



Published in final edited form as:

Curr Protoc Immunol. 2008 May ; CHAPTER: Appendix-IX. doi:10.1002/0471142735.ima01xs81.

Paired Receptor Systems of the Innate Immune System

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Introduction

Upon infection, the host immune system must integrate a constellation of extracellular signals to orchestrate the migration and activation of the multiple cell types required for the development an appropriate response. The host's response must be strong enough to eliminate the pathogen, but at the same time regulated so as not to inflict unwarranted damage to bystander tissues. Cells of the innate immune system are the first to be activated following infection, and therefore, typically play both a vital early effector role and a key regulatory role in both the development and attenuation of the inflammatory response. In addition, innate immune cells are critical in shaping the subsequent adaptive immune response.

As an adaptation to this critical role, innate immune cells express many regulatory receptors. Unlike T cells and B cells, the response of innate immune cells is not generally regulated through antigen specific receptors. Instead, they detect infection through more generalized methods such as the recognition of pathogen-associated molecular patterns or screening for indicators of stress such as modification or absence of MHC class I molecules. Since innate immune responses are not antigen specific, the system requires tight regulatory controls that interpret signals from several receptor-ligand interactions. One mechanism for this regulation is the expression of Paired Receptor Systems.

Paired receptors tune the inflammatory response. Many of the inhibitory receptors within paired systems participate in self tolerance by recognizing ubiquitously expressed endogenous molecules such as MHC class I molecules, cell surface sialic acid modified proteins, or CD200. During infection these markers of self are either downregulated or modified. At the same time, stress related molecules are expressed. The activating siblings of Paired Receptor Systems may recognize these "alert" molecules up-regulated as a consequence of infection or may bind constitutively expressed ligands that gain advantage as inhibitory ligands are downregulated. Alternatively, activating siblings may directly recognize pathogen associated or encoded ligands. Perhaps resolution of this issue will follow the positive identification of more activating ligands. Regardless, it is clear that these paired systems play critical roles in overall regulation of innate immunity.

In this table we review paired receptors involved in the innate immune system. For purposes of this review we define "Paired Receptors" as families of related membrane proteins that show the following characteristics: 1) encoded by different genes, but located as a gene cluster on a given chromosomes, 2) have significant homology within their extracellular domains, 3) expressed on overlapping immune populations and, 4) confirmed to have both activating and inhibitory members. For simplicity in nomenclature, whenever possible we have used the official gene nomenclature provided by NCBI and listed all other names in the alias field. In addition, we have provided a listing of both mouse and human paired systems as some families exist in both species whereas others are important in the study of either human or murine models of disease.

Table 1

Family	Receptor	Cellular Expression	Chromosome location	Other names	Receptor characteristics	Cytoplasmic tyrosine motifs	Ligands(s)	Action	References
CD200r	Cd200r1	Granulocytes, Monocytes, DCs, Macrophages, Mast cells, T cells, NKT cells, B cells	16	CD200R, Mox2r, OX2R	Type I transmembrane protein, 2 Ig-like domains	None	CD200	Inhibition	Wright GJ, et al. 2000. <i>Immunity</i> . 13: 233 Wright GJ, et al. 2003. <i>J Immunol</i> . 171:3034 Vieites JM, et al. 2003. <i>Gene</i> . 311: 99 Hatherley D, et al. 2005. <i>J Immunol</i> . 175: 2469 Voehringer D, et al. 2004. <i>J Biol Chem</i> . 279: 54117 Wright GJ, et al. 2003. <i>J Immunol</i> . 171: 3034 Hatherley D, et al. 2005. <i>J Immunol</i> . 175: 2469 Wright GJ, et al. 2003. <i>J Immunol</i> . 171: 3034 Hatherley D, et al. 2005. <i>J Immunol</i> . 175: 2469 Izawa K, et al. 2007. <i>J Biol Chem</i> . Apr 16.
CD200r	Cd200r3	Basophils, Mast cells, Monocytes, DCs, B cells	16	mCD200RLb	Type I transmembrane protein, 2 Ig-like domains, Associates with DAPI2	None	Unknown	Activation	
CD200r	Cd200r4	Macrophages, Monocytes, Granulocytes, Mast cells, DCs, NK, NKT, B cells	16	mCD200RLa, Cd200r2	Type I transmembrane protein, 2 Ig-like domains, Associates with DAPI2	None	Unknown	Activation	
CD300	4732429D16Rik	Granulocytes, Macrophages, Mast cells	11	CLM5, LMIR4, cIm-5, RP23-331L12.3	Type I transmembrane protein, 1 Ig-like domain, Associates with FcR γ chain	None	Unknown	Activation	
CD300	CD300a	Macrophages, Mast cells, DCs, Granulocytes, B cells, Eosinophils	11	LMIR1, CIm8, MMAC8, Pigr4, mepir1, MAIR-1a	Type I transmembrane, 1 Ig-like domain	ITIMs	Unknown	Inhibition	Munitz A, et al. 2006. <i>J Allergy Clin Immunol</i> . 118: 1082 Kumagai H, et al. 2003. <i>Biochem Biophys Commun</i> . 307: 719 Yotsumoto K, et al. 2003. <i>J Exp Med</i> . 198: 223 Bachelet I, et al. 2005. <i>J Immunol</i> . 175: 7989 Martinez-Barriocanal A and Sayos J. 2006. <i>J Immunol</i> . 177: 2819
CD300	Cd300b (AAV56360)	Myeloid cells	11	mIREM-3	Type I transmembrane protein, 1 Ig-like domain, Associates with DAPI2 and other unidentified molecules	None	Unknown	Activation	
CD300	Cd300c	Monocytes, Neutrophils, T cells, B cells	11	CIm6	Type I transmembrane protein, Charged lysine residues in TM	None	Unknown	Activation?	Chung DH, et al. 2003. <i>J Immunol</i> . 171: 6541
CD300	CD300d	Macrophages, a subset of B cells, Mast cells	11	LMIR2, CLM4, DIgR1, Igsf7, Cd300c, MAIR-II	Type I transmembrane, Ig-like receptor, Associates with either DAPI2, DAPI0 or FcR γ chain	None	Unknown	Activation	Kumagai H, et al. 2003. <i>Biochem Biophys Commun</i> . 307: 719 Nakahashi C et al. 2007. <i>J Immunol</i> . 178: 765 Yotsumoto K, et al. 2003. <i>J Exp Med</i> . 198: 223 Tumbull IR, et al. 2007. <i>Nature Rev</i> . 7: 155 Chung DH, et al. 2003. <i>J Immunol</i> . 171: 6541
CD300	Cd300e	Myeloid cells	11	CLM2; TREM5; Cd300le	Type I transmembrane protein, Charged lysine residue in TM	None	Unknown	Activation?	
CD300	Cd300f	DCs	11	CLM1, CLIM1, Digr2, IREM1, Pigr3, Igsf13, F730004D16Rik, LMIR3	Type I transmembrane protein, 1 Ig-like domain	2 ITIMs	Unknown	Inhibition	Shi L, et al. 2006. <i>Blood</i> . 108: 2678 Álvarez-Errico D, et al. 2007. <i>J Immunol</i> . 178: 808 Izawa K, et al. 2007. <i>J Biol Chem</i> . Apr 16.
Clec5	Clec4a2	DCs, Neutrophils, B cells, Monocytes, Macrophages	6	DCIR, Dcirl, Clec5f6	Type II transmembrane protein, C-type lectin	ITIMs	Unknown	Inhibition	Bates EE, et al. 1999. <i>J Immunol</i> . 163: 1973 Kanazawa N, et al. 2004. <i>Immunobiology</i> . 209: 179

