I.1. Role of Immunity

I.1.1. Some Definitions

Immunology is the study of the immune system and the body's defense mechanisms against external agents (infectious, toxic, tumorous) or foreign bodies (grafts, cells from another individual).

Immunity refers to the defense mechanisms of a living organism against foreign agents, particularly infectious ones, or internal threats, such as tumor transformation, that may jeopardize its proper functioning or survival.

Immunity, therefore, is the set of biological mechanisms that allow an organism to recognize and tolerate what belongs to itself (self) and to recognize and reject what is foreign (non-self).

The collection of organs, tissues, cells, and molecules that work together to resist infections is called the **immune system**.

The **immune response** is the activation of the immune system's mechanisms in response to the recognition of "non-self." Two types of responses come into play:

A) Innate (or Natural) Immune Response:

- This is an immediate response, corresponding to a constitutive, non-adaptive action.
- It relies on a broad distinction between self and non-self.
- The innate immune response is the first line of defense against infectious and pathogenic agents in our environment.
- It is immediate and functional for 3 to 5 days.
- It involves various defense mechanisms:
    - **Constitutive mechanisms**, such as the skin-mucous barrier.
    - **Induced mechanisms**, such as phagocytosis and the inflammatory response, which involve phagocytic cells and cytokines.

B) Adaptive (or Specific or Acquired) Immune Response:

- This response emerged approximately 500 million years ago in the first vertebrates.
- It is specific to the antigen because the cells of adaptive immunity, lymphocytes, carry a single type of receptor capable of recognizing an antigenic determinant (also called an epitope).
- The adaptive response is limited in time to the eradication of the aggressor, and it retains memory of it.
- Its recognition of self is limited, particularly because during their production in primary lymphoid organs, most adaptive immune cells that recognize self-antigens are eliminated.

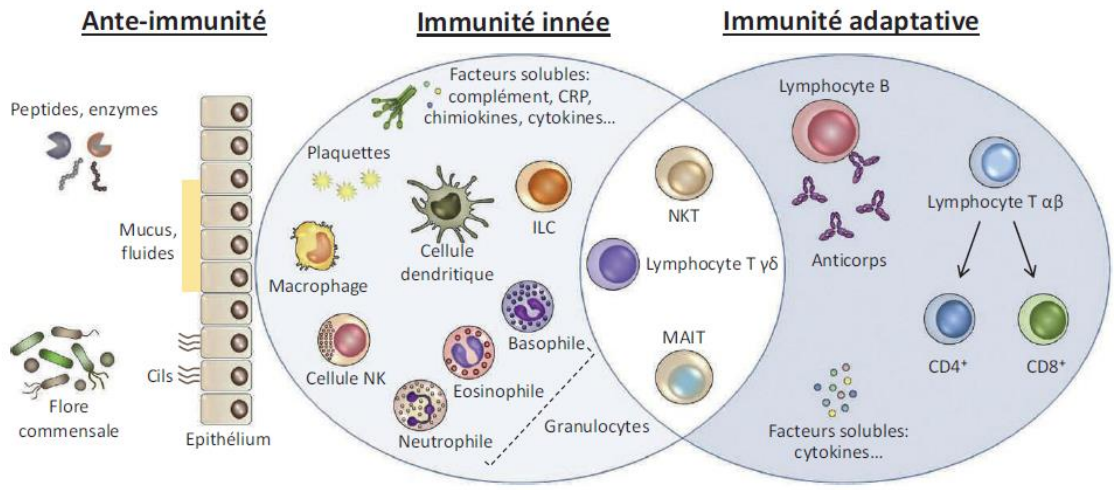

Fig 1: The immune response

The immune response is triggered because the immune system receives "danger" signals, and certain cells are capable of recognizing, through a set of receptors (**Pathogen Recognition Receptors** or **PRRs**), molecular patterns associated with pathogens (**Microbe-Associated Molecular Patterns** or **MAMPs**) or danger signals (**Danger-Associated Molecular Patterns** or **DAMPs**). Meanwhile, other cells of the adaptive immune system recognize, through a receptor specific to each cell, molecules or antigens identified as foreign to our organism, referred to as non-self-antigens.

