Unit-2

Unit I: Immunology- Fundamental concepts and anatomy of the immune system; Components of innate and acquired immunity; Phagocytosis; Complement and Inflammatory responses; Haematopoesis; Organs and cells of the immune system- primary and secondary lymphoid organs-Bone marrow, thymus, lymph nodes, spleen; Lymphatic system; Lymphocyte circulation; Lymphocyte homing; Mucosal and Cutaneous associated Lymphoid tissue (MALT and CALT); Mucosal Immunity. Toll-like receptors, inflammation. Antigens - haptens, antigenicity and immunogenicity.

Unit II: Humoral and Cell-Mediated Immune responses, primary and secondary immune modulation, Immunoglobulins: Basic structure, Classes and Subclasses of immunoglobulins, ADCC; antigenic determinants; B and T cell epitopes; B and T cell receptors; Immune responses generated by B and T lymphocytes; activation and differentiation of B and T cells, Memory B cell maturation, activation and differentiation; Cell-mediated effector functions; Functional T Cell Subsets; Cell-mediated immune responses, Cytokines-properties, receptors and therapeutic uses. Structure and function of antibody molecules; Multigene organization of immunoglobulin genes; Immunoglobulin superfamily; Generation of antibody diversity.

Unit III: Major Histocompatibility Complex - MHC genes, MHC and immune responsiveness and disease susceptibility, HLA typing; MHC molecules, antigen processing and presentation, endogenous antigens, exogenous antigens, non-peptide bacterial antigens and super-antigens.

Unit IV: Antigen-antibody interactions- Kinetics of immune response; Precipitation, agglutination and complement mediated immune reactions; Advanced immunological techniques; RIA, ELISA, Western blotting, ELISPOT assay, immunofluorescence, flow cytometry and immunoelectron microscopy; Surface plasmon resonance, Biosenor assays for assessing ligand–receptor interaction, CMI techniques- lymphoproliferation assay, Mixed lymphocyte reaction, Cell Cytotoxicity assays, Apoptosis, Microarrays.

Unit V: Clinical Immunology: Immunity to Infection Hypersensitivity – Type I-IV; Autoimmunity; Types of autoimmune diseases; Mechanism and role of CD4+ T cells; MHC and TCR in autoimmunity; Treatment of autoimmune diseases; Transplantation immunology– Immunological basis of graft rejection; congenital and acquired immunodeficiencies. Cancer: Tumor immunology; Oncogenes, Tumor Suppressor Genes; Immune response to tumors and tumor evasion of the immune system.

PAPER- III (BCH 303) **MAX.MARKS – 100**

IMMUNOLOGY

UNIT-I The biochemical basis of immunology- Innate immunity, Specific acquired immunity, Immunoglobulin Classification, structure and biochemical basis of function, variable domain bind antigen, MHC, T-cells, B-cells, receptors. Antigens haptens, recognition of antigen – primary interaction its detection and application.

UNIT –II Major Histocompatibility Complex (MHC) Genes and product- Polymorphism of MHC genes, Role of MHC antigens in immune Reponses, MHC antigens in transplantation.

UNIT- III Measurement of antigen-antibody interactions – Production of polyclonal and monoclonal antibodies: Principles techniques and applications. Agglutination and precipitation techniques, RIA, ELISA, IRMA, immunofluorescence assays. Measurement of T cell activation.

UNIT-IV Acquired immune response: consequences of antigens recognition, product effectors and its control development, adversial strategies, and immunodeficiency. Elementary knowledge of hypersensitivity.

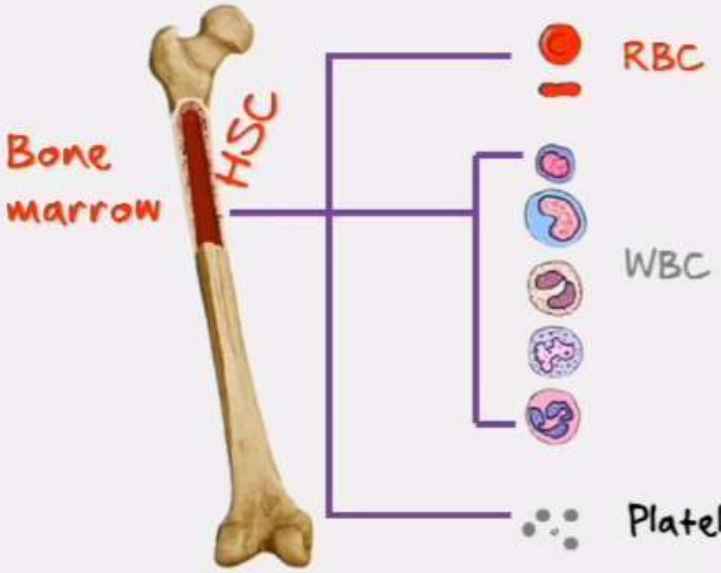
UNIT- V Disorders of immune responses – Autoimmunity, congenital immunodeficiencies, acquired immunodeficiencies, Immune responses to infectious diseases, role of vaccines in the prevention of diseases.

Haematopoiesis

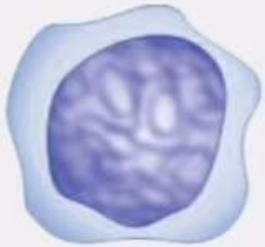
Blood ← Haemato

Poiesis → Formation

The process of formation of blood cells are known as haematopoiesis.



What are haematopoietic stem cells?