Family	Receptor	Cellular Expression	Chromosome location	Other names	Receptor characteristics	Cytoplasmic tyrosine motifs	Ligand(s)	Action	References
Clecs	Clec4b1	DCs, Monocytes, Macrophages, B cells	6	DCAR, Aplra2, Clec4b, mDcar2, DCAR β	Type II transmembrane protein, C-type lectin, Associates with Fc ϵ R γ chain	None	Unknown	Activation	Flornes LM, et al. 2004. Immunogenetics. 56: 506 Kanazawa N, et al. 2002. J Invest. Dermatol. 118: 261 Kanazawa N, et al. 2004. Immunobiology. 209: 179 Kanazawa N, et al. 2003. J Biol Chem. 278: 32645 Robinson MJ, et al. 2006. Nature Immunol. 7: 1258 Aragane Y, et al. 2003. J Immunol. 171: 3801 Taylor PR, et al. 2005. Eur J Immunol. 35: 2163 Robinson MJ, et al. 2006. Nature Immunol. 7: 1258 Fernandes MJ, et al. 1999. Cancer Res. 59: 2709 Bakker A.B, et al. 1999. Proc Natl Acad Sci USA. 96: 9692
Clecs	Clec4n	Monocytes, DCs, Polymorphonuclear cells	6	Clecsf10, dectin2	Type II transmembrane protein, C-type lectin, Fc ϵ R γ chain?	None	weak affinity to mannose	Activation	Arizumi K, et al. 2000. J Bio Chem. 275: 20157
Clecs	Clec5a	Macrophages, Monocytes	6	Md11, Ly100, Clecsf5	Type II transmembrane protein, C-type lectin, Associates with DAP12	None	Unknown	Activation	Ryan JC, et al. 2001. Immunol Rev. 181: 126 Giorda et al. 1990. Science. 249: 1298 Plougastel et al. 2001. Immunogenetics 53: 592
Clecs	Clec7a	Macrophages, DCs, Monocytes, T cells, Polymorphonuclear cells	6	BGR, Clecsf12, β -GR	Type II transmembrane protein, C-type lectin	ITAM-like motif (YxxL)	β -1,3-linked and β -1,6-linked glucans	Activation	Carlyle JR, et al. 2004. Proc Natl Acad Sci USA. 101: 3527
Klrb	Klrb1a	NK cells, NKT cells	6	Ly55a, NKR-PIA, Nkrp1-a, NKR-PI 2	C-type lectin, Type II transmembrane protein, Believed to associate with Fc ϵ R γ chain	YxxL motif	Clr	Activation or Inhibition	Trowsdale et al. 2001. Immunol Rev 181: 20 Ryan JC, et al. 2001. Immunol Rev. 181: 126 Giorda et al. 1990. Science. 249: 1298 Plougastel et al. 2001. Immunogenetics 53: 592
Klrb	Klrb1b	NK cells, NKT cells	6	Ly55b, NKR-PIB, Nkrp1-b, NKR-PI 34	C type lectin, Type II transmembrane protein	ITIM	Unknown	Inhibition	USA. 101: 3527
Klrb	Klrb1c	NK cells, NKT cells	6	117187	C type lectin, Type II transmembrane protein, Associates with Fc ϵ R γ chain	none	Unknown	Activation	Ryan JC, et al. 2001. Immunol Rev. 181: 126 Giorda et al. 1990. Science. 249: 1298 Plougastel et al. 2001. Immunogenetics 53: 592
Klrb	Klrb1d	NK cells, NKT cells	6	Ly55d, Nkrp1d, NKR-PI D	C type lectin, Type II transmembrane protein	ITIM	Clr-b	Inhibition	Ryan JC, et al. 2001. Immunol Rev. 181: 126 Giorda et al. 1990. Science. 249: 1298 Plougastel et al. 2001. Immunogenetics 53: 592
Klrb	Klrb1f	NK cells, CD8 ⁺ T cells, DCs	6	Nkrp1f, NKR-PI F, Nkrp1-f	C type lectin, Type II transmembrane protein, Charged arginine residue in TM	None	Clr-g	Activation?	Plougastel et al. 2001. Immunogenetics 53: 592 Iizuka K, et al. 2003. Nat Immunol. 4: 801 Iizuka K, et al. 2003. Nat Immunol. 4: 801 Tian W, et al. 2005. Cell Immunol. 234: 39
Ly49	Ly49A	NK cells, NKT cells, some T cells	6	-	C-type lectins homodimers, Ly49A-like subfamily of Inhibitors	ITIM	D ^{dk}	Inhibition	Plougastel B, et al. 2001. Immunogenetics. 53: 209 Karlhofer et al. 1992. Nature 358: 66 Smith et al. 1994. J. Immunol. 153: 1068 Chan et al. 1989. J. Immunol. 142: 1727

Family	Receptor	Cellular Expression	Chromosome location	Other names	Receptor characteristics	Cytoplasmic tyrosine motifs	Ligand(s)	Action	References
Ly49	Ly49B	Myeloid cells	6	-	C-type lectin; homodimers, Distantly related to inhibitory Ly49s	ITIM	D ^d , D ^b , D ^k , K ^b , K ^d	Inhibition	Hanke et al. 1999, Immunity 11: 67 Wong et al. 1991, J. Immunol. 147: 1417 Scarpellino et al. 2007, J. Immunol. 178: 1277
Ly49	Ly49C	NK cells, NKT cells, some T cells	6	-	C-type lectins, Homodimers, Ly49C/I-like subfamily of inhibitors	ITIM	D ^{b,dk} , K ^d	Inhibition	Gays et al. 2006, J. Immunol. 177: 5840 Hanke et al. 1999, Immunity 11: 67 Brennan et al. 1996, J. Exp. Med. 184: 2085 Stoneman et al. 1995, J. Exp. Med. 182: 305
Ly49	Ly49D	NK cells	6	-	C-type lectins, Homodimers, Associates with DAPI2, Ly49A-like subfamily of activators	None	D ^{d,sp}	Activation	Ortaldo et al. 1999, J. Immunol. 163: 5269 Smith et al. 1994, J. Immunol. 153: 1068 Mason et al. 1996, J. Exp. Med. 184: 2119,
Ly49	Ly49E	NK cells, NKT cells, some T cells	6	-	C-type lectins, Homodimers, Ly49C/I-like subfamily of inhibitors	ITIM	?	Inhibition	Makrigiannis et al. 2001, J. Immunol. 166: 5034
Ly49	Ly49F	NK cells, NKT cells, some T cells	6	-	C-type lectins, Homodimers, Ly49C/I-like subfamily of inhibitors	ITIM	?	Inhibition	Smith et al. 1994, J. Immunol. 153: 1068 Gays et al. 2005, J. Immunol. 175: 2938
Ly49	Ly49G	NK cells, NKT cells, some T cells	6	-	C-type lectins; homodimers, Ly49C-like subfamily of inhibitors	ITIM	D ^d , L ^d	Inhibition	Fraser et al. 2002, Eur. J. Immunol. 32: 868 Smith et al. 1994, J. Immunol. 153: 1068 Gays et al. 2005, J. Immunol. 175: 2938
Ly49	Ly49H	NK cells	6	-	C-type lectin, Homodimer, Associates with DAPI2, Ly49C/I-like subfamily of activators	None	D ^b , and m157 in B6 mice	Activation	Hanke et al. 1999, Immunity 11: 67 Mason et al. 1995, J. Exp. Med. 182: 293 Smith et al. 1994, J. Immunol. 153: 1068 Brennan et al. 1996, J. Exp. Med. 184: 2085
Ly49	Ly49I	NK cells, NKT cells, some T cells	6	-	C-type lectins, Homodimers, Ly49C/I-like subfamily of inhibitors	ITIM	K ^d , D ^k , D ^d (in B6 mice), m157 (in 129 mice)	Inhibition	Gosselin et al. 1999, J. Leuk. Biol. 66: 165
Ly49	Ly49J	NK cells, NKT cells, some T cells	6	-	C-type lectins, Homodimers, Ly49C/I-like subfamily of inhibitors	ITIM	?	Inhibition	Hanke et al. 1999, Immunity 11: 67 Makrigiannis et al. 2001, J. Immunol. 166: 5034
Ly49	Ly49L	NK cells	6	-	C-type lectin, Homodimer, Associates with DAPI2, Ly49C/I-like subfamily of activators	None	Unknown	Activation	McQueen et al. 1999, Immunogenetics 48: 174
Ly49	Ly49O	NK cells, NKT cells, some T cells	6	-	C-type lectins homodimers, Ly49A-like subfamily of Inhibitors	ITIM	D ^{b,dk} , L ^d	Inhibition	McQueen et al. 1999, Immunogenetics 48: 174 Makrigiannis et al. 2000, J. Leuk. Biol. 68: 765
Ly49	Ly49P	NK cells	6	-	C-type lectins, Homodimers, Associates with DAPI2, Ly49A-like subfamily of activators	None	D ^{dk} (in NOD mouse strain)	Activation	Makrigiannis et al. 1999, J. Immunol. 163: 4931 Silver et al. 2000, J. Immunol. 165: 1771
Ly49	Ly49Q	pDC	6	-	C-type lectin; homodimers, Distantly related to inhibitory Ly49s	ITIM	K ^b	Inhibition	Makrigiannis et al. 2002, Genomics 79: 437
Ly49	Ly49R	NK cells	6	-	C-type lectins, Homodimers, Associates with DAPI2,	None	D ^{b,dk} , L ^d	Activation	Tai et al. 2007, Mol. Immunol. 44: 2638 Toyama-Sorimachi et al. 2005, J. Immunol. 174: 4621 Scarpellino et al. 2007, J. Immunol. 178: 1277 Makrigiannis et al. 2001, J. Immunol. 166: 5034

