Killer-cell immunoglobulin-like receptor (KIR) nomenclature report, 2002

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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) (Marsh *et al*., 2002). 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 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 are 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.

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 (Long *et al*., 1996). 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 (Vilches & Parham, 2002). Where two or more genes have very similar structures and have very similar sequences, they may be given the same number but distinguished by a final letter, for example the *KIR2DL5A* and *KIR2DL5B* genes (Gomez-Lozano *et al*., 2002). 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 which 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'*, where 'n' represents the next number in the series.

Perhaps the simplest solution to naming alleles of a recombinant gene is to assign the allele the gene name of the gene contributing the Ig-like domains, providing sufficient homology is maintained. In such situations where the 3′ region of the recombinant allele is inconsistent with the L/S designation of the gene, a suffix would be

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Table 1. KIR gene names

Gene symbol	Protein symbol	Description	Aliases	Reference or submitting author
KIR2DL1	KIR2DL1	killer-cell immunoglobulin-like receptor, two domains, long cytoplasmic tail, 1	cl-42, nkat1, 47.11, p58.1, CD158a	Colonna & Samaridis (1995); Wagtmann *et al.* (1995a)
KIR2DL2	KIR2DL2	killer-cell immunoglobulin-like receptor, two domains, long cytoplasmic tail, 2	cl-43, nkat6, CD158b1	Colonna & Samaridis (1995); Wagtmann *et al.* (1995a)
KIR2DL3	KIR2DL3	killer-cell immunoglobulin-like receptor, two domains, long cytoplasmic tail, 3	cl-6, nkat2, nkat2a, nkat2b, p58, CD158b2	Colonna & Samaridis (1995); Wagtmann *et al.* (1995a)
KIR2DL4	KIR2DL4	killer-cell immunoglobulin-like receptor, two domains, long cytoplasmic tail, 4	103AS, 15.212, CD158d	Selvakumar *et al.* (1996)
KIR2DL5A	KIR2DL5A	killer-cell immunoglobulin-like receptor, two domains, long cytoplasmic tail, 5A	KIR2DL5.1, CD158f	Vilches *et al.* (2000c)
KIR2DL5B	KIR2DL5B	killer-cell immunoglobulin-like receptor, two domains, long cytoplasmic tail, 5B	KIR2DL5.2, KIR2DL5.3, KIR2DL5.4	Vilches *et al.* (2000c)
KIR2DS1	KIR2DS1	killer-cell immunoglobulin-like receptor, two domains, short cytoplasmic tail, 1	EB6Actl, EB6ActII, CD158 h	Biassoni *et al.* (1996)
KIR2DS2	KIR2DS2	killer-cell immunoglobulin-like receptor, two domains, short cytoplasmic tail, 2	cl-49, nkat5, 183Actl, CD158j	Colonna & Samaridis (1995); Wagtmann *et al.* (1995a)
KIR2DS3	KIR2DS3	killer-cell immunoglobulin-like receptor, two domains, short cytoplasmic tail, 3	nkat7	Dohring *et al.* (1996)
KIR2DS4	KIR2DS4	killer-cell immunoglobulin-like receptor, two domains, short cytoplasmic tail, 4	cl-39, KKA3, nkat8, CD158i	Wagtmann *et al.* (1995a); Dohring *et al.* (1996)
KIR2DS5	KIR2DS5	killer-cell immunoglobulin-like receptor, two domains, short cytoplasmic tail, 5	nkat9, CD158g	Dohring *et al.* (1996)
KIR2DP1	KIR2DP1	killer-cell immunoglobulin-like receptor, two domains, pseudogene 1	KIRZ, KIRY, KIR15, KIR2DL6	Vilches *et al.* (2000c)
KIR3DL1	KIR3DL1	killer-cell immunoglobulin-like receptor, three domains, long cytoplasmic tail, 1	cl-2, NKB1, cl-11, nkat3, NKB1B, AMB11, KIR, CD158e1	Colonna & Samaridis (1995)
KIR3DL2	KIR3DL2	killer-cell immunoglobulin-like receptor, three domains, long cytoplasmic tail, 2	cl-5, nkat4, nkat4a, nkat4b, CD158k	Colonna & Samaridis (1995)
KIR3DL3	KIR3DL3	killer-cell immunoglobulin-like receptor, three domains, long cytoplasmic tail, 3	KIRC1, KIR3DL7, KIR44, CD158z	Torkar *et al.* (1998)
KIR3DS1	KIR3DS1	killer-cell immunoglobulin-like receptor, three domains, short cytoplasmic tail, 1	nkat10, CD158e2	Dohring *et al.* (1996)
KIR3DP1	KIR3DP1	killer-cell immunoglobulin-like receptor, three domains, pseudogene 1	KIRX, KIR48, KIR2DS6, KIR3DS2P, CD158c	Vilches *et al.* (2000c)

