



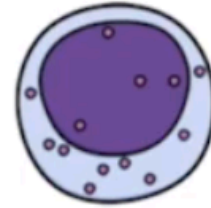
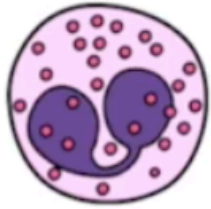
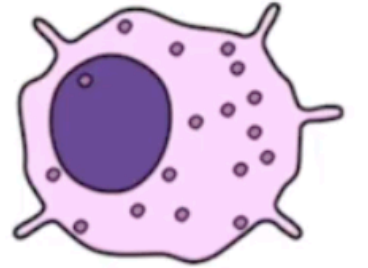
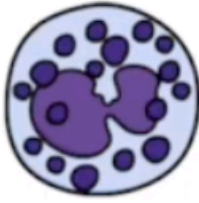
Cells of the Immune System

Lecture-3-

By

Harmand Ali

CELLS OF THE IMMUNE SYSTEM



DESTROY

PATHOGENS

ABNORMAL
CELLS

VIRALLY
INFECTED

TUMOUR
CELLS

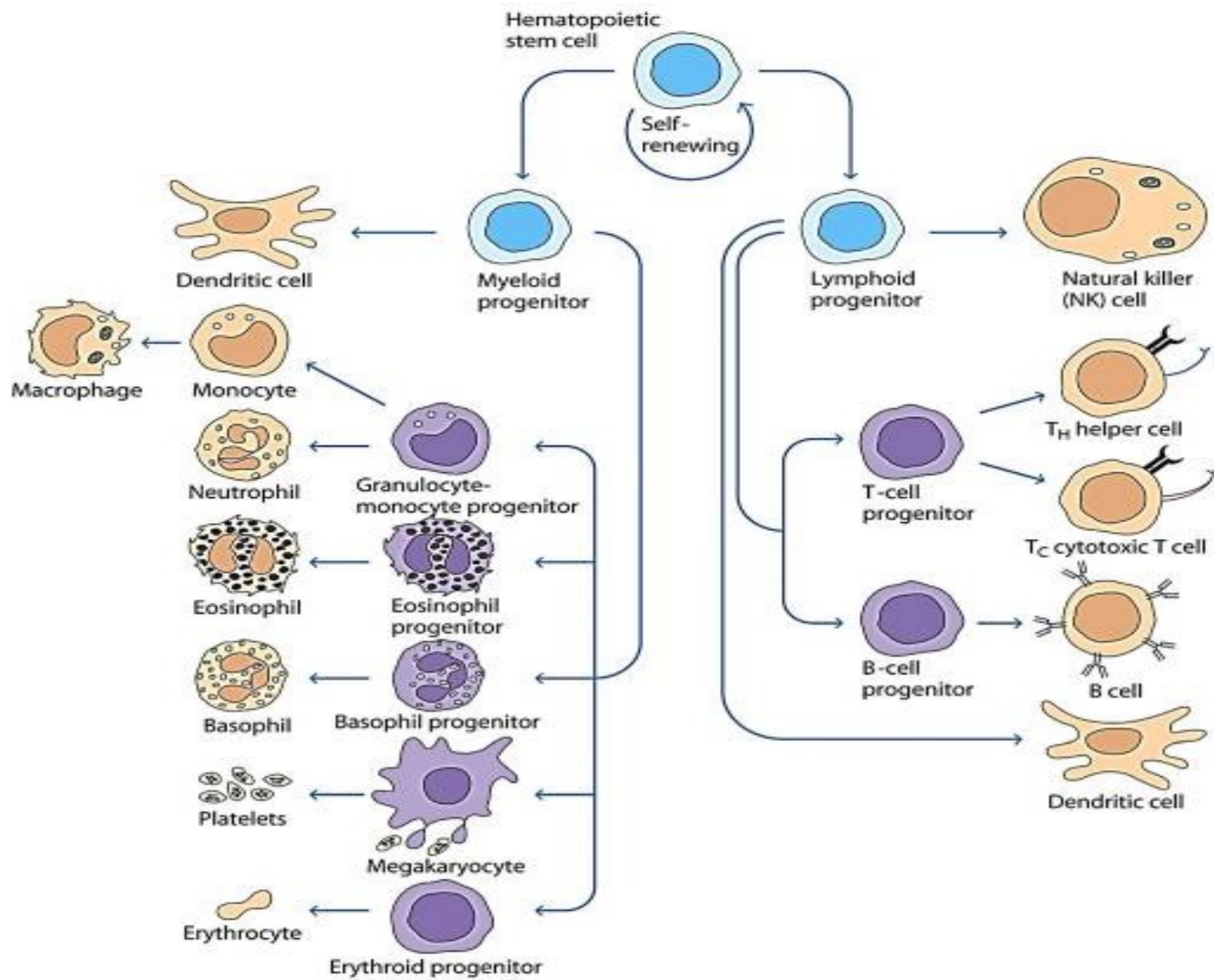
FAMILY TREE

ORIGIN

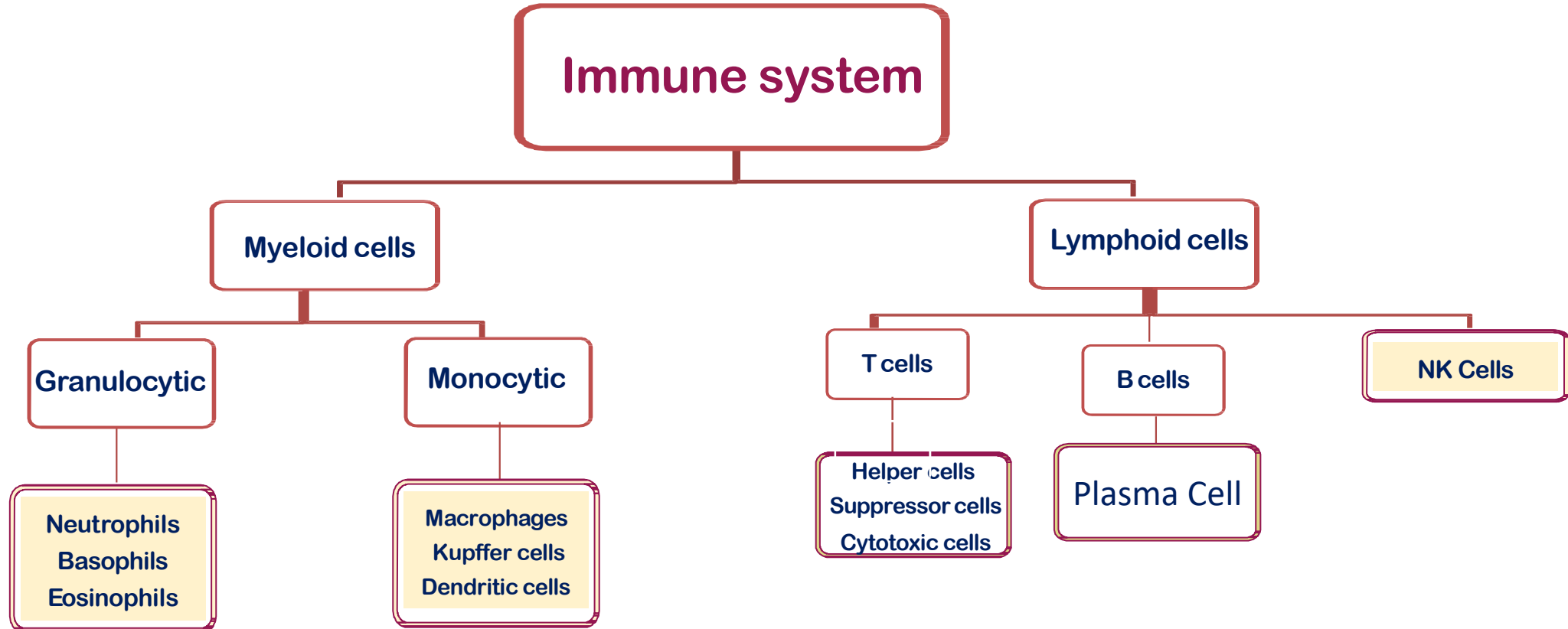
DEVELOPMENT

RELATE

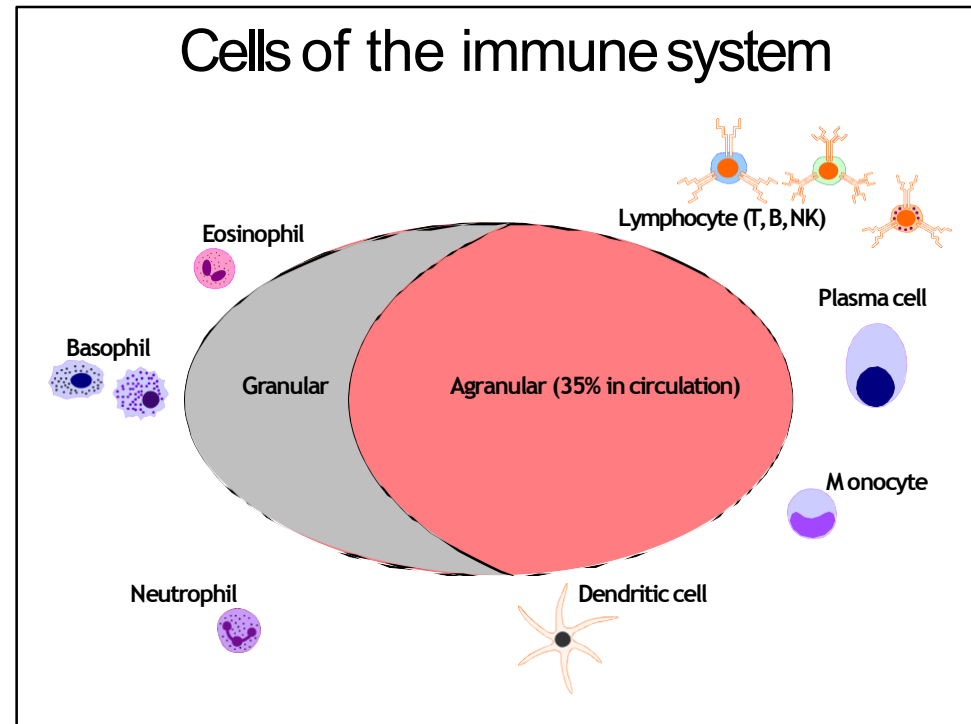
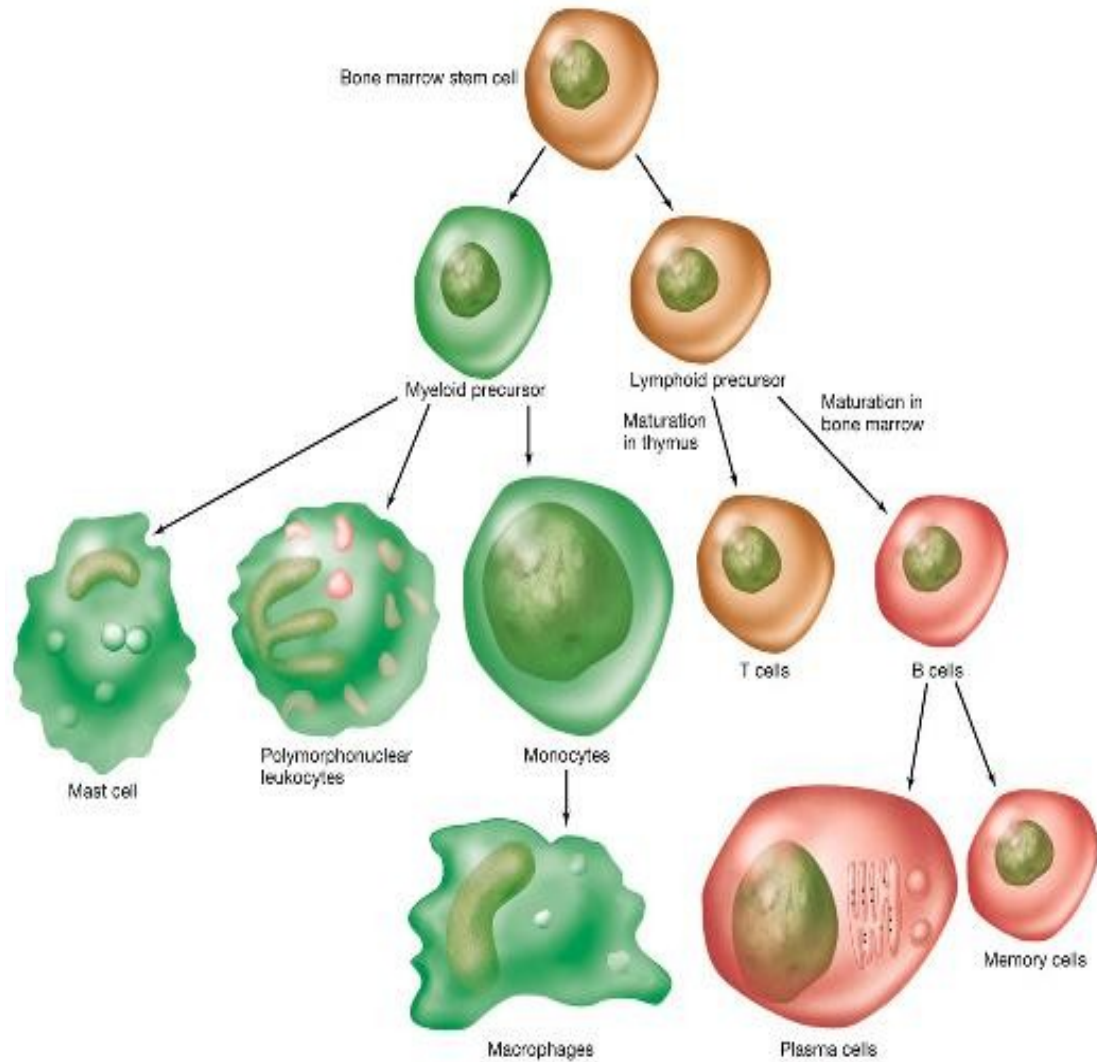
INTERACT



