

Mary Carrington • Paul Norman

# The KIR Gene Cluster

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Killer cell immunoglobulin-like receptors (KIRs) are members of a group of regulatory molecules found on subsets of lymphoid cells. They were first identified by their ability to impart some specificity on natural killer (NK) cytotoxicity. The *KIR locus*, containing a family of polymorphic and highly homologous genes, maps to chromosome 19q13.4 within the 1 Mb leukocyte receptor complex (LRC). The LRC also encodes the leukocyte Ig-like receptor family (LILR), the leukocyte-associated inhibitory receptor (LAIR) family, and the Fc $\gamma$  receptor. *KIR* genes are tandemly arrayed over about 150 kb, with the remarkable feature that gene content varies between haplotypes. The discovery of KIR has also imparted an additional function on the human leukocyte antigen (HLA) class I molecules, which are encoded by genes within the major histocompatibility complex (MHC; chromosome 6). Through their interaction with KIR isotypes that inhibit natural killer (NK) cell activity, certain HLA class I molecules are now known to protect healthy cells from spontaneous destruction by NK-cell-mediated cytotoxicity. Other KIR isotypes stimulate the activity of NK cells. Thus, KIR are likely to play a significant role in the control of the immune response, which would explain the associations observed between certain *KIR* genes in rheumatoid arthritis, psoriatic arthritis and control of HIV disease progression. The degree of HLA/KIR compatibility may also determine the success rate of haematopoietic cell replacement therapy for certain leukemias.

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# The KIR Gene Cluster

Mary Carrington<sup>1</sup> and Paul Norman<sup>2</sup>

Created: May 28, 2003.

## Introduction

Killer cell immunoglobulin-like receptors (KIRs) are members of a group of regulatory molecules found on subsets of lymphoid cells. They were first identified by their ability to impart some specificity on natural killer (NK) cytotoxicity (1, 2). The *KIR locus*, containing a family of polymorphic and highly homologous genes, maps to chromosome 19q13.4 within the 1 Mb leukocyte receptor complex (LRC; Figure 1). The *LRC* also encodes the leukocyte Ig-like receptor family (LILR; see Box 1 and discussion below), the leukocyte-associated inhibitory receptor (LAIR) family, and the Fc $\alpha$  receptor. *KIR* genes are tandemly arrayed over about 150 kb, with the remarkable feature that gene content varies between haplotypes (3). The discovery of KIR has also imparted an additional function on the human leukocyte antigen (HLA) class I molecules, which are encoded by genes within the major histocompatibility complex (*MHC*; chromosome 6). Through their interaction with KIR isotypes that inhibit natural killer (NK) cell activity, certain HLA class I molecules are now known to protect healthy cells from spontaneous destruction by NK-cell-mediated cytotoxicity. Other KIR isotypes stimulate the activity of NK cells. Thus, KIR are likely to play a significant role in the control of the immune response, which would explain the associations observed between certain *KIR* genes in rheumatoid arthritis (4), psoriatic arthritis (5) and control of HIV disease progression (6). The degree of HLA/KIR compatibility may also determine the success rate of haematopoietic cell replacement therapy for certain leukemias (7, 8).

NK cells are an important component of the innate immune system; they participate in early responses against infected or transformed cells by production of cytokines and direct cytotoxicity (9–13). HLA molecules precipitate adaptive aspects of anti-pathogen defense by presenting peptide fragments to immune effector cells (14, 15). Cytotoxic T lymphocytes (CTL) interact with the HLA class I-peptide complex on target cells via the T cell receptor (TCR), which instigates cytolytic activity if the peptide is considered foreign. HLA class I expression can be down-regulated in virally-infected or transformed cells, rendering the cells resistant to cytotoxicity by CTLs. However, aberrant levels of class I expression can result in spontaneous destruction by NK cells (16–18), a concept originally termed the "missing-self hypothesis" (19). Although neither the ligand nor the direct mode of action of many NK receptors is known, it is widely accepted that normal cells are protected from spontaneous killing when they express an appropriate ligand for an inhibitory receptor expressed by the cytotoxic cell (NK or CTL). NK cells need to discriminate between healthy and infected or transformed cells, corresponding with the observed phenotypic dominance of KIR-mediated inhibition over activation (20–23). Furthermore, inhibition by non-HLA specific NK receptors can override potential activation signals (24).

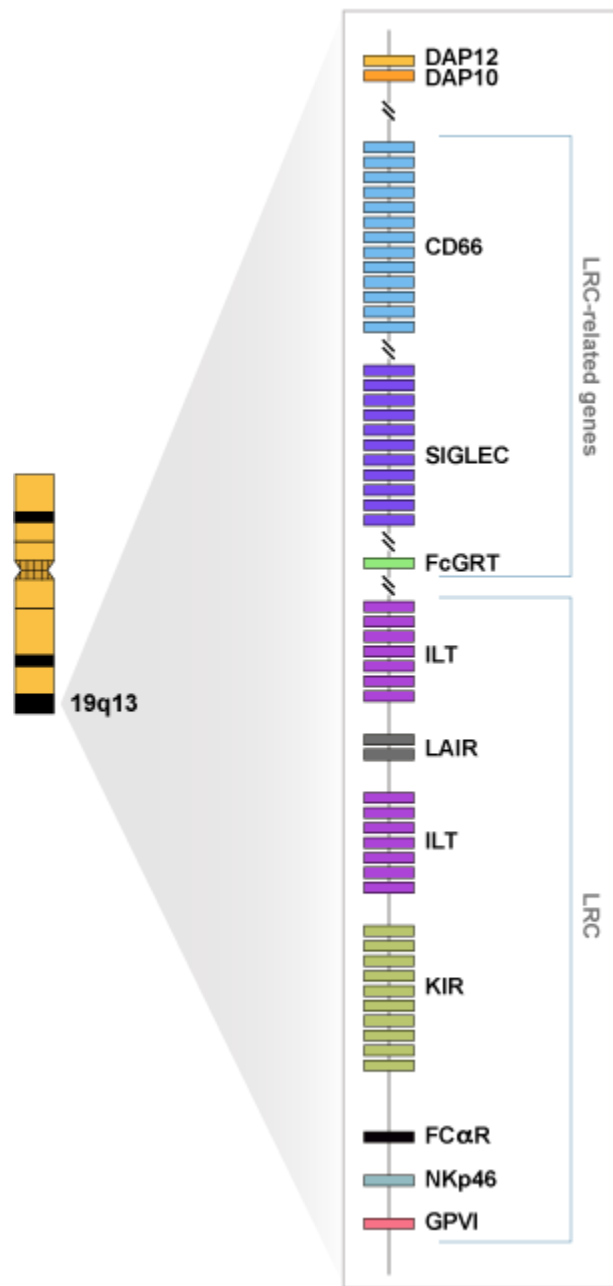
Studies performed over the last few years have revealed extensive diversity at the KIR gene locus, which stems from both its polygenic and multi-allelic polymorphism (3). As a consequence, there is only a small probability that two randomly selected individuals will have the same KIR genotype (25). *KIR* gene expression patterns can vary clonally (26), adding yet another layer of complexity to the system. Diversity at the locus may be the result of selection pressures, in a manner analogous to that proposed for the *HLA* loci. Thus, disease resistance conferred by the *KIR* locus is likely to vary in a haplotypic manner depending on disease type.

LILR are genetically, structurally and functionally related to KIR and may be their ancestral predecessors (27) (Box 1). Several investigators identified the molecules independently, which has led to inconsistencies in

nomenclature systems. The LILRs are also known as ILT [immunoglobulin-like transcript; (28)], LIR [leukocyte inhibitory receptor; (29)], MIR [macrophage inhibitory receptor; (30)] and HM transcripts (31). LILR is the more recently derived and HUGO-endorsed **nomenclature**. The molecules were identified in binding studies of immune evasion by CMV (29), and in expression screening for human homologues of mouse leukocyte inhibitory receptors (28, 30, 31). Like KIRs, LILRs can interact with HLA class I (29, 32–34), are expressed by a range of immunologically active cells, including NK (31, 35), and have the potential to regulate the immune response through inhibition or activation of cytolytic activity (28, 35–37). *LILR* genes have been found in a wide variety of species (38–40) and the number of loci appears to be relatively stable (41). The duplicated sub-cluster organization of the *LILR* gene complex is conserved between humans and chimpanzees (38), unlike *KIR* haplotypes, which have distinct arrangements that are specific to each of these species (42). LILRs have either two or four extracellular Ig domains and a long or short cytoplasmic tail. Long cytoplasmic tails contain up to four immunoreceptor tyrosine-based inhibitory molecules (ITIM) (43) and therefore have the capacity to inhibit cellular activity. LILR with short cytoplasmic domains can associate with molecules containing ITAMs and contribute to cell activation. LILRA3 (ILT6) is unique in that it does not possess a cytoplasmic domain, and may be secreted (31, 44). Also, much of the *LILRA3* gene is missing on some haplotypes due to a 7kb deletion in the region (45). Ligands are not known for all of the LILR, but some, such as LILRB1 (ILT2), can bind to HLA class I (Table 1). Thus, their functions and ligand specificities described so far suggests that LILR and KIR have overlapping and potentially complementary functions.

The *LILR* region in both human and chimpanzees consists of two sub-clusters of six or seven loci in opposite transcriptional orientation separated by two *LAIR* genes (27, 38, 46), which encode molecules that interact with epithelial cell adhesion molecule (EPCAM) (47). *LILRB3* is highly polymorphic, as 18 variants were observed among only 50 individuals (45, 48). Twelve alleles have been identified for *LILRA3* (Table 1) (49).





**Figure 1. Map of the Leukocyte Receptor Complex.** At least 40 members of the Ig superfamily map to 19q13 within the extended LRC. The adapter genes *DAP12* (KARAP) and *DAP10* (KAP10) map to the centromeric end of the complex on band 19q13.1. The *Siglecs* and *CD66* loci are extensive and more complex than indicated in this map. The LRC incorporates the *ILT* and *KIR* genes, and genes encoding *FcαR*, the activating receptor gene *NKp46*, and the collagen-binding receptor *GPVI*. (Adapted from Ref. 58, with permission from Dr. John Trowsdale and Blackwell Publishing Ltd.)

**Table 1. Known LILR, cellular distribution, and ligands.**

LILR	Alias	Alleles	Expression	Action	Ligand
LILRA1	LIR-6	3	Monocytes, B cells	Activating	?
LILRA2	ILT1, LIR-7	7	Myeloid lineage	Activating	FcE
LILRA3	ILT6, LIR-4, HM31, HM43	12	NK, T, Mono	? Activating	?
LILRA4	ILT7	3		Activating	?

Table 1 continued from previous page.

LILR	Alias	Alleles	Expression	Action	Ligand
<a href="#">LILRB1</a>	ILT2, CD85, LIR-1, MIR-7	8	NK, T, B, Mono	Inhibiting	HLA Class I, cmv-UL18
<a href="#">LILRB2</a>	ILT4, LIR-2, MIR-10	6	Monocytes, dendritic cells	Inhibiting <sup>a</sup>	HLA A, B, G, (cmv-UL18)
<a href="#">LILRB3</a>	ILT5, LIR-3	21	Monocytes, NK?	Inhibiting	not HLA
<a href="#">LILRB4</a>	ILT3, LIR-5, HM18	6	Monocytes, Dendritic cells	Inhibiting <sup>a</sup>	?
<a href="#">LILRB5</a>	LIR-8	2	NK	Inhibiting	?
	<a href="#">ILT8</a>	1		Activating	?
	<a href="#">ILT9</a>	1		NA	n/a
	<a href="#">ILT10</a>	1		?	?
	<a href="#">ILT11</a>	1		?	?

LILR: leukocyte immunoglobulin-like receptor; ILT: immunoglobulin-like transcript; LIR: leukocyte inhibitory receptor; MIR: macrophage inhibitory receptor; NA: not applicable.

<sup>a</sup>May be involved in suppressing, rather than preventing an immune response (207).

### Box 1. Unique LILR sequences.

The following sequences are in no particular order, apart from those for *LILRA3*.

#### **LILRA1 (LIR-6)**

[AF025530](#) (LIR6a), [NM\\_006863](#)

[AF025529](#) (LIR6b)

[BC032238](#) (may have truncated cytoplasmic domain, similar to *LILRA3*)

LocusLink: [11024](#)

#### **LILRA2 (ILT1, LIR-7)**

ILT1: [U82275](#) (*LILRA2*), [NM\\_006866](#)

LIR-7: [AF025531](#)

ILT1C1: [AF106246](#), [AF106247](#), [AF106248](#), [AF106249](#), [AF106250](#), [AF106251](#), [AF106252](#), [AF106253](#), [AF106254](#), [AF106255](#); [AH008080](#) (not to be confused with the original ILT1c, below)

ILT1C2: [AF106262](#), [AF106263](#), [AF106264](#), [AF106265](#), [AF106266](#), [AF106267](#), [AF106268](#), [AF106269](#), [AH008081](#)

ILT1C3: [AF106254](#), [AF106255](#), [AF106256](#), [AF106257](#), [AF106258](#), [AF106259](#), [AF106260](#), [AF106261](#), [AH007465](#)

ILT1C4: [AF106270](#), [AF106271](#), [AF106272](#), [AF106273](#), [AF106274](#), [AF106275](#), [AF106276](#), [AF106277](#), [AH007466](#)

[BC017412](#) (= [BC027916](#))

ILT1p: [U70665](#) and "ILT1-like": [AF041034](#)

Splice variants of [U82275](#): ILT1a: [U82276](#), ILT1b; [U82277](#), ILT1c: [U82278](#)

Box 1 continues on next page...

*Box 1 continued from previous page.*

LocusLink: 11027

### **LILRA3 (ILT6, LIR-4, HM31, HM43)**

In the order they were submitted and named (49), based on the KIR nomenclature (55).

\*001: [U91926](#), [AF482768](#)

\*002: [U91927](#)

\*00301: [AF014923](#), [AC010518](#), [AF482767](#)

\*00302: [AF482769](#)

\*004: [AF025527](#)

\*005del: [AL355172](#)

\*00601: [AF482766](#)

\*00602: [AF482762](#)

\*007: [AF482763](#)

\*008: [AF482764](#)

\*009: [AF482765](#)

\*010: [BC028208](#)

LocusLink: 11026

### **LILRA4 (ILT7)**

ILT7: [AF041261](#) = [NM\\_012276](#)

ILT7v1: [AF283989](#)

[BC038829](#)

LocusLink: 23547

### **LILRB1 (ILT2, CD85, LIR-1, MIR-7)**

LIR-1: [AF009221](#) = [AF004230](#) (MIR-7) (possible extra codon in [AF009221](#))

[AF009220](#) = [BC015731](#) = [NM\\_006669](#)

ILT2: [U82279](#)

ILT2a: [AF009005](#)

ILT2b: [AF009006](#)

ILT2c: [AF009007](#)

LIR-1v1: [AF283984](#)

*Box 1 continues on next page...*

*Box 1 continued from previous page.*

LIR-1v2: [AF283985](#)

[AK094834](#)

PDB: [1G0X](#) (208).

LocusLink: [10859](#)

### **LILRB2 (ILT4, LIR-2, MIR-10)**

MIR-10: [AF004231](#)

ILT4 clone 1: [AF000574](#)

ILT4 clone 26: [AF011565](#) = clone 17 (splice variant of cl26): [AF011566](#)

MIR-10: [NM\\_005874](#), [AF025528](#)

LIR-2v1: [AF283986](#)

LIR-2v2: [AF283987](#)

Crystal structure: (209).

LocusLink: [10288](#)

### **LILRB3 (ILT5, LIR-3)**

LIR3v1: [AF025533](#)

HL9: [U91928](#) = [NM\\_006864](#) (LIR-3, LILRB3)

cl16: [AF000575](#)

cl17.1: [AF009632](#)

cl17.11: [AF009633](#)

cl17.6: [AF009634](#)

cl17.7: [AF009635](#)

cl17.8: [AF009636](#)

cl19: [AF009637](#)

cl22: [AF009638](#)

cl31: [AF009639](#)

cl33: [AF009640](#)

cl36: [AF009641](#)

cl40: [AF009642](#)

cl6: [AF009643](#)

*Box 1 continues on next page...*

*Box 1 continued from previous page.*

cl41: [AF009644](#)

cl DC.1: [AF031553](#)

cl17.18: [AF031554](#)

cl17.23: [AF031555](#)

cl17.3: [AF031556](#)

LocusLink: 11025

### **LILRB4 (ILT3, LIR-5, HM18)**

LIR-5: [AF025532](#)

ILT3: [U82979](#)

ILT3v1: [AF072099](#) (genetic sequence)

LILRB4: [NM\\_006847](#) = [U91925](#) (hm18)

LIR-5v1: [AF283988](#)

[BC026309](#)

?extra codon in [U89279](#) and [AF283988](#)

LocusLink: 11006

### **LILRB5 (LIR-8)**

[AF025534](#) = [NM\\_006840](#)

[BC025704](#) (synonymous)

LocusLink: 10990

### **ILT8**

[AF041262](#) = [NM\\_024318](#)

(+ [BC041708](#) ?)

LocusLink: 79168

### **ILT9p**

[AF072102](#)

LocusLink: 79167

### **ILT10**

[AF072100](#)

LocusLink: 79166

*Box 1 continues on next page...*

Box 1 continued from previous page.

## ILT11

AF212842

LocusLink: 58534

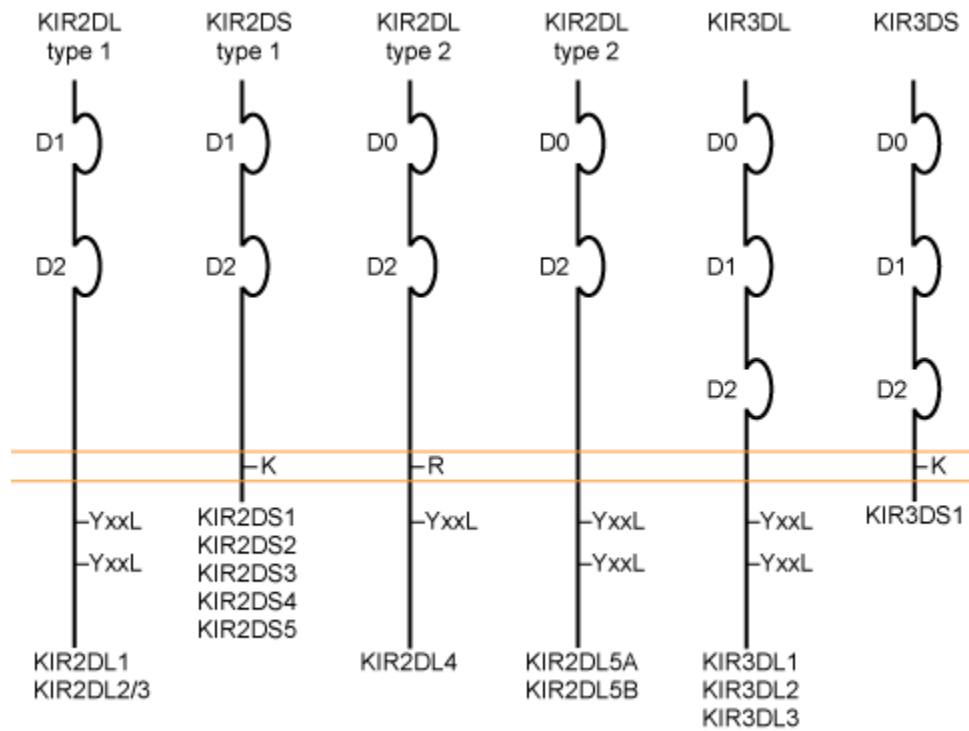
## KIR Nomenclature

About 14 expressed *KIR* genes have been identified (Table 2) and two systems have been generated for naming them. The most commonly used nomenclature system accounts for their protein structure and consists of four major subdivisions based on two features: the number of extracellular Ig domains (2D or 3D) and characteristics of the cytoplasmic tail (Figure 2) (see [PROW](#) and/or the [HUGO-endorsed](#) nomenclatures). They have also been named according to the CD nomenclature system as CD158a, CD158b, etc., based on an approximate centromeric–telomeric order of the genes on chromosome 19 (50). Unfortunately, the CD nomenclature does not reflect structure, function, expression or localization (51). This system also presents the possibility of confusion with the monoclonal antibodies, CD158a and CD158b, since each binds to several different KIR molecules. The CD nomenclature is not used routinely, and the Human Genome Organization (HUGO) nomenclature system will be used throughout this report.

Irrespective of the number of Ig subunits, the cytoplasmic domain of KIR are either long (designated "L") or short ("S"). KIR with long cytoplasmic domains are inhibitory by virtue of the immunoreceptor tyrosine-based inhibition motifs (ITIMs) present in their cytoplasmic domains. Short-tailed KIR transmit activating signals through their interaction with the adaptor molecule, DAP-12 (DNAX activation protein of 12kD; this molecule is also known as killer cell activating receptor-associated protein or KARAP), which contains immunoreceptor tyrosine-based activation motifs (ITAMs) (52, 53). DAP-12 is also a member of the immunoglobulin superfamily and is encoded at the centromeric end of the *LRC*. ITIMs and ITAMs are characteristic of several immunologically important receptors, such as CD5, CD22 and FcγRII (54).

Two *KIR* pseudogenes (*2DP* or *3DP*) have been identified (Table 2): *2DP1*, which shares high sequence similarity with two-domain *KIR* genes, and *3DP1*, which is similar to *3DL3* in portions of the gene, but may represent an ancestral *KIR* gene. The pseudogenes have been given various names in the literature, and an alias key and Accession numbers are provided at ([www.gene.ucl.ac.uk/nomenclature/genefamily/kir.html](http://www.gene.ucl.ac.uk/nomenclature/genefamily/kir.html)).

Allelic variation has been observed for most of the *KIR* genes and names for alleles at several of the most polymorphic loci have been specified based on nomenclature used for *HLA* loci (25, 55). The nomenclature for allelic variants is not complete, but a report that goes some way toward addressing this issue is now available (215).



**Figure 2. Domain structure of the KIR molecules.** KIR genes are members of the Ig-superfamily and express molecules with either two or three extracellular Ig-like domains. The cytoplasmic domains of the inhibitory receptors contain ITIM (I/VxYxxL/V) sequences, whereas a charged amino acid residue, which facilitates interaction with the adaptor molecule [DAP12/KARAP](#), is located in the transmembrane of the activating receptors. [KIR2DL4](#) contains signature sequences of both activating and inhibitory receptors.

**Table 2. KIR gene names.**

Symbol	Name	Aliases	Accession no. *	No. of alleles	Reference
<a href="#">KIR2DL1</a>	killer cell immunoglobulin-like receptor, two domains, long cytoplasmic tail, 1	cl-42, nkat1, 47.11, p58.1, CD158a	<a href="#">L41267</a>	10	(81, 82)
<a href="#">KIR2DL2</a>	killer cell immunoglobulin-like receptor, two domains, long cytoplasmic tail, 2	cl-43, nkat6, CD158b1	<a href="#">L76669</a>	5	(82, 85)
<a href="#">KIR2DL3</a>	killer cell immunoglobulin-like receptor, two domains, long cytoplasmic tail, 3	cl-6, nkat2, nkat2a, nkat2b, p58, CD158b2	<a href="#">L41268</a>	10	(81, 82)
<a href="#">KIR2DL4</a>	killer cell immunoglobulin-like receptor, two domains, long cytoplasmic tail, 4	103AS, 15.212, CD158d	<a href="#">X97229</a>	18	(181, 210)
<a href="#">KIR2DL5A</a>	killer cell immunoglobulin-like receptor, two domains, long cytoplasmic tail, 5A	KIR2DL5.1, CD158f	<a href="#">AF217485</a>		(75, 76)
<a href="#">KIR2DL5B</a>	killer cell immunoglobulin-like receptor, two domains, long cytoplasmic tail, 5B	KIR2DL5.2, KIR2DL5.3, KIR2DL5.4	<a href="#">AF217486</a>		(75, 76)
<a href="#">KIR2DS1</a>	killer cell immunoglobulin-like receptor, two domains, short cytoplasmic tail, 1	EB6ActI, EB6ActII, CD158h	<a href="#">X89892</a>	4	(210)
<a href="#">KIR2DS2</a>	killer cell immunoglobulin-like receptor, two domains, short cytoplasmic tail, 2	cl-49, nkat5, 183ActI, CD158j	<a href="#">L76667</a>	8	(82, 85)
<a href="#">KIR2DS3</a>	killer cell immunoglobulin-like receptor, two domains, short cytoplasmic tail, 3	nkat7	<a href="#">L76670</a>	3	(85)
<a href="#">KIR2DS4</a>	killer cell immunoglobulin-like receptor, two domains, short cytoplasmic tail, 4	cl-39, KKA3, nkat8, CD158i	<a href="#">L76671</a>	9	(85, 213)

Table 2 continued from previous page.

Symbol	Name	Aliases	Accession no. *	No. of alleles	Reference
<a href="#">KIR2DS5</a>	killer cell immunoglobulin-like receptor, two domains, short cytoplasmic tail, 5	nkat9, CD158g	<a href="#">L76672</a>	3	(85)
KIR2DP1	killer cell immunoglobulin-like receptor, two domains, pseudogene 1	KIRZ, KIRY, KIR15, KIR2DL6	<a href="#">AF204908</a>	?	(75)
<a href="#">KIR3DL1</a>	killer cell immunoglobulin-like receptor, three domains, long cytoplasmic tail, 1	cl-2, NKB1, cl-11, nkat3, NKB1B, AMB11, KIR, CD158e1	<a href="#">L41269</a>	22	(81)
<a href="#">KIR3DL2</a>	killer cell immunoglobulin-like receptor, three domains, long cytoplasmic tail, 2	cl-5, nkat4, nkat4a, nkat4b, CD158k	<a href="#">L41270</a>	20	(81)
<a href="#">KIR3DL3</a>	killer cell immunoglobulin-like receptor, three domains, long cytoplasmic tail, 3	KIRC1, KIR3DL7, KIR44, CD158z	<a href="#">AF352324</a>	7	(27)
<a href="#">KIR3DS1</a>	killer cell immunoglobulin-like receptor, three domains, short cytoplasmic tail, 1	nkat10, CD158e2	<a href="#">L76661</a>	6	(85)
KIR3DP1	killer cell immunoglobulin-like receptor, three domains, pseudogene 1	KIRX, KIR48, KIR2DS6, KIR3DS2P, CD158c	<a href="#">AF204919</a>	4	(75)

\* Some of these sequences have not been confirmed in a second study.

## KIR Gene Sequences

Well over 100 *KIR* sequences have been deposited into either the EMBL or GenBank nucleotide sequence databases. A number of the entries are partial cDNA or genomic sequences and some are identical to a portion of the full-length version. We have generated an alignment of the full-length cDNA sequences (Box 2). Accession numbers of these sequences are provided in Table 2. Each unassigned *KIR* sequence identified in GenBank was designated as an allele of a specific *KIR* gene if it differed by <2% from the consensus sequence of that *KIR* gene (42, 56).

### Box 2. Alignment of full-length KIR cDNA sequences.

All *KIR* sequences deposited in GenBank were included in this alignment, some of which have not been confirmed in a second study. When identical sequences were deposited, the longest was used here. *KIR* sequences that were not assigned to a particular *KIR* gene were designated as alleles of a specific *KIR* gene if they differed by <2% from the consensus sequence of that gene. A curated alignment of confirmed *KIR* sequences can be found at <http://www.ebi.ac.uk/ipd/kir>

Key: - identity with consensus sequence; . gap; \* deletion. Note: AY059417 is a hybrid of 3DL1 and 3DL2.