Haematopoietic stem cells

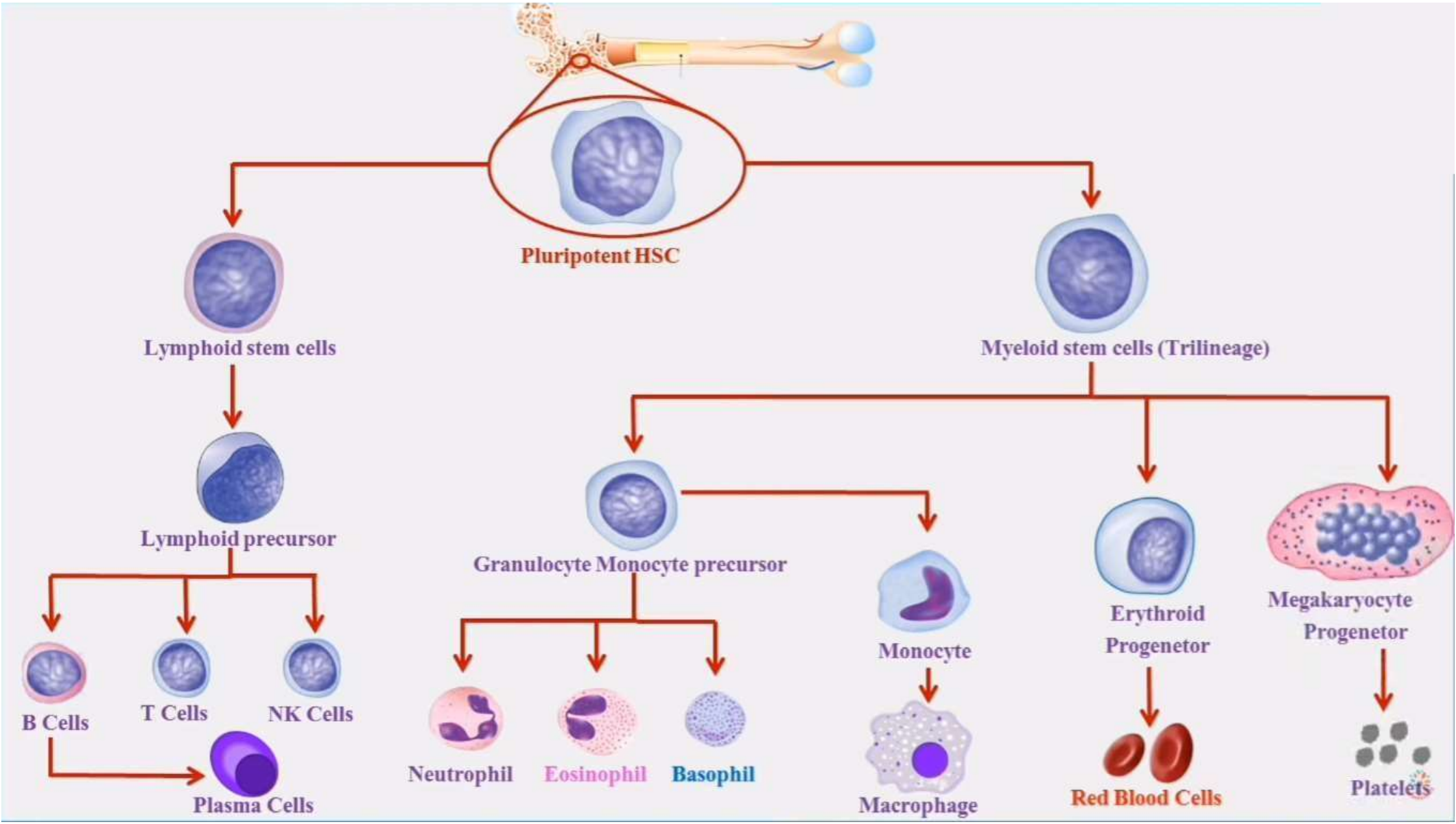
Blood Cells

Haematopoiesis

- Haematopoiesis is the formation of blood cellular components.
- All cellular blood components are derived from haematopoietic stem cells.
- In a healthy adult person, approximately 10^{11}–10^{12} new blood cells are produced daily in order to maintain steady state levels in the peripheral circulation.

