Cells, Organs, and Microenvironments of the Immune System

innate immune cells that mount a first line of defense against pathogen, antigen-presenting cells that communicate the infection to lymphoid cells, which coordinate the adaptive response and generate the memory cells, which prevent future infections.

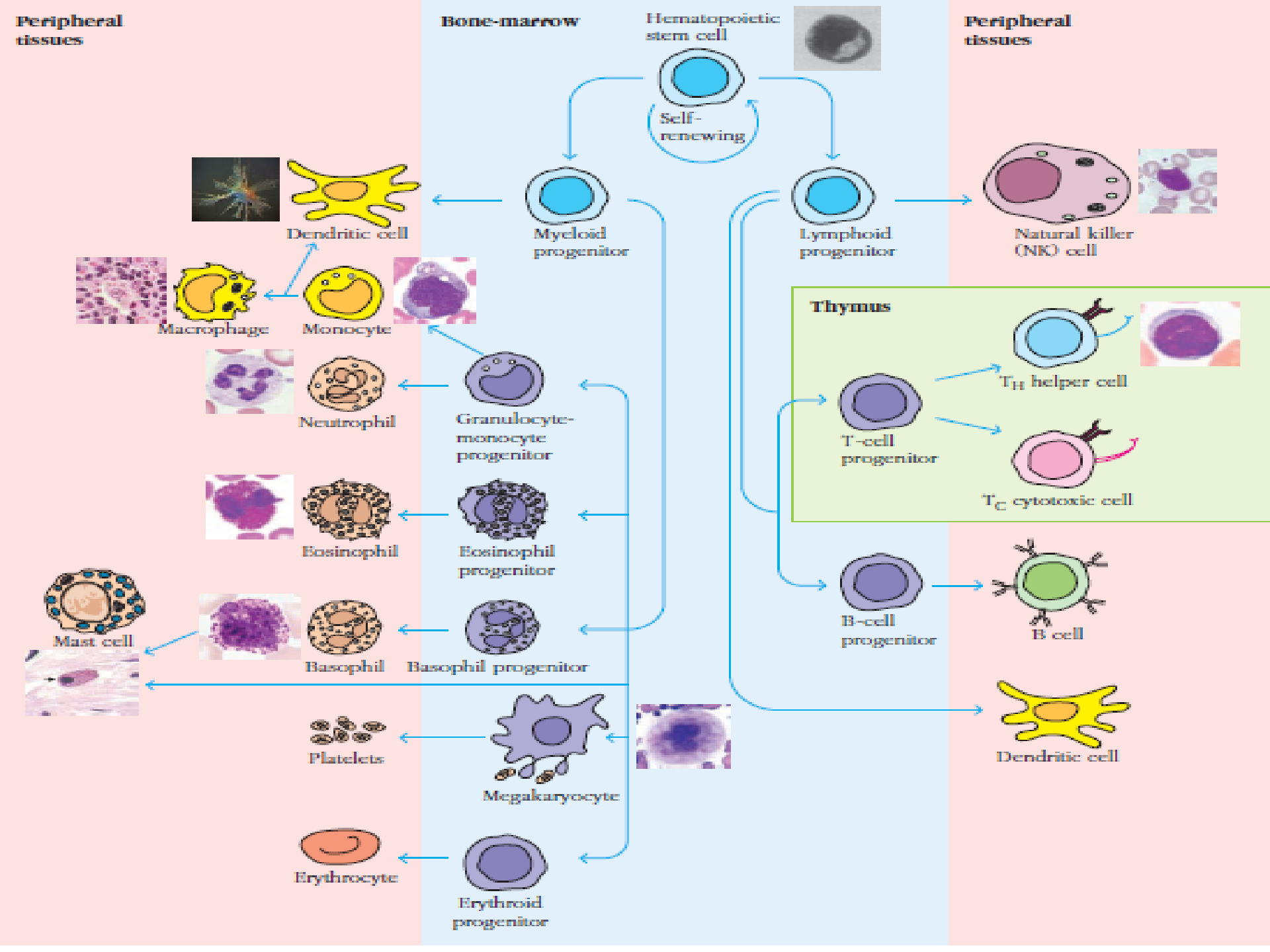
-- **Primary lymphoid organs—** including the bone marrow and the thymus—regulate the development of immune cells from immature precursors.

--**Secondary lymphoid organs—**including the spleen, lymph nodes, and specialized sites in the gut and other mucosal tissues—coordinate the encounter of antigen with antigen-specific lymphocytes and their development into effector and memory cells.

