



# HIV Cure Research

## An Introductory Factsheet

April 2020

*This fact sheet provides basic information on HIV cure research. For more basic fact sheets visit [www.avac.org/resources](http://www.avac.org/resources). Visit [www.avac.org/cureiculum](http://www.avac.org/cureiculum) to access a suite of educational material on HIV cure topics.*

### What does the term “AIDS cure” mean?

The term “cure” refers to strategies that eliminate HIV from a person’s body, or permanently control the virus and render it unable to cause disease. A “sterilizing” cure would completely eliminate the virus from the body. This type of cure is impossible to measure with current technology. Remission, sometimes referred to as long-term viral suppression off ART (without drugs), or sustained viral remission, would suppress viral load, keeping it below the level of detection without the use of ART. The virus would be undetectable on the most sensitive tests currently available, but traces of the virus may remain in the body and could lead to reinfection. Just like cancer, a person in remission may be undetectable for many years and then rebound with a strain of virus dormant in their body.

Researchers are still debating and discovering what it means to be cured of HIV. Although some cases of remission have been reported, almost all have now rebounded. It takes time to be certain that HIV can no longer cause disease.

### What types of cure strategies are being investigated today?

There are three broad strategies being explored. Each takes a different approach to the fundamental challenge of HIV infection—the ability of HIV to hide in cells that are inactive (also called resting cells) and not dividing. As long as the cells are not dividing, the virus isn’t copying itself and is considered “latent”. Cells that carry latent virus are, collectively, referred to as viral reservoirs. Most of the viral reservoir is in memory CD4+ T cells (latent immune cells), which are designed to live in the body a long time. A truly effective cure will either have to eliminate these viral reservoirs or ensure that an activated virus cannot reestablish infection in the body.

#### Shock and kill

This two-step strategy aims to flush (or shock) the virus out of resting cells with a latency reversing drug and then follow up with another intervention (likely something from the strategies below) to effectively kill infected cells. Many of the shock agents being considered are currently used as cancer treatments, although researchers are trying to discover new drugs as well. The kill component of this one-two punch could involve a therapeutic vaccine (which is different than a vaccine for prevention, see the vaccine fact sheet), if an effective one can be developed. The kill may also involve interventions to intensify or improve the immune response to HIV.

#### Gene therapy/manipulation

Some strategies to change the cells so that HIV can’t infect them involve editing genes to remove a protein receptor known as CCR5—the door HIV uses to enter CD4+ T Cells. Another approach modifies immune cells to better detect latent infected cells in the body. Another especially complex strategy would remove HIV from the DNA of infected cells. Researchers are working on developing a method to deliver gene editing technology directly into the body without removing cells. Currently, all gene modification involves extracting immune cells from HIV-positive individuals, modifying them and then reinfusing them back into the participant. The challenges are significant. It’s difficult to collect immune cells infected with HIV, and no one yet knows the quantity of modified genes needed to achieve results. The hope is modified genes would quickly spread through the whole body.

### Resources and links

AVAC ([www.avac.org/cure](http://www.avac.org/cure))

International AIDS Society  
([www.iassociety.org](http://www.iassociety.org))

Michael Palm Basic HIV  
Science, Vaccines and Cure  
Project Blog  
([tagbasicscienceproject.typepad.com](http://tagbasicscienceproject.typepad.com))

## Immune modulation

Immune modulators refer to any type of drug or procedure that causes some type of sustained change in the immune system to better fight HIV. Successful immune modulation would both identify latent cells holding the virus BEFORE the cells reactivate, and intensify the capacity to kill HIV once cell division begins again.

Researchers are exploring natural killers and neutralizers of HIV and how to make them more potent through immune modulation. These include HIV-specific CD8+ T cells, NK cells and broadly neutralizing antibodies. Another immune modulation that could make a difference involves turning off immune cells' "exhaustion markers" that signal a cell to die.

## What challenges face cure research?

Many issues make cure research difficult. First, there is no clear way to measure the HIV reservoir. The two most accessible approaches measure the number of HIV RNA copies in the blood, or the number of HIV DNA copies in cells. But HIV RNA in the blood does not detect viral copies already integrated into resting cells. Measuring DNA often doesn't provide an accurate picture either, since the cheapest and most available technologies cannot distinguish replication-competent virus from damaged, harmless virus. A more precise measure or assay, called the *quantitative viral outgrowth assay*, requires the use of large numbers of cells and cannot be done with a simple blood draw.

Unknown risks and benefits associated with all these current strategies represent a second major challenge to cure research. Trial participants must be able to understand these risks and potential benefits. In order to test for a cure, participants must stop treatment to enable researchers to look for a viral rebound of HIV. There are no standardized guidelines for how to time such "treatment interruptions" and minimize risks for trial participants and their partners. Finally, cure strategies may look different for men, women and children—biological differences between sexes and differences in adult versus pediatric immune systems mean that it is unlikely there will be a one-size-fits-all cure approach.

## What happens next?

Cure research is expanding, with a range of trials planned or under way. See [avac.org/pxrd](http://avac.org/pxrd) for a list of these trials.

## How can advocates get involved?

Many of the research strategies being developed require expensive equipment and specific training to administer. To show success or failure additional resources may be needed. These resources are not available in most global settings. Advocates can increase awareness around the need for these technologies in order to prepare for future cure trials in humans.

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**About AVAC** | AVAC is a non-profit organization that uses education, policy analysis, advocacy and a network of global collaborations to accelerate the ethical development and global delivery of new HIV prevention options as part of a comprehensive response to the pandemic.