

## **Theory Explains Why Some With HIV Survive Longer**

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Credit: NIAID

A group of researchers in Boston announced a new theory this week that may help to explain a longstanding mystery in AIDS research: why some people with HIV survive for decades without ever developing AIDS.

Described in the scientific journal *Nature*, the research highlights the secret workings of a genetic trait that may allow some immune systems to better wage war on the virus than others. Like many new theories in science, though, it is likely to be debated -- at least one expert in the field who was not involved with the research is already cautioning that



further work needs to be done.

The one thing that all experts agree upon, however, is that understanding why some people with <u>HIV</u> can survive longer than others has broad implications for the global epidemic. Their secrets may lead to effective vaccines against the virus, which infects more than 33 million people worldwide and kills millions of people every year.

## The Mystery Of The Non-Progressors

Doctors who treat people with HIV have known for years that the virus affects people differently. Some catch it and develop AIDS very quickly, sometimes dying within a few months, while others live with HIV for a few years without symptoms, though they develop AIDS eventually. New drugs and treatment strategies have helped people live longer than ever in the last 15 years -- saving some 2.9 million lives in the past two decades, according to estimates by the Joint United Nations Program on HIV/AIDS.

About one out of every 200 people who catch HIV are considered "longterm non-progressors" or "elite controllers" because they can live for many years with the virus without developing AIDS. Even the most sensitive tests often cannot detect the virus in their bloodstream.

"Some of our patients have been infected for more than 27 years and have not had any blips or declines in their CD4+ count [a measure of progress towards AIDS]," said immunologist Mark Connors, who works with non-progressors at the National Institute of Allergy and Infectious Diseases in Bethesda, MD.

Numerous studies have followed these people, seeking to understand how their bodies control HIV so well when so many others succumb to the virus. What accounts for this difference is the crux of the new theory



by the team in Boston, led by Arup Chakraborty of MIT in collaboration with Bruce Walker at Massachusetts General Hospital.

## Part Genes, Part Luck

According to Chakraborty, one of the reasons why non-progressors can control HIV so well is a combination of good genes and good luck.

About half of all the people who have natural HIV resistance share a genetic trait known as "HLA-B57," a particular form of the gene that makes a molecule known as HLA. This molecule plays a part in developing the immune system's killer T <u>cells</u>, which seek out and destroy cells infected by HIV and other viruses.

In general, HLA helps to delete T cells that are too reactive and could cause a whole host of problems by damaging healthy tissue.

Chakraborty and his colleagues used computer simulations to study the diversity of interactions between HLA and killer T cells, and they determined that the HLA-B57 variation of the gene tends to remove fewer developing killer T cells. This creates a population of these killer T cells that are cross-reactive and may be better at fighting HIV, keeping up with the virus as it constantly mutates.

Having the HLA-B57 trait by itself is not enough for natural resistance --99 percent of people who have it are not non-progressors -- but for a lucky few it could lead to cross-reactive killer T cells that can recognize a wider range of HIV.

"This ability to have cross-reactive T cells gives you better control of the <u>virus</u>," said Chakraborty.

Some researchers, including Connors, remain unconvinced.



"It's an interesting idea, but it needs to be backed up by experimental data." he said. "There is no objective data that shows non-progressors have greater cross-reactivity."

If future studies confirm the theory and a way can be found to artificially induce such broadly-reactive killer T cells in people, researcher might be able to design a <u>vaccine</u> to do just that -- though there is no guarantee that such a vaccine would ultimately prove effective, as the history of AIDS vaccine trials has shown more than once.

Source: Inside Science News Service

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