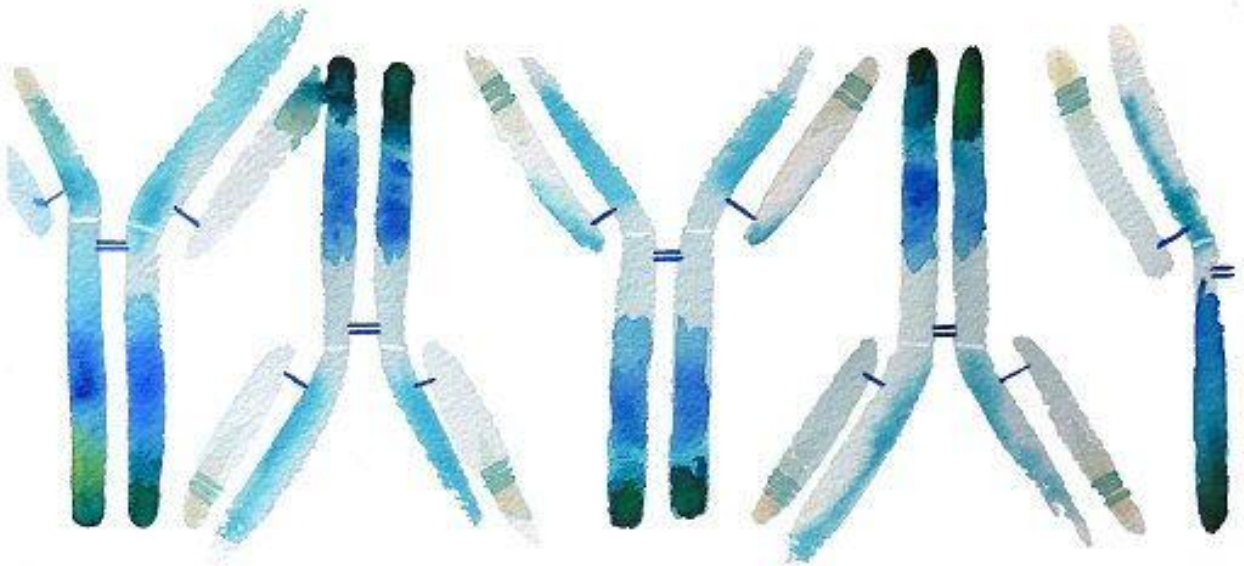
Medical Immunology

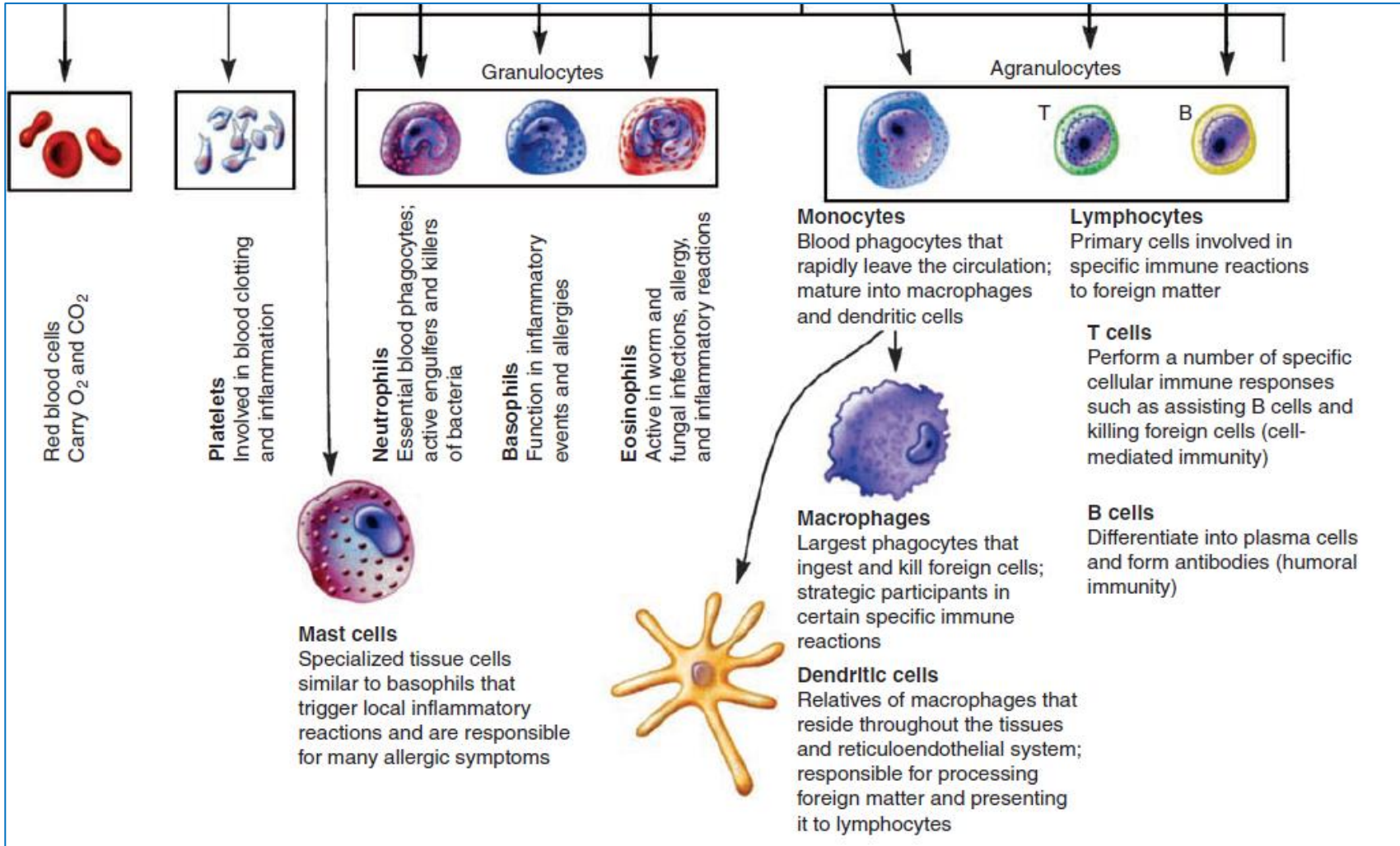


Anas Abu-Humaidan
M.D. Ph.D.

Lecture 3

Cells of the immune system

- **Phagocytes**
- **Mast Cells, Basophils, Eosinophils**
- **Antigen-Presenting Cells**
- **Lymphocytes**



Cells of the immune system / Antigen presenting cells

- Antigen-presenting cells (APCs) are cell populations that are specialized to **capture** microbial and other **antigens**, **display** them to **lymphocytes**, and provide signals that **stimulate** the **proliferation** and **differentiation** of the **lymphocytes**.

- The major type of APC that is involved in initiating T cell responses is the **dendritic cell**.

- **Macrophages** and **B cells** as well present antigens to T lymphocytes in different types of immune responses.

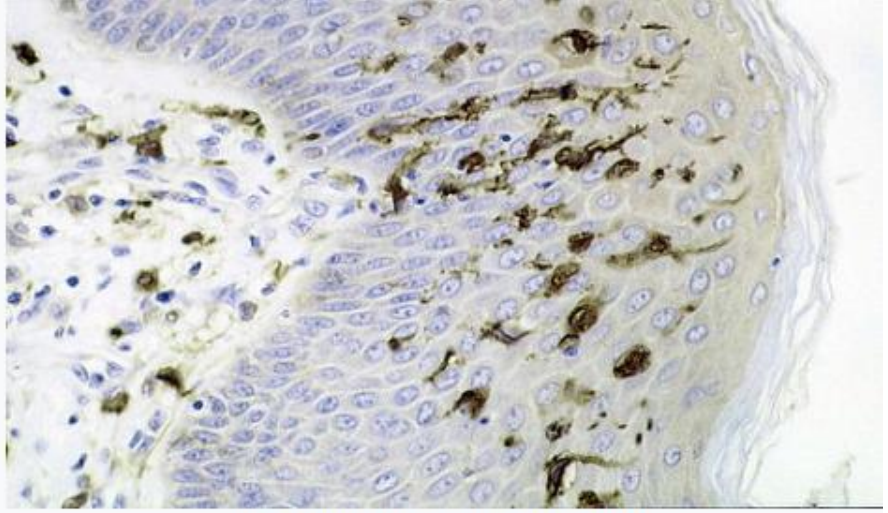
- APCs **link responses of the innate immune system to responses of the adaptive immune** system, and therefore they may be considered components of both systems.

Cells of the immune system / Antigen presenting cells/ Dendritic Cells

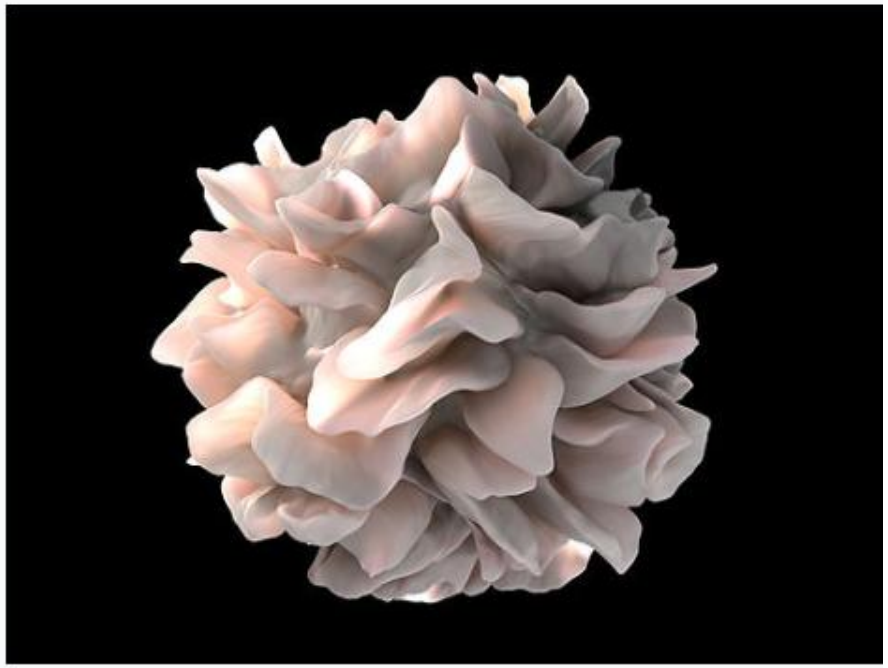
- Dendritic cells are the most important APCs for **activating naive T cells**, and they play major roles in innate responses to infections and in linking innate and adaptive immune responses.