Cells of the immune system



Development of cells involved in the immune response



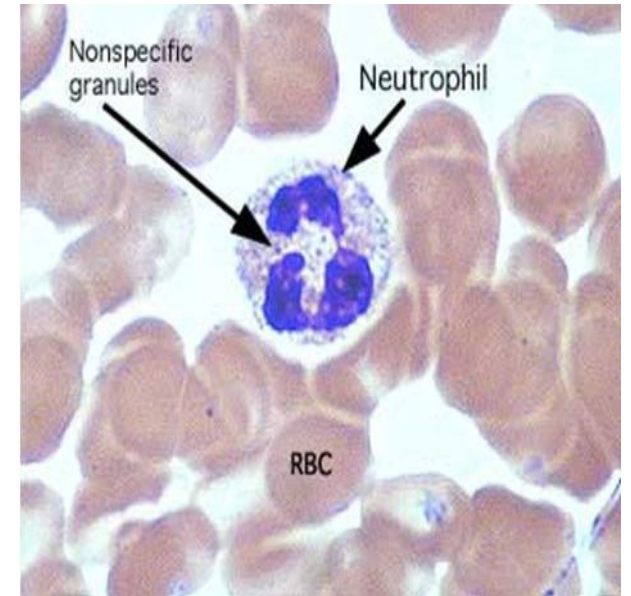
Granulocytes or Polymorphonuclear (PMN) Leukocytes

- A group of white blood cells referred to as granulocytes or polymorphonuclear leukocytes (PMNs).
- Granulocytes are composed of three cell types identified as **neutrophils, eosinophils and basophils**, based on their staining characteristics with certain dyes.
- These cells are predominantly important in the removal of bacteria and parasites from the body, they engulf foreign bodies and destroy them by their powerful enzymes.

Neutrophils

They have multi-lobed nucleus, about **50-70%** of circulating WBC, the granules stain poorly with neutral dye.

- **Primary granules:** contain bactericidal enzymes. (Lysozyme, myeloperoxidase; neutral proteases (elastase); and acid hydrolases (Beta-glucuronidase).
- **Secondary granules:** smaller, contain: (lysozyme, collagenase, lactoferrin and cathepsin B).
- **Phagocytic cells** (can perform phagocytosis and killing of ingested microorganisms). The phagosome fuses with granules to destroy internalized bacteria, oxygen dependent respiratory burst.
- Can not act as APCs.
- Neutrophils are the first cells to arrive as a result of a number of substances produced during an inflammatory response which recruit neutrophils to a site of inflammation.



