review
Haematologica 1994; 79:374-386

REPORT ON THE FIFTH INTERNATIONAL WORKSHOP ON HUMAN LEUKOCYTE DIFFERENTIATION ANTIGENS, BOSTON, NOVEMBER 3-7, 1993

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This paper represents a detailed description of the results and basic studies presented at the *5th International Workshop on Leukocyte Differentiation Antigen* held in Boston on November 3-7, 1993. More than 500 institutions worldwide participated in the Workshop study groups, and approximately 1450 antibodies were investigated, allowing the identification of 48 new CD clusters and the redelineation of 14 previously clustered molecules (see Table 1). All the monoclonal antibodies (mAbs) were analyzed by flow cytometry and the data recorded in a *Leukocyte Differentiation Antigen Database* (LDAD), which represents the source of the information found in this workshop report. A more extensive account of this Workshop will be published by Oxford University Press before the end of 1994.

The workshop was divided into 11 sections and the workshop organizers were the following scientists: Stuart Schlossman, Chairman of the Meeting, Laurence Boumsell (T-cell section), Wally Gilks (Statistical analysis), John Harlan (Endothelial cells), Tadamitsu Kishimoto (Cytokine receptors), Chikao Morimoto (Activation antigens), Jerome Ritz (NK antigens), Stephen Shaw (Cross-lineage *blind panel*), Timothy Springer (Adhesion section), Roy Silverstein (Platelets), Thomas Tedder (B cells), Robert Todd (Myeloid cells).

As in previous workshops (Paris: 1982; Boston: 1984; Oxford: 1986; Vienna: 1989) all mAbs including previously established CD (CD1-CDw78), candidates for CD designation, and those of undefined specificity (the so-called *blind panel*), were submitted to extensive multidisciplinary studies that included flow cytometry, biochemical, molecular, histochemical and serologic analysis. Antibody reactivity was evaluated against more than 80 cell types, and, when possible, flow cytometry data have been expressed in the form of *molecular equivalents of soluble fluorochrome* (MESF), which should be considered the reference unit standard for the quantitation of fluorescence emission by mAbs at the present time. In order to achieve this goal, it was necessary to use together with the required mAbs, FITC or PE (as pertinent) pre-mixed quantitative microbead calibration standards, which permitted a comparison between the fluorescence intensity of cells stained for the required antibodies and that expressed by calibration microbeads. The calculation of MESF was based on the evaluation of the peak channel expressed by cells and different populations of microbeads (four or five, depending on the type and source of beads). The values for the slope, intercept and correlation coefficient allowed calculation of the regression line, which gave precise information on the linearity and stability of the instrument response, the noise level of the flow cytometer, the MESF values of the stained and unstained cells, the resolution indexes for fluorescence, and the coefficient of variation (CV) of microbead fluorescence. The minimum detection threshold (also termed *calculated sensitivity* or *instrument fluorescence threshold*) of the flow

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Acknowlegdments: this work was supported by CNR, ACRO project (Ferrara), University of Turin and CNR (Turin). S.M. is the recipient of a grant from AIRC. F.L. is especially indebted to Prof. Stephen Shaw (Experimental Immunology Branch, National Institutes of Health, Bethesda, USA) for giving him to access to the Leukocyte Differentiation Antigen Database (LDAD) software program.
Received April 22, 1994; accepted May 24, 1994.

cytometer corresponds to the MESF value for the blank beads, and provides meaningful data on the sensitivity of the instrument in detecting fluorescence signals. Using microbeads has the added advantage of allowing a comparison of flow cytometry data over time and between one laboratory and another, and of permitting easy calculation of the number of binding sites present per cell after staining with the various mAbs.

The CD system (CD stands for *cluster of designation*) for classifying monoclonal antibodies and their specific antigens was established at the first workshop on leukocyte differentiation antigens (Paris: 1982), where the rule was also introduced that at least two mAbs that recognize the same molecule are required in order to assign a new CD. It was further recommended that the term CD be used for the clustered antibodies and the term *CD molecule* or *CD antigen* be used for antigens.

The CDw (*w* stands for *workshop*) designation was to be given to those reagents whose reactivity had not been completely defined, and therefore would have to be re-evaluated in future workshops. However, a number of molecules, like glycolipids, cannot be evaluated by immunoprecipitation studies, and therefore a CD cluster can also be defined in the absence of detailed biochemical data or of the molecular weight.

A brief description of the 48 new CD clusters and the 14 CD groups re-defined during this workshop is presented in the following sections of this report, which is subdivided into 9 headings according to the preferential cell-type binding of mAbs. A brief description of some previously established clusters, which were not submitted to redefinition during this workshop is also given later on, since the novelty of the results was, in our opinion, noteworthy.

T section (5 new CD molecules)

CD98. This antigen is a disulfide-linked 125 kD heterodimeric membrane glycoprotein consisting of 2 chains: an 80-90 kD glycosylated heavy chain and a 40 kD nonglycosylated light chain. This molecule is also called 4F2 and has its human gene location on chromosome 11 at band q12-q22. CD98 mAbs inhibit lectin-induced mitogenesis of human T cells by 50%, but do not inhibit T-cell-mediated antibody-dependent cellular cytotoxicity or NK-cell-mediated cytotoxicity; therefore the function of this molecule seems to be concerned with cell activation and proliferation. CD98 is also comitogenic for T cells incubated with anti-CD3 and soluble CD2 mAbs. This molecule enhances Ca^{++} flux mediated by Na^{+}/Ca^{++} exchangers. CD98 is weakly expressed on resting T lymphocytes, but the antigen levels significantly increase following lectin or alloantigenic T-cell stimulation. Thymocytes, monocytes, endothelial cells, stromal cells, epithelial cells, keratinocytes, T cell lines and some myeloid cell lines were found to be reactive with CD98 mAbs. Almost all actively dividing cells strongly express this antigen. The eleven mAbs (clones: 4F2; GRV1; HuLy m10; KS-4; KS-7; L 289; BU 53, etc.) produced so far have been found to be specific for the heavy chain. No mAbs are available for the light chain.

CD99. This identifies MIC2 (also termed E2 or GRP2), which is involved in rosette formation with sheep or human erythrocytes. Four mAbs (clones: 0662; 12E7; 013; MEM-131) recognize this molecule, which has a molecular weight of 32 kD. It is expressed on human T cells, thymocytes, B cells, NK cells, endothelial cells, myeloid cell lines (HL60, etc.) and, to a lesser extent, on $CD34^{+}$ bone marrow progenitor cells. Its gene location is chromosome Yp11.2.