- They have long **membranous projections** and **phagocytic capabilities** and are widely distributed in lymphoid tissues, mucosal epithelium, and organ parenchyma.

- In response to activation by microbes, conventional dendritic cells in skin, mucosa, and organ parenchyma **become mobile, migrate to lymph nodes, and display microbial antigens to T lymphocytes**.

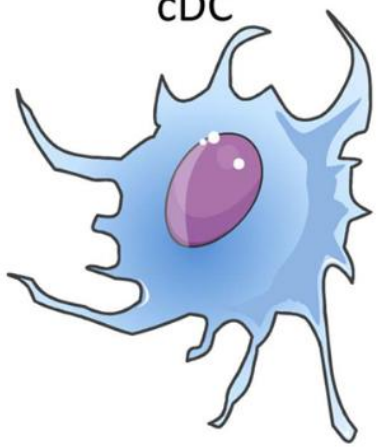
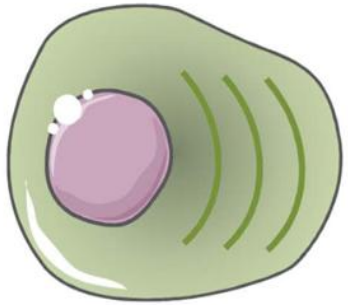
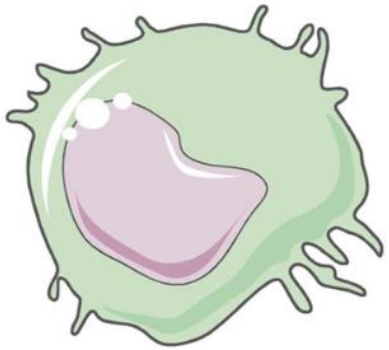


Dendritic cells in skin



Artistic rendering of the surface of a human dendritic cell illustrating sheet-like processes that fold back onto the membrane surface.

Innate immunity/ Dendritic cells

APC type	cDC	pDC	Monocyte / Macrophage
			
Primary functions	T cell priming and functional polarization, Induction of Immunity vs Tolerance	Interferon-α/β production Innate defenses against viruses	Tissue homeostasis Trophic and scavenger functions Microbicidal compound production

DC include two main cell types, the **plasmacytoid DC (pDC**) that are **expert in type I interferon synthesis** upon viral stimulation and the **conventional DC (cDC)** that are specialized in **antigen capture**, **processing**, and **presentation for T-cell priming.**

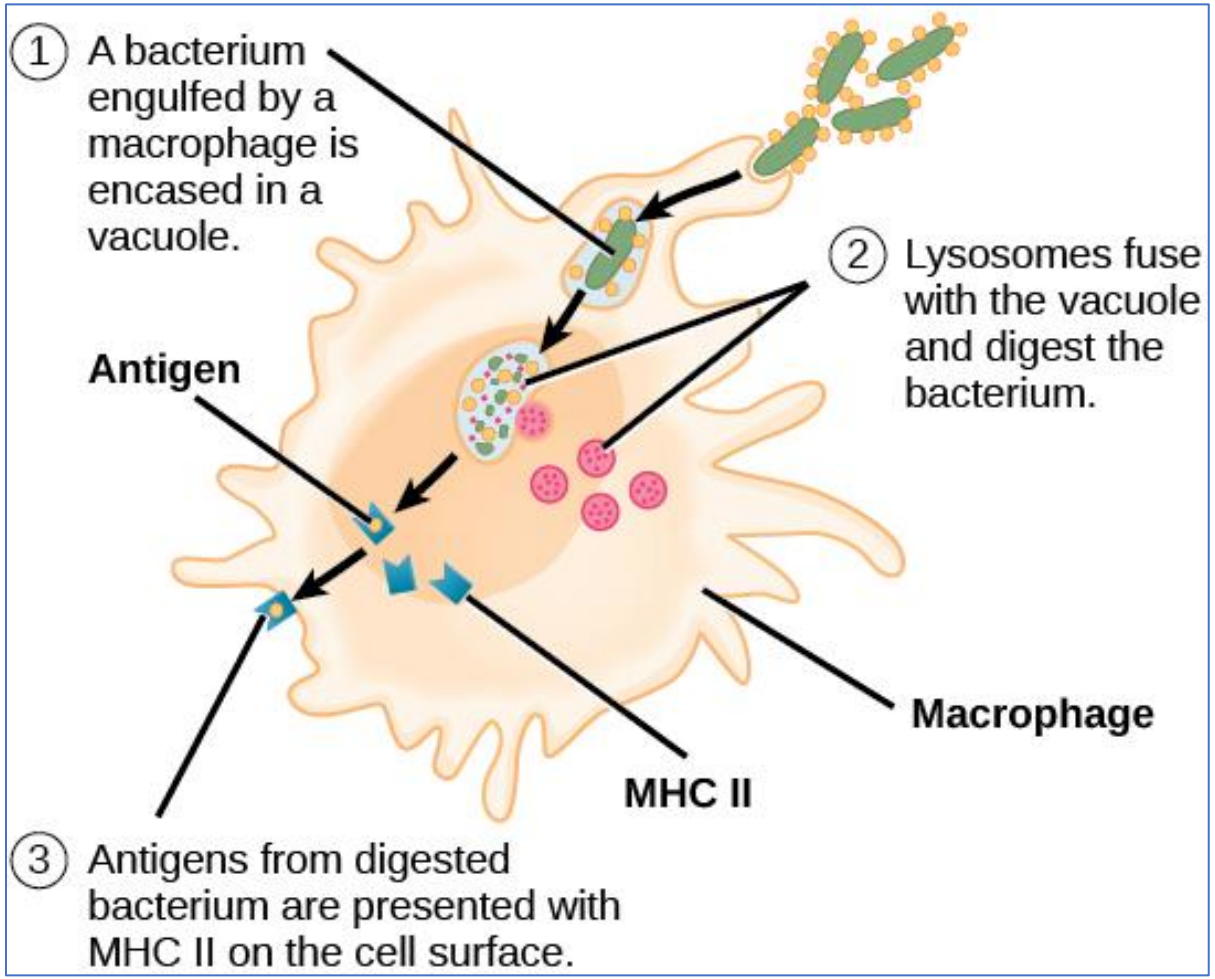
- **Follicular dendritic cells (FDCs)** are cells with membranous projections that are found intermingled in specialized collections of activated B cells, called **germinal centers**, in the lymphoid follicles of the lymph nodes, spleen, and mucosal lymphoid tissues.

- FDCs are not derived from precursors in the bone marrow and are of mesenchymal origin, they are **non migratory**.

- FDCs trap antigens complexed to antibodies or complement products and display these antigens on their surfaces for recognition by B lymphocytes.

- **Macrophages present** antigen **to helper T lymphocytes** at the sites of infection, which leads to **helper T cell activation and production of molecules** that further **activate** the **macrophages**. This process is important for the eradication of microbes that are ingested by the phagocytes but resist killing.

- **B cells present** antigens to helper T cells in lymph nodes and spleen, which is a key step in the cooperation of helper T cells with B cells in humoral immune responses to protein antigens.

