

Preexisting Viral Immunity Impacts Vaccine-Induced Immune Responses

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Recombinant viral vectors, such as recombinant adenovirus serotype 5 (rAd5), have shown promise in HIV vaccine development for their ability to induce strong HIV-1-specific cellular immune responses. Vectored vaccines have been used in clinical efficacy trials, but because Ad5 is a common cold virus, many people already have antibodies against Ad5 that can neutralize Ad5 vector infectivity. While previous work has shown that preexisting Ad5-neutralizing antibodies (humoral immunity) can dampen the HIV-specific cellular immune response induced by vaccination with rAd5, little was known about Ad5-specific cellular immunity after natural Ad5 exposure or vaccination using an Ad5 vector. Following the results of the Step Study, Dr. Nicole Frahm, Vaccine and Infectious Disease Division, and colleagues examined how these cellular immune responses against Ad5 could impact HIV-specific T cell responses.

Ad-specific CD4+ T cells were detected in 54% of Ad5-seronegative placebo recipients, and 74% of Ad5-seropositive placebo recipients. In vaccine recipients, the magnitude of these Ad-specific CD4+ T-cells increased significantly, and was not affected by baseline Ad5 serostatus. Regardless of the prevaccination Ad5 neutralizing antibody titer, higher-magnitude baseline Ad-specific CD4+ T cell responses were associated with a reduction in the magnitude of memory HIV-specific CD4+ T cell responses measured 1 year after vaccination.

To better understand these pre-vaccination Ad5-specific T cell responses in Ad5-seronegative individuals, Frahm and colleagues mapped Ad-specific T cells to different proteins that comprised various parts of the Ad5 genome. They found that the adenovirus regions targeted by Ad5-specific T cells were conserved in Ad5 and other adenovirus vectors that are currently being developed for vaccine trials. This study is the first to look beyond the effects of neutralizing antibodies to the Ad5 vector and determine how vector-specific cellular immunity impacts the HIV-specific T cell induced by the MRKAd5 HIV-1 vaccine. These findings have important implications for future vaccine design, and indicate that careful examination of cellular immune responses to other cross-reactive adenoviruses from multiple subgroups may be necessary.

[Frahm N, DeCamp AC, Friedrich DP, Carter DK, Defawe OD, Kublin JG, Casimiro DR, Duerr A, Robertson MN, Buchbinder SP, Huang Y, Spies GA, De Rosa SC, McElrath MJ](#). 2011. Human adenovirus-specific T cells modulate HIV-specific T cell responses to an Ad5-vectored HIV-1 vaccine. *Journal Clinical Investigation*. 122:359-367