CD99R. This molecule functions as CD99 32kD restricted. Six mAbs (clones: FMC29; HI147; HI170; HIT4; D44; L129) identify this antigen, which is expressed on activated T cells, monocytes, endothelial and stromal cells.

CD100. This antigen, with a molecular weight of 40 kD, is also referred to as BB18 or GR3. Five mAbs (clones: 148-2D12; A8; BB18; BD16; F937G2) have been identified so far that recognize this molecule. Both PHA-stimulated and resting T cells express this antigen; a weak posi-

tivity has also been found on B cells, monocytes, neutrophils, and fetal T lymphocytes.

CDw101. This molecule has a molecular weight of 140 kD; it is also known as GR14, BA27 or BB27. The two mAbs (clones: BA27; BB27) belonging to this cluster react with a subset of PHA-stimulated and resting T cells, NK cells, monocytes and endothelial cells.

NK section (1 new CD molecule)

CD57. This 110 kD molecule is present on large granular lymphocytes, a subset of $CD8^+$ cells, and a small subset of $CD4^+/CD45RO^+$ T cells in the germinal center of lymph nodes. It is also found on a substantial subset of $CD4^+$ cells from renal allograft recipients, and on a $CD4^+/CD7^-$ T-cell subpopulation from HIV-infected (human immunodeficiency syndrome) patients. Furthermore, in patients with HIV infection the number of $CD4^+/CD57^+$ cells increases with the advancing stage of the disease, suggesting a role for this marker in the monitoring of the disease. Neuroectodermal-derived cells express this antigen, which identifies the myelin-associated antigen (MAG) and detects a sulfated carbohydrate epitope expressed on a part of the N-CAM (CD56) molecule. It functions as a ligand for cytotactin, which is involved in cell-cell adhesion. Seven mAbs (IOT 10, Leu7, LN7, NC1, TB02, TB04, UC!.1) belong to this group.

CD94. This is a 43 kD molecule consisting of two subunits. Its common name is KP43. The 3 mAbs (clones: HP-3B1; HP-3D9; XA185) recognizing this molecule are strongly reactive (MESF values range from 500,000 to 700,000) with blood NK cells and TNF- activated endothelial cells.

Cytokine section (13 new CD molecules)

CDw116. This is a receptor for the GM-CSF growth factor. CD116 is a high affinity receptor composed of α and β subunits with molecular weights of 80 and 130 kD, respectively. The α subunit binds GM-CSF with low affinity; the beta subunit (common to IL3 and IL5 receptors) does not bind GM-CSF, but its association with the α-subunit generates high affinity receptors for GM-CSF. The human gene location of the α-subunit is Xp22.32,Yp11.3. Its function is to promote the growth and differentiation of neutrophils, eosinophils and monocytes from bone marrow multipotent precursors. GM-CSF induces tyrosine phosphorylation of a set of proteins similar to IL-3; engagement of the receptor also results in activation of tyrosine kinases, GTP binding proteins (G-proteins), and increased expression of CD35 (complement receptor 1) and CD11/CD18 antigens. It also induces glucose transport, ion fluxes and the expression of a variety of genes. The only mAb (clone: hGMCSFR-M1) that has been defined as recognizing this molecule reacts with monocytes, neutrophilic granulocytes, myeloid and monocyte precursors, $CD34^+$ (middle intensity) hematopoietic progenitors, B and T fetal lymphocytes, endothelial cells, fibroblasts, HL60, KG1a and U937 cell lines. Breast and lung carcinoma cell lines, as well as osteogenic cell lines are stained by CD116 antibodies. Blast cells from acute myeloid leukemias or hybrid acute leukemias may express this receptor. At least two other mAbs (M5D12, 4B5-FC) seem to recognize GM-CSF R, but their reactivity with cells transfected with GM-CSF R cDNA produced conflicting results.

CD117. This identifies an extracellular epitope of the proto-oncogene c-kit, which has been reported to be the receptor for a growth factor encoded by the steel locus (stem-cell-factor receptor). The interaction between c-kit and its ligand plays a fundamental role in the development of stem and progenitor cells. This 145 kD antigen is made up of five Ig-related superficial domains and belongs to subclass III of the tyrosine kinase receptors. In humans, it is expressed on 20-30% of $CD34^+$ bone marrow cells, mobilized and cord blood progenitors, 50% of endothelial cells, and on mast cell lines, B cell lines, and NK cell lines. Eight mAbs (reference mAb: 17F11) have been identified so far.

CDw119. This functions as a receptor for γ-IFN (γ-interferon) and has a molecular weight of 90 kD. Its human gene location is 6q23-q24.

Table 1. List of new clusters (CD) defined or re-defined during the 5th International Workshop on Leukocyte Differentiation Antigens (Boston, 1993).

