The Journal of Immunology

CD Nomenclature 2015: Human Leukocyte Differentiation Antigen Workshops as a Driving Force in Immunology

Pablo Engel, Laurence Boumsell, Robert Balderas, Armand Bensussan, Valter Gattei, Vaclav Horejsi, Bo-Quan Jin, Fabio Malavasi, Frank Mortari, Reinhard Schwartz-Albiez, Hannes Stockinger, Menno C. van Zelm, Heddy Zola and Georgina Clark

J Immunol 2015; 195:4555-4563; ;
doi: 10.4049/jimmunol.1502033
http://www.jimmunol.org/content/195/10/4555

The Journal of Immunology is published twice each month by
The American Association of Immunologists, Inc.,
1451 Rockville Pike, Suite 650, Rockville, MD 20852

Print ISSN: 0022-1767 Online ISSN: 1550-6606.

Immunology Notes and Resources

The Journal of Immunology

CD Nomenclature 2015: Human Leukocyte Differentiation Antigen Workshops as a Driving Force in Immunology

Pablo Engel,* Laurence Boumsell,† Robert Balderas,‡ Armand Bensussan,§ Valter Gattei,¶ Vaclav Horejsi,‖ Bo-Quan Jin,# Fabio Malavasi,** Frank Mortari,†† Reinhard Schwartz-Albiez,‡‡ Hannes Stockinger,§§ Menno C. van Zelm,¶¶ Heddy Zola,‖‖ and Georgina Clark##

CD (cluster of differentiation) Ags are cell surface molecules expressed on leukocytes and other cells relevant for the immune system. CD nomenclature has been universally adopted by the scientific community and is officially approved by the International Union of Immunological Societies and sanctioned by the World Health Organization. It provides a unified designation system for mAbs, as well as for the cell surface molecules that they recognize. This nomenclature was established by the Human Leukocyte Differentiation Antigens Workshops. In addition to defining the CD nomenclature, these workshops have been instrumental in identifying and determining the expression and function of cell surface molecules. Over the past 30 y, the data generated by the 10 Human Leukocyte Differentiation Antigens Workshops have led to the characterization and formal designation of more than 400 molecules. CD molecules are commonly used as cell markers, allowing the identification and isolation of leukocyte populations, subsets, and differentiation stages. mAbs against these molecules have proven to be essential for biomedical research and diagnosis, as well as in biotechnology. More recently, they have been recognized as invaluable tools for the treatment of several malignancies and autoimmune diseases. In this article, we describe how the CD nomenclature was established, present the official updated list of CD molecules, and provide a rationale for their usefulness in the 21st century. *The Journal of Immunology*, 2015, 195: 4555–4563.

In the early days of mAb technology, a plethora of human cell surface molecules was identified and described. To avoid confusion and enhance the field, Human Leukocyte Differentiation Antigens (HLDA) Workshops were organized that implemented a standard nomenclature for clusters of Abs that reacted with a specific Ag, providing consistency and uniformity in manuscripts referring to identical molecules. This standardization is commonly referred to as the cluster of differentiation (CD) nomenclature. At present, CD markers range from CD1 to CD371, with some CDs covering a group of closely related proteins or carbohydrates (e.g., CD1a, CD1b, CD1c, and CD1d). In this review, we aim to explain the CD nomenclature system and provide a rationale for its usefulness in an age of rAbs and Ab therapies.

CD Definition and Nomenclature

A nondescriptive CD number is assigned to a group or cluster of mAbs that recognize the same cell surface molecule (e.g., CD2 or CD3). The CD designation refers to a group of mAbs shown by the statistical method of cluster analysis to recognize a particular cellular-differentiation pattern. The CD nomenclature is also used to name the molecule itself. For example, CD4 designates both the group of mAbs recognizing the CD4 cell surface molecule, as well as the CD4 molecule itself.

A lowercase "w" preceding the number designation stands for "workshop" (e.g., CDw12) and indicates that the CD designation is tentative; it denotes an insufficiently characterized Ab or molecule. In some cases, it corresponds to a molecule defined by only one Ab submitted to the HLDA Workshops. Most of the provisional CDw-designated Ags of the early workshops turned out to correspond to clusters of mAbs recognizing carbohydrate epitopes, which after proper biochemical identification received their own CD number (e.g., CD176 = Thomsen-Friedenreich, carbohydrate Ag) (1).

Uppercase letters following a CD number designate a spliced variant of the extracellular domain of a cell surface molecule. For example, CD45RA or CD45RO corresponds to splice variants

*Immunology Unit, Department of Cell Biology, Immunology, and Neurosciences, Medical School, University of Barcelona, Barcelona 08036, Spain; †INSERM, Paris 75014, France; ‡BD Biosciences, San Jose, CA 95131; §INSERM U976, Hospital Saint Louis, University of Paris, Paris 75010, France; ¶Clinical and Experimental Onco-Hematology Unit, Oncological Referral Center, Aviano 33081, Italy; ‖Institute of Molecular Genetics, Czech Academy of Sciences, Prague 142 20, Czech Republic; #Department of Immunology, The Fourth Military Medical University, Xi'an 710032, China; **Laboratory of Immunogenetics and Center for Experimental Research and Medical Studies, Department of Medical Sciences, University of Turin, Turin 10126, Italy; ††R&D Systems, Bio-Techne Corporation, Minneapolis, MN 55413; ‡‡Tumor Immunology Program, German Cancer Research Center, Heidelberg 69120, Germany; §§Institute for Hygiene and Applied Immunology, Centre for Pathophysiology, Infectiology, and Immunology, Medical University of Vienna, Vienna 1090, Austria; ¶¶Department of Immunology, Central Clinical School, Monash University, Melbourne, Victoria 3004, Australia; ‖‖Child Health Research Institute and University of Adelaide, Adelaide 5000, Australia; and ##Dendritic Cell Research, Australian and New Zealand Army Corps Research Institute, University of Sydney, Sydney 2139, Australia

ORCIDs: 0000-0001-8410-252X (P.E.); 0000-0002-6386-7475 (B.-Q.J.); 0000-0002-3367-4998 (F. Mortari); 0000-0001-7741-2482 (R.S.-A.); 0000-0001-6404-4430 (H.S.); 0000-0003-4161-1919 (M.C.v.Z.); 0000-0003-0664-6518 (H.Z.).

Received for publication September 15, 2015. Accepted for publication September 15, 2015.