Remarkably, all functionally specialized, mature blood cells (red blood cells, granulocytes, macrophages, dendritic cells, and lymphocytes) arise from a single cell type, the **hematopoietic stem cell (HSC) .**

– The process by which HSCs differentiate into mature blood cells is called **hematopoiesis.**

-- Two primary lymphoid organs are responsible for the development of stem cells into mature immune cells: the bone marrow where HSCs reside and give rise to all cell types; and the thymus, where T cells complete their maturation.


Peripheral tissues
Bone-marrow
Peripheral tissues
Hematopoietic stem cell
Self-renewing
Myeloid progenitor
Lymphoid progenitor
Dendritic cell
Natural killer (NK) cell
Macrophage
Monocyte
Thymus
T_H helper cell
T-cell progenitor
T_C cytotoxic cell
Neutrophil
Granulocyte-monocyte progenitor
Eosinophil
Eosinophil progenitor
B-cell progenitor
B cell
Mast cell
Basophil
Basophil progenitor
Platelets
Megakaryocyte
Dendritic cell
Erythrocyte
Erythroid progenitor

Cells of the Myeloid Lineage Are the First Responders to Infection

Cells that arise from a common myeloid progenitor (CMP)

include red blood cells (erythroid cells) as well as various types of white blood cells (myeloid cells such as granulocytes, monocytes, macrophages, and some dendritic cells).

-- Granulocytes

Granulocytes are at the front lines of attack during an immune response and are considered part of the innate immune system.

Granulocytes are white blood cells (leukocytes) that are classified as neutrophils, basophils, mast cells, or eosinophils on the basis of differences in cellular morphology and the staining of their characteristic cytoplasmic granules.

Neutrophils constitute the majority (50% to 70%) of circulating leukocytes and are much more numerous than eosinophils (1%–3%), basophils (1%), or mast cells (1%). After differentiation in the bone marrow, neutrophils are released into the peripheral blood and circulate for 7 to 10 hours before migrating into the tissues, where they have a life span of only a few days. In response to many types of infections, the number of circulating neutrophils increases significantly and more are recruited to tissues. The resulting transient increase in the number of circulating neutrophils, called **leukocytosis**, is used medically as an indication of infection(phagocytosis).

Neutrophils are the dominant first responders to infection and the main cellular components of pus, where they accumulate at the end of their short lives.

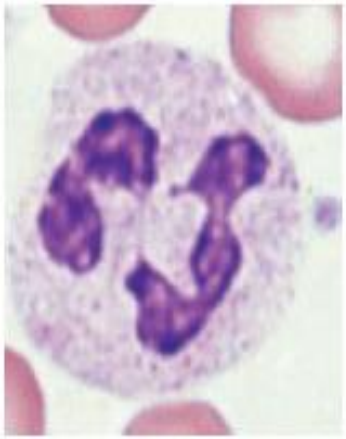
Basophils are non phagocytic granulocytes that contain large granules filled with basophilic proteins (i.e., they stain blue in standard H&E staining protocols).

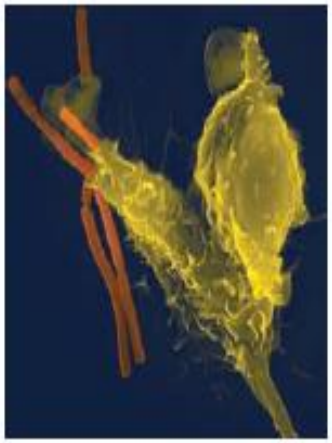
Basophils are relatively rare in the circulation, but can be very potent. In response to binding of circulating antibodies, basophils release the contents of their granules. Histamine, one of the best known proteins in basophilic granules, increases blood vessel permeability and smooth muscle activity.

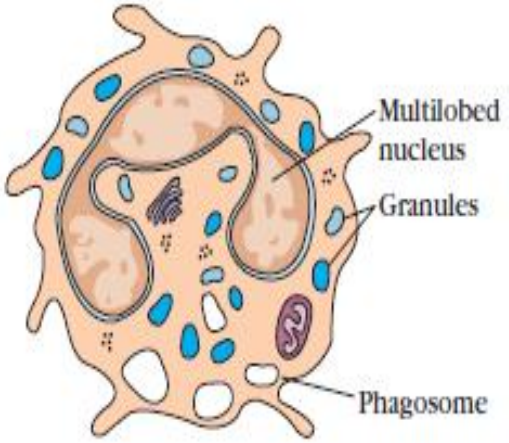
Mast cells : are released from the bone marrow into the blood as undifferentiated cells; they mature only after they leave the blood. Mast cells can be found in a wide variety of tissues, including the skin, connective tissues of various organs, and mucosal epithelial tissue of the respiratory, genitourinary, and digestive tracts. Like circulating basophils, these cells have large numbers of cytoplasmic granules that contain histamine and other pharmacologically active substances. Mast cells also play an important role in the development of allergies.