Family	Receptor	Cellular Expression	Chromosome location	Other names	Receptor characteristics	Cytoplasmic tyrosine motifs	Ligand(s)	Action	References
Ly49	Ly49S	NK cells, NKT cells, some T cells	6	-	Ly49A-like subfamily of activators C-type lectins, Homodimers, Ly49C/I-like subfamily of inhibitors	ITIM	?	Inhibition	Makrigiannis et al. 2001. J. Immunol. 166: 5034
Ly49	Ly49T	NKT cells, some T cells	6	-	C-type lectins, Homodimers, Ly49G-like subfamily of inhibitors	ITIM	?	Inhibition	Makrigiannis et al. 2001. J. Immunol. 166: 5034
Ly49	Ly49U	NK cells	6	-	C-type lectin, Homodimer, Associates with DAPI2, Ly49C/I-like subfamily of activators	None	D ^b	Activation	Makrigiannis et al. 2001. J. Immunol. 166: 5034
Ly49	Ly49V	NK cells, NKT cells, some T cells	6	-	C-type lectins homodimers, Ly49A-like subfamily of inhibitors	ITIM	D ^{d,b,k} , K ^{b,d,k} , L ^d	Inhibition	Makrigiannis et al. 2001. J. Immunol. 166: 5034
Ly49	Ly49W	—	6	-	C-type lectin, Homodimer, Associates with DAPI2, Ly49G-like subfamily of activators	D ^{d,k} (in NOD mouse strain)	Unknown	Activation	Silver et al. 2001. J. Immunol. 166: 2333
NKG2	NKG2A/B	NK cells, Activated CD8 ⁺ , NKT cells	6	CD159A, Klrc1	Heterodimerizes with CD94	2 ITIMs	Qa-1 (b)	Inhibition	Salcedo et al. 1998. Eur J Immunol. 28: 4356 Vance et al. 1998. J Exp Med. 188: 1841 Smith et al. 2001. Immunol Rev. 181: 115 Barten et al. 2001. Trends Immunol. 22: 52 Lohwasser et al. 1999. Eur J Immunol. 29: 755
NKG2	NKG2C	NK cells, Activated CD8 ⁺ cells, NKT cells	6	Klrc2	C-type lectin, Heterodimerizes with CD94, Associates with DAPI2	None	Qa-1 (b)	Activation	Salcedo et al. 1998. Eur J Immunol. 28: 4356 Vance et al. 1999. J Exp Med. 190: 1801 Smith et al. 2001. Immunol Rev. 181: 115 Barten et al. 2001. Trends Immunol. 22: 52 Lohwasser et al. 1999. Eur J Immunol. 29: 755
NKG2	NKG2D	NK cells, Activated CD8 ⁺ , LPS-activated macrophages	6	None	C-type lectin, Associates with DAPI10	None	H60, RAE-1	Activation	Ho et al. 1998. Proc Natl Acad Sci USA. 95: 6320 Smith et al. 2001. Immunol Rev. 181: 115 Cerwenka et al. 2000. Immunity. 12: 721 Lanier LL. 2003. Curr Opin Immunol. 15: 308
NKG2	NKG2D-S (short form)	NK cells, T	6	None	C-type lectin, Associates with DAPI12 and DAPI10	None	H60, RAE-1	Activation	Giffillan S et al. 2002. Nature Immunol. 3: 1150 Diefenbach A et al. 2002. Nature Immunol. 3: 1142 Lanier LL. 2003. Curr Opin Immunol. 15: 308
NKG2	NKG2E	Activated CD8 ⁺ cells	6	Klrc3	C-type lectin, Heterodimerizes with CD94, Associates with DAPI2	None	Qa-1 (b)	Activation	Vance RE. et al. 1999. J Exp Med. 190: 1801 O'Callaghan CA. et al. 2000. Microbes Infect. 2: 371
PILR	Pilra	Granulocytes, Macrophages	5	FDFF03	1 Ig-like domain	ITIM	CD99 like molecules	Inhibition	Fournier NJ. et al. 2000. Immunol. 165: 1197
PILR	Pilrb1	NK cells, Macrophages, DCs, Granulocytes	5	Fdact, Pilrb, FDFACT	1 Ig-like domain, Associates with DAPI2	None	CD99 like molecules	Activation	Shiratori I. et al. 2004. J Exp Med. 199: 525 Fournier NJ. et al. 2000. Immunol. 165: 1197 Shiratori I. et al. 2004. J Exp Med. 199: 525

