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Meeting Abstract

Immune correlates in HIV infection: application to vaccines

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Abstract

Despite evidence that CD8+ T cells play an important role in the control of viral replication and disease progression in HIV-infected individuals, the specific CD8+ T-cell function(s) responsible for this activity remain unclear. We examined simultaneously five separate CD8+ T-cell functional parameters: degranulation ability (CD107a), cytokine expression (IFNγ, TNFα, IL2), and chemokine production (MIP1b) in HIV-specific T cells from HIV progressors ($n = 79$) and elite long-term non-progressors ($n = 9$). We found that the functional profile of HIV-specific CD8+ T cells in progressors is limited compared to nonprogressors. While the total magnitude of the CD8+ T-cell response did not correlate inversely with viral load, the magnitude and proportion of the most functional component of the CD8+ T-cell response did. In addition, other virus infections and vaccinations known to provide life-long protection against virus infections were characterized by highly poly-functional CD8+ T-cell responses.

We have also dissected the functions of virus-specific CD4+ T cells, and found that with prolonged maturation, virus-specific CD4+ T cells can express many direct effector functions. Some of these functions could be associated with *in vivo* protection from HIV infection. These include class II-restricted killer T cell activity and production of MIP-1b. Studies from HIV-infected subjects show that CD4+ T cells that produce MIP-1b are less susceptible to HIV infection *in vivo* than cells that do not produce MIP-1b. Thus, the T-cell response to HIV and other virus infections is complex, and the quality of the response may be more important to monitor than the quantity.

We have developed flow cytometric panels to monitor 5 separate T-cell functions, and multiple surface phenotypes, which we use to assess the spectrum of T-cell functions induced by our vaccines. These panels will be used to evaluate new vaccine platforms.