

Experts Propose Transmissible Gene Therapy to Halt the HIV Epidemic

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Researchers have outlined an intriguing model that could help slow the spread of HIV better than test-and-treat models or a modestly effective HIV vaccine. Their theory, [published](#) online March 17 in the journal PLoS Computational Biology and [reported](#) by aidsmap, details how a gene therapy that curbs HIV production could be given to people with HIV. If these people were to have unsafe sex with someone else, they would pass along the gene therapy, essentially limiting the effects of HIV if the virus were to take hold in their sex partner.

The new gene therapy technology uses tiny pieces of genetic code called therapeutic interfering particles (TIPs) packaged inside of a lentivirus. The TIPs can't reproduce on their own. They depend on genes produced by HIV. In the body of someone who is HIV-positive, the TIPs essentially steal HIV's genetic material and, because they reproduce faster than the virus, outcompete HIV in the body and prevent it from replicating at its normally high rate.

If a person with both HIV and TIPs in the body were to have unprotected sex or share injection equipment with an HIV-negative person, they would theoretically be less likely to pass on HIV—because the TIPs have caused HIV levels to drop—but they would be likely to pass on the TIPs. The person infected with the TIPs would have the TIPs genes sitting dormant inside of them until they did acquire HIV. When that happens, the TIPs would hopefully keep their HIV levels low enough that they wouldn't easily pass on HIV to others. What makes the technology so exciting is that giving the gene therapy to just one HIV-positive partner could spread TIPs throughout their entire sexual or drug-using network, thus substantially lowering HIV transmission rates for all involved.

"TIPs are molecular parasites that 'piggyback' on HIV [transmission networks] to spread between individuals," said Leor Weinberger, PhD, from the University of California at San Diego, the senior scientist on the team.

Weinberger and his colleagues devised their model based on a desire to reach a critical juncture of high-risk individuals whom experts call "super spreaders." Such individuals, who typically make up less than 20 percent of a sexual or drug-using network, are actually responsible for 80 percent or more of all new infections. Because such individuals are often not in care and are undiagnosed, they are incredibly difficult to reach.

Using data from several real world databases from areas in Africa with the most out-of-control HIV epidemics, Weinberger's team conducted computer simulations that modeled the effect of five scenarios on the rate of new infections and overall prevalence of HIV over a 30- to 50-year period. Those scenarios included: aggressively testing all HIV-negative people and placing those found to be positive on treatment (test and treat), offering a 30 percent effective vaccine in a community, offering a 50 percent effective vaccine, using TIPs that reduce HIV levels by 0.5 logs in those infected and using TIPs that could reduce HIV levels by 1.5 logs.

The team found that either TIPs scenario cut HIV infections and prevalence by 30 to 50 times more than the test and treat approach or either vaccine. They estimate that that this huge difference in efficacy was due to the fact that TIPs spread quickly and easily throughout an entire sexual network, while test and treat and vaccine approaches rely on the laborious process of finding such individuals, usually long after they have acquired HIV and spread it to others.

The authors caution that there is a lot of laboratory and clinical work that must first be done before TIPs can be judged feasible enough to continue study. For one thing, the specific TIPs must be tested in animals first to ensure that they don't actually amplify HIV replication rather than slow it down. Scientists will also need to judge how long the TIPs last in the body.

Weinberger said that his team will be working with medical ethicists to determine if it would be ethical to introduce a transmissible new therapy, such as TIPs, into a population of people.

Nevertheless, the authors comment that a single injection of TIPs into a relatively small number of HIV-positive people has the potential to far outstrip either test and treat or a vaccine in cutting new infections—and at a fraction of the cost.