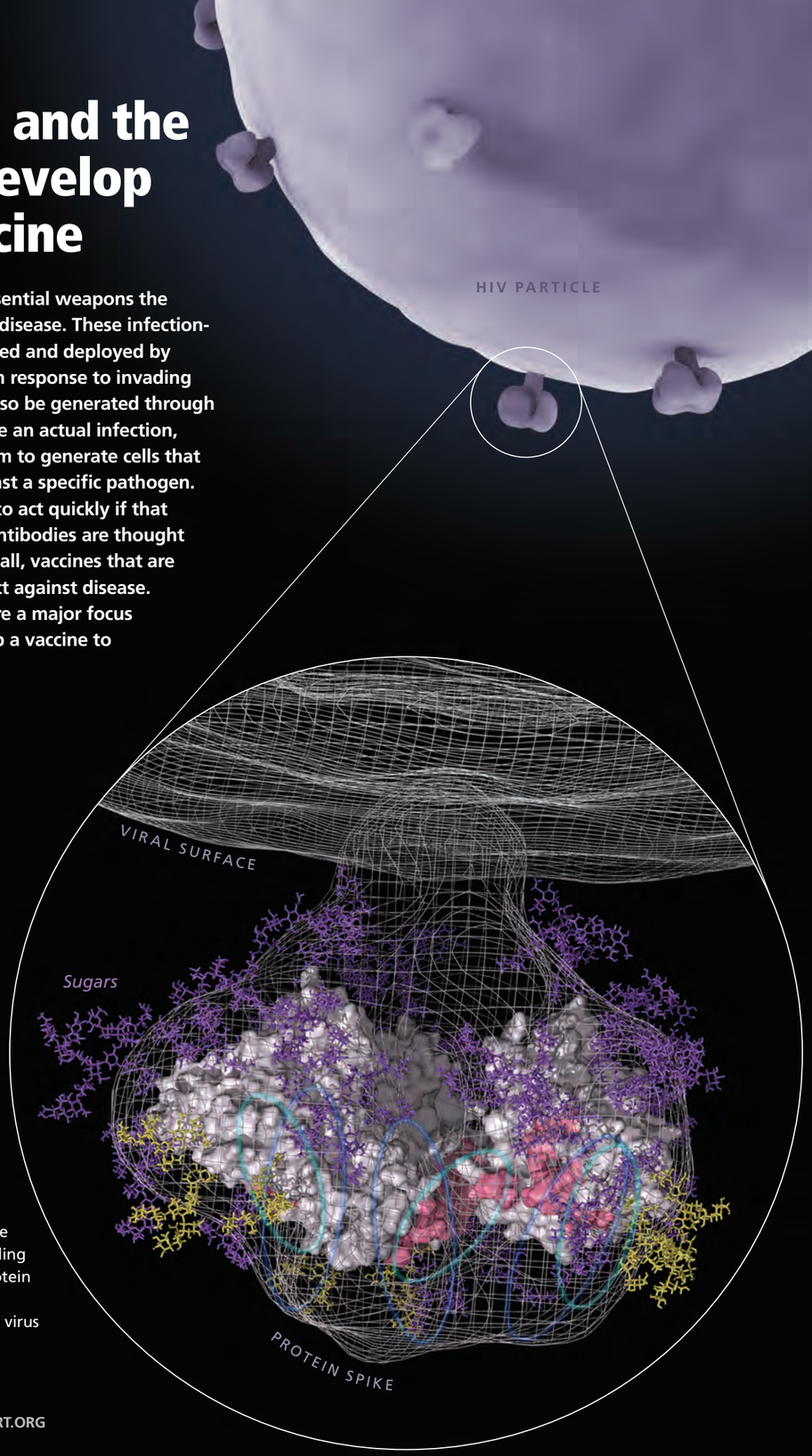
Antibodies and the Quest to Develop an HIV Vaccine

Antibodies are one of the essential weapons the body uses to defend against disease. These infection-fighting proteins are generated and deployed by the human immune system in response to invading pathogens. Antibodies can also be generated through vaccination. Vaccines simulate an actual infection, provoking the immune system to generate cells that can produce antibodies against a specific pathogen. These cells lie in wait, ready to act quickly if that pathogen enters the body. Antibodies are thought to be the reason most, if not all, vaccines that are used today are able to protect against disease. Because of this, antibodies are a major focus of research efforts to develop a vaccine to protect against HIV/AIDS.