CD	ANTIGEN NAME	MOLECULAR WEIGHT (KD)	TARGET CELLS	no. of mAbs	WORKSHOP SECTION
CD15s	SLe-X		Mo, E, act-G, G, act-L	1	ADHESION
CD16	FcγRIII	48	NK, Mo, G	12	MYELOID CELL
CD16b	FcγRIIIb	40	G	1	MYELOID CELL
CD32	FcγRII	40	Mo, B, B lines, CD34+,Myeloid lines	8	MYELOID CELL
CD42a	GPIX	23	Plt, act-Plt, M	5	PLATELET
CD42b	GPIBα chain	135-145	G, Mo,F, B lines, CD34+	12	PLATELET
CD42c	GPIBβ chain	23	idem	1	PLATELET
CD42d	GPV	85	Plt	1	PLATELET
CD44	H-CAM	80-90	act-L, pre-B, B, CD34+, E, G, Mo	21	ADHESION
CD44R	CD44 Restricted epitope		act-L, pre-B, B, G, Mo, CD34+prog	1	ADHESION
CD49a	VLA-1	210	act-E, NK, F,act-B, act-T, act-Mo	2	ADHESION
CD49b	VLA-2	165	B,Mo,E,Plt,F,CD34+	8	ADHESION
CD49c	VLA-3	125	B,T,Mo,E,S	3	ADHESION
CD49d	VLA-4	150-180	act-T,Thy, act-E, CD34+	6	ADHESION
CD49e	VLA-5	135/25	memory T, act-E, E, Plt	6	ADHESION
CD49f	VLA-6	120-125	act-T, NK, act-E, E, Mo, S	5	ADHESION
CD50	ICAM-3	124	NK, Mo, G, CD34+LO and MID, act-E, act-Plt	17	ADHESION
CD51/61	$a^{v}/\beta 3$ integrin		act-T, Plt, Hemat cell lines	2	ADHESION
CD52	CAMPATH-1	21-28	NK,T, Mo, B, S, CD34+HI, CD34+MID, CD34+LO	2	CROSS LINEAGE
CD62E	ELAM-1	115	act-E, B lines, Plt, Megakaryoblast	10	ADHESION
CD62L	LAM-1	75-80	E, B, G, Mo, act-T	4	ADHESION
CD62P	P-selectin	150	G, Mo, act-Plt	12	ADHESION
CD66acde	CEA family	170-200	Eo, N, Bone marrow prog	9	MYELOID CELL
CD66a	BGP of CEA family	180-200	G, Bone marrow prog	none	MYELOID CELL
CD66b=CD67	CGM6 gene product	95-100		4	MYELOID CELL
CD66c	NCA	90-95	G, Mo, Eo, B lines, E lines	8	MYELOID CELL
CD66d	CGM	30		one for CD66de	MYELOID CELL
CD66e	CEA molecule	180-200	G, Mo, S	none	MYELOID CELL
CDw70	ligand for CD27	55,75,95,110,170	act-B, B lines, NK lines, T lines, Thy	3	ACTIVATION
CDw76	CD76	unknown	mature B, T, G	2	B CELL
CD79a	MB-1 (mIgM)	33-40	B restricted: from pre-B to Plasm	1	B CELL
CD79b	B29 (mIgM)	33-40	idem	1	B CELL
CD80	B7/BB1	60	proliferating B, secreting B, HTLV-1-T	6	B CELL
CD81	TAPA-1	22	act-B, act-T, Hemat cell lines, E	5	B CELL
CD82	R2	50-53	act-L, E, weakly on CD34+ bone marrow prog	2	B CELL
CD83	HB15A	43	act-B, act-T, splenic B, DRC, Lymphoblastoid cells	2	B CELL
CDw84		73	act-L, CD34+ HI and MID, act-Plt	3	B CELL
CD85	VMP-55,GHI-75	120-83	Mo, B, T	3	B CELL

CD86	GR65, FUN-1	80	act-B, B, T, Lymphoblastoid lines	3	B CELL

Table 1. (continued).

CD87	UPA-R	50-65	act-G, act-Mo, G, Mo, F, Megakaryoblast	6	MYELOID CELL
CD88	C5a-R	42	act-G, G, Mo, Eo	2	MYELOID CELL
CD89	IgA-R	55-70	G, Mo, Myeloid and Monocyte lines	5	MYELOID CELL
CDw90	Thy-1	25-35	HEV, T lines, Thy, F, CD34+	1	MYELOID CELL
CD91	α2M-R	200	G, Mo, T, Plt, fetal F, act-Plt	5	MYELOID CELL
CDw92		70	act-L, G, E, act-E, CD34+, Hemat cell lines	2	MYELOID CELL
CD93		120	G, Mo, Eo, NK lines, B lines, E	4	MYELOID CELL
CD94	KP43	43	NK, act-E	3	NK CELL
CD95	FAS, APO-1	43	G, Mo, L, Myeloid lines	4	ACTIVATION
CD96	Tactile	160	E, Myeloid lines	2	ACTIVATION
CD97	GR1,BL/KDD/F12	74-80-89	G, Mo, B and T lines	4	ACTIVATION
CD98	4F2	80-40	T, Mo, E, Myeloid lines, T lines	11	T CELL
CD99	MIC-2	32	T, NK, E, B	4	T CELL
CD99R	CD99 restricted	32	act-T, Mo, E	6	T CELL
CD100	BB18;GR3	150	act-T, T, Mo	5	T CELL
CDw101	BB27;GR14	140	act-T, NK, Mo	2	T CELL
CD102	ICAM-2	60	T, B, NK, Mo, E, act-G	3	ADHESION
CD103	HML-1	150-25	act-E, M	7	ADHESION
CD104	β4 integrin	220	E, Mo, G, fetal B, S	4	ADHESION
CD105	ENDOGLOBIN	95	CD34+, T, B, Mo, G	10	ENDOTHELIUM
CD106	VCAM-1;INCAM-110	110	B lines, NK lines,S	5	ENDOTHELIUM
CD107a	LAMP-1	110	KG1a, HL60, HUT78, Plt	3	PLATELET
CD107b	LAMP-2	120	Plt, E, act-Plt, act-E	2	PLATELET
CD108	GR2	80	Splenic B, act-T, S	2	ADHESION
CDw109	GR56;8A3;7D1	170-150	Thy, act-L, adhese and act-Plt	2	ENDOTHELIUM
CD115	M-CSF-R	150	Mo, MØ, Bone marrow prog, fetal B	12	MYELOID CELL
CDw116	GM-CSFR	75-85	Mo and G prog, Mo, G, fetal B, fetal T	1	CYTOKINE
CD117	SCF-R	145	CD34+, Mast cell line, B lines, NK lines, E	8	CYTOKINE
CDw119	IFNγR	90	Mo,MØ, CD34+, Hemat cell lines	1	CYTOKINE
CD120a	TNF-R type I	55	Epithelial cells, Mast cell line, S	5	CYTOKINE
CD120b	TNF-R type II	75	G, Mo, B,T, NK act-B, act-T, act-NK	3	CYTOKINE
CDw121a	IL-1R type I	80	NK, NK lines, T, E, Thy, F	1	CYTOKINE
CDw121b	IL-1R type II	68	act-L, G, act-G, Mo	1	CYTOKINE
CD122	IL-2R b chain	75	NK lines, B lines	6	CYTOKINE
CD124	IL-4R	140	MØ, fetal B, pre-B, Myeloid lines	1	CYTOKINE
CD126	IL-6R α subunit	80	G, Mo, CD4+, Plasm, EBV-B	19	CYTOKINE
CDw127	IL-7R	75	Thy, pro-B,pre-B, act-L, CD34+, NK	1	CYTOKINE
CDw128	IL-8R	58-67	B, B lines, S	2	CYTOKINE
CDw130	IL-6R β subunit	130	act-E, E, NK, Mo, Plt, EBV-B, Plasm	1	CYTOKINE

Legend: Plt=platelets;Mo=monocytes; G=granulocytes; MØ=macrophages; E=endothelial cells; F= fibroblasts; S=stromal cells; Eo=eosinophils; DRC=dendritic reticulum cells; Thy=thymocytes; Plasm=plasma cells; act=activated; prog=progenitors; CD34+ HI=high intensity, LO=low intensity; MID=middle intensity; lines=cell lines; HEV=high endothelial venules.

