

Killer-cell Immunoglobulin-like Receptor (KIR) Nomenclature Report, 2002

Steven G. E. Marsh, Peter Parham, Bo Dupont, Daniel E. Geraghty, John Trowsdale, Derek Middleton, Carlos Vilches, Mary Carrington, Campbell Witt, Lisbeth A. Guethlein, Heather Shilling, Christian A. Garcia, Katharine C. Hsu, and Hester Wain

INTRODUCTION

During discussion at the WHO Nomenclature Committee for Factors of the HLA System meeting in Victoria, Canada, in May 2002, it was decided to form a subcommittee to coordinate the naming of alleles of the genes encoding the killer-cell immunoglobulin-like receptors (KIRs) [1]. These genes are encoded on chromosome 19 (19q13.4) and have varying degrees of polymorphism. The receptors encoded by the *KIR* genes are expressed by natural killer (NK) cells and a subset of T cells and some of them have been shown to have specificity for determinants of human leukocyte antigen (HLA) class I molecules. The extracellular ligand-binding part of KIR consists of two or three immunoglobulin (Ig)-like domains. The discussions which took place in Victoria further to earlier discussions on KIR nomenclature at the NK Polymorphism meeting (27–29 July 2001) in Cambridge, UK. In addition, a request has been made by the International Union of Immunological Societies (IUIS) to provide a standardized nomenclature for the expressed protein products of the KIR genes.

From the Anthony Nolan Research Institute, London, United Kingdom; Stanford University School of Medicine, Stanford, CA; Sloan-Kettering Institute for Cancer Research, New York, NY; Fred Hutchinson Cancer Center, Seattle, WA; Cambridge University, Cambridge, United Kingdom; Northern Ireland Tissue Typing Laboratory, Belfast, United Kingdom; Hospital Puerta de Hierro, Madrid, Spain; Frederick Cancer Research & Development Centre, Frederick, MD; Royal Perth Hospital, Perth, Australia; University of Washington, Seattle, WA; University College London, London, United Kingdom.

Address reprint requests to: Dr. Steven G. E. Marsh, Anthony Nolan Research Institute, Royal Free Hospital, Pond Street, Hampstead, London NW3 2QG, United Kingdom. Tel: (+44) 20-7284 8321; Fax: (+44) 20-7284 8331; E-mail: marsh@ebi.ac.uk.

Received March 7, 2003; accepted March 7, 2003.

KIR GENE NOMENCLATURE

The first KIRs to be defined were inhibitory receptors, and when initially coined, the acronym stood for killer-cell inhibitory receptor. With appreciation that this family of molecules included both activating and inhibitory receptors, the KIR acronym was retained and is now accepted as an abbreviation for Killer-cell Immunoglobulin-like Receptor [2]. Unlike HLA genes, which for practical and historical reasons are named by the WHO Nomenclature Committee for Factors of the HLA System, the naming of KIR genes is the responsibility of the HUGO Genome Nomenclature Committee (HGNC). Agreement was reached with the HGNC for naming the *KIR* genes, and a total of 17 genes have been recognized and named (Table 1), the ones most recently assigned being *KIR2DL5A*, *KIR2DL5B*, *KIR2DP1*, *KIR3DL3*, and *KIR3DP1*. The subcommittee will continue to work closely with the HGNC in the future to ensure all newly described genes are assigned appropriate names.

The names given to the *KIR* genes are based on the structures of the molecules they encode. The first digit following the KIR acronym corresponds to the number of Ig-like domains in the molecule and the “D” denotes “domain.” The D is followed by either an “L,” indicating a “Long” cytoplasmic tail, an “S” indicating a “Short” cytoplasmic tail, or a “P” for “pseudogenes.” The final digit indicates the number of the gene encoding a protein with this structure. Thus *KIR2DL1*, *KIR2DL2*, and *KIR2DL3* all encode receptors having two extracellular Ig-like domains and a long cytoplasmic tail [3]. Where two or more genes have very similar structures and have very similar sequences, they may be given the same

