Novel vaccine approach offers hope in fight against HIV

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Philip Johnson, M.D., chief scientific officer at the Children's Hospital of Philadelphia, led the SIV study. Credit: The Children's Hospital of Philadelphia

A research team may have broken the stubborn impasse that has frustrated the invention of an effective HIV vaccine, by using an approach that bypasses the usual path followed by vaccine developers. By using gene transfer technology that produces molecules that block infection, the scientists protected monkeys from infection by a virus closely related to HIV—the simian immunodeficiency virus, or SIV—that causes AIDS in rhesus monkeys.

"We used a leapfrog strategy, bypassing the natural immune system response that was the target of all previous HIV and SIV vaccine

candidates," said study leader Philip R. Johnson, M.D., chief scientific officer at The Children's Hospital of Philadelphia. Johnson developed the novel approach over a ten-year period, collaborating with K. Reed Clark, Ph.D., a molecular virologist at Nationwide Children's Hospital in Columbus, Ohio.

The study appeared today in the online version of *Nature Medicine*.

Johnson cautioned that many hurdles remain before the technique used in this animal study might be translated into an HIV vaccine for humans. If the technique leads to an effective HIV vaccine, such a vaccine may be years away from realization.

Most attempts at developing an HIV vaccine have used substances aimed at stimulating the body's immune system to produce antibodies or killer cells that would eliminate the virus before or after it infected cells in the body. However, clinical trials have been disappointing. HIV vaccines have not elicited protective immune responses, just as the body fails on its own to produce an effective response against HIV during natural HIV infection.

The approach taken in the current study was divided into two phases. In the first phase, the research team created antibody-like proteins (called immunoadhesins) that were specifically designed to bind to SIV and block it from infecting cells. Once proven to work against SIV in the laboratory, DNA representing SIV-specific immunoadhesins was engineered into a carrier virus designed to deliver the DNA to monkeys. The researchers chose adeno-associated virus (AAV) as the carrier virus because it is a very effective way to insert DNA into the cells of a monkey or human.

In the second part of the study, the team injected AAV carriers into the muscles of monkeys, where the imported DNA produced

immunoadhesins that entered the blood circulation. One month after administration of the AAV carriers, the immunized monkeys were injected with live, AIDS-causing SIV. The majority of the immunized monkeys were completely protected from SIV infection, and all were protected from AIDS. In contrast, a group of unimmunized monkeys were all infected by SIV, and two-thirds died of AIDS complications. High concentrations of the SIV-specific immunoadhesins remained in the blood for over a year.

Further studies need to be conducted if this technique is to become an actual preventive measure against HIV infection in people, Johnson said. "To ultimately succeed, more and better molecules that work against HIV, including human monoclonal antibodies, will be needed," he and his co-authors conclude. Finally, added Johnson, their approach may also have potential use in preventing other infectious diseases, such as malaria.

More information: Johnson et al, "Vector-mediated gene transfer engenders long-lived neutralizing activity and protection against SIV infection in monkeys," Nature Medicine, published online May 17, 2009. (dx.doi.org/10.1038/nm.1967)

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