Transmissible Treatment Proposed for HIV Could Target Superspreaders to Curb Epidemic

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Biochemist Leor Weinberger and colleagues at the University of California, San Diego and UCLA have proposed a fundamentally new intervention for the HIV/AIDS epidemic based on engineered, virus-like particles that could subdue HIV infection within individual patients and spread to high-risk populations that are difficult for public health workers to reach.

With a model that considers the effects of the proposed treatment on several scales, from interference with HIV in infected cells to viral loads in individual patients to the prevalence of HIV in large populations, they determined that the engineered particles could work in concert with current treatments for HIV infection and lower the prevalence of infection more effectively than current drugs or proposed vaccines alone. Their findings will appear in the March 17 issue of *PLoS Computational Biology*.

"Dr. Weinberger's idea to use engineered virus-derived particles to combat infectious diseases is truly provocative," said James Anderson, M.D., Ph.D., Director of the Division of Program Coordination, Planning, and Strategic Initiatives. Anderson oversees the NIH Common Fund, which supports a series of exceptionally high impact, trans-NIH programs including the NIH Director's New Innovator Award, which Weinberger received in 2009.

Piggyback parasite

The engineered particles, called therapeutic interfering particles or TIPs, would persist for years in an individual patient and could be packed with genes that disrupt the functioning of HIV. Weinberger's team has succeeded in creating functional prototypes in the lab.

"TIPs are molecular parasites that 'piggyback' on HIV to spread between individuals," Weinberger said. The engineered particles use the same outer envelope as HIV but lack the genes for components of this structure and the enzymes needed to assemble it. They can only replicate, infect additional cells and transmit to new individuals by stealing these elements from HIV. Until the host cell is infected with HIV, TIPs remain dormant.

In an HIV-infected individual, TIPs would transmit to others in the same ways as the natural virus - through unprotected sex or shared needles, for example. That means TIPs would, by design, penetrate high-risk populations that are responsible for a disproportionate share of the spread of disease and can be particularly difficult for public-health officials to reach.

Using an epidemiological model, Weinberger and colleagues compared the predicted effects of the treatment they propose with current drug campaigns and hypothetical vaccines and found that TIPs could be more effective.

An intervention using TIPs could lower the number of people infected with HIV in sub-Saharan Africa to one thirtieth the current level in about 30 years, they found. Optimistic predictions for vaccine campaigns or currently

available antiretroviral therapy would lower the number of HIV-infected people by less than one half the current level over the same period of time.

TIPs wouldn't replace other therapies, Weinberger said, "In part, we are arguing that TIPs could be used in conjunction with current antiretroviral drug therapy or vaccine campaigns, and could enhance the efficacy of these campaigns at the population level."

Precedence for transmissible treatments

Weinberger acknowledges that an infectious treatment raises ethical concerns and is working with bioethicists to explore the unique issues associated with any use of TIPs in more detail.

He also points out that vaccines already in use can spread from one person to another. People who receive the oral polio vaccine, for example, "shed" the weakened version of the virus that is the basis of the vaccine and this can transmit immunity to other individuals. Public health officials see this transmission as a benefit; it is one reason why this form of polio vaccine was chosen for the worldwide effort to eradicate the disease.

Co-authors include James Lloyd-Smith, a theoretical ecologist at UCLA, and Vincent Metzger, a graduate student in Weinberger's group. This work was funded by a grant from the Bill and Melinda Gates Foundation and an NIH Director's Innovators Award to Leor Weinberger.

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