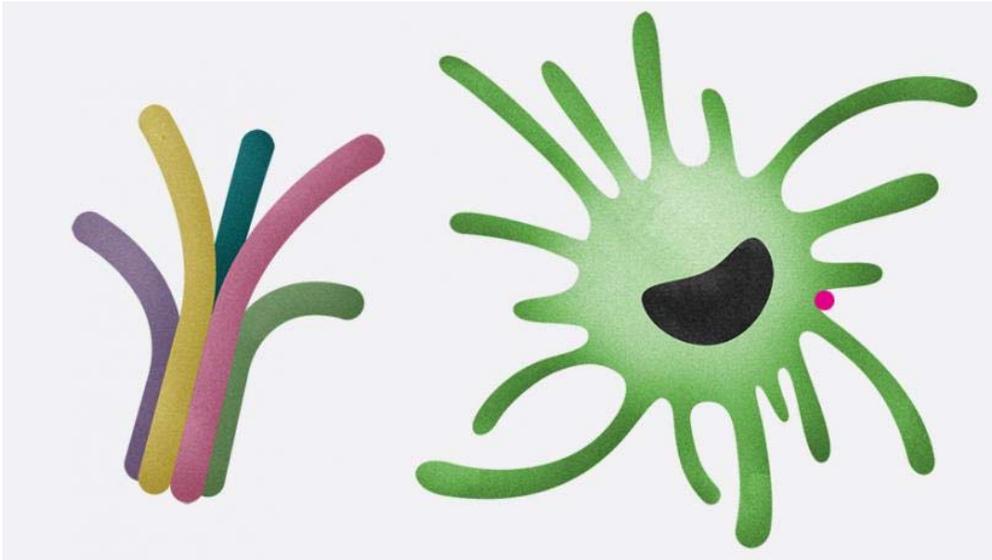


Immune responses



Complement and dendritic cell. Bret Syfert, 'Big Picture' CC BY

The innate immune system

Once barriers like the skin and mucosal membranes are breached, the immune system's second line of defence against invading pathogens is its non-specific (innate) response.

This response is rapid, short-lived and generic, and it lacks any memory of previous infections. Through pattern recognition receptors, cells involved in the innate response can recognise pathogens like bacteria and viruses but can't distinguish between, say, the viruses that cause measles and flu. Important components of innate immunity are described below.

Natural killer cells

True to their name, natural killer (NK) cells' natural inclination is to kill everything they meet. What stops them is the recognition of self markers – major histocompatibility complex (MHC) proteins – on the surface of the cells they make contact with. Virus-infected cells and cancer cells have fewer of these markers and so are more likely than healthy self cells to be killed. NK cells release chemicals called cytokines, which alert and attract other immune cells.

Phagocytes

Cells that engulf – or phagocytose – microbes or other cells that are infected, damaged or dying. Most cells are capable of phagocytosis, but the immune system employs specialist phagocytes like macrophages and neutrophils to deal with foreign matter. They begin by wrapping themselves around the offender, enclosing it in a vesicle called a phagosome before breaking down the contents with hydrolytic enzymes. The remains are presented (so-called antigen presentation) to other specialised immune cells that initiate a more targeted immune response.

Inflammation

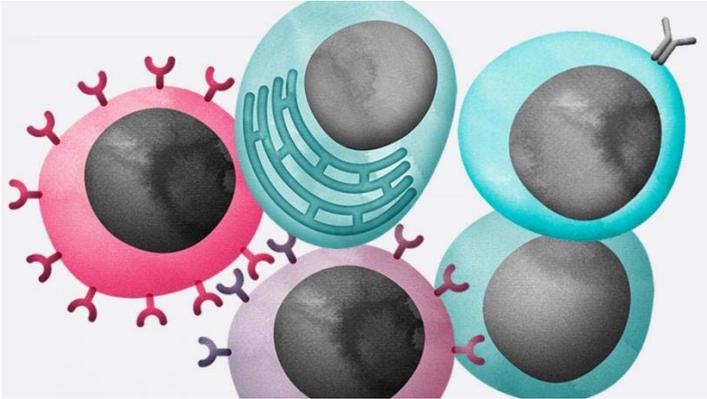
When the receptors of cells involved in the non-specific immune system are engaged by pathogens, the cells release molecules that trigger inflammation. Increased blood flow brings in more cells to deal with the problem, and also leads to swelling and pain, which alert you to the fact that something is wrong. Greater

blood flow also causes an increase in temperature, which can inhibit the replication of some bacteria and viruses.

Complement

A set of around 30 proteins in the blood plasma that can be activated by the presence of microbes or antibody–antigen complexes. Complement (see drawing, above left) can destroy pathogens and activate phagocytic cells.

B cells and T cells give us an immunological memory



B cells and T cells, Bret Syfert, 'Big Picture' CC BY

In mammals, the specific (adaptive) immune system provides long-lasting protection against specific microbes or substances. It maintains a 'memory' of all the previous infections it has fought.

B cells, which are made in the bone marrow, produce antibodies. These proteins attach to very specific non-self markers, or antigens, of pathogens. T cells, which are made in the bone marrow but then mature in the thymus gland, express cell-surface receptors that fit the antigens on pathogens.

Cells specific to lots of different diseases patrol our bodies all the time. When they come across something that they recognise as a potential threat, they work to eliminate it. The B-cell response involving antibodies is often referred to as the humoral immune response, whereas T cells are associated with the cell-mediated immune response.

However, immune responses generally require a coordinated attack involving components of both the humoral and cell-mediated responses, and the specific and non-specific branches.

