



How Some HIV Controllers Contain the Virus

A small subset of people living with HIV are able to control viral replication without antiretroviral treatment.

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Currently living in Sacramento, Loreen Willenberg, a 66-year-old landscape designer with HIV, is among a group referred to as “elite controllers,” individuals who aren’t on antiretroviral medications, have no symptoms of illness and possess a robust immune system with disease-fighting CD4 and CD8 T-cells that are highly active against HIV. According to the National Institutes of Health (NIH), elite controllers account for less than 0.5% of people living with HIV.

“In my case, the folks at the NIH showed me film captured under a fluorescent microscope that showed my cells at work,” she says. “My CD8s homed in on the HIV-infected CD4 cells faster than the cells of most people living with HIV, which is remarkable. I’m like this natural born destroyer of infected cells! It’s crazy stuff!”

As Willenberg watched in wonder, her CD8 cells emitted two substances: one, a protein called perforin, poked holes in the infected cell’s wall; the second, an enzyme called granzyme B, slipped through the perforation and signaled the infected CD4 cell to kill itself.

“Apparently, my CD8s are among the most potent that they’ve ever witnessed in a human being,” she says. “Within an hour, that process happens, and that cell is dead. The level of production of perforin and granzyme B from within my CD8 cells is several-fold higher than that of most people living with HIV, and that’s what the NIH taught me about my case.”

But an additional adjective elevates the already elite Willenberg into an even higher tier. Researchers have classified her as an exceptional elite controller because she’s exhibited no progression of HIV for more than 25 years.

Willenberg explains that, not counting the minor viral blip that occurred 20 years ago when she developed a bad case of the flu, she’s been undetectable for over 28 years. “No symptoms, no loss of CD4s and a balanced ratio between my CD4 and CD8 cells,” she says. “CD8 cells are the soldiers that support the general—the CD4 cells—in its fight. The CD8s are actually natural killers.”

In July, Willenberg will have achieved 29 years of being undetectable. “I know elite controllers who

are in their 35th year or fourth decade of this control, so I think, basically, the story is one of hope,” she says.

After a pause, she adds, “So how do we make that happen in other people? Is that a vaccine? God, I hope so!”

In a recent study, researchers shed light on how Willenberg and about 60 other elite controllers keep HIV in check. In these individuals, HIV’s genetic blueprint is locked away in the genome of resting immune cells in such a way that it can’t be used to produce new virus. The researchers were unable to find any intact HIV after looking in more than 1.5 billion of her cells.

Scientists think that in elite controllers, HIV frequently occupies genetic areas they call “gene deserts” that don’t allow the virus to replicate. The HIV genes there are only inactive viral DNA.

“I believe Loreen might indeed meet anyone’s definition of a cure,” says study coauthor Steven Deeks, MD, of the University of California at San Francisco.

The question now is whether scientists can develop treatments to enable the millions of typical people with progressive HIV to become more like elite controllers.

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