Eosinophils

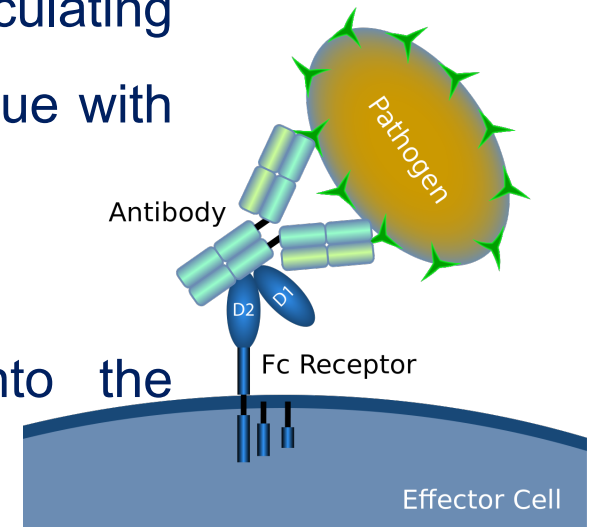
They represent 1-3% of circulating WBCs, possess a bi-lobed nucleus and a heavily granulated cytoplasm. Granules stain orange/red with the acidic dye Eosin Y.

- Sometimes phagocytic but do not act as APCs.
- The major role of the eosinophil is thought to be against **parasites**, particularly parasitic worms.
- Eosinophils kill by ADCC (antibody dependent cell-mediated cytotoxicity) by binding to parasite - specific **IgE** via cell surface FcεRs.
- When eosinophils bind to IgE on the surface of a worm, the cell is triggered to degranulate.
- The contents of the granules cause damage to the worm's tegument. There are many hydrolytic enzymes present in the granules responsible for the anti-helminthic activity. One component which is unique to the eosinophils - and highly toxic to worms - is a substance known as Major Basic Protein (MBP).

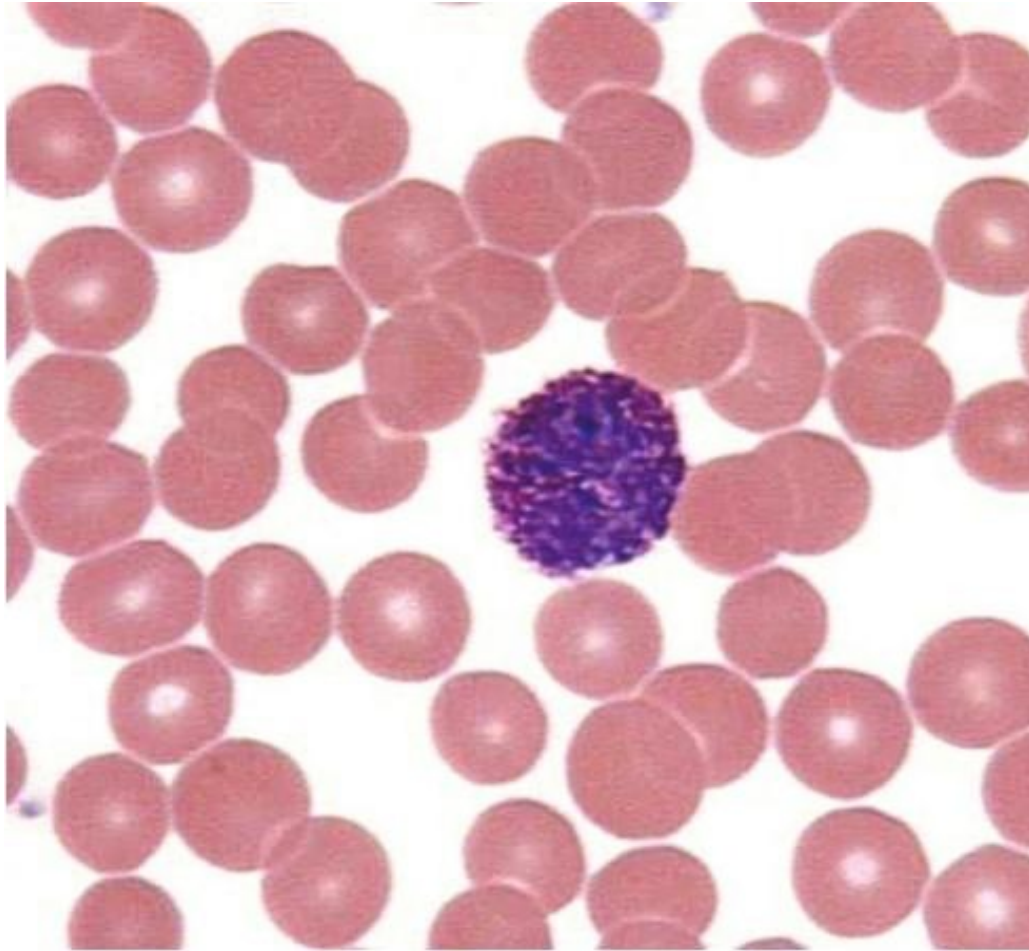


Basophils

- They are present only in the bloodstreams, and represent <1% of circulating WBC, has lobed nucleus--more variable, large coarse granules stain blue with basic dye methylene blue. They bear **Fc receptors for IgE (FceRs)**.
- They play a major role in the allergic response when they release their granules (containing histamine, serotonin, heparin, prostaglandin, etc into the bloodstreams following exposure to specific allergens).
- When an individual is exposed to an allergen, allergen specific IgE is produced, which binds to the surface of basophils.
- Upon re-exposure to the allergen, the allergen binds to IgE on the surface of basophils resulting in degranulation.

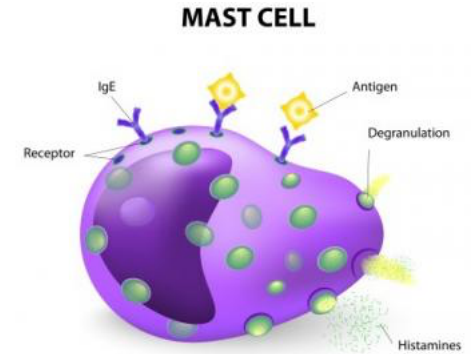


Basophils and Mast cell



Mast Cells

- Mast cells are released from the bone marrow as undifferentiated precursor cells and do not differentiate until they enter the tissues (skin, connective tissue, mucosal epithelium, etc.)
- Morphology and function similar to circulating basophils - but clearly derived from a distinct cell lineage.
- Mast cells bear Fc receptors for IgE (FcεRs) and contain large numbers of cytoplasmic granules which also play important role in the allergic response.
- They produce a variety of cytokines (**TNF** is produced and stored within the cytoplasm of the mast cell, and it can be released quickly following mast cell activation).