This molecule has sequence similarity with the IFN-α/β receptor. IFN leads to macrophage activation, B cell differentiation and expression of class I and class II MHC in several cell types; IFN-γ receptor binds IFN with high affinity but is unable to transduce the biological response to IFN in transfected cells, which indicates that additional elements are required to generate a functional receptor. IFNγR is expressed on monocytes, macrophages, a subset of B lymphocytes, bone marrow $CD34^+$ progenitors, fibroblasts, and some myelo-monocytic, erythroid and lymphoid cell lines. One mAb is known (clone: GIR-208).

CD120a. This functions as TNFRI (*tumor necrosis factor receptor type I*) and binds TNFα and TNFβ with relatively high affinity. It has a molecular weight of 55 kD and its human gene location on 12p13.2. It is a member of the NGFR (*nerve growth factor receptor*) superfamily. The large majority of hemopoietic cells exhibit one or both of the two receptors for TNF; TNFRI is expressed at high fluorescence intensity on epithelial, stromal cells, and some myeloid cell lines (KG1α and HK60). Both receptors co-modulate with the FAS antigen, and this activity seems to play a role in anti-Fas-mediated cytotoxicity. Five mAbs (clones: htr-9; MR1-1; MR1-2; MR1-3, MR1-4) are known.

CD120b. This is also known as TNFRII (*TNF receptor type II*). It has the same affinity as TNFRI and its gene is on chromosome 1 at band p36.3-p36.2. This 75 kD molecule is expressed on activated and cytokine-stimulated B, T, and NK cells. B, T and NK cell lines are also positive for CD120. It is also weakly expressed on neutrophilic granulocytes and monocytes. Three mAbs are known (clones: hTNFR-M1; MR2-1; utr-1).

CDw121a. This 80 kD antigen is also referred to as IL-1 (interleukin) receptor type I. The CD121 gene maps to a region (chromosome 2q12) that also encodes IL1 receptor type II, IL1α and IL1β. This antigen is composed of three Ig-similar domains and a cytoplasmic domain that is required for signal transduction. IL1 mediates thymocyte and T-cell activation, fibroblast proliferation, induction of acute phase proteins and inflammatory reactions. Both IL1 receptors bind IL1α and IL1β with high affinity, but they have different IL1 binding and processing properties. IL1R type I is weakly expressed on thymocytes, T cells, fibroblasts, endothelial cells, stromal cells and some NK cell lines. One mAb is confirmed (clone: hIL-1R1-M1).

CDw121b. This 68 kD molecule is also termed IL1-R type II and has the same amino acid sequence as the type I receptor except for the cytoplasmic domain, which is smaller and unable to transduce signals. It is expressed on resting and activated neutrophils and monocytes, PHA-stimulated lymphocytes, the K562 and mast cell lines, and weakly on B cells. One mAb is known (clone: hIL-1R2-M2).

CD122. This is a receptor for the β chain of IL2. It has a molecular weight of 75 kD. The six mAbs (reference clone: MIK-b1) so far defined are reactive with lectin-stimulated lymphocytes, IL2-stimulated NK cell lines, and B cell lines.

CD124. This is also called IL4-R and is a member of the cytokine receptor superfamily. Its molecular weight is 140 kD and the gene maps to chromosome 16p21.1-p11.2. IL4 is a growth factor for pre-activated B cells and T cells, and enhances the synthesis of IgG1 and IgE and the expression of MHC class II molecules in B cells and macrophages. IL4 induces macrophage activation and synergizes with colony stimulating factors in inducing the proliferation of hemopoietic cells. IL4-R is expressed on pre-B, B cells, fetal B cells, $CD34^+$ hemopoietic precursors and macrophages. One mAb is known (clone: hIL-GR-M57).

CD126. This is a receptor for the α-subunit of IL6. This 80 kD molecule consists of many Ig-similar epitopes. Its gene is on chromosome 1. IL6 is a growth factor for myeloma cells, B cells, activated and EBV-transformed B and T cell lines. It induces differentiation and prolifera-

tion of hemopoietic precursors. The IL6-Rα subunit is expressed on neutrophils and monocytes. It is also present on HL60 and KG1a cell lines. EBV-transformed B cells, plasma cells and myeloma cells are strongly reactive with CD126 antibodies. Nineteen mAbs (clones: PM1; B-C22; B-E23; B-F19; B-F22; B-G18 as reference) belong to this cluster.

CDw127. This is a 75 kD molecule and functions as a receptor for IL7. IL7 stimulates the proliferation of pro-B and pre-B cells, thymocytes and mature T cells and induces the activation of monocytes. One mAb (clone:hIL-7R-M20) is known and is weakly reactive with $CD34^+$ bone marrow progenitors, thymocytes, PHA-stimulated lymphocytes, pro-B cells, pre-B cells. The intensity of staining is strong on resting NK cells (MESF >100,000) and weak on IL2-activated NK cells.

CDw128. This is the receptor for IL8 and comprises two transmembrane forms with low and high affinity for IL8. Two mAbs (clones: B-F25; B-G20) recognize this 58-67 kD molecule, which is found on resting and activated T lymphocytes (MESF values: 1000-10,000), monocytes, neutrophils. High reactivity has been shown by B lymphoblastoid cell lines and stromal cells. IL8 is a chemotactic stimulus for neutrophils, basophils and T lymphocytes, and increases adhesion to endothelial cells. IL8 binding to IL8-R induces a transient expansion in intracellular calcium levels. Both NAP-2/bTG (neutrophil activating peptide-2) and melanoma growth factor stimulating activity (MGSA/GRO) compete with this molecule for binding to IL8-R.

