Immunology and the Immune System

See online here

The knowledge of fundamental immunological functions are essential for every physician, no matter if an exam in physiology or immunology lies ahead or not. We summarised relevant facts for you that you should bear in mind beyond your study for exams.

Immune System

The human immune system combines cell-mediated and humoral components that interact in various ways to protect body cells from pathogens. The immune system is subdivided into a nonspecific innate immune system.

Innate immune system

- The **nonspecific (innate) immune system** includes undirected and immediate defense mechanisms that follow a pathogenic invasion. This involves the elimination of pathogens (bacteria) by **phagocytes** and natural killer cells (focusing on viruses and intracellular pathogens), the induction of a **local and systemic inflammation (complement system, cytokines)**, including the attraction (**chemotaxis**) of nonspecific and specific immune cells

to the focus of inflammation, the **opsonization** of pathogens for nonspecific and specific immune cells (complement system), and the activation of a specific immune response.

Adaptive immune system

- The **specific (adaptive) immune** system is responsible for the late and targeted immune response during symptomatic/asymptomatic infections. Unlike the innate immune system, the adaptive immune system is **highly specific for particular pathogens**. Moreover, it is able to **create immunological memory** and to distinguish between endogenous and foreign pathogens.

The adaptive immune system consists of **B and T lymphocytes** and **immunoglobulins** that are secreted by activated B cells (plasma cells).

	Innate immunity	**Adaptive immunity**
Cell-mediated	Phagocytes: macrophages, neutrophil granulocytes, NK cells	T lymphocytes (CD4+, CD8+) B lymphocytes
Humoral	Complement system, cytokines	Plasma cells respectively antibodies

Secondary Lymphoid Organs: Lymph Nodes and Lymphoid Follicles

Antigens arrive in the lymph nodes (filtration stations) with the circulating lymph in the course of an infection. There they are presented to **naïve lymphocytes** that circulate between the bloodstream and lymphoid organs. If their surface receptors fit the particular antigen, they **are activated** by the influence of various stimuli (see below), **proliferating** and **differentiating** into **effector cells**.

If certain antigens invade through the mucosa, they are withheld in the mucosa-associated lymphoid tissue (lymphoid follicles, Peyer's patches) and presented to the lymphocytes there.

T Lymphocytes

Antigen presentation to T cells by dendritic cells

For naïve T lymphocytes to be activated, they need to be presented an antigen by specialized **antigen-presenting cells**. This occurs within the secondary lymphoid organs (lymph nodes, Payer's patches, tonsils, and others); **dendritic cells** present epitopes of an antigen to the naïve T cells using special surface proteins called **major histocompatibility complex (MHC) proteins**.

As soon as the T cell recognizes a matching antigen with the help of its antigen-specific **T cell receptor**, binding between the T cell receptor and antigen-presenting MHC protein is induced.

For the T cell activation process to be completed, a second signal is required from dendritic cells. This second signal is given by the B7 protein expressed on the surface of dendritic cells. The B7 protein binds to the CD28 receptor on the T cell. This completes

the activation of the naïve T cell to an effector T cell. The reason for the second signal is to confirm that the antigen epitope presented is a foreign antigen and not from the human body. This prevents the development of autoimmunity.

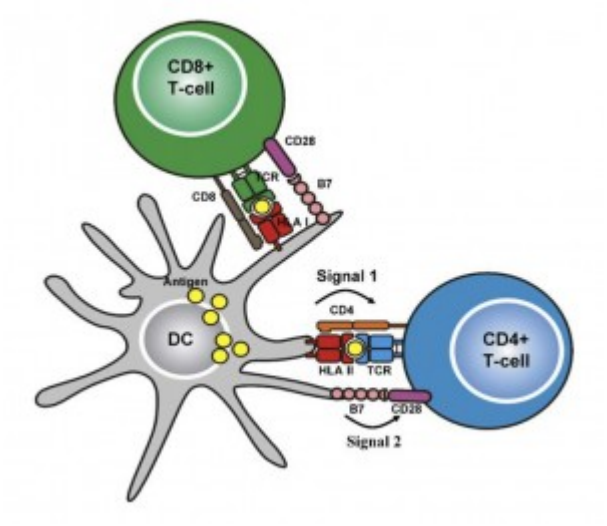


Image: T lymphocytes

As mentioned above, upon activation, the naïve T cell becomes an effector T cell. Naïve T cells carry either the CD4 or CD8 receptor on their surface. The activation of these 2 types of naïve T cells has a different response as described below.

- **CD4+ T cells (T helper cells)** mature to Th1 cells or Th2 cells. **Th1 cells** release cytokines in order to activate macrophages (IFNy, IL2), whose mission is to **modulate local inflammatory processes**. **Th2** cells express another cytokine pattern. They are necessary for the **activation of B lymphocytes** to plasma cells and play an essential role in antibody class switching (**isotype switching**) during the later humoral immune reaction (see below).
- **CD8+ cells** differentiate into **cytotoxic T cells** which are equipped with various lytic enzymes. Their function is to destroy cells that are infected with **intracellular pathogens (viruses)**.

