New study shows a single experimental shot reduces HIV levels 1,000-fold

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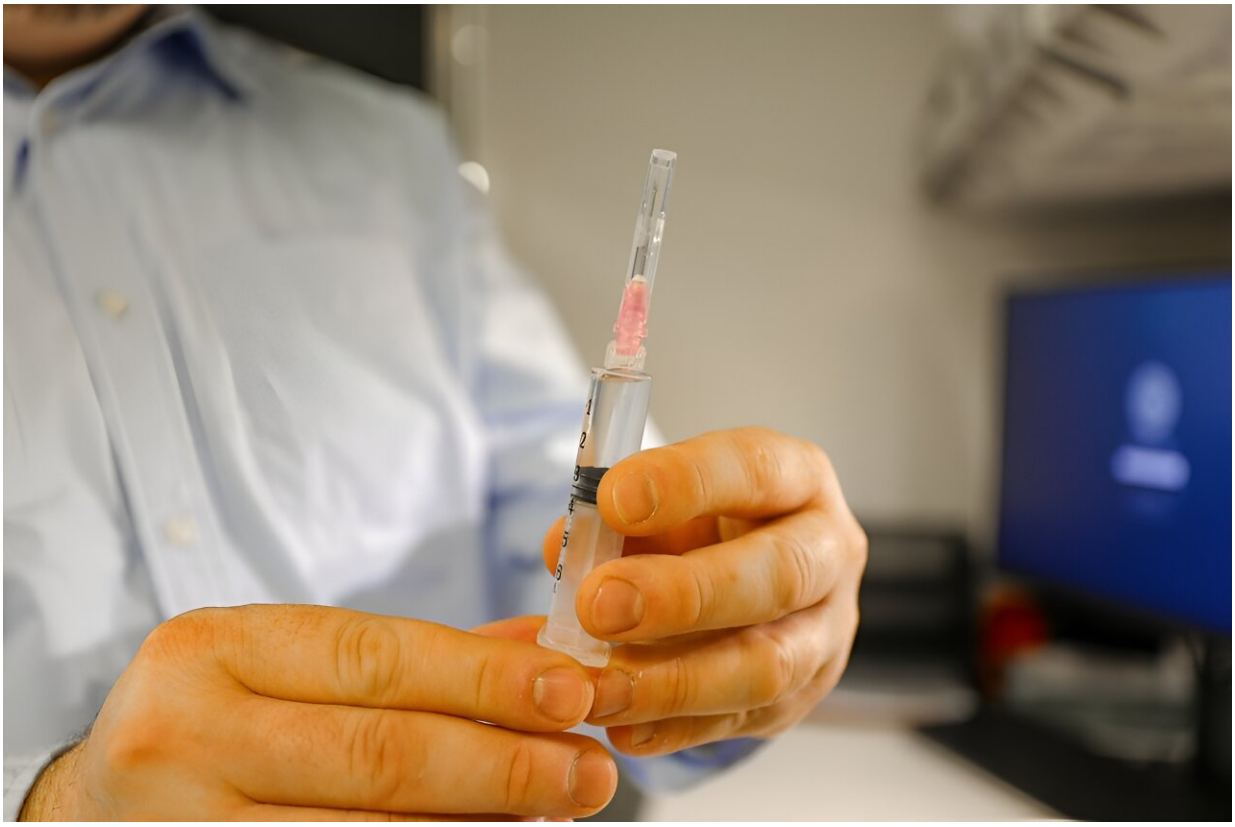

A study in nonhuman primates found a dramatic decrease in levels of the monkey form of HIV after one shot of Therapeutic Interfering Particles, or TIPs. The study's results suggest that one TIP shot could prevent a person living with HIV from passing the virus onto anyone else. Results from this research will be used to inform a planned clinical trial in people. Credit: OHSU/Christine Torres Hicks

A single shot of an experimental injection dramatically reduces levels of the monkey form of HIV in nonhuman primates for at least 30 weeks, according to a study published today in *Science*. The new research suggests that the lab-made shot has the potential to offer a simple and durable alternative to the current standard treatment for people living with HIV, which is effective but demanding.