TABLE 1 KIR gene names

Gene Symbol	Protein symbol	Description	Aliases	Reference or submitting author
<i>KIR2DL1</i>	KIR2DL1	Killer cell immunoglobulin-like receptor, two domains, long cytoplasmic tail, 1	cl-42, nkat1, 47.11, p58.1, CD158a	(10, 11)
<i>KIR2DL2</i>	KIR2DL2	Killer cell immunoglobulin-like receptor, two domains, long cytoplasmic tail, 2	cl-43, nkat6, CD158b1	(10, 11)
<i>KIR2DL3</i>	KIR2DL3	Killer cell immunoglobulin-like receptor, two domains, long cytoplasmic tail, 3	cl-6, nkat2, nkat2a, nkat2b, p58, CD158b2	(10, 11)
<i>KIR2DL4</i>	KIR2DL4	Killer cell immunoglobulin-like receptor, two domains, long cytoplasmic tail, 4	103AS, 15.212, CD158d	(12)
<i>KIR2DL5A</i>	KIR2DL5A	Killer cell immunoglobulin-like receptor, two domains, long cytoplasmic tail, 5A	KIR2DL5.1, CD158f	(13)
<i>KIR2DL5B</i>	KIR2DL5B	Killer cell immunoglobulin-like receptor, two domains, long cytoplasmic tail, 5B	KIR2DL5.2, KIR2DL5.3, KIR2DL5.4	(13)
<i>KIR2DS1</i>	KIR2DS1	Killer cell immunoglobulin-like receptor, two domains, short cytoplasmic tail, 1	EB6ActI, EB6ActII, CD158h	(14)
<i>KIR2DS2</i>	KIR2DS2	Killer cell immunoglobulin-like receptor, two domains, short cytoplasmic tail, 2	cl-49, nkat5, 183ActI, CD158j	(10, 11)
<i>KIR2DS3</i>	KIR2DS3	Killer cell immunoglobulin-like receptor, two domains, short cytoplasmic tail, 3	nkat7	(15)
<i>KIR2DS4</i>	KIR2DS4	Killer cell immunoglobulin-like receptor, two domains, short cytoplasmic tail, 4	cl-39, KKA3, nkat8, CD158i	(11, 15)
<i>KIR2DS5</i>	KIR2DS5	Killer cell immunoglobulin-like receptor, two domains, short cytoplasmic tail, 5	nkat9, CD158g	(15)
<i>KIR2DP1</i>	KIR2DP1	Killer cell immunoglobulin-like receptor, two domains, pseudogene 1	KIRZ, KIRY, KIR15, KIR2DL6	(13)
<i>KIR3DL1</i>	KIR3DL1	Killer cell immunoglobulin-like receptor, three domains, long cytoplasmic tail, 1	cl-2, NKB1, cl-11, nkat3, NKB1B, AMB11, KIR, CD158e1	(10)
<i>KIR3DL2</i>	KIR3DL2	Killer cell immunoglobulin-like receptor, three domains, long cytoplasmic tail, 2	cl-5, nkat4, nkat4a, nkat4b, CD158k	(10)
<i>KIR3DL3</i>	KIR3DL3	Killer cell immunoglobulin-like receptor, three domains, long cytoplasmic tail, 3	KIRC1, KIR3DL7, KIR44, CD158z	(16)
<i>KIR3DS1</i>	KIR3DS1	Killer cell immunoglobulin-like receptor, three domains, short cytoplasmic tail, 1	nkat10, CD158e2	(15)
<i>KIR3DP1</i>	KIR3DP1	Killer cell immunoglobulin-like receptor, three domains, pseudogene 1	KIRX, KIR48, KIR2DS6, KIR3DS2P, CD158c	(13)

number but distinguished by a final letter; for example, the *KIR2DL5A* and *KIR2DL5B* genes [4]. The similarity of these two genes suggests they are related by a recent gene duplication event.

