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Cellular Immunology 236 (2005) 17–20
Cellular Immunology
www.elsevier.com/locate/ycimm

The Eighth Human Leucocyte Differentiation Antigen (HLDA8) Workshop: Natural killer cell section report

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Received 28 March 2005; accepted 12 May 2005
Available online 12 September 2005

Abstract

Monoclonal antibodies submitted to the natural killer (NK) cell section of the Eighth International Workshop on Human Leucocyte Differentiation Antigens (HLDA8) comprised those to known clusters of differentiation (CD), those to well-characterised molecules without a CD nomenclature, and those to unknown molecules. From the HLDA8 workshop, the seven well-characterised molecules in the NK cell panel were assigned a CD classification. These were NKG2D (CD314), LAIR-1 (CD305), NKp46 (CD335), NKp44 (CD336), NKp30 (CD337), CRACC (CD319), and NKG2C (CD159c).

Keywords: NK cells; CD nomenclature; NKG2D; LAIR-1; NKp46; NKp44; NKp30; CRACC; NKG2C

1. Introduction

Natural killer (NK) cells express an array of activating and inhibitory receptors on their cell surface [1,2]. These receptors are clonally distributed and the NK cell response against target cells is a balance between signalling through activation and inhibitory receptors determined by expression of ligands on target cells. Ligands for some of these receptors are induced by viral infection, malignant transformation or stress. Although many of these receptors were originally described for NK cells, many are present also on subsets of T cells and on other cells of the immune system.

There are three families of receptors recognising class I MHC ligands, and most were assigned a CD nomenclature in previous HLDA workshops. Members of these families have inhibitory activity, whilst others have activating activity. The inhibitory function of class I MHC receptors is mediated through immunotyrosine based inhibitory motifs (ITIM) in the cytoplasmic domain. Activating receptors have a charged amino acid residue in their transmembrane domain allowing association with adaptor proteins that contain immunotyrosine based activation motifs (ITAM) to effect activation [2].

The killer Ig-like receptor (KIR) family, was assigned the nomenclature CD158 in HLDA7 [3], and this included alphabetical notation for the 14 members. Members of the CD158 family differ in the number of Ig-like domains (2 or 3) and whether the cytoplasmic domain is long (inhibitory receptor) or short (activating receptor). The genes for these receptors have the human genome organisation (HUGO) nomenclature based on this structural definition. For example CD158a is the product of *KIR2DL1* and CD158h is the product of *KIR2DS1*. CD158d (*KIR2DL4*) has both inhibitory and activating functions. Only the inhibitory receptors have been shown definitively to bind class I MHC alleles.

The CD94/NKG2A (inhibitory) and the CD94/NKG2C (activating) C-type lectin superfamily receptors bind the non-classical class I molecule, HLA-E. The common chain for these receptors, CD94, was assigned in HLDA5. NKG2A, the partner that with CD94 forms the inhibitory receptor, was assigned CD159a in HLDA7 [3].

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doi:10.1016/j.cellimm.2005.08.003

The gene nomenclature for these receptors is, *KLRD1* (CD94), *KLRC1* (NKG2A), and *KLRC2* (NKG2C).

CD85 is a 13 member family of Ig-superfamily receptors on many hematopoietic cells. The alphabetical subclassification of the CD85 family was assigned in HLDA7. CD85j is present on NK cells and functions as an inhibitory receptor that binds the monomorphic α3 domain of class I MHC. CD85j was previously termed ILT2 or LIR1, and the gene nomenclature is *LILRB1*.

