

Immune Responses to Viruses

Kerry Laing, Fred Hutchinson Cancer Research Centre, Seattle, USA

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Via cytotoxic cells

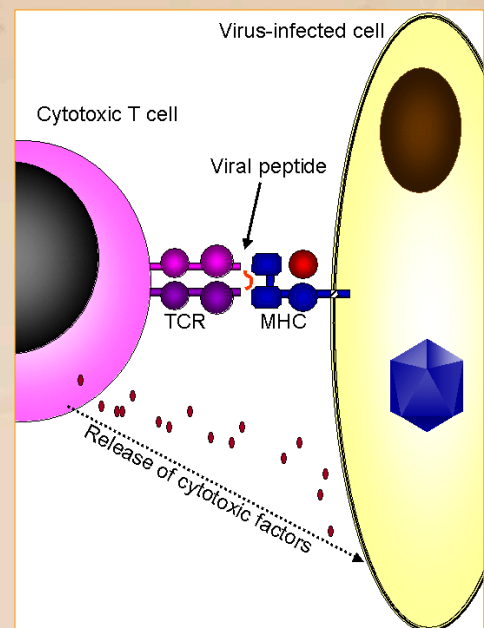
When a virus infects a person (host), it invades the cells of its host in order to survive and replicate. Once inside, the cells of the immune system cannot 'see' the virus and therefore do not know that the host cell is infected. To overcome this, cells employ a system that allows them to show other cells what is inside them – they use molecules called **class I major histocompatibility complex proteins** (or **MHC class I**, for short) to display pieces of protein from inside the cell upon the cell surface. If the cell is infected with a virus, these pieces of peptide will include fragments of proteins made by the virus.

A special cell of the immune system called a **T cell** circulates looking for infections. One type of T cell is called a **cytotoxic T cell** because it kills cells that are infected with viruses with toxic mediators. Cytotoxic T cells have specialised proteins on their surface that help them to recognise virally-infected cells. These proteins are called **T cell receptors (TCRs)**. Each cytotoxic T cell has a TCR that can specifically recognise a particular antigenic peptide bound to an MHC molecule. If the T cell receptor detects a peptide from a virus, it warns its T cell of an infection. The T cell releases **cytotoxic factors** to kill the infected cell and, therefore, prevent survival of the invading virus (**Figure 1**).

Viruses are highly adaptable, and have developed ways to avoid detection by T cells. Some viruses stop MHC molecules from getting to the cell surface to display viral peptides. If this happens, the T cell doesn't know there's a virus inside the infected cell.

However, another immune cell specialises in killing cells that have a reduced number of MHC class I molecules on their surface – this cell is a **natural killer cell** or **NK cell** for short. When the NK cell finds a cell displaying fewer than normal MHC molecules it releases toxic substances, in a similar way to cytotoxic T cells, which kill the virally-infected cell.

Cytotoxic cells are armed with preformed mediators. Cytotoxic factors are stored inside compartments called **granules**, in both cytotoxic T cells and NK cells, until contact with an infected cell triggers their release. One of these mediators is **perforin**, a protein that can make pores in cell membranes; these pores allow entry of other factors into a target cell to facilitate destruction of the cell. Enzymes called **granzymes** are also stored in, and released from, the granules. Granzymes enter target cells through the holes made by perforin.



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Once inside the target cell, they initiate a process known as programmed cell death or **apoptosis**, causing the target cell to die. Another released cytotoxic factor is **granulysin**, which directly attacks the outer membrane of the target cell, destroying it by lysis. Cytotoxic cells also newly synthesise and release other proteins, called **cytokines**, after making contact with infected cells. Cytokines include **interferon- γ** and **tumour necrosis factor- α** , and transfer a signal from the T cell to the infected, or other neighbouring cells, to enhance the killing mechanisms.

Via interferons

Virally infected cells produce and release small proteins called **interferons**, which play a role in immune protection against viruses. Interferons prevent replication of viruses, by directly interfering with their ability to replicate within an infected cell. They also act as signalling molecules that allow infected cells to warn nearby cells of a viral presence - this signal makes neighbouring cells increase the numbers of MHC class I molecules upon their surfaces, so that T cells surveying the area can identify and eliminate the viral infection as described above.

Via antibodies

Viruses can also be removed from the body by **antibodies** before they get the chance to infect a cell. Antibodies are proteins that specifically recognise invading pathogens and bind (stick) to them. This binding serves many purposes in the eradication of the virus:

- Firstly, the antibodies neutralise the virus, meaning that it is no longer capable of infecting the host cell.
- Secondly, many antibodies can work together, causing virus particles to stick together in a process called **agglutination**. Agglutinated viruses make an easier target for immune cells than single viral particles.
- A third mechanism used by antibodies to eradicate viruses, is the activation of phagocytes. A virus-bound antibody binds to receptors, called Fc receptors, on the surface of phagocytic cells and triggers a mechanism known as **phagocytosis**, by which the cell engulfs and destroys the virus.
- Finally, antibodies can also activate the complement system, which opsonises and promotes phagocytosis of viruses. Complement can also damage the envelope (phospholipid bilayer) that is present on some types of virus.