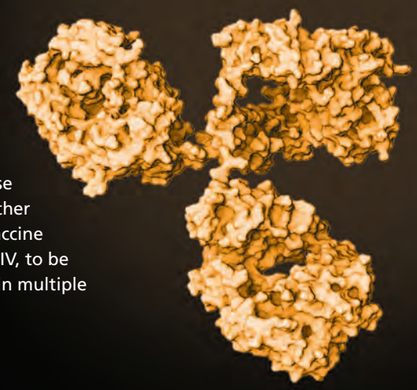


THE HIV SPIKE

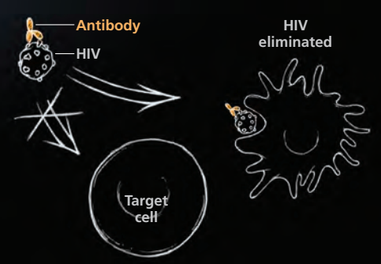
The surface of HIV is dotted with spikes made of proteins. Researchers use special microscopes and X-rays that allow them to study the structure of HIV's protein spikes and create images like this one. Because these protein spikes are the only exposed part of the virus, they are a target for antibodies that are generated against HIV. However, HIV's protein spikes are coated with bulky sugar molecules, shown here in purple, that act as armor, shielding the virus from antibodies. The protein spikes on HIV are also constantly changing their shape, helping the virus to avoid antibodies.

ANTIBODIES

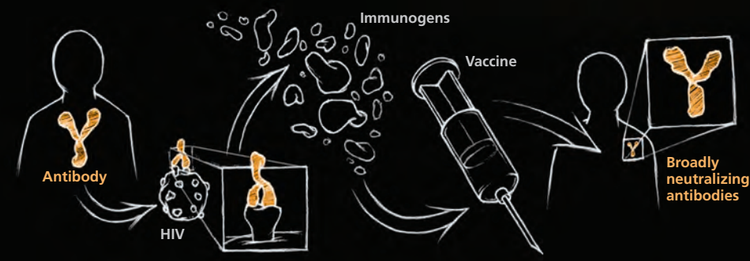
The immune systems of individuals infected with HIV eventually generate antibodies against the virus. Researchers can isolate these antibodies from blood and study them to gather clues about the types of antibodies an HIV vaccine might need to trigger, prior to exposure to HIV, to be able to block the virus. Antibodies can work in multiple ways, some of which are described below.



HOW NEUTRALIZATION WORKS



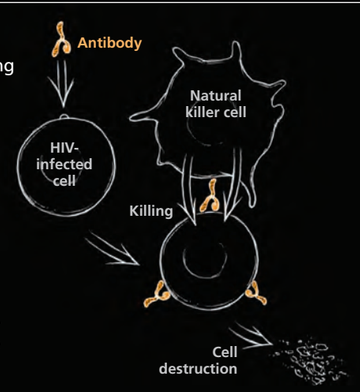
1 HIV, like any virus, must enter cells to cause an infection. Antibodies that attach their arms to HIV's protein spikes can stop HIV from entering its target cells. Such antibodies are called neutralizing antibodies because they inhibit or neutralize the virus. After HIV is tagged by neutralizing antibodies, specialized immune cells destroy the virus, eliminating it from the body.



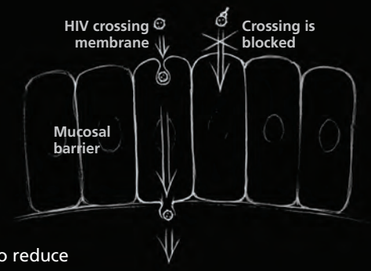
2 HIV is one of the most variable viruses ever discovered. This represents a major challenge for vaccine development. To combat HIV's variability, researchers are trying to design vaccine candidates that can induce antibodies that neutralize many HIV variants, so-called broadly neutralizing antibodies. Several new broadly neutralizing antibodies were recently isolated from HIV-infected volunteers. Scientists are now working backward to construct an HIV vaccine candidate based on these antibodies. First, they study where on HIV the antibody attaches. Then, they design an immunogen, the component of a vaccine that stimulates the immune system, which has a structure similar to the part of HIV where the antibody attaches. These immunogens will then be tested to see if they generate broadly neutralizing antibodies in vaccinated individuals.

OTHER ANTIBODY FUNCTIONS

1 Antibodies can also inhibit HIV by facilitating the destruction of virus-infected cells. When the arms of an antibody attach to an HIV-infected cell, immune cells called natural killer cells can then be recruited and become attached to the tip of the antibody. These cells then kill the HIV-infected cell.



2 Antibodies may also inhibit the virus's ability to cross mucosal surfaces, the body's first-line defense against sexual transmission of HIV. Recently, a combination vaccine candidate was shown to reduce the risk of HIV infection by 31%. The antibodies induced by this candidate could not neutralize HIV, but may have worked in one of these other ways.



GRAPHIC: JENNY WANG, JARED TRAVNICEK

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