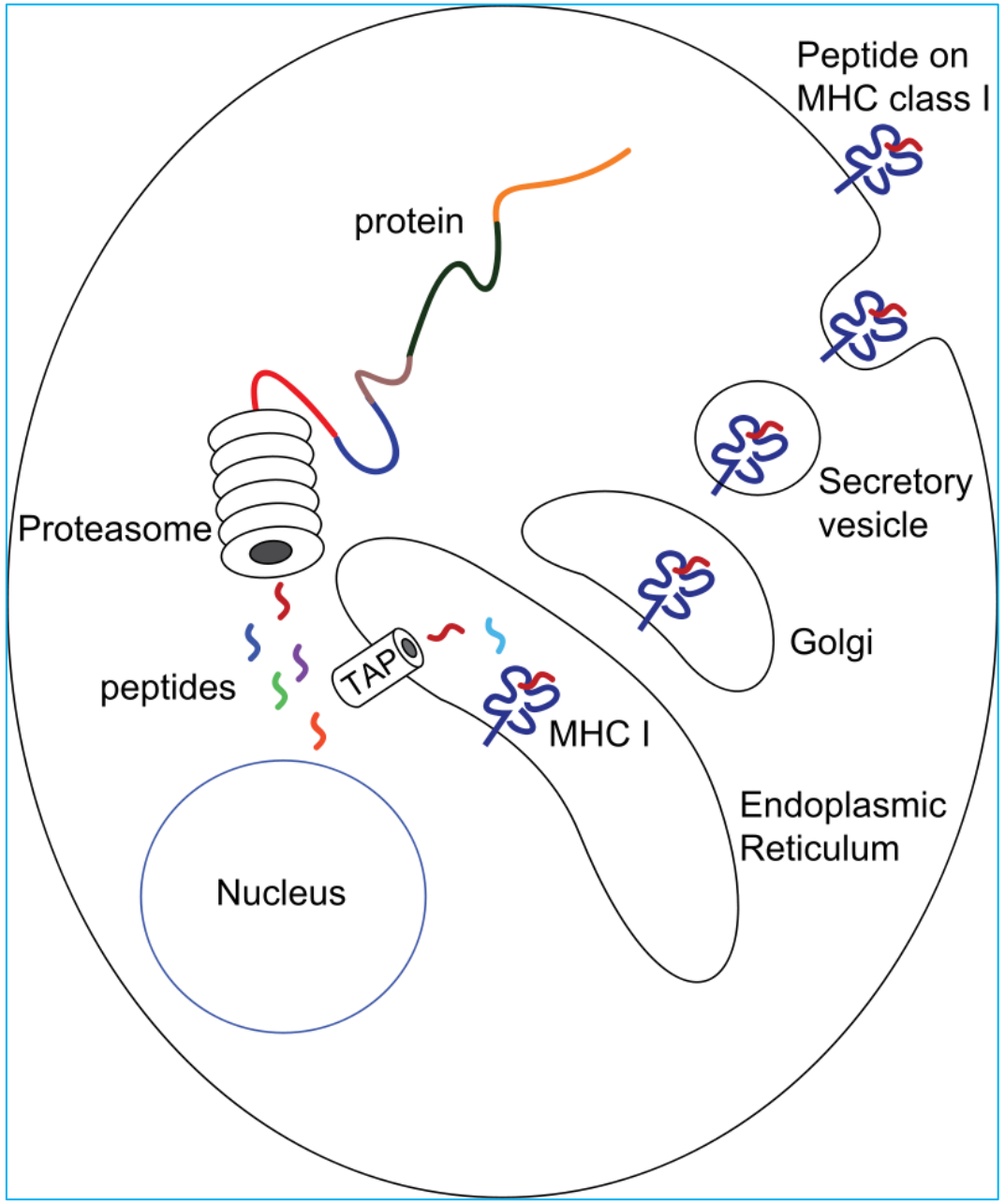


Major histocompitability complex I

- Their function is **to display peptide fragments of proteins from within the cell** to cytotoxic T cells; this will trigger an immediate response from the immune system against a particular non-self antigen displayed with the help of an MHC class I protein.

- The **proteasome** is a macromolecule that consists of 28 subunits, of which half affect proteolytic activity.

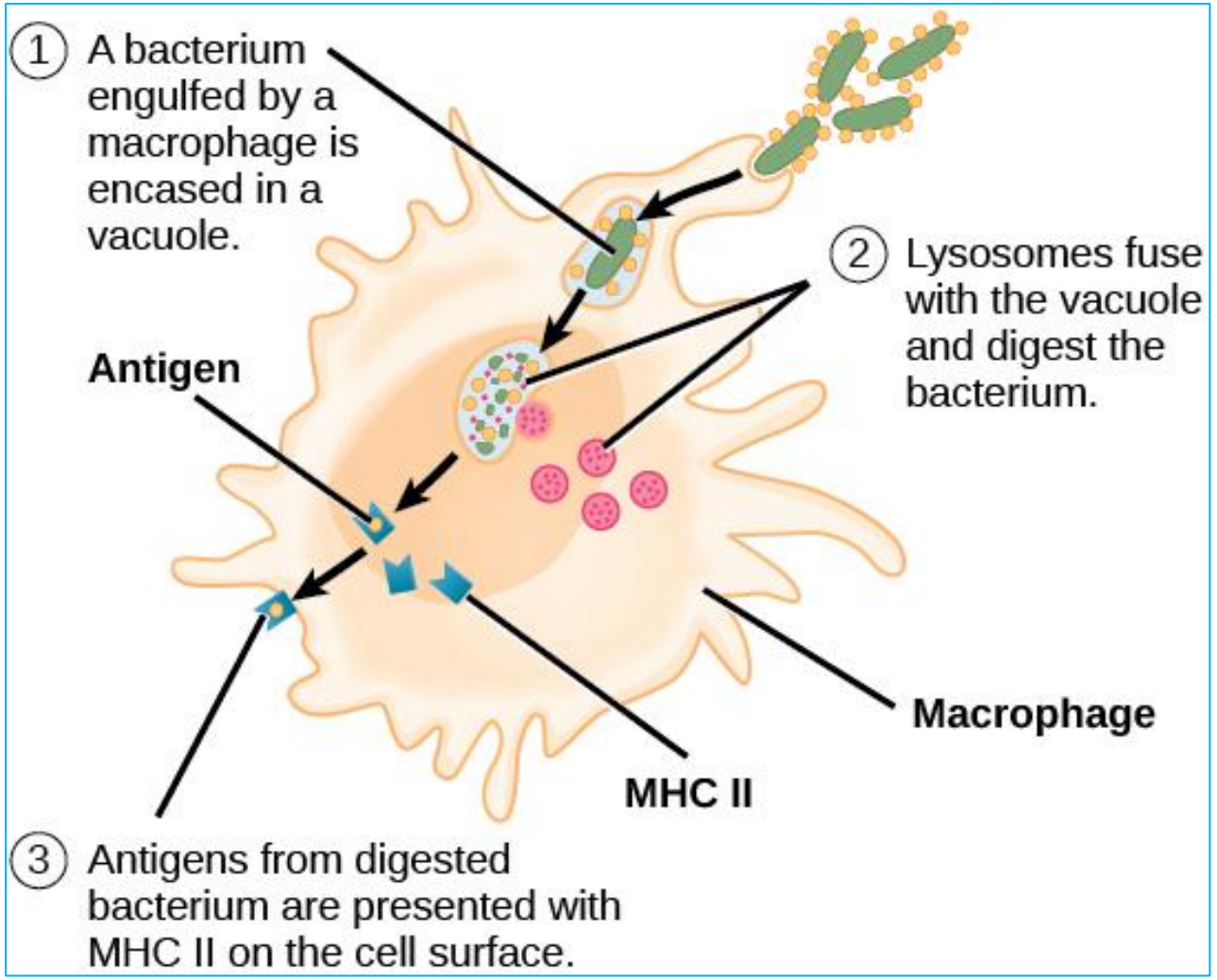
- Cells constantly break down proteins and present them on MHC I.



Major histocompitability complex II

- Normally found only on professional antigen-presenting cells such as **dendritic cells**, **Macrophages**, **B cells** and some **endothelial cells.**

- The antigens presented by class II peptides are derived from **extracellular proteins** (not cytosolic as in MHC class I).



