

## KLRK1 (killer cell lectin-like receptor subfamily K, member 1)

### Identity

Other names	<b>CD314</b> <b>D12S2489E</b> <b>NKG2D</b> <b>NKG2-D</b>
Hugo	<b><u>KLRK1</u></b>
Location	12p13.2
Local_order	KLRK1 is flanked by KLRD1 (CD94) on the centromeric and KLRC4 (NKG2F) on the telomeric side. The 3' end of the KLRC4 transcript includes the first non-coding exon found at the 5' end of the adjacent KLRK1 gene transcript.
Note	KLRK1 is on chromosome 12p13.2-p12.3 at 10,416,857-10,454,012. KLRK1 is a member of the C-type lectin-like family of type II cell surface glycoproteins. It is expressed by NK cells, CD8+ T cells, gamma/delta-TcR+ T cells, and a minor subset of CD4+ T cells. KLRK1 associates with the DAP10 transmembrane adapter protein and transmits activating signalings into these lymphocytes.

### DNA/RNA

Note	KLRK1 is present on chromosome 12 within a cluster of genes referred to as the "NK complex" (NKC) because several genes that are preferentially expressed by NK cells are located in this region, including on the centromeric side KLRD1 (CD94) and on the telomeric side KLRC4 (NKG2F), KLRC3 (NKG2E), KLRC2 (NKG2C), and KLRC1 (NKG2A).
Description	The KLRK1 gene is 37,793 bases located on the negative strand of chromosome 12 spanning 10,416,219 to 10,454,012 bp. ENTREZ database predicts 12 exons. Three alleles of KLRK1 differing by substitutions at only two nucleotide positions, of which one is nonsynonymous and the other synonymous, have been reported.
Transcription	There is evidence for alternative splicing of KLRK1, but only one isoform encoding a functional protein has been described in humans. In one of the KLRK1 splice variants the fourth exon of KLRC4 is spliced to the 5-prime end of KLRK1. KLRK1 is transcribed by NK cells, gamma/delta-TcR+ T cells, CD8+ T cells and some CD4+ T cells. Transcription of KLRK1 is enhanced by stimulation of NK cells with IL-2 or IL-15 and decreased by culture with TGF-beta.

### Protein

Note	KLRK1 is a type II membrane glycoprotein expressed as a disulfide-bonded homodimer on the cell surface. Expression of KLRK1 on the cell surface requires its association with DAP10, which is a type I adapter protein expressed as a disulfide-bonded homodimer. On the cell surface, the receptor complex is a hexamer; two disulfide-bonded KLRK1/NKG2D homodimers each paired with two DAP10 disulfide-bonded homodimers. A charged amino acid residue (aspartic acid) centrally located within the transmembrane region of DAP10 forms a salt bridge with a charged amino acid residue (arginine) in the transmembrane region of KLRK1/NKG2D to stabilize the receptor complex.
Description	KLRK1 is a type II membrane protein comprising 216 amino acids with a predicted molecular weight of 25143 kD. The protein has an N-terminal intracellular region, a transmembrane domain, and a C-terminal extracellular region with a single C-type lectin-like domain. KLRK1 is expressed on the cell surface as a disulfide-bonded homodimer with a molecular weight of approximately 42 kd when analyzed under reducing conditions and approximately 80 kd under non-reducing conditions.

A cysteine residue just outside the transmembrane region forms the disulfide bond joining the two subunits of the homodimer. There are three potential sites for N-linked glycosylation in the extracellular region of KLRK1.

Treatment of the KLRK1 glycoprotein with N-glycanase reduces the molecular weight to approximately the size of the core polypeptide. The protein has an N-terminal intracellular region, a transmembrane domain, a membrane-proximal stalk region, and an extracellular region with a single C-type lectin-like domain.

Expression	KLRK1 is transcribed by NK cells, gamma/delta-TcR+ T cells, CD8+ T cells and some CD4+ T cells.
Localisation	KLRK1 is expressed as a type II glycoprotein on the cell surface of NK cells, gamma/delta-TcR+ T cells, CD8+ T cells and some CD4+ T cells.
Function	<p>KLRK1 binds to at least seven distinct ligands: MICA, MICB, ULBP-1, ULBP-2, ULBP-3, ULBP-4, and RAET1G. These ligands are type I glycoproteins with homology to MHC class I.</p> <p>The KLRK1 ligand are frequently over-expressed on tumor cells, virus-infected cells, and "stressed" cells.</p> <p>The crystal structure of KLRK1 bound to MICA has been reported. After binding to its ligand, KLRK1 transmits an activating signal via the DAP10 adapter subunit. DAP10 has a YxxM motif in its cytoplasmic domain, which upon tyrosine phosphorylation binds to <a href="#">Vav</a> and the p85 subunit of PI3-kinase, causing a downstream cascade of signaling in T cells and NK cells.</p>
Homology	<p>NKG2-D type II integral membrane protein [<i>Pan troglodytes</i>] NP_001009059</p> <p>NKG2D protein [<i>Macaca mulatta</i>] NP_001028061</p> <p>NKG2D receptor [<i>Macaca fascicularis</i>] CAD19993</p> <p>NKG2D [<i>Callithrix jacchus</i>] ABN45890</p> <p>NKG2D [<i>Papio anubis</i>] ABO09749</p> <p>NKG2-D type II integral membrane protein [<i>Pongo pygmaeus</i>] Q8MJH1</p> <p>putative immunoreceptor NKG2D [<i>Bos taurus</i>] CAJ27114</p> <p>NKG2-D type II integral membrane protein [<i>Sus scrofa</i>] Q9GLF5</p> <p>NKG2-D isoform a [<i>Mus musculus</i>] NP_149069</p> <p>NKG2-D isoform b [<i>Mus musculus</i>] NP_001076791</p> <p>killer cell lectin-like receptor subfamily K, member 1 [<i>Rattus norvegicus</i>] NP_598196</p>

#### Mutations

Note None identified.