Certain *KIR* genes have arisen through recombination

between two other *KIR* genes and are effectively functional hybrids of the parent genes. The question for gene nomenclature is whether the recombinant gene should have a new unique name or be given a name that in some way represents its evolutionary ontogeny. If we consider

a hypothetical recombination between *3DL1* and *3DL2*, we could name the new product according to these parent genes, either by concatenating their names (*i.e.*, *3DL13DL2*) or by arbitrarily choosing to name the gene after the parent that has contributed the 5' end of its sequence (*i.e.*, *3DL1* if the recombination was 5' *3DL1* × *3DL2* 3' or *3DL2* if the recombination was 5' *3DL2* × *3DL1* 3'). This system of naming derived from the parent gene makes many assumptions about the nature of the recombination and the function of the new gene and presumes that there have been no further modifications to the gene that would merit providing a new name. The alternative of assigning a new name to the recombinant gene using the same criteria that have been applied in naming all other new *KIR* genes (based on domain structure, cytoplasmic tail length and sequence similarity) avoids the ambiguities of these assumptions. In this case, the new gene could be assigned *3DL*"*n*," in which "*n*" represents the next number in the series.

Perhaps the simplest solution to naming alleles of a recombinant gene is to assign the allele with the gene name of the gene contributing the Ig-like domains, providing sufficient homology is maintained. In such situations in which the 3' region of the recombinant allele is inconsistent with the L/S designation of the gene, a suffix would be added to the allele name to indicate the aberrant nature of the allele. Using this nomenclature, it would be possible to rename the alleles of the *3DS1* gene, which behave as alleles of the *3DL1* gene, in the *3DL1* series with an "S" suffix to indicate their short tail.

KIR PROTEIN NOMENCLATURE

Consistent with standard genetic nomenclature, the names of genes and alleles are given in italic typeface. The names for the *KIR* proteins are the same as those used for the *KIR* genes; however, they will be presented as normal typeface (Table 1).

Like other cell surface molecules of the immune system, the *KIR* molecules have also been given a CD designation and are recognized as members of the CD158 series (see the list of aliases and previous designations given in Table 1) [5–7].

KIR ALLELE NOMENCLATURE

Following the success of the nomenclature used for HLA alleles, it was decided to name *KIR* allele sequences in an analogous fashion. After the gene name, an asterisk will be used as a separator before a numerical allele designation. The first three digits of the numerical designation will be used to indicate alleles that differ in the sequences of their encoded proteins. The next two digits will be used to distinguish alleles that only differ by synonymous (noncoding) differences within the coding se-

quence. The final two digits will be used to distinguish alleles that only differ by substitutions in an intron, promoter, or other noncoding region of the sequence. A complete listing of all *KIR* allele sequences assigned official names can be found in Table 2.

Evidence exists indicating that the *3DS1* and *3DL1* genes behave as alleles of the same gene. It is likely that at some time in the future the alleles of these genes will be combined under one gene name. To avoid confusion, it has been decided to name the alleles of both genes in a single numeric series, thus *3DL1**001 to *3DL1**009 are followed by *3DS1**010 to *3DS1**014. Likewise the alleles of the *2DL5A* and *2DL5B* genes have also been named in a single series because of the similarity of these sequences.

NAMING KIR HAPLOTYPES

The *KIR* gene family forms part of the leukocyte receptor complex (LRC), which includes several related gene families that encode cell-surface receptors of the immune system and have extracellular regions made up of Ig-like domains. Within the LRC the *KIR* genes appear the most variable. In addition to allelic polymorphism, there is haplotypic variability due to the different number and kind of *KIR* genes. This situation is analogous to that of the HLA-DRB genes, but contrasts with that of the HLA class I gene organization, which is relatively fixed. Because haplotypic diversity is a major contributor to the population diversity of *KIR* and of NK cell repertoires, there was agreement amongst the committee that it would be useful to devise a robust and versatile nomenclature system that could be used to describe the gene content of different *KIR* haplotypes. With this in mind it was suggested that each *KIR* haplotype be designated "KH," followed by a hyphen and then a unique three-digit number, assigned sequentially indicating the different haplotypes. This system would allow 999 *KIR* haplotypes to be named.