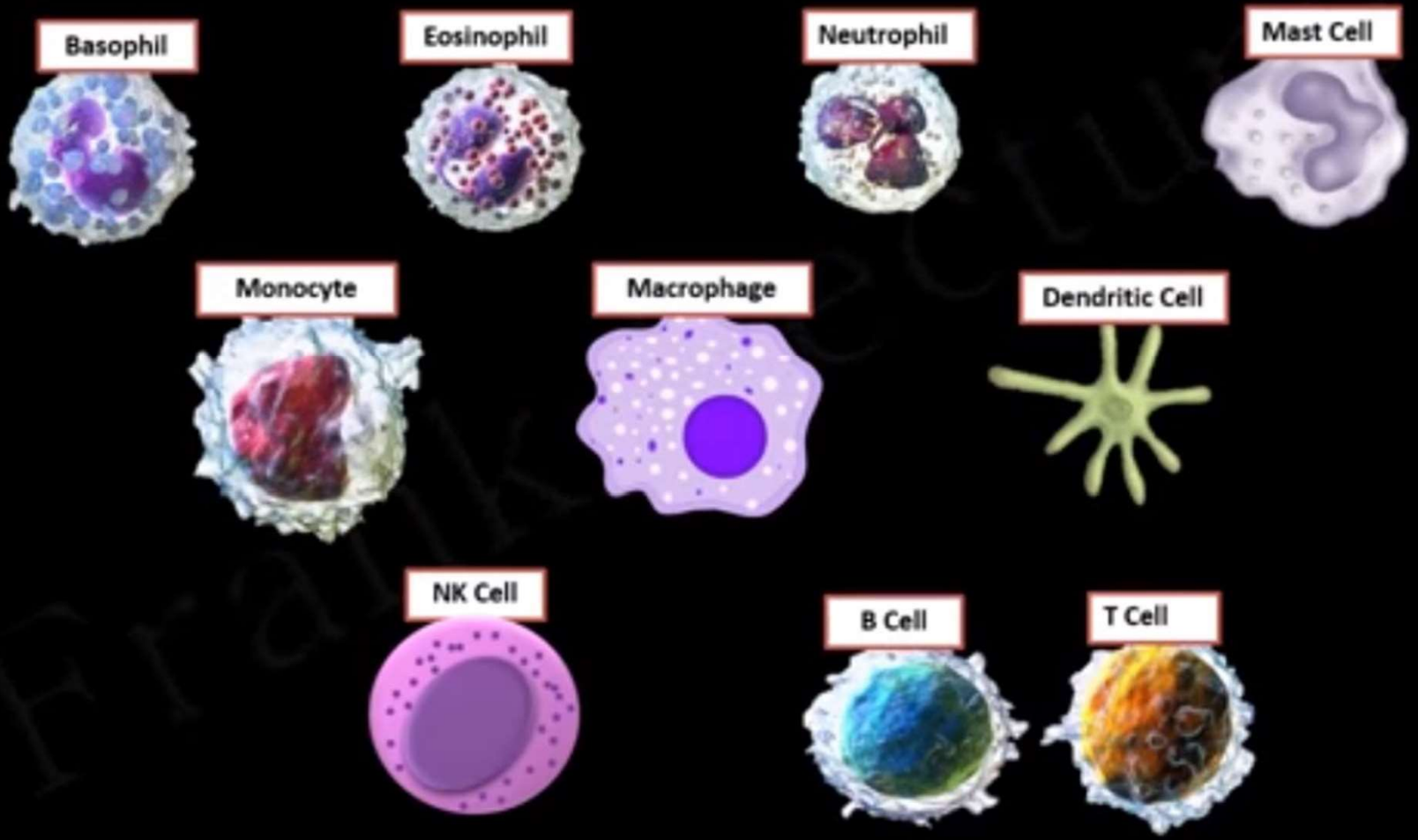
- **Haematopoietic stem cells (HSCs)**
  - Haematopoietic stem cells (HSCs) reside in the medulla of the bone (**bone marrow**) and have the unique ability to give rise to all of the different mature blood cell types and tissues.
  - **HSCs are self-renewing cells**: when they proliferate, at least some of their daughter cells remain as HSCs, so the pool of stem cells is not depleted.This phenomenon is called asymmetric division.

- The other daughters of HSCs (myeloid and lymphoid progenitor cells) can follow any of the other differentiation pathways that lead to the production of one or more specific types of blood cell, but cannot renew themselves.
- The pool of progenitors is heterogeneous and can be divided into two groups;
- long-term self-renewing HSC and
- short-terms self-renewing HSC.


Pluripotent HSC
Lymphoid stem cells
Myeloid stem cells (Trilineage)
Lymphoid precursor
Granulocyte Monocyte precursor
B Cells
T Cells
NK Cells
Plasma Cells
Neutrophil
Eosinophil
Basophil
Monocyte
Macrophage
Erythroid Progenetor
Red Blood Cells
Megakaryocyte Progenetor
Platelets

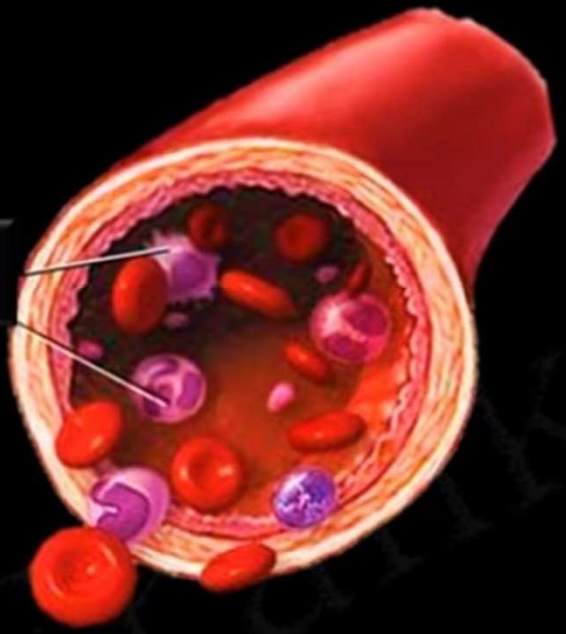
- All blood cells are divided into three lineages.
  - **Erythroid cells** are the oxygen carrying red blood cells. Both reticulocytes and erythrocytes are functional and are released into the blood. In fact, a reticulocyte count estimates the rate of **erythropoiesis.**
  - **Lymphocytes** are the cornerstone of the adaptive immune system. They are derived from common lymphoid progenitors. The lymphoid lineage is primarily composed of T-cells and B-cells (types of white blood cells). This is **lymphopoiesis**.
  - **Myelocytes**, which include granulocytes, megakaryocytes and macrophages and are derived from common myeloid progenitors, are involved in such diverse roles as innate immunity, adaptive immunity, and blood clotting. This is **myelopoiesis**.
- **Granulopoiesis** (or granulocytopoiesis) is haematopoiesis of granulocytes.
- **Megakaryocytopoiesis** is haematopoiesis of megakaryocytes.

