

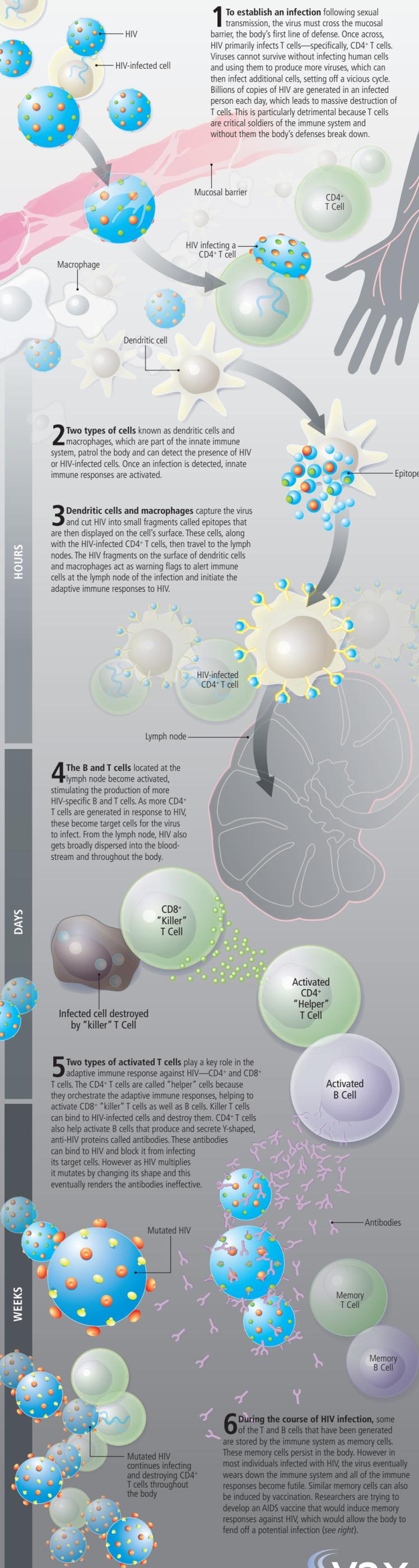
Understanding the Immune System and AIDS Vaccine Strategies

HUMANS ARE REPEATEDLY EXPOSED to various disease-causing organisms known as pathogens, including viruses and bacteria, which pose a threat to their health. The body defends itself against these foreign invaders using an incredibly complex network of cells, molecules, tissues, and organs, which together make up the immune system.

There are two categories of defenses the immune system uses to combat pathogens: innate and adaptive. The innate immune responses are the first responders against an invading virus, acting within hours. These responses are not specific, so whether the pathogen is a cold virus or HIV, the response will be very similar. Innate immune responses don't always clear an infection. Instead they help control the virus until the adaptive immune responses are ready to kick in. The adaptive immune responses take days to weeks to activate, partly because they are produced in response to a specific pathogen. Adaptive responses are further divided into two types: cellular and antibody responses.

The adaptive immune responses are orchestrated by two main classes of cells: B cells, which produce antibodies, and T cells, which conduct cellular immune responses. B and T cells are generated in the bone marrow and thymus (shown in red) and from there migrate throughout the body. They mature in the lymph nodes, spleen, and the mucosal tissues that line the intestine, nasal, respiratory, and genital tracts. B and T cells travel between tissues and organs using a network of vessels known as the lymphatic system. Lymph nodes occur where lymphatic vessels converge and are the communication hubs where different cells of the immune system meet and greet.

HOW HIV INTERACTS WITH THE IMMUNE SYSTEM



1 To establish an infection following sexual transmission, the virus must cross the mucosal barrier, the body's first line of defense. Once across, HIV primarily infects T cells—specifically, CD4+ T cells. Viruses cannot survive without infecting human cells and using them to produce more viruses, which can then infect additional cells, setting off a vicious cycle. Billions of copies of HIV are generated in an infected person each day, which leads to massive destruction of T cells. This is particularly detrimental because T cells are critical soldiers of the immune system and without them the body's defenses break down.