#### Implicated in

<b>Entity</b>	Cancer
<b>Note</b>	Many types of cancer (carcinomas, sarcomas, lymphomas, leukemias) over-express the ligands for KLRK1. In some cases, this renders the tumor cells susceptible to killing by activated KLRK1-bearing NK cells. Some tumors shed or secrete soluble ligands that bind to KLRK1 and down-regulate expression of the KLRK1 receptor on NK cells and T cells, potentially to evade attack by these immune effector cells.
<b>Entity</b>	Viral Infection
<b>Note</b>	Viral infection of cells can induce transcription and cell surface expression of ligands for KLRK1, rendering these infected cells susceptible to attack by NK cells and T cells. Some viruses, for example cytomegalovirus, encodes proteins that intercept the ligand proteins intracellularly and prevent their expression on the surface of virus-infected cells.
<b>Entity</b>	Rheumatoid Arthritis
<b>Note</b>	An expansion of CD4+,CD28- T cells expressing KLRK1 was observed in the joints of patients with rheumatoid arthritis and KLRK1 ligands were detected on synovial cells in the inflamed tissue.
<b>Entity</b>	Type I Diabetes
<b>Note</b>	Peripheral blood NK cells and T cells in patients with type I diabetes demonstrate a slightly decreased amount of expression of KLRK1 on the cell surface, independent disease duration, similar to prior observations in the NOD mouse.

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## Nomenclature

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## Cards

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## Genomic and cartography

[KLRK1](#) - [12p13.2](#) [chr12:10416220-10451632 - 12p13.2-p12.3](#) (hg18-Mar\_2006)

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## Gene and transcription

[AF260135](#) [ ENTREZ ]

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[AF439512](#) [ ENTREZ ]

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## Protein : pattern, domain, 3D structure

[11480](#)

## Protein Interaction databases

## Polymorphism : SNP, mutations, diseases

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#### Bibliography

**DNA sequence analysis of NKG2, a family of related cDNA clones encoding type II integral membrane proteins on human natural killer cells.**

Houchins JP, Yabe T, McSherry C, Bach FH.  
J Exp Med 1991; 173(4): 1017-1020.  
Medline [2007850](#)

**The genomic organization of NKG2C, E, F, and D receptor genes in the human natural killer gene complex.**

Glienke J, Sobanov Y, Brostjan C, Steffens C, Nguyen C, Lehrach H, Hofer E, Francis F.  
Immunogenetics 1998; 48(3): 163-173.  
Medline [9683661](#)

**Activation of NK cells and T cells by NKG2D, a receptor for stress-inducible MICA.**

Bauer S, Groh V, Wu J, Steinle A, Phillips JH, Lanier LL, Spies T.  
Science 1999; 285(5428): 727-729.  
Medline [10426993](#)

**An activating immunoreceptor complex formed by NKG2D and DAP10.**

Wu J, Song Y, Bakker AB, Bauer S, Spies T, Lanier LL, Phillips JH.  
Science 1999; 285(5428): 645-647.

[Hs.387787](#)

[stimulatory C-type lectin receptor signaling pathway \[Amigo\]](#) [stimulatory C-type lectin receptor signaling pathway](#)

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**Other databases**

**Probes**

[KLRK1 Related clones \(RZPD - Berlin\)](#)

**PubMed**

[71 Pubmed reference\(s\) in LocusLink](#)

Medline [10426994](#)

**ULBPs, novel MHC class I-related molecules, bind to CMV glycoprotein UL16 and stimulate NK cytotoxicity through the NKG2D receptor.**

Cosman D, Mullberg J, Sutherland CL, Chin W, Armitage R, Fanslow W, Kubin M, Chalupny NJ. *Immunity* 2001; 14(2): 123-133.

Medline [11239445](#)

**Complex structure of the activating immunoreceptor NKG2D and its MHC class I-like ligand MICA.**

Li P, Morris DL, Willcox BE, Steinle A, Spies T, Strong RK. *Nat Immunol* 2001; 2(5): 443-451.

Medline [11323699](#)

**Tumour-derived soluble MIC ligands impair expression of NKG2D and T-cell activation.**

Groh V, Wu J, Yee C, Spies T. *Nature* 2002; 419(6908): 734-738.

Medline [12384702](#)

**Stimulation of T cell autoreactivity by anomalous expression of NKG2D and its MIC ligands in rheumatoid arthritis.**

Groh V, Bruhl A, El-Gabalawy H, Nelson JL, Spies T. *Proc Natl Acad Sci U S A* 2003; 100(16): 9452-9457. Epub 2003 Jul 23.

Medline [12878725](#)

**The activating NKG2D receptor assembles in the membrane with two signaling dimers into a hexameric structure.**

Garrity D, Call ME, Feng J, Wucherpfennig KW. *Proc Natl Acad Sci U S A* 2005; 102(21): 7641-7646. Epub 2005 May 13.

Medline [15894612](#)

**Altered natural killer cells in type 1 diabetic patients.**

Rodacki M, Svoren B, Butty V, Besse W, Laffel L, Benoist C, Mathis D. *Diabetes* 2007; 56(1):177-185.

Medline [17192480](#)

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