

Substantial Inpatient Differences In The Breadth And Specificity Of Hiv-specific Cd8+ T-cell Interferon-gamma And Proliferation Responses.

McKinnon, LR; Ball, TB; Wachih, C,; Chinga, N; Maingi, A; Luo, M; Fowke, K R; Plummer, FA

Date: 2008-10

Abstract:

HIV vaccine design and evaluation require a better understanding of protective immune responses. HIV-specific CD8+ T-cell responses have been characterized extensively using interferon-gamma (IFN-gamma) enzyme-linked immunosorbent spot (ELISPOT) assays, which do not always correlate with control of viral replication or disease progression. Alternative aspects of CD8+ T-cell responses, in particular those associated with a central memory (T_{cm}) phenotype, may be more protective against disease progression. To determine the extent that the breadth and specificity of HIV-specific CD8+ T-cell responses differ based on immunological readout, we screened in HIV-infected Kenyan sex workers for responses to HIV Env using IFN-gamma ELISPOT and 6-day carboxyfluorescein succinimidyl ester-based proliferation assays. This comparison revealed substantial differences in the epitopes recognized when the assay readout was IFN-gamma versus proliferation. Although 24 and 41 IFN-gamma and proliferative responses were identified, overlapping specificity was observed for only 5 responses. Breadth also differed between assays in several patients. Env-specific IFN-gamma breadth was found to correlate inversely with CD4 count ($r = -0.66$, $P = 0.005$), although this was not the case for proliferation. These data suggest that efforts to define HIV-specific CD8+ T-cell responses may need to be revisited using additional immunological readouts.