Monocytes and macrophages

They represent 5-8% of WBCs. Monocytes enter the tissues through the process of extravasation accompanied by certain changes include:

(Cells enlargement, increase in numbers of intracellular organelles and complexity, acquire increased phagocytic ability, increase in secretion of many soluble factors)

•**Macrophages** play the following important roles:

1)Phagocytosis

2)Antimicrobial activity

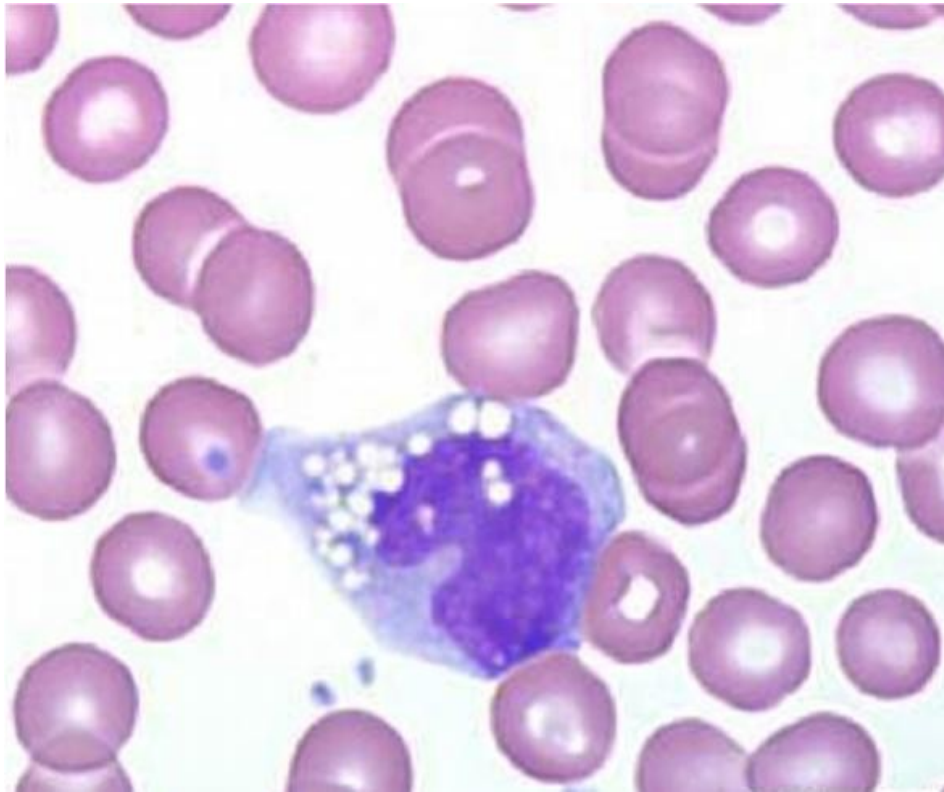
3)Secretion of soluble factors

•**Macrophages** are activated by a variety of stimuli in the course of an immune response.

- One of the earliest activating signals comes from chemokines.

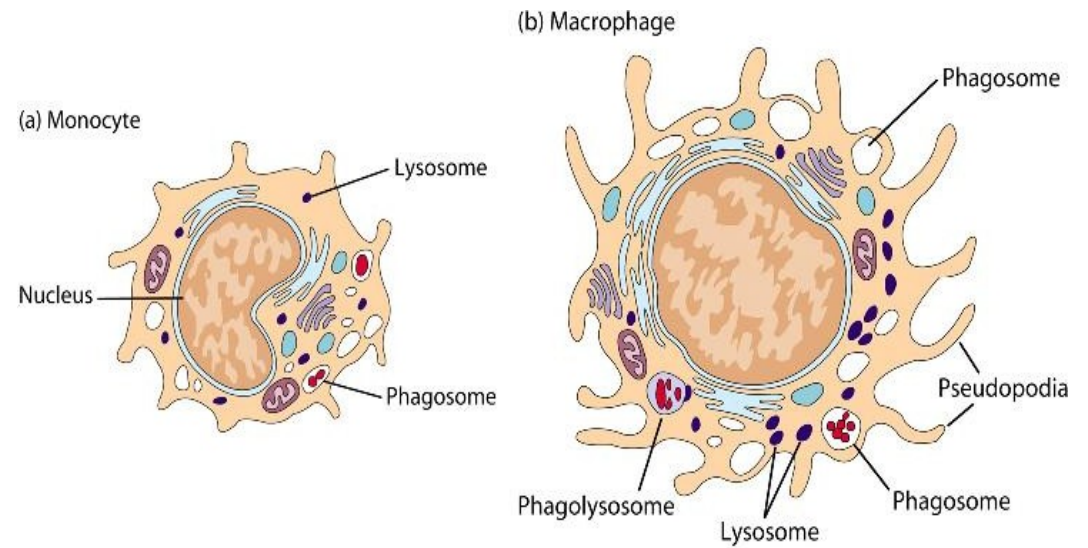
- Phagocytosis itself is an important activating stimulus.