Cells of the Immune System

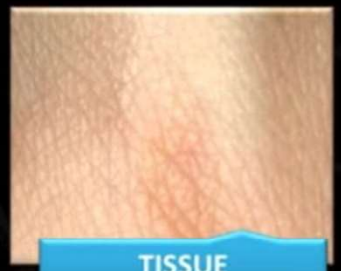


Cells of the Immune System

WBCs

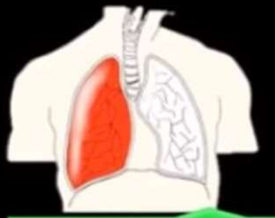


FIXED MACROPHAGES

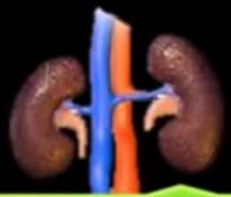


TISSUE MACROPHAGES

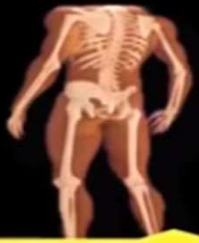
MICROGLIAL CELLS



ALVEOLAR MACROPHAGES



MESANGIAL CELLS



OSTEOCLASTS

KUPFFER CELLS

CYTOKINES

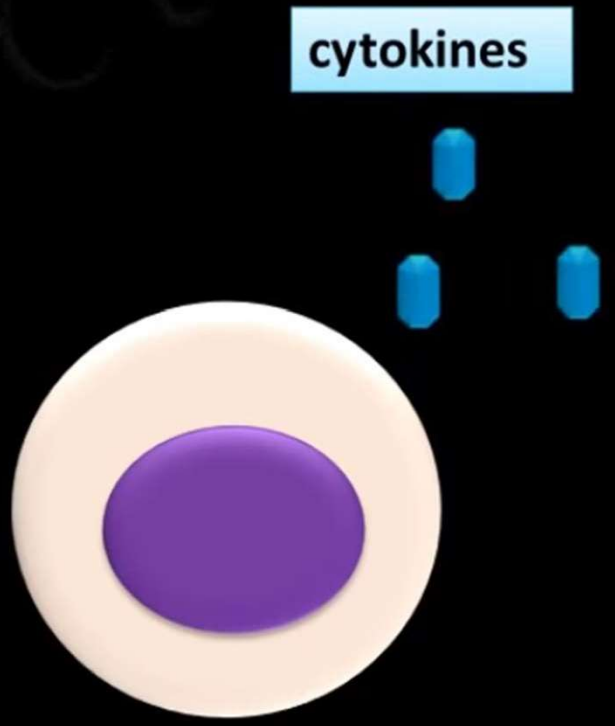
- Hormone-like substances
- Soluble molecules, some are membrane bound molecules

CYTOKINES

- Hormone-like substances
- Soluble molecules, some are membrane bound molecules
- Chemically they can be protein or glycoprotein
- Molecular mass is less than 30kDa

