Molecular and genetic basis of immunity.

Major histocompatibility complex. Humoral and cellular immunity. Antibodies. Cytokines, interferons and the complement system.

1. Describe the main histocompatibility complex and its role in human immunity.
2. Explain what humoral and cellular immunity is.
3. Classify and characterize proteins involved in humoral and cellular immunity.
4. Describe congenital and acquired disorders of human immunity.

Every multicellular organism, including our own, constantly has to be on guard not to be gobbled up by others, as it constitutes a potential source of valuable organic molecules. The ability to resist being used as "food" automatically confers a selective advantage. Over the course of evolution, this has led to the development of highly sophisticated defense systems in multicellular organisms.

To maintain the integrity of our organism, it is essential to distinguish between biological structures that have to be fought off –ideally, everything that poses a danger to our organism— and structures that must not be attacked, e.g., the cells of our own body, or useful bacteria in our gut. This problem is not at all trivial, as dangerous attackers from the worlds of viruses, bacteria and parasites consist of largely the same molecules as the human body.

Immunity can be defined as a complex biological system endowed with the capacity to recognize and tolerate whatever belongs to the self, and to recognize and reject what is foreign (non-self).

Antigen, substance that is capable of stimulating an immune response, specifically activating lymphocytes, which are the body's infection-fighting white blood cells. In general, two main divisions of antigens are recognized: foreign antigens (or heteroantigens) and autoantigens (or self-antigens). Foreign antigens originate from outside the body. Examples include parts of or substances produced by viruses or microorganisms (such as bacteria and protozoa), as well as substances in snake venom, certain proteins in foods, and components of serum and red blood cells from other individuals. Autoantigens, on the other hand, originate within the body. Normally, the body is able to distinguish self from nonself, but in persons with autoimmune disorders, normal bodily substances provoke an immune response, leading to the generation of autoantibodies. An antigen that induces an immune response—i.e., stimulates the lymphocytes to produce antibody or to attack the antigen directly—is called an immunogen. On the surface of antigens are regions, called antigenic determinants, that fit and bind to receptor molecules of complementary structure on the surface of the lymphocytes. The binding of the lymphocytes' receptors to the antigens' surface molecules stimulates the lymphocytes to multiply and to initiate an immune response—including the production of antibody, the activation of cytotoxic cells, or both—against the antigen. The amount of antibody formed in response to stimulation depends on the kind and amount of antigen involved, the route of entry to the body, and individual characteristics of the host.

Molecular and cellular components make up the immune system. The function of these components is divided up into nonspecific mechanisms, those which are **innate** to an organism, and responsive responses, which are **adaptive** to specific pathogens. These two systems work closely together and take on different tasks.

The innate immune system is the phylogenically oldest component of the human immune system.

The innate immune system is the body's first line of defense against germs entering the body. It responds in the same way to all germs and foreign substances, which is why it is sometimes referred to as the "nonspecific" immune system. It acts very quickly. The innate immune system has only limited power to stop germs from spreading, though. The innate immune system is always general, or *nonspecific*, meaning anything that is identified as foreign or *non-self* is a target for the innate immune response.

The innate immune system consists of

- Protection offered by the skin and mucous membranes
- Protection offered by the immune system cells (defense cells) and proteins

Defects in innate immunity are associated with invasive, life-threatening infection. Inappropriate activation of the innate immune system can lead to autoinflammatory states. The innate immune system directs the subsequent development of adaptive immune responses

The adaptive immune system, also called *acquired immunity*, uses specific antigens to strategically mount an immune response. Unlike the innate immune system, which attacks only based on the identification of general threats, the adaptive immunity is activated by exposure to pathogens, and uses an immunological memory to learn about the threat and enhance the immune response accordingly. The adaptive immune response is much slower to respond to threats and infections than the innate immune response, which is primed and ready to fight at all times.

The adaptive immune system is made up of:

- T lymphocytes in the tissue between the body's cells
- B lymphocytes, also found in the tissue between the body's cells
- Antibodies in the blood and other bodily fluids

The major proteins of the immune system are predominantly signaling proteins (often called cytokines), antibodies, and complement proteins.

The cells of the immune system are represented by a variety of cell populations of lymphocytes, macrophages, microphages and platelets. The total weight of immune cells in an adult is about 1 kg.

The cells of the immune system can be categorized as lymphocytes (T-cells, B-cells and NK cells), neutrophils, and monocytes/macrophages. These are all types of white blood cells.

Characteristics of immune system

There are 4 main properties of immunity: existence of
1- cell immunity
2-humoral immunity
3-passive immunity
4 –ability to individual “education” of immune system

Immune system disorders

The immune system is a complex and highly developed system, yet its mission is simple: to seek and kill invaders

The immune system protects against infectious disease, but it may also at times cause disease. Disorders of the immune system fall into two broad categories: (1) those that arise when some aspect of the host’s immune mechanism fails to prevent infection (immune deficiencies) . Immune deficiencies could be primary and acquired

(2) those that occur when the immune response is directed at an inappropriate antigen, such as a noninfectious agent in an allergic reaction, the body’s own antigens in an autoimmune response, or the cells of a transplanted organ in graft rejection.

Literature:

1. Alberts et al, pp. 1297-1342.
2. Lodish et al, pp. 1079-1134.