CDw130. Is known as gp130 and represents the IL6-R β subunit. This 130 kD molecule mediates signal transduction but is unable to bind IL6 without the cooperation of other molecules. One mAb has been identified (clone: AM64) and has reactivity with resting and TNF-activated endothelial cells, NK cells, monocytes, platelets, myeloid and myeloblastic cell lines. It is strongly expressed on EBV-transformed B cells, plasma cells, myeloma cells.

Adhesion section (4 new CD molecules)

CD15s. The SLe-X molecule is the sialylated form of CD15. This 50-65 kD molecule functions as a ligand for the cell adhesion molecules CD62 and ELAM-1 (endothelial-leukocyte adhesion molecule-1). It is expressed on endothelial cells, monocytes (MESF: 100,000), resting and activated granulocytes, PHA-stimulated T lymphocytes (MESF> 500,000). Resting T cells express this molecule at low density. One mAb (clone:CSLEX-1) has been developed so far.

CD44. Its common name is phagocytic glycoprotein-1 (Pgp-1) or H-CAM (hyaluronate-cellular adhesion molecule). This antigen has a molecular weight of 80-90 kD and its gene is found on chromosome 11 at band p13. The CD44 membrane proximal region consists of several variants generated by the alternative splicing of at least five different exons.

CD44R identifies domain No. 9 only (the only mAb belonging to this CD is FW11.24). The molecule has extensive O-linked glycosylation and the extracellular domain has six potential N-linked glycosylation sites. CD44 recognizes the main cell surface receptor for hyaluronate and this interaction mediates binding of lymphocytes to high endothelial venules. This receptor is therefore involved in lymphocyte trafficking and endothelial cell recognition. This antigen has been reported to be expressed on resting and PHA-stimulated T cells, pre-B lymphocytes, mature B cells, neutrophils and monocytes (MESF: 500,000-1,000,000). $CD34^+$ bone marrow precursors and endothelial cells are strongly positive for mAbs belonging to this cluster (MESF 1,000,000). Twenty-one mAbs (A3D8; 156-3C11;A1G3; 50B4; BRIC222; BRIC214; 212-3; BRIC235; BU52 as reference) are known.

CD49a. Is also known as α1 integrin chain or VLA-1 molecule (*very late antigens*), and belongs to the integrin CD49/29 family. It has a molecular weight of 210 kD. CD49α/29 mediates RGD-dependent (Arg-Gly-Asp sequence that is important for some adhesive reactions with extracellular proteins) and RGD-independent adhesion with the extracellular matrix.

Ligands vary for each CD49; CD49α has its ligands in collagen and laminin. Two mAbs (clones: IB3.1; SR84) are present in this cluster; they react with TNF-stimulated endothelial cells (MESF: 500,000), NK, activated T and B cells, blood monocytes, and resting and IL1-activated fibroblasts.

CD49b. Is also referred to as α2 integrin chain or VLA-2 molecule. This 165 kD molecule has its gene location on chromosome 5. The CD49b/CD29 complex binds predominantly collagen and laminin. This antigen is found on B cells and monocytes. Resting and activated platelets, endothelial cells, $CD34^+$ bone marrow cells and fibroblasts are strongly stained by the eight mAbs (clones: 6F1; 12F1; 5E8; AK-7; GI14; Gi9; HAS3; P1E6) which are clustered into this group.

CD49c. Is the α3 integrin chain or VLA-3. Its ligands are laminin, fibronectin and (weakly) collagen. This 125 kD molecule is expressed on splenic B cells, monocytes, T cells, resting and TNF-stimulated endothelial cells (MESF 10,000-500,000), and on stromal cells, which are strongly positive (MESF: 900,000). Three mAbs (clones: 10.1.2; A3IIF5; J143) have been defined.

CD49d. Is also referred to as α4 integrin chain or VLA-4 molecule. Its gene location is on chromosome 2p31-q32. This 150 -80-70 kD molecule is a ligand for fibronectin and Peyer's patch high endothelial venules. CD49d/CD29, unlike other integrins, specifically recognizes VCAM-1 (*vascular-cell adhesion molecule-1*) on activated endothelial cells and induces homotypic aggregation in T, B, and U937 cells. Resting T cell express intermediate levels of CD49d, CD49e, CD49f, but when activated the degree of positivity significantly increases. CD49d is also present on thymocytes, endothelial cells (resting and activated), $CD34^+$ bone marrow cells (MESF: 10,000), and weakly on B cells, fetal and adult fibroblasts. Six mAbs (clones: L25; 5D5; 8F2; 9F10; HP1/7; HP2/1) are known.

CD49e. It identifies the α5 integrin chain or VLA-5 molecule, which has a molecular weight of 135/25 kD. It is a fibronectin ligand and is present on memory T cells, resting endothelial cells, platelets, $CD34^+$ bone marrow progenitors, stimulated and resting granulocytes and monocytes. Six mAbs (clones: X6; mAb16; SAM-1; mAb11; 2H6; 3D3) are known.

CD49f. This molecule (MW 120-125 kD) recognizes the α6 integrin chain or VLA-6, and is a ligand of laminin, fibronectin. It is expressed on resting and TNF-activated endothelial cells, NK cells, stromal cells (MESF: 500,000), activated T cells, monocytes, (MESF: 10,000), platelets and weakly on resting T cells. Five mAbs (clones: BQ16; 135-13C; 450-30A1; J8H; S3-41) have been included in this cluster.

CD50. This 124 kD molecule is also termed ICAM-3 (intercellular adhesion molecule-3). It is a ligand of LFA-1 and is present on $CD34^+$LO (*low intensity*) and $CD34^+$ MID (*middle intensity*) bone marrow cells, TNF-stimulated endothelial cells, B and T lymphocytes, NK cells, monocytes and neutrophils. It is weakly expressed on activated platelets. Seventeen mAbs (reference mAbs: 152-2D11; CBR-IC3/1; CBR-IC3/2; 101-1D2; 140-11; BRIC79) form this cluster.

CD51/61. Is known as α^V/β3 integrin, a chain associated with CD61, and functions as a vitronectin receptor. CD51/61 binds and recognizes RGD (Arg-Gly-Asp) sequences in the extracellular matrix protein, vitronectin, von Willebrand factor, fibrinogen and thrombospondin. RDG is important for some adhesive reactions with extracellular proteins. It is found on monocytes, activated T cells, endothelial cells, myeloid, monocytic, myeloblastic, B lymphoid cell lines. It is weakly expressed on platelets. Two mAbs (clones: 23C6; LM609) are known.