Eosinophils, like neutrophils, are motile phagocytic cells that can migrate from the blood into the tissue spaces. Their phagocytic role is significantly less important than that of neutrophils, and it is thought that they play their most important role in the defense against multicellular parasitic organisms, including worms. They can be found clustering around invading worms, whose membranes are damaged by the activity of proteins released from eosinophilic granules.

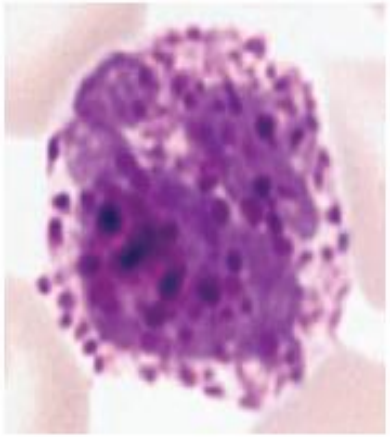
(a) Neutrophil

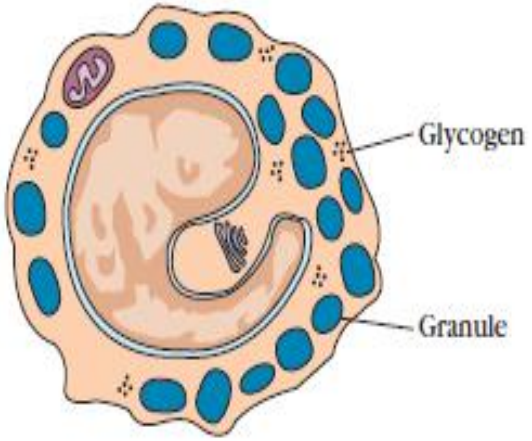




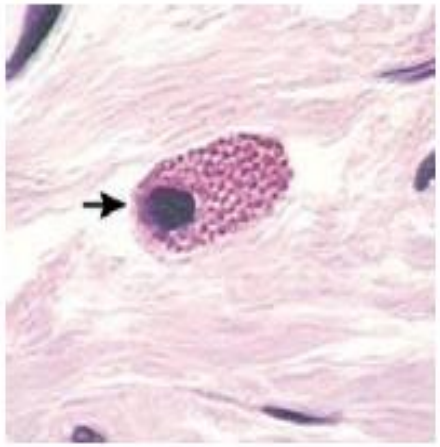


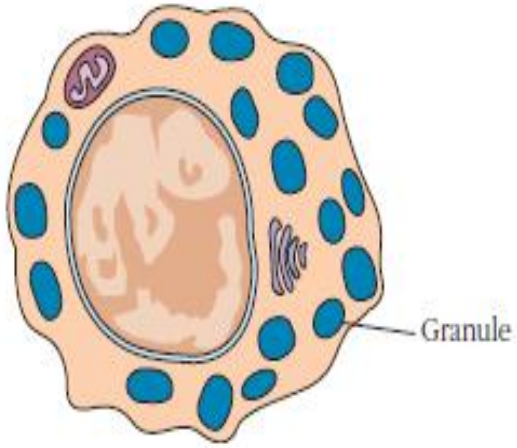
(b) Basophil



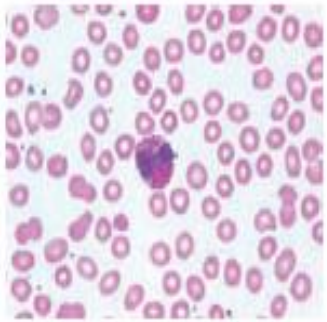


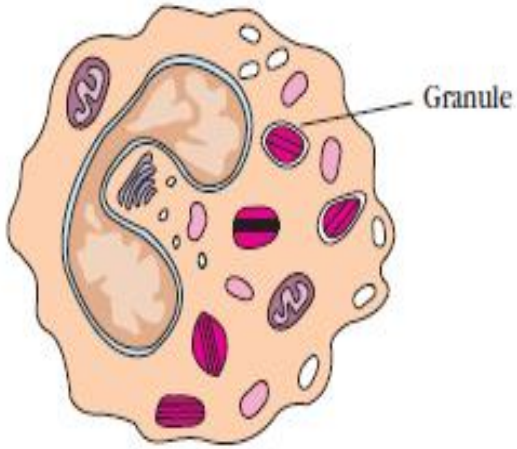
(c) Mast cell





(d) Eosinophil





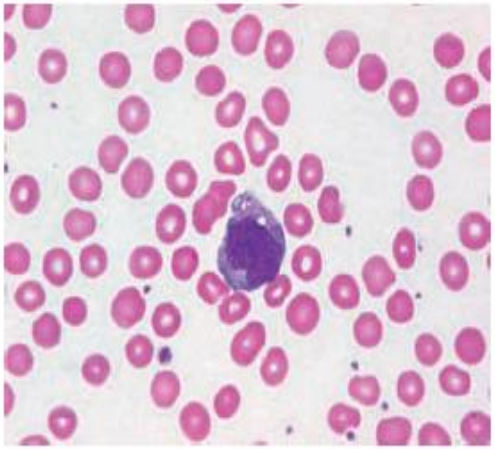
Myeloid Antigen-Presenting Cells

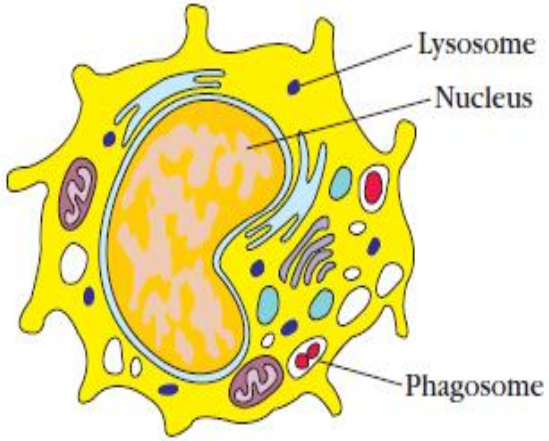
- Myeloid progenitors also give rise to a group of phagocytic cells (monocytes, macrophages, and dendritic cells) that have **professional antigen-presenting cell (APC)** function. Myeloid APCs are considered cellular bridges between the innate and adaptive immune systems because they