

New insights into HIV-1 specific cytotoxic T-lymphocyte responses in exposed, persistently seronegative Kenyan sex workers

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Abstract:

A clearer understanding of HIV-1 specific immune responses in highly-exposed, persistently seronegative (HEPS) subjects is important in developing models of HIV-1 protective immunity. HIV-1 specific cytotoxic T-lymphocytes (CTL) have been described in a cohort of HEPS Kenyan sex workers, and recent work has further elucidated these responses. CTL specific for HIV-1 Env were found in the blood of over half the sex workers meeting criteria for HIV resistance, and in some women recognized unmapped epitopes. The proportion of women with Env-specific CTL increased with the duration of uninfected HIV exposure, suggesting that these responses were acquired over time. CD8+ lymphocyte responses directed against predefined HIV-1 CTL epitopes from various HIV-1 genes were found in the blood and genital tract of >50% resistant sex workers, at a ten-fold lower frequency than in infected subjects. The epitope specificity of CD8+ responses differs between HEPS and HIV infected women, and in HEPS the maintenance of responses appears to be dependent on persistent HIV exposure. Several HIV-1 'resistant' sex workers have become HIV infected over the past 6 years, possibly related to waning of pre-existing HIV-specific CTL, and infection has often been associated with a switch in the epitope specificity of CD8+ responses. These findings suggest that vaccine-induced protective HIV immunity is a realistic goal, but that vaccine strategies of boosting or persistent antigen may be necessary for long-lived protection