Family	Receptor	Cellular Expression	Chromosome location	Other names	Receptor characteristics	Cytoplasmic tyrosine motifs	Ligands(s)	Action	References
PIR	Lilrb3	Mast cells, Macrophages, B cells, Granulocytes, DCs, Neurons	7	Gp91, Lilrb3, Pirb	6 Ig-like domains	1 ITIM and 2 ITSMs	H-2K ^b , 2K ^k , 2K ^d , 2D ^d , 2L ^d , HLA-G	Inhibition	Takai T. 2005. <i>Immunology</i> . 115: 433 Chen CC. et al. 2002. <i>Immunol Res</i> . 26: 191 Liang S. et al. 2002. <i>Eur J Immunol</i> . 32: 2418 Ujike A et al. 2002. <i>Nat Immunol</i> . 3: 542 Syken J. et al. 2006. <i>Science</i> . 313: 1795 Kubagawa H. et al. 1997. <i>Proc Natl Acad Sci USA</i> . 94: 5261 Takai T. 2005. <i>Immunology</i> . 115: 433 Colonna M. 2003. <i>Nature Rev Immunol</i> . 3: 1
PIR	PirA1	Mast cells, Macrophages, DCs, Granulocytes	7	Pir, 6M21, Ly89, PIR-A1	6 Ig-like domains, Associates with Fcγ chain	None	H-2 molecules, HLA-G	Activation	Brinkman-Van der Linden EC. et al. 2003. <i>Mol Cell Biol</i> . 23: 4199 Crocker PR. and Varki A. 2001. <i>Immunology</i> . 103: 137 Crocker PR. et al. 2002. <i>Curr Op Structure Biol</i> . 12: 609 Crocker PR. et al. 2007. <i>Nature Rev Immunol</i> . 7: 255
Siglec	Siglec-3	Monocytes, Macrophages	7	Cd53, gp67	Type I transmembrane protein, 2 Ig-like domains	ITIM and ITSM	Sialic acids	Inhibition	Aizawa H. et al. 2003. <i>Genomics</i> . 82: 521 Zhang JQ. 2004. <i>Eur J Immunol</i> . 34: 1175 Yu Z. et al. 2001. <i>Biochem J</i> . 353: 483 Crocker PR. et al. 2007. <i>Nature Rev Immunol</i> . 7: 255
Siglec	Siglece	Neutrophils, Monocytes, Macrophages, Eosinophils, NK cells, DCs, Some B cells	7	Cd170, Siglec5, Siglec9, Siglec11, mSiglec-E	Type I transmembrane protein, 3 Ig-like domains	ITIM and ITSM	Sialic acids	Inhibition	Zhang M. et al. 2007. <i>Blood</i> . 109: 4280 Aizawa H. et al. 2003. <i>Genomics</i> . 82: 521 Angata T. et al. 2001. <i>J Biol Chem</i> . 276: 45128 Crocker PR. et al. 2007. <i>Nature Rev Immunol</i> . 7: 255
Siglec	Siglecf	Eosinophils	7	Siglec5; mSiglec-F	Type I transmembrane protein, 4 Ig-like domains	ITIM and ITSM	Sialic acids (α2,3-linkages > α2,6-linkages)	Inhibition	Crocker PR. et al. 2007. <i>Nature Rev Immunol</i> . 7: 255 Crocker PR. et al. 2007. <i>Nature Rev Immunol</i> . 7: 255
Siglec	Siglecg	Eosinophils, B cells	7	Siglec-G; Siglec10; mSiglec-G	Type I transmembrane protein, 5 Ig-like domains	ITIM and ITSM	Sialic acids	Inhibition	Aizawa H. et al. 2003. <i>Genomics</i> . 82: 521 Blasius AL. et al. 2006. <i>Blood</i> . 107: 2474 Blasius AL. et al. 2006. <i>Trends Immunol</i> . 27: 255 Zhang J. et al. 2006. <i>Blood</i> . 107: 3600 Crocker PR. et al. 2007. <i>Nature Rev Immunol</i> . 7: 255
Siglec	Siglech	Plasmaocytoid DCs	7	Siglec-H	Type I transmembrane protein, 2 Ig-like domains, Associates with DAP12	None	Sialic acids	Inhibition of IFNα pathway	Sano S. et al. 1997. <i>FEBS Lett</i> . 411: 327 Barclay AN. and Brown M.H. 2006. <i>Nature Rev Immunol</i> . 6: 457 Lahoud MH. et al. 2006. <i>J Immunol</i> . 177: 372
SIRP	Sirpα	Myeloid cells, Neurons	2	Sirp-α, P84, SIRP, SHP-1, CD172a, Ptpnsl1, SHPS-1, Bit	3 Ig-like domains	ITIMs	CD47, Surfactant proteins A and D	Inhibition	Hayashi A. et al. 2004. <i>J Biol Chem</i> . 279: 29450 Barclay AN. and Brown M.H. 2006. <i>Nature Rev Immunol</i> . 6: 457 Keller MS. Et al. 2004. <i>J Mol Biol</i> . 344: 1175
SIRP	Sirpβ1	Macrophages, Neutrophils	3	Sirpβ, SIRP-β	3 Ig-like domains, Associates with DAP12	None	Unknown	Activation	Murakami Y. et al. 2007. <i>J Immunol</i> . 178: 1144 Chung DH. et al. 2002. <i>Eur J Immunol</i> . 32: 59 Bouchon A. et al. 2001. <i>Nature</i> . 410: 1103
TREM	Trem1	A subset of monocytes and macrophages, Neutrophils, Granulocytes	17	-	Type I transmembrane protein, 1 Ig-like domain, Associates with DAP12	None	Unknown	Activation	

Family	Receptor	Cellular Expression	Chromosome location	Other names	Receptor characteristics	Cytoplasmic tyrosine motifs	Ligand(s)	Action	References
TREM	Trem2	Activated macrophages, DCs, Osteoclasts, Microglia	17	Trem2a, Trem2b, Trem2c	Type I transmembrane protein, 1 Ig-like domain, Associates with DAP12	None	Unknown	Activation/Inhibition	Daws MR, et al. 2003. <i>J. Immunol.</i> 171: 594 Tumbull IR et al. 2006. <i>J Immunol.</i> 177: 5520 Hamerman JA, et al. 2006. <i>J Immunol.</i> 177: 2051 Humphrey MB, et al. 2006. <i>J Bone Miner Res.</i> 21: 237 Chung DH, et al. 2002. <i>Eur J Immunol.</i> 32: 59
TREM	Trem3	Myeloid cells	17	-	Type I transmembrane protein, 1 Ig-like domain, Associates with DAP12	None	Unknown	Activation	

Table 2

Human		Family	Receptor	Cellular Expression	Chromosome location	Other names	Receptor characteristics	Cytoplasmic tyrosine motifs	Ligands(s)	Action	References
CD200R	CD200R1	Macrophages, Neutrophils, Monocytes, DCs, Mast cells, T cells, NKT cells, B cells	3	OX2R, MOX2R, CD200R, HCRTR2	Type I transmembrane protein, 2 Ig-like domains	None	None	CD200	Inhibition	Minas K. et al. 2006. Crit Rev Immunol. 26: 213 Wright GJ et al. 2003. J Immunol. 171: 3034	
CD200R	CD200R2	Basophils, Mast cells	3	CD200RLa	Type I transmembrane protein, 2 Ig-like domain, Associates with DAPI2	None	None	Unknown	Activation	Wright GJ. et al. 2003. J Immunol. 171: 3034 Voehringer D. 2004. J Biol Chem. 279: 54117	
CD300	CD300A	Eosinophils, Mast cells	17	IRC1, IRC2, IRp60, IGSF12, CMRF35H, CMRF35H9	Type I transmembrane protein, 1 Ig-like domain,	3 ITIMs	Unknown	Unknown	Inhibition	Munitz A. et al. 2006. Blood. 107: 1996 Bachelet I. et al. 2005. J Immunol. 175: 7989	
CD300	CD300C	Monocytes, Neutrophils, T cells, B cells	17	CMRF35A1, CMRF35A, CMRF35, IGSF16	Type I transmembrane protein, 1 Ig-like domain, Adaptor molecule	None	None	Unknown	Activation	Clark GL. et al. 2001. Tissue Antigens. 57: 415	
CD300	CD300E	Monocytes, Myeloid DCs, Macrophages	17	CLM2, IREM2, CD300LE	Type I transmembrane protein, 1 Ig-like domain, Associates with DAPI2	None	None	Unknown	Activation	Aguilar H. et al. 2004. J Immunol. 173: 6703 Clark GJ. et al. 2007. J Immunother. 30: 303	
CD300	CD300LB	Myeloid cells	17	CLM7, IREM3, TREM5	Type I transmembrane protein, 1 Ig-like domain, Associates with DAPI2 and unidentified molecules	Tyrosine-based motif	Unknown	Unknown	Activation	Martinez-Barriocanal A. and Sayos J. 2006. J Immunol. 177: 2819	
CD300	CD300LF	Myeloid cells	17	CLM1, NKIR, IREM1, CD300f, IgSFI3	Type I transmembrane protein, 1 Ig-like domain	2 ITIMs	Unknown	Unknown	Inhibition	Marquez J. A. et al. 2007. J Mol Biol. 367: 310 Alvarez-Errico D. et al. 2007. J Immunol. 178: 808	
CLEC	CLEC12A	Monocytes, Macrophages, DCs, Granulocytes	12	CLL1, MICL, CLL-1, DCAL-2	Type II transmembrane protein, C-type lectin	1 ITIM	Unknown	Unknown	Inhibition	Alvarez-Errico D. et al. 2004. Eur J Immunol. 34: 3690 Marshall AS. et al. 2004. J Biol Chem. 279: 14792 Bakker AB. et al. 2004. Cancer Res. 64: 8443 Robinson MJ. et al. 2006. Nat Immunol. 7: 1258	
CLEC	CLEC2B	Macrophages, Granulocytes, Monocytes	12	AICL, IFNRG1, CLECSF2	Type II transmembrane protein, C-type lectin	?	NKp80		Activation	Welte S. et al. 2006. Nature Immunol. 7: 1334	
CLEC	CLEC2D	NK cells	12	LLT1, OCIL, CLAX	Type II transmembrane protein, C-type lectin	?	KLRB1 (NKR-PIA)		Activation	Boles KS. et al. 1999. Immunogenetics. 50: 1 Lebbink RJ. and Meygaard L. 2007. Mol Immunol. 44: 2153 Aldemir H. et al. 2005. J Immunol. 176: 7791	
CLEC	CLEC4A	DCs, Neutrophils, B cells, Monocytes, Macrophages	12	DCIR, LLI, DDB27, CLECSF6, HDCGC13P	Type II transmembrane protein, C-type lectin	1 ITIM	Unknown	Unknown	Inhibition	Rosen DB. Et al. 2005. J immunol. 176: 7796 Mathew PA. et al. 2004. Mol Immunol. 40: 1157 Kanazawa N. et al. 2004. Immunobiology. 209: 179 Bates EE. et al. 1999. J Immunol. 163: 1973	