CD62E. This is also known as ELAM-1 (*endothelial leukocyte adhesion molecule-1*), or E-Selectin molecule. It is a member of the selectin family of cellular adhesion molecules.

Together with CD62-L and CD62-P, this 115 kD antigen mediates the interaction of activated platelets with neutrophils and monocytes, and is responsible for the rolling attachment of neutrophils to activated endothelium. It has high expression on stimulated endothelial cells, megakaryocytes and activated platelets, weak expression on B lymphoid cell lines. Ten mAbs (clones: ENA 2; H18/7; H4/18; 3B7; 7A9, 4D10; BB11; CL-3; ENA 1; HAE-1a) have been identified.

CD62L. Is also termed LAM-1 (*leukocyte adhesion molecule-1*) or L-selectin. This 75-80 kD antigen is expressed on endothelial cells, B lymphocytes, activated T lymphocytes, neutrophils, monocytes, and weakly on NK cells. Four mAbs (clones: FMC46; LAM1-3; SK11; Dreg-56) are known.

CD62P. This 150 kD molecule is also called P-selectin, PADGEM, or GMP-140. This α granule protein is a member of the selectin family of leukocyte adhesion proteins and mediates the interaction of activated platelets with neutrophils, monocytes and endothelium. The activation process is Ca^{++} dependent. CD62P is expressed on granulocytes, monocytes and activated platelets. Twelve mAbs (reference mAbs: G1; P3-38; G2; G3; KCG-1; W40; S2-51) are known.

CD102. This 60 kD molecule is also referred to as ICAM-2 (*intercellular adhesion molecule-2*), and has its gene location on chromosome 17q23-q25. ICAM-2 is a ligand for the integrin LFA-1 (*leukocyte function antigen-1*) but, unlike ICAM-1, it is not a ligand for CD11b. Inflammatory mediators do not influence ICAM-2 expression on endothelium or lymphocytes. Together with other molecules ICAM-2 transduces signals for T cells activated via the T-cell receptor. It is present on T cells, B cells, NK cells, monocytes, activated and resting granulocytes, platelets and $CD34^{+}$ cells; strong positivity has been found on endothelial cells (MESF >1,000,000). Three mAbs (clones: CBR-IC2/1; CBR-IC2/2; 6D5) have been clustered in this group.

CD103. Is also named HML-1 and seems to be an $\alpha\beta$ integrin. This 150-25 kD molecule is expressed on TNF-activated endothelial cells, weakly on monocytes. Six mAbs (2G5.1; BER-ACT8; HML-1; LF61; F3F7; FGF1) are known.

CD104. This designation refers to the β4 integrin chain of 220 kD. It belongs to the integrin family and is a ligand of laminin and epithelial basal membrane epidesmosomes. Endothelial cells, monocytes, neutrophils, fetal B lymphocytes and stromal cells were found to be positive for the four CD104 mAbs (clones: 439-9B; 450-11A1; AA3; UM-A9) thus far defined.

CD108. This 80 kD antigen is also called GR2. It is expressed on endothelial cells, activated T cells, splenic and activated B lymphocytes, some myeloid cell lines and stromal cells. Two mAbs (clones: MEM-121; MEM-150) are known.

B section (9 new CD molecules)

CD79a. Is part of the B cell antigen receptor complex (mIgM). CD79a is also termed MB-1 and represents the α chain of the α/β complex for the IgM receptor. This 33-40 kD molecule is also referred to as a specific antigen receptor, and can function as a signal for B cells following exposition to multivalent antigens that cross-link many mIg molecules. Transmembrane signalling through surface mIg induces B-cell activation via MB-1 and B29 molecules. MB-1 expression is B restricted (from pre-B cells to plasma cells). One mAb (clone:HM47) is known.

CD79b. B29 is the β chain of the α/β complex for the IgM receptor. It has a molecular weight of 33-40 kD, and shows the same reactivity and function as CD79a. One mAb (clone: SN8) is known.

CD80. Is commonly called B7/BB1. This 60 kD antigen is a ligand for CD28 and is a co-stimulator for the alloactivation of T cells. The antigen is not found on resting B cells but is upregulated on B cells activated with a variety

of substances (EBV, anti-Ig M, IL2, IL4 ept). It is present on proliferating and Ig-producing B cells, and HTLV-1 transformed T cells. Six mAbs (clones: 104; 133; 49; B7-g; BB1; L307) form this cluster.

CD81. This antigen is also termed TAPA-1 and is a transmembrane molecule of 22 kD. Its function is to transduce proliferation signals. It is present on activated and resting T cells, endothelial cells, a subset of $CD34^+$ cells, myeloid, lymphoid and monocytoid cell lines. It is not found on quiescent cells. Five mAbs (clones: 1D6; 4TM-1; 5A6; JS64; JS81) are known.

CD82. Its common name is R2. It has been postulated that this 50-53 kD molecule can transduce proliferation signals. It is weakly expressed on all hemopoietic cells, endothelial cells and stromal cells (MESF: 10,000-300,000). Its expression increases on activated lymphocytes and on cell lines in active proliferation. Two mAbs (clones: 4F9; IAG) are known.

CD83. This 43 kD molecule is also referred to as HB15A. It seems to be responsible for dendritic cell antigen presentation. It is expressed on dendritic cells, activated T and B cells, splenic B cells and lymphoblastoid cell lines. Two mAbs (HB15a; HB15b) are known.

CDw84. The function of this 73 kD molecule is unknown. It is expressed on monocytes, bone marrow progenitors expressing CD34 at intermediate- strong intensity, PHA-stimulated lymphocytes, and activated platelets. Three mAbs (clones: 152-1D5; 153-4D9; 2G7) are known.

CD85. Is also known as VMP-55 and GHI-75. This 120-83 kD molecule is expressed by monocytes, B and T lymphocytes, and 30-40% of bone marrow progenitors. Two mAbs (clones: GHI/75; VMP55) belong to this cluster.

CD86. This antigen, also called GR65 or FUN-1, is present on activated and resting B cells, T cells and some lymphoid cell lines. Two mAbs (clones: BU63; FUN-1) are known.