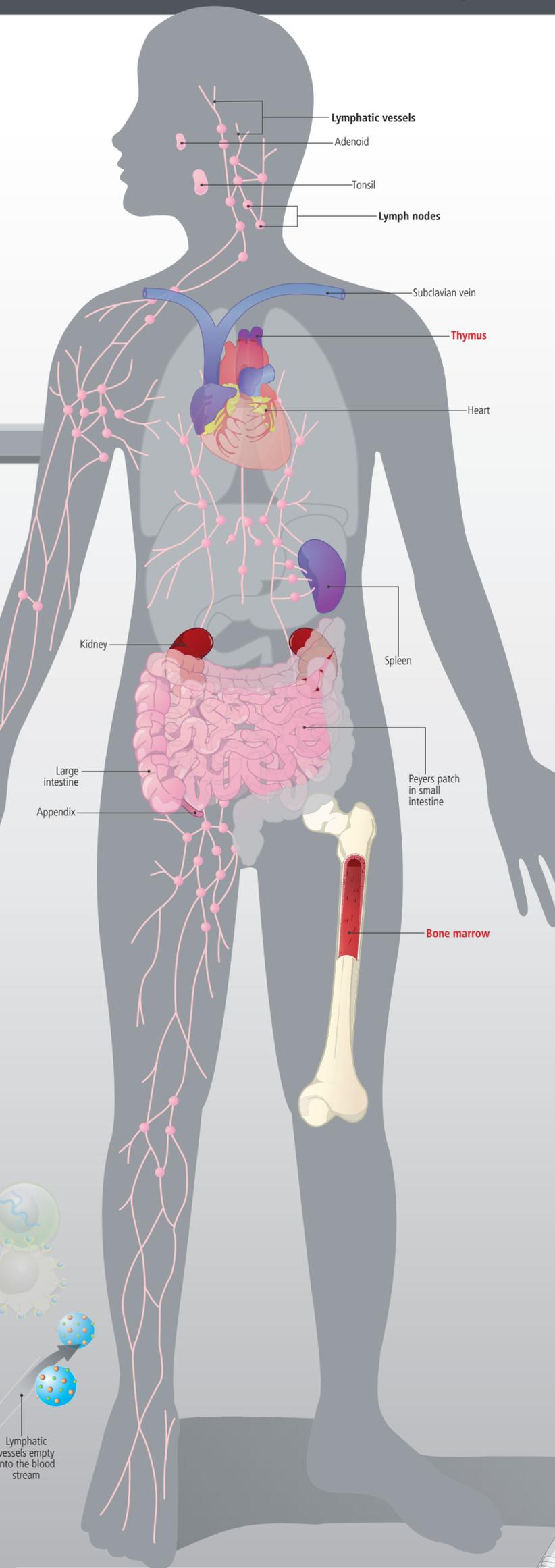
2 Two types of cells known as dendritic cells and macrophages, which are part of the innate immune system, patrol the body and can detect the presence of HIV or HIV-infected cells. Once an infection is detected, innate immune responses are activated.

3 Dendritic cells and macrophages capture the virus and cut HIV into small fragments called epitopes that are then displayed on the cell's surface. These cells, along with the HIV-infected CD4+ T cells, then travel to the lymph nodes. The HIV fragments on the surface of dendritic cells and macrophages act as warning flags to alert immune cells at the lymph node of the infection and initiate the adaptive immune responses to HIV.

4 The B and T cells located at the lymph node become activated, stimulating the production of more HIV-specific B and T cells. As more CD4+ T cells are generated in response to HIV, these become target cells for the virus to infect. From the lymph node, HIV also gets broadly dispersed into the bloodstream and throughout the body.