- Macrophages are further activated by cytokines secreted by T helper cells [IFN- gamma], and by mediators of the inflammatory response as well as by various microbial products (such as LPS)



Monocyte

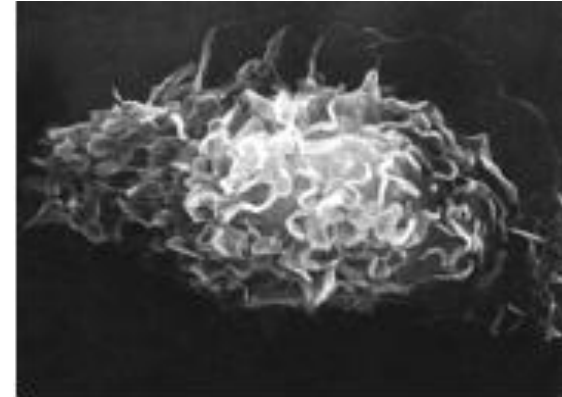
Monocyte vs MΦ



Macrophages

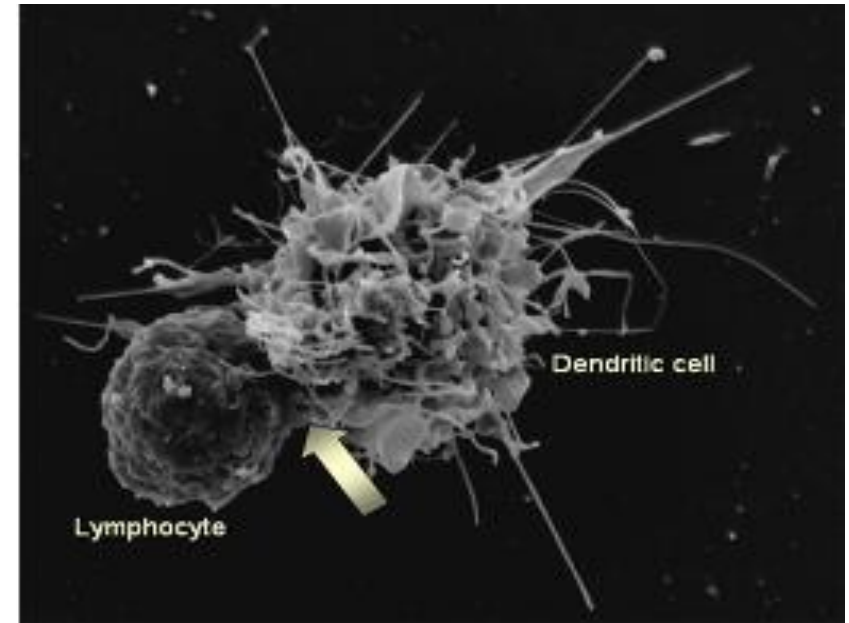
These cells are derived from the bone marrow and have a variety of functions in the immune response:

- Phagocytosis
- Secretion of cytokines
- The cells performing these various functions have differing microscopic appearances but they are grouped together as the mononuclear phagocytic system.

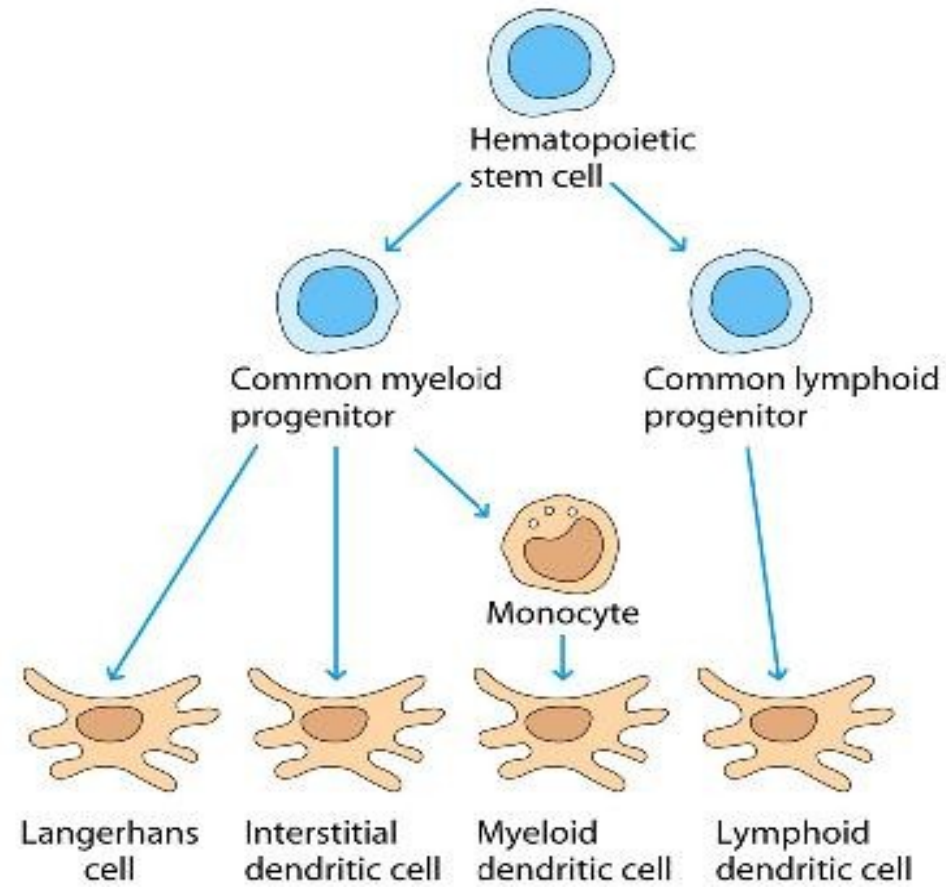


Dendritic Cells

- They are phagocytic cells and originate in the bone marrow
- Act as antigen presenting cells (APC). Can capture antigen or bring it to the lymphoid organs where an immune response is initiated.
- They can be found in the structural compartment of the lymphoid organs as well as in the bloodstreams and other tissues of the body



