How the immune system works

The sophisticated communication network our cells use to rally against infection

Dr. Christos Tsoukas

The immune system is a complicated yet very adaptable protective system. It defends the body from attack by destroying microorganisms (germs) and cancer cells. It's composed of an extraordinarily variable and elaborate collection of cells and molecules that are able to work in harmony to eliminate a limitless range of foreign invaders. The system relies on an intricate and dynamic communications network between the many different kinds of immune cells.

Dr. Christos Tsoukas is an Associate Professor of Immunology at McGill University and practices at the Immune Deficiency Treatment Centre at the McGill University Health Centre, Montreal General Hospital site.

The mission: Identify and eliminate

The immune system has two major functions: recognition and response. Immune system cells recognize anything that's not a normal component of our body. The foreign substance (also called antigen) may be an infectious agent, a cancer or a transplanted organ. Once a foreign invader is recognized, the body rapidly develops an attack to eliminate or neutralize it. Immune cells remember information on the invader, and when the same microorganism re-invades, this memory response activates a very rapid and powerful immune force to eliminate it.

Lines of defense

Barriers

The body's first defense involves barriers to the entry of microorganisms. The most important are the skin and mucous membranes, such as

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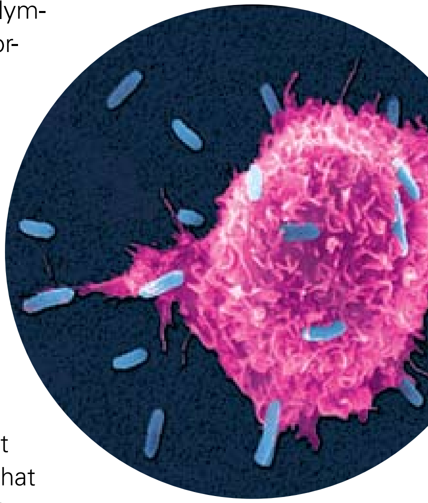
the lining of the mouth, airways, lungs, digestive and genital systems. These mechanical barriers can prevent foreign microbes from entering the body, but tissue damage, as a result of a wound or an invading microorganism, can cause a break in these barriers. As well, mucous membranes aren't as strong a barrier as skin, which is why HIV doesn't go through the skin but can go through the mucous membranes. The reason condoms are recommended to prevent transmission of HIV is to create a barrier between the virus and the mucous membranes.

Counterintelligence

In addition to barrier defenses, the body uses a more sophisticated system known as the adaptive immune system. This system has long-term memory and is responsible for self-recognition, so that it doesn't mount attacks against the body's own components. Most immune system cells are white blood cells, of which there are many types. Macrophages and neutrophils are two types that circulate in the blood and survey the body for foreign substances. When they find foreign antigens, such as bacteria, they ingest and destroy them. In the process of killing foreign invaders, they also transmit identifiable parts of the microbe to another white cell—the lymphocyte. Lymphocytes are critically important in adaptive immunity. These cells not only help destroy microbes, they also coordinate the overall immune response.



There are three major classes of lymphocytes: T cells, B cells and Natural Killer (NK) cells. The T cell has a molecule on its surface called the T cell receptor, which can receive information about the invader (antigen) from the macrophages. B cells make antibodies, which are molecules that attach to an antigen and weaken it so that other immune system cells can destroy it more easily. NK cells recognize and kill tumours and cells in the body that have been infected with viruses.

T cells: intelligence operatives

For the T cell to become activated to respond against antigens, it must come into contact with particular molecules on the surface of macrophages. Once activated, T cells evolve to become the *effector cells* and *memory cells* that are required to mount the initial campaign against infection and stave off future infections efficiently. If the T cells don't become activated, they die and are cleared by the body.

There are two different types of T cells: the CD4 or helper cell and the CD8 or suppressor cell. The CD4 cell is perhaps the most important immune cell of the body. It's the commander of all immune cells and provides help and guidance to other cells, in particular CD8 cells, in the fight against invaders. Unfortunately, the CD4 cell is also the target of HIV.

HIV's mission: Infiltrate and destroy

CD4 T cells are named for the CD4 protein molecule found on their surface, which is normally used to communicate with macrophages. This same molecule is the main receptor for HIV as it enters

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Effector cells and memory cells

Effector cells

These populations of cells have been specifically activated by an antigen during the immune response and can stimulate/focus the activity of an immune response leading to the elimination of the antigen.

Memory cells

After the human body has recovered from a disease, B cells produce memory cells that attack the disease-causing organism if it invades again. This second response is much quicker than the first, thus preventing symptoms of the disease from occurring.