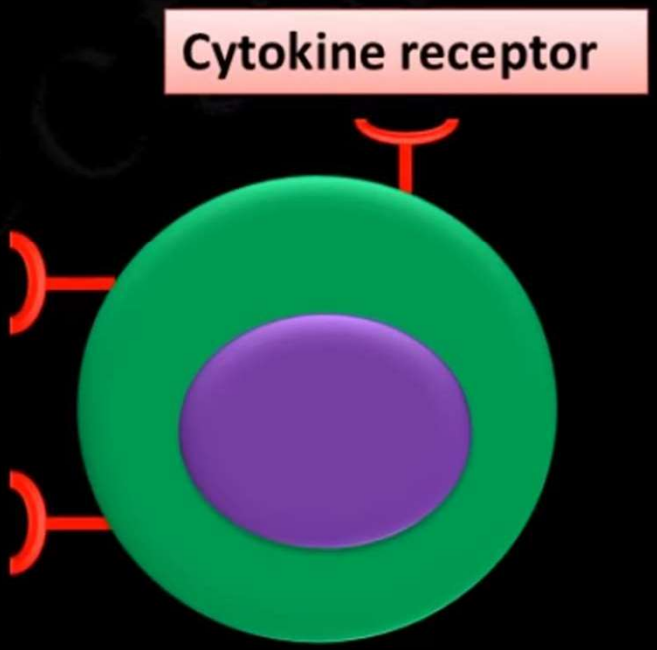
CYTOKINES

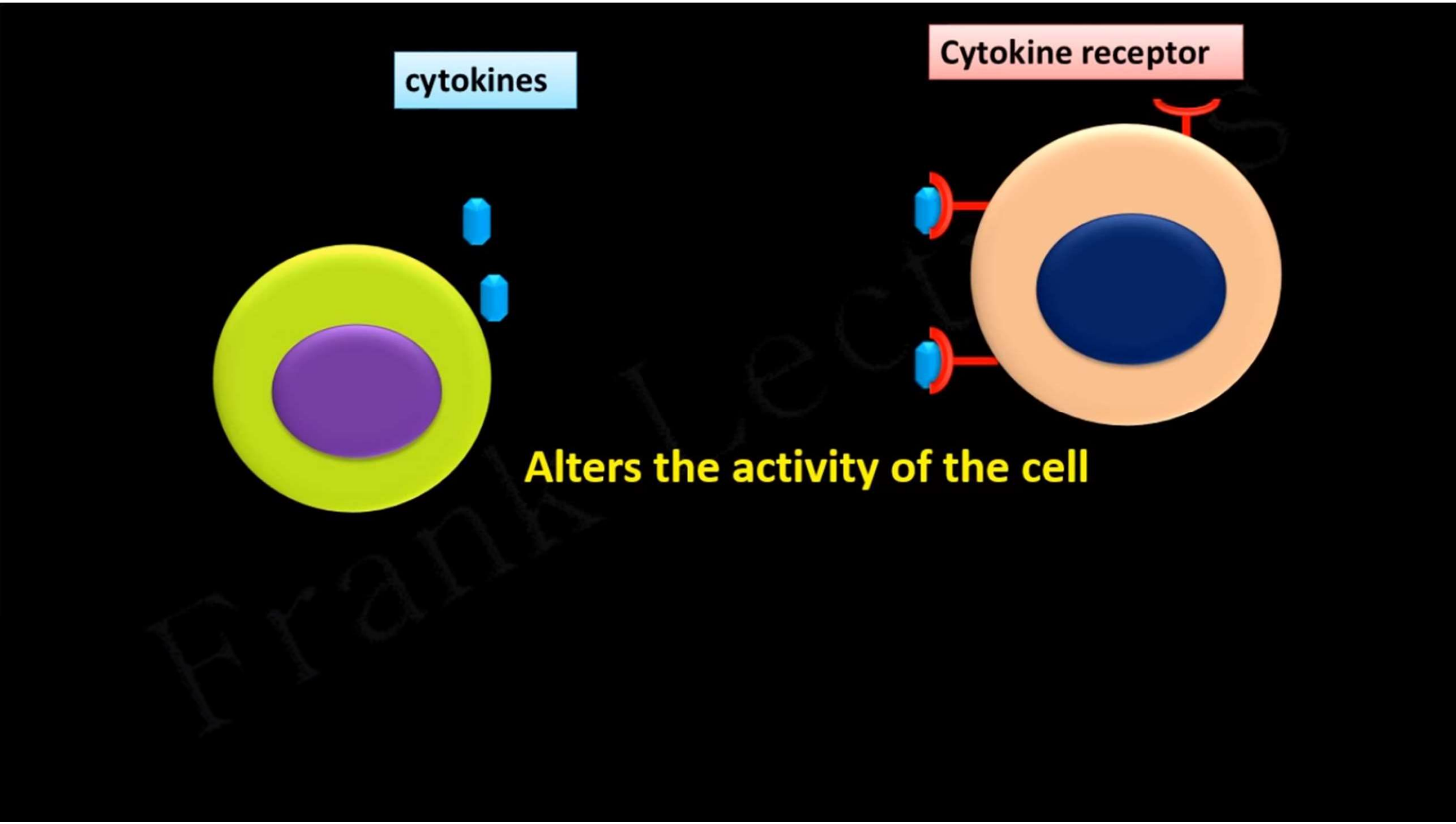
- Produced and secreted by wide variety of cells
- Act as intercellular mediators

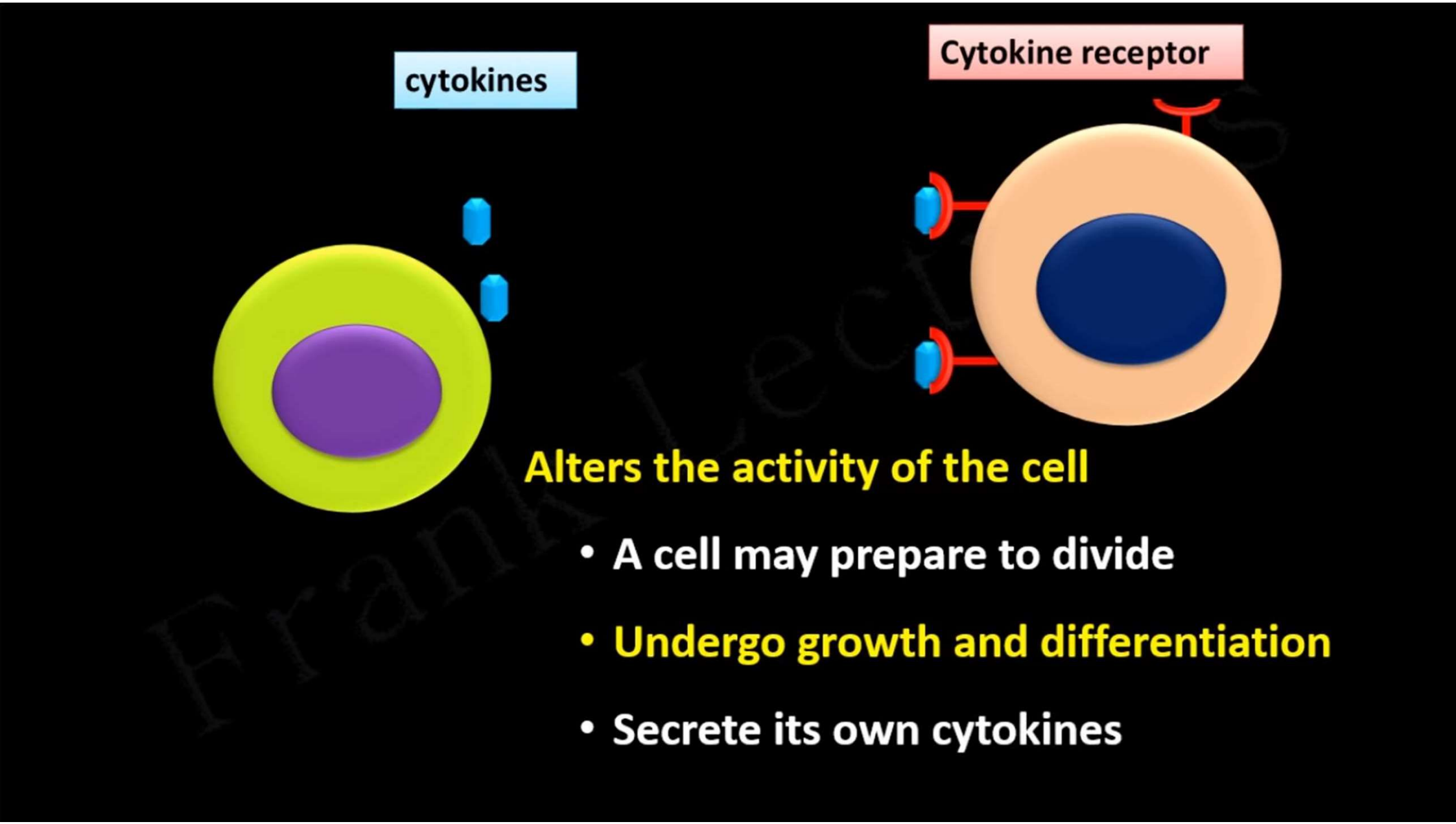


CYTOKINES

- Cytokines bind to specific receptors on the surface of other cells.