Family	Receptor	Cellular Expression	Chromosome location	Other names	Receptor characteristics	Cytoplasmic tyrosine motifs	Ligands(s)	Action	References
CLEC	CLEC4C	Plasmacytoid DCs, Monocytes, Macrophages, Neutrophils	12	DLEC, HECL, BDCA2, CD303, CLECSF7, CLECSF11	Type II transmembrane protein, C-type lectin, Adaptor molecules unknown	None	Unknown	Activation or Inhibition	Dzionic A. et al. 2001. J Exp Med. 194: 1823 Dzionic A. et al. 2002. Hum Immunol. 63: 1133 Kanazawa N. et al. 2004. Immunobiology. 209: 179 Sato et al. 2006. J Biol Chem. 281: 38854 Gavino AC. et al. 2005. Exp Dermatol. 14: 281 Robinson MJ. et al. 2006. Nat Immunol. 7: 1258 Kanazawa N. et al. 2004. Immunobiology. 209: 179 Gersuk GM. et al. 2006. J Immunol. 176: 3717 Underhill DM. et al. 2005. Blood. 106: 2543 Robinson MJ. et al. 2006. Nat Immunol. 7: 1258 Lee MS. et al. 2007. Mol Cells. 23: 1 Willment JA. et al. 2005. Eur J Immunol. 35: 1539 Lanier LL. et al. 1994. J Immunol. 153: 2417 Pozp D. et al. 2006. J Immunol. 176: 2397 Lebbink RJ. and Meygaard L. 2007. Mol Immunol. 44: 2153 Aldemir H. et al. 2005. J Immunol. 176: 7791 Rosen DB. Et al. 2005. J immunol. 176: 7796 Welte S. et al. 2006. Nature Immunol. 7: 1334
CLEC	CLEC6A	Monocytes, Macrophages, Neutrophils, DCs, B cells, Activated CD4 ⁺ T cells	12	CLECSF10, dectin-2	Type II transmembrane protein, C-type lectin, Associates with Fc γ receptor	None	Hyphal components of some fungi	Activation	
CLEC	CLEC7A	Macrophages, DCs, Monocytes, T cells, B cells, Eosinophils, Polymorphonuclear cells	12	DECTIN1, CLECSF12, BGR	Type II transmembrane protein, C-type lectin	ITAM-like motif (YxxL)	β -1,3-linked and β -1,6-linked glucans	Activation	
CLEC	KLRB1	NK cells, NKT cells, T cells	12	NKR-P1A, NKR-P1, NKR, CD161, CLEC5B	Type II transmembrane protein, C-type lectin	?	CLEC2D (LLT1)	Activation or Inhibition	
CLEC	KLRF1	NK cells	12	NKp80, CLEC5C	Type II transmembrane protein, C-type lectin, Homodimer, Lack of charged residues	?	CLEC2B (A1CL)	Activation	
CLEC	KLRG1	Some NK cells and T cells	12	2F1, MAFA, MAFA-L, CLEC15A, MAFA-2F1, MGC13600	Type II transmembrane protein, C-type lectin	1 ITIM	Cadherins	Inhibition	Lebbink RJ. and Meygaard L. 2007. Mol Immunol. 44: 2153 Ito M. et al. 2006. J Exp Med. 203: 289 Grundermann C. et al. 2006. J Immunol. 176: 1311 Stewart C.A. et al. 2005. Proc Natl Acad Sci USA. 102: 13224 Colonna M. and Samaridis J. Science. 1995. 268: 405 Wagtmann N. et al. 1995. Immunity. 2: 439 Boyington JC. et al. 2001. Mol Immunol 38: 1007 Lanier LL. et al. Annu Rev Immunol 2005. 23: 225 Parham P. 2005. Nature Rev Immunol. 5: 201
KIR	KIR2DL1	NK, NKT cells, T cells	19	NKAT, 47,11, CL-42, NKAT1, p58,1, CD158a, KIR-K3, KIR-K9, KIR221, KIR-K64, KIR-K65	Type I transmembrane protein, 2 Ig-like domains	2 ITIMs	HLA-C N77/K80	Inhibition	