Downloads: alignment ([text](#)); ([PDF](#)); sequences ([fasta](#)); consensus ([text](#)).

```

1 100 2d11_u24078  .-----c-
                               -t-----t- -----t ----- t-----
-----
                               -----
2d11_ac011501  ..... ..-----t-
                               -----t ----- t-----
-----
                               ----- 2d11_af285431 .....c- -t-----t-
                               -----t ----- t-----
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                               ----- 2d11_l41267 .....- -t-----t-

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Box 2 continues on next page...



Box 2 continued from previous page.

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-----t ----- t-----
-----
----- 2d11_u24076 .....c- c-t-g-cgt-
-----t ----- t--t-----
-----
----- 2d11_af022045 .....
..... ---- t-----
-----
----- 2d11_af135560 .....
.....
...
..... 2d11_af285432 .....
.....
...
kirg2_af001885-8 .....
.....
...
kir221_af133901
.....
...
2ds1_al133414 .....
.----- ----- -c-----
-----
----- 2ds1_x98858 .....
..... ----
-----
----- 2ds1_x89892 .....
.----- ----- -c-----
-----
----- 2ds1_af285437 .....
.....
...
.----- ----- 2d12_u24075 .....
..... -a-a-----
-----
----- 2d12_al133414 .....
..... -a-a-----
-----
----- 2d12_l76669 .....
..... -a-a-----
-----
----- 2d12_af285433 .....
.....
...
.----- ----- 2d12_af285434 .....
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.----- ----- 2ds2_al133414 .....
..----- -a-a-----
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----- 2ds2_l41347 .....
..----- -a-a-----
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Box 2 continues on next page...

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----- 2ds2_x89893 .....
.....
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-----g- 2ds2_af285439 .....
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----- 2ds2_af285438 .....
.....
...
.----- kir2d_aj002102 .....
.....c-
-----
----- kir2d_aj002103 .....
.....
-----
----- kir2d_aj002105 .....
.....
-----
----- 2d13_u97173-80 .-----
-----t-----
-----
          2d13_af082936-9 .-----a-
a-----
-----t-----
          2d13_af022048
-----
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2d13_af285435 .....
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.....-a-a-----t--
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----- 2d13_176663 .....
.....-a-a-----t--
-----
----- 2d13_u73395 .....
.-----a-a-----
-----
----- 2d13_u96190 .....
.....
...
..... kir412_af134312-6 .-----
-----a-a-----
-----t-----
kircl23_af133896-900 .....
.....
...
          2ds3_x97231 ctgagcta--
--t-----t-----c-----a-----

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Box 2 continues on next page...

Box 2 continued from previous page.

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a--
----- g-----
2ds3_af022047 .....
.....
-----
-----g----- 2ds3_176670 .....
.....
-----
-----g----- 2ds4_ac011501 .....
-----a-- t-----
-----
----- 2ds4_af215832 .....
.....
...
..... 2ds4_aj417555 .....
.....
-----
----- 2ds4_af002255 .-----t--
-----a-- t-----
-----
----- 2ds4_176671 .....
.....a-- t-----
-----
----- 2ds4_af285440 .....
.....a-- t-----
-----
----- 2ds4_x94609 .-----
-----a-- t-----
-----
----- 2ds4_u96188 .....
.....
...
..... 2ds4_af082961 .....
.....
...
..... 2ds4_aj417554 .....
.....
-----
----- 2ds5_al133414 .....
.....a-----
c----
----- 2ds5_af272389 .....
.....
c----
----- 2ds5_176672 .....
.....t--- a-----
c----
----- 2d14_bc028137 *****
***agaa-t g-ac-tgt- -----a-c- -c---a-- t-c---a-- -
c-----
-----gac- --a-t-tg-- 2d14_af285436 *****
***agaa-t g-ac-tgt- -----a-c- -c---a-- t-c---a-- -
c-----
-----gac- --a-t-tg-- 2d14_af002980 *****
***agaa-t g-ac-tgt- -----a-c- -c---a-- t-c---a-- -

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

c-----
-----gac- --a-t-tg-- 2d14_u71199 *****
***agaa--t g-ac--tgt- -----a-c- -c---a--- t-c---a-- -
c-----
-----gac- --a-t-tg-- 2d14_x97229 *****
***..... -tgt- -----a-c- -c---a--- t-c---a-- -
c-----
-----gac- --a-t-tg-- 2d14_ac011501 *****
***..... -tgt- -----a-c- -c---a--- t-c---a-- -
c-----
-----gac- --a-t-tg-- 2d14_al133414 *****
***..... .c--tgt- -----a-c- -c---a--- t-c---a-- -
c-----
-----gac- --a-t-tg-- 2d14_af002979 *****
***..... -tgt- -----a-c- -c---a--- t-c---a-- -
c-----
-----gac- --a-t-tg-- 2d14_af276292 *****
***..... -tgt- -----a-c- -c---a--- t-c---a-- -
c-----
-----gac- --a-t-tg-- 2d14_ay052496 *****
***.....
..... 2d14_ay052498 *****
***.....
..... 2d14_af002256 *****
***..... -tgt- -----a-c- -c---a--- t-c---a-- -
c-----
-----gac- --a-t-tg-- 2d14_af034772 *****
***..... -tgt- -----a-c- -c---a--- t-c---a-- -
c-----
-----gac- --a-t-tg-- 2d14_af034771 *****
***..... -tgt- -----a-c- -c---a--- t-c---a-- -
c-----
-----gac- --a-t-tg-- 2d14_x99480 *****
***..... -tgt- -----a-c- -c---a--- t-c---a-- -
c-----
-----gac- --a-t-tg-- kir2d1_x99481 *****
***..... -tgt- -----a-c- -c---a--- t-c---a-- -
c-----
-----gac- --a-t-tg-- kirg9p_af110032-5 *****
***..... -tgt- -----a-c- -c---a--- t-c---a-- -
tg--
kir2d1_y13054 *****
***** ***..... -tgt- -----a-c- -c---a--- t-c---
a--
-c----- -gac- --a-t-tg-- 2d15_af217486 .-----
-----t-
-----
----- 2d15_af204903 .-----
-----a-----
----- 2d15_af260138-41 .-----t-

```

Box 2 continues on next page...



Box 2 continued from previous page.

```

                                3dl1_af208688
                                .....
...
                                .....
3dl1_af208689 .....
                                .....
...
                                ..... 3dl1_af262968 .....
                                .....
...
                                ..... 3dl1_af262969 .....
                                .....
...
                                ..... ..a----g- 3dl1_af262970 .....
                                .....
...
                                ..... 3dl1_af262971 .....
                                .....
...
                                ..... 3dl1_af262972 .....
                                .....
...
                                ..... 3dl1_af262973 .....
                                ..... .----t----
-----
                                -----g-c- --a----g- 3dl1_af262974 .....
                                ..... .----t----
-----
                                -----g-c- --a----g-
3dl_af105231-9 .....
                                ..... .----t---- -----g-c- --
a----g-
                                3dl_x97230 .....
                                ..... .-----
-----
                                -----g -----g-c- --a----g-
3ds1_aj417558 .....
                                .....
...
                                ..... ..a----g- 3ds1_176661 .....
                                ..... -----
-----g
                                -----g-c- --a----g- 3ds1_af022044 .....
                                ..... -----t----
-----g
                                -----g-c- --a----g- 3ds1_al133414 .....
                                ..... -----t----
-----g
                                -----g-c- --a----g- 3ds1_u73396 .....
                                ..... -----
-----g
                                -----g-c- --a----g- 3ds1_x97233 .....
                                ..... -----
-----g
                                -----g-c- --a----g- 3dl2_x93595 ..... .-----t

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

----- -c-----
c-----
----- 3d12_ay059418 .....
.....
..... 3d12_ay059419 .....
.....
..... 3d12_ay059420 .....
.....
..... 3d12_141270 .....
----- -c-----
c-----
----- 3d12_al133414 .....
----- -ct-----
c-----
----- 3d12_176665 .....
----- -c-----
c-----
----- 3d12_176666 .....
----- -c-----
c-----
----- 3d12_u30272 .....
----- -ct-----
c-----
----- 3d12_x93596 .....
----- -c-----
c-----
----- 3d12_af262966 .....
.....
..... 3d12_af262965 .....
.....
..... 3d12_af263617 .....
----- -c-----
c-----
-----
3d12_af082963-7 .....
.....
..... 3d12_af208683 .....
.....
3d12_af208684 .....
.....
..... 3d12_af208685 .....
.....
..... 3d12_af208686 .....
.....
.....

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

..... 3d12_af208687 .....
.....
...
..... 3d12_aj276125 .....
..... -ct-----
c-----
----- kircl_ac006293 .-----a----
-----
-----g ----c---- kircl_af072407-10 .-----a----
-----g ----
c----
          kircl_af352324
          .....-----
-----g ----c----
3d13_al133414 .....
-----
-----g ----c---- 3d13_ay083462 .....
.....
...
          kir44b_af204912-14
          .....
          .....g ----c----
kirx_af082931-5 .....
.....
          kirz_ac006293
          .....-----
c-----
----- kir15_af204906-8
-----
-----
kiry_af082940-7 .....
-----
          kirx_al133414
          .....-t-
-----
kirx_ac011501 .....-t-
*****
          ***** kir48_af204918-20
          .....
...
          .....
kir222_af133901 ..ctgagct-
-----
*****
          ***** kir411_af134311-2 .....

```

Box 2 continues on next page...



Box 2 continued from previous page.

```

...
.....
..... Consensus -CTGAGCTGG
GGCGCGGCCG CCTGTCTGCA CCGGCAGCAC
      CATGTCGCTC ATGGTCGTCA GCATGGCGTG TGTTGGGTTT TTCTTGCTGC
      AGGGGGCCTG 101 200 2d11_u24078 ----- -.....
.....
...
..... 2d11_ac011501 ----- . -----
----- g----- ----a---c ----- --c-***-- --t----
t--
---a----- t-c-ta--t- 2d11_af285431 ----- -.....
.....
...
..... 2d11_141267 ----- -.....
.....
...
..... 2d11_u24076 ----- -.....
.....
...
..... 2d11_af022045 ----- -.....
.....
...
..... 2d11_af135560 .....
.....
...
..... 2d11_af285432 .....
.....
...
kirg2_af001885-8 .....
.....
..... kir221_af133901
.....
..... 2ds1_al133414
----- -----
----- g----- ----a---c ----- --c-***-- t-t----
t--
---a----- t-c-ta--t- 2ds1_x98858 ----- -.....
.....
...
..... 2ds1_x89892 ----- -.....
.....
...
..... 2ds1_af285437 ----- -.....
.....
...
..... 2d12_u24075 ----- -----
----- g----- -----c t----- --t-***-- --t--c-
t--
----- --c-ta--t- 2d12_al133414 ----- . -----
----- g----- -----c t----- --t-***-- --t--c-
t--

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

----- --c-ta--t- 2d12_176669 ----- -.....
.....
...
..... 2d12_af285433 ----- -.....
.....
...
..... 2d12_af285434 ----- -.....
.....
...
..... 2ds2_a1133414 -----
----- g----- -----c t----- --t-***-- --t--c-
t--
----- --c-ta--t- 2ds2_141347 ----- -.....
.....
...
..... 2ds2_x89893 ----- -.....
.....
...
..... 2ds2_af285439 ----- -.....
.....
...
..... 2ds2_af285438 ----- -.....
.....
...
..... kir2d_aj002102 ----- -.....
.....
...
..... kir2d_aj002103 ----- -.....
.....
...
..... kir2d_aj002105 ----- -.....
.....
...
..... 2d13_u97173-80 -----
----- g-----
-----a--c ----- --c-***-- --t---t- --a----- t-c-
ta--t-
      2d13_af082936-9 -----
g-----
-----c t----- --t-***-- --t--c-t- ----- --c-
ta--t-
      2d13_af022048
----- g----- c
t-----
--t-***-- --t--c-t- ----- --c-ta--t- 2d13_af285435
----- -.....
...
..... 2d13_176662 ----- -.....
.....
...
..... 2d13_176663 ----- -.....
.....
...
..... 2d13_u73395 ----- -.....

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

.....
...
..... 2d13_u96190 .....
.....
..... kir412_af134312-6 -----
----- g-----
-----c t----- --t-***-- --t-c-t-- ----- --c-
ta--t-
      kircl23_af133896-900 ..... .----- -----
g-----
-----c t----- --t-***-- --t-c-t-- ----- --c-
ta--t-
      2ds3_x97231 -----
-.....
-..... 2ds3_af022047 -----
.....
..... 2ds3_176670 -----
.....
..... 2ds4_ac011501 -----g--. -----
----- g-t--a-- -----c t----- --c-***a- --
t-----
---a----- --c-aa--t- 2ds4_af215832 ..... .-----
----- g-t--a-- -----c t----- --c-***a- --
t-----
---a----- --c-aa--t- 2ds4_aj417555 -----g--- .....
.....
..... 2ds4_af002255 -----g--- .....
.....
..... 2ds4_176671 -----g--- .....
.....
..... 2ds4_af285440 -----g--- .....
.....
..... 2ds4_x94609 -----g--- .....
.....
..... 2ds4_u96188 .....
.....
..... 2ds4_af082961 .....
.....
..... 2ds4_aj417554 -----g--- .....
.....
..... 2ds5_al133414 -----
----- g-t--a-- -----c t----- --c-***a- --

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

t-----
----- --c-aa--t- 2ds5_af272389 ----- -.....
.....
...
..... 2ds5_176672 ----- -.....
.....
...
..... 2d14_bc028137 -g---c-t- -----
----- -tgc----- ----- --a-----
-----
----- 2d14_af285436 -g---c-t- -----
----- -tgc----- ----- --a-----
-----
----- 2d14_af002980 -g---c-t- -----
----- -tgc----- ----- --a-----
-----
----- 2d14_u71199 -g---c-t- -----
----- -tgc----- ----- --a-----
-----
----- 2d14_x97229 -g---c-t- -----
----- -tgc----- ----- --a-----
-----
----- 2d14_ac011501 -g---c-t- -----
----- -tgc----- ----- --a-----
-----
----- 2d14_al133414 -g---c-t- -----
----- -tgc----- ----- --a-----
-----
----- -g----- 2d14_af002979 -g---c-t- -----
----- -tgc----- ----- --a-----
-----
----- 2d14_af276292 -g---c-t- -----
----- -tgc----- ----- --a-----
-----
----- 2d14_ay052496 .....
.....
...
..... 2d14_ay052498 .....
.....
...
..... 2d14_af002256 -g---c-t- -.....
.....
...
..... 2d14_af034772 -g---c-t- -----
----- -tgc----- ----- --a-----
-----
----- 2d14_af034771 -g---c-t- -----
----- -tgc----- ----- --a-----
-----
----- 2d14_x99480 -g---c-t- -----
----- -tgc----- ----- --a-----
-----
----- kir2d1_x99481 -g---c-t- -.....
.....
...

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

..... kirg9p_af110032-5 -g---c-t- -----
----- -tgc-----
g-----
          kir2dl_y13054 -g---c-t-
----- -tgc-----
a-----
-----a-----
-----g-----
t-----
---t---g --c---t- 2d15_af204903 -a-----
-----g-----
t-----
---t---g --c---t- 2d15_af260138-41 -a-----
-----a----- --t----- --t---g --
          2d15_af217487
-----g-----
----- --t----- --t---g --c---t- 2dlx_af271608 -
-----g-----
---t---g --c---t- 2dlx_af272157 -a----- --a---
-----g-----
---t---g --c---t- 2dlx_af271607 -a----- --a---
-----g-----
---t---g --c---t- 3d11_bc028206 t----cat- -----
-----c-----
-----a----- 3d11_ay059417 .....
-----a-----
-----a----- 3d11_u30274 t----cat- -----
-----a-----
-----a----- 3d11_u31416 t----c-t- -----
-----a----- 3d11_af022049 t----c-t- -----
-----a----- 3d11_u33328 t----c-t- -----
-----a----- 3d11_af103010 t----c-t- -----
-----a----- 3d11_af104848-56 t----c-t- -----
-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

-----a-
                                3d11_af103011
                                t----c-t- -----c -----
-----
-----a- 3d11_af103013
t----c-t- -----
-----
-----a- 3d11_af103012 t----c-t- -----
-----
-----a-
3d11_af082956-9 .....
...
                                3d11_af208688
                                .....
-----
3d11_af208689 .....
-----
-----a- 3d11_af262968 .....
..-a- -----
-----
-----a- 3d11_af262969 t----cat- -----
--a- -----
-----
-----a-a- 3d11_af262970 .....
..-a- -----
-----
-----a-a- 3d11_af262971 .....
..-a- -----
-----
-----a- 3d11_af262972 .....
-----
-----
-----a- 3d11_af262973 t----c-t- -----
-----
-----a- 3d11_af262974 t----c-t- -----
-----
-----a-a- 3d1_af105231-9 t----c-t- -----
-----
-----a-
                                3d1_x97230 t----cat-
-----a- -----
-----
-----a- 3ds1_aj417558 t----cat-
-----
-----
-----a- 3ds1_l76661 t----cat- -----

```

Box 2 continues on next page...



Box 2 continued from previous page.

```

...
3d12_af208683
-----
3d12_af208684 .....
g--
g--
g--
g--
g--
g--
t-----
-----c-----
c----t-
-----t-
-----t-
t-----
...
kirx_af082931-5 .....
...
kirz_ac006293
-----
--c-***-- --t---t- ----- t-c-ta--t- kir15_af204906-8
-----
-----g-----t
-----
--c-***-- --t---t- ----- t-c-ta--t-
kiry_af082940-7 .....
...

```

Box 2 continues on next page...



Box 2 continued from previous page.

```

                                kirx_al133414
-----t-                                -----c-----c
-ga----a- --t--g-- --a----g --c----t- kirx_ac011501
***** *-----
g--                                -----c-----t- -ga----a- --t--
---a----g --c----t- kir48_af204918-20
-a----- -----c-----c -
c-----t-
-ga----a- --t--g-- --a----g --c----t- kir222_af133901
***** *-----
g--                                -----c-----t- -ga----a- --t--
---a----g --c----t- kir411_af134311-2 .....
.....
..... Consensus GCCACATGAG
GGTGGTCAGG ACAAGCCCTT CCTGTCTGCC
                                TGGCCAGCG CTGTGGTGCC TCGAGGAGGA CACGTGACTC TTCGGTGTCA
                                CTATCGTCGT 201 300 2d11_u24078 .....
.....
..... 2d11_ac011501 -----c----gt--
---a-g-- --t--gg-g- ct--c--tga gc--t--aa- -t-----t g-a-
c---c-
tt----- ----- 2d11_af285431 .....
.....
..... 2d11_141267 .....
.....
..... 2d11_u24076 .....
.....
..... 2d11_af022045 .....
.....
..... 2d11_af135560 .....
.....
..... 2d11_af285432 .....
.....
kirg2_af001885-8 .....
.....
                                kir221_af133901
.....
..... 2ds1_al133414
-----c----gt--
---a-g-- --t--gg-g- ct--c--tga gc--t--aa- -t-----t g-a-
c---c-

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

tt----- ----- 2ds1_x98858 .....
.....
...
..... 2ds1_x89892 .....
.....
...
..... 2ds1_af285437 .....
.....
...
..... 2d12_u24075 ----- -c---gt--
-----g--- -gt--gg-g- ct--c--tga gc--t--aa- -----t g-a-
c---c-
tt----- ----- 2d12_al133414 ----- -c---gt--
-----g--- -gt--gg-g- ct--c--tga gc--t--aa- -----t g-a-
c---c-
tt----- ----- 2d12_l76669 .....
.....
...
..... 2d12_af285433 .....
.....
...
..... 2d12_af285434 .....
.....
...
..... 2ds2_al133414 ----- -c---gt--
-----g--- -gt--gg-g- ct--c--tga gc--t--aa- -----t g-a-
c---c-
tt----- ----- 2ds2_l41347 .....
.....
...
..... 2ds2_x89893 .....
.....
...
..... 2ds2_af285439 .....
.....
...
..... 2ds2_af285438 .....
.....
...
..... kir2d_aj002102 .....
.....
...
..... kir2d_aj002103 .....
.....
...
..... kir2d_aj002105 .....
.....
...
a-g--- --t--gg-g-
-----
g-
..... 2d13_u97173-80 ----- -c---gt-- ---
ct--c--tga gc--t--aa- -t-----t g-a-c---c- tt-----
2d13_af082936-9 ----- -c---gt-- ---a-g--- -gt--gg-
ct--c--tga gc-----aa- -----t g-a-c---c- tt-----

```

Box 2 continues on next page...



Box 2 continued from previous page.

```

...
..... 2ds4_x94609 .....
.....
...
..... 2ds4_u96188 .....
.....
...
..... 2ds4_af082961 .....
.....
...
..... 2ds4_aj417554 .....
.....
...
..... 2ds5_al133414 ----- -c---gt--
-----g-t --t-gg-g- ct--c--tga gc--t--aa- -----t g-a-
a---c-
tt----- ----- 2ds5_af272389 .....
.....
...
..... 2ds5_l76672 .....
.....
...
..... 2d14_bc028137 ----- tc---c---
-----ga-- --t-gg-- ct--c--tga gc--t--aa- -----t g-a-c--
t--
-c---ta-- ----- 2d14_af285436 ----- tc---c---
-----ga-- --t-gg-- ct--c--tga gc--t--aa- -----t g-a-c--
t--
-c---ta-- ----- 2d14_af002980 ----- tc---c---
-----ga-- --t-gg-- ct--c--tga gc--t--aa- -----t g-a-c--
t--
-c---ta-- ---c----- 2d14_u71199 ----- tc---c---
-----ga-- --t-gg-- ct--c--tga gc--t--aa- -----t g-a-c--
t--
-c---ta-- ---c----- 2d14_x97229 ----- tc---c---
-----ga-- --t-gg-- ct--c--tga gc--t--aa- -----t g-a-c--
t--
-c---ta-- ----- 2d14_ac011501 ----- tc---c---
-----ga-- --t-gg-- ct--c--tga gc--t--aa- -----t g-a-c--
t--
-c---ta-- ----- 2d14_al133414 ----- tc---c---
-----ga-- --t-gg-- ct--c--tga gc--t--aa- -----t g-a-c--
t--
-c---ta-- ----- 2d14_af002979 ----- tc---c---
-----ga-- --t-gg-- ct--c--tga gc--t--aa- -----t g-a-c--
t--
-c---ta-- ---c----- 2d14_af276292 ----- tc---c---
-----ga-- --t-gg-- ct--c--tga gc--t--aa- -----t g-a-c--
t--
-c---ta-- ----- 2d14_ay052496 .....
.....
...
..... 2d14_ay052498 .....
.....

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

..... 2d14_af002256 .....
.....
...
..... 2d14_af034772 ----- tc---c---
-----ga-- --t--gg--- ct--c--tga gc--t--aa- -----t g-a-c--
t--
-c---ta-- ----- 2d14_af034771 ----- tc---c---
-----ga-- --t--gg--- ct--c--tga gc--t--aa- -----t g-a-c--
t--
-c---ta-- ----- 2d14_x99480 ----- tc---c---
-----ga-- --t--gg--- ct--c--tga gc--t--aa- -----t g-a-c--
t--
-c---ta-- ----- kir2dl_x99481 .....
.....
...
..... kirg9p_af110032-5 ----- tc---c---
-----ga-- --t--gg---
-----
ct--c--tga gc--t--aa- -----t g-a-c--t-- -c---ta--
kir2dl_y13054 -----
tc---c--- -----ga-- --t--gg--- ct--c--tga gcc-t--aa-
-----t
g-a-c--t-- -c---ta-- ----- 2d15_af217486 -----c--
tc---gt--
----- --t--gg-g- ct--c--tga gc--t--aa- -a-----t g-
a----a-
-c----- ----- 2d15_af204903 -----c-- tc---gt--
----- --t--gg-g- ct--c--tga gc--t--aa- -a-----t g-
a----a-
-c----- ----- 2d15_af260138-41 -----c-- tc---gt--
----- --t--gg-g-
ct--c--tga gc--t--aa- -a-----t g-a-----a- -c-----
-----
2d15_af217487
-----c-- tc---gt-- ----- --t--gg-g- ct--c--tga gc--t--
aa-
-a-----t g-a-----a- -c----- ----- 2dlx_af271608
-----c-- tc---gt--
----- --t--gg-g- ct--c--tga gc--t--aa- -a-----t g-
a----a-
-c----- ----- 2dlx_af272157 -----c-- tc---gt--
----- --t--gg-g- ct--c--tga gc--t--aa- -a-----t g-
a----a-
-c----- ----- 2dlx_af271607 -----c-- tc---gt--
----- --t--gg-g- ct--c--tga gc--t--aa- -a-----t g-
a----a-
-c----- ----- 3d11_bc028206 a-----
a----- --a-a---- ac--t--cat ct---tgg- ----- a-g--
g----
--a----a-- -----a 3d11_ay059417 a-----
a----- --a-a---- aca-t--cat ct---tgg- ----- a-
g-----
--a----a-- -----a 3d11_u30274 a-----
a----- --a-a---- aca-t--cat ct---tgg- ----- a-
g-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

--a---a-- -----a 3d11_u31416 a-----
a----- --a-a--- ac--t--cat ct---tgg- ---t----- a-
g-----

--a---a-- -----a 3d11_af022049 a-----
a----- --a-a--- ac--t--cat ct---tgg- ---t----- a-
g-----

--a---a-- -----a 3d11_u33328 a-----
a----- --a-a--- ac--t--cat ct---tgg- ---t----- a-
g-----

--a---a-- -----a 3d11_af103010 a-----
a----- --a-a--- ac--t--cat ct---tgg- ---t----- a-
g-----

--a---a-- -----a 3d11_af104848-56 a-----
a----- --a-a--- ac--t--cat ct---tgg- ---t----- a-g----- --a---a--
-----a

3d11_af103011
a----- --a-a--- ac--t--cat ct---
tgg-
---t----- a-g----- --a---a-- -----a 3d11_af103013
a----- --a-a--- ac--t--cat ct---tgg- ---t----- a-
g-----

--a---a-- -----a 3d11_af103012 a-----
a----- --a-a--- ac--t--cat ct---tgg- ---t----- a-
g-----

--a---a-- -----a
3d11_af082956-9 .....
...

3d11_af208688
a----- --a-a--- ac--t--cat ct---
tgg-
---t----- a-g----- --a---a-- -----a 3d11_af208689
a----- --a-a--- ac--t--cat ct---tgg- ---t----- a-
g-----

--a---a-- -----a 3d11_af262968 a-----
a----- --a-a--- aca-t--cat ct---tgg- ----- a-
g-----

--a---a-- -----a 3d11_af262969 a-----
a----- --a-a--- aca-t--cat ct---tgg- ----- a-
g-----

--a---a-- -----a 3d11_af262970 a-----
a----- --a-a--- aca-t--cat ct---tgg- ----- a-
g-----

--a---a-- -----a 3d11_af262971 a-----
a----- --a-a--- aca-t--cat ct---tgg- ----- a-
g-----

--a---a-- -----a 3d11_af262972 a-----
a----- --a-a--- ac--t--cat ct---tgg- ---t----- a-
g-----

--a---a-- -----a 3d11_af262973 a-----
a----- --a-a--- ac--t--cat ct---tgg- ---t----- a-
g-----

```

Box 2 continues on next page...



Box 2 continued from previous page.

```

g-----
----- 3d12_x93596 -----
----- --a-a-g- ac--t--cat ct----gg- ----- a-
g-----
----- 3d12_af262966 -----
----- --a-a-g- ac--t--cat ct----gg- ----- a-
g-----
----- 3d12_af262965 -----
----- --a-a-g- ac--t--cat ct----gg- ----- a-
g-----
----- 3d12_af263617 -----
----- --a-a-g- ac--t--cat ct----gg- ----- a-
g-----
-----
3d12_af082963-7 .....
...
          3d12_af208683
----- --a-a-g- ac--t--cat ct----
gg-
----- a-g----- 3d12_af208684
-----
----- --a-a-g- ac--t--cat ct----gg- ----- a-
g-----
----- 3d12_af208685 -----
----- --a-a-g- ac--t--cat ct----gg- ----- a-
g-----
----- 3d12_af208686 -----
----- --a-a-g- ac--t--cat ct----gg- ----- a-
g-----
----- 3d12_af208687 -----
----- --a-a-g- ac--t--cat ct----gg- ----- a-
g-----
----- 3d12_aj276125 -----
----- --a-a-g- ac--t--cat ct----gg- ----- a-
g-----
----- kircl_ac006293 -----g -a---gt--
c----- ----g-g- ct--c--tga gc--t--aa- ----- g-a-
c-----
tc----- kircl_af072407-10 -----g -a---gt--
--c----- ----g-g-
ct--c--tga gc--t--aa- ----- g-a-c----- tc-----
-----
          kircl_af352324
-----g -a---gt-- --c----- ----g-g- ct--c--tga gc--t--
aa-
----- g-a-c----- tc----- 3d13_al133414
-----g -a---gt--
--c----- ----g-g- ct--c--tga gc--t--aa- ----- g-a-
c-----
tc----- 3d13_ay083462 .....
...
          kir44b_af204912-14
-----tg -a---gt-- --c----- ----g-g- ct--c--tga gc--t--

```

Box 2 continues on next page...