Two kinds of *KIR* haplotype have been described based upon gene content and are designated A and B. No single specific criterion distinguishes all A and B haplotypes, a current working definition being as follows. Group B haplotypes are characterized by one or more of the following genes: *KIR2DL5*, *KIR2DS1*, *KIR2DS2*, *KIR2DS3*, *KIR2DS5*, and *KIR3DS1*. Conversely, group A haplotypes are characterized by the absence of all these genes. As a consequence of these differences, the B haplotypes have more genes encoding activating *KIR* than A haplotypes. Different investigators have used different criteria to distinguish A and B haplotypes, and certain haplotypes are assigned differently when using these different criteria ([8, 9] and other refs). The committee felt that the distinction between A and B haplotypes is a useful one, having potential biological and medical sig-

TABLE 2 KIR allele names

Allele name	Previous name	Cell ID	Accession number	Reference or submitting author
<i>2DL1*001</i>	NKAT1	?	L41267	(10)
<i>2DL1*002</i>	cl-42	?	U24076	(11)
<i>2DL1*00301</i>	cl-47.11	NK-lib	U24078	(11)
<i>2DL1*00302</i>	2DL1M, 2DL1v2	MU	AF285431	(17)
<i>2DL1*004</i>	2DL1v	NV	AF022045	(18)
<i>2DL1*005</i>	2DL1W102, 2DL1v3	WC	AF285432	(17)
<i>2DL2*001</i>	cl-43	?	U24075	(11)
<i>2DL2*002</i>	NKAT6	?	L76669	(15)
<i>2DL2*003</i>	2DL2v2, 2DL2M	MU	AF285434	(17)
<i>2DL2*004</i>	2DL2v1	WC	AF285433	(17)
<i>2DL3*001</i>	NKAT2, cl-6	?, NK3.3	L41268, U24074	(10, 11)
<i>2DL3*002</i>	NKAT2a	?	L76662	(15)
<i>2DL3*003</i>	NKAT2b	?	L76663	(15)
<i>2DL3*004</i>	KIR-023GB	?	U73395	(19)
<i>2DL3*005</i>	2DL3v	PP	AF022048	(18)
<i>2DL3*006</i>	2DL3W308	WC	AF285435	(17)
<i>2DL4*00101</i>	NK3.3#27	NK3.3	X99480	(20)
<i>2DL4*00102</i>	2DL4v1	PP, NV	AF034771	(18)
<i>2DL4*00201</i>	15.212	?	X97229	(20)
<i>2DL4*00202</i>	2DL4v2	PP, NV	AF034772	(18)
<i>2DL4*003</i>	KIR103AS	YT, NK92	U71199	(12)
<i>2DL4*004</i>	KIR103LP	?	AF002979	(21)
<i>2DL4*005</i>	2DL4v3	NV	AF034773	(18)
<i>2DL4*006</i>	2DL4v4	RR	AF285436	(17)
<i>2DL4*007</i>	—	LP	AF276292	A. Selvakumar, New York, USA
<i>2DL5A*001</i>	2DL5.1	NV, XX-1060P11	AF204903, AF217485, AL133414	(13, 22, 23)
<i>2DL5B*002</i>	2DL5.2	NV	AF217486	(22)
<i>2DL5B*003</i>	2DL5.3	WCS	AF217487	(22)
<i>2DL5B*004</i>	2DL5.4	CC	AF260138, AF260139, AF260140, AF260141	(22)
<i>2DS1*001</i>	Eb6ActI	PA	X89892	(14)
<i>2DS1*002</i>	2DS1v	NV	AF022046	(18)
<i>2DS1*003</i>	Eb6ActII	GT	X98858	(24)
<i>2DS1*004</i>	2DS1v1	WC	AF285437	(17)
<i>2DS2*001</i>	NKAT5, cl-49	?, ?	L41347, U24079	(10, 11)
<i>2DS2*002</i>	183ActI	23D	X89893	(14)
<i>2DS2*003</i>	TG14#35	TG14	AJ002103	R. Biassoni, Genova, Italy
<i>2DS2*004</i>	2DS2v1	WC	AF285438	(17)
<i>2DS2*005</i>	2DS2v2	FC	AF285439	(17)
<i>2DS3*00101</i>	NKAT7	?	L76670	(15)
<i>2DS3*00102</i>	59C_K3	Pag1	X97231	R. Biassoni, Genova, Italy
<i>2DS3*00103</i>	2DS3v	NV	AF022047	(18)
<i>2DS4*00101</i>	cl-39, cl-17, KKA3_34-52	?, ?, 4053, Mal 43-52	U24077, AF002255, AJ417555, X94609	(11, 25, 26), HW. Chan, Pittsburgh, USA
<i>2DS4*00102</i>	NKAT8	?	L76671	(15)
<i>2DS4*002</i>	2DS4v1	RR	AF285440	(17)

