OBJECTIVES: To determine whether CD8 T lymphocytes from HIV-1-infected patients expressing B*5701 and B*5703 show broad cross-reactivity against different variants of a conserved p24 epitope, which might account for the good prognosis of HIV-1-infected individuals with HLA-B*57. DESIGN: B*5701+ and B*5703+ were recruited from Nairobi, Kenya and from Oxford, UK. All patients had been HIV positive for at least 8 years and could be categorized as slow progressors. METHODS: CD8 cytotoxic T cell clones were generated from B*5701+ and B*5703+ donors and tested for their ability to recognize clade variants of an index p24 epitope in standard cytolytic assays. Cross-reactive responses in freshly isolated peripheral blood mononuclear cells (PBMC) were assessed by interferon-gamma (IFNgamma) production and tetramer binding. RESULTS: Broad cross-clade reactivity for both cytolysis and tetramer binding was observed in CD8 T cell clones from patients harbouring the index epitope sequence. Patterns of cross-reactivity were similar in freshly isolated PBMC but varied between individuals in terms of strength and breath of responses generated. One common variant induced an unusual response with tetramer binding but often failed to induce IFNgamma production, and another was a weak stimulator of both IFNgamma and cytolytic activity. CONCLUSION: B*5701+ and B5703+ donors demonstrate broad functional cross-reactivity to both common and rare variants of a dominant p24 epitope, which could be relevant to the association of B*57 alleles with slow progression to AIDS.