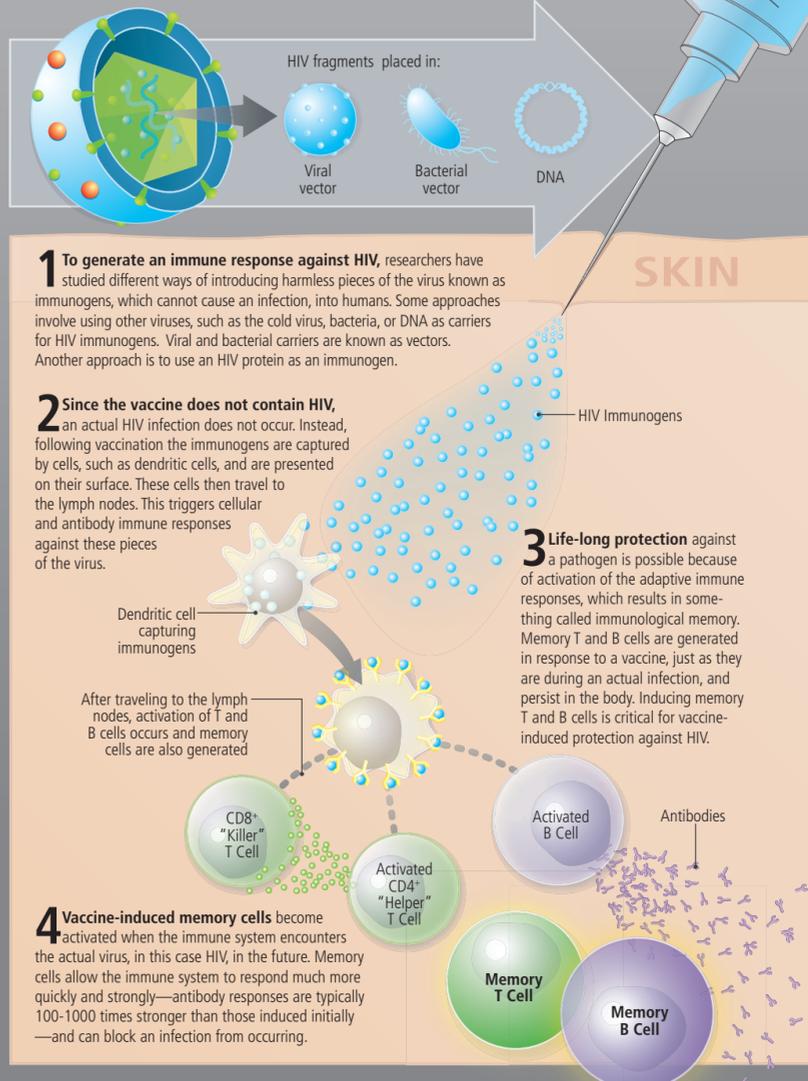
5 Two types of activated T cells play a key role in the adaptive immune response against HIV—CD4+ and CD8+ T cells. The CD4+ T cells are called "helper" cells because they orchestrate the adaptive immune responses, helping to activate CD8+ "killer" T cells as well as B cells. Killer T cells can bind to HIV-infected cells and destroy them. CD4+ T cells also help activate B cells that produce and secrete Y-shaped, anti-HIV proteins called antibodies. These antibodies can bind to HIV and block it from infecting its target cells. However as HIV multiplies it mutates by changing its shape and this eventually renders the antibodies ineffective.

6 During the course of HIV infection, some of the T and B cells that have been generated are stored by the immune system as memory cells. These memory cells persist in the body. However in most individuals infected with HIV, the virus eventually wears down the immune system and all of the immune responses become futile. Similar memory cells can also be induced by vaccination. Researchers are trying to develop an AIDS vaccine that would induce memory responses against HIV, which would allow the body to fend off a potential infection (see right).



CURRENT STRATEGIES IN AIDS VACCINE RESEARCH

Vaccines are a highly effective way to train the immune system to combat pathogens. Scientists only began studying the immune system after the concept of vaccination was discovered. Researchers are currently exploring multiple strategies in an effort to develop an effective AIDS vaccine.



1 To generate an immune response against HIV, researchers have studied different ways of introducing harmless pieces of the virus known as immunogens, which cannot cause an infection, into humans. Some approaches involve using other viruses, such as the cold virus, bacteria, or DNA as carriers for HIV immunogens. Viral and bacterial carriers are known as vectors. Another approach is to use an HIV protein as an immunogen.

2 Since the vaccine does not contain HIV, an actual HIV infection does not occur. Instead, following vaccination the immunogens are captured by cells, such as dendritic cells, and are presented on their surface. These cells then travel to the lymph nodes. This triggers cellular and antibody immune responses against these pieces of the virus.

3 Life-long protection against a pathogen is possible because of activation of the adaptive immune responses, which results in something called immunological memory. Memory T and B cells are generated in response to a vaccine, just as they are during an actual infection, and persist in the body. Inducing memory T and B cells is critical for vaccine-induced protection against HIV.

4 Vaccine-induced memory cells become activated when the immune system encounters the actual virus, in this case HIV, in the future. Memory cells allow the immune system to respond much more quickly and strongly—antibody responses are typically 100-1000 times stronger than those induced initially—and can block an infection from occurring.