

Abstract:

HIV-specific cytotoxic T-lymphocytes (CTL) are believed to play a key part in the control of virus levels throughout HIV infection. An important goal of a potential prophylactic vaccine against HIV is therefore to elicit a strong CTL response which is broadly cross-reactive against a diverse range of HIV strains. We have detected HIV-specific CTL in two groups of highly-exposed but persistently seronegative female sex workers in Africa which show extensive cross-reactivity between different viral sequences. In a small group of women exposed to both HIV-1 and HIV-2 in Gambia, studied over 4 years, we have repeatedly detected HLA-B35-restricted CTL which exhibit cross-reactivity between the HIV-1 and HIV-2 sequences of the CTL epitopes. In women with particularly intense exposure to what are likely to be multiple clades of HIV-1 in Nairobi Kenya, we have detected CTL directed towards epitopes conserved between HIV-1 clades. In neither group is there any evidence that variation in CCR5 sequence or expression is responsible for their apparent resistance to HIV infection. However, in seropositive donors from Oxford infected with African strains of HIV-1, we have defined CTL responses which are specific for particular clades and have mapped some unique A clade CTL epitopes, together with others to highly-conserved regions of the virus. Further information about the extent of cross-reactive CTL immunity will be important for future vaccine design and evaluation.