Activation section (3 new CD molecules)

CDw70. Is probably a ligand for CD27. It has a molecular weight of 55, 75, 95, 110, 170 kD, and is expressed on activated B cells, a subset of T cells, B and NK cell lines, thymic cells. Four mAbs (clones: BU69; HNC-142; KI-24; LD6) have been identified.

CD95. This 43 kD molecule is termed FAS or APO-1 and its gene is located on chromosome 10q24.1. It mediates cytotoxicity and may be important in apoptosis and negative selection in the thymus. It is co-modulated with the TNF receptor. CD95 is present on lectin-stimulated T cells, granulocytes, monocytes, lymphoid and myeloid cell lines. Four mAbs (clones: 7C11; ANTI-FAS; APO-1; IPO-4) have been clustered.

CD96. Is referred to as tactile and has a molecular weight of 160 kD. It is strongly expressed on TNF-activated endothelial cells, myeloid cell lines. The KG1α cell line has been shown to express this antigen at high fluorescence intensity (MESF: 300,000). Two mAbs (clones: G8.5; TH-111) belong to this cluster.

CD97. This 74-80-89 kD antigen is also known as GR1, BL/kDD/F12. It is expressed on B and T cell lines, peripheral monocytes, granulocytes, and weakly on bone marrow CD34+ cells. Four mAbs (clones: BL-AC (F2); VIM3; VIM3B; VIM3C) are known.

Myeloid section (8 new CD molecules)

CD16. Is a transmembrane molecule of 48 kD. It functions as FcγRIII, which is a low affinity receptor for aggregated IgG. There are two distinct forms of CD16 encoded by two linked genes (mapped to chromosome 1q23) that encode for a transmembrane and a GPI-linked form. CD16 binds IgG complexed to antigens and mediates phagocytosis and ADCC. Twelve mAbs (reference mAbs: 3G8; B88-9; 2/1AG.1; BW209/2; DJ130c; GRM1) recognize the complete FcγRIIIb, which is present on NK, monocytes, resting and activated granulocytes (MESF: 1,000,000).

CD16b. Is termed GPI-linked restricted form (FcγRIIIb). This 40 kD molecule is selectively expressed on granulocytes. One mAb (clone: 1D3) is known.

CD32. Its common name is FcγRII and it represents a low affinity receptor for aggregated IgG. This 40 kD molecule can induce IgG-mediated phagocytosis and oxidative burst in monocytes and neutrophils, while it is a negative signal for B cells. It is strongly expressed on monocytes, granulocytes (MESF: 500,000), myeloid and myeloblastic cell lines (HL60, KG1, etc.), and weakly on B cell lines, B cells, $CD34^+$ bone marrow cells, and resting and activated platelets. Eight mAbs (clones: IV.3; 2ZC115; AT10; FLI8.2; CIKM5; FLI8.26; KB61; KU79) have been clustered in this group.

CD34. In addition to the Q-bend 10 mAb, 15 new reagents have been verified as recognizing CD34 antigen, the most direct evidence being reactivity with cells transfected with CD34 cDNA and binding to CD34 protein. The CD34 gene is localized on chromosome 1q32. It has been shown that lymph node $CD34^+$ high endothelial venules are a ligand for L-selectin. Antibodies belonging to this cluster react with hematopoietic progenitor and stem cells, fibroblasts and vascular endothelium. At least three epitopes (class I, II and III) of the molecule have been identified on the basis of their differential sensitivity to enzymatic cleavage with neuraminidase, chymopapain and glycoprotease from *Pasteurella haemolytica*. Umbilical cord blood and mobilized progenitor cells express this antigen, but the degree of positivity is variable depending on the mAb utilized for cell reactivity evaluation. The HPCA2 (clone: 8G12) mAb was clustered during this workshop, and based on experiments for enzyme sensitivity it was found to recognize class III epitopes. Examples of class II and class I antibodies are Q-bend 10 and BI3C5 mAb, respectively.

CD66 a,c,d,e. This 170-200 kD molecule consists of CEA (carcinoembryonic antigen) family complex antigens. Nine mAbs (reference mAbs: CBL-gran/1; B1.1; b18.7.7; D11-AD11) belong to this cluster, which is found to be reactive with neutrophils, eosinophils, endothelial cells, monocytes, and bone marrow myeloid progenitors.

CD66a. This is BGP and has a molecular weight of 180-200 kD. It is a CEA molecule belonging to the adhesion molecule family and is expressed on granulocytes and myeloid progenitors. So far no antibodies have been developed.

CD66b. Corresponds to CD67 and is a CGM6 gene product. It is a member of CEA family of adhesion molecules. This 95-100 kD unit is also called p100 molecule and its membrane attachment occurs through a GPI anchor. It is found on eosinophils, resting and activated neutrophils (MESF: 800,000-1,000,000). Five mAbs (clones: B13.9; MF25.1; G10F5; 80H3; BL-B7) are known.

CD66c. This 90-95 kD molecule is also termed NCA. It belongs to the CEA adhesion molecule family. It is expressed on neutrophils, monocytes, eosinophils, endothelium and on B cell lines. Eight mAbs (reference mAbs: 12G7; 13H10; 9A6; B6.2) have been clustered.

CD66d. CGM molecule belongs to the CEA family. It has a molecular weight of 30 kD. No mAbs are known for this particular molecule but one (clone: COL-1) has been found to recognize the CD66de complex.

CD66e. Is termed CEA and has a molecular weight of 180-200 kD. It is weakly expressed on granulocytes, monocytes, stromal cells.

CD87. Is referred to as UPA-R and is a receptor for urokinase type plasminogen activator. This antigen, with a molecular weight of 50-65 kD, is expressed on resting and TNF-activated endothelial cells (MESF: 10,000-400,000), PHA and IL2-stimulated lymphocytes, activated and resting granulocytes, activated and resting monocytes, megakaryocytes, and IL1-stimulated fibroblasts (MESF: 500,000). Six mAbs

(clones: 100; 109; 3B10; 68; L21; VIM5) are known.

CD88. Is a receptor for C5a of the complement cascade. C5a is produced by cleavage of C5 during complement activation and it is a potent chemoattractant peptide for monocytes and granulocytes. C5a receptor is internalized as phagocytes move toward the inflammatory site. It acts as a stimulus for degranulation and respiratory burst in neutrophils, monocytes and mast cells. This 42 kD molecule is expressed on eosinophils, resting and activated granulocytes and monocytes. Two mAbs (clones: S5/1; W17/1) are known.

