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.