(Continued)

TABLE 2 KIR allele names (*Continued*)

Allele name	Previous name	Cell ID	Accession number	Reference or submitting author
2DS4*003	Deletion V, KIR1D	3321	AJ417554	(26, 27)
2DS5*001	NKAT9	?	L76672	(15)
2DS5*002	—	NV	AF208054	(28)
2DS5*003	—	WC	AF272389	(28)
2DP1*001	KIR15	NV	AF204906, AF204907, AF204908	(13)
2DP1*002	—	CTB-61M7	AC011501	(29)
3DL1*00101	NKAT3, cl-11, AMB11.115	?, ?, AMB11	L41269, U30274, X94262	(10, 30, 31)
3DL1*00102	Nnkat-3	?	AF262968	(32)
3DL1*002	NKB1, cl-2	NKB1, ?	U31416, U30273	(30, 33)
3DL1*003	3DL1v	NV	AF022049	(18)
3DL1*00401	W204	WC	AF262970	(32)
3DL1*00402	M322	MU	AF262969	(32)
3DL1*006	NJN55	?	AF262972	(32)
3DL1*007	r3k10	RR	AF262973	(32)
3DL1*008	r3k2	RR	AF262974	(32)
3DL1*009	—	3321, 4053	AJ417556, AJ417557	(34)
3DL2*001	NKAT4	?	L41270	(10)
3DL2*002	cl-5, AMC5	?, ?	U30272, X94374	(30, 31)
3DL2*003	1.1, NKAT4A	?, ?	X94373, L76665	(15, 31)
3DL2*004	17.1C	?	X93595	(31)
3DL2*005	NKAT4b	?	L76666	(15)
3DL2*006	3DL2Wv2	WC	AF262966	(32)
3DL2*007	b3DL2b	BS	AF262965	(32)
3DL2*008	r3k17	RR	AF262967	(32)
3DL2*009	rrk100	RR	AF263617	(17)
3DL2*010	—	?	AY059418	(35)
3DL2*011	—	?	AY059419	(35)
3DL2*012	—	?	AY059420	(35)
3DL3*001	KIRCI	?	AF072407, AF072408, AF072409, AF072410	(16)
3DL3*00201	KIR44a	NV, UV5HL9-5B	AF204909, AF204910, AF204911, AC006293	(13, 29)
3DL3*00202	KIR44b	NV	AF204912, AF204913, AF204914	(13)
3DL3*003	KIRC1	XX-1060P11	AL133414	(23)
3DL3*004	3DL7	?	AF352324	(36)
3DS1*010	NKAT10, 3DS1*001	?	L76661	(15)
3DS1*011	C97.12#5, 3DS1*002	?	X97233	R. Biassoni, Genova, Italy
3DS1*012	KIR-123FM, 3DS1*003	?	U73396	(19)
3DS1*013	3DS1v, 3DS1*004	NV	AF022044	(18)
3DS1*014	3DS1*005	4373	AJ417558	(34)
3DP1*001	KIR48a	NV	AF204915, AF204916, AF204917	(13)
3DP1*002	KIRX	XX-1060P11	AL133414	(23)
3DP1*00301	KIR48b	NV	AF204918, AF204919, AF204920	(13)
3DP1*00302	2DS6	CTB-61M7	AC011501	(29)

nificance, and that efforts should be made to develop a consistent and logical set of criteria for distinguishing them. It was proposed that as part of the haplotype nomenclature the letters A or B would follow the three-

digit number. So a haplotype may, for example, be named KH-001A or KH-022B.