cytokines
Cytokine receptor
Alters the activity of the cell


cytokines
Cytokine receptor
Alters the activity of the cell
• A cell may prepare to divide
• Undergo growth and differentiation
• Secrete its own cytokines

CYTOKINES

- INTERLEUKINS
- TUMOR NECROSIS FACTOR
- INTERFERONS
- COLONY- STIMULATING FACTORS
- CHEMOKINES

INTERLEUKINS (ILs)

- In Latin, "inter" means between and In Greek "leukos" means white
- Cytokines produced by one leukocyte acting on another leucocyte.
- Though cells other than leukocytes may also use interleukins.

INTERLEUKINS (ILs)

- About 35 interleukins have been identified

- They are named interleukin (IL) followed by number which represents sequence in which they were discovered (IL-1 to IL-35)

COLONY-STIMULATING FACTORS (CSFs)

- Essential for the growth and differentiation of immature leukocytes in the bone marrow i.e. red blood cells, monocytes, granulocytes and lymphocytes

- Ensure that the body is supplied with sufficient white blood cells of all types

INTERLEUKINS (ILs)

- In Latin, "inter" means between and In Greek "leukos" means white
- Cytokines produced by one leukocyte acting on another leucocyte.
- Though cells other than leukocytes may also use interleukins.

INTERLEUKINS (ILs)

- About 35 interleukins have been identified

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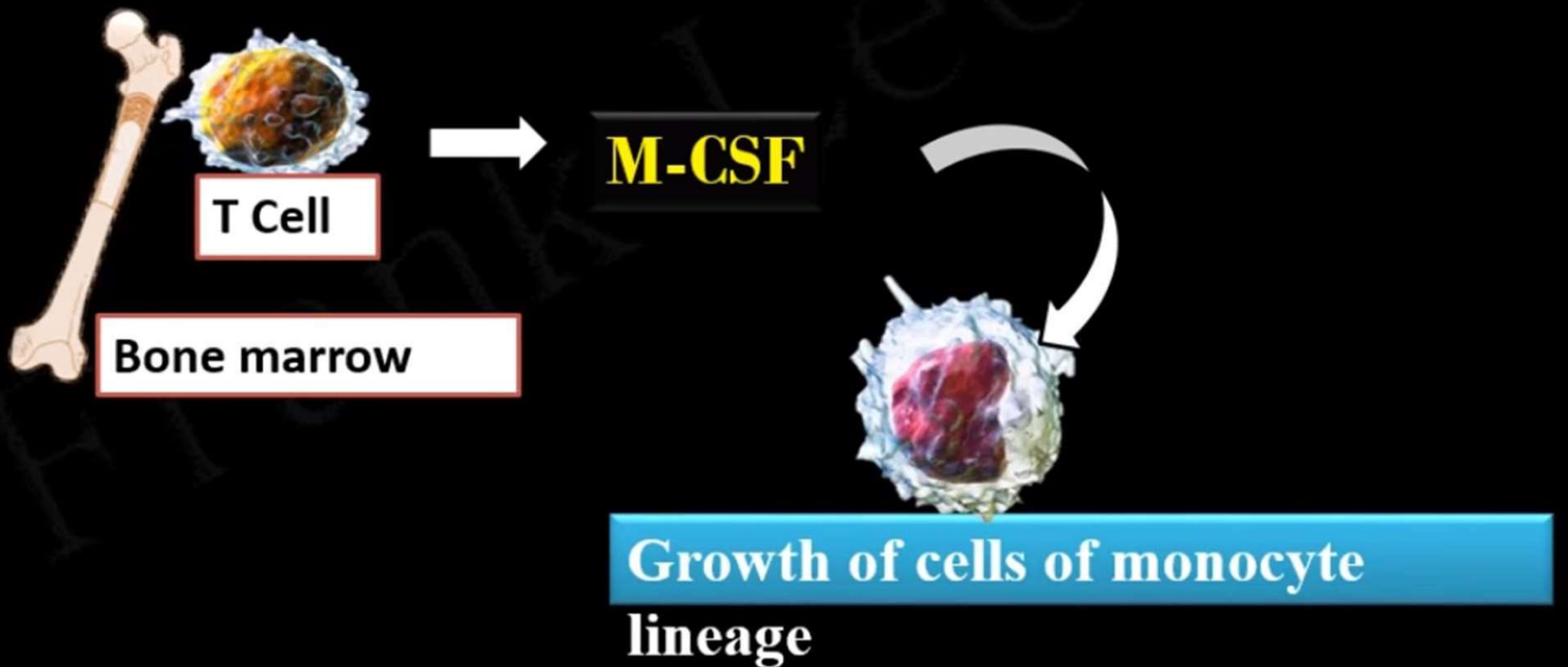
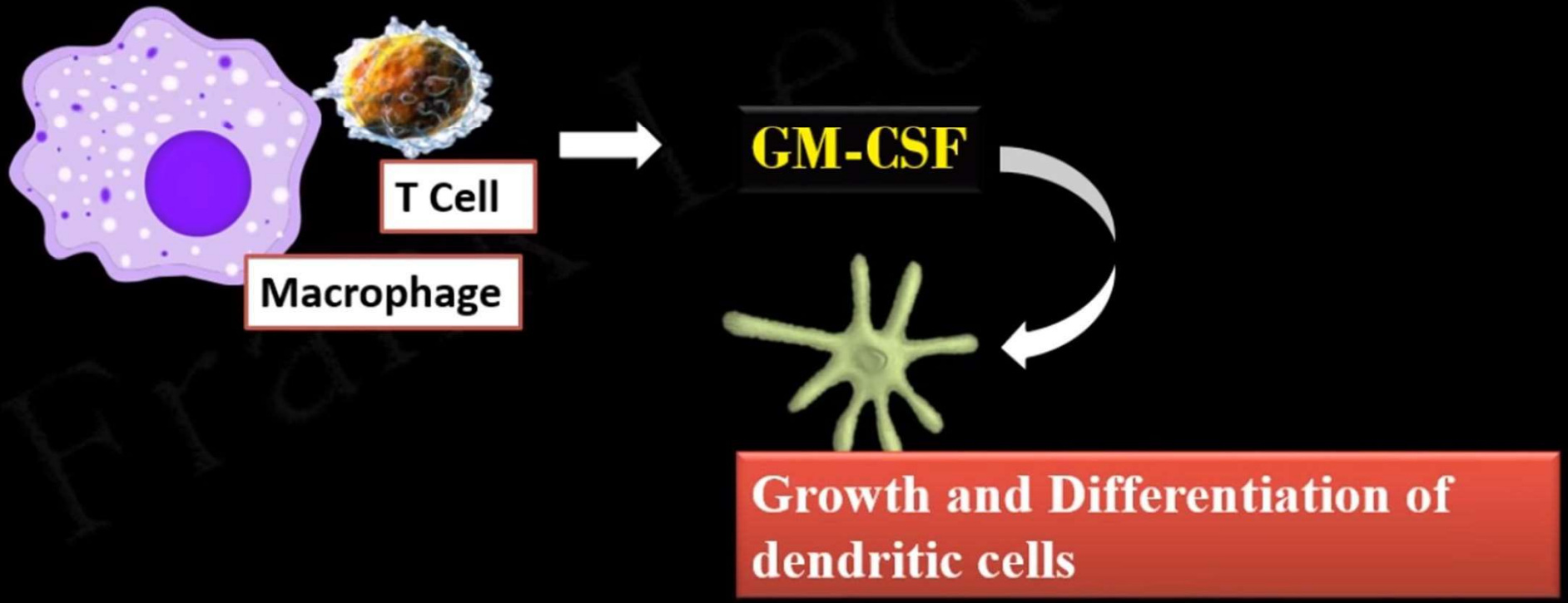
COLONY-STIMULATING FACTORS (CSFs)