Box 2 continued from previous page.

```

aa-
kirx_af082931-5 ..... -a---gt-- --c----- ----g-g-
                        ct--c--tga gc--t--aa- ----- g-a-c----- tc-----
-----
                        kirz_ac006293
aa-                      ----- -c---gt-- ---a-g--- --t--gg-g- ct-gca-tga gc--t--
                        -----t g-a----c- tt----- ----kir15_af204906-8
aa-                      ----- -c---gt-- ---a-g--- --t--gg-g- ct-gca-tga gc--t--
                        -----t g-a----c- tt----- ----
kiry_af082940-7 .....
...
                        kirx_al133414
aa-                      -----g -a---gt-- --c----- ----g-g- ct--c--tga gc--t--
                        ---g----- gaa-c-c-g- tt---a--- ----kirx_ac011501
-----g -a---gt--
                        --c----- ----g-g- ct--c--tga gc--t--aa- ---g----- gaa-c-
c-g-
                        tt---a--- ----kir48_af204918-20
                        -----g -a---gt-- --c----- ----g-g- ct--c--tga gc--t--
aa-
                        ---g----- gaa-c-c-g- tt---a--- ----kir222_af133901
-----g -a---gt--
                        --c----- ----g-g- ct--c--tga gc--t--aa- ---g----- gaa-c-
c-g-
                        tt---a--- ----kir411_af134311-2 .....
...
                        ..... Consensus GGGTTTAACA
ATTTTCATGCT GTACAAAGAA GACGG-ATCC
                        --GT-CC--- --TCCAC--C AGAATATTCC -G-AGAGCTT CATCATGGGC
                        CCTGTGACCC 301 400 2d11_u24078 .....
...
                        .....---- 2d11_ac011501 -----c-- -----t
                        -c----- ----a- ----a--- -g----- ----
-----
                        -a----c-- ----2d11_af285431 .....
...
                        .....---- 2d11_l41267 .....
...
                        .....---- 2d11_u24076 .....
...
                        .....---- 2d11_af022045 .....
...
                        .....---- 2d11_af135560 .....

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

...
                .....---- 2d11_af285432 .....
                .....
...
                .....----
kirg2_af001885-8 .....
                .....
...
                kir221_af133901
                .....
...
                ..... 2ds1_al133414
-----c-- -----t
                -c----- -a- -a- -g-----
-----
                -a----c-- ----- 2ds1_x98858 .....
                .....
...
                .....---- 2ds1_x89892 .....
                .....
...
                .....---- 2ds1_af285437 .....
                .....
...
                .....---- 2d12_u24075 -c----*a- -----a---
                .....-a- ----- -g----- -a-----
-----
                -----g-- --t----- 2d12_al133414 -c----*a- -----a---
                .....-a- ----- -g----- -a-----
-----
                -----g-- --t----- 2d12_l76669 .....
                .....
...
                .....---- 2d12_af285433 .....
                .....
...
                .....---- 2d12_af285434 .....
                .....
...
                .....---- 2ds2_al133414 -c----*a- -----a---
                .....-a- ----- -g----- -a-----
-----
                -----g-- --t----- 2ds2_l41347 .....
                .....
...
                .....---- 2ds2_x89893 .....
                .....
...
                .....---- 2ds2_af285439 .....
                .....
...
                .....---- 2ds2_af285438 .....
                .....
...
                .....---- kir2d_aj002102 .....

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

...
kir2d_aj002103
...
kir2d_aj002105
...
2d13_u97173-80 -----c-- -----t -
c----- -----a--
-----a---- -g----- ----- -a----c--
-----
2d13_af082936-9 -c----ca- -----a-- -----
a-
----- -g----- -a----- ----- -g--- ---
t-----
2d13_af022048
-c----ca- -----a-- -----a- ----- -
g-----
-a----- ----- -g--- ---t-----
2d13_af285435 .....
...
2d13_176662 .....
...
2d13_176663 .....
...
2d13_u73395 .....
...
2d13_u96190 .....
...
kir412_af134312-6 -c----ca- -----a--
----- -g----- -a----- ----- -g--- ---
t-----
kircl23_af133896-900 -c----ca- -----a-- -----
-----a-
----- -g----- -a----- ----- -g--- ---
t-----
2ds3_x97231 .....
...
-----t-
2ds3_af022047 .....
...
-----t- 2ds3_176670 .....
...
-----t- 2ds4_ac011501 -gt----- -----t
-----c---- -----a- ----- -g-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

-----
                -----g--- ----- 2ds4_af215832 -gt----- -----t
                -----c--- -----a- ----- -g----- -----
-----
                ----- ..... 2ds4_aj417555 .....
                .....
...
                .....---- 2ds4_af002255 .....
                .....
...
                .....---- 2ds4_l76671 .....
                .....
...
                .....---- 2ds4_af285440 .....
                .....
...
                .....---- 2ds4_x94609 .....
                .....
...
                .....---- 2ds4_u96188 .....
                .....
...
                ..... 2ds4_af082961 .....
                .....
...
                ..... 2ds4_aj417554 .....
                .....
...
                .....---- 2ds5_al133414 -gt----ca- -----t
                -----c--- -----a- ----- -g---g--- -----
-----
                -----g--- -----t- 2ds5_af272389 .....
                .....
...
                .....--t- 2ds5_l76672 .....
                .....
...
                .....--t- 2d14_bc028137 -----c-- -----
                -----a- ---tt----- g----- ---a-----
-----
                -----***** 2d14_af285436 -----c-- -----
                -----a- ---tt----- g----- ---a-----
-----
                -----***** 2d14_af002980 -t----c-- -----
                -----a- ---tt----- g----- ---a-----
-----
                -----***** 2d14_u71199 -t----c-- -----
                -----a- ---tt----- g----- ---a-----
-----
                -----***** 2d14_x97229 -----c-- -----
                -----a- ---tt----- g----- ---a-----
-----
                -----***** 2d14_ac011501 -----c-- -----
                -----a- ---tt----- g----- ---a-----
-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

----- ***** 2d14_al133414 -----c-- -----
-----a- ---tt----- g----- ----a-----
-----
----- ***** 2d14_af002979 -----c-- -----
-----a- ---tt----- g----- ----a-----
-----
----- ***** 2d14_af276292 -----c-- -----a--
-----a- ---tt-g--- g----- ----a-----
-----
----- ***** 2d14_ay052496 .....
.....
...
..... ***** 2d14_ay052498 .....
.....
...
..... ***** 2d14_af002256 .....
.....
...
..... ***** 2d14_af034772 -----c-- -----
-----a- ---tt----- g----- ----a-----
-----
----- ***** 2d14_af034771 -----c-- -----
-----a- ---tt----- g----- ----a-----
-----
----- ***** 2d14_x99480 -----c-- -----
-----a- ---tt----- g----- ----a-----
-----
----- ***** kir2dl_x99481 .....
.....
...
..... ***** kirg9p_af110032-5 -----c-- -----
-----a- ---tt-----
g----- ----a-----
*****
          kir2dl_y13054 -----c--
-----a- ---tt----- g----- ----a-----
-----
----- ***** 2d15_af217486 -t----c--
-----g-g----- -t-a-----
-----g--- ----- ***** 2d15_af204903 -t----c-- -----
-----g----- -t-a----- -a-----
-----g--- ----- ***** 2d15_af260138-41 -t----c-- -----
-----g----- -t-a----- -a----- -----g--- -----
*****
          2d15_af217487
-t----c-- ----- -----g----- -t--
a-----
-a----- ----- ***** 2dlx_af271608 -
-----g-g----- -t-a-----
-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

-----g--- -----**** 2dlx_af272157 -t-----c-- -----
-----g--- -----**** 2dlx_af271607 -t-----c-- -----
-----g--- -----**** 3dl1_bc028206 -----a----
-c-----
a--
-----aa 3dl1_ay059417 -----a----
-c-----
g--
-----aa 3dl1_u30274 -----a----
-c-----
g--
-----aa 3dl1_u31416 -----a----
-c-----
g--
-----aa 3dl1_af022049 -----a----
-c-----
g--
-----aa 3dl1_u33328 -----a----
-c-----
g--
-----aa 3dl1_af103010 -----a----
-c-----
c-----
-----aa 3dl1_af104848-56 -----a----
-----g--
-----aa
3dl1_af103011
-----a---- -c-----
-----g-- -----aa 3dl1_af103013
-c-----
g--
-----aa 3dl1_af103012 -----a----
-c-----
g--
-----aa
3dl1_af082956-9 .....
-----
3dl1_af208688
-----a---- -c-----
-----g-- -----aa 3dl1_af208689
-c-----
g--
-----aa 3dl1_af262968 -----a----
-c-----
g--

```

Box 2 continues on next page...



Box 2 continued from previous page.

```

-----
-----aa 3d12_141270 -----
-----g-- -----t- -----
-----
-----aa 3d12_a1133414 -----
-----g-- -----t- -----a-----
-----
-----aa 3d12_176665 -----
-----g-- -----t- -----
g--
-----aa 3d12_176666 -----
-----g-- -----t- -----
g--
-----aa 3d12_u30272 -----
-----g-- -----t- -----
-----
-----aa 3d12_x93596 -----
-----g-- -----t- -----
g--
-----aa 3d12_af262966 -----
-----g-- -----t- -----a-----
-----
-----aa 3d12_af262965 -----
-----g-- -----t- -----a-----
-----
-----aa 3d12_af263617 -----
-----g-- -----t- -----
-----
-----aa
3d12_af082963-7 .....
-aa
          3d12_af208683
-----g-g-----t-
-----aa 3d12_af208684
-----gg-----t- -----
-----aa 3d12_af208685 -----
-----gg-----t- g-----
-----aa 3d12_af208686 -----
-----gg-----t-t-----
-----aa 3d12_af208687 -----
-----g-----t-----
-----aa 3d12_aj276125 -----
-----g-----t-----
-----aa kircl_ac006293 -----
-----t-ca-----
tg--
-----kircl_af072407-10 -----

```

Box 2 continues on next page...





Box 2 continued from previous page.

```

-----
----- --a----- 2d11_af285431 -----
----- --g----- -----g
-----
----- --a----- 2d11_l41267 -----
-----
----- --a----- 2d11_u24076 -----
-----
----- --a----- 2d11_af022045 -----
----- --g----- -----
-----
----- --a----- 2d11_af135560 -----t---
----- --a----- -----g
-----
----- --a----- 2d11_af285432 -----
----- --g----- -----
-----
----- --a-----
kirg2_af001885-8 .....
...
kir221_af133901
...
..... 2ds1_al133414
-----
----- --g----- -----
-----
----- --a----- 2ds1_x98858 -----
----- --g----- -----
-----
----- --a----- 2ds1_x89892 -----
----- --g----- -----
-----
----- --a----- 2ds1_af285437 -----
----- --g----- -----
-----
----- --a----- 2d12_u24075 -----
----- --g----- -----
-----
-----g----- 2d12_al133414 -----
----- --g----- -----
-----
-----g----- 2d12_l76669 -----
----- --g----- -----
-----
-----g----- 2d12_af285433 -----
-----
-----
-----g-----c----- 2d12_af285434 -----
----- --g----- -----
-----
-----g----- 2ds2_al133414 -----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

-----
-----g----- 2ds2_141347 -----
-----
-----g----- 2ds2_x89893 -----
-----
-----g----- 2ds2_af285439 -----
-----
-----g----- 2ds2_af285438 -----
-----
-----g----- kir2d_aj002102 -----
-----t-----
-----g----- kir2d_aj002103 -----
-----
-----g----- kir2d_aj002105 -----
-----
-----g----- 2d13_u97173-80 -----
-----g-----
c-----
                2d13_af082936-9 -----
-----g-----
c-----
                2d13_af022048
-----g-----
-----g----- 2d13_af285435
-----
-----g-----c----- 2d13_176662 -----
-----
-----g-----c----- 2d13_176663 -----
-----
-----g-----c----- 2d13_u73395 -----
g-----
-----g----- 2d13_u96190 -----
-----
-----g-----c----- kir412_af134312-6 -----
-----a-----
c-----
                kircl23_af133896-900 -----a--

```

Box 2 continues on next page...



Box 2 continued from previous page.

```

*****
***** 2d14_af285436 *****
*****
*****
***** 2d14_af002980 *****
*****
*****
***** 2d14_u71199 *****
*****
*****
***** 2d14_x97229 *****
*****
*****
***** 2d14_ac011501 *****
*****
*****
***** 2d14_al133414 *****
*****
*****
***** 2d14_af002979 *****
*****
*****
***** 2d14_af276292 *****
*****
*****
***** 2d14_ay052496 *****
*****
*****
***** 2d14_ay052498 *****
*****
*****
***** 2d14_af002256 *****
*****
*****
***** 2d14_af034772 *****
*****
*****
***** 2d14_af034771 *****
*****
*****
***** 2d14_x99480 *****
*****
*****
***** kir2d1_x99481 *****
*****
*****
***** kirg9p_af110032-5 *****
*****
*****
***** kir2d1_y13054 *****
*****
*****
***** 2d15_af217486 *****
*****
*****

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

*****
***** 2d15_af204903 *****
*****
*****
***** 2d15_af260138-41 *****
*****
*****
***** 2d15_af217487 *****
*****
***** 2d1x_af271608 *****
*****
***** 2d1x_af272157 *****
*****
***** 2d1x_af271607 *****
*****
***** 3d11_bc028206 -----
----- g----g---
--a----- 3d11_ay059417 -----
----- g----g---
--a----- 3d11_u30274 -----
----- g----g---
--a----- 3d11_u31416 -----
----- g----g---
--a----- 3d11_af022049 -----
----- g----g---
--a----- 3d11_u33328 -----
----- g----g---
--a----- 3d11_af103010 -----
----- g----g---
--a----- 3d11_af104848-56 -----
----- g----g--- --a-----
-----
3d11_af103011 ----- g----
g---
--c----- --a----- 3d11_af103013
----- g----g---
--a----- 3d11_af103012 -----
----- g----g--- --t-----

```

Box 2 continues on next page...



Box 2 continued from previous page.

```

-----
--a----- 3ds1_x97233 -----
-----      g-----g-----
-----
--a----- 3d12_x93595 -----
-----g-----c-----g-----
-----
----- 3d12_ay059418 -----
-----g-----c-----g-----
-----
----- 3d12_ay059419 -----
-----g-----c-----g-----
-----
----- 3d12_ay059420 -----
-----g-----c-----g-----
-----
----- 3d12_141270 -----
-----g-----c-----g-----
-----
----- 3d12_a1133414 -----
-----g-----c-----g-----
-----
----- 3d12_176665 -----
-----g-----c-----g-----
-----
----- 3d12_176666 -----
-----g-----c-----g-----
-----
----- 3d12_u30272 -----
-----g-----c-----g-----
-----
----- 3d12_x93596 -----
-----g-----c-----g-----
-----
----- 3d12_af262966 -----
-----g-----c-----g-----
-----
----- 3d12_af262965 -----
-----g-----c-----g-----
-----
----- 3d12_af263617 -----
-----g-----c-----g-----
-----
-----t----- 3d12_af082963-7 -----
-----g-----c-----g-----.....
-----
3d12_af208683
-----g-----c-----ga-----c-----
-----c----- 3d12_af208684
-----ga-----c-----g-----
-----
3d12_af208685 -----

```

Box 2 continues on next page...



Box 2 continued from previous page.

```

c-----
----- --ga----- c----- g-----
-----
----- 3d12_af208686 -----
----- --ga----- c----- g-----
-----
----- c----- 3d12_af208687 -----
--g----- --ga----- c----- g-----
-----
----- 3d12_aj276125 -----
----- --ga----- c----- g-----
-----
----- kircl_ac006293 -----
----- --g- g- g- -----
-----g--- --g--- kircl_af072407-10 -----
-----g- g- g- -----g- -----
g----
kircl_af352324
-----g- g-----
g--
-----g--- --g--- 3d13_al133414
-----g- g- g-----
-----g--- --g--- 3d13_ay083462 .....
.....
...
..... kir44b_af204912-14
-----g-----
g--
-----g--- --g--- kirx_af082931-5
-----g-----
g----
kirz_ac006293
-----g--- -c----- kir15_af204906-8
-----g--- ----- kiry_af082940-7
-----g-----
c-----
kirx_al133414
-----
----- kirx_ac011501
-----
----- kir48_af204918-20
-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

----- kir222_af133901
-----
----- kir411_af134311-2 .....
.....
..... Consensus CCACAGAAAA
CCTTCCCTCC TGGCCACCC AGGTCCCCTG
      GTGAAATCAG AAGAGACAGT CATCCTGCAA TGTTGGTCAG ATGTCATGTT
      TGAGCACTTC 501 600 2d11_u24078 -----
--t--c-- ----- a-a-----
-----
-----a-- -g----c-- 2d11_ac011501 -----
--t--c-- ----- a-a-----
-----
-----a-- -g----c-- 2d11_af285431 -----
--t--c-- ----- a-a-----
-----
-----a-- -g----c-- 2d11_l41267 -----
--t--c-- ----- a-a-----
-----
-----a-- -g----c-- 2d11_u24076 -----
--t--c-- ----- a-a-----
-----
-----a-- -g----c-- 2d11_af022045 -----
--t--c-- ----- a-a-----
-----
-----a-- -g----c-- 2d11_af135560 -----
--t--c-- ----- a-a-----
-----
-----a-- -g----c-- 2d11_af285432 -----
--t--c-- ----- a-a-----
-----
-----a-- -g----c--
kirg2_af001885-8 .....
.....
..... kir221_af133901
.....
..... 2ds1_al133414
-----
--t--c-- ----- a-a-----
-----
-----a-- -g----a-- 2ds1_x98858 -----
--t--c-- ----- a-a--c-- -----
-----
-----a-- -g----a-- 2ds1_x89892 -----
--t--c-- ----- a-a-----
-----
-----a-- -g----g-- 2ds1_af285437 -----
--t--c-- ----- a-a-----
-----
-----a-- -g----a-- 2d12_u24075 -----a--a

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

--t----- -----a-- ----- --a----- ----- -
a-----
----- 2d12_al133414 ----- --a---a
--t----- -----a-- ----- --a----- ----- -
a-----
----- 2d12_176669 ----- --a---a
--t----- -----a-- ----- --a----- ----- -
a-----
----- 2d12_af285433 ----- c---a---a
--t----- -----a-- ----- --a----- ----- -
-----
-----t--- ----- 2d12_af285434 ----- --a---a
--t----- -----a-- ----- --a----- ----- -
a-----
----- 2ds2_al133414 ----- -----a
--a----- -----a-- ----- --a----- ----- -
-----
----- 2ds2_141347 ----- -----a
--a----- -----a-- ----- --a----- ----- -
-----
----- 2ds2_x89893 ----- -----a
--a----- -----a-- ----- --a----- ----- -
-----
----- 2ds2_af285439 ----- -----a
--a----- -----a-- ----- --a----- ----- -
-----
----- 2ds2_af285438 ----- -----a
--a----- -----a-- ----- --a----- ----- -
-----
----- kir2d_aj002102 ----- -----a
--a----- -----a-- ----- --a----- ----- -
-----
----- kir2d_aj002103 ----- -----a
--a----- -----a-- ----- --a----- ----- -
-----
----- kir2d_aj002105 ----- -----a
--a----- -----a-- ----- --a----- ----- -
-----
-----g----- 2d13_u97173-80 ----- --a---a --
t----- -----a--
-----
----- 2d13_af082936-9 ----- --a---a --t----- -----
a--
----- --a----- ----- -----
-----
----- 2d13_af022048 -----
----- --a---a --t----- ----- -----
a-----
----- ----- 2d13_af285435
----- --a---a
--t----- -----a-- ----- --a----- -----t---
-----
----- 2d13_176662 ----- --a---a
--t----- -----a-- ----- --a----- -----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

-----
--t-----          ----- 2d13_176663 ----- -a-a
-----a-----          ----- -a-----
-----
--t-----          ----- 2d13_u73395 ----- -a-a
-----a-----          ----- -a-----
-----
--t-----          ----- 2d13_u96190 ----- -a-a
-----a-----          ----- -a-----
-----
--t-----          ----- kir412_af134312-6 ----- -a-a
-----a-----          -----
-----
-----a-----          kircl23_af133896-900 ----- -a-a -t-----
-----a-----          ----- -a-----
-----
-----c-----          2ds3_x97231 -----
-----c-----          ----- -c -t -c----- -a-at-----
-----
-----c-----          ----- -g-----g-- 2ds3_af022047 -----
-----c-----          ----- -t -c----- -a-at-----
-----
-----c-----          ----- -g-----g-- 2ds3_176670 ----- -c
-----c-----          ----- -t -c----- -a-at-----
-----
-----c-----          ----- -g-----g-- 2ds4_ac011501 ----- -a
-----c-----          ----- -t -ca----- -a----- -a----- -t-----
-----
-----c-----          ----- -t----- 2ds4_af215832 .....
-----c-----          .....
...
-----c-----          ..... 2ds4_aj417555 ----- -a
-----c-----          ----- -t -ca----- -a----- -a----- -t-----
-----
-----c-----          ----- -t----- 2ds4_af002255 ----- -a
-----c-----          ----- -t -ca----- -a----- -a----- -t-----
-----
-----c-----          ----- -t----- 2ds4_176671 ----- -a
-----c-----          ----- -t -ca----- -a----- -a----- -t-----
-----
-----c-----          ----- -t----- 2ds4_af285440 ----- -a
-----c-----          ----- -t -ca----- -a----- -a----- -t-----
-----
-----c-----          ----- -t----- 2ds4_x94609 ----- -a
-----c-----          ----- -t -ca----- -a----- -a----- -t-----
-----
-----c-----          ----- -t----- 2ds4_u96188 ----- -a
-----c-----          ----- -t -ca----- -a----- -a----- -t-----
-----
-----c-----          ----- -t----- 2ds4_af082961 .....
-----c-----          .....
...

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

..... 2ds4_aj417554 -----a
--t--ca-- -----a-- ----- --a----- -t---
-----
-----t--- ----- 2ds5_al133414 -----c
--t--cc-- ----- --a-at-----
g-----
-----g----ca- 2ds5_af272389 -----c
--t--cc-- ----- --a-at-----
g-----
-----g----ca- 2ds5_l76672 -----c
--t--cc-- ----- --a-at-----
g-----
-----g----ca- 2d14_bc028137 *****
*****
*****
***** 2d14_af285436 *****
*****
*****
***** 2d14_af002980 *****
*****
*****
***** 2d14_u71199 *****
*****
*****
***** 2d14_x97229 *****
*****
*****
***** 2d14_ac011501 *****
*****
*****
***** 2d14_al133414 *****
*****
*****
***** 2d14_af002979 *****
*****
*****
***** 2d14_af276292 *****
*****
*****
***** 2d14_ay052496 *****
*****
*****
***** 2d14_ay052498 *****
*****
*****
***** 2d14_af002256 *****
*****
*****
***** 2d14_af034772 *****
*****
*****
***** 2d14_af034771 *****
*****
*****
***** 2d14_x99480 *****

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

*****
*****
***** kir2dl_x99481 *****
*****
***** kirg9p_af110032-5 *****
*****
***** kir2dl_y13054 *****
*****
***** 2d15_af217486 *****
*****
***** 2d15_af204903 *****
*****
***** 2d15_af260138-41 *****
*****
***** 2d15_af217487 *****
*****
***** 2dlx_af271608 *****
*****
***** 2dlx_af272157 *****
*****
***** 2dlx_af271607 *****
*****
***** 3d11_bc028206 t----- a-----
c----- c-c-ca---- -g-----c- -a----- -----
t--
----- 3d11_ay059417 t----- a-----
c----- c-c-ca---- -g-----c- -a----- -----
t--
----- 3d11_u30274 t----- a-----
c----- c-c-ca---- -g-----c- -a----- -----
t--
----- 3d11_u31416 t----- a-----
c----- c-c-ca---- -g-----c- -a----- -----
t--
----- 3d11_af022049 t----- a-----
c----- c-c-ca---- -g-----c- -a----- -----
t--
----- 3d11_u33328 t----- a-----
c----- c-c-ca---- -g-----c- -a----- -----
t--
----- 3d11_af103010 t----- a-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

t--          c----- c-c-caa--- --g----c- -a----- -----
c----- c-c-caa---          ----- 3d11_af104848-56 t----- a-----
--g----c- -a-----          ----- t-- -----
          3d11_af103011
t----- a----- c----- c-c-caa--- --g----c- -
a-----          ----- t-- ----- 3d11_af103013
t----- a-----
cc----- c-c-caa--- --g----c- -ac----- -----
t--          ----- 3d11_af103012 t----- a-----
c----- c-c-ca--- --g----c- -a----- -----
t--          ----- 3d11_af082956-9 t----- a-----c
tcta-tc--- c-c-c-----
-----c- -a----- -----
          3d11_af208688
t----- a----- c----- c-c-ca--- --g----c- -
a-----          ----- t-- ----- 3d11_af208689
t----- a-----
c----- c-c-ca--- --g----c- -a----- -----
t--          ----- 3d11_af262968 t----- a-----
c----- c-c-ca--- --g----c- -a----- -----
t--          ----- 3d11_af262969 t----- a-----
c----- c-c-ca--- --g----c- -a----- -----
t--          ----- 3d11_af262970 t----- a-----
c----- c-c-ca--- --g----c- -a----- -----
t--          ----- 3d11_af262971 t----- a-----
c----- c-c-ca--- --g----c- -a----- -----
t--          ----- 3d11_af262972 t----- a-----
c----- c-c-ca--- --g----c- -a----- -----
t--          -----t--- ----- 3d11_af262973 t----- a-----
c----- c-c-ca--- --g----c- -a----- -----
t--          ----- 3d11_af262974 t----- a-----
c----- c-c-ca--- --g----c- -a----- -----
t--          ----- 3d1_af105231-9 t----- a-----
c----- c-c-ca--- --g----c- -a----- -----
          3d1_x97230 t-----
a----- c----- c-c-ca--- --g----c- -a-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

----- 3ds1_aj417558 t-----
a-----
c----- c-c-ca--- -g----c- -a----- -----
t--
----- t----- 3ds1_l76661 t----- a---t----
c----- c-c-ca--- -g----c- -a----- -----
t--
----- t----- 3ds1_af022044 t----- a---t----
c----- c-c-ca--- -g----c- -a----- -----
t--
----- t----- 3ds1_al133414 t----- a---t----
c----- c-c-ca--- -g----c- -a----- -----
t--
----- t----- 3ds1_u73396 t----- a---t----
c----- c-c-ca-a-- -g----c- -a----- -----
t--
----- t----- 3ds1_x97233 t----- a---t----
c----- c-c-ca--- -g----c- -a----- -----
t--
----- t----- 3d12_x93595 t----- -----
c--g----- c-c-ca-a-- -g----c- -a----- -----
-----
----- --t----- 3d12_ay059418 t----- -----
c--g----- c-c-ca--- -g----c- -a----- -----
-----
----- --t----- 3d12_ay059419 t----- -----
c--g----- c-c-ca--- -g----c- -a----- -----
-----
----- --t----- 3d12_ay059420 t----- -----
c--g----- c-c-ca-a-- -g----c- -a----- -----
-----
----- --t----- 3d12_l41270 t----- -----
c--g----- c-c-ca--- -g----c- -a----- -----
-----
----- --t----- 3d12_al133414 t----- -----
c--g----- c-c-ca--- -g----c- -a----- -----
-----
----- --t----- 3d12_l76665 t----- -----
c--g----- c-c-ca--- -g----c- -a----- -----
-----
----- --t----- 3d12_l76666 t----- -----
c--g----- c-c-ca-a-- -g----c- -a----- -----
-----
----- --t----- 3d12_u30272 t----- ----t----
c--g----- c-c-ca--- -g----c- -a----- -----
-----
----- --t----- 3d12_x93596 t----- -----
c--g----- c-c-ca-a-- -g----c- -a----- -----
-----
----- --t----- 3d12_af262966 t----- -----
c--g----- c-c-ca--- -g----c- -a----- -----
-----
----- --t----- 3d12_af262965 t----- -----
c--g----- c-c-ca--- -g----c- -a----- -----
-----

```

Box 2 continues on next page...



Box 2 continued from previous page.

```

----- ---t----- 3d12_af263617 t-----
c--g----- c-c-ca---- --g-----c- -a-----
-----
c--g----- c-c-ca----          3d12_af082963-7 t-----
--g-----c- -a-----
t-----
          3d12_af208683
t----- c--g----- c-c-ca---- --g-----c- -
a-----
----- 3d12_af208684
t-----
c--g----- c-c-ca---- --g-----c- -a-----
-----
----- ---t----- 3d12_af208685 t-----
c--g----- c-c-ca---- --g-----c- -a-----
-----
----- ---t----- 3d12_af208686 t-----
c--g----- c-c-ca-g- --g-----c- -a-----
-----
----- ---t----- 3d12_af208687 t-----
c--g----- c-c-ca---- --g-----c- -a-----
-----
----- ---t----- 3d12_aj276125 t-----
c--g----- c-c-ca---- --g-----c- -a-----
-----
t-----a          ---t----- kircl_ac006293 -----
ca-g----- c-c----- --g-----c- -----c--- -c-gt---c ---
t-----g--- -----ca- kircl_af072407-10 -----
-----c- -----c--- -c-gt---c ---t-----a t-----g--- -----
          kircl_af352324
c--- ----- ca-g----- c-c----- --g-----c- -----
-----c--- -c-gt---c ---t-----a t-----g--- -----ca- 3d13_al133414
-----
t-----a          ca-g----- c-c----- -----c- -----c--- -c-gt---c ---
...
          3d13_ay083462 .....
          ..... kir44b_af204912-14
c--- ----- ca-g----- c-c----- --g-----c- -----
-----c--- -c-gt---c ---t-----a t-----g--- -----ca- kirx_af082931-5
----- ca-g----- c-c-----
ca- --g-----c- -----c--- -c-gt---c ---t-----a t-----g--- -----
          kirz_ac006293
a----- -----a---a --t---c--- -----a--- --c----- --
-----t----- -----g kir15_af204906-8
-----c a-t---c--- -----a--- --c----- --

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

a-----
-----g kiry_af082940-7
-----a---a --t--c-- -----a--
-----c----- --a----- ----t---- -----
-----g
kirx_al133414
-----a --t--t--- -----c-----
-----g----c-- kirx_ac011501
-----a
--t--t--- -----c-----
-----g----c-- kir48_af204918-20
-----a --t--t--- -----c-----
-----g----c-- kir222_af133901
-----a
--t--t--- -----c-----
-----g----c-- kir411_af134311-2 .....
.....
..... Consensus CTTCTGCACA
GAGAGGGGAT GTCTAAGGAC ACTTTGCGCC
TCATTGGAGA GCTCCATGAT GGGGTCTCCA AGGCCAACTT CTCCATCGGT
CCCATGATGC 601 700 2d11_u24078 -a----g-- -----
-----g-- -----
-----t----- 2d11_ac011501 -a----g-- -----
-----g-- -----
-----t----- 2d11_af285431 -a----g-- -----
-----g-- -----
-----t----- 2d11_141267 -a----g-- -----
-----g-- -----
-----t----- 2d11_u24076 -a----g-- -----
-----g-- -----
-----t----- 2d11_af022045 -a----g-- -----
-----g-- -----
-----t----- 2d11_af135560 -a----g-- -----
-----g-- -----
-----t--c-- 2d11_af285432 -a----g-- -----
-----g-- -----
-----t-----
kirg2_af001885-8 .....
-----
kir221_af133901
.....

```

Box 2 continues on next page...