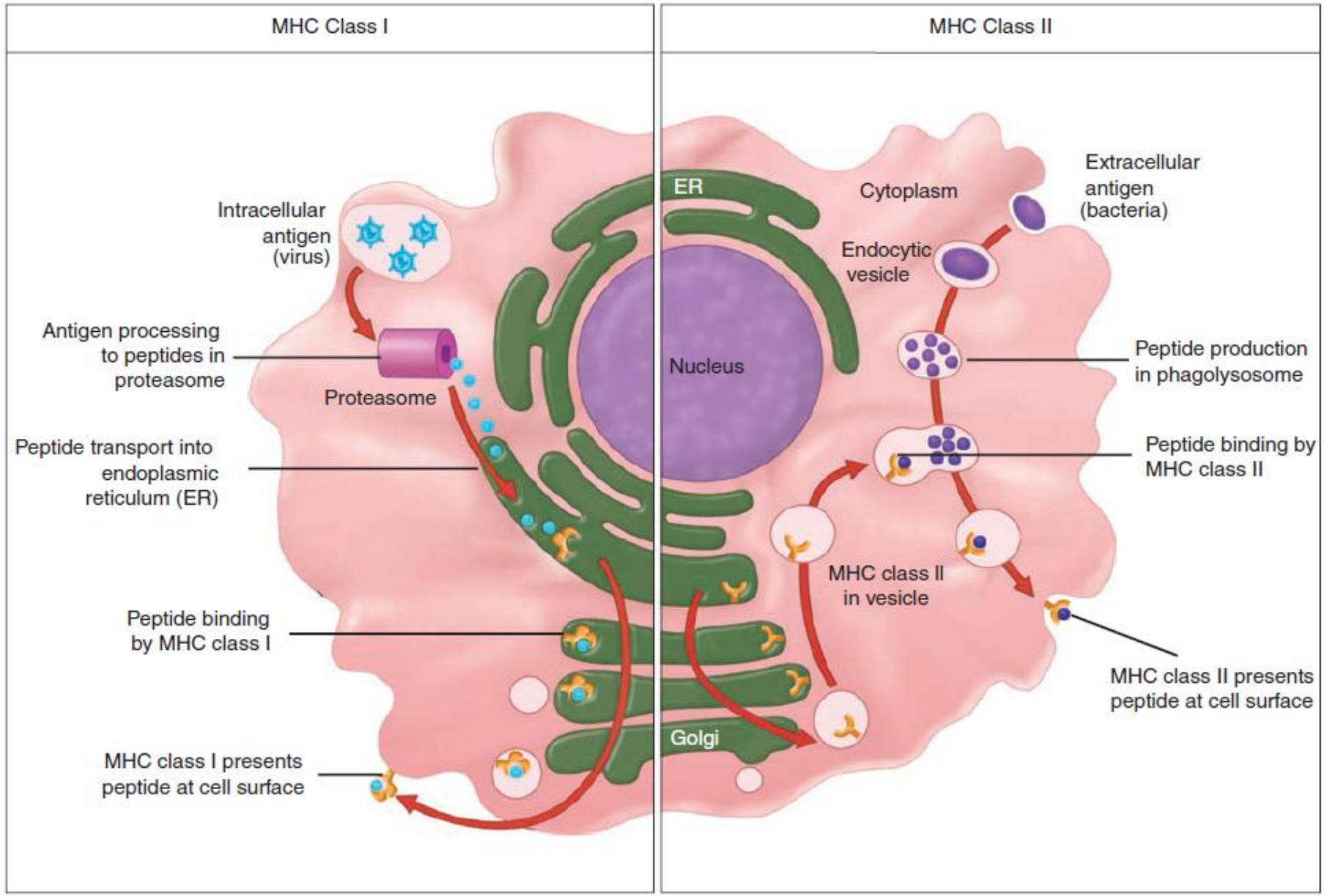
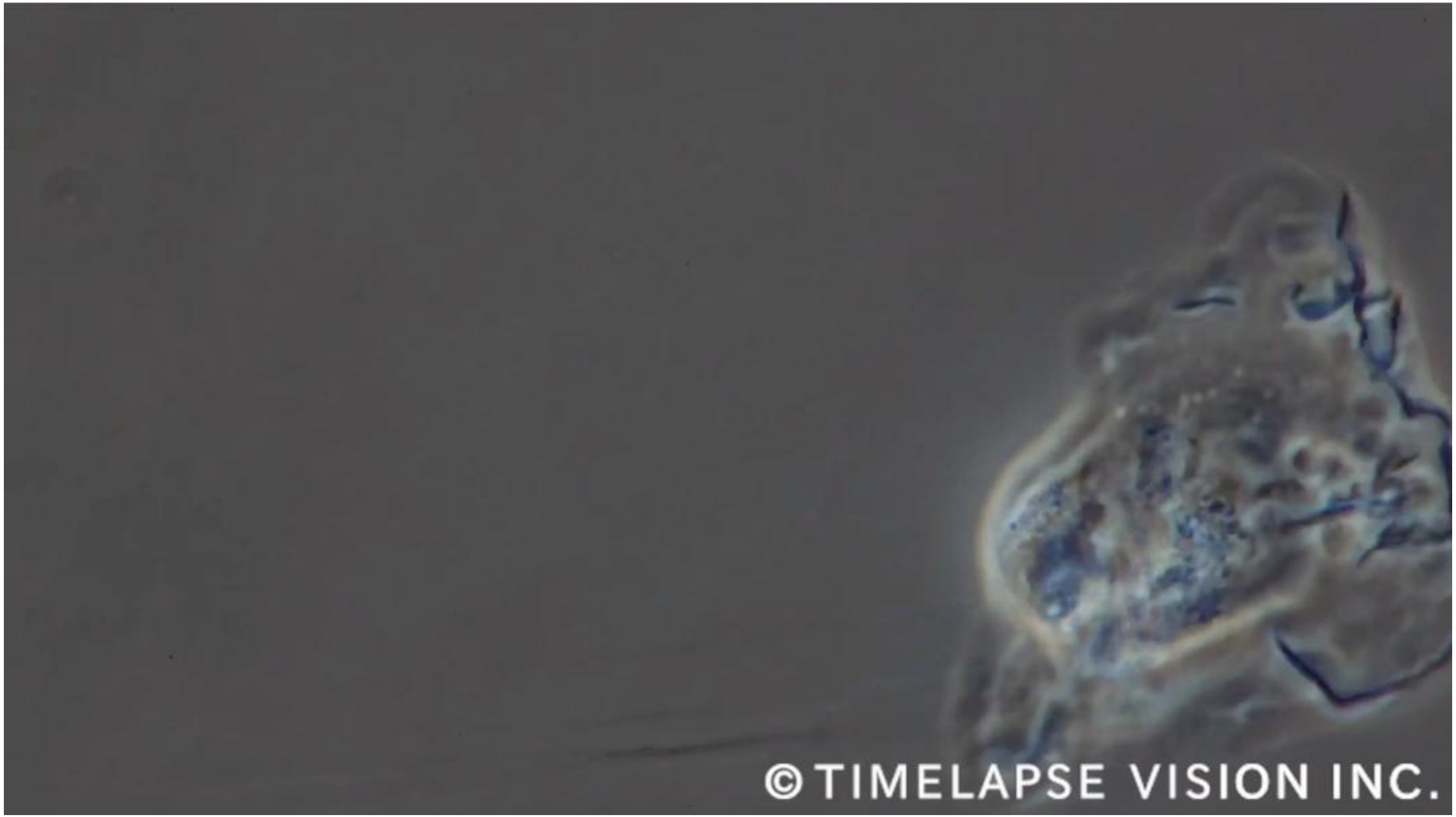


FIGURE 2–11. Antigen processing and presentation. A. Antigens originating in the cytoplasm are digested by the proteasome to peptides. The peptides are bound to the MHC class I molecules in the endoplasmic reticulum (ER) and transported to the surface for presentation. **B.** Antigens originating outside the cell are endocytosed and digested in the phagolysosome. The digested peptides are bound to MHC class II molecules in the ER and transported to the surface for presentation. MHC, major histocompatibility complex.



Dendritic cell presents antigens to **lymphocytes**

Cells of the immune system

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- **Mast Cells, Basophils, Eosinophils**
- **Antigen-Presenting Cells**
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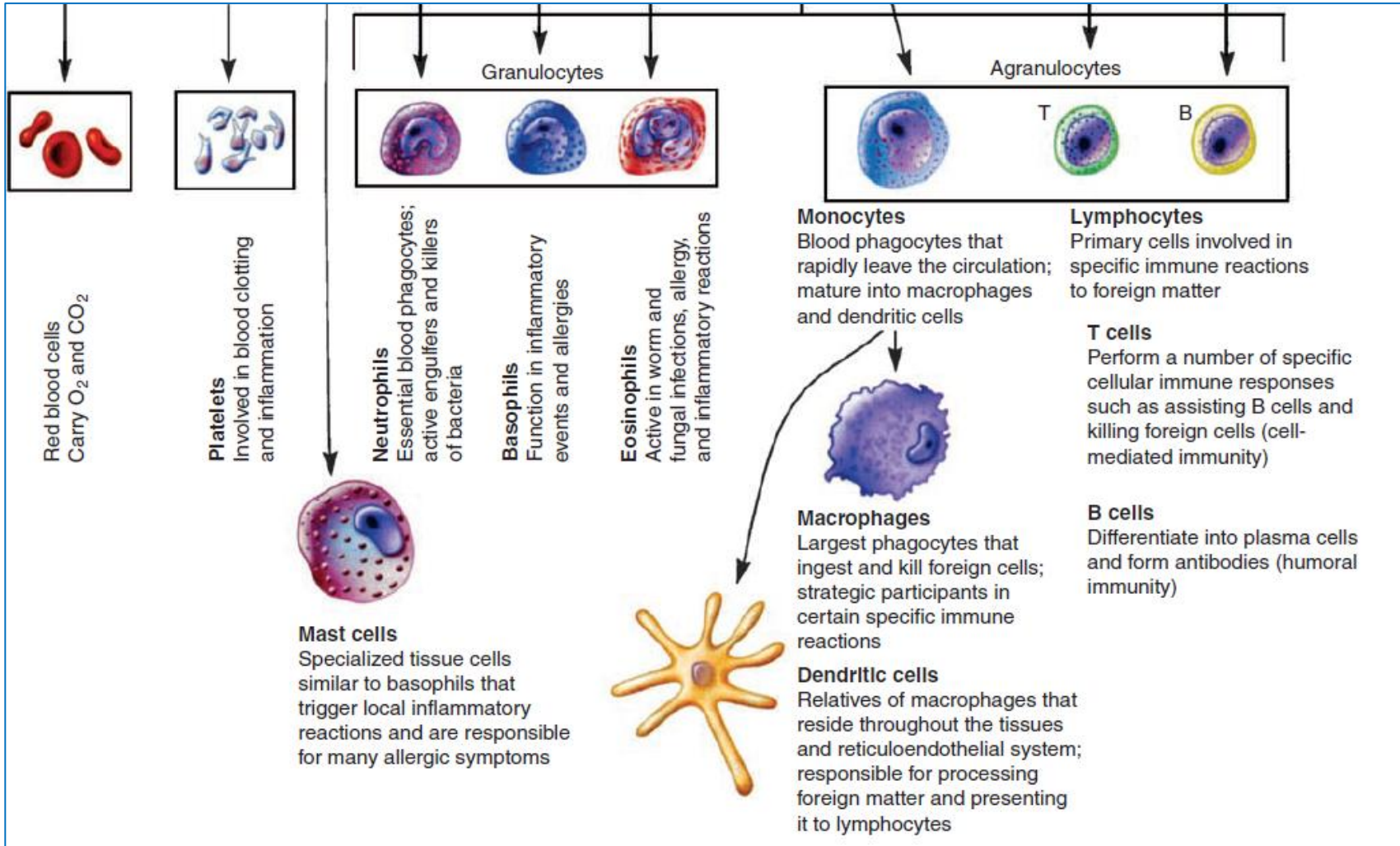
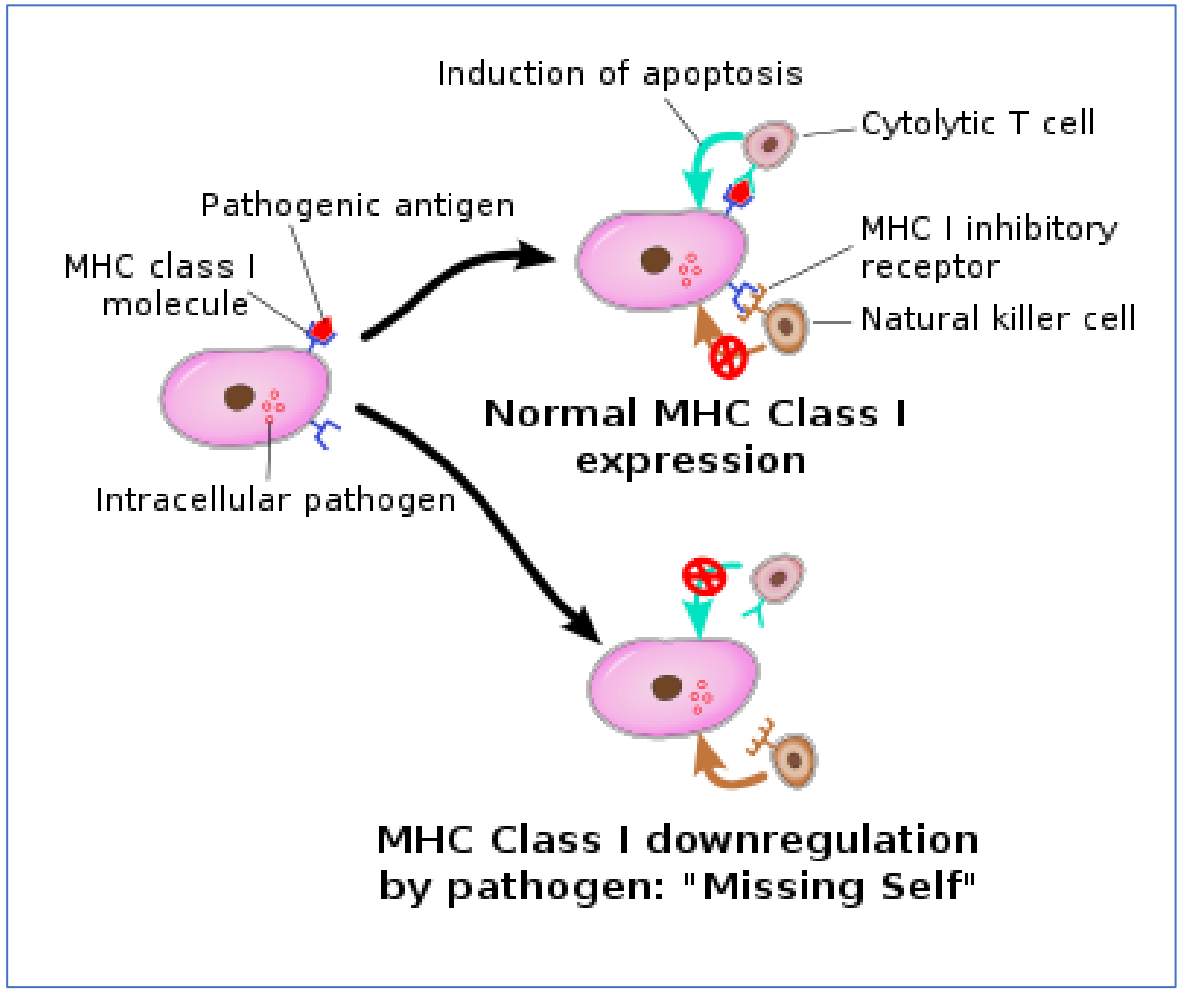


