Method of Prompting Body to Develop Strong HIV Antibodies Shows Early Promise

Researchers used a harmless virus to deliver a gene for a broadly neutralizing HIV antibody to cells, which produced the antibody over time.

March 13, 2020 By Benjamin Ryan

Researchers have made promising initial strides in developing a method of prompting the immune system to produce broadly neutralizing antibodies (bNAbs) against HIV and to sustain that production over time.

In a small early-stage human study, investigators at the National Institute of Allergy and Infectious Diseases (NIAID) used a harmless virus as a vector to deliver to human immune cells a gene for a specific bNAb. They found that a single injection of this treatment led to long-term production of the desired antibody in people with HIV who were on antiretroviral (ARV) treatment.

The study's principal investigator, Joseph P. Casazza, MD, PhD, presented findings from an analysis of the first eight participants to receive the treatment at the 2020 Conference on Retroviruses and Opportunistic Infections in Boston this week.

Research has found that the study's vector, known as the adeno-associated virus serotype 8 (AAV8), is well-tolerated and does not cause disease in humans.

In a previous monkey study, researchers at the NIAID's Vaccine Research Center found that using AAV8 to deliver genes for antibodies against simian immunodeficiency virus (SIV), a simian cousin to HIV, prompted monkeys' immune systems to develop high levels of antibodies against SIV, which in turn protected the animals from acquiring the virus.

The investigators advanced this research into human trials with the Phase I, open-label dose-escalation VRC 603 trial. Thus far, eight people with HIV between ages 30 and 60 have received one of three doses of the AAV8 vector carrying a gene that encodes the HIV bNAb known as VRC07. The doses included 50 billion, 500 billion or 2.5 trillion viral genomes per kilogram of body weight and were provided through an intramuscular (into the muscle, as opposed to under the skin) injection.

VRC07 is currently under investigation in a separate trial as part of a combination bNAb treatment for HIV. Laboratory tests have indicated that the antibody, which was first isolated from the blood of a person living with HIV, can neutralize a wide variety of strains of the virus.

After their single injection, eight out of eight participants in VRC 603, all of whom remained on ARVs, developed VRC07 antibodies. The level of VRC07 in their bodies initially peaked about four to six weeks after the injection and then declined, followed by a slow initial incline starting about 16 weeks after the injection.

The five participants who received the low or intermediate doses of the VRC07 gene have been monitored for one and a half to two years by this point. In three of these people, VRC07 levels have exceeded the initial peak seen at the four-to-six-week post-injection point.

The three individuals who received the highest dose of VRC07 have passed three months since their injection. Two of them have developed an antibody level exceeding the peaks seen in the participants who received the lower doses of the gene.

The treatment has not led to any major side effects. Some participants experienced mild tenderness at the injection site or mild muscle pain, but these reactions were transient.

“To the best of our knowledge, this marks the first time that an AAV-based technology to deliver an antibody gene has resulted in safe and sustained levels of that antibody in blood,” said NIAID Vaccine Research Center director John Mascola, MD. “We hope that further development of this technology will yield a drug-delivery strategy applicable to a broad range of infectious diseases.”

The study authors also monitored the participants to see whether their immune systems developed antibodies against the VRC07 bNAb, as has been known to occur with the use of other antibody treatments. Three of the eight participants did develop antibodies to VRC07. But because all participants remained on ARV treatment with a fully suppressed viral load, it remains unclear what implication this finding has for VRC07’s ability to suppress HIV.

Compared with the monkeys that received the AAV8 vector delivering the VRC07 gene in the previous study, the human participants developed lower levels of the antibody. The study authors are currently analyzing data from this trial, which is still recruiting new members, in order to develop a better grasp of the factors that predict the bNAb level of the bNAb that human cells will produce.

If you’re interested in participating in the trial, which is being conducted in the National Institutes of Health Clinical Center in Bethesda, Maryland, click here to access the ClinicalTrials.gov information page on the trial.

To read the conference abstract, click here.

To read a press release about the study, click here.