Address correspondence and reprint requests to Dr. Pablo Engel, Immunology Unit, Department of Cell Biology, Immunology, and Neurosciences, Medical School, University of Barcelona, Casanova 143, Barcelona 08036, Spain. E-mail address: pengel@ub.edu

Abbreviations used in this article: CD, cluster of differentiation; HCDM, Human Cell Differentiation Molecules; HLDA, Human Leukocyte Differentiation Antigens.

www.jimmunol.org/cgi/doi/10.4049/jimmunol.1502033

of CD45. A lowercase letter following the CD number (e.g., CD1a, CD1b, CD1c, CD1d, or CD1e) indicates several molecules that share a common chain, in this example, β2-microglobulin. Other examples are the integrin chains CD11a, CD11b, and CD11c, all of which share CD18 as a common chain to form different dimers. In other cases, lowercase letters have been used to name different members of the same gene family, as is the case with CD66 (CD66a, CD66b, CD66c, CD66d, CD66e, and CD66f). With regard to carbohydrate CD structures, a lower case suffix represents a modification of the same carbohydrate sequence (e.g., CD15s = sialylated CD15, Lewis^x Ag; CD60b = 9-*O*-acetylated ganglioside GD3) (1). Details of carbohydrate CD Ags and carbohydrate-binding CD proteins can be found at http://glycosciences.de/glycocd/index.php.

The CD nomenclature is also frequently used to describe lymphocyte and leukocyte subsets. A "+" symbol is added as a superscript to a CD number to indicate the presence of that molecule on a cell or cell population, and a "−" superscript indicates its absence, as in $CD3^+CD4^+CD8^-$. If a particular CD molecule is expressed at different levels by a cell subset, the superscript "high" or "low" can be added, as in $CD4^+CD45RA^{low}CD45RO^{high}$.

In the past, an uppercase letter was added to some CDs to group related molecules under the same CD number. This was the case for selectins: CD62L (L-selectin), CD62E (E-selectin), and CD62P (P-selectin). Unfortunately, this turned out to be confusing, because sometimes an "L" was added by some researchers to indicate "ligand," such as for CD154, commonly referred to as CD40L. To avoid confusion, the addition of uppercase "L" has been discontinued. It should be noted that the terms CD5L, CD20L, and CD137L are not approved nomenclature and should be avoided.

HLDA Workshops

HLDA Workshops were created to establish the nomenclature of leukocyte cell surface molecules by using mAbs from different laboratories. Currently, HLDA Workshops are run by the Human Cell Differentiation Molecules (HCDM) organization (http://www.HCDM.org) under the umbrella of the International Union of Immunological Societies/World Health Organization nomenclature and standardization committees.

The history of the HLDA Workshops

With the advent of hybridoma technology to produce mAbs, immunologists began to generate very large numbers of mAbs directed against leukocyte cell surface molecules, generally using whole cells as immunogen. The problem was that several mAbs produced by different laboratories (under different names) were actually directed against the same molecule. This was not always obvious, because the description of the cellular expression pattern reflected the different local interests of the research groups. This resulted in the chaotic naming of molecules, and a Tower of Babel of terminology arose (2). To solve this problem, the first international HLDA Workshop and Conference was organized in 1982 by Alain Bernard and Laurence Boumsell and was cochaired by Jean Dausset, Cesar Milstein, and Stuart F. Schlossman. It was sponsored by INSERM, the Medical Research Council, the World Health Organization, and the International Union of Immunological Societies, mimicking the already existing HLA Workshops that were organized for establishing the nomenclature of HLA alleles (3). The initial goal was to identify groups of mAbs reacting with a common Ag and to agree upon a nomenclature to facilitate better and consistent communication within the scientific community (4). Soon, HLDA workshops proved essential in the identification and characterization of the molecules that populate the surface of hematopoietic cells. The successive workshops provided a forum for the exchange of mAbs and information. Consequently, these workshops were instrumental in unraveling the function of leukocyte cell surface molecules and profoundly transformed our understanding of functional properties of immune cells, as well as their differentiation, maturation, and activation. Ten HLDA Workshops have been organized thus far, with the most recent in 2014 chaired by Georgina Clark.

HLDA Workshop protocol

HLDA Workshops are wet workshops based on an international exchange and blind evaluation of mAbs, submitted by numerous academic laboratories and/or companies. The main goal has consistently been to identify mAbs reacting with a common Ag. The basic strategy was to assess a given mAb's reactivity with a large panel of different lymphoid cells, followed by statistical analysis of the resulting expression data and further examination of the biochemical nature and molecular mass of the target Ag. Although cellular expression analysis remains essential, modern molecular biology techniques are very useful for a clearer identification of the molecular structures of the target Ags than was possible in the earliest workshops (5).

The initial step consists of establishing one or more panels of mAbs that are submitted by academic groups and/or companies. The organizing laboratory aliquots and distributes the mAbs among the participating laboratories. This has been quite challenging. For example, during HLDA5, >100,000 aliquots of 1,450 mAbs were prepared and distributed among the participating laboratories (6).

Participating laboratories perform specific blind studies with the mAbs included in the panel. This allows for the testing of mAb reactivity with multiple cell types using multiple-color flow cytometry. Because these studies require analysis of huge numbers of different types of primary normal and malignant cells and cell lines, this approach is only possible as a combined effort by a large group of laboratories.

Other participating researchers perform additional tests, such as immunohistochemistry on tissue sections or the biochemical characterization of the target molecules using immunoprecipitation, Western blots, or binding studies to the recombinant target molecules.

The flow cytometry expression data are collected by the organizing laboratory and analyzed using a hierarchical clustering algorithm (3). The biochemical and molecular biological data are used to further validate the clustering analysis.

Currently, the designation of new CDs requires submission to the workshop of at least two independent mAbs that recognize the same molecule and present an identical pattern of reactivity. Proof of specific reactivity with transfected cells is mandatory to obtain a CD designation. Such mAbs must specifically recognize the target protein on transfected cells, as well as the endogenous protein on live primary cells. During the last two HLDA Workshops, the cross-reactivity of the Abs