Box 2 continued from previous page.

```
...
a----g-- -----
..... 2ds1_al133414 -
-----
-----t----- 2ds1_x98858 -a----g-- -----
-----
-----t----- 2ds1_x89892 -a----g-- -----
-----
-----t----- 2ds1_af285437 -a----g-- -----
-----g-----
-----t----- 2d12_u24075 -a----- -----
-----
-----c----- 2d12_al133414 -a----- -----
-----
-----c----- 2d12_l76669 -a----- -----
-----
-----c----- 2d12_af285433 -a----- -----
-----
-----c----- 2d12_af285434 -a----- -----
-----
-----c----- 2ds2_al133414 -a----- -----
-----
-----c----- 2ds2_l41347 -a----- -----
-----
-----c----- 2ds2_x89893 -a----- -----
-----
-----c----- 2ds2_af285439 -a----- -----
-----
-----c----- 2ds2_af285438 -a----- -----
-----
-----c----- kir2d_aj002102 -a----- -----
-----
-----c----- kir2d_aj002103 -a----- -----
-----
-----c----- kir2d_aj002105 -a----- -----
-----
-----c----- 2d13_u97173-80 -a----- -----
```

Box 2 continues on next page...

Box 2 continued from previous page.

```

----- c-
-----
2d13_af082936-9 -a-----
----- c-
-----
2d13_af022048
-a-----
----- c- 2d13_af285435 -
a-----
-----
----- c- 2d13_176662 -a-----
-----
----- c- 2d13_176663 -a-----
-----
----- c- 2d13_u73395 -a-----
-----
----- c- 2d13_u96190 -a-----
-----
----- c- kir412_af134312-6 -a-----
----- c-
----- kircl23_af133896-900 -a-----
----- c-
----- 2ds3_x97231 -a----g--
----- c- -----t-
----- 2ds3_af022047 -a----g--
----- c- -----t-
----- 2ds3_176670 -a----g--
----- c- -----t-
----- 2ds4_ac011501 c--t-----a-----
----- c-
-----g---- --t----- 2ds4_af215832 .....
.....
..... 2ds4_aj417555 c--t-----a-----
----- c-
-----g---- --t----- 2ds4_af002255 c--t-----a-----
----- c-

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

-----g---- ---t----- 2ds4_176671 c--t----- ---a-----
-----c-----

-----g---- ---t----- 2ds4_af285440 c--t---a- ---a-----
-----a-----c-----

-----g---- ---t----- 2ds4_x94609 c--t----- ---a-----
-----c-----

-----g---- ---t----- 2ds4_u96188 c--t----- ---a-----
-----c-----

-----g---- ---t----- 2ds4_af082961 .....
.....

...
..... 2ds4_aj417554 c--t----- ---a-----
-----c-----

-----g---- ---t----- 2ds5_al133414 -a----g-- -----
-----g-----

-----g---- ---t----- 2ds5_af272389 -a----g-- -----
-----g-----

-----g---- ---t----- 2ds5_176672 -a----g-- -----
-----g-----

-----g---- ---t----- 2d14_bc028137 *****
*****

***** ***** 2d14_af285436 *****
*****

***** ***** 2d14_af002980 *****
*****

***** ***** 2d14_u71199 *****
*****

***** ***** 2d14_x97229 *****
*****

***** ***** 2d14_ac011501 *****
*****

***** ***** 2d14_al133414 *****
*****

***** ***** 2d14_af002979 *****
*****

***** ***** 2d14_af276292 *****
*****

***** ***** 2d14_ay052496 *****
*****

```

Box 2 continues on next page...



Box 2 continued from previous page.

```

----- a----- t--
c---
-----g-----c 3d11_u30274 t--c-----
----- a----- t--
c---
-----g-----c 3d11_u31416 t--c-----
----- a----- t--
c---
-----g-----c 3d11_af022049 t--c-----
----- a----- t--
c---
-----g-----c 3d11_u33328 t--c-----
----- a----- t--
c---
-----g-----c 3d11_af103010 t--c-----
----- a----- t--
c---
-----g-----c 3d11_af104848-56 t--c-----
----- a----- t--c--- g
-----c
3d11_af103011
t--c----- a-----
----- t--c--- g-----c 3d11_af103013 t--
----- a----- t--
c-----
-----g-----c 3d11_af103012 t--c-----
----- a----- t--
c---
-----g-----c 3d11_af082956-9 t-----
----- t--c---
-----.....
3d11_af208688
t--c----- a-----
----- t--c--- g-----c 3d11_af208689 t--
----- a-a----- t--
c---
-----g-----c 3d11_af262968 t--c-----
----- a----- t--
c---
-----g---g---c 3d11_af262969 t--c-----
----- a-t----- t--
c---
-----g-----c 3d11_af262970 t--c-----
----- a-t----- t--
c---
-----g-----c 3d11_af262971 t--c-----
----- a-t----- t--
c---
-----g-----c 3d11_af262972 t--c-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

----- a----- t--
c---
-----g -----c 3d11_af262973 t--c-----
----- a----- t--
c---
-----g -----c 3d11_af262974 t--c-----
----- a----- t--
c---
-----g -----c 3d1_af105231-9 t--c-----
----- a----- t--c--- -----g
-----c
3d1_x97230 -a-----
-----
-----c----- 3ds1_aj417558 g--c-----
----- a----- t--
c---
-----g ----- 3ds1_176661 g--c-----
----- a----- t--
c---
-----g ----- 3ds1_af022044 g--c-----
----- a----- t--
c---
-----g ----- 3ds1_al133414 g--c-----
----- a----- t--
c---
-----g ----- 3ds1_u73396 g--c-----
----- a----- t--
c---
-----g ----- 3ds1_x97233 g--c-----
----- a----- t--
c---
-----g ----- 3d12_x93595 c--t----- --a-----
-----t-t-----c-----
c---
-----t-t-----c----- 3d12_ay059418 c--t----- --a-----
-----t-t-----c-----
c---
-----t-t-----c----- 3d12_ay059419 c--t----- --a-----
-----t-t-----c-----
c---
-----t-t-----c----- 3d12_ay059420 c--t----- --a-----
-----t-t-----c-----
c---
-----t-t-----c----- 3d12_141270 c--t----- --a-----
-----t-t-----c-----
c---
-----t-t-----c----- 3d12_al133414 c--t----- --a-----
-----t-t-----c-----
c---
-----t-t-----c----- 3d12_176665 c--t----- --a-----
-----t-t-----c-----
c---

```

Box 2 continues on next page...



Box 2 continued from previous page.

```

----- 3d12_176666 c--t----- ---a-----
----t-t- -----c- -----
c---

----- 3d12_u30272 c--t----- ---a-----
----t-t- -----c- -----
c---

----- 3d12_x93596 c--t----- ---a-----
----t-t- -----c- -----
c---

----- 3d12_af262966 c--t----- ---a-----
----t-t- -----c- -----
c---

----- 3d12_af262965 c--t----- ---a-----
----t-t- -----c- -----
c---

----- 3d12_af263617 c--t----- ---a-----
----t-t- -----c- -----
c---

----- 3d12_af082963-7 c--t----- ---a-----
-----c-----
-----

          3d12_af208683
c--t----- ---a----- ----t-t- -----c- -----
-----

-----c----- 3d12_af208684 c--
----t-t- -----c- -----
c---

----- 3d12_af208685 c--t----- ---a-----
----t-t- -----c- -----
c---

----- 3d12_af208686 c--t----- -----
----t-t- -----c- -----
c---

----- 3d12_af208687 c--t----- ---a-----
----t-t- -----c- -a-----
c---

----- 3d12_aj276125 c--t----- ---a-----
----t-t- -----c- -----
c---

----- kircl_ac006293 c--c----- -----
-----tt- -----c- ----ta--- --g----- -g-----
-----

-----g --gt----- kircl_af072407-10 c--c----- -----
----ta--- --g----- -g----- -----g --
gt-----

          kircl_af352324
c--c----- -----tt- -----c- ----ta--- ---
g-----
-g----- -----g --gt----- 3d13_al133414 c--
-----tt- -----c- ----ta--- --g----- -g-----
-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

-----g --gt----- 3d13_ay083462 .....
.....
...
.....----- kir44b_af204912-14
c-c----- -----tt- -----c-- ----ta--- ---
g-----
c-c----- -----tt- -----c--
-----ta--- --g----- -g----- -----g --
gt--.....
      kirz_ac006293
-a----g-- -----
*-----
-----c- ----- kir15_af204906-8
-a----g-- -----
*-----
-----c- ----- kiry_af082940-7 -
a----g-- -----
-----c-
-----
      kirx_al133414
-a----- -----c- ---t-----
-----
-----t----- kirx_ac011501 -
-----c- ---t-----
-----
-----t----- kir48_af204918-20
-a----- -----c- ---t-----
-----
-----t----- kir222_af133901 -
-----c- ---t-----
-----
-----t----- kir411_af134311-2 .....
.....
..... Consensus ATGACCTTGC
AGGGACCTAC AGATGCTACG GTTCTGTTAC
      TCACTCCCCC TATCAGTTGT CAGCTCCCAG TGACCCTCTG GACATCGTGA
      TCACAGGTCT 701 800 2d11_u24078 -----
-----t -----t-----t-----
-----
-----t----- 2d11_ac011501 -----
-----t -----t-----t-----
-----
-----t----- 2d11_af285431 -----
-----t -----t-----t-----
-----
-----t----- 2d11_l41267 -----
-----t -----t-----
-----
-----t----- 2d11_u24076 -----
-----t -----t-----
-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

----- 2d11_af022045 -----
-----t-----t-----
-----
----- 2d11_af135560 -----
-----t-----t-----
-----
----- 2d11_af285432 -----
-----t-----t-----
-----
----- kirg2_af001885-8 -----
-----t-----t-----
-----
kir221_af133901
.....
...
..... 2ds1_al133414
-----t-----t-----
-----
----- 2ds1_x98858 -----
-----t-----t-----
-----
----- 2ds1_x89892 -----
-----t-----t-----
-----
----- 2ds1_af285437 -----
-----t-----t-----
-----
----- 2d12_u24075 -----
-----t-----g-----
-----
----- 2d12_al133414 -----
-----t-----g-----
-----
----- 2d12_176669 -----
-----t-----g-----
-----
----- 2d12_af285433 -----
-----t-----g-----
-----
----- 2d12_af285434 -----
-----t-----g-----
-----
----- 2ds2_al133414 -----
-----tt-----g-----
-----
----- 2ds2_141347 -----
-----tt-----g-----
-----
----- 2ds2_x89893 -----
-----tt-----g-----
-----
----- 2ds2_af285439 -----
-----tt-----g-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

-----
----- 2ds2_af285438 -----
----- tt-----g-----
-----
----- kir2d_aj002102 -----
----- ***-----tt-----g-----
-----
----- kir2d_aj002103 -----
----- tt-----g-----
-----
----- kir2d_aj002105 -----
----- tt-----g-----
-----g----- 2d13_u97173-80 -----
-----t-----g-----
-----
----- 2d13_af082936-9 -----
-----t-----g-----
-----
----- 2d13_af022048 -----
-----t-----
g---
----- 2d13_af285435 -----
-----t-----g-----
-----
----- 2d13_176662 -----
-----t-----g-----
-----
----- 2d13_176663 -----
-----t-----g-----
-----
----- 2d13_u73395 -----
-----t-----g-----
-----
----- 2d13_u96190 -----
-----t-----g-----
-----
----- kir412_af134312-6 -----
-----t-----g-----
-----
----- kircl23_af133896-900 -----
-----t-----g-----
-----
----- 2ds3_x97231 -----
-----t-----g-----
-----t----- 2ds3_af022047 -----
-----t-----g-----
-----t-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

----- 2ds3_176670 -----
-----t-----g-----
-----t
----- 2ds4_ac011501 -----
-----t-----
----- 2ds4_af215832 .....
.....
...
..... 2ds4_aj417555 -----
-----t-----
----- 2ds4_af002255 -----
-----t-----
----- 2ds4_176671 -----
-----t-----
----- 2ds4_af285440 -----
-----t--t-----
----- 2ds4_x94609 -----
-----t-----
----- 2ds4_u96188 -----
-----t-----
----- 2ds4_af082961 .....
.....
...
..... 2ds4_aj417554 -----
-----t-----
***
***** ***** 2ds5_al133414 -----
-----t-----g-----
----- 2ds5_af272389 -----
-----t-----t-----
----- 2ds5_176672 -----c
-----t-----g-----
-----g-----g-----ta
-----g-----gc-----
a-----t-----c--- 2d14_af285436 -----g-----ta
-----g-----t-----gc-----
a-----t-----c--- 2d14_af002980 -----g-----ta
-----g-----gca-----
a-----t-----c--- 2d14_u71199 -----g-----ta
-----g-----gca-----
a-----t-----c--- 2d14_x97229 -----g-----ta

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

-----g--- -----gc-----
-----
a-----t -----c--- 2d14_ac011501 -----g--ta
-----g--- -----gc-----
-----
a-----t -----c--- 2d14_al133414 -----g--ta
-----g--- -----gc-----
-----
a-----t -----c--- 2d14_af002979 -----g--ta
-----g--- -----gc-----
-----
a-----t -----c--- 2d14_af276292 -----g--ta
-----g--- -----gc-----
-----
a-----t -----c--- 2d14_ay052496 .....
.....
-----
a-----t -----c--- 2d14_ay052498 .....
.....
-----
a-----t -----c--- 2d14_af002256 -----g--ta
-----g--- -----gc-----
-----
a-----t -----c--- 2d14_af034772 -----g--ta
-----g--- -----gc-----
-----
a-----t -----c--- 2d14_af034771 -----g--ta
-----g--- -----gca---
-----
a-----t -----c--- 2d14_x99480 -----g--ta
-----g--- -----gca---
-----
a-----t -----c--- kir2dl_x99481 -----g--ta
-----g--- -----gc-----
-----
a-----t -----c--- kirg9p_af110032-5 -----g--ta
-----g--- -----gc-----
-----
c---
-----
kir2dl_y13054 -----
-----g--ta -----g--- -----gc-----
-----
-----a-a-----t -----c--- 2d15_af217486 --t--g---
-----gca---
-----a-t -----2d15_af204903 --t--g--- -----a---
-----gca---
-----a-t -----2d15_af260138-41 --t--g--- -----a---
-----gca--- -----a-----a-t
-----
2d15_af217487
--t--g--- -----a-----gca---

```

Box 2 continues on next page...







Box 2 continued from previous page.

```
-----c--- 3d12_ay059419 -----
-----c--- 3d12_ay059420 -----
-----c--- 3d12_141270 -----
-----c--- 3d12_al133414 -----
-----c--- 3d12_176665 -----
-----c--- 3d12_176666 -----
-----c--- 3d12_u30272 -----
-----c--- 3d12_x93596 -----
-----c--- 3d12_af262966 -----
-----c--- 3d12_af262965 -----
-----c--- 3d12_af263617 -----
-----c--- 3d12_af082963-7 -----
-----t-----
c---
3d12_af208683
-----t-----c--- 3d12_af208684
-----c--- 3d12_af208685 -----
-----c--- 3d12_af208686 -----
-----c--- 3d12_af208687 -----
-----c--- 3d12_aj276125 -----
```

Box 2 continues on next page...

Box 2 continued from previous page.

```

t-----t
-----c--- kircl_ac006293 -----g----
-----t-----
-----tg-t -----t--- kircl_af072407-10 -----g----
-----t-----tg-t -----
t---
      kircl_af352324
-----g-----
t--
-----tg-t -----t--- 3dl3_al133414
-----g-----
-----tg-t -----t--- 3dl3_ay083462 -----g----
-----t-----
-----tg-t -----t--- kir44b_af204912-14
-----g-----
t--
-----tg-t -----t---
kirx_af082931-5 .....
...
      kirz_ac006293
-----t-----
g---
-----kir15_af204906-8
-----t-----
g---
-----kiry_af082940-7
-----t-----g-----
-----kirx_al133414
--g-g-----c-----t- --a-----
g---
-----c--- kirx_ac011501 --
g-g-----c-----t- --a-----g-----
-----c--- kir48_af204918-20
--g-g-----c-----t- --a-----
g---
-----c--- kir222_af133901 --
g-g-----c-----t- --a-----g-----
-----c--- kir411_af134311-2 .....
...
..... Consensus ATATGAGAAA
CCTTCTCTCT CAGCCAGCC GGGCCCCACG
      GTTCAGGCAG GAGAGAACGT GACCTTGTCC TGCAGCTCCC GGAGCTCCTA

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

                TGACATGTAC 801 900 2d11_u24078 -----a-----
-----g-----
t-----
----- 2d11_ac011501 -----a-----
-----g-----
t-----
----- 2d11_af285431 -----a-----
-----g-----
t-----
----- 2d11_l41267 -----a-----
-----g-----
t-----
----- 2d11_u24076 -----a-----
-----g-----
t-----
----- 2d11_af022045 -----a-----
-----g-a-----
a-----
----- 2d11_af135560 -----a-----
-----g-----g-gca-----
-----
----- 2d11_af285432 -----a-----
-----g-----
t-----
----- kirg2_af001885-8 -----a-----
-----g-----t-----
-----
                kir221_af133901
.....
...
-----a-----
-----g-a-----
a-----
----- 2ds1_x98858 -----a-----
-----g-a-----
a-----
----- 2ds1_x89892 -----a-----
-----g-a-----
a-----
----- 2ds1_af285437 -----a-----
-----g-a-----
a-----
----- 2d12_u24075 -----
-----t-t-t-----g-----
-----
----- 2d12_al133414 -----
-----t-t-t-----g-----
-----
----- 2d12_l76669 -----
-----t-t-t-----g-----
-----
----- 2d12_af285433 -----
-----t-t-t-----g-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

-----
-----a----- 2d12_af285434 -----
----- t----t--t -----g--- -----
-----
----- 2ds2_a1133414 -----
----- -----t--t -----g--- -----
-----
----- 2ds2_141347 -----
----- -----t--t -----g--- -----
-----
----- 2ds2_x89893 -----
----- -----t--t -----g--- -----
-----
----- 2ds2_af285439 -----
----- -----t--t -----g--- -----
-----
----- 2ds2_af285438 -----
----- -----t--t -----g--- -----
-----
----- kir2d_aj002102 -----
----- --g-t--t -----g--- -----
-----
----- kir2d_aj002103 -----
----- -----t--t -----g--- -----
-----
----- kir2d_aj002105 -----a-----
----- -----t--t -----g---g-----
-----
----- 2d13_u97173-80 -----
----- -----t--t -----g--- -----t-----
-----
----- 2d13_af082936-9 -----t-----
----- -----g--- -----
-----
----- 2d13_af022048 -----t--t -----g---
-----
----- 2d13_af285435 -----
----- -----t--t -----g--- -----
-----
----- 2d13_176662 -----
----- -----t--t -----g--- -----
-----
----- 2d13_176663 -----
----- -----t--t -----g--- -----
-----
----- 2d13_u73395 -----
----- -----t--t -----g--- -----
-----
----- 2d13_u96190 -----
----- -----t--t -----g--- -----
-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

----- kir412_af134312-6 -----
-----t--t-----
-----g-----
-----
kircl23_af133896-900 -----
-----t--t-----
-----g-----
-----
2ds3_x97231 -----
c-----t--t-----g-----
-----
----- 2ds3_af022047 -----
-----t--t-----g-----
-----
----- 2ds3_176670 ----- c-----
-----t--t-----g-----
-----
----- 2ds4_ac011501 -----a-----
-----g--gca-----
-----
----- 2ds4_af215832 .....
.....
...
..... 2ds4_aj417555 -----a-----
-----g--gca-----
-----
----- 2ds4_af002255 -----a-----
-----g--gca-----
-----
----- 2ds4_176671 -----
-----g--gca-----
-----
----- 2ds4_af285440 -----
-----g--gca--c-----
-----
----- 2ds4_x94609 -----a-----
-----g--gca-----
-----
----- 2ds4_u96188 -----a-----
-----g--gca-----
-----
----- 2ds4_af082961 .....
.....
...
..... 2ds4_aj417554 -----a-----
-----g--gca-----
-----
----- 2ds5_al133414 -----a-----
-----g-----a-----
-----
-----a----- 2ds5_af272389 -----a-----
-----g-----
-----
-----a----- 2ds5_176672 -----a-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

-----c
-----g-----a-----
-----a----- 2d14_bc028137 -----
a----- -t----- --gca---t -----
-----
c-----t ----- 2d14_af285436 -----
a----- -t----- --gca---t -----
-----
c-----t ----- 2d14_af002980 -----
a----- -t----- --gca---t -----
-----
c-----t ----- 2d14_u71199 -----
a----- -t----- --gca---t -----
-----
c-----t ----- 2d14_x97229 -----a-----
a----- -t----- --gca---t -----
-----
c-----t ----- 2d14_ac011501 -----
a----- -t----- --gca---t -----
-----
c-----t ----- 2d14_al133414 -----
a----- -t----- --gca---t -----
-----
c-----t ----- 2d14_af002979 -----
a----- -t----- --gca---t -----
-----
c-----t ----- 2d14_af276292 -----
a----- -t----- --gca---t -----
-----
c-----t ----- 2d14_ay052496 -----a-----
a----- -t----- --gca---t -----
-----
c-----t ----- 2d14_ay052498 -----
a----- -t----- --gca---t -----
-----
c-----t ----- 2d14_af002256 -----
a----- -t----- --gca---t -----
g-----
c-----t ----- 2d14_af034772 -----
a----- -t----- --gca---t -----
-----
c-----t ----- 2d14_af034771 -----
a----- -t----- --gca---t -----
-----
c-----t ----- 2d14_x99480 -----a-----
a----- -t----- --gca---t -----
-----
c-----t ----- kir2d1_x99481 -----a-----
a----- -t----- --gca---t -----
-----
c-----t ----- kirg9p_af110032-5 -----
a----- -t-----
----- --gca---t ----- c-----t
-----
kir2d1_y13054 -----

```

Box 2 continues on next page...







Box 2 continued from previous page.

```

c----- 3ds1_a1133414 -----g
a-----  -----g ----- a----- a--
t--

c----- 3ds1_u73396 -----g
a-----  -----g ----- a----- a--
t--

c----- 3ds1_x97233 -----g
a-----  -----g ----- a----- a--
t--

c----- 3d12_x93595 -----g----- a-----
-----  -----g----- a-----
a-----

----- 3d12_ay059418 -----g----- a-----
-----  -----g----- a-----
a-----

----- 3d12_ay059419 -----g----- a-----
-----  -----g----- a-----
a-----

----- 3d12_ay059420 -----g----- a-----
-----  -----g----- a-----
a-----

----- 3d12_141270 -----g----- a-----
-----  -----g----- a-----
a-----

----- 3d12_a1133414 -----g----- a-----
-----  -----g----- a-----
a-----

----- 3d12_176665 -----g----- a-----
-----  -----g----- a-----
a-----

----- 3d12_176666 -----g----- a-----
-----  -----g----- a-----
a-----

----- 3d12_u30272 -----g----- a-----
-----  -----g----- a-----
a-----

----- 3d12_x93596 -----g----- a-----
-----  -----g----- a-----
a-----

----- 3d12_af262966 -----g----- a-----
-----  -----g----- a-----
a-----

----- 3d12_af262965 -----g----- a-----
-----  -----g----- a-----
a-----

----- 3d12_af263617 -----g----- a-----
-----  -----g----- a-----
a-----

----- 3d12_af082963-7 -----g----- a-----
-----  -----g----- a-----
g----- a----- a----- *-----

-----
3d12_af208683
-----g----- a----- -----g-----
-----

```

Box 2 continues on next page...



Box 2 continued from previous page.

```

a----          ---t----- -t---t--- -----t -----c---- -----
-----kir48_af204918-20
-----a----- ---t----- -t---t--- -----
-----t-----
-----c---- ----a---- -----kir222_af133901
-----a-----
a----          ---t----- -t---t--- -----a--- -----t-----c---- -----
-----kir411_af134311-2 .....
...
..... Consensus CATCTATCCA
GGGAGGGGGA GGCCCATGAA CGTAGGCTCC
          CTGCAGTGCC CAAGGTCAAC GGAACATTCC AGGCCGACTT TCCTCTGGGC
          CCTGCCACCC 901 1000 2d11_u24078 -----
-----a----- --a----- -----g- a-----
-----2d11_ac011501 -----
-----a----- --a----- -----g- a-----
-----2d11_af285431 -----
-----a----- --a----- -----g- a-----
-----2d11_l41267 -----
-----a----- --a----- -----g- a-----
-----2d11_u24076 -----
-----a----- --a----- -----g- a-----
-----2d11_af022045 -t-----
-----a----- --a----- -----g- a-----
-----2d11_af135560 -----
-----a----- --a----- -----g- a-----
-----..... 2d11_af285432 -----
-----a----- --a----- -----g- a-----
-----a-----
-----a----- --g- a-----
-----kir221_af133901
.....
..... 2ds1_al133414 -
t-----
-----a-----
-----2ds1_x98858 -t-----
-----a----- --g- a-----
-----2ds1_x89892 -t-----
-----a----- --g- a-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

-----
----- 2ds1_af285437 -t-----
----- --a-----g- a-----
-----
----- 2d12_u24075 -----a--
----- --a-----
-----
-----t-- ----- 2d12_al133414 -----a--
----- --a-----
-----
----- 2d12_l76669 -----a--
----- --a-----
-----
-----t-- ----- 2d12_af285433 -----a-- g-----
----- --a-----
-----
----- 2d12_af285434 -----a--
----- --a-----
-----
----- 2ds2_al133414 -----a--
----- -----t-----
-----
----- 2ds2_l41347 -----a--
----- -----t-----
-----
----- 2ds2_x89893 -----a--
----- -----t-----
-----
----- 2ds2_af285439 -----a--
----- -----t-----
-----
----- 2ds2_af285438 -----a--
----- -----t-----
-----
----- kir2d_aj002102 -----a--
----- -----t-----
-----
----- kir2d_aj002103 -----a--
----- -----t-----
-----
----- kir2d_aj002105 -----a--
----- -----t-----
-----
----- ..... 2d13_u97173-80 -----a--
-----
-----
----- 2d13_af082936-9 -----a--
-----
-----a-----
-----
----- 2d13_af022048
-----
-----
----- 2d13_af285435

```

Box 2 continues on next page...



Box 2 continued from previous page.

```

-----          -----g- -----          -----t--
-----          ..... 2ds4_af082961 .....
.....
.....          ..... 2ds4_aj417554 -----t--
-----          -----g- -----          -----t--
-----          --c----- 2ds5_al133414 -----          -----
-----          -----a-----g- a-----
-----          -----t---- 2ds5_af272389 -----          -----
-----          -----a-----g- a-----
-----          -----t---- 2ds5_l76672 -----g- -----
-----          -----a-----g- a-----
-----          -----t---- 2d14_bc028137 -----a--- -----
-----          --a-ga- -----g-c -----
c----
-----          ----- 2d14_af285436 -----a--- -----
-----          --a-ga- -----g-c -----
c----
-----          ----- 2d14_af002980 -----a--- -----
-----          --a-ga- -----g-g -----
c----
-----          ----- 2d14_u71199 -----a--- -----
-----          --a-ga- -----g-g -----
c----
-----          ----- 2d14_x97229 -----a--- -----
-----          --a-ga- -----g-c -----
c----
-----          ----- 2d14_ac011501 -----a--- -----
-----          --a-ga- -----g-c -----
c----
-----          ----- 2d14_al133414 -----a--- -----
-----          --a-ga- -----g-c -----
c----
-----          ----- 2d14_af002979 -----a--- -----
-----          --a-ga- -----g-c -----
c----
-----          ----- 2d14_af276292 -----a--- -----
-----          --a-ga- -----g-c -----
c----
-----          ----- 2d14_ay052496 -----a--- -----
-----          --a-ga- -----g-c -----
c----
-----          ----- 2d14_ay052498 -----a--- -----
-----          --a-ga- -----g-c -----
c----
-----          ----- 2d14_af002256 -----a--- -----
-----          --a-ga- -----g-c -----
c----
-----          ----- 2d14_af034772 -----a--- -----
-----          --a-ga- -----g-c -----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

c----
----- 2d14_af034771 -----a---
----- a-ga- -----g-g -----
c----
----- 2d14_x99480 -----a---
----- a-ga- -----a -----g-g -----
c----
----- kir2d1_x99481 -----a---
----- a-ga- -----g-c -----
c----
----- ..... kirg9p_af110032-5 -----a---
----- a-ga- -----g-c -----c-----
-----
kir2d1_y13054 -----a---
----- a-ga- -----g-c -----
a----
-----c----- 2d15_af217486 -----
-----c-----
---a---c ---a----- a---t--- -----g-c -----
-----t----- 2d15_af204903 -----c-----
-----c ---a----- a---t--- -----g-c -----
-----t----- 2d15_af260138-41 -----c-----
-----c ---a-----
...
2d15_af217487
-----c-----c ---a----- a---t--- -----
g-c
-----c-----
---a---c ---a----- a---t--- -----g-c -----
-----t----- 2d1x_af272157 -----c-----
---a---c ---a----- a---t--- -----g-c -----
-----t----- 2d1x_af271607 -----c-----
---a---c ---a----- a---t--- -----g-c -----
-----t----- 3d11_bc028206 -----
-----c----- -----g-c -----
-----c----- 3d11_ay059417 -----
-t-----c----- -t---g-c -a-----
-----c----- 3d11_u30274 -----
-----c----- -----g-c -----
-----c----- 3d11_u31416 -----
-----c----- -----g-c -----
-----c----- 3d11_af022049 -----
-----c----- -----g-c -----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

-----
----- 3d11_u33328 -----
----- -c- -----g-c-----
-----
----- ..... 3d11_af103010 -----
----- -c- -----g-c-----
-----
----- 3d11_af104848-56 -----
----- -g-c-----
-----
----- 3d11_af103011 -----
----- -c- -----
g-c-----
----- 3d11_af103013 -----
----- -c- -----g-c-----
-----
----- 3d11_af103012 -----
----- -c- -----g-c-----t--
-----
----- 3d11_af082956-9 -----
----- .....
...
----- 3d11_af208688 -----
----- -c- -----
g-c-----
----- ..... 3d11_af208689 -----
----- -a-----
----- -c- -----g-c-----
a-----
----- ..... 3d11_af262968 -----
----- -c- -----g-c-----
-----
----- 3d11_af262969 -----
--t----- -c- -----t-g-c-----
-----
----- 3d11_af262970 -----
--t----- -c- -----t-g-c-----
-----
----- 3d11_af262971 -----
--t----- -c- -----t-g-c-----
-----
----- 3d11_af262972 -----
----- -t-c----- -t-g-c-----
-----
----- 3d11_af262973 -----
----- -c- -----g-c-----
-----
----- 3d11_af262974 -----
----- -c- -----g-c-----
-----
----- 3d11_af105231-9 -----
----- -c-----

```

Box 2 continues on next page...



