New nomenclature for Fc receptor–like molecules

To the editor:

Newly identified Fc receptor–like genes are referred to in various publications as Fc receptor homologs (*FcRH*)[1], immunoglobulin superfamily receptor translocation-associated genes (*IRTA*)[2], immunoglobulin-Fc-gp42–related genes (*IFGP*)[3], Src homology 2 domain–containing phosphatase anchor proteins (*SPAP*) or B cell crosslinked by anti–immunoglobulin M–activating sequences (*BXMAS*). Eight human and six mouse Fc receptor–like genes have been identified. Correspondence organized by the International Committee on Standardized Genetic Nomenclature for Mice, the Mouse Genomic Nomenclature Committee and the Human Genome Organisation Gene Nomenclature Committee has emphasized the need for a unified nomenclature to classify these genes and has proposed the term 'Fc receptor–like' ('*FCRL*' or '*Fcrl*').

The chromosomal position and genomic organization of '*FCRL*' family is conserved with that of the 'classical' Fc receptor ('*FCR*') gene family. *FCRL1–FCRL5* are tandemly located in the 1q21–23 region near *FCGR1*, whereas *FCRL6* is located closer to *FCER1A*. *FCRL1–FCRL6* encode type I transmembrane glycoproteins containing three to nine extracellular immunoglobulin domains and cytoplasmic immunoreceptor tyrosine-based activation–like motifs and/or immunoreceptor tyrosine-based inhibition motifs (**Fig. 1**, top). FCRL1 contains a charged residue in its transmembrane region, but the transmembrane portions of FCRL2–FCRL6 are hydrophobic and uncharged. FCRL1–FCRL5 are 'preferentially' expressed by B cells, whereas FCRL6 is expressed mainly by T cells and natural killer cells.

Two additional human '*FCRL*' genes, originally called *FcRL* (also known as *FREB* or *FcRX*) and *FcRL2* (also known as *FREB2* or *FcRY*)[4], have unusual features that justify their designation as a separate subfamily. These genes are located in the low-affinity '*FCR*' locus on chromosome 1q23 and contain two or three immunoglobulin domains (**Fig. 1**, top). However, *FcRL* lacks exons encoding a split signal peptide, a genomic organization characteristic of other '*FCR*' and '*FCRL*' genes. Both *FcRL* and *FcRL2* are expressed by B cells as well as nonlymphoid cells and encode immunoglobulin-like molecules that lack transmembrane regions and tyrosine-based signaling motifs, but distinctly have C-terminal mucin-like regions. The nomenclature we suggest for these genes is *FCRLA* (for *FcRL*) and *FCRLB* (for *FcRL2*).

The mouse '*Fcr*' locus is divided between chromosomes 1 and 3. The genes originally called *FcRH1* (also known as *Ifgp1*), *FcRH2* (also known as *Ifgp2* and *Msr2*) and *FcRH3* are positioned near *Fcgr1* on chromosome 3 and encode proteins containing two to five immunoglobulin domains with or without transmembrane regions[5] (**Fig. 1**, bottom). *FcRH1* and *FcRH3* are expressed by B cells and encode molecules containing cytoplasmic tyrosine-based signaling motifs. Uniquely, *FcRH2* does not cluster with *FcRH1* and *FcRH3*, lacks a human ortholog or lymphoid expression and encodes a molecule containing a C-terminal type B scavenger receptor cysteine-rich domain without a

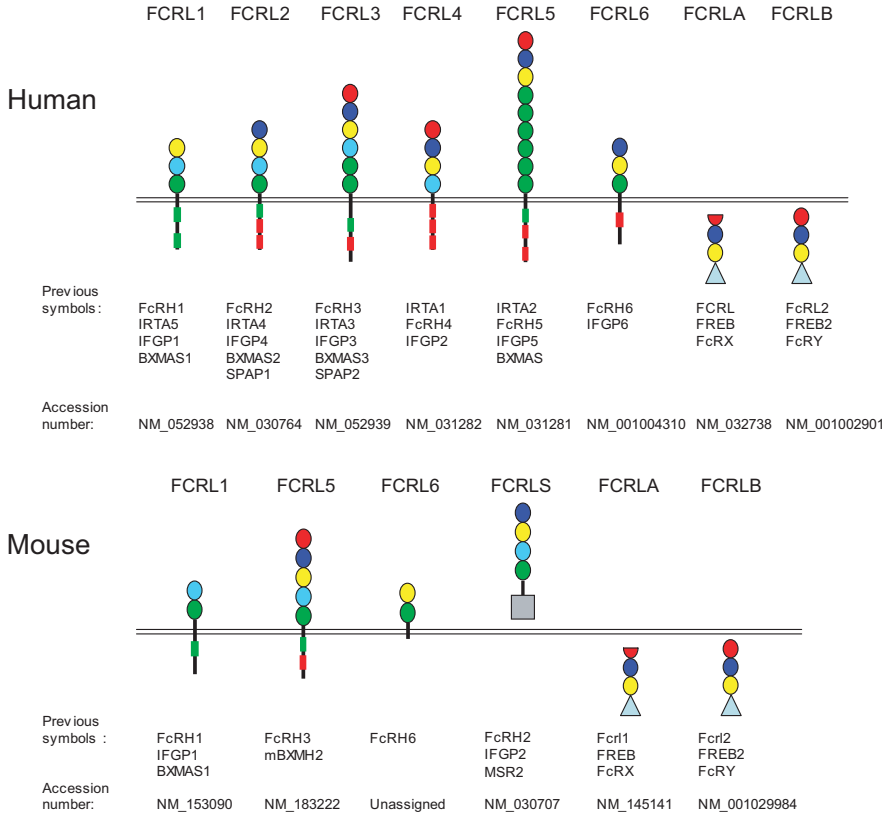

Figure 1 Human and mouse Fc receptor–like proteins. Colors of immunoglobulin domains indicate their phylogenetic relationships. Immunoreceptor tyrosine-based inhibition motifs, red boxes; immunoreceptor tyrosine-based activation–like motifs, green boxes; type B scavenger receptor cysteine-rich domain, gray box; mucin-rich regions, blue triangles. The first domain of FCRLA corresponds to a partial immunoglobulin domain and the full-length isoforms of both FCRLA and FCRLB are intracellular proteins. Accession numbers are for GenBank.

transmembrane region. We support the assignment of the symbol *Fcrl1* for the gene previously known as *FcRH1* and the symbol *Fcrl5* for the gene previously known as *FcRH3* (given its sequence identity and surrounding genomic homology) and propose the symbol *Fcrls* for *FcRH2* (to emphasize that it has a scavenger receptor cysteine-rich motif).

Three additional mouse '*Fcrl*' genes are located near the low-affinity '*Fcr*' locus on mouse chromosome 1. *FcRH6*, *FcRL* (also known as *Freb* and *FcRX*) and *FcRL2* (also known as *Freb2* and *FcRY*) are located in syntenic regions relative to their human orthologs. The new names we suggest for these genes are *Fcrl6*, *Fcrla* and *Fcrlb*, respectively.

Expression patterns, functions and ligands of Fc receptor-like molecules are being investigated and additional splice isoforms may be identified. We propose the designation 'v' followed by a number, such as Fcrl1_v1, to designate splice variants. As cluster designations are assigned, we anticipate modifications of the nomenclature to accommodate this new extended receptor family.

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