Domain Shuffling has been the Main Mechanism Forming New Hominoid Killer Cell Ig-like Receptors.

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The killer cell Ig-like receptor (*KIR*) gene family encodes MHC class I-specific receptors, which regulate NK cell responses and are also expressed on subpopulations of T cells. *KIR* haplotypes vary in gene content, which, in combination with allelic polymorphism, extensively diversifies the *KIR* genotype both within and between human populations. Species comparison indicates that formation of new *KIR* genes and loss of old ones are frequent events, so that few genes are conserved even between closely related species. In this regard, the hominoids define a time frame that is particularly informative for understanding the processes of *KIR* evolution and its potential impact on killer cell biology. *KIR* cDNA were characterized from PBMC of three gorillas, and genomic DNA were characterized for six additional individuals. Eleven gorilla *KIR* genes were defined. With attainment of these data, a set of 75 *KIR* sequences representing five hominoid species was assembled, which also included rhesus monkey, cattle, and rodent *KIR*. Searching this data set for recombination events, and phylogenetic analysis using Bayesian methods, demonstrated that new *KIR* were usually the result of recombination between loci in which complete protein domains were shuffled. Further phylogenetic analysis of the *KIR* sequences after removal of confounding recombined segments showed that only two *KIR* genes, *KIR2DL4* and *KIR2DL5*, have been preserved throughout hominoid evolution, and one of them, *KIR2DL4*, is also common to rhesus monkey and hominoids. Other *KIR* genes represent recombinant forms present in a minority of species, often only one, as exemplified by 8 of the 11 gorilla *KIR* genes.