Box 2 continued from previous page.

```

----- g--c -----
-----
3d1_x97230 -----a--
----- a-----
-----
----- 3ds1_aj417558 -----
----- c--- -----g--c -----
-----
----- 3ds1_176661 -----
----- c--- -----g--c -----
-----
----- 3ds1_af022044 -----
----- c--- -----g--c -----
-----
----- 3ds1_al133414 -----
----- c--- -----g--c -----
-----
----- 3ds1_u73396 -----
----- c--- -----g--c -----
-----
----- 3ds1_x97233 -----
----- c--- -----g--c -----
-----
----- 3d12_x93595 -----
----- c-ct g---g--t- ----- a-----
-----
----- 3d12_ay059418 -----
----- c-ct g---g--t- ----- a-----
-----
----- 3d12_ay059419 -----
----- c-ct g---g--t- ----- a-----
-----
----- 3d12_ay059420 -----
----- c-ct g---g--t- ----- a-----
-----
----- 3d12_141270 -----
----- c-ct g---g--t- ----- a-----
-----
----- 3d12_al133414 -----
----- c-ct g---g--t- ----- a-----
-----
----- ..... 3d12_176665 -----
----- c-ct g---g--t- ----- a-----
-----
----- 3d12_176666 -----
----- c-ct g---g--t- ----- a-----
-----
----- 3d12_u30272 -----
----- c-ct g---g--t- ----- a-----
-----
----- 3d12_x93596 -----
----- c-ct g---g--t- ----- a-----
-----
----- ..... 3d12_af262966 -----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

----- -c-ct g---g-t- ----- -a-----
-----
----- 3d12_af262965 -----
----- -c-ct g---g-t- ----- -a-----
-----
----- 3d12_af263617 -----
----- -a-c-ct g---g-t- ----- -a-----
-----
----- 3d12_af082963-7
-----c-ct
g---g-t- ----- -a-----
-----
----- 3d12_af208683
----- -c-ct g---g-t-
-----
----- -a----- 3d12_af208684
-----
----- -c-ct g---g-t- ----- -a-----
-----
----- 3d12_af208685 -----
----- -c-ct g---g-t- ----- -a-c-----
-----
----- 3d12_af208686 -----
----- -c-ct g---g-t- ----- -a-----
-----
----- 3d12_af208687 -----
----- -c-ct g---g-t- ----- -a-----
-----
----- 3d12_aj276125 -----
----- -c-ct g---g-t- ----- -a-----
-----
----- kircl_ac006293 -----a -----
----- -c-ct g--c--c- -----g-c -----
cc---
-----* ***** kircl_af072407-10 -----a -----
-----c-ct
g--c--c- -----g-c -----cc--- -----*
*****
----- kircl_af352324
-----a ----- -c-ct g--c--c- -----
g--c
-----cc--- ----- ***** 3d13_al133414
-----a -----
----- -c-ct g--c--c- -----g-c -----
cc---
----- ***** 3d13_ay083462 -----
----- -c-ct g--c--c- -----g-c -----
cc---
----- ***** kir44b_af204912-14
-----a -----
-----
----- *****
kirx_af082931-5 .....
*****

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

kirz_ac006293
-----a-----
-----
-----kir15_af204906-8
-----a-----
-----
-----kiry_af082940-7
-----
-----
kirx_al133414
-----
g--c
tt-----*****kirx_ac011501
-----g--c tt-----
-----*****kir48_af204918-20
-----
-----*****kir222_af133901
-----g--c tt-----
-----*****kir411_af134311-2
-----
...
-----Consensus ACGGAGGGAC
CTACAGATGC TTCGGCTCTT TCCGTGACTC
TCCCTACGAG TGGTCAAAC TCGAGTGACCC ACTGCTTGTT TCTGTCACAG
GAAACCCTTC 1001 1100 2d11_u24078 --a-----
-----g-----c-----a-----
-----.. 2d11_ac011501 --a-----
-----c-----c-----a-----
-----.. 2d11_af285431 --a-----
-----c-----c-----a-----
-----.. 2d11_l41267 --a-----
-----c-----c-----a-----
-----.. 2d11_u24076 --a-----
-----c-----c-----a-----
-----.. 2d11_af022045 --a-----
-----g--c-----c-----a-----
-----.. 2d11_af135560
-----
...
-----2d11_af285432 --a-----
-----c-----c-----a-----
-----.. kirg2_af001885-8 --a-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

-----c
-----c -----a-----
-----..
kir221_af133901
--a-----c-----c
-----
-a-----.. 2ds1_al133414 --
a-----
-----g---c -----a--t-----
-----
-----aa-- --ct----- 2ds1_x98858 --a-----
-----g---c -----a--t-----
-----
-----aa-- --ct----- 2ds1_x89892 --a-----
-----g---c -----a--t-----
-----
-----aa-- --ct----- 2ds1_af285437 --a-----
-----c-----a--t-----
-----
-----aa-- --ct----- 2d12_u24075 --a-----
-----t---c -----c-----a-----
-----
-----.. 2d12_al133414 --a-----
-----t---c -----c-----a-----
-----
-----.. 2d12_176669 --a-----
-----t---c -----c-----a-----
-----
-----.. 2d12_af285433 --a-----
-----g---c -----c-----a-----
-----
-----.. 2d12_af285434 --a-----
-----t---c -----c-----a-----
-----
-----.. 2ds2_al133414 --a-----
-----c-----t-----
-----
-----aa-- --ct----- 2ds2_141347 --a-----
-----c-----t-----
-----
-----aa-- --ct----- 2ds2_x89893 --a-----
-----c-----t-----
-----
-----aa-- --ct----- 2ds2_af285439 --a-----
-----c-----a-----
-----
-----aac-- --ct----- 2ds2_af285438 --a-----
-----g---c -----
-----
-----aa-- --ct----- kir2d_aj002102 --a-----
-----c-----t--- --t-----c-----
-----
----- --c---tg-t kir2d_aj002103 --a-----
-----c-----t--- --t-----c-----
-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

----- --c---tg-t kir2d_aj002105 .....
..... .-----t--- --t----- --c-----
-----
----- --c---tg-t 2d13_u97173-80 --a----- -t-----
----- ----g----c
----- t-----
-----t-
          2d13_af082936-9 --a----- ----g----
c
----- t-----
-----t-
          2d13_af022048
--a----- ----g----c -----
-----
t----- ----t- 2d13_af285435 --
a-----
----- ----g----c ----- t-----
-----
-----t- 2d13_176662 --a----- -t-----
----- ----g----c ----- t-----
-----
-----t- 2d13_176663 --a-----
----- ----g----c ----- t-----
-----
-----t- 2d13_u73395 --a-----
----- ----g----c ----- t----- t-----
-----
-----t- 2d13_u96190 .....
.....
...
kir412_af134312-6 .....
.....
...
          kircl23_af133896-900 --a----- ----
g----c
----- t-----
-----t-
          2ds3_x97231 --a-----
----- ----c----- ----a--
-----
-----aac- --ct----- 2ds3_af022047 --a-----
----- ----c----- ----a--
-----
-----aac- --ct----- 2ds3_176670 --a-----
----- ----c----- ----a--
-----
-----aac- --ct----- 2ds4_ac011501 --a-----
----- ----c----- ----a-- t-----
-----
-----aa- --ct----- 2ds4_af215832 .....
.....
...
          2ds4_aj417555 --a-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

-----c -----a-- t-----
-----aa-- --ct----- 2ds4_af002255 --a-----
-----c -----a-- t-----
-----aa-- --ct----- 2ds4_176671 --a-----
-----c -----a-- t-----
-----aa-- --ct----- 2ds4_af285440 --a-----
-----c -----a-- t-----
-----aa-- --ct----- 2ds4_x94609 --a-----
-----c -----a-- t-----
-----aa-- --ct----- 2ds4_u96188 .....
.....
...
..... 2ds4_af082961 .....
.....
...
..... 2ds4_aj417554 --a-----
-----c -----a-- t-----
-----aa-- --ct----- 2ds5_al133414 --a-----
-----g--c -----a-----
-----aac-- --ct----- 2ds5_af272389 --a-----
-----g--c -----a-----
-----aac-- --ct----- 2ds5_176672 --a-----
-----g--c -----a-----
-----aac-- --ct----- 2d14_bc028137 t-----
-----t----- --t-g-- --t-c-g-- a--
ta-----
---c----- -----t--- 2d14_af285436 t-----
-a----- --t----- --t-g-- --t-c-g-- a--
ta-----
---c----- -----t----- 2d14_af002980 t-----
-a----- --t----- --t-g-- --t-c-g-- a--
ta-----
---c----- -----t----- 2d14_u71199 t-----
-a----- --t----- --t-g-- --t-c-g-- a--
ta-----
---c----- -----t----- 2d14_x97229 t-----
-----t----- --t-g-- --t-c-g-- a--
ta-----
---c----- -----t--- 2d14_ac011501 t-----
-----t----- --t-g-- --t-c-g-- a--
ta-----
---c----- -----t--- 2d14_al133414 t-----
-----t----- --t-g-- --t-c-g-- a--
ta-----
---c----- -----t----- 2d14_af002979 t-----
-a----- --t----- --t-g-- --t-c-g-- a--

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

ta-----
                ---c----- ----- 2d14_af276292 t-----
                ----- --t----- ----t-g-- ----- t-c-g---- a--
ta-----
                ---c----- -----t--- 2d14_ay052496 t-----
                ----- --t----- ----t-g-- ----- t-c-g---- a--
ta-----
                ---c----- -----t--- 2d14_ay052498 t-----
                ----- --t----- ----t-g-- ----- t-c-g---- a--
ta-----
                ---c----- ----- 2d14_af002256 t-----
                ----- --t-----
-.....
                ..... 2d14_af034772 t-----
                ----- --t----- ----t-g-- ----- t-c-g---- a--
ta-----
                ---c----- -----t--- 2d14_af034771 t-----
                ----- --t----- ----t-g-- ----- t-c-g---- a--
ta-----
                ---c----- ----- 2d14_x99480 t-----
                ----- --t----- ----t-g-- ----- t-c-g---- a--
ta-----
                ---c----- -----t--- kir2dl_x99481 .....
                .....
...
                ..... kirg9p_af110032-5 t-----c
----- --t-----
                ----t-g-- ----- t-c-g---- a-ta---- ---c-----
t---
                kir2dl_y13054 t-----
                ----- --t-----
-.....
                ..... 2d15_af217486 -----ca
t-----
                ----- --t-g-- ----- -a-----
-----
                ---ct-----t- 2d15_af204903 -----ca t-----
                ----- --t-g-- ----- -a-----
-----
                ---ct-----t-
2d15_af260138-41 .....
                .....
...
                2d15_af217487
                -----ca t----- --t-g--
-----
                -a----- --ct-----t- 2dlx_af271608
-----ca t-----
                ----- --t-g-- ----- -a-----
-----
                ---ct-----t- 2dlx_af272157 -----ca t-----
                ----- --t-g-- ----- -a-----
-----
                ---ct-----t- 2dlx_af271607 -----ca t-----
                ----- --t-g-- ----- -a-----

```

Box 2 continues on next page...





Box 2 continued from previous page.

```

-----
-----t- 3d11_af262971 -----
-a-----t- ----- -a-----
-----
-----t- 3d11_af262972 -----
-a-----t- ----- -a-----
-----
-----t- 3d11_af262973 -----
-a-----t- -----
-----
-----t- 3d11_af262974 -----
-a-----t- ----- -a-----
-----
-----t- 3d1_af105231-9 -----
a-----t--
-----t-
-----
t-----
-----g---c -----
-----t- 3ds1_aj417558 -----
-a-----t- -----t- ----- -a-----
-----aa-- --ct----- 3ds1_l76661 -----
-a-----t- -----t- ----- -a-----
-----aa-- --ct----- 3ds1_af022044 -----
-a-----t- -----t- ----- -a-----
-----aa-- --ct----- 3ds1_al133414 -----
-a-----t- -----t- ----- -a-----
-----aa-- --ct----- 3ds1_u73396 -----
-a-----t- -----t- ----- -a-----
-----aa-- --ct----- 3ds1_x97233 -----
-a-----t- -----t- ----- -a-----
-----aa-- --ct----- 3d12_x93595 -----
-a-----t- ----t-tg-- ----- t-----
-----t- -----t- 3d12_ay059418 -----
-a-----t- ----t-tg-- ----- t-----
-----t- -----t- 3d12_ay059419 -----
-a-----t- ----t-tg-- ----- t-----
-----t- -----t- 3d12_ay059420 -----
-a-----t- ----t-tg-- ----- t-----
-----t- -----t- 3d12_l41270 -----
-a-----t- ----t-tg-- ----- t-----
-----t- -----t- 3d12_al133414 .....

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

...
.....
3d12_176665 -----
-a----- -t- -t-tg- -t-----
-----
-----t- -----t- 3d12_176666 -----
-a----- -t- -t-tg- -t-----
-----
-----t- -----t- 3d12_u30272 -----
-a----- -t- -t-tg- -t-----
-----
-----t- -----t- 3d12_x93596 .....
..... .-t-tg- -t-----
-----
-----t- -----t- 3d12_af262966 -----
-a----- -t- -t-tg- -t-----
-----
-----t- -----t- 3d12_af262965 -----
-a----- -t- -t-tg- -t-----
-----
-----t- -----t- 3d12_af263617 -----
-a----- -t- -t-tg- -t-----
-----
-----t- -----t-
3d12_af082963-7 .....
...
3d12_af208683
.....
3d12_af208684 .....
...
3d12_af208685 .....
...
3d12_af208686 .....
...
3d12_af208687 .....
...
3d12_aj276125 -----
-a----- -t- -t-tg- -t-----
-----
-----t- -----t- kircl_ac006293 *****
***** -t- -----
----- -c--tg-t kircl_af072407-10 *****
*****
-----t- --a----- ----- -c--
tg-t
kircl_af352324
***** ***** .-t- --

```

Box 2 continues on next page...



Box 2 continued from previous page.

```

----- *-- --g-----
t-----a-
-----c ---t--c--- 2d11_u24076 .-----
----- *-- --g-----
t-----a-
-----c ---t--c--- 2d11_af022045 .-----
---t----- *-- --g-----
t-----a-
-----c ---t--c--- 2d11_af135560 .....
.....
...
..... 2d11_af285432 .-----
----- *-- --g-----
t-----
-----c ---t--c--- kirg2_af001885-8 .-----
-----
-----t----- --g----- -----t-----a-----c---t---
c---
      kir221_af133901
g----
-----t-----a-----c----- 2ds1_al133414
-----g----- *-----
-----c--- 2ds1_x98858 -----
-----g----- *-----
-----c--- 2ds1_x89892 -----
-----g----- *-----
-----c--- 2ds1_af285437 -----
-----g----- *-----
-----c--- 2d12_u24075 .-----
----- *-- --g-----
t-----
-----c ---t--c--- 2d12_al133414 .-----
----- *-- --g-----
t-----
-----c ---t--cc--- 2d12_176669 .-----
----- *-- --g-----
t-----
-----c -----c--- 2d12_af285433 .-----
----- *-----
t-----a-
-----c ---t--tc--- 2d12_af285434 .-----
----- *-- --g-----
t-----
-----c ---t--c--- 2ds2_al133414 -----
-----
*... ..
..... 2ds2_141347 -----
----- *-----
-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

-----c--- 2ds2_x89893 -----
-----*-- -----
-----c--- 2ds2_af285439 -----
-----g-- -at-----g-----
g----
-----c--- 2ds2_af285438 -----
-----*-- -----
-----c--- kir2d_aj002102 -----
-----tg-----*-- -----
-----c--- kir2d_aj002103 -----
-----tg-----*-- -----
-----c--- kir2d_aj002105 -----
-----tg-----*-- -----
-----c--- 2d13_u97173-80 c-----
-----*-- -t-----
-----g-----
-----c--- 2d13_af082936-9 c-----
-----*-- -t-----
-----c--- 2d13_af022048 -----
c-----g-----*--
t-----
-----c----- 2d13_af285435
-----g-----*-- -t-----
-----c--- 2d13_176662 c-----
-----g-----*-- -t-----
-----c--- 2d13_176663 c-----
-----g-----*-- -t-----
-----c--- 2d13_u73395 c-----
-----g-----*-- -t-----
-----c--- 2d13_u96190 .....
...
kir412_af134312-6 .....
...
-----c--- kircl23_af133896-900 c-----
-----*-- -t-----
-----c--- 2ds3_x97231 -----
-----g-----*-- -at-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

-----g-
-----g-----g----- 2ds3_af022047 -----
-----
-----g-----*-- -at-----g-----
g----
----- 2ds3_176670 -----
-----g-----*-- -at-----g-----
g----
----- 2ds4_ac011501 -----
-----g-----*-- -----
-----
-----c--- 2ds4_af215832 .....
.....
...
..... 2ds4_aj417555 -----
-----g-----*-- -----
-----
-----c--- 2ds4_af002255 -----
-----g-----*-- -----
-----
-----c--- 2ds4_176671 -----
-----g-----*-- -----
-----
-----c--- 2ds4_af285440 -----
-----g-----*-- -----
-----
-----c--- 2ds4_x94609 -----
-----g-----*-- -----
-----
-----c--- 2ds4_u96188 .....
.....
...
..... 2ds4_af082961 .....
.....
-----
-----c--- 2ds4_aj417554 -----
-----g-----*-- -----
-----
-----c--- 2ds5_al133414 -----
-----*-- -at-----g-----
g----
----- 2ds5_af272389 -----
-----*-- -at-----g-----
g----
----- 2ds5_176672 -----
-----*-- -at-----g-----
g----
----- 2d14_bc028137 ----t-c-----
-----a-----**-----a-----
g--ac
----- 2d14_af285436 ----t-c-----
-----a-----*-----a-----
g--ac
----- 2d14_af002980 ----c-----
-----a-----**-----a-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

g--ac
----- 2d14_u71199 -----c--
-----a- -----*g-- -----a-
g--ac
----- 2d14_x97229 -----t-c--
-----a- -----*-- -----a-
g--ac
----- 2d14_ac011501 -----t-c--
-----a- -----*g-- -----a-
g--ac
----- 2d14_al133414 -----t-c--
-----a- -----*-- -----a-
g--ac
----- 2d14_af002979 -----t-c--
-----a- -----*-- -----a-
g--ac
----- 2d14_af276292 -----t-c--
-----a- -----**-- -----a-
g--ac
----- 2d14_ay052496 -----t-c--
-----a- -----*-- -----a-
g--ac
-----... 2d14_ay052498 -----t-c--
-----a- -----*-- -----a-
g--ac
-----... 2d14_af002256 .....
..... -----a-
g--ac
----- 2d14_af034772 -----t-c--
-----a- -----*-- -----a-
g--ac
----- 2d14_af034771 -----t-c--
-----a- -----*-- -----a-
g--ac
----- 2d14_x99480 -----t-c--
-----a- -----*-- -----a-
g--ac
----- kir2dl_x99481 .....
..... -----a-
g--ac
----- kirg9p_af110032-5 -----t-c--
-----a- -----*-- -----a- -----g-ac
-----
kir2dl_y13054 .....
..... -----a-
a-----
-----g-ac ----- 2d15_af217486 -----t---
-----
---t---c -----*g-- -----
c---g
----- 2d15_af204903 -----t---
---t---c -----*g-- -----
c---g
-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

2d15_af260138-41 .....
...
                2d15_af217487
-----t--- -----t---c -----*g---
-----
-----t--- -----
c---g
-----t---c -----*g--- -----g- ----
----- 2dlx_af271608
c---g
-----t---c -----*g--- -----g- ----
----- 2dlx_af272157 -----t--- -----
c---g
-----t---c -----*g--- -----g- ----
----- 2dlx_af271607 -----t--- -----
c---g
-----t---c -----*g--- -----
----- 3d11_bc028206 c-----
-----t--- -----*-- -----
-----c c----c--- 3d11_ay059417 c-----
g---g
-----t--- -----*g--- -----
-----t---c--- 3d11_u30274 c-----
-----t--- -----*-- -----
-----c c----c--- 3d11_u31416 c-----
-----t--- -----*-- -----
-----c c----c--- 3d11_af022049 c-----
-----t--- -----*-- -----
-----c c----c--- 3d11_u33328 c-----
-----t--- -----*-- -----
-----c c----c--- 3d11_af103010 c-----
-----t--- -----*-- -----
t-----
-----c c----c--- 3d11_af104848-56 c-----
-----t--- -----
c---
-----*-- -----c c----
                3d11_af103011
c-----t--- -----*--
-----c c----c--- 3d11_af103013
c-----
-----t--- -----*-- -----
-----c c----c--- 3d11_af103012 c-----
-----t--- -----*-- -----
-----c c----t---
3d11_af082956-9 .....
...

```

Box 2 continues on next page...



Box 2 continued from previous page.

```

                                3d11_af208688
                                .....
...
                                .....
3d11_af208689 .....
...
                                .....
                                ..... 3d11_af262968 c-----
-----t----- *-----g-----
-----c c-----c--- 3d11_af262969 c-----
-----t-----a----- *-----
-----c c-----c--- 3d11_af262970 c-----
-----t-----a----- *-----
-----c c-----c--- 3d11_af262971 c-----
-----t----- *-----
-----c c-----c--- 3d11_af262972 c-----
-----t----- *-----
-----c c-----c--- 3d11_af262973 c-----
-----t----- *-----
-----c c-----c--- 3d11_af262974 c-----
-----t----- *-----
-----c c-----c--- 3d1_af105231-9 c-----
-----t-----
----- *-----c c-----
c---
                                3d1_x97230 c-----
-----g----- *-----t-----
-----
----- 3ds1_aj417558 -----
----- *-----
-----**-----c--- 3ds1_l76661 -----
----- *-----
-----**-----c--- 3ds1_af022044 -----
-----
-----**-----c--- 3ds1_al133414 -----
----- *-----
-----**-----c--- 3ds1_u73396 -----
-----
-----**-----c--- 3ds1_x97233 -----
-----
-----**-----c--- 3d12_x93595 c-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

g---g          -t-----  -----  ----*g----  -----  -----  -----
-----  ---t---c--  3d12_ay059418  c-----  -----
-t-----  -----  ----*g----  -----  -----
g---g          -----  ---t---c--  3d12_ay059419  c-----  -----
-t-----  -----  ----*g----  -----  -----
g---g          -----  ---t---c--  3d12_ay059420  c-----  -----
-t-----  -----  ----*g----  -----  -----
g---g          -----  ---t---c--  3d12_l41270  c-----  -----
-t-----  -----  ----*g----  -----  -----
g---g          -----  ---t---c--  3d12_al133414  .....
.....
...
.....  .....  3d12_l76665  c-----  -----
-t-----  -----  ----*g----  -----  -----
g---g          -----  ---t---c--  3d12_l76666  c-----  -----
-t-----  -----  ----*g----  -----  -----
g---g          -----  ---t---c--  3d12_u30272  c-----  -----
-t-----  -----  ----*g----  -----  -----
g---g          -----  ---t---c--  3d12_x93596  c-----  -----
-t-----  -----  ----*g----  -----  -----
g---g          -----  ---t---c--  3d12_af262966  c-----  -----
-t-----  -----  ----*g----  -----  -----
g---g          -----  ---t---c--  3d12_af262965  c-----  -----
-t-----  -----  ----*g----  -----  -----
g---g          -----  ---t---c--  3d12_af263617  c-----  -----
-t-----  -----  ----*g----  -----  -----
g---g          -----  ---t---c--
3d12_af082963-7 .....
c--          .....  -----  -----g--g-----  ---t---
          3d12_af208683
.....
...
3d12_af208684 .....
.....
...          .....  3d12_af208685 .....
.....
...          .....  3d12_af208686 .....
.....
...

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

..... 3d12_af208687 .....
.....
...
..... 3d12_aj276125 c-----
-t----- *g-----
g---g
----- --t--c-- kircl_ac006293 -----
----- -tg----- *g----- -t-----
----- kircl_af072407-10 -----
----- -tg-----
----- *g----- -t-----
----- kircl_af352324 -----
----- -tg----- *g-----
t-----
----- 3d13_al133414 -----
----- -tg----- *g----- -t-----
----- 3d13_ay083462 .....
.....
...
..... kir44b_af204912-14 .....
.....
..... kirx_af082931-5
c----- --c----- --tgg-----
----- *g----- -t-----
----- kirz_ac006293 -----
c----- -g--*-
----- -c --t--c-- kir15_af204906-8
.....
..... kiry_af082940-7
c-----
----- **----- -c ---t--
c---
kirx_al133414
*****
***** kirx_ac011501
*****
***** kir48_af204918-20
*****
***** kir222_af133901
*****
***** kir411_af134311-2 -----

```

Box 2 continues on next page...



Box 2 continued from previous page.

```

----- 2d12_176669 -----
----- a-----a-----
-----*
----- 2d12_af285433 -----
----- a-----a-----
-----*
a----- 2d12_af285434 -----
----- a-----a-----
-----*
----- 2ds2_a1133414 --t-----a
----- t-----t -a-----t-----
-----*
----- 2ds2_141347 --t-----a
----- t-----t -a-----t-----g
-----*
-----g----- 2ds2_x89893 --t-----a
----- t-----t -
a.....
..... 2ds2_af285439 --t-----g---a
----- t-----t -a-----t-----
-----*
c----- 2ds2_af285438 --t-----a
----- t-----t -a-----t-----
-----*
-----g----- kir2d_aj002102 --t-----a
----- t-----t -a-----t-----g
-----*
-----g----- kir2d_aj002103 --t-----a
----- t-----t -a-----t-----g
-----*
-----g----- kir2d_aj002105 --t-----a
----- t-----t -a-----t-----g
-----*
-----g----- 2d13_u97173-80 -----
-----*
...
2d13_af082936-9 -----
t----
----- a-----* -----
-----
2d13_af022048
----- t-----a-----
-----* a----- 2d13_af285435
----- t-----a-----
-----*
a----- 2d13_176662 -----
----- t-----a-----
-----*
a----- 2d13_176663 -----
----- a-----a-----
-----*
----- 2d13_u73395 -----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

-----*
-----t-----t-----a-----
a----- 2d13_u96190 .....
.....
...
kir412_af134312-6 .....
.....
kircl23_af133896-900 -----
-----t-----
-----a-----*-----
-----
2ds3_x97231 --t-----
---g---a -----t-----t -a----- ---
t----- . .....
g---a
-----*
c----- 2ds3_176670 --t----c- ---g---a
-----t-----t -a----- ---t-----
-----*
c----- 2ds4_ac011501 --t----- -----a
-----t-----t -a----- ---t-----
-----*
-----g- ----- 2ds4_af215832 .....
.....
...
-----g- ----- 2ds4_aj417555 --t----- -----a
-----t-----t -a----- ---t-----
-----*
-----g- ----- 2ds4_af002255 --t----- -----a
-----t-----t -a----- ---t-----
-----*
-----g- ----- 2ds4_176671 --t----- -----a
-----t-----t -a----- ---t-----
-----*
-----g- ----- 2ds4_af285440 --t----- -----a
-----t-----t -a----- ---t-----
-----*
c----- 2ds4_x94609 --t----- -----a
-----t-----t -a----- ---
t----- . .....
.....
2ds4_u96188 .....
.....
...
-----g- ----- 2ds4_af082961 --t----- -----a
-----t-----t -a----- ---t-----
-----*
-----g- ----- 2ds4_aj417554 --t----- -----a
-----t-----t -a----- ---t-----
-----*
-----g- ----- 2ds5_al133414 --t----- ---g---a
-----t-----t -a----- ---t-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

-----*
c----- 2ds5_af272389 --t----- --g---a
-----  t-----t -a----- --t-----

-----*
c----- 2ds5_176672 --t----- --g---a
-----  t-----t -a----- --t-----

-----*
c----- 2d14_bc028137 -----
-----  ----- a-----

-----g*
----- ag---- 2d14_af285436 -----
-----  ----- a-----

-----g*
----- ag---- 2d14_af002980 -----
-----  ----- a-----

-----g*
----- ag---- 2d14_u71199 -----
-----  ----- a-----

-----g*
----- ag---- 2d14_x97229 -----
-----  ----- a-----

-----g*
----- ag---- 2d14_ac011501 -----
-----  ----- a-----

-----g*
----- ag---- 2d14_al133414 -----
-----  ----- a-----

-----g*
----- ag---- 2d14_af002979 -----
-----  ----- a-----

-----g*
----- ag---- 2d14_af276292 -----
-----  ----- a-----

-----g*
----- ag---- 2d14_ay052496 .....
.....

...
..... 2d14_ay052498 .....
.....

...
..... 2d14_af002256 -----
-----  ----- a-----

-----g*
----- ag---- 2d14_af034772 -----
-----  ----- a-----

-----g*
----- ag---- 2d14_af034771 -----
-----  ----- a-----

-----g*
----- ag---- 2d14_x99480 -----
-----  ----- a-----

-----g*
----- ag---- kir2d1_x99481 -----
-----  ----- a-----

-----g*

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

----- ag----- kirg9p_af110032-5 -----
----- a----- g* -----
ag----
      kir2dl_y13054 --t-----
----- a-----
----- g* ----- ag---- 2d15_af217486 -----
t-----
----- t----- c--
----- t* -----
c----- 2d15_af204903 ----- t-----
----- t----- c--
----- t* -----
c-----
2d15_af260138-41 .....
...
      2d15_af217487
----- t----- t-----
----- c----- t* c----- 2dlx_af271608
----- t----- c--
----- t* -----
c----- 2dlx_af272157 ----- t-----
----- t----- c--
----- t* -----
c----- 2dlx_af271607 ----- t-----
----- t----- c--
----- t* -----
c----- 3d11_bc028206 -----
-g-----
----- * -----
----- g----- 3d11_ay059417 ----- t-----
g--*
----- g----- 3d11_u30274 -----
----- * -----
----- g----- 3d11_u31416 -----
----- * -----
----- g----- 3d11_af022049 -----
----- * -----
----- g----- 3d11_u33328 -----
----- * -----
----- g----- 3d11_af103010 -----
----- * -----
g----- 3d11_af104848-56 -----
----- * -----

```

Box 2 continues on next page...



