

LESSON 9: THE BODY FIGHTS BACK

This lesson is not a complete description of the immune system. If you want to know more about how the immune system works, there are nine drawing lessons devoted to this topic in module 3 of my Mapping the Body with Art curriculum, available on my website. Here in this lesson, I will just mention a few aspects of the immune system that are aimed at viruses.

The first layer of defense is physical barriers that block viruses from entering. Skin does a great job of keeping viruses out, because the top layer of skin is made of dead cells. Viruses can only enter living cells that have receptors. Dead cells are like a brick wall to a virus. The surface layer of cells in moist places like the mouth, nose, throat, lungs, and intestines, have specialized cells that can make mucus. Viruses can get stuck in mucus and be unable to function. Mucus mostly ends up going to the stomach (as we swallow mucus that we sniff or cough up) and the acid in the stomach can kill many viruses. (Of course, some viruses like to be in the stomach, but most do not.)

If a virus gets past the physical barriers and enters cells, the next layer of defense kicks in. There are phagocytes ("eating cells") roaming around, eating every foreign object in their path. The biggest eater is called the **macrophage**. ("Macro" means "big," and "phage" means "eater.") A similar cell is the **dendritic cell**, which gets its name from its long branch-like arms. ("Dendri" means "branch.") Both of these cells engulf all particles they come across. If a virus is taken in by one of these eaters, it will not have a chance to do its usual attachment-and-entry routine, it will not be able to uncoat and replicate, and will be digested inside one of the eater cell's lysosomes. (**Lysosomes** are big endosomes filled with digestive enzymes.) These eating cells will also put some of the digested pieces onto their own type of MHC clip (MHC-2) and post them on their surface.

If the virus gets past the phagocytes, it will likely be able to enter one of the body cells. However, cells have sensing devices floating around in their cytoplasm that can detect viral RNA. (Examples include RIG-1 and MDA5.) Usually they sense double-stranded RNA, which is never made by a cell. Even if a virus doesn't have a dsRNA genome, it will produce some dsRNA as a temporary by-product of genome replication. When a sensor molecule comes into contact with the viral RNA, it will change shape (a "conformational change") and this will then cause it to be able to interact with another cellular protein. This reaction will allow another reaction, and then another, like a chain reaction, with the end result being the production of a protein message called **interferon** (IFN). There are three types of interferon: alpha, beta and gamma. They all cause the cell to produce many anti-viral proteins, but can do so in a slightly different way. (These anti-viral proteins have been discovered so recently that it is hard to find out details about them.) Interferon also acts as a message to other cells to warn them that one of their neighbors has been infected, and to call immune system cells to come to the site of infection.

MDA5 can detect uncapped RNA, which is why influenza does its "cap-snatching." The measles virus has a way to block the action of MDA5. Toll-like receptors (TLRs) are located on the outside surface of macrophages and dendritic cells. TLR-3 is the best at sensing viral RNA. When activated, TLR-3 will start that complicated chain reaction that will lead to interferon production.

If the virus gets past this defense system, and finds a body cell with a receptor it can attach to, it will enter the cell and start to replicate. But little pieces of viral protein will start appearing in the clips in the MHC-1 flags of that cell, as it constantly sends flags to the surface. A white blood cell called a Natural Killer (NK) is able to "feel" what the clips are holding. If it is not a body protein (or it is a bad body protein such as cancer), the NK cell will use **perforin** to kill the cell. Imagine a tiny gun shooting bullets that, when they land, assemble themselves into a ring. The ring builds itself on the surface of the cell, so you end up with a hole in the cell membrane. Along with the proteins for the hole, there are also proteins called **granzymes**, which are classified as toxins because they cause cell death. The granzymes go down through the hole and into the cell where they begin a chain of events that ends with the DNA being shredded to bits. With no DNA, the cell can't do anything and it slowly shrivels and disintegrates. (Macrophages then come and eat up the pieces.) When a cell dies in this way, we call it **apoptosis**. Many cells in your body are programmed to live only a short time then die. Programmed cell death is one of the ways your body stays healthy.

If the virus tries to trick the NK cell and prevent the viral-protein-carrying flags from going to the surface (like we saw with herpes) the NK cell can still detect that something is wrong. It can count the number of flags on the surface and if there are none, or very few, it will assume something is wrong and kill the cell. (A few viruses have ways to make the cell put up fake flags!)

All the defense strategies we have discussed so far are part of the body's non-specific, or "innate" system. This system reacts the same way to all pathogens. If the virus gets past the innate system, it meets the "adaptive" immune system. This system acts specifically to individual pathogens. These cells can tell influenza from coronavirus. The system involves interaction between macrophages, dendritic cells, T cells and B cells.

Macrophages and dendritic cells have flags called MHC-2. They put samples of what they have eaten into the clips on MHC-2. Helper T cells come along and "feel" these samples. Each T cell "knows" a sample pattern that does not belong to the body. If the helper T has a match to the viral protein, it will be activated. It will hopefully come across a killer T cell that has found that same pattern sticking to a cell's MHC-1 clip. The killer T "gets permission" from the helper T, and then the killer T uses perforin to kill the cell.

B cells make Y-shaped proteins called **antibodies**. Each B cell is capable of matching one particular protein shape that might be found on a pathogen. If it runs into a helper T cell that has been activated by a macrophage, and the helper T's sample matches the shape of the B cell's antibody, the B cell will be told to make thousands of its antibodies. The antibodies might match a virus's glycoproteins and stick to them, preventing the virus from attaching. Or the antibodies could stick to the capsid proteins. In both cases, macrophages will eat anything with antibodies stick to it, so they gobble up viruses with antibodies.