The collaborative study between Oregon Health & Science University and the University of California San Francisco found Therapeutic Interfering Particles, or TIPs, reduced HIV levels in nonhuman primates by at least 1,000-fold in five of six treated subjects. The primate form of HIV was so low in one treated animal that the virus became undetectable.

TIPs are small, lab-engineered segments of the HIV virus that do not cause disease. TIPs reproduce so rapidly that they compete with HIV and are designed to suppress HIV in an infected person. The study's corresponding author, University of California San Francisco virologist Leor Weinberger, Ph.D., first came up with the idea for TIPs in the early 2000s through computational research. He then refined the concept with laboratory research and mouse models.

"There's really nothing that can change the course of disease like this," said co-author Nancy Haigwood, Ph.D., a professor at OHSU's Oregon National Primate Research Center. "If TIPs can reduce HIV in people like it has in our nonhuman primate study, this technology could open the door to alternative approaches to HIV care and mean people won't have to take medications for the rest of their lives. That is incredibly exciting."

Four years ago, Weinberger proposed a joint study with Haigwood, who has focused her four-decade research career on testing HIV and AIDS vaccines and treatments in nonhuman primate models. For this study,

teams of UCSF and OHSU researchers evaluated TIPs in nonhuman primates for the first time. Results from this research will be used to inform a planned clinical trial in people.

"This 20-year-long research journey opens the door to a future where people living with HIV may no longer have to adhere to continual drug regimens," Weinberger said. "These primate studies show the promise of a single-dose TIP intervention and are a strong indicator of efficacy in human trials.

"The real test, of course, will be the upcoming human clinical trials," he continued. "But, if TIPs prove effective, we could be on the brink of a new era in HIV treatment that could bring hope to millions of people—particularly in areas where access to antiviral drugs remains a challenge."

Promising treatment, prevention

The current standard HIV treatment involves taking a personalized combination of antiretroviral medications on a daily basis. Antiretroviral therapy enables people to live long, full lives and can enable most people to achieve undetectable HIV levels. However, the medications are potent and can cause numerous side effects, including diarrhea, fatigue, mood changes and high cholesterol. And missing scheduled antiretroviral therapy doses can lead HIV to become resistant to that combination of drugs, leaving a patient with fewer treatment options.

Another treatment option is lab-made antibodies, but the infusions must be given regularly throughout a person's lifetime. Having the option of a single, long-lasting injection could reduce both the burden and the expense of HIV treatment.

For this study, the research team—including Ann J. Hessell, Ph.D., a

professor at OHSU's Oregon National Primate Research Center, and professor Jacob Estes, Ph.D., director of OHSU's Vaccine & Gene Therapy Institute—injected nonhuman primates with TIPs and then exposed them to the primate form of HIV 24 hours later. An additional four nonhuman primates were infected, but not treated, and served as controls for the study.

Scientists observed all 10 of the nonhuman primates for 30 weeks, regularly analyzing samples of blood and tissue from the lymph nodes, where reservoirs of HIV are concentrated in people living with HIV. Repeated, quantitative analyses showed all but one of the treated animals consistently had substantially lower levels of both HIV DNA and RNA than the controls.

The 1,000-fold reduction in HIV levels that the team observed is three times more than what can delay people with HIV from developing AIDS.

Using data from this study, the researchers conducted mathematical modeling to determine that a single TIP injection has the potential to permanently reduce viral levels below the World Health Organization's threshold for HIV transmission. This means that while the findings need to be confirmed with human studies, the study's results suggest that one TIP shot could prevent a person living with HIV from passing the virus onto anyone else.

The research team also did not observe recombination, or when two different viral strains infect a single cell at the same time and the strains exchange genetic material to create a hybrid with portions of both strains. Recombination is a major cause of HIV variation, which partly makes the virus so challenging to treat. The absence of recombination indicates that TIPs won't make managing HIV more difficult down the road.

Weinberger, Haigwood and colleagues are conducting a follow-up nonhuman primate study to assess how a single TIPs injection could work after infection is already established and controlled with antiretroviral therapy, to control virus when the therapy is halted.

More information: Fathima N. Nagoor Pitchai et al, Engineered deletions of HIV replicate conditionally to reduce disease in nonhuman primates, *Science* (2024). DOI: 10.1126/science.adn5866

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