Combination Treatment Shows Promise in Targeting Viral Reservoir in Monkeys

An antibody treatment plus an immune-stimulating agent delayed viral rebound in primates infected with HIV-like virus.

October 5, 2018 By Benjamin Ryan

Primates infected with an HIV-like virus, SHIV, in some cases experienced at least a six-month delay in their viral rebound after stopping antiretroviral (ARV) treatment when they were first additionally treated with a combination of a broadly neutralizing antibody and an immune-stimulating agent.

Preliminary results from the study were presented in March at the 2018 Conference on Retroviruses and Opportunistic Infections (CROI) in Boston.

Publishing their findings in the journal Nature, researchers infected 44 rhesus monkeys with a strain of virus known as SHIV-SF 162P3 and started the primates on treatment with Truvada (tenofovir disoproxil fumarate/emtricitabine) plus Tivicay (dolutegravir) seven days after infection.

Ninety-six weeks into ARV treatment, the monkeys were divided into four groups of 11 primates each. One group received five infusions spaced two weeks apart of 10 milligrams per kilogram of body weight of the broadly neutralizing antibody PGT121. A second group received 10 oral doses spaced two weeks apart of 0.15 mg per kg of the immune-stimulating agent GS-9620. A third group received both regimens that the first and second group received. And a fourth control group received placebo treatments.

One hundred thirty weeks into the study, by which time 16 weeks had passed since the monkeys last received any of the additional antibody or immune-stimulating treatments, the study authors interrupted the primates' ARV treatment and monitored them for viral rebound—virus rising above a fully suppressed level.

All the monkeys in the control group quickly experienced viral rebound, as did nearly all the animals that received only GS-9620. Five of the 11 monkeys that received the combination of PGT121 and GS-9620 experienced no viral rebound within six months of being taken off ARVs; the six monkeys in this group that did experience viral rebound experienced much lower peak viral loads than the animals in the control group. The monkeys that received only PGT121 experienced a modest delay in viral rebound.

“The combination of the antibodies and the immune stimulant led to optimal killing of HIV-infected cells,” study author Dan H. Barouch, MD, PhD, a professor of medicine at Harvard Medical School, said in a press release. “Together, our data suggest a mechanism by which the combination therapy stimulated innate immunity and rendered infected cells more susceptible to elimination. This study provides an initial proof-of-concept showing a potential strategy to target the viral reservoir.”

Dan Barouch speaks at CROI 2018 in Boston.Benjamin Ryan

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

To read the study abstract, click here.

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