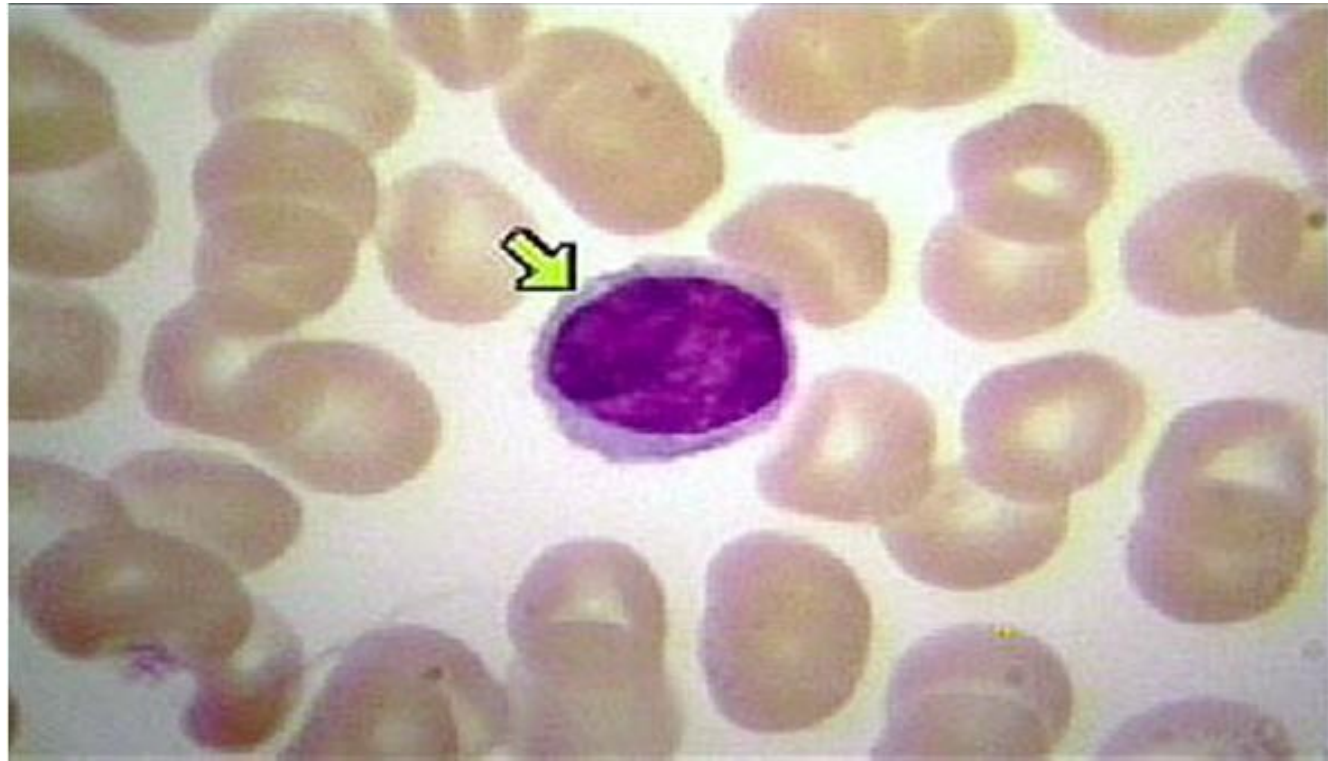
Developmental Pathway of DCs



Lymphocyte

- These cells are responsible for the specific immune response, and represent about 20-40% of circulating WBC. Extravasate and enter the tissues – return 99% of cells in lymph
- Contain a single nucleus, little visible cytoplasm around their nucleus.
- Mainly classified into T-lymphocytes and B-lymphocytes and natural killer cells.
- T and B lymphocytes are small, motile, non-phagocytic cells which cannot be distinguished from each other morphologically.
- Once stimulated with antigen enlarges into a blast cell. Lymphoblasts further differentiate into effector cells [Plasma cells, T-helper cells, T-cytotoxic cells] or memory cells.
- The memory cells are long-lived cells that reside in the G₀ phase of the cell cycle until activated by a secondary encounter with antigen.
- Different lineages or different maturational stages of lymphocytes can be distinguished by their expression of **membrane CD molecules** (Cluster of Differentiation (CD))

Lymphocyte

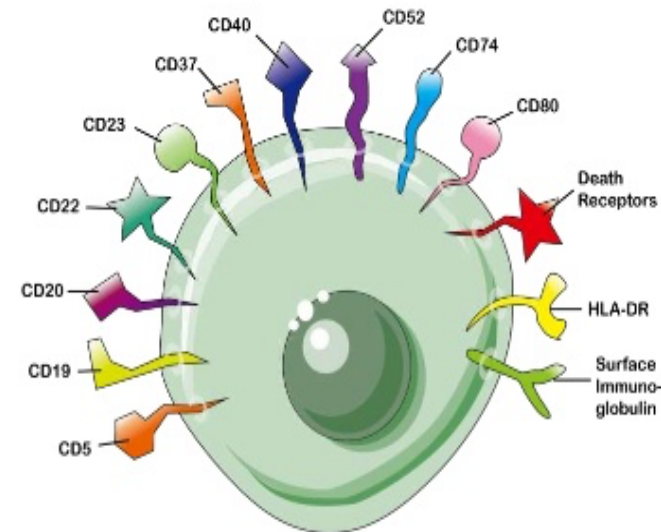


Identifying Cell Using the CD Nomenclature

CD is a collection of antibodies that recognize an antigen found on a particular differentiated cell type or types.

