Scientists Set the Stage for Combination HIV-Antibody Treatment and Prevention

Three antibodies combined into one protected monkeys against a simian version of HIV, opening the door for human trials.

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Researchers have reached an important milestone in the long-range effort to harness the power of so-called broadly neutralizing antibodies against HIV for use as treatment and prevention of the virus. Experiments in monkeys found that synthesizing three such antibodies into one protected the primates against exposure to SHIV, a simian version of HIV developed for research purposes.

Compared with individual antibodies, the “trispecific” antibody, which contains three prongs, each of which affects a different site on the surface, or envelope, of HIV, proved superior in thwarting the virus in the test animals. This finding suggests that, just as with standard antiretroviral (ARV) treatment, a combination-therapy approach will prove the most potent and put up the highest barrier against resistant virus.

Publishing their findings in the journal Science, National Institutes of Health (NIH) researchers, working in partnership with the Paris-based pharmaceutical company Sanofi, conducted extensive laboratory tests to identify the most promising double or triple combinations of antibodies. They used Sanofi’s technology to combine these antibodies into single, multipronged antibodies. Ultimately, they found that the combination that best attacked HIV included the antibodies VRC01, PGDM1400 and 10E8v4.

Scientists are currently investigating VRC01 in a pair of large, multiyear Phase III clinical trials to determine its efficacy as pre-exposure prophylaxis (PrEP) against HIV when infused every eight weeks.

The researchers in the trispecific antibody study infused eight macaque monkeys with VRC01, eight monkeys with PGDM1400 and eight monkeys with the triple-pronged antibody. Five days later, they exposed all the monkeys to two strains of SHIV. One strain of the virus was vulnerable to attack by VRC01 and the trispecific antibody but resistant to PGDM1400, while the other strain was vulnerable to attack by PGDM1400 and the trispecific antibody but resistant to VRC01.

Five of the eight monkeys (62.5 percent) that received PGDM1400 and six of the eight (75 percent) that received VRC01 became infected with SHIV. None of the animals that received the trispecific antibody were infected.

Sanofi and the National Institute for Allergies and Infectious Diseases (NIAID), a division of the NIH, are gearing up for a Phase I human trial of the trispecific antibody to begin in 2018. The trial will test the antibody's safety and how it is metabolized in HIV-negative individuals. NIAID is also looking into launching another Phase I trial of the trispecific antibody among HIV-positive individuals.

Scientists hope that successful clinical trials—there are three main phases before a new treatment may receive approval from the Food and Drug Administration—may yield a new way to treat and prevent the virus, with intermittent infusions of antibodies.

The study authors believe that this method of combining antibodies could also lead to new treatments for infectious diseases other than HIV, as well as autoimmune diseases and cancers.

To read the study abstract, click here.

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