P11-03. Mucosal Trafficking and Differentiation of Vaccine-Elicited CD8+ T-Lymphocytes

Retrovirology

Poster presentation

P11-03. Mucosal trafficking and differentiation of vaccine-elicited CD8+ T-lymphocytes

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Background

We have previously demonstrated that intramuscular immunization with recombinant adenovirus (rAd)-based HIV/SIV vaccine candidates elicits robust mucosal CD8+ T-lymphocyte responses (Kaufman et al., J Immunol 2009, 181: 4188–98). Elucidating the mechanisms underlying the priming, trafficking and differentiation of rAd-elicited mucosal CD8+ T-lymphocytes may prove critical for optimizing mucosal cellular immunity generated by these vaccine vectors.

Methods

rAd-elicited CD8+ T-lymphocyte priming and trafficking were evaluated using adoptive transfer studies in C57BL/6 mice. The genotypic and phenotypic properties of vaccine-elicited CD8+ T-lymphocytes were characterized in systemic and mucosal microenvironments using gene expression profiling and polyfunctional intracellular cytokine staining.

Results

Using adoptive transfer of CFSE-labeled T-lymphocytes, we demonstrated that intramuscular rAd immunization induced CD8+ T-lymphocyte priming in peripheral lymph nodes draining the inoculation site but not at distant systemic or mucosal lymphoid inductive sites. Primed CD8+ T-lymphocytes subsequently migrated to mucosal lymphoid inductive sites, including mesenteric lymph nodes and Peyer's patches, upregulated mucosal homing markers and acquired the capacity to traffic to mucosal effector surfaces. The influx of systemic vaccine-elicited CD8+ T-lymphocytes into mucosal tissues accounted for the vast proportion mucosal CD8+ T-lymphocyte responses generated by intramuscular rAd immunization. Vaccine-elicited CD8+ T-lymphocytes migrating to the intestinal mucosa rapidly acquired genotypic properties typical of gut-resident T-lymphocytes, which included upregulation of genes involved in both immune activation and senescence. Mucosal vaccine-elicited CD8+ T-lymphocytes also retained the capacity to elaborate multiple effector functions, including TNF-α, IFN-γ and IL-2 production and cytotoxic degranulation.

Conclusion

Intramuscular rAd immunization licenses vaccine-elicited systemic CD8+ T-lymphocytes to traffic to mucosal surfaces and undergo microenvironment-specific patterns of differentiation. These data have important implications for the development of vaccines against mucosal pathogens.