Table I. List of CD molecules

CD	Other Names	Gene Family	Gene Name	Gene Number
CD1a	R4, HTA1	Ig superfamily	CD1a	909
CD1b	R1	Ig superfamily	CD1b	910
CD1c	R7	Ig superfamily	CD1c	911
CD1d	R3	Ig superfamily	CD1d	912
CD1e	R4	Ig superfamily	CD1e	913
CD2	LFA-2	Ig superfamily	CD2	914
CD3e	T3, Leu4, OKT3	Ig superfamily	CD3G	917
CD4	T4, Leu3a, OKT4	Ig superfamily	CD4	920
CD5	Leu-1	Scavenger receptor superfamily	CD5	921
CD6	T12	Scavenger receptor superfamily	CD6	923
CD7	gp40	Ig superfamily	CD7	924
CD8a	T8, Leu2, OKT8	Ig superfamily	CD8A	925
CD8b	CD8b	Ig superfamily	CD8B	926
CD9	p24, MRP-1	Tetraspanin family	CD9	928
CD10	CALLA, gp100, NEP	Peptidase protein family	MME	4311
CD11a	LFA-1	Integrin family	ITGAL	3683
CD11b	Mac-1	Integrin family	ITGAM	3684
CD11c	p150	Integrin family	ITGAX	3687
CD13	APN, gp150	Peptidase protein family	ANPEP	290
CD14	LPS R	Leucine-rich repeat family	CD14	929
CD15	Lewis X	Carbohydrate		
CD15u	3-sulfo Lex	Carbohydrate		
CD15s	Sialyl Lex	Carbohydrate		
CD15su	6-sulfo-sialyl Lex	Carbohydrate		
CD16	CD16a, FcγRIIIA	Ig superfamily	FCGR3A	2214
CD16b	FcYRIIIB	Ig superfamily	FCGR3B	2215
CD17	Lactosylceramide	Carbohydrate		
CD18	b2 integrin	Integrin family	ITGB2	3689
CD19	B4	Ig superfamily	CD19	930
CD20	B1, Bp35	Membrane-spanning 4A family	MS4A1	931
CD21	CR2, EBV-R, C3dR	Regulator of complement activation gene family	CR2	1380
CD22	BL-CAM, Siglec-2	Ig superfamily	CD22	933
CD23	FcεRII, BLAST-2	C-type lectin family	FCER2	2208
CD24	BA-1, HAS	Sialomucin family	CD24	934
CD25	Tac, p55, IL-2Ra	Cytokine receptor family	IL2RA	3559
CD26	Dipeptidyl peptidase IV	Ectodomain family	DPPA	1803
CD27	T14, S152, TNFRSF7	TNFR superfamily	TNFRSF7	939
CD28	Tp44, T44	Ig superfamily	CD28	940
CD29	Integrin b1	Integrin family	ITGB1	3688
CD30	Ki-1, TNFRSF8	TNFR superfamily	TNFRSF8	943
CD31	PECAM-1, endocam	Ig superfamily	PECAM1	5175
CD32	FcγRII	Ig superfamily	FCGR2A	2212
CD33	p67, Siglec-3	Ig superfamily	CD33	945
CD34	gp10-120, mucosialin, MY10	Sialomucin family	CD34	947
CD35	CR1, C3b/C4b-R	Regulator of complement activation gene family	CR1	1378
CD36	GPIV, gpIIIb	Scavenger receptor superfamily	CD36	948
CD37	gp52-40	Tetraspanin family	CD37	951
CD38	T10, ADP-ribosyl cyclase	Ectoenzyme family	CD38	952
CD39	Entpd1, NTPDase-1	Ectoenzyme family	ENTPD1	953
CD40	TNFRSF5	TNFR superfamily	TNFRSF5	958
CD41	GPIIb	Integrin family	ITGA2B	3674
CD42a	GPIX	Leucine-rich repeat family	GP9	2815
CD42b	GPIBa	Leucine-rich repeat family	GP1BA	2811
CD42c	GPIBb	Leucine-rich repeat family	GP1BB	2812
CD42d	gpv	Leucine-rich repeat family	GP5	2814
CD43	Sialophorin, leukosialin	Sialomucin family	SPN	6693
CD44	HCAM, Pgp-1	Hyaluronic acid receptor family	CD44	960
CD45	LCA, T200	Protein tyrosine phosphatase family	PTPRC	5788
CD45RA	Leu18	Protein tyrosine phosphatase family	Spliced variant	5788
CD45RB		Protein tyrosine phosphatase family	Spliced variant	5788
CD45RC		Protein tyrosine phosphatase family	Spliced variant	5788
CD45RO	UCHL-1	Protein tyrosine phosphatase family	Spliced variant	5788
CD46	MCP	Regulator of complement activation gene family	MCP	4179
CD47	Integrin-associated protein	Ig superfamily	CD47	961
CD48	BLAST1, BCM1, SLAMF2	Ig superfamily	CD48	962
CD49a	VLA4-1a, a1 integrin	Integrin family	ITGA1	3672
CD49b	VLA4-2a, a2 integrin	Integrin family	ITGA2	3673
CD49c	VLA4-3a, a3 integrin	Integrin family	ITGA3	3675
CD49d	VLA4-4a, a4 integrin	Integrin family	ITGA4	3676
CD49e	VLA4-5a, a5 integrin	Integrin family	ITGA5	3678
CD49f	VLA4-6a, a6 integrin	Integrin family	ITGA6	3655
CD50	ICAM-3	Ig superfamily	ICAM3	3385

(*Table continues*)

Table I. (*Continued*)