make contact with a pathogen at the site of infection and communicate this encounter to T lymphocytes in the lymph node ("antigen presentation"). Each APC can respond to pathogens and secrete proteins that attract and activate other immune cells. Each can ingest pathogens via phagocytosis, digest pathogenic proteins into peptides, then present these peptide antigens on their membrane surfaces.

❑ Monocytes

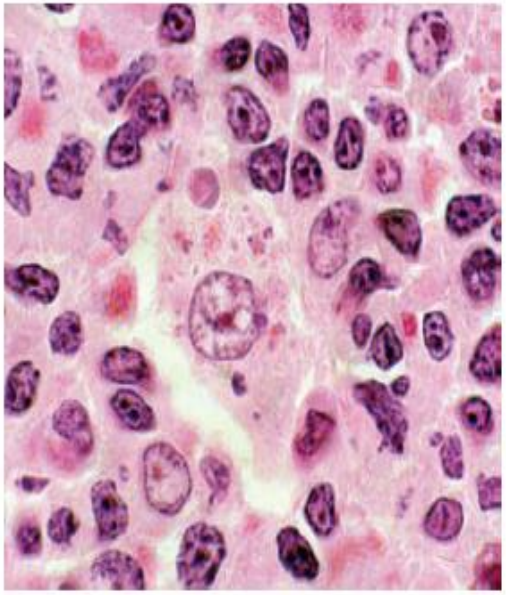
make up about 5% to 10% of white blood cells and are a heterogeneous group of cells that migrate into tissues and differentiate into a diverse array of tissue-resident phagocytic cells, including macrophages and dendritic cells. During hematopoiesis in the bone marrow, granulocyte-monocyte progenitor cells differentiate into promonocytes, which leave the bone marrow and enter the blood, where they further differentiate into mature monocytes. Two broad categories of monocytes have recently been identified. *Inflammatory monocytes* enter tissues quickly in response to infection. *Patrolling monocytes*, a smaller group of cells that crawl slowly along blood vessels, provide a reservoir for tissue-resident monocytes in the absence of infection