Family	Receptor	Cellular Expression	Chromosome location	Other names	Receptor characteristics	Cytoplasmic tyrosine motifs	Ligands(s)	Action	References
KIR	KIR2DL2	NK cells, NKT cells, T cells	19	NKAT6, p58.2, CD158b, CD158B1	Type I transmembrane protein, 2 Ig-like domains	2 ITIMs	HLA-C S77/N80	Inhibition	Boyington JC, et al. 2001. Mol Immunol 38: 1007 Lanier LL, et al. Annu Rev Immunol. 2005. 23: 225 Parham P. 2005. Nature Rev Immunol. 5: 201
KIR	KIR2DL3	NK, NKT cells, T cells	19	p58, CL-6, NKAT, GL183, NKAT2, CD158b, NKAT2A, NKAT2B, NKR-K7, CD158B2, KIR-K15, KIR-K7c, p58 KIR, KIR-023GB	Type I transmembrane protein, 2 Ig-like domains	2 ITIMs	HLA-C S77/N80	Inhibition	Colonna M, and Samaridis J. Science. 1995. 268: 405 Lanier LL, et al. Annu Rev Immunol. 2005. 23: 225 Parham P. 2005. Nature Rev Immunol. 5: 201
KIR	KIR2DL4	CD56high NK cells and IL-2 activated NK cells	19	G9P, CD158D, KIR103, KIR103AS	Type I transmembrane protein, 3 Ig-like domains, Associates with FcR γ chain, Recruits SHP-2	ITIM	HLA-G	Activation/Inhibition	Faure M, and Long EO. 2002. J Immunol. 168: 6208 Goodridge JP, et al. 2003. J Immunol. 171: 1768 Rajagopalan S, et al. 2001. 167: 1877
KIR	KIR2DL5A	NK cells, T cells	19	CD158F, KIR2DL5, KIR2DL5.1, KIR2DL5.3	Type I transmembrane protein, 3 Ig-like domains	2 ITIMs	Unknown	Inhibition	Lanier LL, et al. Annu Rev Immunol. 2005. 23: 225 Kikuchi-Maki A, et al. 2003. J Immunol. 171: 3415 Gomez-Lozano N, et al. 2002. Immunogenetics. 54: 314 Estefania E, et al. 2007. J Immunol. 178: 4402 Yusa S, et al. 2004. J Immunol. 172: 7385
KIR	KIR2DL5B	NK cells, T cells	19	KIR2DL5, KIR2DL5.2, KIR2DLX	Type I transmembrane protein, 3 Ig-like domains	2 ITIMs	Unknown	Inhibition	Lanier LL, et al. Annu Rev Immunol. 2005. 23: 225 Gomez-Lozano N, et al. 2002. Immunogenetics. 54: 314 Estefania E, et al. 2007. J Immunol. 178: 4402 Yusa S, et al. 2004. J Immunol. 172: 7385
KIR	KIR2DS1	NK cells	19	p50.1; CD158H; CD158a	Type I transmembrane protein, 2 Ig-like domains, Associates with DAP12	None	HLA-C weakly, Peptide specificity is similar to KIR2DL1	Activation	Lanier LL, et al. Annu Rev Immunol. 1998. 16: 4402 Stewart C.A, et al. 2005. Proc Natl Acad Sci USA. 102: 13224 Snyder MR, et al. 2004. J Immunol 173: 3725 Saulquin X, et al. 2003. J Exp Med. 197: 933 Lanier LL, et al. 1998. Nature. 391: 1998
KIR	KIR2DS2	NK cells	19	NKAT5, CD158J, CD158b, p58 KIR	Type I transmembrane protein, 2 Ig-like domains, Associates with DAP12	None	Very low affinity to HLA-C S77/N80 with uncertainty	Activation	Stewart C.A, et al. 2005. Proc Natl Acad Sci USA. 102: 13224 Becker S, et al. 2003. Hum Immunol 64: 183 Lanier LL, et al. 1998. Nature. 391: 1998
KIR	KIR2DS3	NK cells	19	NKAT7	Type I transmembrane protein, 2 Ig-like domains, Associates with DAP12	None	Unknown	Activation	Stewart C.A, et al. 2005. Proc Natl Acad Sci USA. 102: 13224 Becker S, et al. 2003. Hum Immunol 64: 183 Lanier LL, et al. 1998. Nature. 391: 1998

Family	Receptor	Cellular Expression	Chromosome location	Other names	Receptor characteristics	Cytoplasmic tyrosine motifs	Ligands(s)	Action	References
KIR	KIR2DS4	NK cells, NKT cells	19	KKA3, KIR1D, NKAT8, CD158I, KIR412	Type I transmembrane protein, 2 Ig-like domains, Associates with DAP12	None	Non-MHC class I protein	Activation	Lanier LL, et al. <i>Annu Rev Immunol.</i> 2005; 23: 225 Lanier L.J., et al. <i>Annu Rev Immunol.</i> 2005; 23: 225 Katz et al. 2004. <i>J Immunol.</i> 173: 1819
KIR	KIR2DS5	NK cells	19	NKA T9, CD158G	Type I transmembrane protein, 2 Ig-like domains, Associates with DAP12	None	Unknown	Activation	Becker S, et al. 2003. <i>Hum Immunol.</i> 64: 183 Lanier LL, et al. <i>Annu Rev Immunol.</i> 2005; 23: 225
KIR	KIR3DL1	NK cells, NKT cells, T cells	19	KIR, CL-2, NKBI, AMB11, CL-11, NKAT3, NKBI, KIR-G1, NKAT10, CD158E1, CD158E2, KIR3DS1, CD158E1/2	Type I transmembrane protein, 3 Ig-like domains	2 ITIMs	HLA-A-Bw4, HLA-B-Bw4	Inhibition	Lanier LL, et al. <i>Annu Rev Immunol.</i> 2005; 23: 225 Stewart CA, et al. 2003. <i>J Immunol.</i> 170: 6073 Yawata M, et al. 2006. <i>J Exp Med.</i> 203: 633 Carr WH, Et al. 2005. <i>J Immunol.</i> 175: 5222
KIR	KIR3DL2	NK cells, T cells	19	p140, NKAT4, CD158K, NKAT4B	Type I transmembrane protein, 3 Ig-like domains	2 ITIMs	HLA-A	Inhibition	Stewart-Jones GBE, et al. 2005. <i>Eur J Immunol.</i> 35: 341 Chan HW, et al. 2003. <i>J Exp Med.</i> 197: 245 Meenagh A, et al. 2004. <i>Tissue Antigens.</i> 64: 226
KIR	KIR3DL3	NK cells, T cells	19	KIR44, KIRCI, CD158Z, KIR3DL7, KIR3DL3var	Type I transmembrane protein, 3 Ig-like domains	2 ITIMs	Unknown	Inhibition	Lanier LL, et al. <i>Annu Rev Immunol.</i> 2005; 23: 225 Jones DC, et al. 2006. <i>Immunogenetics.</i> 58: 614 Trundley AE, et al. 2006. <i>Immunogenetics.</i> 57: 904 Long EO, et al. 2001. <i>Immunol. Rev.</i> 181: 223
KIR	KIR3DS1	NK cells, NKT cells, T cells	19	NKAT10, CD158E2	Type I transmembrane protein, 3 Ig-like domains, Associates with DAP12	None	Unknown	Activation	Lanier LL, et al. <i>Annu Rev Immunol.</i> 2005; 23: 225 Pascal V, et al. 2007. <i>J Immunol.</i> in press Lanier LL, et al. <i>Annu Rev Immunol.</i> 2005; 23: 225 O'Connor GM. 2007. <i>J Immunol.</i> 178: 235 Carr WH. 2007. <i>J Immunol.</i> 178: 647
LILR	LILRA1	Monocytes	19	LIR6, CD85I	4 Ig-like domains, Associates with FcR γ chain	None	Recognize classical and b2m free heavy chain form of HLA-B27	Activation	Trundley A, et al. 2007. <i>Eur J Immunol.</i> 3: 780 Borges L, et al. 1997. <i>J Immunol.</i> 159: 5192 Colonna M. 2003. <i>Nature Rev Immunol.</i> 3: 1 Allen RL, et al. 2001. <i>J Immunol.</i> 167: 5543 Tedla N, et al. 2003. <i>Proc Natl Acad Sci USA.</i> 100: 1174 Brown D, et al. 2004. <i>Tissue Antigens.</i> 64: 215

