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Long-acting shot prevents infection with HIV analogue

Periodic injection keeps monkeys virus-free and could confer as long as three months of protection in humans.

Brendan Borrell

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A study in macaques has raised hopes that preventing HIV infection in humans will soon be as easy as a shot in the arm four times a year. In a proof-of-concept study, researchers have shown that an antiviral drug injected into the muscle protects monkeys from infection for weeks afterward.

“We believe it’s a very practical, feasible approach to HIV prevention,” says David Ho, a virologist at the Aaron Diamond AIDS Research Center in New York and a co-author of the study, which is published online today in *Science*[1].

In the absence of a proven vaccine, ‘pre-exposure prophylaxis’ with drugs used to treat the infection has become one of the most promising strategies to cut down HIV infection rates among high-risk populations, including people living in sub-Saharan Africa, intravenous-drug users and men who have sex with men. A 2010 study[2] found that among men who have sex with men, those who took a combination of tenofovir and emtricitabine daily reduced their risk of contracting HIV by more than 90%. However, not everyone in the trial — which lasted for several months — took the medication every day, and among all participants who received the pill, HIV infection rates dropped by only 44%.

Shot in the dark

Ho and his colleagues, who include researchers from drug-maker GlaxoSmithKline in Research Triangle Park, North Carolina, studied an experimental drug called GSK744. GSK744 is a highly potent analogue of dolutegravir (sold as Tivicay), which was approved by the US Food and Drug Administration for HIV treatment last year.

GSK744 works by interfering with the enzyme that HIV uses to insert its DNA into the human genome. This blocks the key step needed for the AIDS virus to replicate itself, and the viral DNA simply degrades inside the cell.

Turning the drug into an injection depended on its chemical properties. Because GSK744 is not soluble in water, the researchers melted it and crystallized it into nanoparticles, which they suspended in solution. When this fluid is injected into muscle, Ho explains, it

forms a ‘depot’ and slowly seeps into the blood and tissues, including the rectum, where HIV exposure can occur. “The depot allows the agent to be around for three to four months,” says Ho.

To test the drug’s effectiveness, Ho and his team squirted a solution containing a hybrid of the simian and human AIDS-causing viruses into the rectums of 16 macaque monkeys once a week for eight weeks. Half of the macaques received two injections of GSK744 during that period. The other half, which served as the control group, did not.

All the macaques in the control group became infected, typically within two weeks. All of the macaques receiving GSK744 were protected.

A follow-up experiment showed that a single dose of GSK744 protected monkeys for 5–10 weeks on average. Because humans metabolize the drug much more slowly than macaques do, Ho thinks it will remain effective in humans for up to three months.

Jonathan Mermin, director of the US National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention at the US Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia, says that the CDC is presenting data from a similar study in macaques this week at the Conference on Retroviruses and Opportunistic Infections in Boston, Massachusetts. He says that those results show that the shot is also effective warding off infections after exposure through the vagina, and that it is now time to start testing the strategy in humans.

“It’s hard to get healthy people to take a pill or put on a salve every day,” notes Robert Schooley, an infectious-disease specialist at the University of California in San Diego, who was not involved in the study. An injection strategy, he says, is “a very important avenue to pursue”.

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References

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