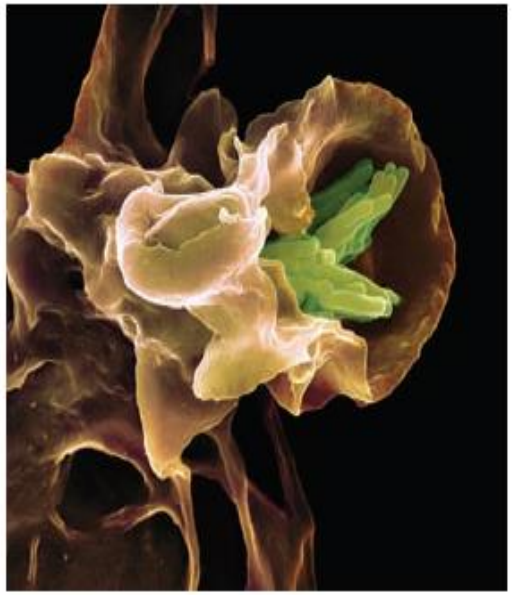
(a) Monocyte

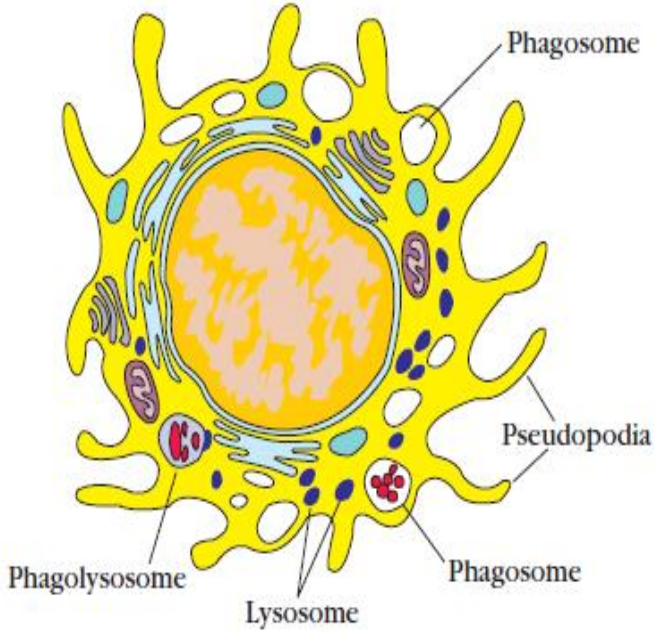




(b) Macrophage



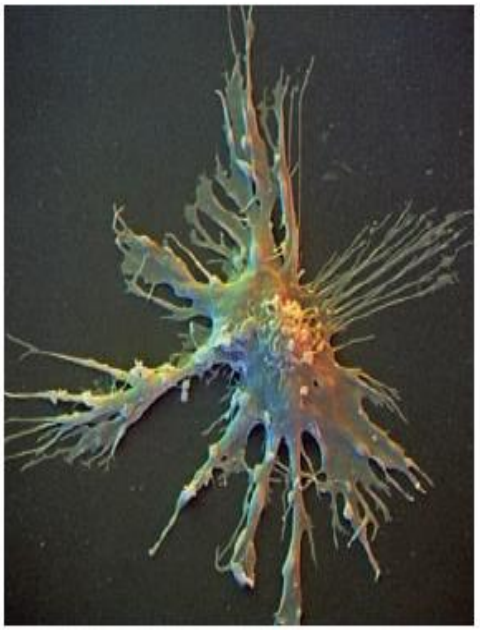


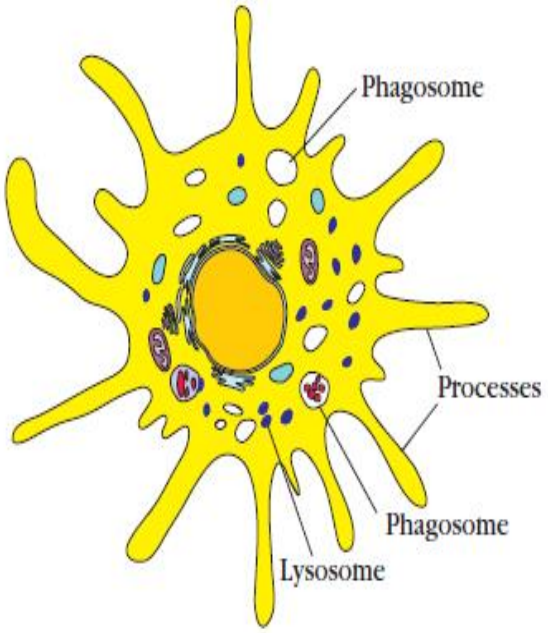


Megakaryocytes :

Megakaryocytes are large myeloid cells that reside in the bone marrow and give rise to thousands of **platelets**, very small cells (or cell fragments) that circulate in the blood and participate in the formation of blood clots. Although platelets have some of the properties of independent cells, they do not have their own nuclei.

(c) Dendritic cell





(d) Megakaryocyte