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A potential HIV-1 vaccine based on the elicitation of cellular immune responses

Emilio A. Emini

Merck Research Laboratories, West Point, PA

Abstract

It is now well-accepted that viral-specific cellular immune responses play an important role in controlling HIV-1 infection in persistently infected individuals. Although a vaccine designed to prevent infection with the virus would preferably elicit both specific cellular immune responses as well as virus-neutralizing antibodies, the latter goal has yet to be achieved. Accordingly, a substantial effort has been placed on the development of a vaccine that would, minimally, prime for anti-HIV-1 cellular immunity. A number of different vaccine vector delivery systems are currently under investigation. We have focused on the use of replication-defective adenoviral vectors expressing various HIV-1 genes. We have demonstrated that these vectors can potently elicit specific CD8+ and CD4+ T-cell responses in non-human primates. These responses, in turn, mediate the positive modification of the persistent virus infection, following immunodeficiency virus challenge, as manifested by clinically significantly lower virus levels compared with control animals. We have established a statistically significant correlation between the vaccine-elicited cellular immune response and the associated antiviral effect. Preliminary data from ongoing phase I trials have shown the replication-defective adenovirus vaccine vector to be immunogenic in humans.

In continuing preclinical studies, we are addressing questions involving the practical use of such vaccine vectors. We have developed vector platforms based on adenovirus serotypes that exhibit low seroprevalence in the human population. This was done in an effort to minimize the potentially detrimental effects of pre-existing antibody-based immunity to the vector. These alternate vector types have proven to be reasonably immunogenic in non-human primates. In addition, we have determined that use of the adenovirus vectors in "heterologous" prime-boost immunization strategies along with naked DNA vectors or poxvirus vectors yield substantial increases in the cellular immune response. Finally, in immunodeficiency virus-infected monkeys, in which virus levels are suppressed subsequent to the use of antiretroviral drug therapy, immunization with the replication-defective vectors leads to a specific CD8+ and CD4+ T-cell response, encouraging the further evaluation of this vaccine approach for possible therapeutic use.

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