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 (see 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) (Moretta *et al.*, 1997; André *et al.*, 2001; Pascal *et al.*, 2002).

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 (non-coding) differences within the coding sequence. The final two digits will be used to distinguish alleles that only differ by substitutions in an intron, promoter, or other non-coding 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 numerical series, thus *3DL1*001–3DL1*009* are followed by *3DS1*010–3DS1*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.

Table 2. KIR allele names

Allele name	Previous name	Cell ID	Accession number	Reference or submitting author
2DL1*001	NKAT1	?	L41267	Colonna & Samaridis (1995)
2DL1*002	cl-42	?	U24076	Wagtmann *et al.* (1995a)
2DL1*00301	cl-47.11	NK-lib	U24078	Wagtmann *et al.* (1995a)
2DL1*00302	2DL1M, 2DL1v2	MU	AF285431	Rajalingam *et al.* (2001)
2DL1*004	2DL1v	NV	AF022045	Valiante *et al.* (1997)
2DL1*005	2DL1W102, 2DL1v3	WC	AF285432	Rajalingam *et al.* (2001)
2DL2*001	cl-43	?	U24075	Wagtmann *et al.* (1995a)
2DL2*002	NKAT6	?	L76669	Dohring *et al.* (1996)
2DL2*003	2DL2v2, 2DL2M	MU	AF285434	Rajalingam *et al.* (2001)
2DL2*004	2DL2v1	WC	AF285433	Rajalingam *et al.* (2001)
2DL3*001	NKAT2, cl-6	?, NK3.3	L41268, U24074	Colonna & Samaridis (1995); Wagtmann *et al.* (1995a)
2DL3*002	NKAT2a	?	L76662	Dohring *et al.* (1996)
2DL3*003	NKAT2b	?	L76663	Dohring *et al.* (1996)
2DL3*004	KIR-023GB	?	U73395	Selvakumar *et al.* (1997a)
2DL3*005	2DL3v	PP	AF022048	Valiante *et al.* (1997)
2DL3*006	2DL3W308	WC	AF285435	Rajalingam *et al.* (2001)
2DL4*00101	NK3.3#27	NK3.3	X99480	Cantoni *et al.* (1998)
2DL4*00102	2DL4v1	PP, NV	AF034771	Valiante *et al.* (1997)
2DL4*00201	15.212	?	X97229	Cantoni *et al.* (1998)
2DL4*00202	2DL4v2	PP, NV	AF034772	Valiante *et al.* (1997)
2DL4*003	KIR103AS	YT, NK92	U71199	Selvakumar *et al.* (1996)
2DL4*004	KIR103LP	?	AF002979	Selvakumar *et al.* (1997b)
2DL4*005	2DL4v3	NV	AF034773	Valiante *et al.* (1997)
2DL4*006	2DL4v4	RR	AF285436	Rajalingam *et al.* (2001)
2DL4*007	—	LP	AF276292	A. Selvakumar (New York, USA)
2DL5A*001	2DL5.1	NV, XX-1060P11	AF204903, AF217485, AL133414	Vilches *et al.* (2000a,c); Wilson *et al.* (2000)
2DL5B*002	2DL5.2	NV	AF217486	Vilches *et al.* (2000a)
2DL5B*003	2DL5.3	WCS	AF217487	Vilches *et al.* (2000a)
2DL5B*004	2DL5.4	CC	AF260138, AF260139, AF260140, AF260141	Vilches *et al.* (2000a)
2DS1*001	Eb6ActI	PA	X89892	Biassoni *et al.* (1996)
2DS1*002	2DS1v	NV	AF022046	Valiante *et al.* (1997)
2DS1*003	Eb6ActII	GT	X98858	Biassoni *et al.* (1997)
2DS1*004	2DS1v1	WC	AF285437	Rajalingam *et al.* (2001)
2DS2*001	NKAT5, cl-49	?, ?	L41347, U24079	Colonna & Samaridis (1995); Wagtmann *et al.* (1995a)
2DS2*002	183ActI	23D	X89893	Biassoni *et al.* (1996)
2DS2*003	TG14#35	TG14	AJ002103	R. Biassoni (Genova, Italy)
2DS2*004	2DS2v1	WC	AF285438	Rajalingam *et al.* (2001)
2DS2*005	2DS2v2	FC	AF285439	Rajalingam *et al.* (2001)
2DS3*00101	NKAT7	?	L76670	Dohring *et al.* (1996)
2DS3*00102	59C_K3	Pag1	X97231	R. Biassoni (Genova, Italy)
2DS3*00103	2DS3v	NV	AF022047	Valiante *et al.* (1997)
2DS4*00101	cl-39, cl-17, KKAS_34–52	?, ?, 4053, Mal 43–52	U24077, AF002255, AJ417555, X94609	Wagtmann *et al.* (1995a); Bottino *et al.* (1996); Maxwell *et al.* (2002); H. W. Chan (Pittsburgh, USA)
2DS4*00102	NKAT8	?	L76671	Dohring *et al.* (1996)
2DS4*002	2DS4v1	RR	AF285440	Rajalingam *et al.* (2001)
2DS4 *003	Deletion V, KIR1D	3321	AJ417554	Maxwell *et al.* (2002); Hsu *et al.* (2002b)
2DS5*001	NKAT9	?	L76672	Dohring *et al.* (1996)
2DS5*002	—	NV	AF208054	Vilches *et al.* (2000b)
2DS5*003	—	WC	AF272389	Vilches *et al.* (2000b)
2DP1*001	KIR15	NV	AF204906, AF204907, AF204908	Vilches *et al.* (2000c)
2DP1*002	—	CTB-61M7	AC011501	Martin *et al.* (2000)