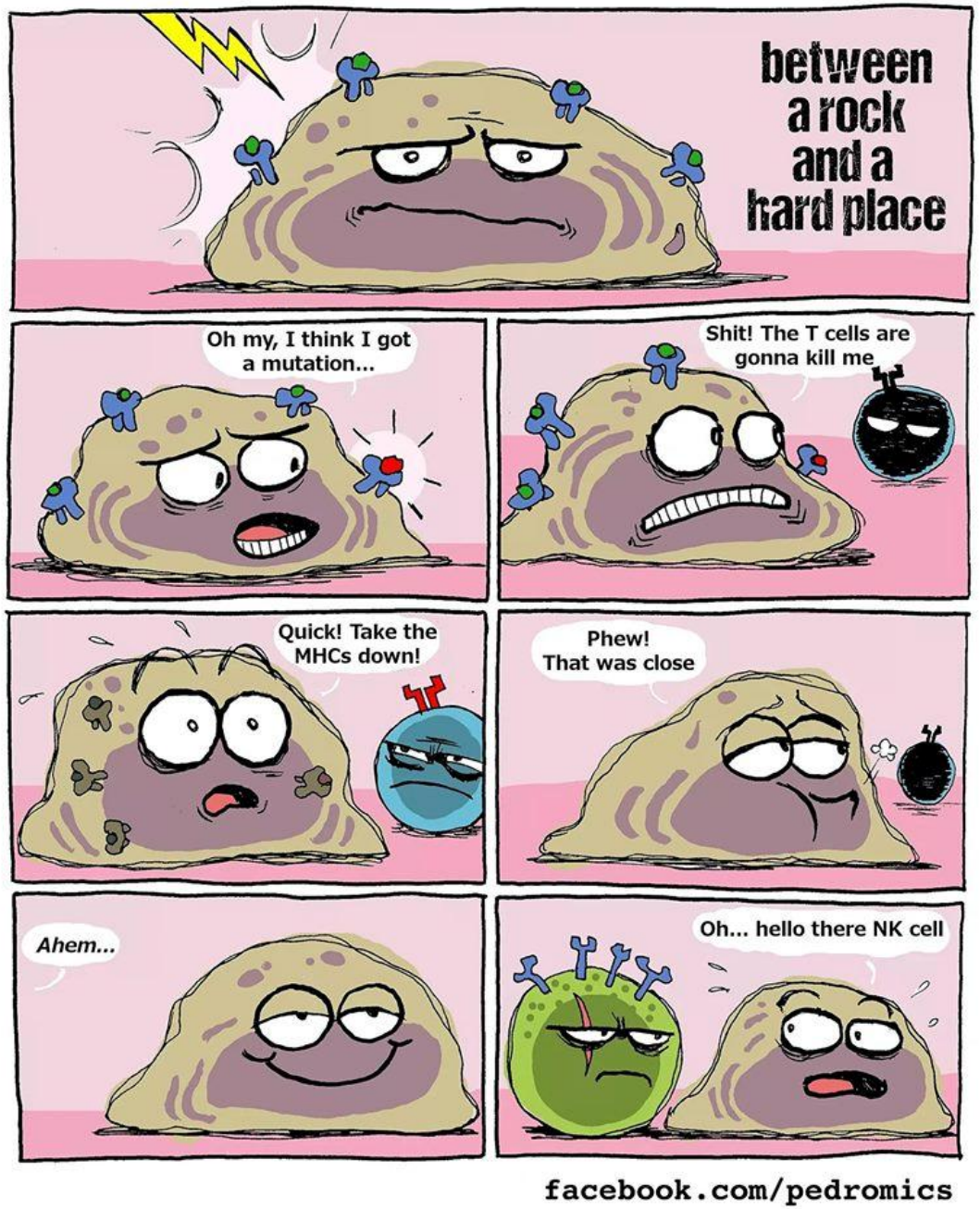
- Natural killer (NK) cells are **lymphocytes** distinct from T and B cells that play important roles in innate immune responses **mainly against intracellular viruses and bacteria.**

- The term natural killer derives from the fact that these cells are capable of performing their killing function **without** a need for **clonal expansion** and **differentiation.**

- Most NK cells express inhibitory receptors that recognize **class I major histocompatibility complex (MHC)** molecules, which are cell surface proteins normally expressed on almost all healthy cells in the body



Cells of the immune system / Lymphocytes / Natural killer (NK) cells



Cells of the immune system / Lymphocytes

- Lymphocytes consist of distinct subsets that are **different in their functions** and protein products, but are **morphologically similar**.

- **B** (**B**ursa of Fabricius) lymphocytes originate in the **b**one marrow and **early maturation** occurs there. Also, **T** (**T**hymus) lymphocytes originate in the bone marrow, but **mature** in the **thymus**.

- Membrane proteins are used as **phenotypic markers** to **distinguish distinct populations of lymphocytes**