CD	Other Names	Gene Family	Gene Name	Gene Number
CD51	Vitronectin R	Integrin family	ITGAV	3685
CD52	CAMPATH-1	Sialomucin family	CD52	1043
CD53	TSPAN2	Tetraspanin family	CD53	963
CD54	ICAM-1	Ig superfamily	ICAM1	3383
CD55	DAF	Regulator of complement activation gene family	DAF	1604
CD56	NCAM	Ig superfamily	NCAM1	4684
CD57	HNK-1, 3-0-sulfated glucuronic acid	Carbohydrate		
CD58	LFA-3	Ig superfamily	CD58	965
CD59	Protectin H19	Regulator of complement activation gene family	CD59	966
CD60a	GD3	Carbohydrate		
CD60b	9-0-acetyl GD3	Carbohydrate		
CD60c	7-0-acetyl GD3	Carbohydrate		
CD61	gpIIIa, b3 integrin	Integrin family	ITGB3	3690
CD62E	E-selectin, ELAM-1	C-type lectin family	SELE	6401
CD62L	L-selectin	C-type lectin family	SELL	6402
CD62P	P-selectin	C-type lectin family	SELP	6403
CD63	LAMP-3, LIMP, MLA1	Tetraspanin family	CD63	967
CD64	FcγRI, FcRI	Ig superfamily	FCGR1A	2209
CD65	Ceramide-dodecasaccharide 4c	Carbohydrate		
CD65s	α2,3-sialylatedceramidedodecasaccharide 4c	Carbohydrate		
CD66a	BGP, CEACAM1, NCA-160	Ig superfamily	CEACAM1	634
CD66b	NCA-95, CGM6	Ig superfamily	CEACAM8	1088
CD66c	NCA	Ig superfamily	CEACAM6	4680
CD66d	CGM1	Ig superfamily	CEACAM3	1084
CD66e	CEA	Ig superfamily	CEACAM5	1048
CD66f	PSG, Sp-1	Ig superfamily	PSG1	5669
CD68	Macrosialin, gp110	Sialomucin	CD68	968
CD69	AIM, VEA	C-type lectin family	CD69	969
CD70	Ki-24, CD27L, TNFSF7	TNF superfamily	TNFSF7	970
CD71	TfR, T9, transferin receptor	Transferin receptor family	TFRC	7037
CD72	Lyb-2	C-type lectin family	CD72	971
CD73	ECTO-5′Nucleotidase	Ectoenzyme family	NT5E	4907
CD74	li, invariant chain	No family assigned	CD74	972
CD75	N-acetyllactosamine	Carbohydrate		
CD75s	CDw76, 2,6-sialylated N-acetyllactosamine	Carbohydrate		
CD77	Globotriaosylceramide, Gb3, BLA, CTH	Glycosphingolipid		
CD79a	Iga, MB1	Ig superfamily	CD79A	973
CD79b	Igb, B29	Ig superfamily	CD79B	974
CD80	B7, B7-1, BB1	Ig superfamily	CD80	941
CD81	TAPA-1	Tetraspanin family	CD81	975
CD82	R2,4F9, C33	Tetraspanin family	KAI1	3732
CD83	HB15	Ig superfamily	CD83	9308
CD84	SLAMF5	Ig superfamily	CD84	8832
CD85a	LIR-3, ILT5, LILRB3,	Ig superfamily	LILRB3	11025
CD85d	LIR-2, ILT4, LILRB2	Ig superfamily	LILRB2	10288
CD85j	LIR-1, ILT2	Ig superfamily	LILRB1	10859
CD85k	LIR-5, ILT3	Ig superfamily	LILRB4	11006
CD86	B70, B7-2	Ig superfamily	CD86	942
CD87	uPAR, urokinase receptor	Ly-6 superfamily	PLAUR	5329
CD88	C5aR	G protein–coupled receptor superfamily	C5R1	728
CD89	IgA R, FcaR	Ig superfamily	FCAR	2204
CD90	Thy-1	Ig superfamily	THY1	7070
CD91	LRP, a2M-R	Low-density lipoprotein receptor family	LRP1	4035
CD92	CTL1, CHTL1	Solute carrier family	SLS44A1	23446
CD93	CDw93, C1qR1, GR11	C-type lectin family	CD93	22918
CD94	Kp43	C-type lectin family	KLRD1	3824
CD95	TNFRSF6, Fas, APO-1	TNFR superfamily	TNFRSF6	355
CD96	TACTILE, EMR1, BL-KDD/F12	Ig superfamily	CD96	10225
CD97	EMR1	G-protein coupled receptor superfamily	CD97	976
CD98	FRP-1, 4F2	Solute carrier family	SLC3A2	6520
CD99	MIC2, E2	Sialomucin family	CD99	4267
CD99R	E2	Sialomucin family	CD99 variant	
CD100	SEMA4D	Semaphorin family	SEMA4D	10507
CD101	V7, P126	Ig superfamily	IGSF2	9398
CD102	ICAM-2	Ig superfamily	ICAM2	3384
CD103	HML-1, Integrin aE-subunit	Integrin family	ITGAE	3682
CD104	TSP-1180, Integrin b4-subunit	Integrin family	ITGB4	3691
CD105	Endoglin	TGF-β superfamily	ENG	2022
CD106	VCAM-1, INCAM-110	Ig superfamily	VCAM1	7412
CD107a	LAMP-1	LAMP family	LAMP1	3916
CD107b	LAMP-2	LAMP family	LAMP2	3920
CD108	SEMA7A, GPI-gp80, JMH, Sema K1	Semaphorin family	SEMA7A	8482

(*Table continues*)

Table I. (*Continued*)

CD	Other Names	Gene Family	Gene Name	Gene Number
CD109	Platelet activation factor, 8A3, E123	Alfa2 macroglobulin family	CD109	135228
CD110	TPO-R, c-mpl	Cytokine receptor family	MPL	4352
CD111	PRR1, Nectin-1, Hve C1	Ig superfamily	PVRL1	5818
CD112	PRR2, Nectin-2, Hve B	Ig superfamily	PVRL2	5819
CD113	PVRL3, Nectin-3	Ig superfamily	PVRL3	25945
CD114	G-CSFR, HG-CSF3R	Cytokine receptor family	CSF3R	1441
CD115	M-CSFR, CSF-1R	Ig superfamily	CSF1R	1436
CD116	GM-CSFR a-subunit	Cytokine receptor family	CSF2RA	1438
CD117	SCFR, c-kit	Protein kinase superfamily	KIT	3815
CD118	LIFR	Cytokine receptor family	LIFR	3977
CD119	IFNγ receptor a-chain, IFNYR, IFNYRa	Cytokine receptor family	IFNGR1	3459
CD120a	TNFRI, TNFRp55, TNFRSF1A	TNFR superfamily	TNFRSF1A	7132
CD120b	TNFRII, TNFRp75, TNFRSF1B	TNFR superfamily	TNFRSF1B	7133
CD121a	Type I IL-1R	Ig superfamily	IL1R1	3554
CD121b	Type II IL-1R	Ig superfamily	IL1R2	7850
CD122	IL-2/15Rb, p75	Cytokine receptor family	IL2RB	3560
CD123	IL-3Ra	Cytokine receptor family	IL3RA	3563
CD124	IL-4Ra	Cytokine receptor family	IL4R	3566
CD125	IL-5Ra	Cytokine receptor family	IL5RA	3568
CD126	IL-6Ra	Cytokine receptor family	IL6RA	3570
CD127	IL-7Ra, p90	Cytokine receptor family	IL7RA	3575
CD129	IL-9Ra	Cytokine receptor family	IL9R	3581
CD130	gp130	Cytokine receptor family	IL6ST	3572
CD131	Common b-chain	Cytokine receptor family	CSF2RB	1439
CD132	Common y-chain	Cytokine receptor family	IL2RG	3561
CD133	AC133, PROML1	Prominin family	PROM1	8842
CD134	TNFSF4, OX40	TNFR superfamily	TNFRSF4	7293
CD135	FLT3, STK-1	Ig superfamily	FLT3	2322
CD136	MSP-R	Semaphorin family	MST1R	4486
CD137	4-1BB, TNFRSF9	TNFR superfamily	TNFRSF9	3604
CD138	Syndecan-1, B-B4	Syndecan proteoglycan family	SDC1	6382
CD139		Not cloned		
CD140a	PDGF receptor a polypeptide	Protein kinase superfamily	PDGFRA	5156
CD140b	PDGF receptor b polypeptide	Protein kinase superfamily	PDGFRB	5159
CD141	Thrombomodulin, fetomodulin	C-type lectin family	THBD	7056
CD142	Tissue factor, thromboplastin	Cytokine receptor family	F3	2152
CD143	ACE, peptidyl-dipeptidase A	Metalloendopeptidase family	ACE	1636
CD144	VE-cadherin, cadherin-5	Cadherin superfamily	CDH5	1003
CDw145		Not cloned		
CD146	MCAM. Muc 18, Mel-CAM, s-endo	Ig superfamily	MCAM	4162
CD147	Basigin, M6, EMMPRIN	Ig superfamily	BSG	682
CD148	DEP-1, HPTP-n	Protein tyrosine phosphatase family	PTPRJ	5795
CDw149	Now CD47R	Ig superfamily	CD47	961
CD150	IPO-3, SLAMF1,	Ig superfamily	SLAMF1	6504
CD151	Platelet-endothelial tetra-span Ag 3	Tetraspanin family	CD151	977
CD152	CTLA-4, CTL Ag 4	Ig superfamily	CTLA4	1493
CD153	TNFSF8, CD30L	TNF superfamily	TNFSF8	944
CD154	TNFSF5, CD40L, gp39, TRAP	TNF superfamily	TNFSF5	959
CD155	Poliovirus receptor, nectin-like 5	Ig superfamily	PVR	5817
CD156a	ADAM 8, MS2	ADAM family	ADAM8	101
CD156b	TACE, ADAM17, snake venom–like protease	ADAM family	ADAM17	6968
CD156c	ADAM10	ADAM family	ADAM10	102
CD157	BST-1, BP-3/IF7, Mo5	Ectoenzyme family	BST1	683
CD158e	KIR3DL1, NKB1, NKB1B, NKAT-3	Ig superfamily	KIR3DL1	3811
CD158i	KIR2DS4, NKAT-8	Ig superfamily	KIR2DS4	3809
CD158k	KIR3DL2, NKAT-4, NKAT4B	Ig superfamily	KIR3DL2	3812
CD159a	NKG2A, NKG, KLRC1	C-type lectin family	KLRC1	3821
CD159c	NKG2C, KLRC2	C-type lectin family	KLRC2	3822
CD160	BY55, NK1, NK28	Ig superfamily	CD160	11126
CD161	NKR-P1A	C-type lectin family	KLRB1	3820
CD162	PSGL-1	Sialomucin family	SELPLG	6404
CD163	GHI/61, D11, RM3/1, M130	Scavenger receptor superfamily	CD163	9332
CD164	MUC-24, MGC 24	Sialomucin family	CD164	8763
CD165	AD2, gp 37, SN2	Not cloned	CD165	23449
CD166	ALCAM, KG-CAM, BEN	Ig superfamily	ALCAM	214
CD167a	DDR1	Protein kinase superfamily	DDR1	780
CD167b	DDR2	Protein kinase superfamily	DDR2	4921
CD168	RHAMM	Hyaluronic acid receptor family	HMMR	3161
CD169	Sialoadhesin (Sn), Siglec-1	Ig superfamily	SN	6614
CD170	Siglec-5	Ig superfamily	SIGLEC5	8778
CD171	Neuronal adhesion molecule, L1	Ig superfamily	L1CAM	3897
CD172a	SIRPA, SHPS-1	Ig superfamily	SIRPA	140885