- **M-CSF**: Monocyte colony-stimulating factor



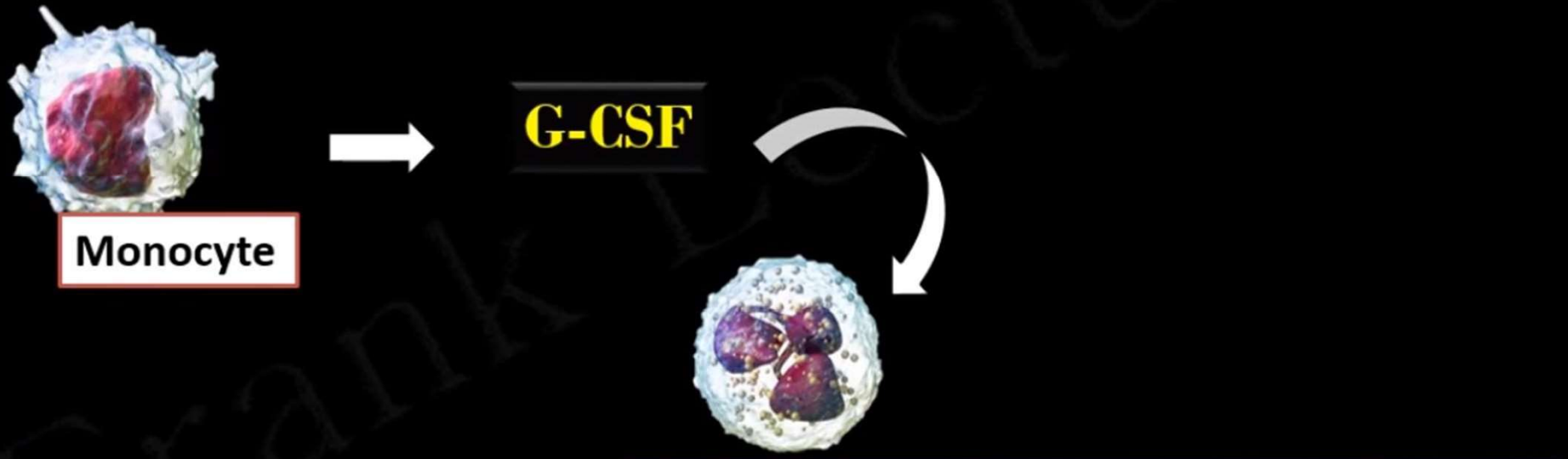
COLONY-STIMULATING FACTORS (CSFs)

- **GM-CSF**: Granulocyte Macrophage colony-stimulating factor



COLONY-STIMULATING FACTORS (CSFs)