I.1.2. Antigens

An **antigen** is a natural or synthetic macromolecule that, when recognized by antibodies or cells of the immune system, is capable of triggering a specific immune response. Antigens are generally proteins, polysaccharides, and their lipid derivatives. The lymphocyte receptor is called a **paratope**, and the antigenic determinant is called an **epitope** (a single antigen can have multiple epitopes, which may be identical or different).

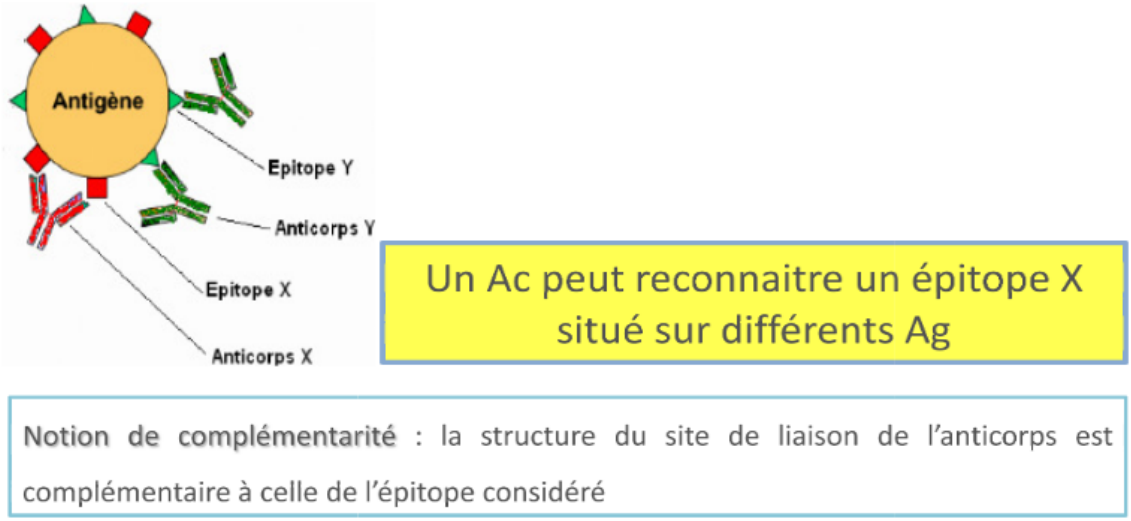

Fig 2: antigen

I.1.2.1. Different Types of Antigens

- **Xenoantigen**: An antigen foreign to the species.
- **Alloantigen**: A molecule that varies among individuals of the same species (e.g., the ABO system).
- **Neoantigen**: An antigen not normally expressed in the organism (e.g., tumor-induced antigens).
- **Autoantigen**: A self-antigen that is normally not recognized by the immune system.
- **Hapten**: A low molecular weight substance (usually a polysaccharide) whose structure varies with each antigen and determines its specificity. It reacts with the corresponding antibody but cannot alone provoke the formation of an immune complex. This formation occurs only after the hapten is associated with a protein or polysaccharide carrier, such as Hemocyanin or Bovine Albumin. This association is essential to confer antigenic properties to the hapten.

I.2. Connection to Daily Life and Major Discoveries

In the 20th century, immunology experienced tremendous progress, contributing significantly to the development of modern medicine. This was made possible by discoveries made during this period, some of which include:

1. **Discovery of the ABO Blood Groups by Karl Landsteiner (1901)**: The importance of this discovery lies in the following:

- It became possible to perform blood transfusions by selecting blood that would not be destroyed by the recipient's immune system (destruction of red blood cells by antibodies). This eliminated major risks of incompatibility.
- It introduced the concept of genetics in a part of the immune system.