Table 2. *Continued*

Allele name	Previous name	Cell ID	Accession number	Reference or submitting author
3DL1*00101	NKAT3, cl-11, AMB11.115	?, ?, AMB11	L41269, U30274, X94262	Colonna & Samaridis (1995); Wagtmann *et al.* (1995b); Pende *et al.* (1996)
3DL1*00102	Nnkat-3	?	AF262968	Gardiner *et al.* (2001)
3DL1*002	NKB1, cl-2	NKB1, ?	U31416, U30273	D'Andrea *et al.* (1995); Wagtmann *et al.* (1995b)
3DL1*003	3DL1v	NV	AF022049	Valiante *et al.* (1997)
3DL1*00401	W204	WC	AF262970	Gardiner *et al.* (2001)
3DL1*00402	M322	MU	AF262969	Gardiner *et al.* (2001)
3DL1*005	3DL1v2	YW	AF262971	Gardiner *et al.* (2001)
3DL1*006	NJN55	?	AF262972	Gardiner *et al.* (2001)
3DL1*007	r3k10	RR	AF262973	Gardiner *et al.* (2001)
3DL1*008	r3k2	RR	AF262974	Gardiner *et al.* (2001)
3DL1*009	—	3321, 4053	AJ417556, AJ417557	Crum *et al.* (2000)
3DL2*001	NKAT4	?	L41270	Colonna & Samaridis (1995)
3DL2*002	cl-5, AMC5	?, ?	U30272, X94374	Wagtmann *et al.* (1995b); Pende *et al.* (1996)
3DL2*003	1.1, NKAT4A	?, ?	X94373, L76665	Pende *et al.* (1996); Dohring *et al.* (1996)
3DL2*004	17.1C	?	X93595	Pende *et al.* (1996)
3DL2*005	NKAT4b	?	L76666	Dohring *et al.* (1996)
3DL2*006	3DL2Wv2	WC	AF262966	Gardiner *et al.* (2001)
3DL2*007	b3DL2b	BS	AF262965	Gardiner *et al.* (2001)
3DL2*008	r3k17	RR	AF262967	Gardiner *et al.* (2001)
3DL2*009	rrk100	RR	AF263617	Rajalingam *et al.* (2001)
3DL2*010	—	?	AY059418	Shilling *et al.* (2002)
3DL2*011	—	?	AY059419	Shilling *et al.* (2002)
3DL2*012	—	?	AY059420	Shilling *et al.* (2002)
3DL3*001	KIRCl	?	AF072407, AF072408, AF072409, AF072410	Torkar *et al.* (1998)
3DL3*00201	KIR44a	NV, UV5HL9–5B	AF204909, AF204910, AF204911, AC006293	Martin *et al.* (2000); Vilches *et al.* (2000c)
3DL3*00202	KIR44b	NV	AF204912, AF204913, AF204914	Vilches *et al.* (2000c)
3DL3*003	KIRC1	XX-1060P11	AL133414	Wilson *et al.* (2000)
3DL3*004	3DL7	?	AF352324	Long *et al.* (2001)
3DS1*010	NKAT10, 3DS1*001	?	L76661	Dohring *et al.* (1996)
3DS1*011	C97.12#5, 3DS1*002	?	X97233	R. Biassoni (Genova, Italy)
3DS1*012	KIR-123FM, 3DS1*003	?	U73396	Selvakumar *et al.* (1997a)
3DS1*013	3DS1v, 3DS1*004	NV	AF022044	Valiante *et al.* (1997)
3DS1*014	3DS1*005	4373	AJ417558	Crum *et al.* (2000)
3DP1*001	KIR48a	NV	AF204915, AF204916, AF204917	Vilches *et al.* (2000c)
3DP1*002	KIRX	XX-1060P11	AL133414	Wilson *et al.* (2000)
3DP1*00301	KIR48b	NV	AF204918, AF204919, AF204920	Vilches *et al.* (2000c)
