

HIV-specific CTL play an important role in the host control of HIV infection. HIV-nef may facilitate escape of HIV-infected cells from CTL recognition by selectively down regulating the expression of HLA-A and HLA-B molecules, while surface expression of HLA-C is unaffected. The HLA-C-restricted CTL responses have previously been largely ignored and poorly characterized. We examined the frequency, function, and phenotype of HLA-C-restricted CTL in ten antiretroviral therapy-naïve Caucasian and African individuals with chronic HIV-1 infection (for at least 8 years; CD4 cell counts in the range of 50-350) who carried the HLA-Cw04 allele. HLA-Cw04-restricted CTL that recognize a conserved epitope within HIV-1 envelope (aa 375-383 SF9) were analyzed using IFN-gamma ELISPOT assays and phenotypic analysis was carried out by flow cytometry. HLA-C-restricted CTL play an important role in the HIV-specific response, and can account for as much as 54% of the total response. HLA-C-restricted CTL are functionally and phenotypically identical to HLA-A- and HLA-B-restricted CTL. HLA-C-restricted CTL in chronic HIV infection are memory cells of an intermediate phenotype, characterized by high CD27 and low CD28 expression and lack of perforin production.