To supplement the haplotype name and provide further information, it was suggested that following the

haplotype designation a 17-digit binary code would indicate the presence or absence of the genes on the haplotype. Each digit in the code would represent a distinct gene: a “1” indicating presence of the gene, a 0’ its absence. Thus a full haplotype name could be given as KH-001A-11100010011011011. This system can readily accommodate the discovery of additional *KIR* genes by simple introduction of another digit. Wherever possible the order of the genes in the full haplotype designation will reflect their order in the genome. However, when digits are added to represent newly discovered genes, they will be placed at the end of the code in the order of their discovery.

To refine haplotype definition, a further series of digits could be used to indicate which allele for each *KIR* gene is present on a haplotype. It is suggested that such an addition would only be made to the nomenclature once it had become a common practice to type *KIR* genes at the allele level.

NAMING KIR GENOTYPES

As well as assigning unique designations to *KIR* haplotypes, it was also thought useful to provide a nomenclature system to describe *KIR* genotypes. It was suggested that each genotype would be indicated by the prefix “KG” followed by a hyphen, in turn followed by a unique four-digit number. This would then be followed with an optional hyphen and 17-digit binary code. As in the naming of haplotypes, the binary code would indicate the presence (a 1) or absence (a 0) of *KIR* genes in the genotype. So a *KIR* genotype may be written KG-0202-1110101101101101. The order of genes would be as used for the haplotype code.

Further refinements of this system to indicate the presence of null alleles or to demonstrate homozygosity of alleles have been suggested. However, in the short term it has been recommended that the community gains familiarity with the system as proposed before implementing any additional complexity.

KIR SEQUENCE DATABASE

In collaboration with the European Bioinformatics Institute, the *KIR*-DB—a database of the nucleotide and protein sequence alignments for all of the officially recognized *KIR* alleles—has been established. Together with the sequences, information is given on the nomenclature assigned to the different *KIR* alleles. In the near future further tools for the submission and analysis of *KIR* sequences will be made available from the web site. The *KIR*-DB may be accessed via the World Wide Web at <http://www.ebi.ac.uk/ipd/kir/>.

REFERENCES

1. Marsh SGE, Albert ED, Bodmer WF, Bontrop RE, Dupont B, Erlich HA, Geraghty DE, Hansen JA, Mach B, Mayr WR, Parham P, Petersdorf EW, Sasazuki T, Schreuder GM, Strominger JL, Svejgaard A, Terasaki PI: Nomenclature for factors of the HLA system, 2002. *Tissue Antigens* 60:407, 2002.
2. Long EO, Colonna M, Lanier LL: Inhibitory MHC class I receptors on NK and T cells: a standard nomenclature. *Immunology Today* 17:100, 1996.
3. Vilches C, Parham P: *KIR*: diverse, rapidly evolving receptors of innate and adaptive immunity. *Annu Rev Immunol* 20:217, 2002.
4. Gomez-Lozano N, Gardiner CM, Parham P, Vilches C: Some human *KIR* haplotypes contain two *KIR2DL5* genes: *KIR2DL5A* and *KIR2DL5B*. *Immunogenetics* 54: 314–319, 2002.
5. Moretta A, Bottino C, Biassoni R. CD158a (p58.1/p50.1) and CD158b (p58.2/p50.2) natural killer receptors for HLA-C alleles: Workshop Panel Report. In Kishimoto T, Kikutani H, von dem Born AEGK, Goyert SM, Masou DY, Miyaska K, Moretta K, Okumura K, Shaw S, Springer TA, Sugamara K, Zola H (eds): *Leucocyte Typing VI: White Cell Differentiation Antigens*. New York, Garland Publishing Inc., 1997:1109.
6. André P, Biassoni R, Colonna M, Cosman LL, Lanier LL, Long EO, Lopez-Botet M, Moretta A, Moretta L, Parham P, Trowsdale J, Vivier E, Wagtmann N, Wilson MJ: New Nomenclature for MHC receptors. *Nature Immunology* 2:661, 2001.
7. Pascal V, Vivier E, André P: CD158 (killer immunoglobulin-like receptors family) report. In: D Mason ed. *Leucocyte Typing VII*. New York: Oxford University Press, 2002:412–413.
8. Uhrberg M, Valiante NM, Shum BP, Shilling HG, Lienert-Weidenbach K, Corliss B, Tyan D, Lanier LL, Parham P: Human diversity in killer cell inhibitory receptor genes. *Immunity* 7:753, 1997.
9. Hsu KC, Chida S, Geraghty DE, Dupont B: The killer cell immunoglobulin-like receptor (*KIR*) genomic region: gene-order, haplotypes and allelic polymorphism. *Immunol Rev* 190:40, 2002.
10. Colonna M, Samaridis J: Cloning of immunoglobulin-superfamily members associated with HLA-C and HLA-B recognition by human natural killer cells. *Science* 268: 405, 1995.
11. Wagtmann N, Biassoni R, Cantoni C, Verdiani S, Malnati MS, Vitale M, Bottino C, Moretta L, Moretta A, Long EO: Molecular clones of the p58 NK cell receptor reveal immunoglobulin-related molecules with diversity in both the extra- and intracellular domains. *Immunity* 2:439, 1995.
12. Selvakumar A, Steffens U, Dupont B: NK cell receptor gene of the *KIR* family with two IG domains but highest homology to *KIR* receptors with three IG domains. *Tissue Antigens* 48:285, 1996.