(*Table continues*)

Table I. (*Continued*)

CD	Other Names	Gene Family	Gene Name	Gene Number
CD172b	SIRPB1	Ig superfamily	SIRPB1	10326
CD172g	SIRPG, SIRPB2	Ig superfamily	SIRPG	55423
CD173	Blood group H	Carbohydrate		
CD174	Blood group Lewis Y	Carbohydrate		
CD175	Tn Ag	Carbohydrate		
CD175s	Sialyl-Tn	Carbohydrate		
CD176	Thomsen-Friedenreich Ag	Carbohydrate		
CD177	NB1, HNA-2a, PRV1	Ly-6 superfamily	PRV1	57126
CD178	TNFSF6, FAS ligand, CD95 ligand	TNF superfamily	TNFSF6	356
CD179a	VPREB1, IGVPB	Ig superfamily	VPREB1	7441
CD179b	Λ 5	Ig superfamily	IGLL1	3543
CD180	RP105, Bgp95	TLR family	LY64	4064
CD181	CXCR1, IL-8R-a	G protein–coupled receptor superfamily	CXCR1	3577
CD182	CXCR2, IL-8R-b	G protein–coupled receptor superfamily	CXCR2	3579
CD183	CXCR3, G protein–coupled receptor 9	G protein–coupled receptor superfamily	CXCR3	2833
CD184	CXCR4, Fusin	G protein–coupled receptor superfamily	CXCR4	7852
CD185	CXCR5, BLR1	G protein–coupled receptor superfamily	CXCR5	643
CD186	CXCR6, BONZON, STRL33, TYMSTR	G protein–coupled receptor superfamily	CXCR6	10663
CD191	CCR1, CC-CKR-1	G protein–coupled receptor superfamily	CCR1	1230
CD192	CCR2, MCP-1-R, CKR2	G protein–coupled receptor superfamily	CCR2	1231
CD193	CCR3, eosinophil eotaxin receptor, CKR3	G protein–coupled receptor superfamily	CCR3	1232
CD194	CCR4	G protein–coupled receptor superfamily	CCR4	1233
CD195	CCR5, CKR5	G protein–coupled receptor superfamily	CCR5	1234
CD196	CCR6, CKR6, LARC receptor	G protein–coupled receptor superfamily	CCR6	1235
CD197	CCR7, EB11, BLR2	G protein–coupled receptor superfamily	CCR7	1236
CDw198	CCR8, CKRL1	G protein–coupled receptor superfamily	CCR8	1237
CD199	CCR9	G protein–coupled receptor superfamily	CCR9	10803
CD200	OX-2	Ig superfamily	CD200	4345
CD201	Endothelial protein C receptor	MHC class family	PROCR	10544
CD202b	TIE2, TEK	Protein kinase superfamily	TEK	7010
CD203c	E-NPP3, PDNP3, PD-1b	Ectoenzyme family	ENPP3	5169
CD204	MSR, SRA, macrophage scavenger receptor	Scavenger receptor superfamily	MSR1	4481
CD205	DEC-205, lymphocyte Ag 75	C-type lectin family	LY75	4065
CD206	Macrophage mannose receptor, CLEC13D	C-type lectin family	MRC1	4360
CD207	Langerin, CLEC4K	C-type lectin family	CD207	50489
CD208	DC-LAMP	LAMP family	LAMP3	27074
CD209	DC-SIGN, CLEC4L	C-type lectin family	CD209	30835
CD210	IL10R-a	Cytokine receptor family	IL10RA	3587
CDw210b	IL10R-b	Cytokine receptor family	IL10RB	3588
CD212	IL-12R-b1	Cytokine receptor family	IL12RB1	3594
CD213a1	IL-13R-a1	Cytokine receptor family	IL13RA1	3597
CD213a2	IL-13R-a2	Cytokine receptor family	IL13RA2	3598
CD215	IL-15R-a	Cytokine receptor family	IL15RA	3601
CD217a	IL-17R-a	Cytokine receptor family	IL17RA	23765
CD218a	IL-18R-a	Ig superfamily	IL18R1	8809
CD218b	IL-18R-b	Ig superfamily	IL18RAP	8807
CD220	Insulin receptor	Protein kinase superfamily	INSR	3643
CD221	IGF1 receptor, type I IGF receptor	Protein kinase superfamily	IGF1R	3480
CD222	IGF2R, mannose-6-phosphate receptor	P-type lectin family	IGF2R	3482
CD223	LAG3	Ig superfamily	LAG3	3902
CD224	GGT1, γ-glutamyl transferase	Peptidase protein family	GGT1	2678
CD225	Leu-13, IFN-induced TM protein 1	IFN-inducible transmembrane protein family	IFITM1	8519
CD226	DNAM-1, PTA-1	Ig superfamily	CD226	10666
CD227	MUC1, DF3 Ag, H23 Ag	Sialomucin family	MUC1	4582
CD228	Melanotransferrin, p97	Transferrin superfamily	MF12	4241
CD229	Ly9, SLAMF3	Ig superfamily	LY9	4063
CD230	Prion protein	Prion family	PRNP	5621
CD231	TALLA-1, TM4SF2	Tetraspanin family	TSPAN7	7102
CD232	VESPR, PLEXIN C1	Plexin family	PLXNC1	10154
CD233	Band 3, AE1, anionexchanger 1	Solute carrier family	SLC4A1	6521
CD234	DARC, Fγ-glycoprotein	G protein–coupled receptor superfamily	DARC	2532
CD235a	Glycophorin A, PAS-2	Glycophorin family	GYPA	2993
CD235b	Glycophorin B, PAS-3	Glycophorin family	GYPB	2994
CD236	Glycophorin C/D	Glycophorin family	GYPC	2995
CD236R	Glycophorin C	Glycophorin family	spliced variant	
CD238	Kell blood group Ag	Peptidase protein family	KEL	3792
CD239	B-CAM, lutheran glycoprotein	Ig superfamily	BCAM	4059
CD240CE	Rh blood group system, Rh30CE	Rh blood group system family	RHCE	6006
CD240DCE	Rh30D/CE	Rh blood group system family	spliced variant	6006
CD240D	RhD, RH1, Rh30D, Rhesus blood group Ag	Rh blood group system family	RHD	6007
CD241	RhAg, Rh50, Rh-associated Ag	Rh blood group system family	RHAG	6005
CD242	ICAM-4, LW blood group	Ig superfamily	ICAM4	3386

