Population Diversity of Killer Cell Ig-like Receptor (KIR) Genes.

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The effector function of natural killer (NK) cell is regulated by the integration of signals transduced by a set of inhibitory and activating killer cell Ig-like receptors (KIR). Thirteen KIR receptors have been identified in humans of which 7 are inhibitory type and 6 are activating type. The number and type of *KIR* genes vary to haplotypes, which produce an extensive genotypic diversity in humans. To understand the environmental pressure on the selection of each *KIR* receptor, we have characterized the presence and absence of 15 *KIR* genes on a panel of 265 unrelated individuals. The panel includes 52 Caucasians, 53 Hispanics, 21 African Americans, 32 Asians and 107 unclassified mixed groups. No population difference was observed in the frequency of five well-defined inhibitory *KIR* genes: *KIR2DL1* (HLA-C^{K80}), *2DL2/3* (HLA-C^{N80}), *2DL4* (HLA-G), *3DL1* (HLA-Bw4) and *3DL2* (HLA-A3 and A11). Three of these inhibitory *KIR* genes (*2DL2/3, 2DL4* and *3DL2*) present ubiquitously in all individuals, and over 95% of the panel carries all the five inhibitory *KIR* genes. The inhibitory KIR receptors provide NK tolerance to healthy cells expressing the HLA class I ligands. Much diversity is seen between the populations in the distribution of activating KIR genes. *KIR3DS1* is abundant in Asians (53%) whereas it occurs with low frequency in African Americans (24%); *KIR2DS2* and *2DS3* are frequent activating KIRs in African Americans (61% and 43% respectively) but occur infrequently in Asians (37% and 25% respectively); *KIR2DS5* is a frequent receptor in Hispanics (45%) and Asians (44%) but occurs at low frequency in Caucasians (27%) and African Americans (29%). The activating receptors recognize pathogen-derived or pathogen-induced molecules expressed on the surface of infected target cells, and trigger NK lysis of targets in antigen independent manner. Ethnic diversity in the distribution of activating KIR genes likely due to the differential selection pressure in populations evolved in distinct geographical areas. A set of 44 *KIR* gene combinations (genotypes) was distinguished in this panel of 265 individuals. The most common genotype (20-30%) in all population encodes inhibitory receptors for all five HLA class I specificities, and one activating KIR2DS4. Nine of the 44 genotypes were novel and not found in previous studies. Further analysis with allelic level will determine the force that drives the diversity of these rapidly evolving immune genes.