MHC Proteins

Just like the existence of 2 different T cell populations with particular functions, there are 2 classes of MHC proteins for different types of antigen presentation:

- **MHC I proteins** occur on the surface of **all nucleated cells** and present proteasomal degraded proteins that are synthesized by the antigen-presenting cell itself (**endogenous peptide**). This includes cell-specific antigens—**viral antigens** that emerge there due to viral replication. MHC 1 proteins interact with **CD8+ T cells** that differentiate into cytotoxic effector cells **(cytotoxic T cells)** when activated.
- **MHC II proteins** occur only on few cells—**dendritic cells, B cells, and macrophages (so-called professional antigen-presenting cells)**. They present various antigens, particularly those of bacterial pathogens that were previously internalized via phagocytosis and interact with naïve **CD4+ T lymphocytes**, which then mature into CD4-positive helper cells.

Note: MHC I proteins present antigens of intracellular pathogens to cytotoxic T cells (→

Destruction of the infected cell). MHC II proteins present antigens of extracellular pathogens to CD4+ cells (→ B cell activation into plasma cells).

B Cells

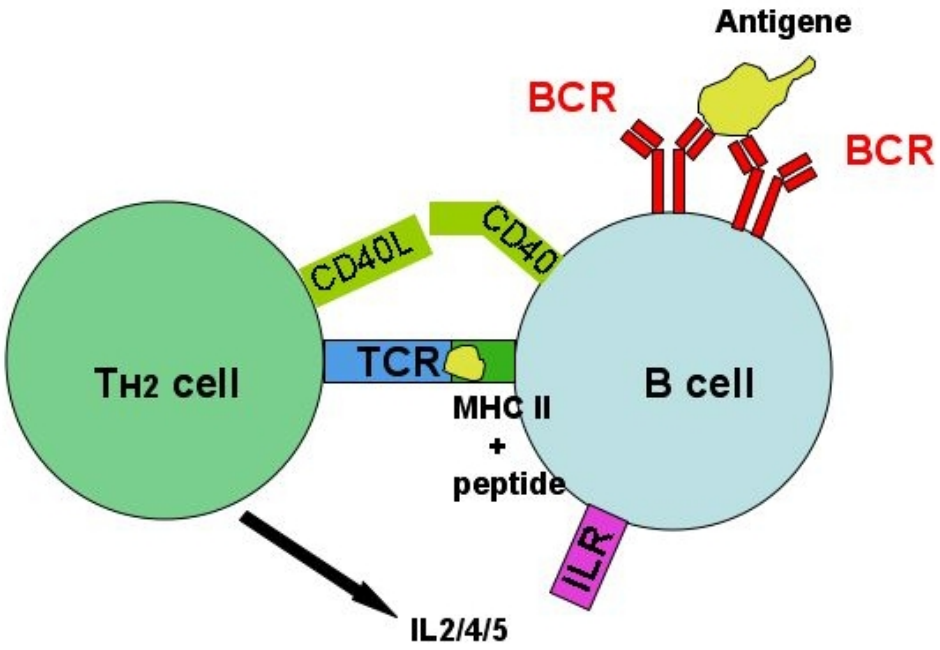
For the activation of naïve B cells, it is not always necessary to have antigens presented by MHC molecules. For the detection of antigens, B cells use **IgM or IgD molecules on their membrane surface (B cell receptor)**, which are able to detect and bind soluble antigens in the blood or lymphoid tissue.

The subsequent activation (clonal expansion) and differentiation into immunoglobulin-secreting plasma cells take place inside the lymphoid tissue:

- **T cell-dependent activation of B cells:** After an antigen that has bound to the B-cell receptor is taken up into the cell, the antigen gets degraded in the lysosome and is prepared for presentation with **MHC II surface proteins**. These proteins interact with the T cell receptor of antigen-specific **CD4+ cells.** The T helper cells thus promote, with the help of further costimulating signals (e.g. the interaction between the CD40 molecule of the B cell and the CD40 ligand of the T cell), the proliferation and differentiation of B cells into plasma cells. This initial activation takes place in the **T cell zone (primary focus)** of lymphoid organs and results in **short-lived plasma cells secreting IgM**. Later on, the B cells migrate from the primary focus to the B cell zones (follicle), where so-called **germinal centers** are built. In these germinal centers, B cells develop a higher antigen affinity by means of complex cell-cell interactions, the cells undergo a change of their antibody pattern (**isotype switching**), and immunological memory cells are built. These newly emerged plasma cells are long-lived and show a modified spectrum of antibodies (IgG, IgE, IgA).

Note: The early humoral immune reaction is classified by the synthesis of IgM, which is replaced by IgG in a later phase of infection.

- **T cell-independent activation of B cells:** Various antigens—for example, **capsular polysaccharides** of some bacteria—can cause a crosslinking of B cell receptors with succeeding B cell activation. In contrast to the T cell-dependent activation of B cells, there are **no immunological memory cells built** on this occasion. There is also none or hardly any immunoglobulin class switching from IgM to IgG.



T cell-independent activation of B cells

Notes