(*Table continues*)

Table I. (*Continued*)

CD	Other Names	Gene Family	Gene Name	Gene Number
CD243	MDR-1, P-glyprotein, pgp 170	ATP-binding cassette transporters superfamily	ABCB1	5243
CD244	2B4, SLAMF4	Ig superfamily	CD244	51744
CD245		Not cloned		
CD246	ALK	Protein kinase superfamily	ALK	238
CD247	TCR z-chain, CD3 ζ	CD3Z/FCER1G family	CD247	919
CD248	TEM1, endosialin, CD164L1	C-type lectin family	CD248	57124
CD249	Aminopeptidase A	Peptidase protein family	ENPEP	2028
CD252	TNFSF4, CD134L	TNF superfamily	TNFSF4	7292
CD253	TRAIL, APO-2 ligand, TL2, TNFSF10	TNF superfamily	TNFSF10	8743
CD254	TNFSF11, TRANCE, RANK ligand	TNF superfamily	TNFSF11	8600
CD256	TNFSF13, APRIL, TALL2	TNF superfamily	TNFSF13	8741
CD257	TNFSF13B, BLyS, BAFF, TALL1	TNF superfamily	TNFSF13B	10673
CD258	TNFSF14, LIGHT	TNF superfamily	TNFSF14	8740
CD261	TNFRSF10A, TRAIL-R1, DR4	TNFR superfamily	TNFRSF10A	8797
CD262	TNFRSF10B, TRAIL-R2, DR5	TNFR superfamily	TNFRSF10B	8795
CD263	TNFRSF10C, TRAIL-R3, DCR1, LIT, TRID	TNFR superfamily	TNFRSF10C	8794
CD264	TNFRSF10D, TRAIL-R4, TRUNDD, DcR2	TNFR superfamily	TNFRSF10D	8793
CD265	TNFRSF11, RANK, TRANCER	TNFR superfamily	TNFRSF11	8792
CD266	TNFRSF12A, TWEAK-R, Fn14, FN14	TNFR superfamily	TNFRSF12A	51330
CD267	TNFRSF13B, TACI	TNFR superfamily	TNFRSF13B	23495
CD268	TNFRSF13C, BAFF receptor, BR3	TNFR superfamily	TNFRSF13C	115650
CD269	TNFRSF17, BCMA, BCM	TNFR superfamily	TNFRSF17	608
CD270	TNFRSF14, LIGHT-R, HVEM	TNFR superfamily	TNFRSF14	8764
CD271	TNFRSF16, NGFR, NTR, LNGFR	TNFR superfamily	NGFR	4804
CD272	BTLA	Ig superfamily	BTLA	151888
CD273	B7-DC, PD-12, PDCD1LG2	Ig superfamily	PDCD1LG2	80380
CD274	B7-H1, PD-L1, PDCD1LG1	Ig superfamily	CD274	29126
CD275	ICOSL, B7-H2	Ig superfamily	ICOSLG	23308
CD276	B7-H3, 4Ig-B7-H3	Ig superfamily	CD276	80381
CD277	BT3.1, BTF5	Ig superfamily	BTN3A1	11119
CD278	ICOS	Ig superfamily	ICOS	29851
CD279	PD1, PDCD1, hPD-1, SLEB2	Ig superfamily	PDCD1	5133
CD280	CLEC13E, Endo180, TEM22, MRC2, UPARAP	C-type lectin family	MRC2	9902
CD281	TLR 1, TIL	TLR family	TLR1	7096
CD282	TLR 2, TLR2, TIL4	TLR family	TLR2	7097
CD283	TLR 3, TLR3	TLR family	TLR3	7098
CD284	TLR 4, TLR4	TLR family	TLR4	7099
CD286	TLR 6, TLR6	TLR family	TLR6	10333
CD288	TLR 8, TLR8	TLR family	TLR8	51311
CD289	TLR 9, TLR9	TLR family	TLR9	54106
CD290	TLR 10, TLR10	TLR family	TLR10	81793
CD292	BMPR1A, ALK-3	Protein kinase superfamily	BMPR1A	657
CDw293	BMPR1B, ALK-6	Protein kinase superfamily	BMPR1B	658
CD294	CRTH2	G protein–coupled receptor superfamily	GPR44	11251
CD295	Leptin R, LEPR, OBR, B219	Cytokine receptor family	LEPR	3953
CD296	ART1	Ectoenzyme family	ART1	417
CD297	ART4, DOK1, DO	Ectoenzyme family	ART4	420
CD298	Na/K ATPase, b3-subunit	Na/K and H/K ATPases b-chain family	ATP1B3	483
CD299	DC-SIGN2, DC-SIGNR, L-SIGN, CD209L	C-type lectin family	CLEC4M	10332
CD300a	CD300a, CMRF35H,IRC1	Ig superfamily	CD300A	11314
CD300c	CD300c, CMRF35A, LIR	Ig superfamily	CD300C	10871
CD300e	CD300e, CMRL35L1	Ig superfamily	CD300E	342510
CD301	MGL, CLECSF14	C-type lectin family	CLEC10A	10462
CD302	DCL1	C-type lectin family	CD302	9936
CD303	BDCA-2, CLECSF11, DLEC, HECL	C-type lectin family	CLECSF7	170482
CD304	BDCA-4, neuropilin, VEGF165R	Neuropilin family	NRP1	8829
CD305	LAIR1	Ig superfamily	LAIR1	3903
CD306	LAIR2	Ig superfamily	LAIR2	3904
CD307a	FCRL1	Ig superfamily	FCRL1	115350
CD307b	FCRL2	Ig superfamily	FCRL2	79368
CD307c	FCRL3	Ig superfamily	FCRL3	115352
CD307d	FCRL4	Ig superfamily	FCRL4	83417
CD307e	FCRL5	Ig superfamily	FCRL5	83416
CD308	FLT1, VEGRF1	Ig superfamily	FLT1	2321
CD309	KDR, FLK1, VEGRF2	Ig superfamily	KDR	3791
CD312	EMR2	EGF family	EMR2	30817
CD314	KLRK1, NKG2D	C-type lectin family	KLRK1	22914
CD315	PTGFRN, FPRP	Ig superfamily	PTGFRN	5738
CD316	IGSF8, PGRL	Ig superfamily	IGSF8	93185
CD317	BST2, TETHERIN	Bone marrow stromal Ag 2 precursor	BST2	684
CD318	CDCP1, SIMA135, TRASK	CUB family	CDCP1	64866
CD319	SLAMF7, CRACC	Ig superfamily	SLAMF7	57823