3DP1*00302	2DS6	CTB-61M7	AC011501	Martin *et al.* (2000)

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 seen for 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 (e.g. Uhrberg *et al*., 1997; Hsu *et al*., 2002a and other references). The committee felt that the distinction between A and B haplotypes is a useful one, having potential biological and medical significance, 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 letter 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, and 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 by an optional hyphen and a 17-digit binary code. As in the naming of haplotypes, the binary code would indicate the presence (1) or absence (0) of KIR genes in the genotype. So a KIR genotype may be written KG-0202-1110101101101111. 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 the *KIR* sequences will be made available from the website. The KIR-DB may be accessed via the World-Wide Web from www.ebi.ac.uk/ipd/kir/.

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References

André, P., Biassoni, R., Colonna, M., Cosman, L.L., Lanier, L.L., Long, E.O., Lopez-Botet, M., Moretta, A., Moretta, L., Parham, P. *et al.* (2001) New nomenclature for MHC receptors. *Nature Immunology*, **2**, 661.

Biassoni, R., Cantoni, C., Falco, M., Verdiani, S., Bottino, C., Vitale, M., Conte, R., Poggi, A., Moretta, A. & Moretta, L. (1996) 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. *Journal of Experimental Medicine*, **183**, 645.

Biassoni, R., Pessino, A., Malaspina, A., Cantoni, C., Bottino, C., Sivori, S., Moretta, L. & Moretta, A. (1997) Role of amino acid position 70 in the binding affinity of p50.1 and p58.1 receptors for HLA-Cw4 molecules. *European Journal of Immunology*, **27**, 3095.

Bottino, C., Sivori, S., Vitale, M., Cantoni, C., Falco, M., Pende, D., Morelli, L., Augugliaro, R., Semenzato, G., Biassoni, R. *et al.* (1996) 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. *European Journal of Immunology*, **26**, 1816.

Cantoni, C., Verdiani, S., Falco, M., Pessino, A., Cilli, M., Conte, R., Pende, D., Ponte, M., Mikaelsson, M.S., Moretta, L. *et al.* (1998) p49, a putative HLA class I-specific inhibitory NK receptor belonging to the immunoglobulin superfamily. *European Journal of Immunology*, **28**, 1980.