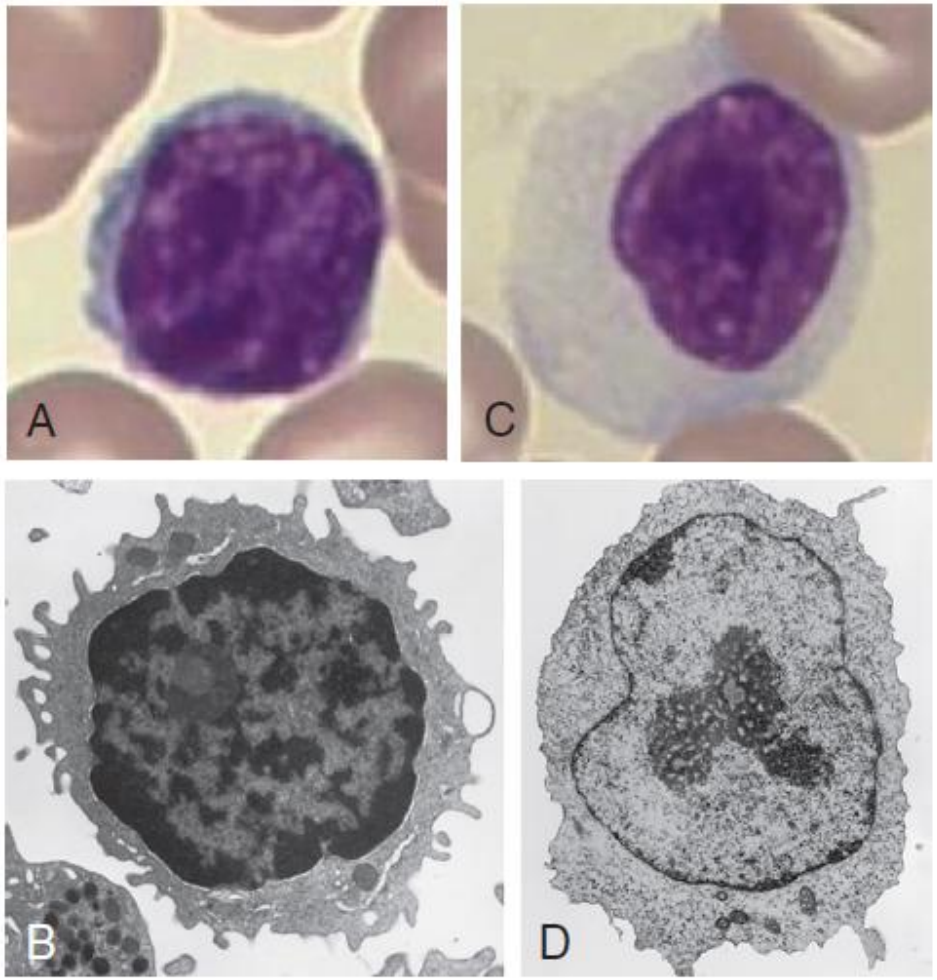
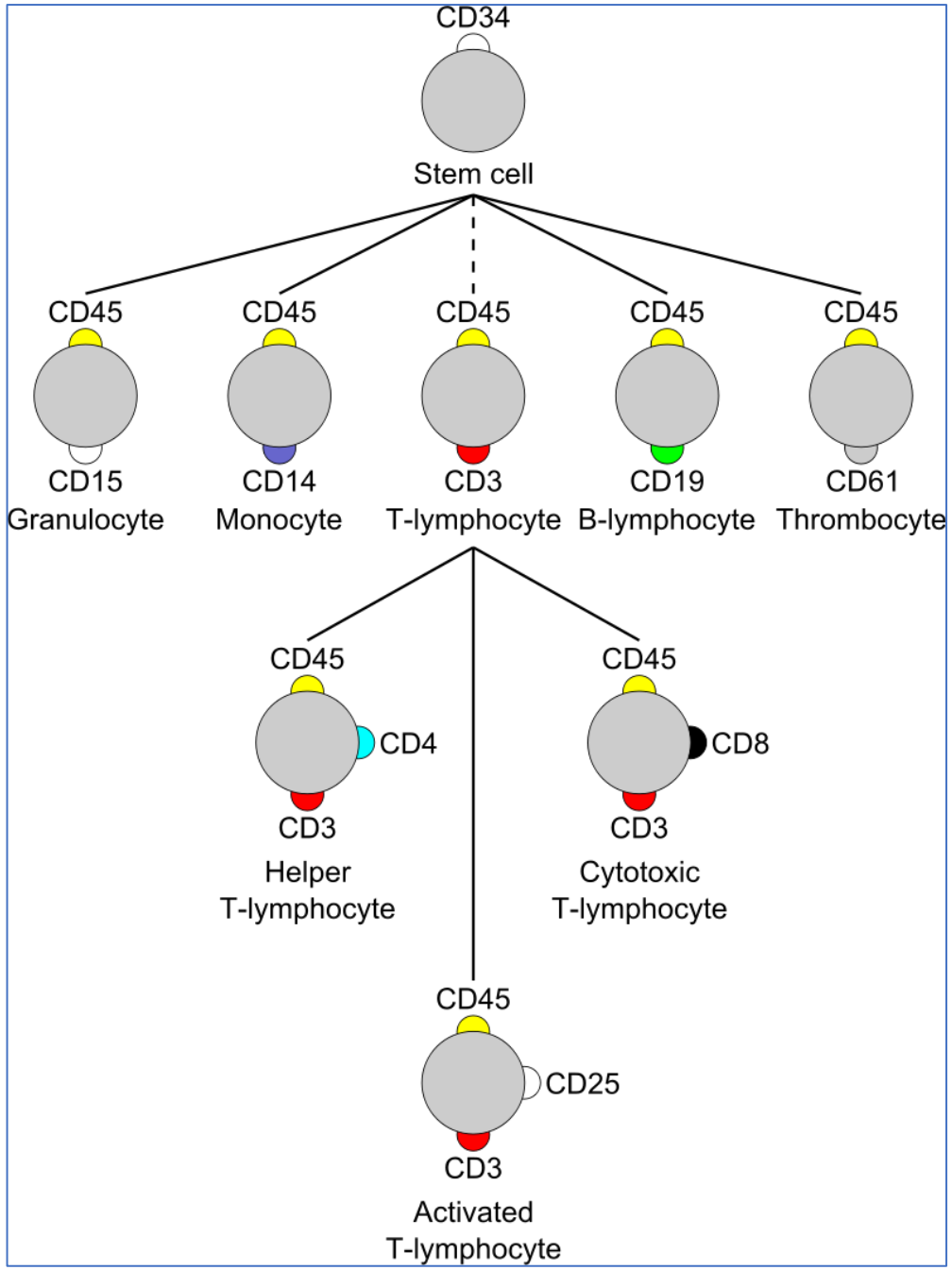


FIGURE 2–7 Morphology of lymphocytes. A, Light micrograph of a lymphocyte in a peripheral blood smear. *(Courtesy of Jean Shafer, Department of Pathology, University of California, San Diego. Copyright 1995-2008, Carden Jennings Publishing Co., Ltd.)* **B,** Electron micrograph of a small lymphocyte. *(Courtesy of Dr. Noel Weidner, Department of Pathology, University of California, San Diego.)* **C,** Light micrograph of a large lymphocyte (lymphoblast). *(Courtesy of Jean Shafer, Department of Pathology, University of California, San Diego. Copyright 1995-2008, Carden Jennings Publishing Co., Ltd.)* **D,** Electron micrograph of a large lymphocyte (lymphoblast). *(From Fawcett DW. Bloom and Fawcett: A Textbook of Histology, 12th ed. Chapman & Hall, New York, 1994. With kind permission of Springer Science and Business Media.)*

Cells of the immune system / Cluster of differentiation

- The cluster of differentiation (CD) is a protocol used for the **identification** and **investigation** of **cell surface molecules** providing targets for immunophenotyping of cells.

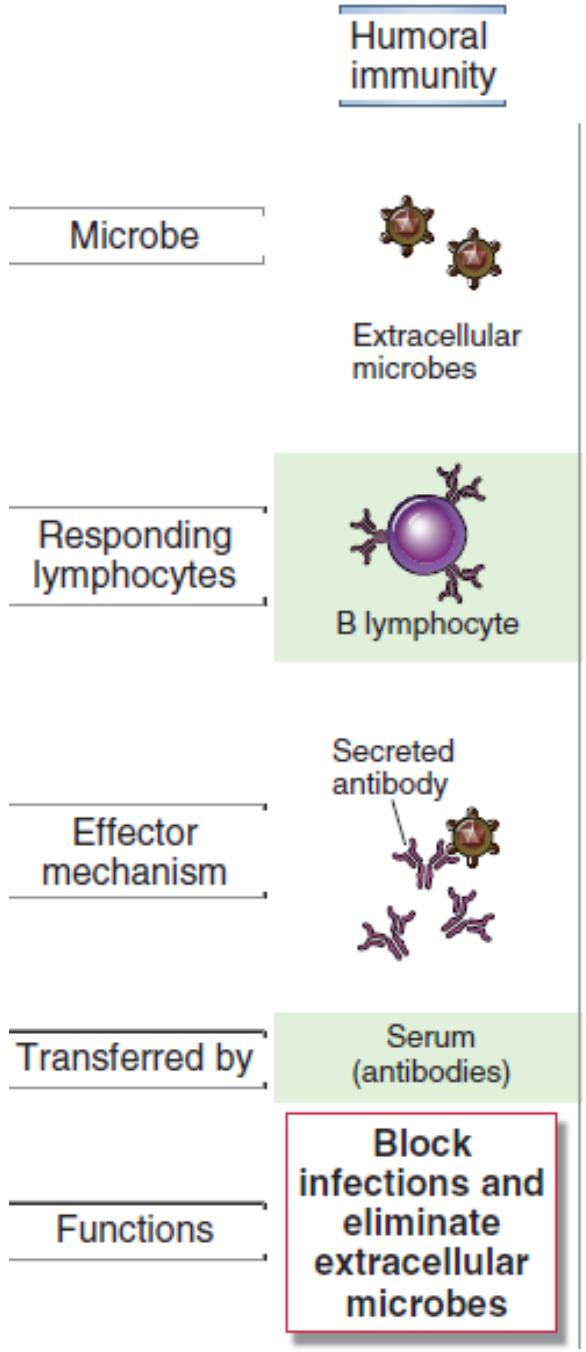
- In terms of physiology, CD molecules can act in numerous ways, often acting as **receptors** or **ligands** important to the cell and some function as **adhesion** molecules.



Cells of the immune system / Lymphocytes/ B-lymphocytes

- B-lymphocytes are the **only cells capable of producing antibodies**.

- They recognize **extracellular (including cell surface) antigens** and differentiate into antibody-secreting **plasma cells**, thus functioning as the mediators of humoral immunity.