Box 2 continued from previous page.

```

-----
                                3d11_af103011
-----
                                -g-----
-----
                                -----*----- 3d11_af103013
-----
-g-----
-----*
-----
----- 3d11_af103012 -----
----- -t----- -c-----
-----*
----- 3d11_af082956-9 -----
g-----
-----
-----
                                3d11_af208688
.....
...
3d11_af208689 .....
...
..... 3d11_af262968 -----
-g-----
-----*
----- 3d11_af262969 -----
-----*
----- 3d11_af262970 --t-----
-----*
----- 3d11_af262971 -----
-g-----
-----*
----- 3d11_af262972 -----
-g-----
-----*
----- 3d11_af262973 -----
----- -t-----
-----*
----- 3d11_af262974 -----
-g-----
-----*
----- 3d1_af105231-9 -----
----- -t-----
-----
-----*-----
-----
                                3d1_x97230 -----
-----
----- -t----- -a-----
-----*----- 3ds1_aj417558 --t-----
----- -a-----
----- -t----- -a----- -t-----
-----*-----
----- 3ds1_176661 --t----- -a-----

```

Box 2 continues on next page...



Box 2 continued from previous page.

```

----- -t----- -g-* -----
-----
3d12_af208683
...
3d12_af208684 .....
...
3d12_af208685 .....
...
3d12_af208686 .....
...
3d12_af208687 .....
...
3d12_aj276125 -----
----- -g----- -t-----
g-*
-----*
----- kircl_ac006293 -----
----- a-----
-----*
----- kircl_af072407-10 -----
----- a-----* -----
-----
kircl_af352324
----- a-----
-----* ----- 3d13_al133414
----- a-----
-----*
----- 3d13_ay083462 .....
...
kir44b_af204912-14
...
kirx_af082931-5
----- a-----* -----
-----
kirz_ac006293
----- t-----
-----* ----- kir15_af204906-8
...
kiry_af082940-7
----- t-----
-----* -----
-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

kirx_al133414
*****
*****
***** kirx_ac011501
*****
*****
***** kir48_af204918-20
*****
***** kir222_af133901
*****
***** kir411_af134311-2 -----
-----a-----
-----*----- Consensus GACTCTGATG
AACAAAGACCC TCAGGAGGTG ACATACGCAC
AGTTGGATCA CTGCGTTTTC ACACAGAGAA AAATCACTC- GCCCTTCTCA
GAGGCCCAAG 1301 1400 2d11_u24078 -----t--t
-----*-----t-----
----- 2d11_ac011501 -----t--t
-----*-----t-----
----- 2d11_af285431 -----t--t
-----*-----t-----
----- 2d11_l41267 -----t--t
-----*-----t-----
----- 2d11_u24076 -----t--t
-----*-----t-----
----- 2d11_af022045 -----t--t
-----*-----t-----
----- 2d11_af135560 .....
...
..... 2d11_af285432 -----t--t
-----*g-----t-----
----- kirg2_af001885-8 -----t--t
-----*-----t-----
kir221_af133901
-----t--t-----*-----tt-----t
----- 2ds1_al133414
-----a--*--t a-----t--t---
c---

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

----- 2ds1_x98858 .....
.....
...
..... 2ds1_x89892 .....
.....
...
..... 2ds1_af285437 -----
-a--*--t a----- -----t--t--
c---
----- 2d12_u24075 -----t--t
-----*--g-----t-----
-----
----- 2d12_al133414 -----t--t
-----*-----t-----
-----
----- 2d12_l76669 -----t--t
-----*--g-----t-----
-----
----- 2d12_af285433 -----t--t
-----*-----g-----t-----
-----
----- 2d12_af285434 -----t--t
-----*-----t-----
-----
----- 2ds2_al133414 -----
-a--*--t a----- -----t--t--
c---
----- 2ds2_l41347 -----
-a--*--t a----- -----t--t--
c---
----- 2ds2_x89893 .....
.....
...
..... 2ds2_af285439 -----g---
-a--*--t a----- -----t-----c-----t--t--
c---
----- 2ds2_af285438 -----
-a--*--t a----- -----t--t--
c---
----- kir2d_aj002102 -----
-a--*--t a----- -----t--t--
c---
----- kir2d_aj002103 -----
-a--*--t a----- -----t--t--
c---
----- kir2d_aj002105 -----
-a--*--t a----- -----t--t--
c---
2d13_u97173-80 .....
...
----- 2d13_af082936-9 -----t--t-----*-----
-----t-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

-----
                                2d13_af022048
-----t--t -----*-----
t-----
-----t--t                                2d13_af285435
-----*----- --t-----
-----
-----2d13_176662 -----t--t
-----*----- --t-----
-----
-----2d13_176663 -----t--t
-----*----- --t-----
-----
-----2d13_u73395 -----t--t
-----*----- --t-----
-----
-----2d13_u96190 .....
...
kir412_af134312-6 .....
...
                                kircl23_af133896-900 -----t--t -----*-----
----- --t----- -----tc-t gc--at-----
-----
                                2ds3_x97231 .....
...
-----g---
-----a--*--t a-----t -----c---t- --t---
c---
-----2ds3_176670 -----g---
-----a--*--t a-----t -----c---t- --t---
c---
-----2ds4_ac011501 -----t- --t---
c---
-----2ds4_af215832 .....
...
-----2ds4_aj417555 -----t- --t---
c---
-----2ds4_af002255 -----t- --t---
c---
-----2ds4_176671 -----t- --t---
c---
-----2ds4_af285440 -----t- --t---

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

c---
----- 2ds4_x94609 .....
.....
...
..... 2ds4_u96188 .....
.....
...
..... 2ds4_af082961 -----
-a--*--t a----- -----t-t- --t--
c---
----- 2ds4_aj417554 -----
-a--*--t a----- -----t- --t--
c---
----- 2ds5_al133414 -----
-a--*--t a----- -----t -----c----t- --t--
c---
----- 2ds5_af272389 -----
-a--*--t a----- -----t -----c----t- --t--
c---
----- 2ds5_l76672 -----
-a--*--t a----- -----t -----c----t- --t--
c---
----- 2d14_bc028137 -g---t--- -----
-----*gt-t a----- -----g-*** *-----
-----
-----t 2d14_af285436 -g---t--- -----
-----*gt-t a----- -----g-*** *-----
-----
-----t 2d14_af002980 -g---t--- -----
-----*gt-t a----- -----g-*** *--a-----
g-----
-----t 2d14_u71199 -g---t--- -----
-----*gt-t a----- -----g-*** *--a-----
g-----
-----t 2d14_x97229 -g---t--- -----
-----*gt-t a----- -----g-*** *-----
-----
-----t 2d14_ac011501 -g---t--- -----
-----*gt-t a----- -----g-*** *-----
-----
-----t 2d14_al133414 -g---t--- -----
-----*gt-t a----- -----g-*** *-----
-----
-----t 2d14_af002979 -g---t--- -----
-----*gt-t a----- -----g-*** *-----
g-----
-----t 2d14_af276292 -g---t--- -----
-----*gt-t a----- -----t-g-*** *-----
-----
-----t 2d14_ay052496 .....
.....
...
..... 2d14_ay052498 .....
.....
...

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

..... 2d14_af002256 -g---t--- -----
----*gt-t a----- -----g-*** *-----
-----
-----t 2d14_af034772 -g---t--- -----
----*gt-t a----- -----g-*** *-----
-----
-----t 2d14_af034771 -g---t--- -----
----*gt-t a----- -----g-*** *--a-----
-----
-----t 2d14_x99480 -g---t--- -----
----*gt-t a----- -----g-*** *-----
-----
-----t kir2d1_x99481 -g---tt--- -----
----*gt-t a----- -----g-*** *-----
-----
-----t kirg9p_af110032-5 -g---t--- -----
----*gt-t a----- -----g-*** *-----
-----t
kir2d1_y13054 -g---t---
-----*gt-t a----- -----g-***
*-----
-----t 2d15_af217486 -----t---
-----c
-a--*---t -----a--- -a-----*** *a-----
a--
----- 2d15_af204903 -----t--- -----c
-a--*---t -----a--- -a-----*** *a-----
a--
2d15_af260138-41 .....
...
2d15_af217487
----t--- -----c -a--*---t -----a--- -a-----
***
*a----- -----a-- ----- 2dlx_af271608
g---t--- -----c
-a--*---t -----a--- -a-----*** *a-----
a--
----- 2dlx_af272157 -----t--- -----c
-a--*---t -----a--- -a-----*** *a-----
a--
----- 2dlx_af271607 g---t--- -----c
-a--*---t -----a--- -a-----*** *a-----
a--
----- 3d11_bc028206 -----t--- -----t
-t--*--- -----a--- -----
-----
----- 3d11_ay059417 -----t--- -----
-----*-----
c---
-----t----- 3d11_u30274 -----t--- -----t
-t--*--- -----a--- -----
-----

```

Box 2 continues on next page...



Box 2 continued from previous page.

```

----- 3d11_u31416 -----t- -----t-
-t--*--- -----a--- -----
-----
----- 3d11_af022049 -----t- -----t-
-t--*--- -----a--- -----
-----
----- 3d11_u33328 -----t- -----t-
-t--*--- -----a--- -----
-----
----- 3d11_af103010 -----t- -----t-
-t--*--- -----a--- -----
-----
..... 3d11_af104848-56 -----t- -----t-
t--*--- -----
-----a--- -----
-----
3d11_af103011
-----t- -----t- -t--*--- -----a---
-----
----- . ..... 3d11_af103013
-t--*--- -----a--- -----
-----
..... 3d11_af103012 -----t- -----t-
-t--*--- -----a--- -----
-----
..... 3d11_af082956-9 -----t- -----t-
t--*--- -----
-----a--- -----
-----
3d11_af208688
.....
...
3d11_af208689 .....
...
..... 3d11_af262968 -----t- -----t-
-t--*--- -----a--- -----
-----
----- 3d11_af262969 -----t- -----t-
-t--*--- -----a--- -----
-----
----- 3d11_af262970 -----t- -----t-
-t--*--- -----a--- -----
-----
----- 3d11_af262971 -----t- -----t-
-t--*--- -----a--- -----
-----
----- 3d11_af262972 -----t- -----t-
-t--*--- -----a--- -----
-----
t----- 3d11_af262973 -----t- -----t-
-t--*--- -----a--- -----
-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

----- 3d11_af262974 -----t- -----t
-t---*--- -----a--- -----
-----
t---*--- -----
-----
          3d1_x97230 -----
-----t-t -----*----- --t-----
-----
----- 3ds1_aj417558 -----
-a---*---t a----- -----t- --t---
c---
----- 3ds1_176661 -----
-a---*---t a----- -----t- --t---
c---
----- 3ds1_af022044 -----
-a---*---t a----- -----t- --t---
c---
----- 3ds1_al133414 -----
-a---*---t a----- -----t- --t---
c---
----- 3ds1_u73396 -----a--- -----
-a---*---t a----- -----a---
-----
.....
..... 3ds1_x97233 -----
-a---*---t a----- -----t- --t---
c---
----- 3d12_x93595 -----t-- -----
-----*-----
c---
-----t----- 3d12_ay059418 -----t-- -----
-----*-----
c---
-----t----- 3d12_ay059419 -----t-- -----
-----*-----
c---
-----t----- 3d12_ay059420 -----t-- -----
-----*-----
c---
-----t----- 3d12_141270 -----t-- -----
-----*-----
c---
-----t----- 3d12_al133414 .....
.....
...
..... 3d12_176665 -----t-- -----
-----*-----
c---
-----t----- 3d12_176666 -----t-- -----
-----*-----
c---
-----t----- 3d12_u30272 -----t-- -----
-----*-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

c---
----- --t----- 3d12_x93596 -----t-- -----
-----*-----
c---
----- --t----- 3d12_af262966 -----t-- -----
-----*-----
c---
----- --t----- 3d12_af262965 -----t-- -----
-----*-----
c---
----- --t----- 3d12_af263617 -----t-- -----
-----*-----
c---
----- --t----- 3d12_af082963-7 -----t-- -----
-----*-----
-----c-----
t-----
          3d12_af208683
...
3d12_af208684 .....
...
          3d12_af208685 .....
...
          3d12_af208686 .....
...
          3d12_af208687 .....
...
          3d12_aj276125 -----
-----*-----
c---
----- --t----- kircl_ac006293 -----
-----g-----t-----t-----
ct--
-----t----- kircl_af072407-10 -----
-----g-----t-----t-----ct-----
-----t-----
          kircl_af352324
g-----
-----t-----t-----cc-----t----- 3d13_al133414
-----g-----t-----t-----
cc--
-----t----- 3d13_ay083462 .....
...
          kir44b_af204912-14

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

...
..... kirx_af082931-5
-----
----- g-----t- --t--ct--
-----t
          kirz_ac006293
----- a---*---t
-----
----- kir15_af204906-8
.....
...
..... kiry_af082940-7
----- a---*---
-----t
-----
          kirx_al133414
*****
***** kirx_ac011501
*****
***** kir48_af204918-20
*****
***** kir222_af133901
*****
***** kir411_af134311-2 -----
----- g-----
-----t-
--t--ct-- -----t Consensus ACACCCCAA
CAGATACCAG CGTGTAACAC GGAACCTCCA
          AATGCTGAGC CCAGATCCAA AGTTGTCTCC TGCCCATGAG CACCACAGTC
          AGGCCTTGAG 1401 1477 2d11_u24078 --cg-----
-----
          2d11_ac011501
--cg-----
----- . 2d11_af285431 --cg-----
-----
          2d11_141267 --cg-----
-----
----- . 2d11_u24076 --cg-----
-----
----- . 2d11_af022045
--cg-----
-----
          2d11_af135560
          2d11_af285432
--cg-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

-----
..... kirg2_af001885-8 --cg-----
-----
cg-----
-----
2ds1_al133414
-----
-----
----- . 2ds1_x98858 .....
-----
2ds1_x89892 .....
-----
...
..... 2ds1_af285437
-----
-----
..... 2d12_u24075 --cg-----
-----
2d12_al133414
--cg-----
-----
----- 2d12_176669 --c-----
-----
2d12_af285433
--tg-----
-----
..... 2d12_af285434 --cg-----
-----
2ds2_al133414
-----
-----
----- . 2ds2_141347 -----
-----
2ds2_x89893 .....
-----
...
..... 2ds2_af285439
-----
-----
----- . 2ds2_af285438 -----
-----
kir2d_aj002102
-----
-----
..... kir2d_aj002103 -----
-----
kir2d_aj002105
-----
----- -a---
c-....
-----
2d13_u97173-80 .....
-----
----- t--
----- -a----- . 2d13_af082936-9
-----
----- . 2d13_af022048

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

-----
.....
..... 2d13_af285435 .....
-----
-----
..... 2d13_176662 -----
-----t-----a-----
2d13_176663 -----
-----t-----
-----
..... 2d13_u73395 -----
-----t-----a-----
-----
----- 2d13_u96190 .....
.....
.....
kir412_af134312-6 ..... kircl23_af133896-900
-----t-----
-----a-----
2ds3_x97231 .....
.....
2ds3_af022047
-----
-----
..... 2ds3_176670 -----
-----
2ds4_ac011501
-----
----- 2ds4_af215832 .....
.....
2ds4_aj417555
-----
-----
..... 2ds4_af002255 -----
-----
2ds4_176671 -----
-----
-----
..... 2ds4_af285440
-----
-----
----- 2ds4_x94609 .....
.....
2ds4_u96188 .....
.....
..... 2ds4_af082961
-----
-----
..... 2ds4_aj417554 -----
-----
2ds5_al133414

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

-----
----- . 2ds5_af272389 -----
-----
2ds5_176672 -----
----- t--
g-----
----- . 2d14_bc028137
----- c-a c-----
ta-----
----- . 2d14_af285436 -----
----- c-a c----- -ta----- .
2d14_af002980
----- c-a c-----
-----
----- . 2d14_u71199 -----
----- c-a c-----
2d14_x97229 -----
----- c-a c----- -ta-----
-----
----- . 2d14_ac011501
----- c-a c-----
ta-----
----- . 2d14_al133414 -----
----- c-a c----- -ta----- .
2d14_af002979
----- c-a c-----
-----
----- . 2d14_af276292 -----
----- c-a c----- . . . . .
2d14_ay052496
. . . . .
...
. . . . . 2d14_ay052498 . . . . .
. . . . .
2d14_af002256
----- c-a c--g-----
ta-----
----- . 2d14_af034772 -----
----- c-a c----- -ta----- .
2d14_af034771
----- c-a c-----
ta-----
----- . 2d14_x99480 -----
----- c-a c----- -ta----- .
kir2dl_x99481 -----
----- c-a c----- -ta-----
-----
----- . kirg9p_af110032-5 -----
----- c-a-----
c----- -ta----- . kir2dl_y13054
-----
----- c--c-a c----- -ta----- .
2d15_af217486
----- t-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

-----
                ----- . 2d15_af204903 -----
                -----t-----
2d15_af260138-41 .....
                ..... 2d15_af217487
-----
                -----t-----
                2dlx_af271608
                -----t-----
-----
                ----- . 2dlx_af272157 -----
                -----t-----
                2dlx_af271607
                -----t-----
-----
                ----- . 3d11_bc028206 -acg-----
                -----a-----
                3d11_ay059417
                ---g-t---
-----
                .....
                ..... 3d11_u30274 -acg-----
                -----a-----
                3d11_u31416 -acg-----
                -----a-----
-----
                ----- . 3d11_af022049
-----
                .....
                ..... 3d11_u33328 -acg-----
                -----a-----
                3d11_af103010
                .....
...
                .....
3d11_af104848-56 .....
                .....
3d11_af103011 .....
                .....
                3d11_af103013
                .....
...
                ..... 3d11_af103012 .....
                .....
3d11_af082956-9 .....
                .....
3d11_af208688 .....
                .....
                3d11_af208689
                .....
...
                ..... 3d11_af262968 -acg-----
                .....
                3d11_af262969

```

Box 2 continues on next page...



Box 2 continued from previous page.

```

--cg-----
-----
..... 3d11_af262970 --cg----- --.....
.....
      3d11_af262971
--cg-----
-----
..... 3d11_af262972 --cg----- --.....
.....
      3d11_af262973
--cg-----
-----
..... 3d11_af262974 -acg----- --.....
.....
      3d1_af105231-9 -acg----- -----a
----- . 3d1_x97230
-----
-----
      3ds1_aj417558
-----
t- .....
..... 3ds1_176661 -----
-----t-- -----t- -----
      3ds1_af022044
-----
-----
..... 3ds1_al133414 -----
-----t-- -----
      3ds1_u73396 .....
.....
..... 3ds1_x97233 -----
-----
t.. .....
..... 3d12_x93595 ---g-t----
-----a- -----a- --a--a--
-----
----- . 3d12_ay059418
---g-t----
-----
..... 3d12_ay059419 ---g-t---- --.....
.....
      3d12_ay059420
---g-t----
-----
..... 3d12_141270 ---g-t---- -----
-----a- -----a- --a--a-- -----
      3d12_al133414
.....
..... 3d12_176665 ---g-t---- -----
-----a- -----a- --a--a-- -----
      3d12_176666 ---g-t----
-----
-----

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

..... 3d12_u30272 ---g-t----
-----a- -----a- --a--a---
-----

----- . 3d12_x93596 ---g-t----
-----a- -----a- --a--a---
-----

----- . 3d12_af262966
---g-t----
--.....
..... 3d12_af262965 ---g-t---- --.....
.....
      3d12_af263617
---g-t----
--.....
..... 3d12_af082963-7 ---g-
t-.....
3d12_af208683 .....
      3d12_af208684
.....
...
..... 3d12_af208685 .....
      3d12_af208686
.....
...
..... 3d12_af208687 .....
      3d12_aj276125
---g-t---- -----
-----
..... kircl_ac006293 -----
t----- c-----
      kircl_af072407-10 ----- t-----
-----
----- c----- . kircl_af352324
-----
t----- -----
      3d13_al133414
----- t-----
-----
----- . 3d13_ay083462 .....
.....
kir44b_af204912-14 .....
..... kirx_af082931-5
----- t-----
----- c----- . kirz_ac006293
-----
-----
kir15_af204906-8 .....
..... kiry_af082940-7
--.....

```

Box 2 continues on next page...

Box 2 continued from previous page.

```

..... kirx_al133414
*****
***** kirx_ac011501
*****
***** kir48_af204918-20
*****
***** kir222_af133901 *****
***** kir411_af134311-2 ----- t-----
-----
----- c----- . Consensus GGGATCTTCT
AGGGAGACAA CAGCCCTGTC TCAAACCGG
                GTTGCCAGCT CCCATGTACC AGCAGCTGGA ATCTGAA

```

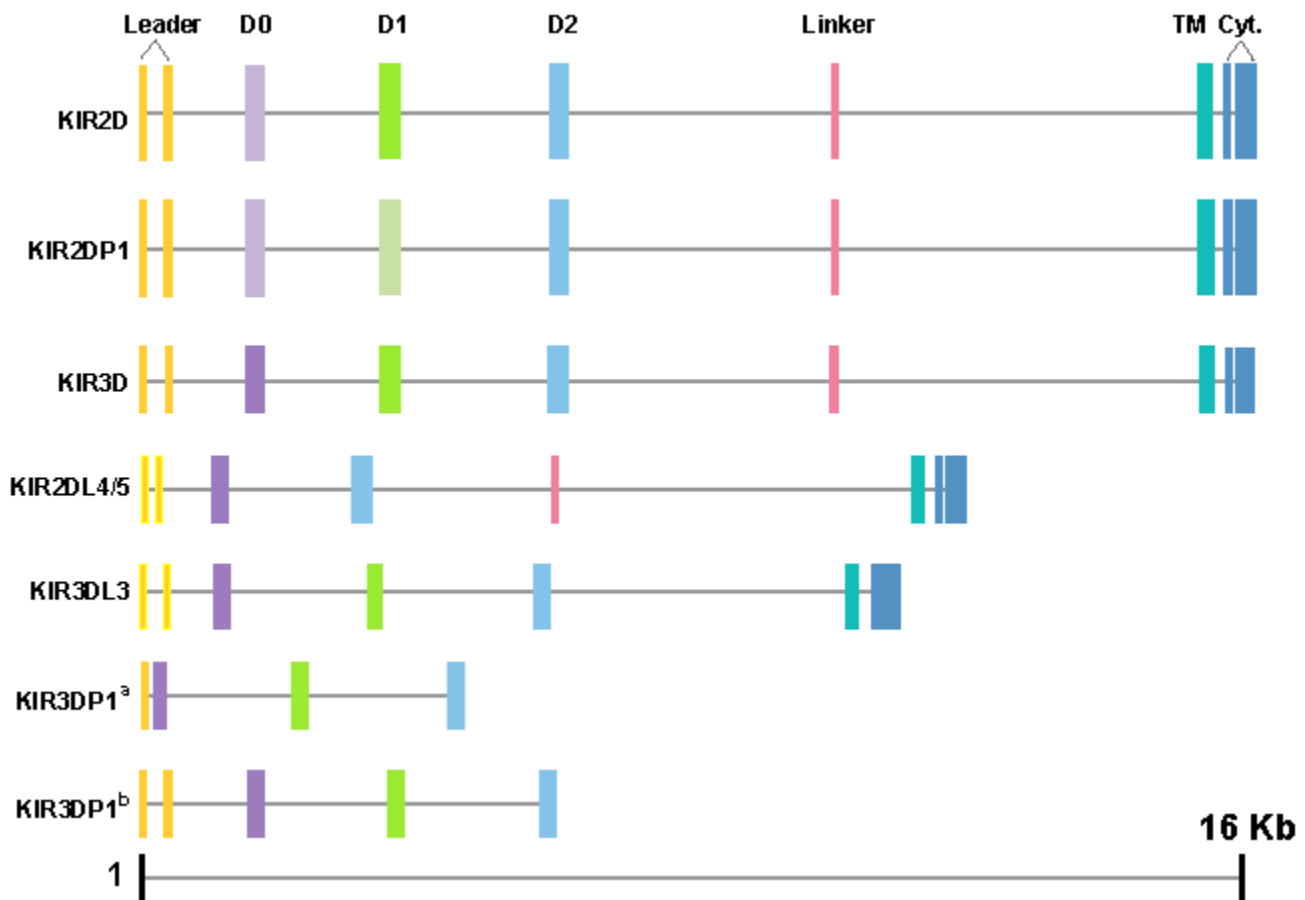
## Exon–Intron Structure of the KIR Genes

Organization of the exon–intron structure of the various *KIR* genes is fairly consistent with the following basic arrangement: the signal sequence is encoded by the first two exons, each Ig domain (D0, D1, and D2, starting from the N-terminus) corresponds to a single exon (exons 3–5, respectively), the linker and transmembrane regions are each encoded by a single exon (exons 6 and 7), and the cytoplasmic domain is encoded by two final exons (Figure 3) (27, 57, 58). *KIR2DL1*, *2DL2/3*, and all *2DS* genes [known as Type 1 two-domain *KIR* genes (59)] have an identical genomic organization to that encoding *KIR* molecules with three Ig domains. However, exon 3 is a pseudoexon in these two-domain *KIR* genes, which often remains in-frame but is eventually spliced out, possibly due to a three-base-pair deletion (59). The protein products of type 1 two-domain *KIR* are therefore missing the D0 domain (60). All NK cells express at least one type 1 2D *KIR* (61). The Type 2 two-domain *KIR*, which include *2DL4*, *2DL5A*, and *2DL5B* (59), are characterized by the complete absence of exon 4 (62), and therefore their protein product has no D1 domain. The *3DL3* gene closely resembles the other *3D* genes, except that it is missing exon 6.

Two *KIR* pseudogenes have been identified and named, although others that closely resemble intact *KIR* genes (and therefore go undetected) may exist on certain haplotypes. *KIR2DP1* (*KIRZ*) is closely related to *2DL2/3* and *2DL1* (>97% homology at the nucleotide level), and contains two pseudoexons, 3 and 4. Pseudoexon 3 of *2DP1* contains the same aberrations as those identified in the Type 1 two-domain *KIR* genes, and a single base pair deletion in pseudoexon 4 of *2DP1* causes a frame shift that introduces a stop codon. A second *KIR* pseudogene, *3DP1* (*KIRX*), is severely truncated and alternate forms of the gene are differentiated by a 1.5kb deletion, which removes exon 2 (27). No transcripts for either *2DP1* or *3DP1* have been identified to date.