Antigen recognition is a key part of the immune response

Antigens are non-self markers that alert cells of the specific (adaptive) immune system to the presence of potential danger. You can remember what antigens do by considering them as antibody generators. Antigens may pose no threat on their own – they are just components, such as proteins, of bacteria or viruses that are recognised by our immune cells.

In the case of the influenza virus, however, the H (haemagglutinin) and N (neuraminidase) protein antigens are actually key to the replication cycle of the virus. Viruses use H to bind to host cells and N to detach themselves as they leave.

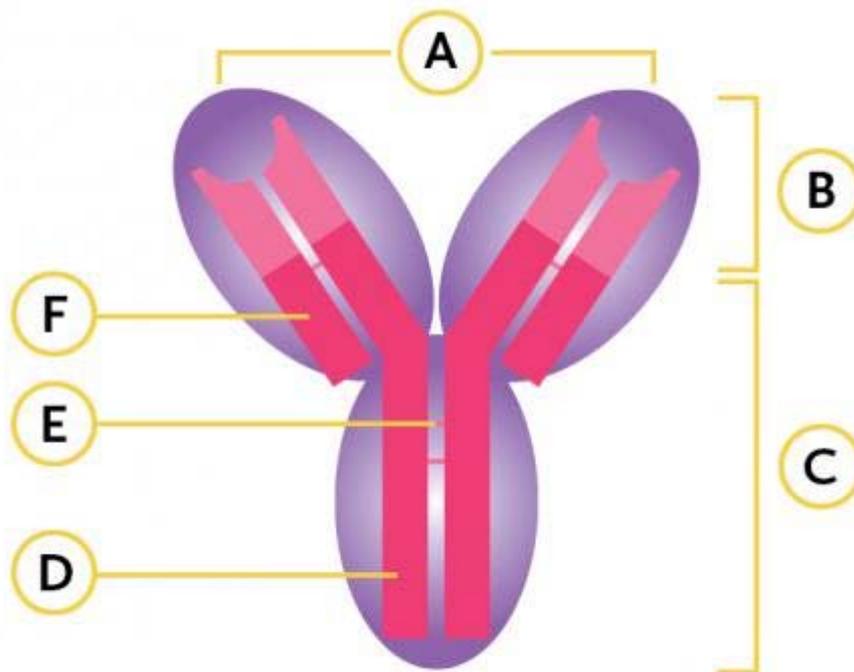
One important way in which the specific and non-specific branches of the immune system cooperate is in the processing and recognition of antigens. Some phagocytes like macrophages can act as antigen-presenting cells, although there are numerous other cells that do this job, including some B cells.

The presenting cells break up foreign substances and then display antigens from them for other immune cells to recognise. The antigens are presented bound to MHC proteins, the same molecules that are used to discriminate between self and non-self.

When they encounter MHC–antigen complexes, immune cells issue a string of immunological orders. Some T cells will send out chemical signals called cytokines, which activate both B cells and other types of T cells.

Antibodies are specialised proteins that bind to antigens

Proteins are considered the workhorses of cells, and antibody proteins play no less of a central role in the body's defence against disease. Antibodies, made by plasma B cells, are Y-shaped globular proteins called immunoglobulins (Ig).



CC BY Big Picture: Immune System'

Annotated diagram of an antibody:

A. Antigen binding sites

B. Variable region

C. Constant region

D. Heavy chain

E. Disulphide bridge

F. Light chain

Each type of antibody binds to a specific antigen. The ability to recognise a specific antigen comes from the diversity within the antibody structure. As for all proteins, antibody structure is determined by the sequence of different amino acids in the protein chain (the primary structure) and how it folds to form a 3D molecule (the tertiary structure).

There are different broad classes of immunoglobulin:

- IgA
- IgD
- IgE
- IgG
- IgM

The classes are defined by the amino acid sequence in the 'stalk', or constant region, of the Y structure. IgA, for instance, is important at the sticky mucosal surfaces where many pathogens try to enter, like in the intestines. IgE in the blood binds to allergens and parasitic worms. And as well as differences in the stalk, there are differences in the amino acid sequences making up the 'arms', or variable regions, of the Y, which bind to antigens. These differences determine which pathogen an antibody is for.

Being able to recognise danger is one thing, but what does the antibody do about it? Lots, actually. Some, like IgA, can neutralise pathogens just by binding to them. Others act as labels for phagocytes, which recognise the stalks of antibodies stuck to the outer surfaces of invading pathogens and proceed to destroy them. Antibodies also trigger components of the non-specific (innate) immune system, including the complement system

We can exploit the ability of antibodies to bind to a specific antigen

Monoclonal antibodies (mAbs) are sets of identical antibodies that come from genetically identical immune cells and all bind to the same substance. Drug developers use them to create drugs capable of targeting specific types of cells.

The breast cancer drug Herceptin (trastuzumab) is a monoclonal antibody that specifically targets breast cancer cells by binding to a protein called HER₂ on the surface of the cells. The HER₂ protein drives the growth of cancer cells and Herceptin blocks that growth.

Antibodies (see annotated image) can also be used in test kits. The pregnancy test, for example, uses an antibody to bind and detect in blood or urine a hormone called human chorionic gonadotropin, which is produced in early pregnancy.

If you have been infected by a particular virus, say, you will have antibodies against it in your body, so monoclonal antibodies are also useful in diagnostic tests. One of the most common methods of detecting HIV uses an antibody-based test called an ELISA – an enzyme-linked immunosorbent assay. It is more accurate a few weeks after initial infection, because it takes a while for the body to build up antibodies against the virus. So early tests are often repeated or alternative methods are used to confirm the diagnosis.