Presentation of an immunodominant immediate-early CD8+ T cell epitope resists human cytomegalovirus immunoevasion.

Control of human cytomegalovirus (HCMV) depends on CD8+ T cell responses that are shaped by an individual's repertoire of MHC molecules. MHC class I presentation is modulated by a set of HCMV-encoded proteins. Here we show that HCMV immunoevasins differentially impair T cell recognition of epitopes from the same viral antigen, immediate-early 1 (IE-1), that are presented by different MHC class I allotypes. In the presence of immunoevasins, HLA-A- and HLA-B-restricted T cell clones were ineffective, but HLA-C*0702-restricted T cell clones recognized and killed infected cells. Resistance of HLA-C*0702 to viral immunoevasins US2 and US11 was mediated by the alpha3 domain and C-terminal region of the HLA heavy chain. In healthy donors, HLA-C*0702-restricted T cells dominated the T cell response to IE-1. The same HLA-C allotype specifically protected infected cells from attack by NK cells that expressed a corresponding HLA-C-specific KIR. Thus, allotype-specific viral immunoevasion allows HCMV to escape control by NK cells and HLA-A- and HLA-B-restricted T cells, while the virus becomes selectively vulnerable to an immunodominant population of HLA-C-restricted T cells. Our work identifies a T cell population that may be of particular efficiency in HCMV-specific immunotherapy.