(*Table continues*)

Table I. (*Continued*)

CD	Other Names	Gene Family	Gene Name	Gene Number
CD320	8D6A	Low-density lipoprotein receptor family	CD320	51293
CD321	F11R, JAM1	Ig superfamily	2321F11R	50848
CD322	JAM2, C21orf43	Ig superfamily	JAM2	58494
CD324	CDH1, E-cadherin	Cadherin superfamily	CDH1	999
CD325	CDH2, N-cadherin	Cadherin superfamily	CDH2	1000
CD326	TACSTD1	EPCAM family	EPCAM	4072
CD327	SIGLEC6, CD33L	Ig superfamily	SIGLEC6	946
CD328	SIGLEC7, AIRM1	Ig superfamily	SIGLEC7	27036
CD329	SIGLEC9, protein FOAP-9	Ig superfamily	SIGLEC9	27180
CD331	FGFR1	Ig superfamily	FGFR1	2260
CD332	FGFR2	Ig superfamily	FGFR2	2263
CD333	FGFR3	Ig superfamily	FGFR3	2261
CD334	FGFR4	Ig superfamily	FGFR4	2264
CD335	NCR1, NKp46	Ig superfamily	NCR1	9437
CD336	NCR2, NKp44	Ig superfamily	NCR2	9436
CD337	NCR3, NKp30	Ig superfamily	NCR3	259197
CD338	ABCG2	ATP-binding cassette transporters superfamily	ABCG2	9429
CD339	JAG1	Jagged ligands family	JAG1	182
CD340	ERBB2, HER2neu	Protein kinase superfamily	ERBB2	2064
CD344	FZD4, FZ-4	G protein–coupled receptor superfamily	FZD4	8322
CD349	FZD9	G protein–coupled receptor superfamily	FZD9	8326
CD350	FZD10	G protein–coupled receptor superfamily	FZD10	11211
CD351	FCAMR	Ig superfamily	FCAMR	8395
CD352	SLAMF6	Ig superfamily	SLAMF6	114836
CD353	SLAMF8	Ig superfamily	SLAMF8	56833
CD354	TREM1	Ig superfamily	TREM1	54210
CD355	CRTAM	Ig superfamily	CRTAM	56253
CD357	TNFRSF18, GITR	TNFR superfamily	TNFRSF18	8784
CD358	TNFRSF21, DR6	TNFR superfamily	TNFRSF21	27242
CD360	IL-21R	Cytokine receptor family	IL21R	50615
CD361	EVI2B	EVI2 family	EVI2B	2124
CD362	SDC2, SYND2	Syndecan proteoglycan family	SDC2	6383
CD363	S1PR1	G protein–coupled receptor superfamily	S1PR1	1901
CD364	Peptidase inhibitor 16, CRIPS9	CAP superfamily	PI16	221476
CD365	TIM1, hepatitis A virus cellular receptor 1	Ig superfamily	HAVCR1	26762
CD366	TIM2, hepatitis a virus cellular receptor 2	Ig superfamily	HAVCR2	84868
CD367	CLEC4A, DCIR, CLECSF6	C-type lectin family	CLEC4A	50856
CD368	CLEC4D, CLECSF8, CLEC-6	C-type lectin family	CLEC4D	338339
CD369	CLEC7A, CLECSF12,DECTIN1	C-type lectin family	CLEC7A	64581
CD370	CLEC9A, DNGR1	C-type lectin family	CLEC9A	283420
CD371	CLEC12A, DCAL-2, CLL-1	C-type lectin family	CLEC12A	160364

The gene names and numbers are approved by the Human Genome Organization gene nomenclature committee (http://www.genenames.org). The Abs validated against these CD molecules are available on the HCDM Web site (http://www.hcdm.org).

with proteins encoded by a common gene family also had to be tested. This is essential if the degree of homology between molecules of the same family is very high. Thus, it is mandatory to exclude cross-reactivity with other related Ags or proteins encoded by other members of the same gene family.

Some participating laboratories test the agonistic or antagonistic effect of the Abs in a variety of functional assays, such as proliferation, apoptosis, or adhesion blocking. Thus, the HLDA Workshop protocol allows the assignment of CD names, and it generates an enormous amount of data on the reactivity of the Abs and the expression and functional characteristics of the target molecules. It represents a very efficient and comprehensive way to independently validate a mAb.

All of the generated data and experiments performed with the submitted mAbs are presented at the HLDA Conferences. These conferences are a valuable forum for discussion of the function of cell surface molecules. A list of the proceedings and references of the different HLDA Conferences and a database with mAbs that were approved by the HLDA Workshops are available at http://www.HCDM.org.

List of Current CD Molecules

Table I shows the current official list of CD molecules. The total number of assigned CDs is 401. The most recent CD designations to be assigned (CD365 to CD371) were established at the HLDA10 Workshop (held in Wollongong, Australia in December 2014). Some CD numbers were dropped because their molecular nature could not be confirmed, or their designation was reassigned (e.g., CDw12, CD67, and CD78). A second set of missing CDs corresponds to CD numbers reserved for molecules for which no useful mAbs have been validated by the HLDA Workshops. These include CD285, CD287, and CD291, corresponding to TLRs, as well as CD255, reserved for TNFF12. The CD label is only valid for those mAbs that have been scrutinized in HLDA Workshops and have fulfilled high-quality criteria. Unfortunately, there are a number of mAbs on the market that misuse the CD label, creating confusion in data interpretation.

