

# The role of cytotoxic T-cells in HIV infection

Rowland-Jones, S; Dong, T; Krausa, P; Sutton, J; Newell, H; Ariyoshi, K; Gotch, F; Sabally, S; Corrah, T; Kimani, J; MacDonald, K; Plummer, F; Ndinya-Achola, JO; Whittle, H; McMichael, A

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## Abstract:

HIV-specific cytotoxic T lymphocytes (CTL) are believed to play a major role in controlling virus levels through the asymptomatic period of HIV infection. For the rational design of an HIV vaccine, we need to know whether protective immunity can ever develop following HIV exposure in people who remain uninfected. We have detected HIV-specific CTL in 5/6 repeatedly exposed, persistently seronegative female sex-workers in The Gambia. Their CTL, repeatedly detected over two years, recognise epitopes presented by HLA-B35 which are cross-reactive between HIV-1 & HIV-2, suggesting they could have been primed first by HIV-2 exposure and subsequently boosted by exposure to HIV-1. Using previously identified clade B HIV-1 epitope peptides, we have now detected HIV-specific CTL in 6/15 highly exposed and apparently HIV-resistant Kenyan prostitutes, predominantly towards epitopes highly conserved between B and the Kenyan A & D clades of HIV-1. This CTL activity towards conserved virus epitopes may represent protective immunity to HIV generated in response to repeated exposure, and prophylactic HIV vaccines should aim to generate similar CTL responses. PIP: During the asymptomatic phase of HIV infection, HIV-specific cytotoxic T lymphocytes (CTL) are believed to play a major role in controlling virus levels. The design of an HIV vaccine requires knowledge about whether protective immunity can ever develop after exposure to the virus and the mechanisms underlying such natural immunity. The authors' research has focused on HIV-specific CTL responses in highly HIV-exposed commercial sex workers in The Gambia, West Africa, and in Nairobi, Kenya. HIV CTL was detected in 5 of 6 repeatedly exposed, persistently seronegative female sex workers in The Gambia. Their CTL recognized epitopes presented by HLA-835 that are cross-reactive between HIV-1 and HIV-2, suggesting they could have been primed first by HIV-2 exposure and subsequently boosted by exposure to HIV-1. Through use of previously identified clade B HIV-1 epitope peptides, the authors also detected HIV-specific CTL in 6 of 15 highly exposed and apparently resistant Kenyan prostitutes, predominantly toward epitopes highly conserved between B and Kenyan A and D clades of HIV-1. This CTL activity toward conserved virus epitopes may represent protective immunity to HIV in response to HIV generated by repeated exposure. HIV vaccines should aim to generate similar CTL responses. There is currently no evidence that genetic factors, other than weak HLA associations, influence susceptibility or resistance to HIV infection.