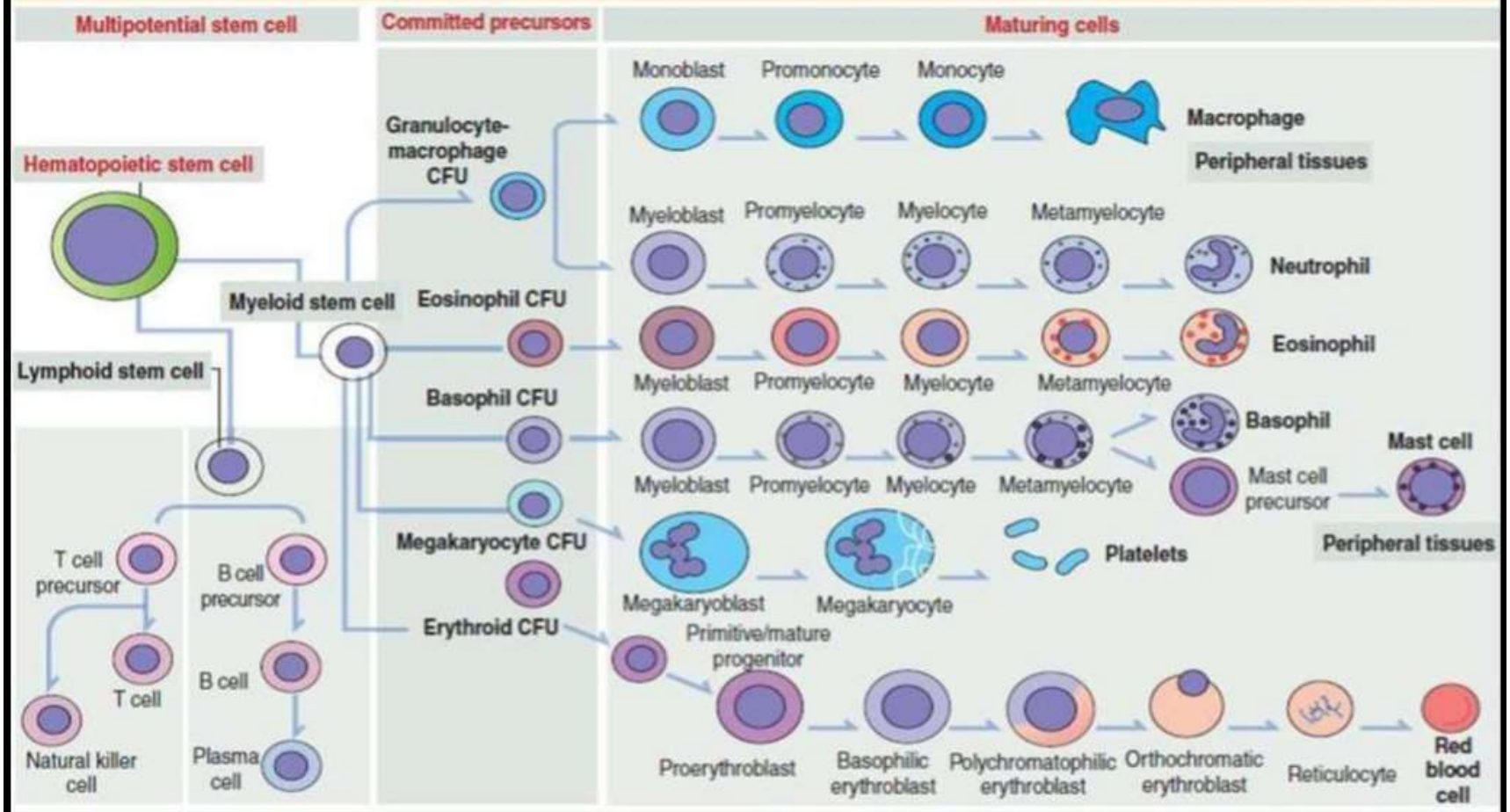
- **G-CSF**: Granulocyte colony-stimulating factor



M-CSF (CSF-1)	Endothelial cells Fibroblasts Macrophages Placenta T cells	Stimulates macrophage differentiation Important for maintenance of mature monocyte function
Erythropoietin	Kidney (?endothelium) Liver	Stimulates erythropoiesis No effect on more primitive progenitors
Interleukin 5 (IL-5)	T cells	Stimulates production of eosinophils Induces terminal B-cell differentiation
G-CSF	Endothelial cells Macrophages Epithelial cells Fibroblasts Neutrophils	Stimulates production of neutrophils Predominantly acts late in hierarchy of development with strong maturational effects
GM-CSF	Endothelial cells Fibroblasts Macrophages T cells NK cells	Stimulates production of neutrophils, macrophages, eosinophils Predominately induces proliferation and differentiation of early myeloid progenitors
Interleukin 3 (IL-3) (multi-CSF)	T cells NK cells	Stimulates production of neutrophils, monocytes, eosinophils, basophils, and platelets Predominately induces proliferation and differentiation of early myeloid progenitors

TABLE 1 Hematopoietic Growth Factors

Figure 6-16. Hematopoietic branching lineage tree



The bone marrow consists of: (1) **Hematopoietic stem cells (HSCs)**, multipotential cells capable of self-renewal. (2) **Committed precursor cells (myeloid stem cell and lymphoid stem cell)**. (3) **Maturing cells**. Maturing cells develop from cells called **colony-forming units (CFUs)**. The **myeloid stem cell** gives rise to CFUs responsible for the regeneration of red blood cells (**erythroid CFUs**), platelets (**megakaryocyte CFUs**), basophils and mast cells (**basophil CFUs**), and eosinophils (**eosinophil CFUs**). Monocytes and neutrophils derive from a common committed progenitor cell (**granulocyte-macrophage CFU**). The **lymphoid stem cell** generates the **B cell progeny** in the **bone marrow** and **T cell progenies** in the **thymus**. They are discussed in detail in Chapter 10, Immune-Lymphatic System.