13. Vilches C, Rajalingam R, Uhrberg M, Gardiner CM, Young NT, Parham P: KIR2DL5, a novel killer-cell receptor with a D0-D2 configuration of Ig-like domains. *J Immunol* 164:5797, 2000.
14. Biassoni R, Cantoni C, Falco M, Verdiani S, Bottino C, Vitale M, Conte R, Poggi A, Moretta A, Moretta L: The human leukocyte antigen (HLA)-C-specific "activatory" or "inhibitory" natural killer cell receptors display highly homologous extracellular domains but differ in their transmembrane and intracytoplasmic portions. *J Exp Med* 183:645, 1996.
15. Dohring C, Samaridis J, Colonna M: Alternatively spliced forms of human killer inhibitory receptors. *Immunogenetics* 44:227, 1996.
16. Torkar M, Norgate Z, Colonna M, Trowsdale J, Wilson MJ: Isotypic variation of novel immunoglobulin-like transcript/killer cell inhibitory receptor loci in the leucocyte receptor complex. *Eur J Immunol* 28:3959, 1998.
17. Rajalingam R, Gardiner CM, Canavez F, Vilches C, Parham P: Identification of seventeen novel KIR variants: fourteen of them from two non-Caucasian donors. *Tissue Antigens* 57:22, 2001.
18. Valiante NM, Uhrberg M, Shilling HG, Lienert-Weidenbach K, Arnett KL, D'Andrea A, Phillips JH, Lanier LL, Parham P: Functionally and structurally distinct NK cell receptor repertoires in the peripheral blood of two human donors. *Immunity* 7:739, 1997.
19. Selvakumar A, Steffens U, Dupont B: Polymorphism and domain variability of human killer cell inhibitory receptors. *Immunol Rev* 155:183, 1997.
20. Cantoni C, Verdiani S, Falco M, Pessino A, Cilli M, Conte R, Pende D, Ponte M, Mikaelsson MS, Moretta L, Biassoni R: p49, a putative HLA class I-specific inhibitory NK receptor belonging to the immunoglobulin superfamily. *Eur J Immunol* 28:1980, 1998.
21. Selvakumar A, Steffens U, Palanisamy N, Chaganti RS, Dupont B: Genomic organization and allelic polymorphism of the human killer cell inhibitory receptor gene KIR103. *Tissue Antigens* 49:564, 1997.
22. Vilches C, Gardiner CM, Parham P: Gene structure and promoter variation of expressed and nonexpressed variants of the KIR2DL5 gene. *J Immunol* 165:6416, 2000.
23. Wilson MJ, Torkar M, Haude A, Milne S, Jones T, Sheer D, Beck S, Trowsdale J: Plasticity in the organization and sequences of human KIR/ILT gene families. *Proc Natl Acad Sci U S A* 97:4778, 2000.
24. Biassoni R, Pessino A, Malaspina A, Cantoni C, Bottino C, Sivori S, Moretta L, Moretta A: Role of amino acid position 70 in the binding affinity of p50.1 and p58.1 receptors for HLA-Cw4 molecules. *Eur J Immunol* 27:3095, 1997.
25. Bottino C, Sivori S, Vitale M, Cantoni C, Falco M, Pende D, Morelli L, Augugliaro R, Semenzato G, Biassoni R, Moretta L, Moretta A: A novel surface molecule homologous to the p58/p50 family of receptors is selectively expressed on a subset of human natural killer cells and induces both triggering of cell functions and proliferation. *Eur J Immunol* 26:1816, 1996.