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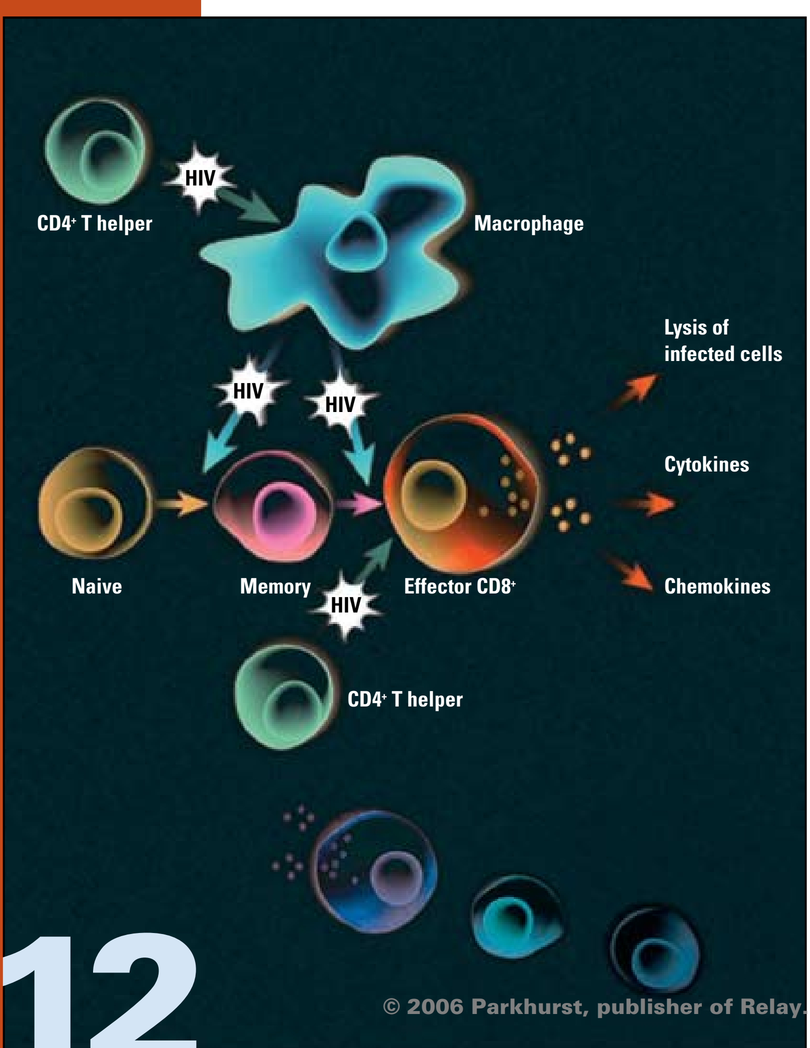
the T cell. HIV uses the CD4 cell to replicate itself, killing the cell in the process. HIV causes progressive loss of CD4 cells, which normally number between 500 and 1,500 cells per cubic millimeter (µL). When enough CD4 T cells are destroyed, communication telling other immune cells they should be fighting invaders is compromised.

After you become infected with HIV, you lose about 60 CD4 cells/µL every year. Once the CD4 count falls below 350 cells/µL, you're at risk for minor infections such as oral candidiasis (thrush) or shingles. When the CD4 count falls below 200 cells/µL, there's a more serious risk of developing potentially fatal opportunistic infections. This is why antiretroviral therapy is suggested at a count of 350 and *required* at a count of 200 cells/µL.

Tracking the losses — and gains

Usually CD4 T cell counts are measured about four times per year. The actual counts are affected by many different factors. Counts are higher in the evening and lower in the morning. Any condition that increases lymphocyte numbers (such as a common cold or other viral infections) or decreases them (chemotherapy) will be reflected in CD4 counts. On the other hand, CD8 T cell counts invariably remain high in a person with HIV and only fall to low levels in very late disease. Healthy individuals without HIV usually have 200-600 CD8 cells/µL. CD8 cells are high in HIV disease because they're required to combat HIV. The ratio of CD4 to CD8 cells may be important in tracking severity of disease and response to treatment. The ratio falls (fewer CD4 to more CD8) with disease progression and improves with effective anti HIV treatment, when CD4 cells have had a chance to regenerate and CD8 cells don't have to work so hard.



Adapted from McMichael AJ et al. Nature 2001; 410:980-987

Antiretrovirals, lifestyle and immune function

Antiretrovirals (ARVs) stop HIV from replicating and thus destroying CD4 cells. With time, individuals on ARVs gradually heal their immune systems. CD4 cell counts increase, CD8 counts decrease and many other immune measurements normalize. It may take years for these changes to occur. It's unknown if the structural damage to sites that are essential to the immune system (such as lymph nodes) is ever fully repaired.

Protecting the immune system as it heals during HIV therapy is important. There are many factors that can affect immune function that should be considered. It has long been known that alcohol suppresses the immune system. Smoking can create chronic stimulation of immune cells in the lungs. Various recreational drugs can have negative effects on the immune system. Attempts should be made to drink alcohol in moderation, quit or minimize smoking and avoid recreational drugs. Rest combined with exercise can provide a healthy environment for the immune system. Avoidance of recurrent infections such as sexually transmitted diseases can also minimize immune activation. Good nutrition can also help replenish essential vitamins and minerals that assist in the recovery process.