Family	Receptor	Cellular Expression	Chromosome location	Other names	Receptor characteristics	Cytoplasmic tyrosine motifs	Ligands(s)	Action	References
LILR	LILRA2	Eosinophils, Basophils, Monocytes, Neutrophils	19	LIR7, ILT1, CD85h	4 Ig-like domains, Associates with FcR γ chain	None	MHC class I?	Activation	Colonna M. 2003. Nature Rev Immunol. 3: 1 Tedla N. et al. 2003. Proc Natl Acad Sci USA. 100: 1174 Sloane DE. et al. 2004. Blood. 104: 2832 Brown D. et al. 2004. Tissue Antigens. 64: 215 Colonna M. 2003. Nature Rev Immunol. 3: 1
LILR	LILRA3	Soluble molecules	19	e3, HM31, HM43, ILT6, LIR4, CD85E, LIR-4	4 Ig-like domains	None	MHC class I?	Activation	Colonna M. 2003. Nature Rev Immunol. 3: 1 Tedla N. et al. 2003. Proc Natl Acad Sci USA. 100: 1174 Sloane DE. et al. 2004. Blood. 104: 2832 Brown D. et al. 2004. Tissue Antigens. 64: 215 Colonna M. 2003. Nature Rev Immunol. 3: 1
LILR	LILRA4	Plasmacytoid DCs	19	ILT7, CD85g	4 Ig-like domains, Associates with FcR γ chain	None	Unknown	Activation or Inhibition	Brown D. et al. 2004. Tissue Antigens. 64: 215 Cao W. et al. 2006. J Exp Med. 203: 1399
LILR	LILRA5	Neutrophils, Monocytes, Myelomonocytic cells	19	CD85, LIR9, CD85F, ILT11, LILRB7	2 Ig-like domains, Associates with FcR γ chain, Extracellular domain can be a soluble molecule	None	Unknown Do not bind to classical and nonclassical MHC class I	Activation	Borges L. et al. 2003. Blood. 101: 1484 Brown D. et al. 2004. Tissue Antigens. 64: 215 Shiroishi M. et al. 2006. J Bio Chem. 281: 19536
LILR	LILRB1	Monocytes, DCs, NK cells, T cells, B cells, Neutrophils, Eosinophils	19	LIR1, ILT2, CD85, CD85j	4 Ig-like domains	4 ITIMs	MHC class I molecules (Preferentially HLA-G), HCMV UL18	Inhibition	Tedla N. et al. 2003. Proc Natl Acad Sci USA. 100: 1174 Colonna M. 2003. Nature Rev Immunol. 3: 1 Shiroishi M. et al. 2006. Proc Natl Acad Sci USA. 103: 16412 Brown D. et al. 2004. Tissue Antigens. 64: 215 Cosman D. et al. 1997. J Immunol. 7: 273
LILR	LILRB2	Myelomonocytic lineage, Eosinophils, Monocytes	19	CD85D, ILT4, LIR-2, LIR2, MIR-10, MIR10	4 Ig-like domains	3 ITIMs	Recognize many MHC class I molecules, Preferentially HLA-G, free heavy chains of HLA-B27, HCMV UL18	Inhibition	Tedla N. et al. 2003. Proc Natl Acad Sci USA. 100: 1174 Colonna M. 2003. Nature Rev Immunol. 3: 1 Shiroishi M. et al. 2006. Proc Natl Acad Sci USA. 103: 16412 Allen RL. et al. 2001. J Immunol. 167: 5543 Brown D. et al. 2004. Tissue Antigens. 64: 215
LILR	LILRB3	Eosinophils, Basophils, Monocytes, Neutrophils	19	HL9, ILT5, LIR3, CD85A	4 Ig-like domains	4 ITIMs	Unknown, Does not bind to B27	Inhibition	Tedla N. et al. 2003. Proc Natl Acad Sci USA. 100: 1174 Colonna M. 2003. Nature Rev Immunol. 3: 1 Sloane DE. et al. 2004. Blood. 104: 2832 Brown D. et al. 2004. Tissue Antigens. 64: 215
LILR	LILRB4	Monocytes	19	LILR5, LIR5, ILT3, CD85K	2 Ig-like domains	3 ITIMs	Unknown, Does not bind to B27	Inhibition	Colonna M. 2003. Nature Rev Immunol. 3: 1 Tedla N. et al. 2003. Proc Natl Acad Sci USA. 100: 1174 Brown D. et al. 2004. Tissue Antigens. 64: 215 Vlad G. et al. 2006. Int Immunopharmacol. 6: 1889

Family	Receptor	Cellular Expression	Chromosome location	Other names	Receptor characteristics	Cytoplasmic tyrosine motifs	Ligands(s)	Action	References
LILR	LILRB5	Monocytes	19	LILR8, CD85C	4 Ig-like domains	2 ITIMs	Unknown	Inhibition	Colonna M. 2003. <i>Nature Rev Immunol.</i> 3: 1 Tedla N. et al. 2003. <i>Proc Natl Acad Sci USA.</i> 100: 1174 Brown D. et al. 2004. <i>Tissue Antigens.</i> 64: 215 Borges L. et al. 1997. <i>J Immunol.</i> 159: 5192
NKG2	KLRC1	NK, Activated CD8 ⁺ , NKT cells	12	NKG2, NKG2A, CD159A	Type II transmembrane protein, C type lectin, Heterodimerizes with CD94	2 ITIMs	HLA-E	Inhibition	Lanier LL. et al. <i>Annu Rev Immunol</i> 2005; 23: 225 Kabat A. et al. 2002. <i>J. Immunol.</i> 169: 1948 Michaelsson J. et al. 2002. <i>J Exp Med.</i> 196: 1403 Brett KK. 2005. <i>J Immunol.</i> 174: 2878 Houchins JP. et al. 1991. <i>J Exp Med.</i> 173: 1017
NKG2	KLRC2	NK, Activated CD8 ⁺ cells, NKT cells	12	NKG2C, CD159c	Type II transmembrane protein, C type lectin, Heterodimerizes with CD94, associates with DAPI2	None	HLA-E	Activation	Lanier LL. et al. <i>Annu Rev Immunol.</i> 2005; 23: 225 Hikami K. et al. 2003. <i>Genes Immun.</i> 4: 160 Houchins JP. et al. 1991. <i>J Exp Med.</i> 173: 1017 Brett KK. 2005. <i>J Immunol.</i> 174: 2878
NKG2	KLRC3	NK, Activated CD8 ⁺ cells	12	NKG2E	Type II transmembrane protein, C type lectin, Heterodimerizes with CD94, Associates with DAPI2	None	HLA-E	Activation	Lanier LL et al. 1998. <i>Immunity.</i> 8: 693 Brett KK. 2005. <i>J Immunol.</i> 174: 2878 Adamkiewicz TV. et al. 1994. <i>Immunogenetics.</i> 39: 218 Glienke J. et al. 1998. <i>Immunogenetics.</i> 48: 163
NKG2	KLRK1	NK, CD8 ⁺ T, $\gamma\delta$ T, LPS-activated macrophages	12	CD314, NKG2D, KLR	Type II transmembrane protein, C type lectin, Homodimer, Associates with DAPI0	None	MICA/MICB, ULBP	Activation	Raulat DH. 2003. <i>Nat Rev Immunol.</i> 3: 781 Lanier LL. 2003. <i>Curr Opin Immunol.</i> 15: 308 Groh V. et al. 2002. <i>Nature.</i> 419: 734 Sutherland CL. et al. 2002. <i>J Immunol.</i> 168: 671
PILR	PILRA	Monocytes, Macrophages, Granulocytes	7	PILR α , FDF03	1 Ig-like domain	ITIMs	CD99 related molecule	Inhibition	Mousseau DD. et al. 2000. <i>J Biol Chem.</i> 275: 4467 Koga T. et al. 2004. <i>Nature.</i> 428: 758 Fournier N. et al. 2000. <i>J Immunol.</i> 165: 1197
PILR	PILRB	Leukocytes	7	PILR β , FDFACT1, FDFACT2	1 Ig-like domain, Charged lysine residue in TM	None	Unknown	Activation	Mousseau DD. et al. 2000. <i>J Biol Chem.</i> 275: 4467 Fournier N. et al. 2000. <i>J Immunol.</i> 165: 1197
SIGLEC	SIGLEC10	Eosinophils, Monocytes, NK cells, Neutrophils, B cells	19	SLG2, PRO940	Type I transmembrane protein, 5 Ig like-domains	ITIM and ITSM	Sialic acids (α 2,3 linkages = α 2,6-linkages)	Inhibition	Li N. et al. 2001. <i>J Biol Chem.</i> 276: 28106 Clark HF. et al. 2003. <i>Genome Res.</i> 13: 2265