26. Maxwell LD, Wallace A, Middleton D, Curran MD: A common KIR2DS4 deletion variant in the human that predicts a soluble KIR molecule analogous to the KIR1D molecule observed in the rhesus monkey. *Tissue Antigens* 60:254, 2002.
27. Hsu KC, Liu X-R, Selvakumar A, Mickelson E, O'Reilly RJ, Dupont B: Killer Ig-like receptor haplotype analysis by gene content: evidence for genomic diversity with a minimum of six basic framework haplotypes, each with multiple subsets. *J Immunol* 169:5118, 2002.
28. Vilches C, Pando MJ, Rajalingam R, Gardiner CM, Parham P: Discovery of two novel variants of KIR2DS5 reveals this gene to be a common component of human KIR 'B' haplotypes. *Tissue Antigens* 56:453, 2000.
29. Martin AM, Freitas EM, Witt CS, Christiansen FT: The genomic organization and evolution of the natural killer immunoglobulin-like receptor (KIR) gene cluster. *Immunogenetics* 51:268, 2000.
30. Wagtman N, Rajagopalan S, Winter CC, Peruzzi M, Long EO: Killer cell inhibitory receptors specific for HLA-C and HLA-B identified by direct binding and by functional transfer. *Immunity* 3:801, 1995.
31. Pende D, Biassoni R, Cantoni C, Verdiani S, Falco M, di Donato C, Accame L, Bottino C, Moretta A, Moretta L: The natural killer cell receptor specific for HLA-A allotypes: a novel member of the p58/p70 family of inhibitory receptors that is characterized by three immunoglobulin-like domains and is expressed as a 140-kD disulphide-linked dimer. *J Exp Med* 184:505, 1996.
32. Gardiner CM, Guethlein LA, Shilling HG, Pando M, Carr WH, Rajalingam R, Vilches C, Parham P: Different NK cell surface phenotypes defined by the DX9 antibody are due to KIR3DL1 gene polymorphism. *J Immunol* 166:2992, 2001.
33. D'Andrea A, Chang C, Franz-Bacon K, McClanahan T, Phillips JH, Lanier LL: Molecular cloning of NK1. A natural killer cell receptor for HLA-B allotypes. *J Immunol* 155:2306, 1995.
34. Crum KA, Logue SE, Curran MD, Middleton D: Development of a PCR-SSOP approach capable of defining the natural killer cell inhibitory receptor (KIR) gene sequence repertoires. *Tissue Antigens* 56:313, 2000.
35. Shilling HG, Guethlein LA, Cheng NW, Gardiner CM, Rodriguez R, Tyan D, Parham P: Allelic polymorphism synergizes with variable gene content to individualize human KIR genotype. *J Immunol* 168:2307, 2002.
36. Long EO, Barber DF, Burshtyn DN, Faure M, Peterson M, Rajagopalan S, Renard V, Sandusky M, Stebbins CC, Wagtman N, Watzl C: Inhibition of natural killer cell activation signals by killer cell immunoglobulin-like receptors (CD158). *Immunol Rev* 181:223, 2001.