SARS-CoV-2 Rapidly Evolves in People with Advanced HIV

Researchers uncover how COVID-19 virus variants may emerge in people with weakened immune systems.

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A NIAID study revealed how some variants of SARS-CoV-2—the virus that causes COVID-19—could evolve. The researchers used cutting-edge technology to examine genes from SARS-CoV-2 in people with and without HIV who also had COVID-19, looking at the different copies of the virus in individuals over time. They found that people with advanced HIV—as defined by reduced numbers of immune cells called CD4+ T cells—had dozens of SARS-CoV-2 variants in their bodies, compared to just one major variant in most people without HIV and people with HIV who had higher numbers of CD4+ T cells.

Like other viruses, SARS-CoV-2 evolves quickly. When the virus enters the body, it makes more copies of itself. During this process, called replication, the virus's genetic material can change, or mutate, to arrive at new viral variants. Variants of concern (VOCs) are viral variants with traits that make them more dangerous—by causing worse disease, finding new ways to evade the immune system, or spreading more easily.

It has been difficult to determine how new VOCs of SARS-CoV-2 arise. Some studies suggest that when people who are immune compromised get SARS-CoV-2, their bodies provide conditions that can promote variants by allowing the virus to linger during a weakened immune response. These prolonged infections could provide a sort of sandbox for different gene mutations to arise and test the body's defenses, allowing for more new variants to evolve and spread. HIV can cause immune deficiency if its replication is not controlled by antiretroviral therapy (ART). ART taken as prescribed suppresses HIV viral replication and prevents or reduces immune system damage.

To examine how VOCs may emerge, Eli Boritz, MD, PhD, chief of the Virus Persistence and Dynamics Section at NIAID's Vaccine Research Center, partnered with researchers at the South African National Institute of Communicable Diseases to conduct the study in a unique cohort of individuals with COVID-19 in South Africa. The study group included 47 people with and without HIV, 12 of whom had advanced HIV, characterized as having CD4+ T cell counts lower than 200 cells/mm^3. [Results were published August 22 in Nature.]

The research team investigated SARS-CoV-2 evolution in the study group using advanced technology developed in Dr. Boritz's lab called high-throughput, single-genome amplification and sequencing (HT-SGS). This approach enabled them to obtain genetic information from thousands of individual SARS-CoV-2 viruses per sample, providing a snapshot of the different mutations present at a given time and allowing for analysis of viral evolution at a level of detail previously unavailable. They looked at the gene for the SARS-CoV-2 spike protein—which the virus uses to enter cells—to see which variants were present throughout the course of COVID-19 and found significant differences in the SARS-CoV-2 variants between the study participants.

People with advanced HIV who had COVID-19 were found to have multiple variants of SARS-CoV-2, and the population of viruses in each person became more diverse and evolved over the course of the infection. The median number of SARS-CoV-2 variants in people with advanced HIV was 47, and some individuals had over 100 detectable variants throughout the infection. In people without advanced HIV (those either without HIV or with HIV and CD4+ T cell numbers above 200 cells/mm^3), the population of viruses in each individual was generally uniform. Most of these participants had only one major variant of SARS-CoV-2 in their bodies, with little evidence that the virus evolved during infection.

The findings reveal extensive variation of SARS-CoV-2 in people with advanced HIV and provide further understanding towards how new variants arise and adapt in people with compromised immune systems. More research is needed to understand how SARS-CoV-2 infection in people with advanced HIV and other immune deficits may contribute to the emergence of new VOCs. This work additionally highlights the importance of research to understand, treat, and prevent HIV, COVID-19 and immune conditions, as well as ensuring access to treatment for people with HIV and working towards a cure.

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