. Immunol.* **137,** 1270.

SANCHEZ-MADRID, F., NAGY, J.A., ROBBINS, E., SIMON, P. & SPRINGER, T.A. (1983) A human leukocyte differentiation antigen family with distinct α-subunits and a common β-subunit. *J. exp. Med.* **158,** 1785.

SCHWARTING, R., STEIN, H. & WANG, C.T. (1985) The monoclonal antibodies αS-HCL 1 (α Leu 14) and αS-HCL 3 (α Leu-M5) allow the diagnosis of hairy cell leukemia. *Blood* **65,** 974.

SHAW, S. (1987) Characterization of human leukocyte differentiation antigens. *Immunol. Today* **8,** 1.

SPRINGER, T.A., THOMPSON, W.S., MILLER, L.J., SCHMALSTIEG, F.C. & ANDERSON, D.C. (1984) Inherited deficiency of the Mac-1, LFA-1, p150,95 glycoprotein family and its molecular basis. *J. exp. Med.* **160,** 1901.

SPRINGER, T.A., TEPLOW, D.B. & DREYER, W.J. (1985) Sequence homology of the LFA-1 and Mac-1 leukocyte adhesion glycoproteins and unexpected relation to leukocyte interferon. *Nature* **314,** 540.

SPRINGER, T.A. & ANDERSON, D.C. (1986) The importance of the Mac-1, LFA-1 glycoprotein family in monocyte granulocyte adherence, chemotaxis, and migration into inflammatory sites: insights from an experiment of nature. In: *Biochemstry of Macrophages.* (Ciba Foundation Symposium No. 118) p. 102. Pitman, London.

STEPLEWSKI, Z., LUBECK, M.D. & KOPROWSKI, H. (1983) Human macrophages armed with murine IgG2a antibodies to tumors destroy human cancer cells. *Science* **221,** 865.

STRASSMANN, G., SPRINGER, T.A., SOMERS, S.D. & ADAMS, D.O. (1986) Mechanisms of tumor cell capture by activated macrophages: evidence for involvement of lymphocyte function associated (LFA)-1 antigen. *J. Immunol.* **136,** 4328.

TODD, R.F., ARNAOUT, M.A., ROSIN, R.E., CROWLEY, C.A., PETERS, W.A. & BABIOR, B.M. (1984) Subcellular localization of the large subunit of Mo1 (Mo1 alpha; formerly gp110), a surface glycoprotein associated with neutrophil adhesion. *J. clin. Invest.* **74,** 1280.

UNKELESS, J.C. (1986) Heterogeneity of human and murine Fcγ receptors. In: *Biochemistry of Macrophages.* (Ciba Foundation Symposium 118) p. 89. Pitman, London.

WALPORT, M.J., ROSS, G.D., MACKWORTH-YOUNG, C., WATSON, J.V., HOGG, N. & LACHMANN, P.J. (1985) Family studies of erythrocyte complement receptor type 1 levels: reduced levels in patients with SLE are acquired, not inherited. *Clin. exp. Immunol.* **59,** 547.

WILSON, J.G., WONG, W.W., SCHUR, P.H. & FEARON, D.T. (1982) Mode of inheritance of decreased C3b receptors on erythrocytes of patients with systemic lupus erythematosus. *N. Eng. J. Med.* **307,** 981.

WRIGHT, D.G. & GALLIN, J.I. (1979) Secretory responses of human neutrophils: exocytosis of specific (secondary) granules by human neutrophils during adherence *in vitro* and during exudation *in vivo*. *J. Immunol.* **123,** 285.

WRIGHT, S.D., CRAIGMYLE, L.S. & SILVERSTEIN, S.C. (1983) Fibronectin and serum amyloid P component stimulate C3b- and C3bi-mediated phagocytosis in cultured human monocytes. *J. exp. Med.* **158,** 1338.

WRIGHT, S.D. & JONG, M.J.C. (1986) Adhesion-promoting receptors on human macrophages recognize *Escherichia coli* by binding to lipopolysaccharide. *J. exp. Med.* **164,** 1876.