A number of other NK cell receptors have not yet been assigned a CD nomenclature. NKG2D (*KLRK1*) is an activating receptor of the C-type lectin superfamily, unrelated to other NKG2 receptors, that binds the stress-induced proteins MICA/B and the UL-16 binding proteins (ULBP1, 2, 3, and 4). LAIR-1 (*LAIR1*) is an inhibitory receptor of the Ig-superfamily present on many hematopoietic cells [4]. The natural cytotoxicity receptors (NCR) NKp46 (*NCR1*), NKp44 (*NCR2*), and NKp30 (*NCR3*) are NK cell specific activating receptors [5]. NKp46 and NKp30 are expressed on resting and activated NK cells, whilst NKp44 is expressed only on activated NK cells. The NCRs belong to the Ig-superfamily and display one or two Ig-like domains and have a charged amino acid in their transmembrane domain that allows association with the ITAM-bearing adaptor molecules CD3ζ and FcεRIγ (NKp30, NKp46) or DAP-12 (NKp44) to transduce their activating signals. NKG2C, which partners CD94 as an activating receptor, uses DAP-12 as its adaptor molecule [2]. The CD2-like receptor activating cytotoxic cells (CRACC) [6] (*SLAMF7*), is present on NK cells and activates cytotoxicity. CRACC also is present on cytotoxic T cells, activated B cells, and mature dendritic cells.

2. Materials and methods

The mAbs submitted to the NK cell section of HLDA8 are listed in Table 1. The mAbs included those

Table 1
HLDA8 NK cell section mAb panel

Code	Clone	Submitter	Immunogen	Specificity	Isotype	Species
80174	AF12-7H3	Winkels	KG-1a	CD56	IgG1	M
80175	AF12-8A7	Winkels	KG-1a	CD56	IgG1	M
80176	MZ3-26G9	Winkels	KG-1a	CD56	IgG1	M
80255	B-E16	Vermot-Desroches	NK cells	CD16	IgG2a	M
80263	B-A19	Vermot-Desroches	U937	CD56	IgG1	M
80279	E63-1337	Hollemweguer	PBMC	T, NK	IgG1	M
80281	2-69	Hollemweguer	NK cells	CD244	IgG2a	M
80290	NKVFS1	Poggi	n/a	KIR2D epitope	IgG1	M
80335	CD56/C5.9	Just	n/a	CD56	IgG2b	M
80340	NK1	Just	n/a	NK CLA (NK cell like Ag)	IgM	M
80390	149810	Houchins	Transfected cells	NKG2D	IgG1	M
80427	6B11	Hollemweguer	Invariant NKT cells	NK-T	IgG1	M
80432	1D11	Hollemweguer	NKL cell line	NKG2D	IgG1	M
80442	9-E2	Hollemweguer	HuIgG fusion protein	NKp46	IgG1	M
80452	162	Hollemweguer	HuIgG fusion protein	CRACC	IgG2b	M
80475	FMU-LAIR1.1	Jin	n/a	LAIR	IgG1	M
80476	FMU-LAIR1.2	Jin	n/a	LAIR	IgG1	M
80477	9.1C3	Jin	n/a	LAIR	IgG2b	M
80525	Z25	Fornelli	NK clones	NKp30	IgG1	M
80526	Z231	Fornelli	NK clone SA260	NKp44	IgG1	M
80527	BAB281	Fornelli	NK clone SE192	NKp46	IgG1	M
80528	ON72	Fornelli	NK clone	NKG2D	IgG1	M
80543	NKTA255	Poggi	n/a	LAIR-1	IgG1	M
80544	210845	Houchins	HuIgG fusion protein	NKp30	IgG2a	M
80545	210847	Houchins	HuIgG fusion protein	NKp30	IgG2a	M
80546	195314	Houchins	HuIgG fusion protein	NKp46	IgG2b	M
80547	D2-9A5	Mandelboim	n/a	NKp46, non-specific	IgG1	M
80548	461-G1	Mandelboim	n/a	NKp46	IgG1	M
80549	WV2	Warren	Polyclonal NK	CD94	IgG1	M
80550	WV4	Warren	Polyclonal NK	CD94	IgM	M
80551	WV6	Warren	Polyclonal NK	CD158b1/b2/j	IgM	M
80655	NAT105C/E3	Roncador	YT cells	Unknown	IgG1	M
80694	134591	Houchins	Transfected cells	NKG2C	IgG1	M
80695	134522	Houchins	Transfected cells	NKG2C	IgG2b	M

n/a, information not available; M, mouse.

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