New nomenclature for MHC receptors

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Killer cell immunoglobulin (Ig)-like receptors (KIRs) as well as Ig-like transcripts (ILTs), which are also known as leukocyte Ig-like receptors (LIRs), are structurally and functionally related transmembrane glycoproteins. These receptors belong to the Ig superfamily and their extracellular portions contain two (KIR2D, LIR5, LIR6b and ILT11), three (KIR3D) or four (ILT1, ILT2, ILT4, ILT5, ILT6, LIR6a and LIR8) Ig domains[1–6]. Unlike KIRs, which are present on NK cells and on T cell subsets, ILTs and LIRs are also expressed on monocytes, macrophages, dendritic cells and B lymphocytes[3,6]. Members of the KIR and ILT and LIR families recognize groups of HLA class I allotypes rather than individual MHC class I–peptide complexes[4]. These receptors can be divided into two groups of inhibitory and activating receptors, according to the nature of their transmembrane and cytoplasmic regions[5]. Receptors with a long cytoplasmic tail—KIR2DL, KIR3DL, ILT2, ILT3, ILT4, ILT5 and LIR8—harbor one or more intracytoplasmic ITIMs, which recruit and activate the protein tyrosine phosphatases SHP-1 and/or SHP-2[5]. Receptors with a short cytoplasmic tail—KIR2DS, KIR3DS, ILT1, ILT7, ILT8, ILT11 and LIR6a—lack ITIMs and harbor a positively charged amino acid residue (arginine or lysine) within their transmembrane domain, which is necessary for association with ITAM-containing polypeptides such as the adaptor KARAP (also called DAP12) (for KIR2DS and KIR3DS) or FcRγ (for ILT)[5]. Phosphorylated ITAMs recruit the protein tyrosine kinases Syk and ZAP70. The one exception to these transmembrane receptors is ILT6 (also called LIR4), which has no transmembrane or cytoplasmic domain and is probably soluble.

For KIR molecules, the first rational nomenclature was based on their protein structure (www.ncbi.nlm.nih.gov/prow/guide/679664748_g.htm). In this nomenclature, KIR members with two Ig domains (KIR2D) and those with three Ig domains (KIR3D) are subdivided into two subfamilies, according to the length of the cytoplasmic tails: inhibitory KIRLs have a long cytoplasmic tail (L) and include one or two ITIMs; activating KIRS have a short cytoplasmic tail (S). For ILT and LIR molecules, inhibitory and activating receptors are described, but no rational nomenclature has been proposed. A single molecule can have two names, for example ILT2 is LIR1 and ILT4 is LIR1. Other molecules—such as ILT7, ILT8, ILT9, ILT10 and ILT11—have no equivalent in the LIR system, and some LIR molecules have no ILT nomenclature, for example LIR8 and LIR6.

During the 7th HLDA workshop (Harrogate, UK, June 2000), a homogeneous CD nomenclature was proposed (**Fig. 1**). It is based on the previous CD designation of some members of these families (for example, CD158a for KIR2DL1, CD158b for KIR2DL2/L3 and CD85 for ILT2) and on the position of the genes on chromosome 19. Indeed, the overall gene organization of these receptor families suggests that they evolved from a common ancestral sequence: 12 clustered KIR loci and 13 ILT (and LIR) loci have been identified in the chromosomal region 19q13.42 within the ~1-mb region designated leukocyte receptor complex (LCR)[7]. In this nomenclature, an alphabetical order has been assigned according to the centromeric-telomeric localization of the genes on chromosome 19. In addition, this nomenclature also accounts for allelic polymorphism of these gene families[7,8]. Allelic forms of the genes are numbered: KIR3DL1 and KIR3DS1 likely represent allelic forms and are therefore referred as to CD158e1 and CD158e2, respectively. The same applies to KIR2DL2 and KIR2DL3, which correspond to CD158b1 and CD158b2, respectively. We propose that this new nomenclature, which corrects and extends the previous CD158 and CD85 designations, be adopted to describe these families of activating and inhibitory leukocyte receptors.

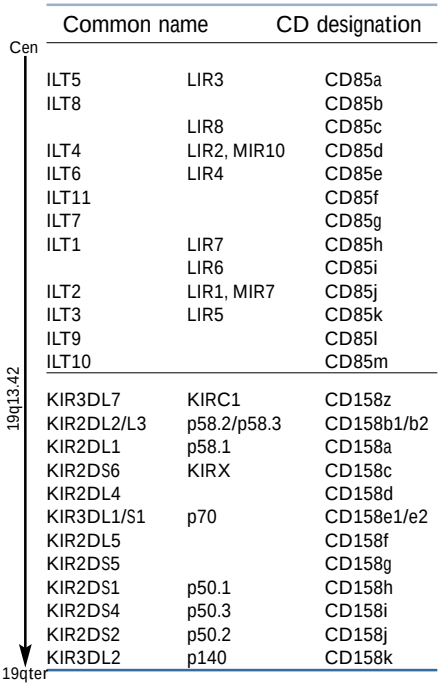

Figure 1. New CD nomenclature for activating and inhibitory MHC receptors. Exceptions to the alphabetical order for KIR genes from their centromeric-telomeric localization on chromosome 19 have been included for CD158z, CD158b and CD158a because CD158a and CD158b had been previously assigned during the 6th HLDA workshop (Kobe, Japan, 1996). KIR2DS3 has not been included in this version of the KIR nomenclature because its location on chromosome 19q13.42 has not yet been determined. Note that another nomenclature for ILT/LIR genes has been proposed (http://www.gene.ucl.ac.uk/users/hester/lilr.html).

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