- CD Cluster Of Differentiation
- Over 300 CD Markers
- T cells, CD4 or CD8 and CD3
- B cells, CD19
- NK cells, CD56
- Monocytes/Macrophages CD14
- Dendritic Cells, CD1c (Human), CD11c (mouse)

X What Is Cluster of Differentiation



- 1 Cluster of differentiation (CD) is a surface marker that identifies a particular differentiation lineage recognized by a group of monoclonal antibodies.
- 2 CD antigens are molecules originally defined as being present on the cell surface of leucocytes and recognized by specific antibody molecules, but now including some intracellular molecules and molecules present on cells other than leucocytes.
- 3 Physiologically, CD antigens do not belong in any particular class of molecules.

T Cell Markers

<u>CD Marker</u>	<u>Function</u>	<u>Expressing Cell</u>
CD3	Identifies <u>all</u> T cells, T cell activation	ALL T CELLS
CD4	Identifies T helper cells of all subsets/ binds MHC II	T helper cells
CD8	Identifies Cytotoxic T cells/ binds MHC I	Cytotoxic T cells
CD28	<u>Signal 2 for T cell activation</u> : Receptor for B7 molecules – ligation is necessary to activate T cells.	T cells
CD25	IL-2 α chain: high affinity IL-2 receptor	Activated T cells and Constitutively on T regulatory cells
CD40L	Ligand for CD40: provides signal to B cells to class switch	T cells
CD45RO	Identifies Memory Cells	Memory T cells
CTLA-4	Inhibitory receptor to end the immune response; induces anergy	T cells
PD-1	Inhibitory receptor indicative of cell exhaustion	T cells (CD8)
FasL	Induces apoptosis when binds to Fas on other cells	Cytotoxic T cells

T and B Lymphocytes

T cells:

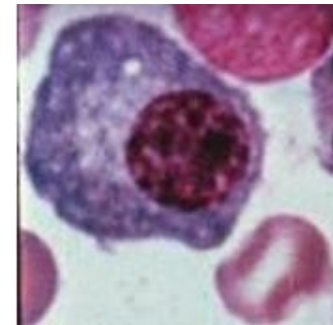
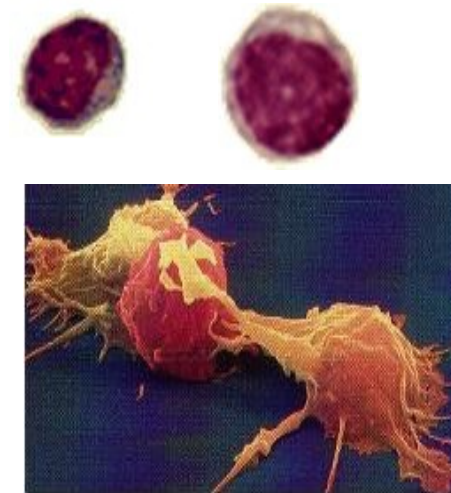
- These cells respond to antigens. Some of them (CD4+) secrete lymphokines which act on other cells involved in the immune response. Others (CD8+, cytotoxic) are able to cause lysis of infected cells.

B Cells

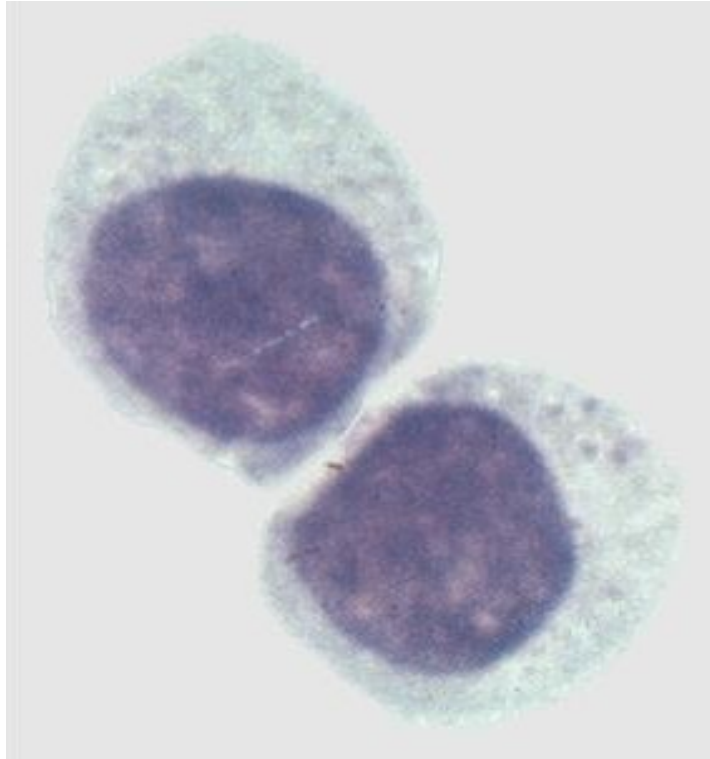
- The major function of B lymphocytes production of antibodies in response to proteins of bacteria, viruses, and tumor cells.

- Antibody production and binding to antigen

Antigen is the foreign substance or antigen, often is critical as a means of signaling other cells to engulf, kill or remove that substance from the body.



Natural killer (NK) cells



- Also known as large granular lymphocytes (LGL)
- Kill virus-infected or transformed cells (Intercellular pathogens).
- It also defend against extracellular pathogens (Bacteria)
- Identified by the CD56+/CD16+/CD3-
- Activated by IL-2 and IFN- γ to become LAK cells

References:

- Abbas, A.K., Lichtman, A.H. and Pillai, S., 2014. *Cellular and molecular immunology E-book*. Elsevier Health Sciences.
- Goldman, A.S. and Prabhakar, B.S., 1996. *Immunology overview*. University of Texas Medical Branch at Galveston, Galveston (TX).
- Abbas, A.K., Lichtman, A.H. and Pillai, S., 2015. *Basic Immunology E-Book: Functions and Disorders of the Immune System*. Elsevier Health Sciences.