

Heterologous HIV Vaccine Regimen Yields Distinct Immunological Advantages

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HIV vaccines are sought to prevent or control infection through the induction of a long lasting memory response. Broadly neutralizing anti-HIV antibodies are difficult to achieve due to variability in the HIV virus. Cellular responses are likely necessary to achieve viral control in a vaccine regimen. Based on previous research and the current HIV vaccine knowledge, it is likely that a prime/boost regimen will be best to elicit both antibody and T-cell responses. A homologous prime/boost, using the same vaccine for each administration, works well for diseases in which neutralizing antibodies are most important. A heterologous approach, using DNA encoding the viral proteins as prime, and then a recombinant viral vector as boost, might increase the quality of T-cell responses and yield long-term memory.

To test this theory, a multicenter clinical trial through the HIV Vaccine Trials Network was conducted, led by Dr. Stephen De Rosa of the Vaccine and Infectious Disease Division. Homologous prime and boosting with a recombinant adenoviral serotype 5 (rAd5) vaccine was compared to a heterologous approach of a DNA prime followed by rAd5 boost. Both types of vaccines encoded specific proteins found in the HIV gene sequence. The study was carried out in healthy HIV-uninfected individuals who did not carry serum antibodies to the viral vector.

The rAd5-rAd5 vaccine regimen gave better protein-specific antibody responses than the heterologous treatment, but did not increase T-cell responses. The heterologous DNA prime followed by Ad5 boost showed limited responses post-prime, but after the boost specific antibody and CD4 T-cell responses were increased. Six months later, antigen-specific cytotoxic T-cells were higher in this treatment group, which may contribute to long lasting memory responses.

This clinical trial demonstrated that repetitive viral vector boosting does not increase the maximum T-cell response. Even if a DNA prime was used, the maximum T-cell response occurs after one rAd5 dose. However, boosting with the rAd5 dramatically increased the antibody responses. Importantly, the heterologous approach of DNA priming altered the nature of the post-boost response, even when T-cell responses were not detected following the DNA prime. This study suggests that vaccine

regimens might need to include a heterologous prime to maximize T-cell responses, along with homologous boosts to generate increased antibody responses.

[De Rosa SC, Thomas EP, Bui J, Huang Y, deCamp A, Morgan C, Kalams SA, Tomaras GD, Akondy R, Ahmed R, Lau CY, Graham BS, Nabel GJ, McElrath MJ, and the National Institute of Allergy and Infectious Diseases HIV Vaccine Trials Network.](#) 2011. HIV-DNA priming alters T cell responses to HIV-adenovirus vaccine even when responses to DNA are undetectable. *Journal of Immunology*187:3391-3401.