## KIR Gene Order and Haplotypic Variability

The *KIRs* are situated within a segment of DNA that has undergone expansion and contraction over time, and inspection of *KIR* haplotypes suggests a history of gene duplication and unequal crossing over in the region. The order of the *KIR* genes along the chromosome has been determined for two distinct haplotypes (Figure 4), providing a framework for their genomic order (27, 46, 63). The genes are organized in a head-to-tail fashion, and each gene is roughly 10–16 kb in length with a sequence of about 2 kb separating each pair of genes, except for a 14 kb stretch of unique sequence upstream of *2DL4*. Variation at the *KIR* gene complex is a function of



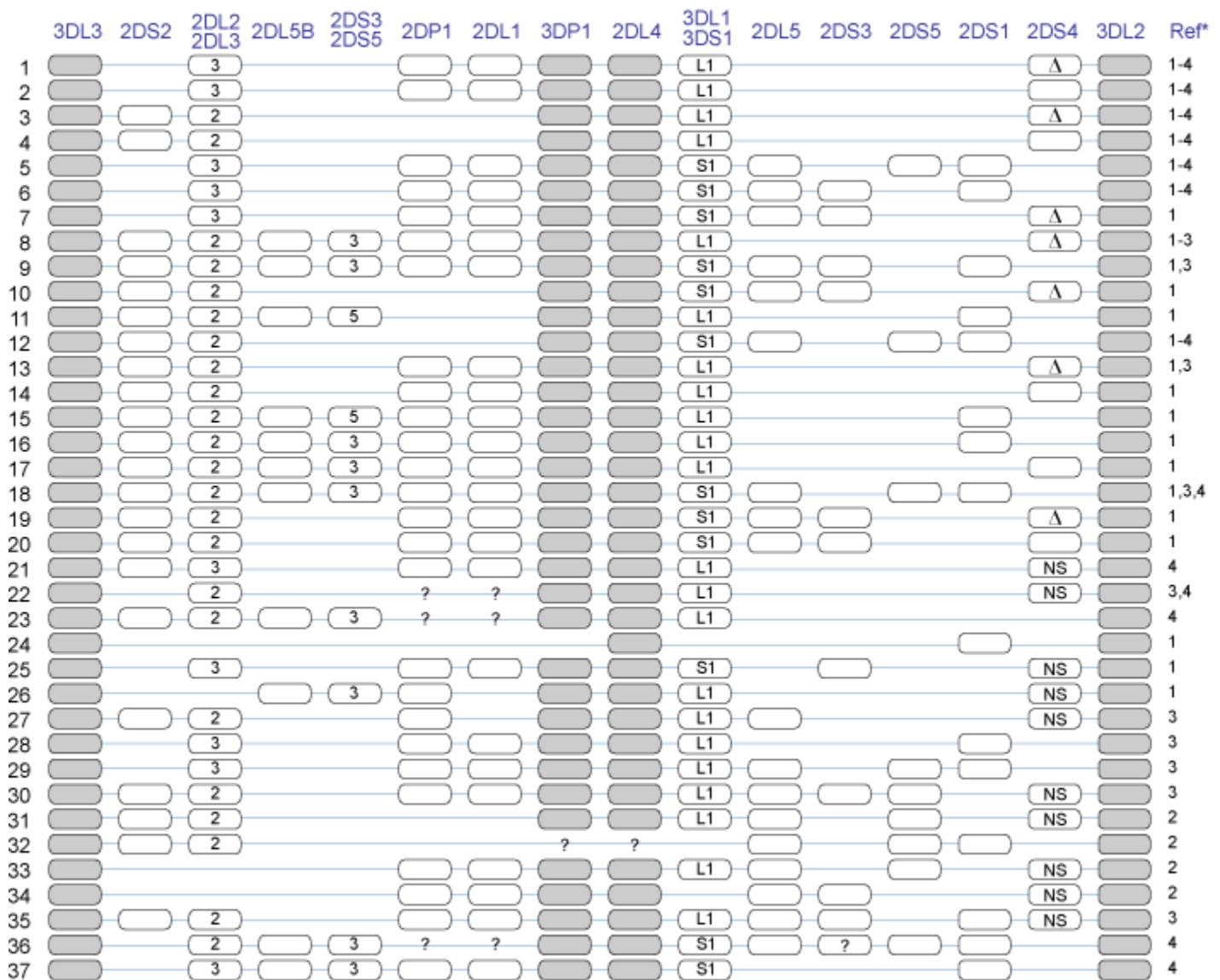
**Figure 3. Exon-intron structure the KIR genes.** Exons encoding the various domains of the KIR molecules are as follows: exons 1 and 2, leader (signal) sequence (yellow); exons 3–5, Ig domains D0, D1, and D2, respectively (purple, green, and blue); exons 6 and 7, linker and transmembrane regions, respectively (pink and turquoise); and exons 8 and 9, cytoplasmic domain (dark blue). The type 1 two-domain *KIR* genes, *KIR2DL1*, *2DL2/3*, and all *2DS* genes, have an identical genomic organization to that encoding KIR molecules with three Ig domains, but exon 3 (encoding D0) of these two domain *KIR*s is a pseudoexon (light purple). Exon 3 is also a pseudoexon in *KIR2DP1*, which also contains a pseudoexon 4 (light green). The Type 2 two-domain *KIR*, which include *2DL4*, *2DL5A*, and *2DL5B*, are characterized by the complete absence of exon 4.



**Figure 4. Gene order of two fully sequenced KIR haplotypes.** The order of the *KIR* genes along the chromosome has been determined for two distinct haplotypes (27, 46, 63). The genes are organized in a head-to-tail fashion, and each gene is roughly 10–16 kb in length with a sequence of about 2 kb separating each pair of genes, except for a 14 kb stretch of unique sequence upstream of *2DL4*.

both allelic polymorphism at several *KIR* genes and variability in the number and types of genes present on any given haplotype (3, 25, 64).

Although *KIR* haplotypes vary in the number and type of genes present (3, 65, 66, 70), the genes *2DL4*, *3DP1*, *3DL2*, and *3DL3* are present on virtually all haplotypes and have therefore been termed framework loci (27). All



**Figure 5. Distinct KIR haplotypes based on gene content.** The haplotypes shown were determined by segregation analysis, but many are not yet definitive. The gene order used in this figure is based on that determined by Hsu *et al.* (51). Segregation analysis cannot always define precisely the gene content of *KIR* haplotypes. Therefore, based on gene frequencies and patterns of linkage disequilibrium between pairs of *KIR* genes, several assumptions based on consistent observations across studies were made in determining some of the haplotypes listed in the figure: (a) *3DL3*, *3DP1*, *2DL4*, and *3DL2* are present on all haplotypes; (b) if *2DS1* is present, *2DS4* is absent and vice versa; (c) if *2DL1* is present, *2DP1* is always present; (d) if *3DS1* is absent, *3DL1* is present. Haplotypes containing the *2DS4* null allele are designated by "Δ" and those in which *2DS4* was not subtyped are marked "NS". [1=(68); 2=(25); 3=(73); 4=(74).]

others exist on only a fraction of the total haplotypic pool. The number of putatively expressed *KIR* genes present on a single haplotype ranges from about 7–12, depending primarily on the presence or absence of activating *KIR* loci (3, 27, 66). Based on gene content, the haplotypes have been divided into two primary sets, termed A and B, which were originally differentiated by the presence of a 24 kb HindIII fragment on Southern blot analysis (3). Haplotype A has seven loci; *2DL1*, *2DL3*, *2DL4*, *2DS4*, *3DL1*, *3DL2* and *3DL3*. Perhaps the most functionally relevant distinction between haplotypes A and B is the number of stimulatory receptors present. Haplotype A contains only a single stimulatory *KIR* gene, *2DS4*, whereas haplotype B contains various combinations of *2DS1*, *2DS2*, *2DS3*, *2DS5*, *3DS1*, and *2DS4*. Furthermore, the *2DS4* gene has a null allele with a population frequency of about 84% (allele frequency of 60%) (67) (and PN, unpublished observation). Thus, some individuals are homozygous for an A haplotype from which no activating *KIR* is expressed (68). The

phenomenon of framework genes supporting areas of variable polygeny is analogous to that seen for *HLA-DR*, in which the *DRA* genes are always present, whereas the *DRB* gene number is variable (69).

The frequencies of haplotypes A and B are roughly equal in Caucasian populations, but on the basis of gene content, haplotype B displays a much greater variety of subtypes. Patterns of linkage disequilibrium (LD) between *KIR* loci (as opposed to LD between alleles of two genes that are both present on all haplotypes) are fixed for the A haplotypes (i.e. A haplotypes differ at the allelic level (25), but not in gene content). Much of what we know about LD patterns among the B haplotypes is based on studies of *KIR* profiles (presence or absence of each gene in a given individual) in groups of unrelated individuals, and they indicate that LD is quite strong between many pairs of genes represented in the group of B haplotypes (3, 65, 66, 70–72). Over 100 different *KIR* profiles have been identified among unrelated individuals, and many distinct gene-content haplotypes have been identified from segregation analysis (Figure 5) (68, 73, 74). The numbers will undoubtedly continue to grow as more individuals and families are screened.

Expansion and contraction of the *KIR* region appears to have occurred due in part to unequal crossing over. One consequence of such molecular genetic events is the possible generation of *KIR* haplotypes that have two (or more) copies of a gene on a single haplotype and the rearrangement of gene order. *2DL5* is the most recently identified *KIR* gene (75) and segregation analysis has indicated that what were once considered alleles of a single *2DL5* locus are actually two different loci, both of which can be present on a single haplotype (74, 76). Interestingly, these genes, termed *2DL5A* and *2DL5B*, are not tandemly located on haplotypes containing both genes, suggesting that they may have arisen due to a mechanism involving nonreciprocal crossing over. The two genes share >99% sequence similarity in both their exons and introns, and would not have been identified as separate loci if family studies of *2DL5* inheritance had not been performed (74, 76). There is at least one haplotype with several *KIR* deleted, including *2DL4* and *3DL1* (72). Since most *KIR* typing methods are designed to determine presence or absence of genes and subtyping of individual *KIR* genes in families has been performed in only a limited number of studies (25, 55, 77), haplotypes containing multiple copies of the same gene would remain undisclosed, further underestimating *KIR* haplotypic diversity.

Frequencies of specific *KIR* haplotypes and the two major haplotypic groups, A and B, vary across ethnically defined populations (65, 66, 70–72, 78–80). The A haplotype has an allele frequency of 75% in Japanese but only 15% in Australian Aborigines [estimated from (71, 79)]. The greatest intra-population haplotype diversity would appear to be in South Asians (72, 80) and the least in Japanese (79). It will be of interest to determine whether significant differences in *KIR* haplotypes across populations might account for variation in disease susceptibility among these groups.

## Allelic Variability

Sequence analysis of *KIR* cDNA has shown that most *KIR* genes contain variable sites, and that some are quite polymorphic (25, 55, 64, 77, 81–91). Allelic polymorphism provides additional diversity to the extent that unrelated individuals identical for both *KIR* haplotypes are unlikely to be observed (25). The variation in *KIR* sequences can occur at positions encoding residues that affect interaction with HLA class I (92–95). Variation tends to occur throughout the gene, unlike the pattern observed in *HLA* class I and II genes where nucleotide variation is restricted primarily to one or two exons (96).

Similarity amongst *KIR* gene sequences and a history of unequal crossing over in the region has clouded the distinction between alleles of a single locus and separate gene loci. *2DS4* and *2DS1* were suggested to be allelic variants of a single locus (3), although more recent data suggests that they represent distinct loci (27, 65). *3DL1* and *3DS1* appear to occupy the same position on different haplotypes (27), and segregation analysis has indicated that they are indeed alleles of a single locus (55). We have previously proposed that *3DS1*, which is substantially less frequent than *3DL1*, arose by an unequal crossover between an ancestral *3DL1* gene and an ancestral activating *KIR* gene (6), based on the high sequence similarity between their extracellular domains and

the observation that they segregate as alleles of a single gene. Nevertheless, rare haplotypes missing both or containing both *3DL1* and *3DS1* have been observed (55, 70). Haplotypes characterized by deletion of *3DL1* / *3DS1* or by the presence of both *3DL1* and *3DS1* may have been derived from unequal crossovers that occurred subsequent to the event that formed *3DS1*. Wilson *et al.* (27) proposed that *2DL2* arose from a non-reciprocal recombination between *2DL1* and *2DL3* based on sequence similarity patterns, which would explain the observation that *2DL2* and *2DL3* also segregate as alleles of the same locus (65, 66, 70, 71). Moreover, the *2DP1* pseudogene, which is located between *2DL1* and *2DL3* and would have been lost in the cross over event, is indeed missing on *2DL2* haplotypes.

*KIR3DL1* and *3DL2*, which encode molecules that bind certain allotypes of the HLA-B and HLA-A, are both quite polymorphic, although the source of variability in the two genes appears to be distinct (55). Recombination is likely to have generated much of the diversity in both genes (25). *KIR3DL1* alleles encode molecules that appear to be expressed at different levels on the surface of NK cells based on antibody binding to *3DL1* allotypes. Allotypes with high, low and no binding have been observed and expression levels correlate with variation at specific amino acid residues of the *3DL1* molecule (55). It will be interesting to consider the functional consequences of these differences in expression patterns. Like the variability that is observed based on KIR gene content, allelic variability and frequencies also appear to distinguish different ethnic groups (83).

Linkage disequilibrium (LD) studies between pairs of polymorphic genes within the *KIR* locus are starting to emerge (25) revealing a pattern of strong allelic disequilibrium between pairs of genes located centromeric and pairs located telomeric of *2DL4*. Although significant in many instances, weaker disequilibrium patterns were observed between pairs of genes located in opposite halves of the locus. In general, patterns of LD that have been observed to date appear to correspond quite well with physical distance between genes.

## Promoter Region Variability

The promoter regions of most *KIR* genes share >91% sequence similarity (26), and may therefore be controlled by similar mechanisms. The promoter regions of *3DL3* and *2DL4*, on the other hand, are more divergent (89% and 69% sequence similarity, respectively). Differences in promoter regions of these framework loci may account for the lack of *3DL3* expression and, alternatively, the expression of *2DL4* in virtually 100% of NK cell clones, a characteristic unique to *2DL4* (26). *2DL5A* appears to be expressed based on measurements of mRNA in NK cells, but the most common allele of *2DL5B* (in Caucasoids) is not expressed (76). Lack of *2DL5B* expression correlates with a mutation in a putative *AML1* transcription factor site in the promoter region, a variant that is also present in the pseudogene *3DP1* (76) and that may prevent expression of these two genes.

## KIR Genotyping

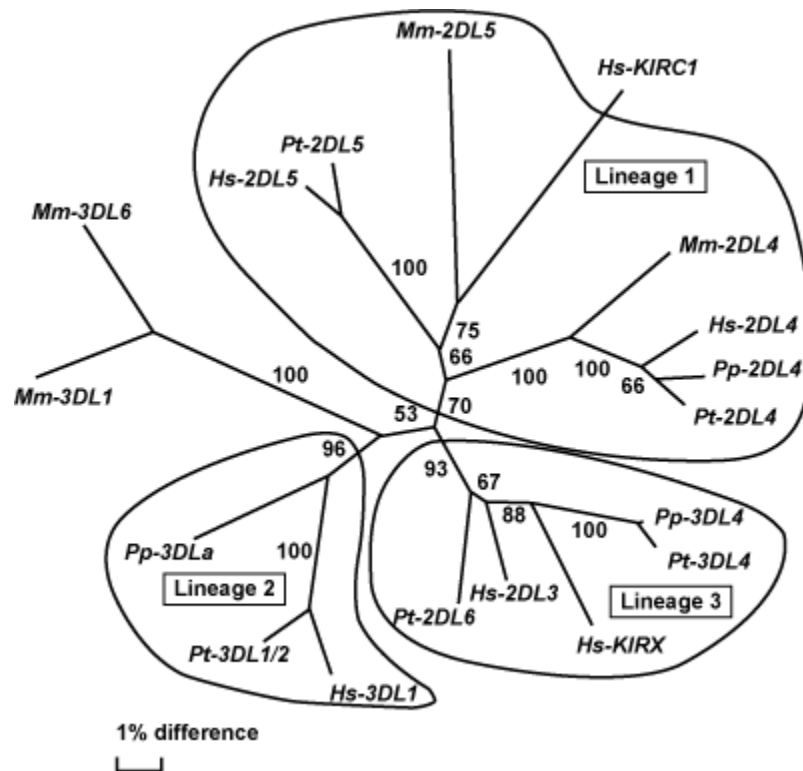
*KIR* genotyping can be locus or allele specific. Locus only typing detects presence or absence of each gene in a given individual, thus providing a profile of the *KIR* repertoire (*KIR* profile). The PCR sequence-specific priming (PCR-SSP) method for *KIR* typing first described by Uhrberg and coworkers (3) has been updated to account for newly discovered loci and previously undetected alleles (65, 72, 78, 97, 98). A PCR sequence-specific oligonucleotide probe (PCR-SSOP) method has also been developed (70, 99). Inter-laboratory collaboration has helped to authenticate the molecular genotyping assay for *KIR* loci (100). Over 100 different *KIR* genotype profiles have been found so far; a summary of those published is shown in Figure 6.

Medium- to high-resolution allele-specific reactions (PCR-SSP) have been described for *2DL1*, *2DL3*, *3DL1* and *3DL2* (25, 55), and a single-stranded conformational polymorphism (SSCP) assay has been used to genotype *2DL4* (77, 91). Development of a comprehensive assay was required for *2DL5* in order to distinguish the two highly homologous loci, *2DL5A* and *2DL5B* (97). Reverse-transcriptase PCR (RT-PCR) based on PCR-SSP is the method of choice for allotyping NK cell clones and remains largely unchanged from that described previously

KIR genes													Number of KIR genes	References	Total	
2DL				3DL			2DS			DS						
1	2	3	4	5	1	2	3	1	2	3	4	5	1			
														7	1-5	305
														9	1-5	134
														11	1,2,4,5	62
														11	1-5	76
														14	2,3,5	37
														13	1-3,5	36
														10	1-3,5	29
														13	1-3,5	29
														10	2,3	21
														12	1-3,5	20
														12	2,3	18
														11	2,3,4,5	19
														12	1-3	16
														13	1-3,5	17
														11	2,3	10
														7	2,3,5	12
														11	1,2	11
														12	2,3	9
														12	1,4	9
														12	1,2	7
														8	1,2	8
														12	2,3	5
														10	1,2	8
														9	4	1
														10	3	6
														10	1-3	7
														13	1,2	9
														12	2,3	7
														12	2,5	11
														11	2,3,5	7
														7	1	5
														11	2,4	4
														10	1,2	4
														9	2	4
														10	2	2
														8	2,3	4
														10	2	3
														9	1,2	2
														10	1,2,5	6
														12	1,3	3
														13	1-3	3
														11	1,2	3
														9	1,3	3
														9	2	3
														10	2	3
														8	3	3
														10	2	2
														12	1	2
														11	2	2
														9	2	2
														11	1,3,5	3
														11	2	2
														11	2,3	2
														9	2	2
														9	1	2
														8	2	2
														10	1,3	2
														9	2,3	2
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														10	2	1
														12	2	1
														11	3,5	2
														12	2	1
														11	2	1
														11	1,5	3
														11	2	1
														11	1	1
														10	1	1
														9	1	1
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														10	2	2
														8	2	1
														8	1	1
														5	2	1
														8	2	1
														10	2	1
														9	2	1
														7	2	1
														10	2	2
														8	5	1
														9	5	1

**Figure 6. KIR genotype profiles observed to date.** Key: Black box: locus detected; white box: absent. Adapted from Ref. 214, with kind permission from Makato Yawata and Begell House Inc. This article is a summary of five studies that included all KIR shown here, as earlier studies did not include 3DL3, 2DL1\*004, 2DL5 and 2DS5. [Refs: 1=(80, n=72); 2=(72, n=659); 3=(73, n=268); 4=(79, n=41), 5=(68, n=85)]. For each profile, the total number of individuals observed from these five studies is shown. To aid other laboratories in assay calibration, KIR genotype profiles of cell lines from the 10th International Histocompatibility Workshop have also been described (100).





**Figure 7. Phylogenetic relationship of KIR gene sequences from four primate species.** KIR cDNA sequences from *Homo sapiens* (Hs), *Pan troglodytes* (Pt), *Pan paniscus* (Pp), and *Macaca mulatta* (Mm) were analyzed using a neighbor-joining method. (Reproduced from Ref. 59, with permission from Dr. Peter Parham and *Annual Review of Immunology*, [Annual Reviews](#).)

(3). Various monoclonal antibodies are available for this purpose, but specificity is limited by the high homology between KIR isotypes.

## Evolutionary Aspects

Comparisons of KIR sequences and haplotypes within and across species indicate that the KIR gene family is evolving rapidly, perhaps in response to species-specific pathogenic organisms (42, 101–103). It was initially thought that KIR were only present in higher primates, although KIR-like sequences have been found recently in lower primates (104, 105), ungulates (106) and other mammals (40). In chimpanzee, the closest living species to humans, ten KIR genes have been identified, only three of which appear to be direct orthologues of human KIR (42). Non-orthologous KIR genes have also been identified in pygmy chimpanzee (102), orangutan (101), rhesus monkeys (105), and baboon (104). The phylogenetic relationship of KIR genes from four different primate species is shown in Figure 7 [reproduced from (59); see also (101, 107)]. Primate species vary in ratios of long tail to short tail KIR genes, and haplotypic structure may also distinguish some species. For example, a common short haplotype of only three KIR genes distinctly characterizes pygmy chimpanzees (102). Comparisons of KIR gene sequences from five species of primates have revealed most lucidly the historical instability of the KIR genes in primate species. Nevertheless, similarities have persisted over millions of years, including the maintenance of 2DL4 in all primate species tested (although all 2DL4 transcripts examined in orangutan prematurely terminated). Further, identical receptor specificity for MHC-Cw molecules was observed in human and chimpanzees, and the two species are xenocompatible in that KIR receptors from chimpanzee can functionally recognize some human MHC class I molecules and vice versa.

Rapid evolution of the KIR locus may have resulted in species-specific characteristics across orders of mammals (108), potentially hampering attempts to clone KIR homologues in some species. KIR have now been detected in

rodents (see; [XM\\_142159](#), [XM\\_142160](#), [AF548540](#), [AF548541](#), [AY152727](#)). Ly49 receptors, which belong to the C-type lectin domain family and are structurally unrelated to KIR, appear to perform the same function in rodents. *Ly49* haplotypes are also complex, containing variable numbers of inhibitory and stimulatory genes (109), some of which are known to recognize mouse class I molecules. Genomes of humans and other primate species contain a single *Ly49*-like gene, which is a pseudogene in humans, gorilla, and chimpanzee (104, 110, 111), but may be functional in cow, baboon and orangutan (101, 104, 106).

It has been suggested that *MHC* class I and *KIR* (and also *Ly49* in mouse) are coevolving (42, 112), such that as selection through infectious disease morbidity alters the frequencies and repertoire of class I variants, *KIR/Ly49* must evolve to maintain or expand the ability to interact with class I in a beneficial manner. Evidence for the co-evolutionary process is illustrated by the observation that mouse class I allotypes lack determinants recognized by KIR, as do human class I allotypes for mouse *Ly49* (86). Along these same lines, the orangutan have *KIR2D* genes that are predicted to encode receptors that specify only the Cw1 epitope (asparagine at position 80) of MHC-Cw molecules, correlating in an evolutionary sense with the observation that allotypes with the Cw2 epitope (lysine at position 80) are missing in this species and only MHC-Cw allotypes with the Cw1 epitope are available for interaction with 2D molecules (101). Additional selective pressures may also act directly on the *KIR* loci during early phases of infection by selecting for variants that enhance innate immune responsiveness, potentially increasing the rate of evolution at a speed surpassing that at the *HLA* class I loci (42, 113). Conforming to this hypothesis, all functional *HLA* class I genes have chimpanzee orthologues (114), but there are only three human-chimpanzee *KIR* orthologues (113). Thus, the portrayal of the *KIR* gene complex as the epitome of "eternal evolutionary restlessness" (58) appears to represent a precise account of the region.

## Individual Molecular Characteristics

### KIR2DL1

*KIR2DL1* is a member of the type 1 (D<sub>1</sub>-D<sub>2</sub>) 2DL subfamily of inhibitory receptors. Exon 3 of *2DL1* is a pseudoexon that would otherwise encode the D<sub>0</sub> domain. Ligands for 2DL1 are HLA-Cw molecules that have Asn77 and Lys80 (Cw\*02/4/5/6/707/12042/15/1602/17). Monoclonal antibodies EB6 (CD158a) and HP3E4 recognize 2DL1, both of which also react with *2DS1* (115, 116). *2DL1\*004* (2DL1v; inhibitory) appears to have been formed by a recombination between *2DL1* and *2DS1*.

**Key references:** *2DL1\*004* (84); allelic variation (25); crystal structure of 2DL1 (94); crystal structure of 2DL1 contacting HLA-Cw4 (92).

#### Unique sequences:

- *2DL1\*001*: [AL41267](#) (NKAT1)
- *2DL1\*002*: [U24076](#) (= [NM14218](#))
- *2DL1\*00301*: [U24078](#)
- *2DL1\*00302*: [AF285431](#) (= [AC011501](#))
- *2DL1\*004*: [AF022045](#)
- *2DL1\*005*: [AF285432](#)
- pseudoexon 3: [AF215827](#) (\*001) and [AC011501](#) (\*00302)

**PDB:** [1NKR](#)

**LocusLink:** [3802](#)

**OMIM:** [604936](#)

**PROW:** [2DL1](#).

## KIR2DL2

**KIR2DL2** is a member of the type 1 (D<sub>1</sub>-D<sub>2</sub>) 2DL subfamily of inhibitory receptors. Exon 3 of *2DL2* is a pseudoexon that would otherwise encode the D<sub>0</sub> domain. Ligands for 2DL2 are HLA-Cw molecules that have Ser77 and Asn80 (Cw\*01/3/7/8/12/13/14/1507/1601 and B\*4601). Monoclonal antibodies GL183 (CD158b) and CH-L recognize 2DL2 as well as **2DL3** and **2DS2** (211, 212).

**Key references:** *2DL2* arose from a non-reciprocal recombination between 2DL1 and 2DL3 (27); 2DL2 and 2DL3 are alleles (66); crystal of 2DL2 (117); crystal structure of 2DL2 contacting HLA-Cw3 (1EFX) (93).

### Unique sequences:

- *2DL2\*001*: [U24075](#) (cl43), [NM\\_014219](#)
- *2DL2\*002*: [L76669](#) (NKAT6a)
- *2DL2\*003*: [AF285433](#)
- *2DL2\*004*: [AF285434](#), [AL133414](#)
- pseudoexon 3: [AF2158292](#) (\*001), [AL133414](#) (\*004)

**PDB:** [1EFX](#)

**LocusLink:** [3803](#)

**OMIM:** [604937](#)

**PROW:** [2DL2](#)

## KIR2DL3

**KIR2DL3** is a member of the type 1 (D<sub>1</sub>-D<sub>2</sub>) 2DL subfamily of inhibitory receptors. Exon 3 of *2DL3* is a pseudoexon that would otherwise encode the D<sub>0</sub> domain. Ligands for 2DL3 are HLA-Cw molecules that have Ser77 and Asn80 (Cw\*01/3/7/8/12/13/14/1507/1601). Monoclonal antibodies GL183 (CD158b) and CH-L recognize 2DL3 as well as **2DL2** and **2DS2** (211, 212).

**Key references:** crystal structure of 2DL3 (118); 2DL3 and 2DL2 are alleles (66).

### Unique sequences:

- *2DL3\*001*: [L41268](#), [NM\\_014511](#), [U24074](#) (NKAT2m)
- *2DL3\*002*: [L76662](#) (NKAT2a)
- *2DL3\*003*: [L76663](#) (NKAT2b)
- *2DL3\*004*: [U73395](#), [NM\\_015868](#) (KIR-023GB)
- *2DL3\*005*: [AF022048](#)
- *2DL3\*006*: [AF285435](#)
- pseudoexon 3: [AF215834](#) (\*002), [AF215835](#) (\*005)
- genomic \*001: [AC000692](#), [AC011501](#)

**PDB:** [1B6U](#)

**LocusLink:** [3804](#)

**OMIM:** [604938](#)

**PROW:** [2DL3](#)

## KIR2DS1

**KIR2DS1** is a type 1 (D<sub>1</sub>-D<sub>2</sub>) two-domain activating receptor. Exon 3 of *2DS1* is a pseudoexon that would otherwise encode the D<sub>0</sub> domain. Ligands for 2DS1 may be HLA-Cw molecules that have Asn77 and Lys80 (Cw\*02/4/5/6/707/12042/15/1602/17). Activating KIR signal by virtue of non-covalent association with the ITAM-bearing adaptor molecule, DAP-12. Monoclonal antibodies EB6 (CD158a) and HP3E4 recognize 2DS1, both of which also react with [2DL1](#) (115, 116).

**Key references:** 2DS1 associated with psoriatic arthritis when ligand for corresponding inhibitory receptor was absent (5).

### Unique sequences:

- 2DS1\*001: [X89892](#)
- 2DS1\*002: [AF022046](#), [NM\\_014512](#), [AL133414](#)
- 2DS1\*003: [X98858](#)
- 2DS1\*004: [AF285437](#)
- Pseudoexon 3: [AF215828](#) (\*002)

**LocusLink:** [3806](#)

**OMIM:** [604952](#)

**PROW:** [2DS1](#)

## KIR2DS2

**KIR2DS2** is a type 1(D<sub>1</sub>-D<sub>2</sub>) two-domain activating receptor. Exon 3 of *2DS2* is a pseudoexon that would otherwise encode the D<sub>0</sub> domain. 2DS2 ligands are HLA-Cw molecules that have Ser77 and Asn80 (Cw\*01/3/7/8/12/13/14/1507/1601). Activating KIR signal by virtue of non-covalent association with the ITAM-bearing adaptor molecule, DAP-12. Monoclonal antibodies GL183 (CD158b) and CH-L recognize 2DS2 as well as [2DL2](#) and [2DL3](#) (211, 212).

**Key references:** 2DS2 implicated in rheumatoid vasculitis (119); single substitution lowers binding affinity compared with 2DL2 (120); 2DS2 associated with psoriatic arthritis when ligand for corresponding inhibitory receptor was absent (5).

