

NK cells and viruses – Defense / Counterdefense

Lewis L. Lanier, Department of Microbiology and Immunology, University of California, San Francisco, CA 94143

Natural killer (NK) cells play a critical role in the early immune response controlling certain viral infections, in particular defense against Herpesviruses. In turn, viruses have devised strategies to avoid detection and elimination by NK cells. The resistance of certain mice to cytomegalovirus (CMV) previously has been shown to be conferred by NK cells and to involve the activating Ly49H receptor. We have shown that Ly49H directly recognizes a viral glycoprotein m157 and provides for NK cell-mediated immunity to CMV. CMV-susceptible mice lack Ly49H and some strains express a related Ly49 inhibitory receptor that may have initially driven selection for the m157 gene in CMV. In addition to Ly49H, NK cells also express another activating receptor, NKG2D, that recognizes the RAE-1 non-classical MHC molecules. CMV infection results in transcriptional induction of the RAE-1 genes; however, expression of these NKG2D ligands is blocked by proteins encoded by CMV. CMV m152 is partially responsible for this and a deletion virus is less virulent in vivo, unless NKG2D is non-functional. Collectively, certain persistent viruses such as CMV, are providing constant selective pressure on both the innate and adaptive immune systems.

References

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