Colonna, M. & Samaridis, J. (1995) Cloning of immunoglobulin-superfamily members associated with HLA-C and HLA-B recognition by human natural killer cells. *Science*, **268**, 405.

Crum, K.A., Logue, S.E., Curran, M.D. & Middleton, D. (2000) Development of a PCR-SSOP approach capable of defining the natural killer cell inhibitory receptor (KIR) gene sequence repertoires. *Tissue Antigens*, **56**, 313.

D'Andrea, A., Chang, C., Franz-Bacon, K., McClanahan, T., Phillips, J.H. & Lanier, L.L. (1995) Molecular cloning of NKB1. A natural killer cell receptor for HLA-B allotypes. *Journal of Immunology*, **155**, 2306.

Dohring, C., Samaridis, J. & Colonna, M. (1996) Alternatively spliced forms of human killer inhibitory receptors. *Immunogenetics*, **44**, 227.

Gardiner, C.M., Guethlein, L.A., Shilling, H.G., Pando, M., Carr, W.H., Rajalingam, R., Vilches, C. & Parham, P. (2001) Different NK cell surface phenotypes defined by the DX9 antibody are due to KIR3DL1 gene polymorphism. *Journal of Immunology*, **166**, 2992.

Gomez-Lozano, N., Gardiner, C.M., Parham, P. & Vilches, C. (2002) Some human KIR haplotypes contain two KIR2DL5 genes: KIR2DL5A and KIR2DL5B. *Immunogenetics*, **54**, 314.

Hsu, K.C., Chida, S., Geraghty, D.E. & Dupont, B. (2002a) The killer cell immunoglobulin-like receptor (KIR) genomic region: gene-order, haplotypes and allelic polymorphism. *Immunological Review*, **190**, 40.

Hsu, K.C., Liu, X.-R., Selvakumar, A., Mickelson, E., O'Reilly, R.J. & Dupont, B. (2002b) 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. *Journal of Immunology*, **169**, 5118.

Long, E.O., Colonna, M. & Lanier, L.L. (1996) Inhibitory MHC class I receptors on NK and T cells: a standard nomenclature. *Immunology Today*, **17**, 100.

Long, E.O., Barber, D.F., Burshtyn, D.N., Faure, M., Peterson, M., Rajagopalan, S., Renard, V., Sandusky, M., Stebbins, C.C., Wagtmann, N. *et al.* (2001) Inhibition of natural killer cell activation signals by killer cell immunoglobulin-like receptors (CD158). *Immunological Review*, **181**, 223.

Marsh, S.G.E., Albert, E.D., Bodmer, W.F., Bontrop, R.E., Dupont, B., Erlich, H.A., Geraghty, D.E., Hansen, J.A., Mach, B., Mayr, W.R. *et al.* (2002) Nomenclature for factors of the HLA system, 2002. *Tissue Antigens*, **60**, 407.

Martin, A.M., Freitas, E.M., Witt, C.S. & Christiansen, F.T. (2000) The genomic organization and evolution of the natural killer immunoglobulin-like receptor (KIR) gene cluster. *Immunogenetics*, **51**, 268.

Maxwell, L.D., Wallace, A., Middleton, D. & Curran, M.D. (2002) 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.

Moretta, A., Bottino, C. & Biassoni, R. (1997) CD158a (p58.1/p50.1) and CD158b (p58.2/p50.2) natural killer receptors for HLA-C alleles: Workshop Panel Report. In: Leucocyte Typing VI: White Cell Differentiation Antigens (ed. by T. Kishimoto, H. Kikutani, A. E. G. K. von dem Born, S. M. Goyert, D. Y. Masou, M. Miyasaka, K. Moretta, K. Okumura, S. Shaw, T. A. Springer, K. Sugamura & H. Zola), p. 1109. Garland Publishing Inc., New York.

Pascal, V., Vivier, E. & André, P. (2002) CD158 (killer immunoglobulin-like receptors family) report. In: *Leucocyte Typing VII* (ed. by D. Mason), p. 412. Oxford University Press, New York.