2. **Discovery of Anaphylaxis by Charles Richet and Paul Portier (1902)**: Anaphylaxis illustrates the harmful, even fatal, effects of the immune system. It is a rapid and severe allergic reaction of the immune system following the reintroduction of an allergen.
3. **Discovery of Human MHC (HLA) by Jean Dausset (1958)**: This is a code present on the surface of our cells, unique to each individual, defining our immunological identity.
4. **First Allograft Transplantation of a Kidney by Joseph Murray (1959)**: This achievement, along with the study of artificial immunosuppression, enabled patients to tolerate their grafts.
5. **Emergence of the Concept of Immune Response Polarization by Goffman RL and Mosmann TR (1986)**: This concept relates to the role of CD4+ T cells: Th1 stimulates the cellular response, while Th2 stimulates the humoral response.
6. **Discovery of Natural Regulatory CD4+ T Cells by Shimon Sakaguchi (1995)**: These cells significantly contribute to maintaining self-tolerance by controlling the autoreactivity of T cells.
7. **Discovery of Genetic Mechanisms Allowing the Body to Produce Antibodies Against Billions of Different Molecules or Antigens by Susumu Tonegawa (Nobel Prize in 1987)**: These mechanisms enable the production of billions of antibody proteins using only a few tens of thousands of genes (random rearrangement of gene segments or recombination).
8. **Discovery of Microbial "Receptors" on Our Cells and the Importance of Dendritic Cells**: Dendritic cells have a unique ability to activate and regulate immunity. These discoveries stem from the research work of Ralph Steinman, Bruce Beutler, and Jules Hoffmann, who were awarded the Nobel Prize in Medicine in 2011.

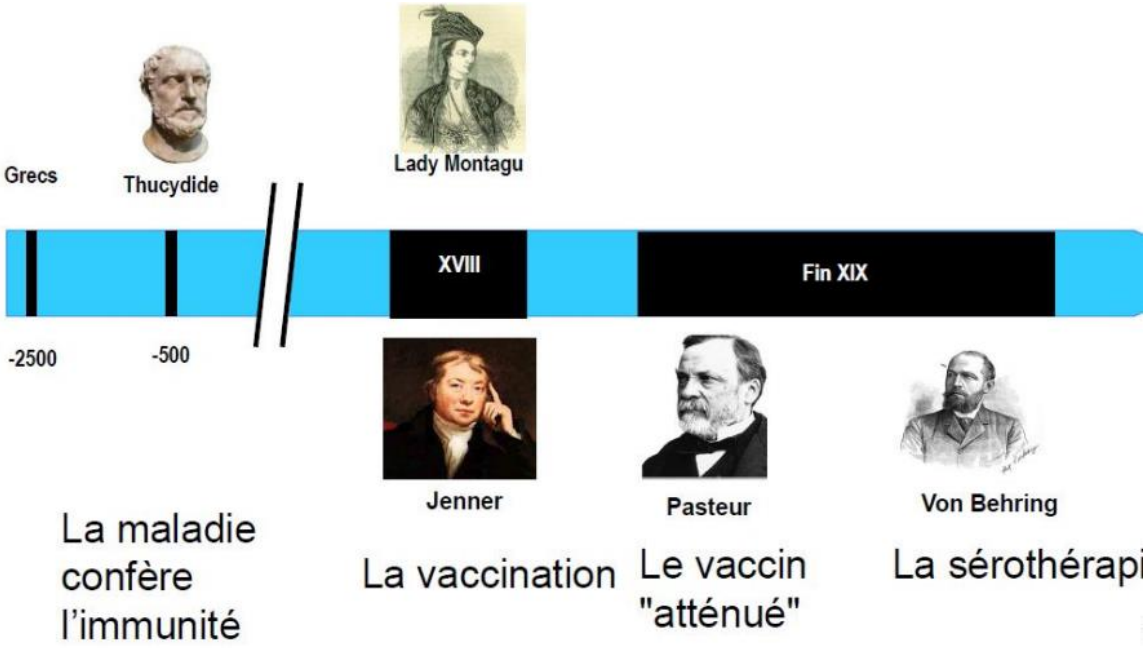

Fig 3: Some contributors in Immunology