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Immunogeneticist helps monitor immune responses in VRC01 phase 1 trial in HIV-infected individuals

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Janardan Pandey, Ph.D., an immunogeneticist specializing in immunoglobulin GM genes at the Medical University of South Carolina, helped monitor for immune responses that could limit the effectiveness of the broadly neutralizing antibody VRC01 in a phase 1 trial of that antibody in HIV-infected individuals led by a team at the Vaccine Research Center (VRC) of the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health. The results of the trial were reported in an article in the Dec. 23, 2015 issue of *Science Translational Medicine*, on which Pandey was a co-author. Pandey's expertise as an immunogeneticist specializing in immunoglobulin GM genes was needed for the trial because the VRC01 antibody is built on the immunoglobulin GM3 platform. "If you give VRC01 antibodies to a person without the gene, they could make antibodies against the VRC01 antibodies, which could reduce their effectiveness," says Pandey. Fortunately, that did not prove an issue in the phase 1 trial, which showed that a single infusion of the VRC01 antibody could suppress the blood plasma level of HIV in infected individuals not taking antiretroviral therapy.

Broadly neutralizing antibodies such as VRC01 are of increasing interest to HIV investigators. They have been isolated from patients with chronic HIV infection who have begun to produce antibodies that are effective at killing many different strains of HIV, but too late in the course of their disease to have a preventive benefit. VRC01, for example, has been shown to neutralize 91% of 200 HIV types from around the world.

In the phase 1 trial conducted at the VRC, 15 HIV-infected patients on antiretroviral therapy (ART) received two infusions of VRC01 28 days apart and eight not on ART received a single infusion. Plasma HIV levels were reduced more than tenfold after VRC01 infusion in six of the eight patients not on ART. In the two people in this group who began the study with the lowest viral loads, the antibody suppressed HIV to extremely low levels for approximately 3 weeks--as long as VRC01 was present at therapeutic concentrations. In the other four people whose HIV levels declined, their viral load fell substantially but did not reach undetectable levels. No decrease was observed in patients whose plasma levels of HIV had already been reduced through ART. VRC01 infusion did not affect the quantity of HIV in blood cells in any of the 23 study patients.

"This is a very promising first step for an HIV treatment approach using broadly neutralizing antibodies, and the first good news for some time for people infected with HIV," says Pandey.

The next step--preventing blood cells from serving as a reservoir of HIV virus -- will likely require new strategies, possibly used in combination. One of these, antibody-dependent cell-mediated cytotoxicity (ADCC), involves binding antigens on the surface of infected cells with antibodies that make them attractive to natural killer cells that can then recognize and destroy them. "We have to make the antibody in a way that it will attract natural killer cells and then they can kill the virally infected cells," says Pandey. Another involves using an adeno-associated virus to deliver genetic instructions for building protective antibodies.

Source:
Medical University of South Carolina