Family	Receptor	Cellular Expression	Chromosome location	Other names	Receptor characteristics	Cytoplasmic tyrosine motifs	Ligand(s)	Action	References
SIGLEC	SIGLECI1	Macrophages, Microglia	19	-	Type I transmembrane protein, 5 Ig-like domains	ITIM and ITSM	Sialic acids ($\alpha 2,8$ -linkages)	Inhibition	Crocker PR, et al. 2007. Nature Rev Immunol. 7: 255 Hayakawa T, et al. 2005. Science. 309: 1693 Angata T et al. 2002. J Biol Chem. 277: 24466 Clark HF, et al. 2003. Genome Res. 13: 2265 Crocker PR, et al. 2007. Nature Rev Immunol. 7: 255 Angata T, et al. 2006. FASEB J. 20: 1964 Crocker PR, et al. 2007. Nature Rev Immunol. 7: 255 Hernandez-Caselles T, et al. 2006. J Leukoc Biol 79: 46 Crocker PR, et al. 2002. Curr Op Structure Biol. 12: 609 Crocker PR, et al. 2007. Nature Rev Immunol. 7: 255 Angata T, et al. 2006. FASEB J. 20: 1964 Avril T, et al. 2005. J Biol Chem. 280: 19843 Erickson-Miller CL, et al. 2003. Exp Hematol. 31: 382 Ghannadan M, et al. 2002. Int Arch Allergy Immunol. 127: 299 Crocker PR, et al. 2007. Nature Rev Immunol. 7: 255 Patel N, et al. 1999. J Biol Chem. 274: 22729 Crocker PR, et al. 2007. Nature Rev Immunol. 7: 255 Nicoll G, et al. 1999. J Biol Chem. 274: 34089 Angata T and Varki A. 2000. Glycobiology. 10: 431 Attrill H, et al. 2006. Biochem. J. 397: 271 Crocker PR, et al. 2007. Nature Rev Immunol. 7: 255 Nutku E, et al. 2000. Blood. 101: 5014 Floyd H, et al. 2000. J. Biol. Chem. 275: 861 Crocker PR, et al. 2007. Nature Rev Immunol. 7: 255 Angata T, and Varki A. 2000. J Biol Chem. 275: 22127 Ikehara Y, et al. 2004. J Biol Chem. 279: 43117 Rapport EM, et al. 2006. Biochemistry Mosc. 71: 496 Crocker PR, et al. 2007. Nature Rev Immunol. 7: 255
SIGLEC	SIGLECI4	Hematopoietic cells	19	-	3 Ig-like domains, Associates with DAP12	None	Sialic acids	Activation	
SIGLEC	SIGLEC3	Myeloid progenitor cells, Monocytes, Activated T cells, Activated NK cells	19	CD33, p67, FLJ00391	Type I transmembrane protein, 2 Ig-like domains	ITIM and ITSM	Sialic acids ($\alpha 2,6$ -linkages > $\alpha 2,3$ -linkages)	Inhibition	
SIGLEC	SIGLEC5	Neutrophils, Macrophages, Monocytes, Basophils, B cells	19	CD170, OBBP2, CD33L2, OB-BP2	Type I transmembrane protein, 4 Ig-like domains	ITIM and ITSM	Sialic acid ($\alpha 2,3$ -linkages = $\alpha 2,6$ -linkages > $\alpha 2,8$ -linkages)	Inhibition	
SIGLEC	SIGLEC6	Neutrophils, B cells, Placental trophoblasts	19	CD33L, OBBP1, CD33L1, CDw327	Type I transmembrane protein, 3 Ig-like domains	ITIM and ITSM	Sialyl Tn antigen	Inhibition	
SIGLEC	SIGLEC7	Granulocytes, Monocytes, NK cells, CD8 + T cells	19	p75, QA79, AIRM1, CDw328, D-siglec, p75/ AIRM1	Type I transmembrane protein, 3 Ig-like-domains	ITIM and ITSM	Sialic acids ($\alpha 2,8$ -linkages > $\alpha 2,6$ -linkages > $\alpha 2,3$ -linkages)	Inhibition	
SIGLEC	SIGLEC8	Eosinophils, Basophils, Mast cells	19	SAF2, MGCS9785, SIGLEC8L	Type I transmembrane protein, 3 Ig-like domains	ITIM and ITSM	Sialic acids ($\alpha 2,3$ -linkages > $\alpha 2,6$ -linkages)	Inhibition	
SIGLEC	SIGLEC9	NK cells, T cells, B cells, Monocytes, Neutrophils	19	CDw329, OBBP-LIKE	Type I transmembrane protein, 3 Ig-like domains	ITIM and ITSM	Sialic acids ($\alpha 2,3$ linkages = $\alpha 2,6$ -linkages)	Inhibition	

Family	Receptor	Cellular Expression	Chromosome location	Other names	Receptor characteristics	Cytoplasmic tyrosine motifs	Ligands(s)	Action	References
SIRP	SIRP- α	Macrophages, Monocytes, DCs, Granulocytes, Neurons, Astrocytes	20	CD172a, SHPS1, P84, MYD-1, BIT, PTPNS1	3 Ig-like domains	ITIMs	CD47, Surfactant proteins A and D	Inhibition	Gardai SJ, et al. 2003. <i>Cell</i> . 115: 13 Seiffert M, et al. 1999. <i>Blood</i> . 94: 3633 Barclay A.N. and Brown M.H. 2006. <i>Nature Rev Immunol</i> . 6: 457 Dietrich J, et al. 2000. <i>J Immunol</i> . 164: 9 Tomasetto E, et al. 2000. <i>Eur J Immunol</i> . 30: 2147 Barclay A.N. and Brown M.H. 2006. <i>Nature Rev Immunol</i> . 6: 457 Piccio L, et al. 2005. <i>Blood</i> . 105: 2421 Barclay A.N. and Brown M.H. 2006. <i>Nature Rev Immunol</i> . 6: 457
SIRP	SIRP- β 1	Macrophages, Neutrophils	20	CD172b, DKFZp686A05192, RP4-576H24.1	3 Ig-like domains, Forms disulphide-linked dimer, Associates with DAPI2	None	Unknown	Activation	Bouchon A, et al. 2000. <i>J Immunol</i> . 164: 4991 Chung DH, et al. 2002. <i>Eur J Immunol</i> . 32: 59 Colonna M, et al. 2003. <i>Nature Rev Immunol</i> . 3: 1
SIRP	SIRP- β 2	NK cells, T cells	20	CD172g, SIRP γ , SIRP-B2, bA77C3.1	3 Ig-like domains, No lysine to associate with adaptor molecules	None	CD47	No signals	Bouchon A, et al. 2000. <i>J Immunol</i> . 164: 4991 Chung DH, et al. 2002. <i>Eur J Immunol</i> . 32: 59 Colonna M, et al. 2003. <i>Nature Rev Immunol</i> . 3: 1
TREM	TREM-1	A subset of monocytes and macrophages, Neutrophils, Granulocytes	6	-	Type I transmembrane protein, 1 Ig-like domain, Associates with DAPI2	None	Unknown	Activation	Bouchon A, et al. 2000. <i>J Immunol</i> . 164: 4991 Chung DH, et al. 2002. <i>Eur J Immunol</i> . 32: 59 Colonna M, et al. 2003. <i>Nature Rev Immunol</i> . 3: 1
TREM	TREM-2	Macrophages, DCs, Osteoclasts, Microglia	6	Trem2a, Trem2b, Trem2c	Type I transmembrane protein, 1 Ig-like domain, Associates with DAPI2	None	Unknown	Activation or Inhibition	Bouchon A, et al. 2000. <i>J Immunol</i> . 164: 4991 Chung DH, et al. 2002. <i>Eur J Immunol</i> . 32: 59 Colonna M, et al. 2003. <i>Nature Rev Immunol</i> . 3: 1