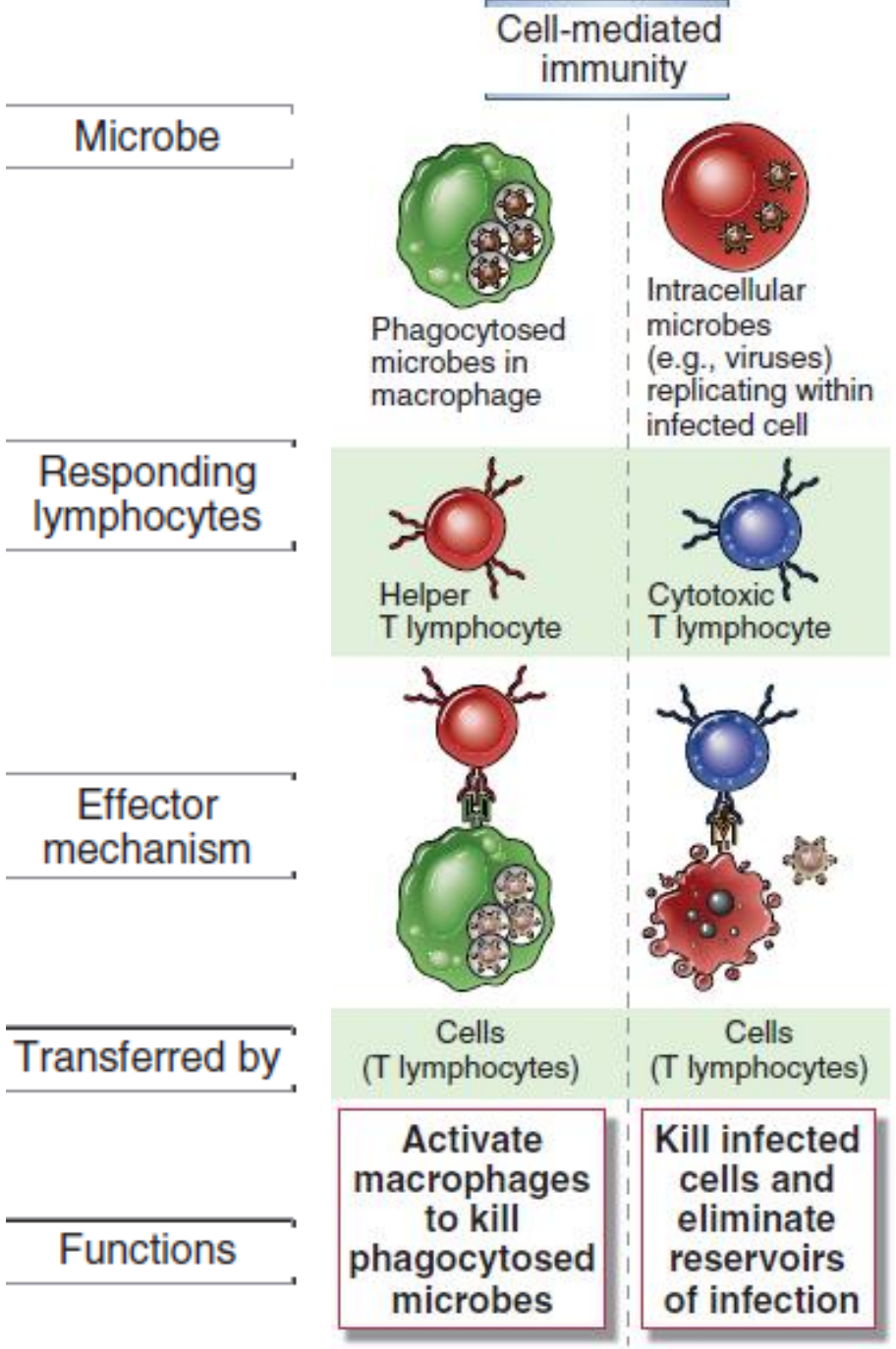


Cells of the immune system / Lymphocytes/ T-lymphocytes

- T lymphocytes, the cells of cell-mediated immunity, **recognize the antigens of intracellular microbes** and either **help** phagocytes to **destroy these microbes** or **directly kill the infected cells**.

- **T cells do not produce antibody molecules**.

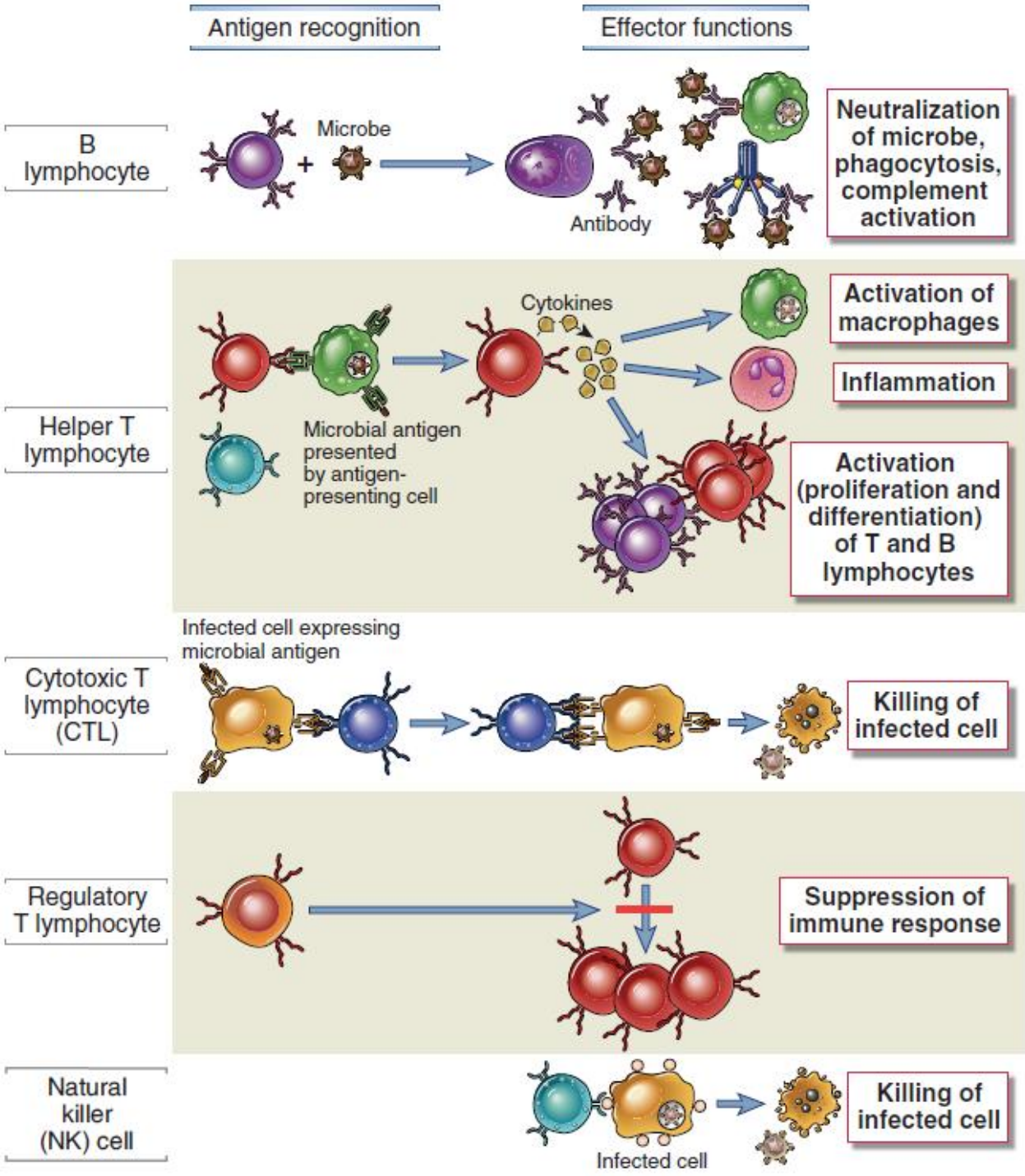
- Their antigen receptors are membrane molecules distinct from but structurally related to antibodies.



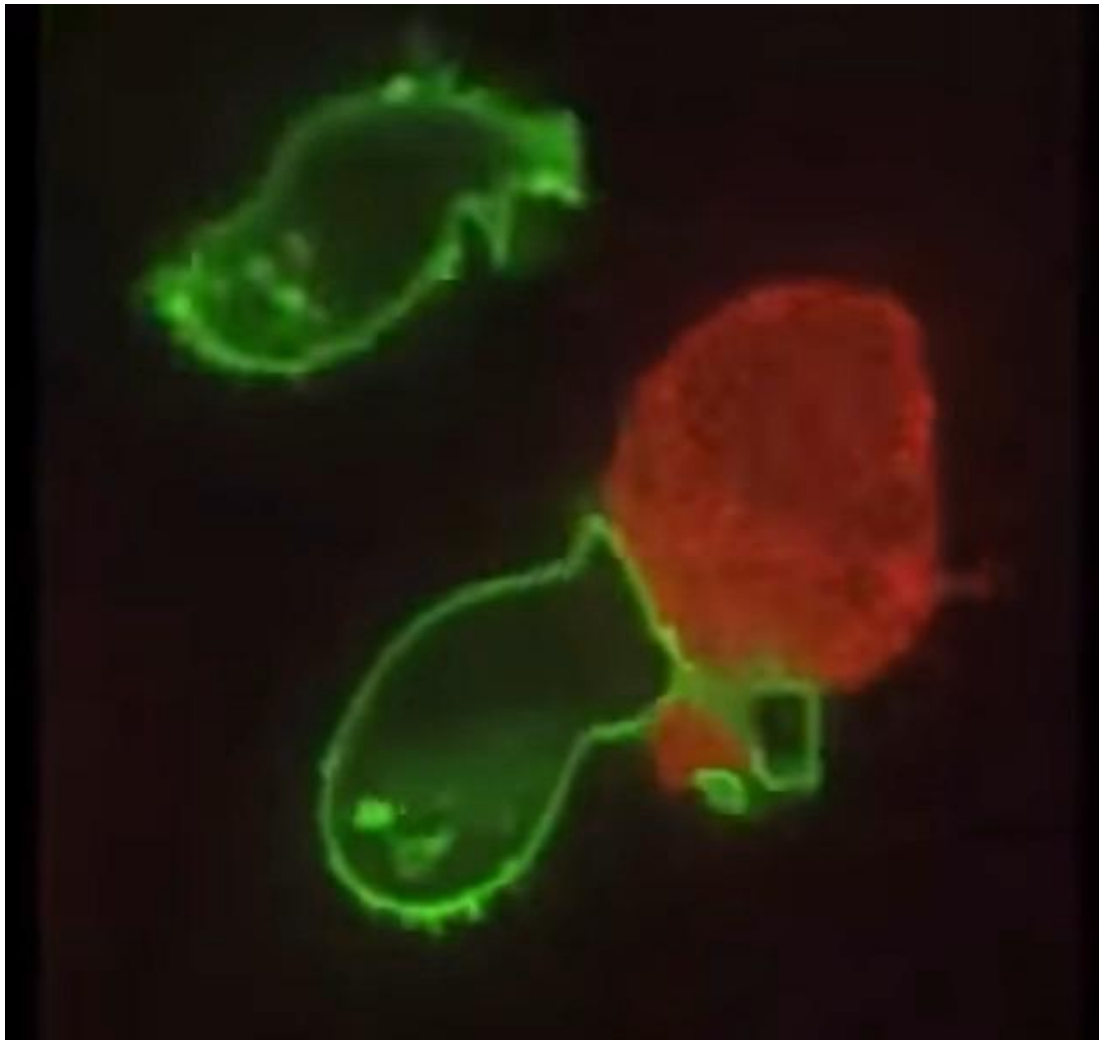
Cells of the immune system / Lymphocytes

- **Humoral immunity** is mediated by molecules in the blood and mucosal secretions, called antibodies, which are produced by cells called B lymphocytes.