CD89. Is the receptor for serum and secretory IgA (IgA-R) and has a molecular weight of 55-70 kD. FcαR promotes IgA-mediated phagocytosis and can induce superoxide anion production in myeloid cell lines. It is present on granulocytes, monocytes, myeloid and monocytoid cell lines. Five mAbs (clones: A3; A59; A62; A77; MY43) are known.

CDw90. This is also called Thy-1. Its physiologic function is unknown. This 25-35 kD molecule is weakly expressed on lineage negative (Li–) $CD34^+$ bone marrow cells, and strongly expressed on thymic epithelial cells, fibroblasts, and on cell lines of T, myeloid and monocytoid origin. It has been shown that 5-25% of cord blood cells, fetal liver, $CD34^+$ bone marrow cells, 92% of fetal fibroblasts and HEV react with CDw90 mAbs. Cell reactivity seems to be confined to the non proliferative cell fraction. One mAb (clone: 5E10) is known.

CD91. α2M-R is a receptor for α2-macroglobulin. This 200 kD antigen is present on T cells, neutrophils, monocytes, adult and fetal fibroblasts, and, to a lesser extent, on activated and resting platelets. Five mAbs (clones: α2MRa-1; α2MRa-2; α2MRA-3,A; α2MRa-5; α2MRb-1,S) are present in this cluster.

CDw92. Its common name is GR9. The function of this 70 kD molecule is unknown. It is expressed on TNF-activated and resting endothelial cells, PHA-stimulated lymphocytes, activated and resting granulocytes, several hematologic cell lines and weakly on $CD34^+$ myeloid progenitors. Two mAbs (clones: VIM15; VIM15b) are known.

CD93. This 120 kD antigen is present on endothelial cells, eosinophils, granulocytes, monocytes, B and NK cell lines. It is also known as GR11. Four mAbs (clones: VIMD2; VIMD2b; WDS4.B4; X2) have been clustered.

CD115. This 150 kD molecule functions as a receptor for the M-CSF-R (*monocyte-macrophage colony-stimulating factor receptor*). It belongs to subclass III of the family of growth factor receptors with tyrosine kinase activity. The human gene location is on chromosome 5q33.2-q33.3. It has been demonstrated that patients with myelodysplastic syndrome can exhibit a loss of both M-CSFR alleles. The interaction of this receptor with its ligand stimulates the proliferation, maturation and survival of cells belonging to the mononuclear phagocyte system. M-CSFR binds the growth factor and this produces kinase activation with stimulation and activation of protein C kinases, which induces gene overexpression. This receptor is found on monocytes, macrophages, and their bone marrow progenitors, fetal B lymphocytes and, to a lesser extent, on megakaryocytes. Twelve mAbs (reference mAbs: 10-4B2-2EG; 11-4C1-1F5; 12-2D6-2D7; 12-3A1-2B8; 12-2A3-1B1; 12-3D3-2F1) are known.

Endothelial section (3 new CD molecules)

CD105. This antigen, with a molecular weight of 95 kD, is also called *endoglobin.* It is an endothelial antigen but it is also present on some B lymphoid and myeloid cell lines, and on a subset of $CD34^+$ bone marrow cells; stromal cells and endothelial cells express large amounts of this molecule (MESF >1,000,000). Ten mAbs (clones: 1G2; 44G4; E9; F430C5; MAEND3; PN-E2) are known; 44G4 antibody is prevalently reactive with $CD34^+$ cells, T cells, B cells, monocytes and granulocytes.

CD106. This 110 kD molecule is also known as INCAM-110, or VCAM-1 (*vascular cellular adhesion molecule-1*). It is a member of the immunoglobulin gene superfamily and is induced on endothelial cells by inflammatory cytokines. This molecule mediates white blood cell adhesion to endothelium via its ligand VLA-4. It is expressed on endothelial cells, stromal cells and a few B cell and NK cell lines. Five mAbs (clones: E1/6; STA; 1G11; 4B9; HAE-2a) are known.

CDw109. This 170-150 kD antigen is also known as GR56, 8A3, 7D1 molecule and is expressed on TNF-activated and resting endothelial cells (MESF=500,000), weakly on PHA-stimulated lymphocytes, thymocytes, myeloid and monocytoid cell lines, activated platelets. Two mAbs (clones: 7D1; 8A3) are known.

Platelet section (2 new CD molecules)

CD42a. GPIX, together with CD42b, is a major component of the platelet surface. This 23 kD molecule is present on activated and resting platelets (MESF: 10,000-500,000), and on 70% of monocytes. Four mAbs (clones: Beb1; BL-H6; GR-P; SZ-1) are known.

CD42b. This 135-145 kD molecule is also referred to as GpIb α chain. It represents the α chain of the GpIb molecule, and its binding to von Willebrand factor is crucial for platelet adhesion at sites of injury. CD42b is also a receptor for thrombin. It is expressed on activated and resting platelets, neutrophils, monocytes, B lymphocytes, fetal and adult fibroblasts and on $CD34^+$ bone marrow progenitors (MESF: 10,000). Many mAbs (reference mAbs: AK-2; Apt2; HIPt; Apt5; C-34; ES85) have been verified as recognizing this molecule.

CD42c. This is referred to as GpIb β chain and has a molecular weight of 23 kD. Its spectrum of reactivity is identical to that of CD42b. One mAb (clone: GI27) is known.

CD42d. Also called GPV, it is glycoprotein V, which is capable of forming a non covalent complex with CD42. This 85 kD antigen has been found to be expressed by platelets and most monocytes (MESF: 10,000). One mAb (clone: Sw16) has been clustered.

Surface α-granule proteins

CD107a. This 110 kD molecule is also known as LAMP-1. It is weakly expressed on activated platelets, KG1α, HL60, HUT-78 cell lines, and on fetal thymic epithelial cells. Three mAbs (clones: ED11; H4A3; H5G11) are known.

CD107b. Is also referred to as LAMP-2. This 120 kD molecule is present on some myeloid cell lines, activated and resting endothelial cells, and weakly expressed on activated and resting platelets. Two mAbs (clones: C3D; H4B4) belong to this group.

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