### Unique sequences:

- 2DS2\*001: [L41347](#) (NKAT5), [NM\\_012312](#)
- 2DS2\*002: [X89893](#)
- 2DS2\*003: [AJ002103](#)
- 2DS2\*004: [AF285438](#)
- 2DS2\*005: [AF285439](#)[AL133414](#)
- Pseudoexon 3: [AF215830](#) (NKAT5)

**LocusLink:** [3807](#)

**OMIM:** [604953](#)

**PROW:** [2DS2](#)

## KIR2DS3

**KIR2DS3** is a type 1 (D<sub>1</sub>-D<sub>2</sub>) two-domain activating receptor. Exon 3 of *2DS3* is a pseudoexon that would otherwise encode the D<sub>0</sub> domain. Its ligand is unknown. Activating KIR signal by virtue of non-covalent association with the ITAM-bearing adaptor molecule, DAP-12.

### Unique sequences:

- 2DS3\*00101: [L76670](#) (NKAT7)
- 2DS3\*00102: [X97231](#)
- 2DS3\*00103: [AF022047](#)
- pseudoexon 3: [AF215831](#) (\*00103)

**LocusLink:** [3808](#)

**OMIM:** [604954](#)

**PROW:** [2DS3](#)

## KIR2DS4

**KIR2DS4** is a type 1 (D<sub>1</sub>-D<sub>2</sub>) two-domain activating receptor. Exon 3 of *2DS4* is a pseudoexon that would otherwise encode the D<sub>0</sub> domain. Ligand unknown. Activating KIR signal by virtue of non-covalent association with the ITAM-bearing adaptor molecule, DAP-12. Some alleles of *2DS4* have a 22bp deletion, which may lead to a truncated molecule (67), occasionally termed KIR1D (68).

**Key references:** Truncated 2DS4 allele (67); truncated 2DS4 on many A haplotypes (68); KIR2DS4 may bind HLA Cw4 (121).

### Unique sequences:

- 2DS4\*00101: [AF024077](#) (cl-39), [AF002255](#)
- 2DS4\*00102: [L76671](#) (NKAT8)
- [X94609](#)
- [AF285440](#)
- Truncated 2DS4: [AJ417554](#) (see also [AC011501.7](#))
- Pseudoexon 3: [AF215832](#) (\*00101)

**LocusLink:** [3809](#)

**OMIM:** [604955](#)

**PROW:** [2DS4](#)

## KIR2DS5

**KIR2DS5** is a type 1 (D<sub>1</sub>-D<sub>2</sub>) two-domain activating receptor. Exon 3 of *2DS5* is a pseudoexon that would otherwise encode the D<sub>0</sub> domain. Ligand unknown. Activating KIR signal by virtue of non-covalent association with the ITAM-bearing adaptor molecule, DAP-12.

**Key references:** (90)

### Unique sequences:

- [L76672](#)
- [AF208054](#)
- [AF215833](#)
- [AF272389](#)
- [AL133414](#)
- Pseudoexon 3: [AF215833](#)

**LocusLink:** [3810](#)

**OMIM:** [604956](#)

**PROW:** [2DS5](#)

## KIR2DL4

**KIR2DL4** is a member of the type 2 (D<sub>0</sub>-D<sub>2</sub>) two-domain receptors. There is no exon 4 (D<sub>1</sub>). 2DL4 may transmit inhibitory, stimulatory, or both types of signals. 2DL4 probably binds to HLA-G. Some alleles of 2DL4 do not have a complete transmembrane domain but it is not clear whether these retain any function.

*2DL4* is present on most haplotypes (a KIR framework locus).

**Key references:** 2DL4 binds to HLA-G (122, 123); or does it?(124); truncated alleles described (77); SNP ([rs649216](#)) (T) associated with truncated 2DL4 (91); 2DL4 is not always present (72); 2DL4 truncated in Orangutan (101); 2DL4 signaling (125, 126).

### Unique sequences:

- 2DL4\*001: [X99480](#) (NK3.3)
- 2DL4\*00201: [X97229](#)
- 2DL4\*00202: [AF034772](#)
- 2DL4\*003: [AF003116](#) (KIR103)
- 2DL4\*004: [AF002979](#)
- 2DL4\*005: [AF034771](#)
- 2DL4\*006: [AF034773](#)
- 2DL4\*007: [AF276292](#)
- [AF276292](#)
- [AL133414](#)

**LocusLink:** [3805](#)

**OMIM:** [604945](#)

**PROW:** [2DL4](#)

## KIR2DL5

**KIR2DL5** is a member of the type 2 (D<sub>0</sub>-D<sub>2</sub>) two-domain receptors. There is no exon 4 (D<sub>1</sub>). 2DL5 is likely to transmit inhibitory signals (Figure 2). Ligand is unknown. *2DL5* is the locus that caused the extra RFLP fragment reported by Uhrberg and coworkers and thus originally defined the *KIR* 'B' haplotype (3, 59). There are two paralogous loci for this KIR. *2DL5A* is in the telomeric *KIR* region and has one known allele, 2DL5A\*001 (see below). *2DL5B* is found in the centromeric *KIR* region and has three known alleles. *2DL5B\*002* is not expressed.

**Key references:** 2DL5 characterized (75); 2DL5B\*002 is not expressed (76); 2DL5 duplicated on some haplotypes (74).

**Unique sequences:**

- 2DL5A\*001: [AF204903](#) and [AF217485](#) (2DL5.1)
- 2DL5B\*002: [AF204905](#) and [AF217486](#) (2DL5.2)
- 2DL5B\*003: [AF217487](#) (2DL5.3)
- 2DL5B\*004: [AF260138](#) (2DL5.4)
- [AF272157](#)
- [AF271607](#)
- [AF271608](#)

**LocusLink:** [57292](#)

**OMIM:** [605305](#)

## KIR3DL1

**KIR3DL1** is a three-immunoglobulin-domain inhibitory receptor. One allele, **3DS1**, is a three-immunoglobulin-domain activating receptor. 3DL1 interacts with HLA-B molecules that contain a Bw4 motif. Two commercially available clones, DX9 and Z27 react with 3DL1. DX9 and Z27 will bind to variants of 3DL1 with differing degrees of affinity; neither bind to 3DS1(55).

**Key references:** 3DL1 polymorphic(83); 3DL1 and 3DS1 alleles: high, low and no expression variants of 3DL1 (55); 3DS1 slows HIV disease progression if the correct HLA ligand is also present (6); 3DS1 rare in Africans (72); locus duplicated on some haplotypes (99).

**Unique sequences:**

- 3DL1\*00101: [L41269](#), [U30274](#), [X94262](#) (NKAT3)
- 3DL1\*00102: [AF262968](#)
- 3DL1\*002: [U31416](#), [U30273](#), [NM\\_013289](#) (NKB1)
- 3DL1\*003: [AF022049](#)
- 3DL1\*00401: [AF262969](#)
- 3DL1\*00402: [AF262970](#)
- 3DL1\*005: [AF262971](#)
- 3DL1\*006: [AF262972](#)
- 3DL1\*007: [AF262973](#)
- 3DL1\*008: [AF262974](#)
- 3DL1: [AF104848](#), [AJ417556](#), [AJ417557](#)
- 3DS1\*004: [AF022044](#)
- 3DS1: [AJ417558](#)
- #3DS1\*001: [L76661](#)
- #3DS1\*002: [X97233](#)
- #3DS1\*003: [U73396](#)
- 3DL1/3DL2 hybrid: [AY059417](#)

#not detected by PCR (55).

**LocusLink:** 3DL1: [3811](#); 3DS1: [3813](#)

**OMIM:** 3DL1: [604946](#) 3DS1: [604957](#)

**PROW:** 3DL1 3DS1

## KIR3DL2

**KIR3DL2** is a three-immunoglobulin-domain inhibitory receptor, which interacts with some HLA-A alleles. Monoclonal antibody DX31 binds to 3DL2.

*3DL2* is present on most, if not all *KIR* haplotypes (a *KIR* framework locus).

**Key references:** 3DL2 polymorphism described (83, 55, 25).

### Unique sequences:

- 3DL2\*001: [L41270](#) (NKAT4m), [AC011501](#)
- 3DL2\*002: [X94374](#), [U30272](#)
- 3DL2\*003: [X94373](#), [L76665](#)
- 3DL2\*004: [X93595](#)
- 3DL2\*005: [L76666](#)
- 3DL2\*006: [AF262966](#)
- 3DL2\*007: [AF262965](#)
- 3DL2\*008: [AF262967](#)
- 3DL2\*009: [AF263617](#)
- 3DL2\*010: [AY054918](#)
- 3DL2\*011: [AY054919](#)
- 3DL2\*012: [AY054920](#)
- [X93596](#) (NK18)
- 3DL1/3DL2 hybrid: [AY059417](#)

**LocusLink:** [3812](#)

**OMIM:** [604947](#)

**PROW:** 3DL2

## KIR3DL3

**KIR3DL3** is a three-immunoglobulin-domain receptor of unknown function or ligand. The 3DL3 gene closely resembles the other 3D genes, except that it is missing exon 6 (stalk region). *3DL3* is present on most, if not all *KIR* haplotypes (a *KIR* framework locus).

### Unique sequences:

- [AF072408](#) (KIR1C1), [AC006293](#)
- [AL133414](#)
- [AF204909](#), [AF2049010](#), [AF204911](#) (KIR44a)
- [AF204912](#), [AF204913](#), [AF204914](#) (KIR44b)
- [AF352324](#) (3DL7)
- [AY083462](#)

**LocusLink:** [115653](#)



## KIR Biology

### KIR Expression

KIR are expressed by classical NK and subpopulations of T cells (127, 128). NK clones from a single individual can vary substantially in the type of KIR molecules they express. Each cell requires at least one inhibitory receptor, such that when there is no appropriate inhibitory KIR–ligand combination, then other types of inhibitory receptor interactions will compensate (26, 129–131). With the exception of null alleles and possibly *3DL3*, all known *KIR* in a given individual's *KIR* gene repertoire are expressed, albeit apparently stochastically in order to generate a large number of different and overlapping subsets of *KIR* expression patterns (26, 132, 133). In heterozygous individuals, NK clones can express none, one or both alleles of *3DL1* and *3DL2*, but usually both alleles of *2DL4* (134). This somatic diversity means that there should be at least one NK clonal population that can respond to downregulation of any single HLA class I isotype (59, 135, 136).

*KIR* expression is likely to involve up to 15 different transcription promoter sequences which are located within 500 bp and 5' to the initiation codon (58). Other mechanisms controlling *KIR* levels are also apparent, including hormonal and cytokine regulation of expression (122, 137). Despite the many potential factors contributing to altered expression, long-term expression levels appear stable (131). The *KIR* locus maps to chromosome 19, whereas *HLA* maps to chromosome 6, and therefore the two loci segregate independently. Thus, NK cells can express *KIR* for which no known HLA ligand is present (129, 138, 139) and can also be expressed in individuals with very low HLA class I expression (140). Nevertheless, HLA can influence the number of peripheral blood *KIR*-expressing cells, but not the level of expression (131).

### KIR Ligands

The ligands for several of the inhibitory *KIR* have been shown to be subsets of HLA class I molecules based on assays measuring binding of inhibitory *KIR* to specific HLA molecules and inhibition of NK-mediated cytolysis of target cells bearing those HLA allotypes [see (59, 141, 142)].

Dimorphisms in the HLA-Cw  $\alpha$ 1 domain that are characterized by Ser77/Asn80 and Asn77/Lys80 define serologically distinct allotypes of HLA-Cw (Cw group 1 and group 2, respectively). *KIR2DL1* and *2DS1* interact with group 2 allotypes, while *2DL2*, *2DL3* and *2DS2* interact with the alternative group 1 allotypes (143–145). The specificity for Cw type is defined entirely by a single substitution at *KIR2D* position 44 (145, 146). Importantly, NK cells expressing only Cw group 2 specific inhibitory receptors can lyse targets that are homozygous for the Cw group 1 allotypes and vice versa.

*KIR3DL1* interacts with HLA-B allotypes that contain Bw4 (112, 147), a serologically-defined motif, and *3DL2* interacts with some HLA-A allotypes (87, 89). No *KIR* has yet been shown to bind allotypes containing Bw6, the alternative to Bw4 positive allotypes. Bw4 and Bw6 are also distinguished by polymorphism at positions 77 and 80. However, additional residues must be required for interaction with *3DL1*, as some HLA-A allotypes possess the Bw4 motif but are not able to bind *3DL1* (112).

*KIR2DL4*, which is unusual by nature of its extracellular domain organization and the possession of only one ITIM, probably interacts with HLA-G (122, 123, 148). A summary of *KIR* isotypes and their specificity are shown in Table 3.

**Table 3. KIR ligand specificity.**

2DL1 and 2DS1	2DL2/3 and 2DS2	3DL1/S1	3DL2	2DL4	2DS4
<b>HLA-C grp 2</b>	<b>HLA-C grp 1</b>	<b>HLA-B Bw4</b>	<b>HLA-A</b>	<b>HLA-G</b>	
C*02	C*01	B*08	A*03		C*04

Table 3 continued from previous page.

2DL1 and 2DS1	2DL2/3 and 2DS2	3DL1/S1	3DL2	2DL4	2DS4
C*04	C*03	B*13	A*11		
C*05	C*07	B*27			
C*06	C*08	B*44			
		B*51			
		B*52			
		B*53			
		B*57			
		B*58			

Ligands for 2DL5, 2DS3, 2DS5, and 3DL3 remain undefined

## KIR Structure

Crystal images of the two Ig domains for each of 2DL1 [1NKR; (94)], 2DL2 [1EFX; (117)] and 2DL3 [1B6U; (118)] are presently available. The ligand-contacting region falls at the membrane distal side of the junction between the Ig domains, which folds the D<sub>1</sub> domain towards the cell surface. 2DL1–3 have similar structures but are distinguished by the angle between the Ig domains. This (hinge) angle appears to be stable (93), so morphological changes upon ligation are unlikely.

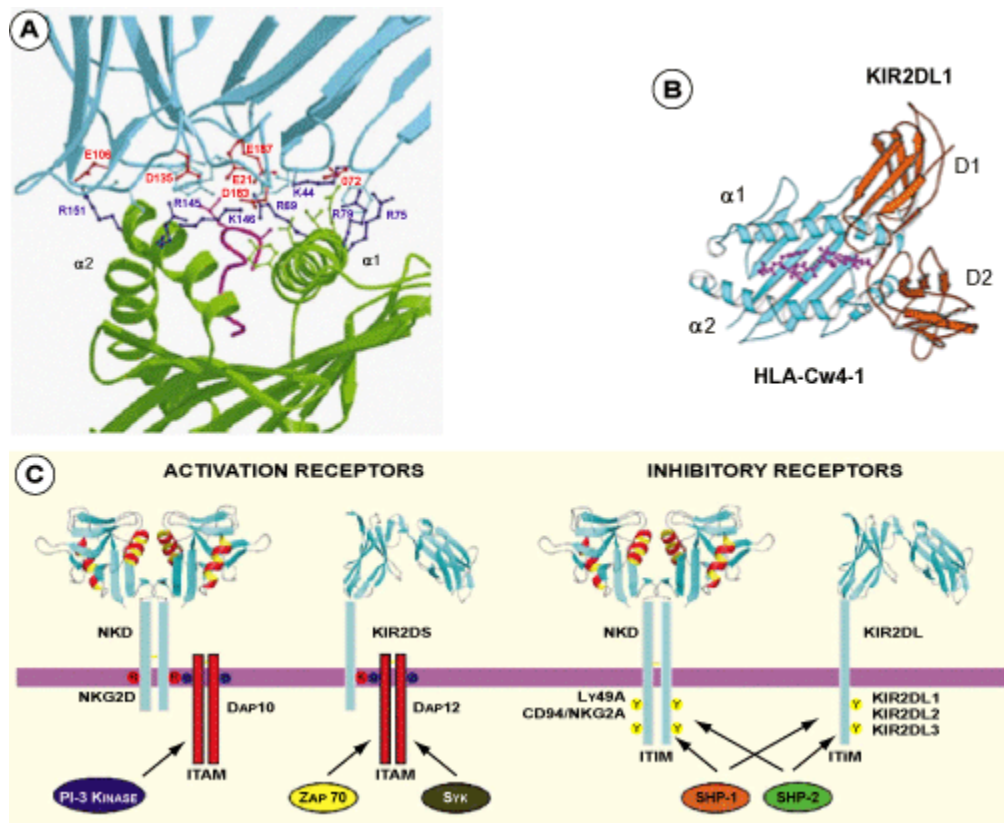
Type 1 2D KIR interact directly with the  $\alpha$ -helices and bound peptide of their HLA ligands (92, 93). Ribbon diagrams of KIR-HLA interactions determined from crystal structures are shown in Figure 8. Six loops contact the MHC molecule, three from D<sub>1</sub>, one from the hinge and two from D<sub>2</sub>; all contact points result from complementary charges (93). There are also several hydrogen bonds, salt bridges and a degree of hydrophobic interaction. These high-resolution images also indicated that the KIR molecule contacts two residues from the bound peptide and forms a hydrogen bond with one of them (92, 93).

The D<sub>1</sub> and D<sub>2</sub> domains of three Ig domain KIR are likely to form a similar interface with Class I as those described for type I 2D KIR (120). Directed mutation experiments have shown that the D<sub>0</sub> domain increases the avidity of this interaction (149), although all three Ig domains of 3DL1 were required for binding to HLA-B\*51 (150).

## KIR Interactions

KIR and TCR have overlapping footprints and therefore cannot bind to the same HLA/peptide complex concurrently (92, 93). This may impart some control over T cell activity over and above direct intracellular signaling, since KIR and TCR would be in competition for HLA ligand binding. The KIR\HLA interaction forms the basis of a natural killer immune synapse during immunosurveillance (151, 152), a process that has been illustrated by confocal microscopy (153). In these images, KIR can be seen inducing a ring formation of HLA-Cw molecules around a cluster of adhesion molecules at the cell surface. Receptor co-aggregation is likely to increase the signaling potential (117, 120). HLA and other membrane molecules may even be captured by the NK cell and either be internalized or remain at the NK cell surface (154, 155). The physiological role for intercellular transfer of HLA molecules remains to be determined, but may represent a novel mechanism for controlling NK cell activity.

Inhibitory KIR can actively prevent the localization of lipid rafts to the immune synapse (156, 157). Rafts contain complexes of activating accessory molecules, potentially explaining the dominant phenotype displayed by inhibitory receptors. The distinct binding affinities of activating compared to inhibitory KIR may also contribute



**Figure 8. Ribbon diagrams of KIR molecules.** (A) The KIR2DL2-Cw3 interface shows charged complementarity. Basic and acidic residues are shown in dark blue and red, respectively. (Reproduced from Ref. 93, with permission from Dr. Peter Sun and Nature Publishing Group.) (B) Shown is the top view of the  $\alpha 1$  and  $\alpha 2$  domains of the HLA-Cw4 molecule bound to KIR2DL1. (Reproduced from Ref. 92, with permission from Dr. Eric Long and Nature Publishing Group.) (C) Activating and inhibitory receptors are shown with their respective signaling motifs (ITIMs and ITAMs) and signaling molecules with which they associate. (Reproduced from Ref. 142, with permission from Dr. David Margulies and Blackwell Publishing Ltd.)

to the dominance of inhibition. For example, 2DL2 has a higher affinity than 2DS2 for HLA-Cw3 due to a single amino acid substitution (120).

NK cells will become activated when inhibition is removed, so activation must involve stimulatory receptors (17). Based on assays measuring target cell killing, stimulatory KIR can mediate NK cell activity through recognition of HLA ligands (158), but little if any direct binding of activating KIR molecules to their putative HLA ligands has been detected and their high affinity, physiological ligands remain in question. Candidate ligands include non-MHC molecules, such as foreign or microbial antigens expressed on infected cells, normal cell surface proteins that are aberrantly expressed, stress-induced proteins or complexes of pathogen-derived peptides bound to MHC class I molecules. Recently, the mouse cytomegalovirus m157 gene product was shown to bind the mouse activating NK cell receptor Ly49H, an interaction that leads to NK cell killing of the infected targets (159–164). Although they lack sequence homology, the mouse Ly49 and human KIR families are considered to be functionally equivalent (165). Ly49H recognition of m157 provides strong support for the possibility that non-HLA molecules can behave as ligands for activating KIR.

As discussed under the section entitled **KIR Ligands**, specificity of inhibitory KIR for HLA-Cw allotypes is dictated to a large extent by the presence of asparagine or lysine at position 80 of the HLA-Cw molecule (115). Crystal structures supported this division of ligand specificity and suggested that the bound peptide also affects KIR binding, as there is a size limit to one of the KIR-contacting residues (92, 93). Although some interactions with KIR have been shown to be independent of peptide (166), several early studies also indicated that specificity depends on the presented peptide (167–171). Peptide-dependent protection of killing by NK cells has been

observed (172, 173). Therefore, it has been suggested that inhibiting and activating receptors specific for the same HLA may respond differentially depending on bound peptides (138, 174). Peptide recognition could provide KIR with one further means for mediating pathogen-specific immunity.

## KIR Signaling

The exact mechanism for signal transmission to KIR transmembrane domains has not been elucidated. Most inhibitory KIR have two ITIMs (Box 2) and these operate in tandem to mediate inhibition (175, 176). ITIM phosphorylation results in association with SHP (Src-homology domain-bearing tyrosine phosphatase), which specifically inhibits the proteins involved in the intracellular activation cascade (177). Activating KIR have no direct signaling properties but associate with the ITAM-bearing adaptor molecule, **DAP12**. **DAP12** and short-tailed KIR associate due to complementarily charged transmembrane residues (52, 53). Ligation of activating KIR leads to phosphorylation of **DAP12**, recruitment of **ZAP-70**/Syk kinase and the induction of an intracellular signaling cascade (178, 179). Also, ligation of activating KIR may control the response by inducing apoptosis of mature cytotoxic cells (180).

One exception to the pattern of division described for stimulatory and inhibitory receptors is **2DL4** (123, 148, 181), which has a long cytoplasmic tail containing only a single ITIM motif. **2DL4** also contains a charged arginine residue in the transmembrane region, which may facilitate interaction with **DAP12**. Thus, it has been proposed that **2DL4** may transmit inhibitory, stimulatory, or both types of signals (125, 126). Some alleles of **2DL4** do not have a complete transmembrane domain (77), but it is not clear whether these are expressed at the cell surface or retain any function.

## NK Development

Classical NK cells develop from CD34<sup>POS</sup> progenitor cells in the bone marrow, in the presence of stromally derived cytokines such as IL15. KIR may be involved in this development (182), suggesting some form of selection for the NK cell receptor repertoire. A sequential pattern of KIR expression during NK maturation may occur, which could ensure self tolerance (133, 183). Clonal NK cell expression of a subset of KIR is stable over time and is predominantly determined by KIR genotype, with only moderate influence from HLA (131), if at all (182). *KIR* promoter methylation correlates with stable KIR expression, but it is not clear at which stage in development methylation patterns are established (134, 184). As KIR can be expressed for which there is no known HLA ligand and vice-versa (129, 138), there appears to be no mechanism for maturation of NK cell clones through selection. The number of functional HLA genes, for example, is controlled to some extent by selection processes in the thymus, where too many HLA molecules would restrict the TCR repertoire and thus reduce immune potential (185). Thus, the constraint placed on *MHC* polygeny may not apply to KIR, potentially explaining the large and varying number of *KIR* genes.

## CD56 Expression

Also known as N-CAM (neural cell adhesion molecule), CD56 is expressed on all NK as well as subpopulations of T cells (186), but its function remains elusive. NK cells expressing low levels of CD56 (CD56<sup>dim</sup>) tend to have more resting cytotoxic activity than those with high levels (CD56<sup>bri</sup>) (13). CD56<sup>dim</sup> NK cells express KIR, whereas CD56<sup>bri</sup> cells do not (187). It is unclear whether CD56 (and KIR) expression on a given NK cell changes with activation state (188) or if two developmental lineages occur (13). Regardless, these observations indicate that KIR expression is intrinsically linked to the cytotoxic potential of an immune cell. CD56<sup>bri</sup> cells are scarce in the periphery but have been found in lymph nodes, where they may play a role in the adaptive immune response (189).



## Disease Phenotypes and Molecular Medicine

### KIR in Adaptive Immunity

KIR can be expressed by  $\alpha\beta$ - and  $\gamma\delta$ - T cells, and they appear to be characteristic of memory CD8<sup>+</sup> T cells, through which they may modify the response to antigenic re-challenge (137, 190, 191). KIR expression appears to be inducible during early clonal expansion of T cells (192). KIR may also be important in the transition to a memory phenotype (183, 193). As the spectrum of response occurs during infection, including self-reactivity, the capacity for reactivation must be controlled. Inhibition of T cell activity by KIR may ensure that a secondary response only occurs when the danger is sufficiently strong. Moreover, expression of inhibitory KIR by T cells during an active response may help cytolytic T cells to remain focused on infected cells (137). T cells that acquire NK activating receptors may be harmful if they do not express appropriate inhibitory KIR (194). Conversely, T cells aberrantly expressing inhibitory KIR may not remove disease cells effectively (137).

### KIR and Disease

Only a limited number of studies addressing genetic associations between *KIR* genes and specific diseases have been reported to date, primarily due to the very recent and ongoing characterization of the genes and their haplotypes. Natural killer cells have been implicated in the defense against infectious diseases, particularly viral infections, through mechanisms involving cytotoxicity and cytokine production (10), presumably mediated in part by stimulatory KIR molecules. Given the receptor–ligand relationship between certain combinations of KIR and HLA class I molecules, it is reasonable to hypothesize a synergistic relationship between these polymorphic loci that may ultimately regulate NK cell mediated immunity against infectious pathogens. Recently, we showed that *3DS1* in combination with *HLA-B* alleles that encode molecules with isoleucine at position 80 (*HLA-B Bw4-80Ile*) resulted in delayed progression to AIDS after HIV infection (6). An additive genetic effect of the two loci was deemed unlikely on the basis that *HLA-B Bw4-80Ile* alleles in the absence of *3DS1* were not associated with AIDS progression, and *3DS1* in absence of *HLA-B Bw4-80Ile* was significantly associated with more rapid progression to AIDS. Thus, a model involving a protective epistatic interaction between *3DS1* and *HLA-B Bw4-80Ile* was proposed whereby *3DS1* receptors bind *HLA-B Bw4-80Ile* (perhaps when they contain HIV peptides), leading to NK cell activation and elimination of HIV-1 infected cells.

Natural selection for resistance to a pathogen can lead to the increase in frequency of alleles that are otherwise deleterious. The extensive diversity of *KIR* haplotypes might suggest the possibility of pleiotropic *KIR* effects on different diseases, whereby a *KIR* gene conferring protection against one disease may predispose to another, perhaps less deadly disease. Two studies have implicated stimulatory *KIR* genes in increased risk of developing specific autoimmune diseases (5, 119). In the first study, *2DS2* was significantly more prevalent amongst patients with rheumatoid vasculitis compared to either normal individuals or patients with rheumatoid arthritis, but no vasculitis (119, 194). CD4<sup>+</sup>CD28<sup>null</sup> T cells, as opposed to NK cells, that expressed *2DS2* were implicated in vascular damage possibly due to stimulatory effects of *2DS2*. The second study reported increased susceptibility to developing psoriatic arthritis amongst individuals with *2DS1* and/or *2DS2*, but only when HLA ligand for their homologous inhibitory receptors, *2DL1* and *2DL2 /3*, were missing (5). The data suggested that absence of ligands for inhibitory KIRs could potentially lower the threshold for NK (and/or T) cell activation mediated through stimulatory receptors, thereby contributing to disease pathogenesis.

Genome-wide linkage studies of celiac disease have suggested that candidate susceptibility loci map to the region of 19q13.4 (5, 195). Using association analyses, Moodie *et al.* (196) showed no association between celiac disease and *KIR* haplotypes distinguished by the presence or absence of *2DL1*, *2DL2*, *2DL3* and *2DL5* that could account for the linkage studies. However, this does not rule out allelic variation at any of the loci.

*2DL4* binds to HLA-G (122, 123), a nonclassical class I molecule that is expressed on the human trophoblast (197), and this receptor–ligand interaction may confer some protection against maternal NK or T cell-mediated

rejection of the hemi-allogeneic fetus. Several alleles of *2DL4* have been identified, some of which are characterized by a single nucleotide deletion that results in the elimination of exon 6 during mRNA production (77), raising the possibility that *2DL4* alleles may vary in their ability to control fetus rejection. However, a study of *2DL4* allelic variation and *KIR* gene frequencies in 45 women who experienced pre-eclampsia compared to 48 normotensive controls indicated no significant differences between the two groups (91).

Recently, KIR molecules have been implicated in reduced risk of relapse in patients with acute myeloid leukemia (AML) who received hematopoietic transplants that were mismatched for KIR ligands (7, 198). KIR ligand incompatibility was defined as absence in recipients of donor class I allelic groups known to be ligands for inhibitory KIRs (*3DL1*, *2DL2* /3, *2DL1* and *3DL2*). The data indicated that donor-versus-recipient NK cell alloreactivity was capable of eliminating leukemia relapse and graft rejection, and it also protected patients against graft-versus-host-disease.

KIR binding specificity for groups of HLA molecules raises the possibility that mechanisms responsible for HLA associations with some diseases may stem from interactions with KIR molecules on NK or T cells, and a limited number of studies have lent strong support to this hypothesis. Further delineation of the diversity at the *KIR* gene complex and development of efficient typing systems will surely foster disease association studies that are plentiful and varied as those that have addressed the *HLA* loci.

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