- **Cell-mediated immunity** is mediated by T lymphocytes.
  viruses and some bacteria, survive and proliferate inside phagocytes and other host cells, where they are inaccessible to circulating antibodies. Defense against such infections is a function of cell mediated immunity, which promotes the destruction of microbes residing in phagocytes or the killing of infected cells to eliminate reservoirs of infection.



Through the action of **perforin**, **granzymes** enter the cytoplasm of the target cell and their serine protease function triggers the **caspase** cascade, which eventually lead to **apoptosis** (programmed cell death).



Cells of the immune system / Lymphocytes

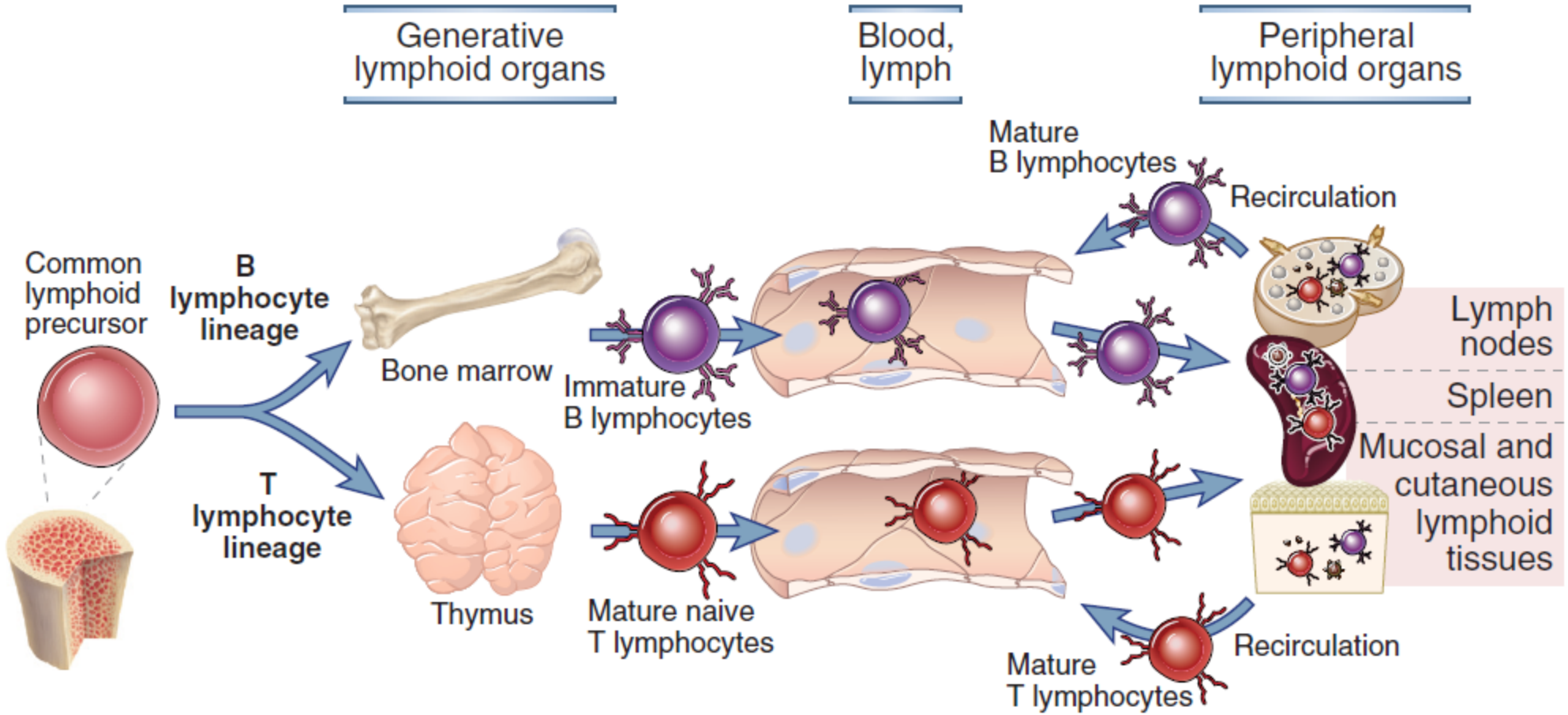
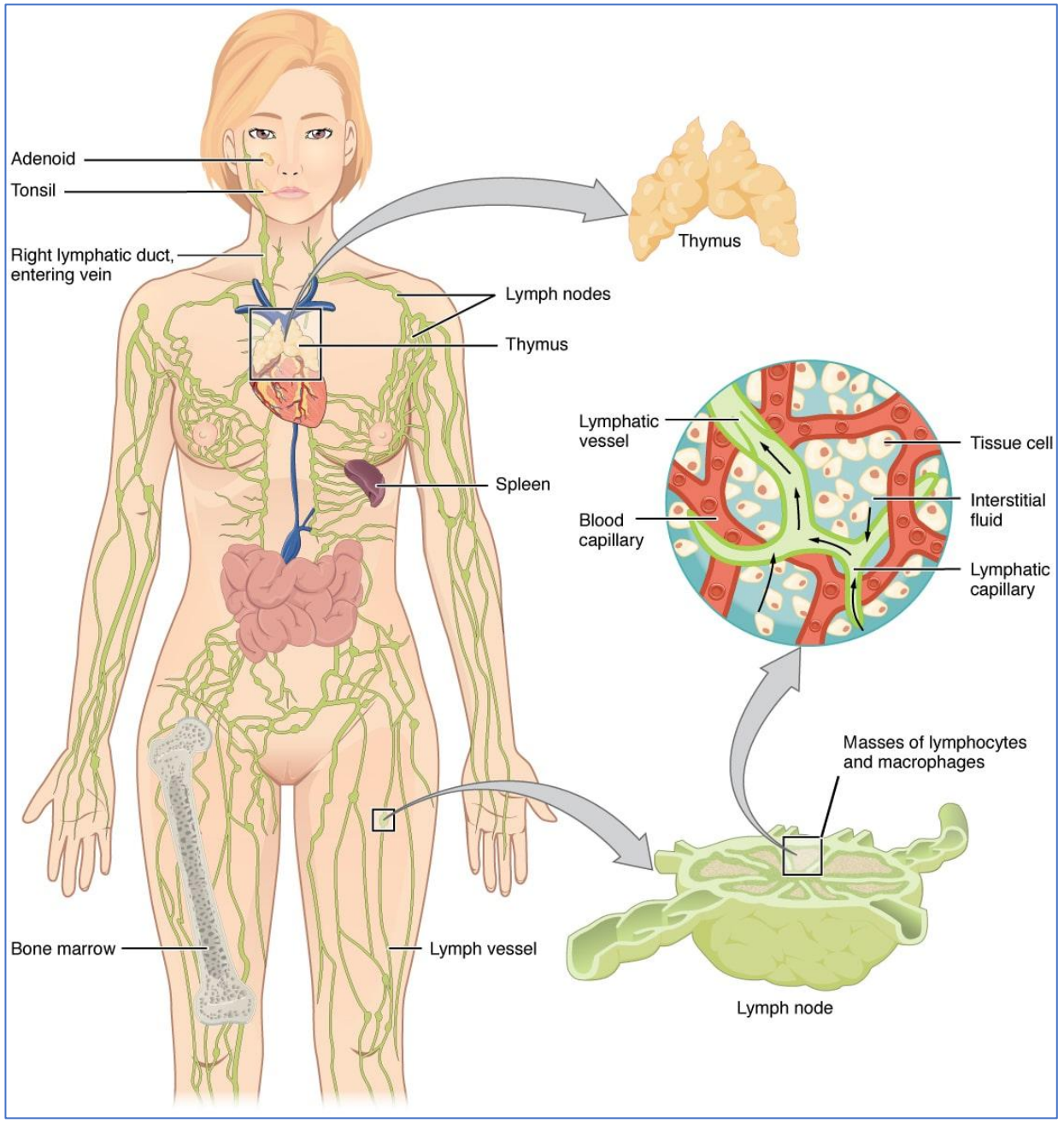


FIGURE 2–5 Maturation of lymphocytes. Lymphocytes develop from bone marrow stem cells and mature in the generative lymphoid organs (bone marrow and thymus for B and T cells, respectively) and then circulate through the blood to secondary lymphoid organs (lymph nodes, spleen, regional lymphoid tissues such as mucosa-associated lymphoid tissues). Fully mature T cells leave the thymus, but immature B cells leave the bone marrow and complete their maturation in secondary lymphoid organs. Naive lymphocytes may respond to foreign antigens in these secondary lymphoid tissues or return by lymphatic drainage to the blood and recirculate through other secondary lymphoid organs.

Cells of the immune system / Lymphocytes

The total number of lymphocytes in a healthy adults about 5×10^{11}. Of these:

- ~2% are in the blood,
- ~10% in the bone marrow,
- ~15% in the mucosal lymphoid tissues of the gastrointestinal and respiratory tracts, and
- ~65% in lymphoid organs (mainly the lymph nodes and spleen)



Further reading:

- Cellular and Molecular Immunology. 7th Edition..

Chapter 2. Cells and tissues of the immune system