Pende, D., Biassoni, R., Cantoni, C., Verdiani, S., Falco, M., di Donato, C., Accame, L., Bottino, C., Moretta, A. & Moretta, L. (1996) 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. *Journal of Experimental Medicine*, **184**, 505.

Rajalingam, R., Gardiner, C.M., Canavez, F., Vilches, C. & Parham, P. (2001) Identification of seventeen novel KIR variants: fourteen of them from two non-Caucasian donors. *Tissue Antigens*, **57**, 22.

Selvakumar, A., Steffens, U. & Dupont, B. (1996) 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.

Selvakumar, A., Steffens, U. & Dupont, B. (1997a) Polymorphism and domain variability of human killer cell inhibitory receptors. *Immunological Review*, **155**, 183.

Selvakumar, A., Steffens, U., Palanisamy, N., Chaganti, R.S. & Dupont, B. (1997b) Genomic organization and allelic polymorphism of the human killer cell inhibitory receptor gene KIR103. *Tissue Antigens*, **49**, 564.

Shilling, H.G., Guethlein, L.A., Cheng, N.W., Gardiner, C.M., Rodriguez, R., Tyan, D. & Parham, P. (2002) Allelic polymorphism synergizes with variable gene content to individualize human KIR genotype. *Journal of Immunology*, **168**, 2307.

Torkar, M., Norgate, Z., Colonna, M., Trowsdale, J. & Wilson, M.J. (1998) Isotypic variation of novel immunoglobulin-like transcript/killer cell inhibitory receptor loci in the leucocyte receptor complex. *European Journal of Immunology*, **28**, 3959.

Uhrberg, M., Valiante, N.M., Shum, B.P., Shilling, H.G., Lienert-Weidenbach, K., Corliss, B., Tyan, D., Lanier, L.L. & Parham, P. (1997) Human diversity in killer cell inhibitory receptor genes. *Immunity*, **7**, 753.

Valiante, N.M., Uhrberg, M., Shilling, H.G., Lienert-Weidenbach, K., Arnett, K.L., D'Andrea, A., Phillips, J.H., Lanier, L.L. & Parham, P. (1997) Functionally and structurally distinct NK cell receptor repertoires in the peripheral blood of two human donors. *Immunity*, **7**, 739.

Vilches, C. & Parham, P. (2002) KIR: diverse, rapidly evolving receptors of innate and adaptive immunity. *Annual Review of Immunology*, **20**, 217.

Vilches, C., Gardiner, C.M. & Parham, P. (2000a) Gene structure and promoter variation of expressed and nonexpressed variants of the KIR2DL5 gene. *Journal of Immunology*, **165**, 6416.

Vilches, C., Pando, M.J., Rajalingam, R., Gardiner, C.M. & Parham, P. (2000b) Discovery of two novel variants of KIR2DS5 reveals this gene to be a common component of human KIR 'B' haplotypes. *Tissue Antigens*, **56**, 453.

Vilches, C., Rajalingam, R., Uhrberg, M., Gardiner, C.M., Young, N.T. & Parham, P. (2000c) KIR2DL5, a novel killer-cell receptor with a D0–D2 configuration of Ig-like domains. *Journal of Immunology*, **164**, 5797.

Wagtmann, N., Biassoni, R., Cantoni, C., Verdiani, S., Malnati, M.S., Vitale, M., Bottino, C., Moretta, L., Moretta, A. & Long, E.O. (1995a) Molecular clones of the p58 NK cell receptor reveal immunoglobulin-related molecules with diversity in both the extra- and intracellular domains. *Immunity*, **2**, 439.

Wagtmann, N., Rajagopalan, S., Winter, C.C., Peruzzi, M. & Long, E.O. (1995b) Killer cell inhibitory receptors specific for HLA-C and HLA-B identified by direct binding and by functional transfer. *Immunity*, **3**, 801.

Wilson, M.J., Torkar, M., Haude, A., Milne, S., Jones, T., Sheer, D., Beck, S. & Trowsdale, J. (2000) Plasticity in the organization and sequences of human KIR/ILT gene families. *Proceedings of the National Academy of Sciences of the USA*, **97**, 4778.