



HIV Science

HIV is a uniquely challenging viral infection for multiple reasons.

The virus contains a microscopic piece of genetic code in the form of ribonucleic acid (RNA). The RNA contains instructions for making more copies of HIV. Unlike deoxyribonucleic acid (DNA), the genetic material that makes up the human genome of humans and many other forms of life, RNA is very sloppy when copying itself. It makes mistakes that can be compared to a spelling error. This means that HIV mutates constantly. There are geographic clusters of similarly mutated forms of HIV found around the world that scientists designate as “clades” or “subtypes.” In North America, South America and Europe, most HIV belongs to clade B. In sub-Saharan Africa, most HIV belongs to clade C.

The mutation of HIV particularly affects the virus’s outer protective **envelope**. This makes it difficult to develop **preventive vaccines**, which typically work by teaching the body to recognize HIV and make **antibodies** that bind to the virus envelope to block infection. HIV’s shape-shifting envelope makes it a moving target for antibodies, and the body doesn’t make antibodies fast enough to keep up with the speed of mutations. While people living with HIV test antibody-positive on standard diagnostic tests, these immune responses are almost always ineffective at controlling the infection and preventing disease progression.

HIV also compromises the immune system by preferentially infecting **CD4 T cells**. CD4 T cells are the helpers, leading the body’s response to infections by coordinating the many other components of the immune system. These include **CD8 T cells**, which target and kill cells infected by viruses or other **pathogens**, and **B cells**, which act as factories for producing antibodies. By targeting and infecting CD4 T cells, HIV leaves the immune system without a leader in its efforts to deal with the virus.

During the process of infecting CD4 T cells, HIV’s viral RNA is converted into DNA, which becomes integrated into a cell’s DNA. This enables HIV to persist in the body for life. Long-lived CD4 T cells containing HIV DNA are a barrier to a cure because they are a

dormant source of virus, as if the virus is “sleeping.” The dormant virus can start making copies again if people stop using anti-retroviral treatment (ART).

Scientists are working on solutions to these challenges. They have identified rare antibodies that can strongly block many different HIV clades that are known as **broadly neutralizing antibodies** (bnAbs for short). They have also developed technologies that allow these antibodies to be copied and produced in large quantities. These laboratory-made antibodies are known as monoclonal antibodies. Studies are underway assessing whether bnAbs can prevent or treat HIV infection when given intravenously (IV) or subcutaneously (SC, meaning given under the skin). These different bnAbs can bind to several different locations on HIV’s envelope, so the studies look at using the bnAbs both individually and in combinations. Different from antibodies that the body makes naturally that last for a long time, bnAbs last for a shorter period of time in the body. Using bnAbs for HIV prevention would require people to receive doses on a regular schedule every few months.

A vaccine that induces bnAbs is widely considered to be the ideal HIV prevention approach. Researchers are making incremental progress toward this goal, but the studies are still at an early stage.

Additional HIV prevention technologies in the research pipeline include new forms of pre-exposure prophylaxis (PrEP) that aim to improve upon, or offer alternatives to, the two available PrEP drugs, Truvada and Descovy. This includes additional technologies, such as long acting injections and vaginal rings. There are also ongoing efforts to develop microbicides that work locally in the vaginal and/or rectal mucosal tissue to block HIV infection at the point of entry.

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