The Future of the CD Workshops

Directly from the start, the HLDA Workshops were very exciting for immunologists, because they provided important

discovery tools that deliver an element of confidence in the world of reagents. The impact of the workshops has been enormous, both in basic immunology and in clinical practice, as exemplified by the applications in clinical diagnosis and treatment of malignancies and immunological diseases (7, 8). Another relevant outcome has been the synergy between research groups and industry. Many companies have commercialized mAbs that researchers have submitted to the HLDA Workshops. More recently, companies have become an important source of mAbs for HLDA Workshops.

What is the importance of the HLDA Workshops in the postgenomic era?

Bioinformatics studies indicate that we have characterized only a fraction, probably just one third, of the cell surface molecules expressed by the cells of the immune system (9, 10). This may be due, in part, to the fact that most of the CDs were defined with mAbs generated from rodents. Direct protein profiling, which reflects the actual levels of protein expression, is limited by the availability of high-quality mAbs against these molecules. Thus, the main goal of the HLDA Workshops is to continue with the characterization of all of the cell surface molecules relevant to the immune system and to immune-mediated diseases and the validation of mAbs against these molecules.

Moreover, there are extensive gaps in our knowledge of CD molecule expression patterns, mainly because of the heterogeneity of the expression studies and the significant changes in flow cytometry technology over the last 30 y. HCDM recently launched a new project called CDMaps, whose objective is to systematically and accurately determine the expression patterns of established CD molecules on all major blood and lymphoid tissue leukocyte subsets, using state-of-the-art multicolor flow cytometry. The use of standardized instrument settings and immunophenotyping protocols with HLDA-approved reagents will generate a data set that is highly reproducible among laboratories (11). Several companies are supporting this project by providing mAbs and the backbone testing cocktails for these tests (http://www.hcdm.org/images/PDF/CDMaps.pdf). Through additional quantification of the number of molecules/cell type, the CDMaps project should generate an enormous database of protein expression profiles that will represent a unique open access resource for basic, translational, and clinical immunology.

Finally, there is an urgent need for independent validation of mAbs. The production of mAbs has become a routine procedure. In recent years, an overwhelming number of mAbs against leukocyte cell surface molecules, as well as other target molecules, have been produced by academic groups and an increasing number of companies. However, a large number of these Abs remain poorly validated. One common observation is that mAbs often recognize recombinant proteins, typically the immunogen, but are unable to react with the endogenous or native protein on live primary cells. The use of improperly validated Abs has resulted in the loss of thousands of work hours, destroyed research projects, and generated false results that have contaminated the scientific literature. The scientific community is increasingly aware of this extremely serious problem (12). Toward the aim of solving this problem, the HLDA Workshop protocol guarantees the validation of submitted mAbs and, therefore, represents an invaluable tool for safeguarding our knowledge of CD molecules and their role in the immune system. This is the reason why the U.S. Food and Drug Administration requested that, for a mAb to be used as a diagnostic reagent, it should be evaluated by the HLDA Workshops. We propose in this article that HLDA Workshop evaluation should be made mandatory for therapeutic mAbs, particularly for biosimilar mAbs targeting leukocyte cell surface molecules. In addition, we suggest adding the CD nomenclature to the International Nonproprietary Name used to designate original and biosimilar mAbs.

Conclusions

HLDA Workshops are a great example of an effective long-term international collaboration across scientific disciplines and laboratories. Future workshops will continue to promote the exchange of reagents between academic groups and industry and will aim to boost the supply of highly characterized mAbs for all cell surface molecules. These workshops will provide a platform to increase our understanding of leukocyte biology and pathology, as well as facilitate the identification of new disease biomarkers and therapeutic targets.

Disclosures

R.B. is an employee of BD Biosciences and F. Mortari of Bio-Techne (R&D Systems). The rest of the authors report no conflict of interest.

Acknowledgments

We thank the International Union of Immunological Societies for its continuous support of the CD Molecule Nomenclature and Leukocyte Standardization Subcommittees.

References

1. Kumar, S., T. Lütteke, and R. Schwartz-Albiez. 2012. GlycoCD: a repository for carbohydrate-related CD antigens. *Bioinformatics* 28: 2553–2555.
2. Springer, T. A. 2002. César Milstein, the father of modern immunology. *Nat. Immunol.* 3: 501–503.
3. Bernard, A., and L. Boumsell. The clusters of differentiation (CD) defined by the First International Workshop on Human Leucocyte Differentiation Antigens. 1984. *Hum Immunol.* 11: 1–10.
4. Boumsell, L. 1996. The international workshops and conferences on human leukocyte differentiation antigens. Birth, current status and future. *Tissue Antigens* 48: 238–241.
5. Zola, H., B. Swart, I. Nicholson, B. Aasted, A. Bensussan, L. Boumsell, C. Buckley, G. Clark, K. Drbal, P. Engel, et al. 2005. CD molecules 2005: human cell differentiation molecules. *Blood* 106: 3123–3126.
6. Schlossman, S. F. 1995. Preface. In *Leucocyte Typing V. White Cell Differentiation Antigens*. S. F. Schlossman, L. Boumsell, W. Gilks, J. M. Harlan, T. Kishimoto, C. Morimoto, J. Ritz, S. Shaw, R. Silverstein, T. Springer, T. F. Tedder, and R. F. Todd, eds. Oxford University Press, Oxford, U.K., p. v–vi.
7. Caligaris-Cappio, F. 2001. How immunology is reshaping clinical disciplines: the example of haematology. *Lancet* 358: 49–55.
8. Zola, H. 2006. Medical applications of leukocyte surface molecules–the CD molecules. *Mol. Med.* 12: 312–316.
9. Díaz-Ramos, M. C., P. Engel, and R. Bastos. 2011. Towards a comprehensive human cell-surface immunome database. *Immunol. Lett.* 134: 183–187.
10. Bock, T., D. Bausch-Fluck, A. Hofmann, and B. Wollscheid. 2012. CD proteome and beyond - technologies for targeting the immune cell surfaceome. *Front. Biosci. (Landmark Ed.)* 17: 1599–1612.
11. Kalina, T., J. Flores-Montero, V. H. van der Velden, M. Martin-Ayuso, S. Böttcher, M. Ritgen, J. Almeida, L. Lhermitte, V. Asnafi, A. Mendonça, et al. 2012. EuroFlow standardization of flow cytometer instrument settings and immunophenotyping protocols. *Leukemia* 26: 1986–2010.
12. Baker, M. 2015. Reproducibility crisis: Blame it on the antibodies. *Nature* 521: 274–276.