(Haematopoiesis)

Haematopoiesis :- is the complex biological process responsible for the continuous production of blood cells throughout life. It ensures the maintenance of adequate numbers of erythrocytes, leukocytes, and platelets, which are essential for oxygen transport, immune defense, and hemostasis. This process is highly regulated by a network of growth factors, cytokines, and transcriptional controls that guide the proliferation, differentiation, and maturation of hematopoietic stem and progenitor cells.

Or

Haematopoiesis :- is defined as the formation and development of all types of blood cells from multipotent hematopoietic stem cells (HSCs). The process involves a hierarchy of progenitor cells that progressively lose self-renewal capacity while acquiring lineage-specific characteristics.

Note: - In healthy adults, approximately **10^{11} to 10^{12} new blood cells** are produced each day to replace aged or damaged cells.

There are two main types of haematopoiesis:

- **Myelopoiesis:** production of erythrocytes, granulocytes, monocytes, and platelets.
- **Lymphopoiesis:** production of B and T lymphocytes, and natural killer (NK) cells

Sites of Haematopoiesis

Haematopoiesis occurs in different anatomical sites throughout development, a process known as **ontogeny of haematopoiesis**.

a. Embryonic Haematopoiesis:

- **Yolk sac stage (2–3 weeks of gestation):** Primitive erythropoiesis begins with the formation of nucleated erythroblasts.
- **Hepatic stage (6 weeks–7 months):** The liver becomes the primary hematopoietic organ; both erythroid and myeloid lineages develop here. The spleen and thymus also contribute.
- **Bone marrow stage (after 7 months):** The bone marrow gradually becomes the dominant hematopoietic tissue and remains so after birth.

Adult Haematopoiesis:-

In adults, haematopoiesis is confined mainly to the **red bone marrow** of the axial skeleton—vertebrae, ribs, sternum, pelvis, and proximal ends of long bones. With age, much of the marrow converts to inactive **yellow marrow** containing adipose tissue. Under stress conditions (e.g., severe anemia or marrow failure), **extramedullary haematopoiesis** may occur in the liver and spleen.

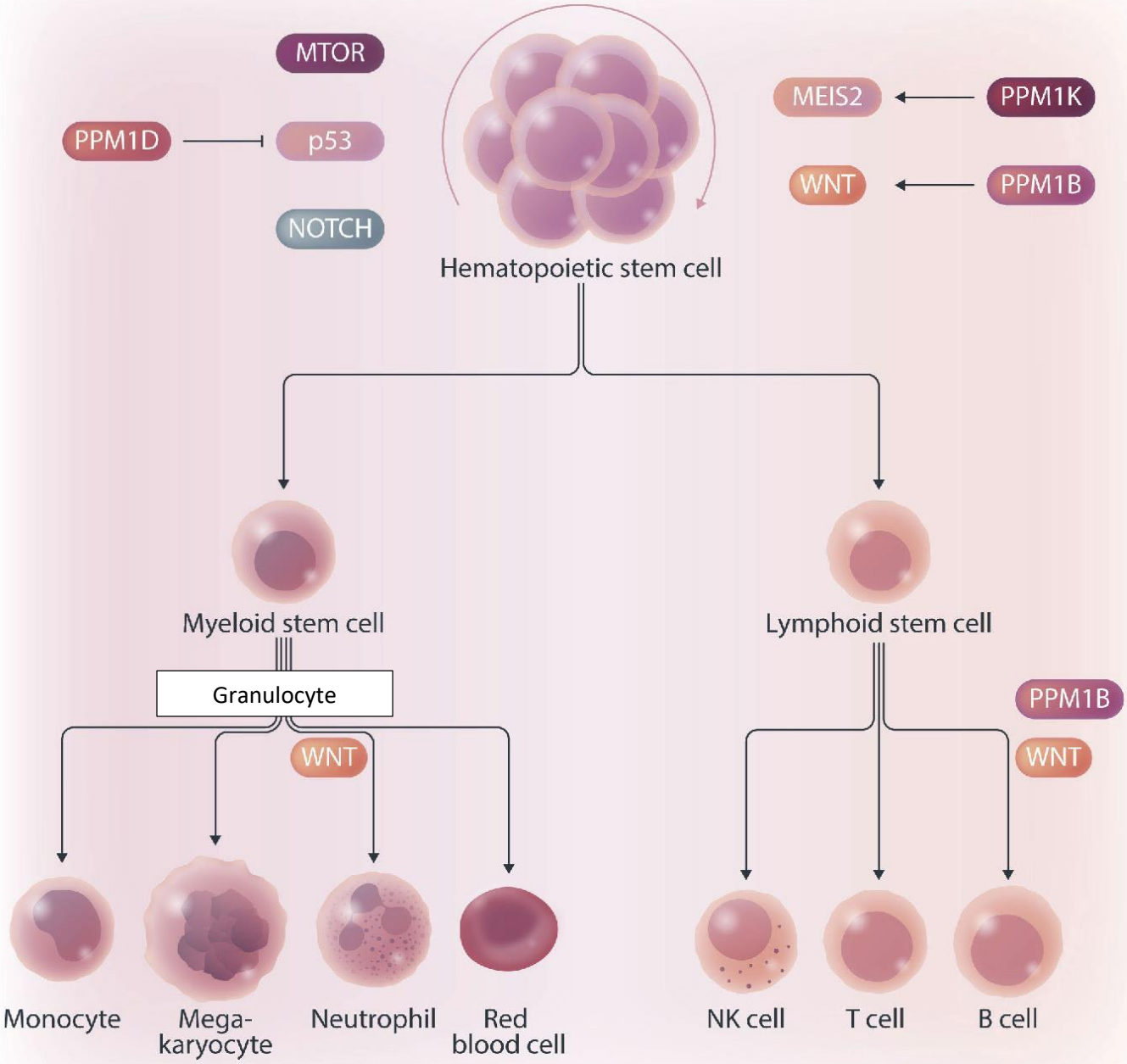
4. Hematopoietic Stem Cells and Differentiation Hierarchy

The foundation of the hematopoietic system is the **hematopoietic stem cell (HSC)**, characterized by its abilities for **self-renewal** and **multipotency**. HSCs give rise to two main progenitor types:

1. **Common Myeloid Progenitor (CMP):** Generates erythrocytes, megakaryocytes (platelets), granulocytes, and monocytes.
2. **Common Lymphoid Progenitor (CLP):** Produces B cells, T cells, and NK cells.

Differentiation follows a hierarchical pattern from HSCs → multipotent progenitors → committed progenitors → precursor cells → mature blood cells.

This process is regulated by a specialized bone marrow microenvironment called the **stem cell niche**, composed of stromal cells, fibroblasts, endothelial cells, and extracellular matrix components.


MTOR
PPM1D
p53
NOTCH
Hematopoietic stem cell
MEIS2
PPM1K
WNT
PPM1B
Myeloid stem cell
Lymphoid stem cell
Granulocyte
WNT
PPM1B
WNT
Monocyte
Mega-
karyocyte
Neutrophil
Red
blood cell
NK cell
T cell
B cell

Regulation of Haematopoiesis

Haematopoiesis is controlled by a balance between intrinsic genetic programs and extrinsic regulatory signals.

Intrinsic regulation:

Transcription factors such as **GATA-1**, **PU.1**, **RUNX1**, and **TAL1** direct lineage-specific gene expression. Mutations in these factors can lead to dysregulated differentiation and hematologic malignancies.

Extrinsic regulation:

Cytokines and cell-to-cell interactions within the bone marrow microenvironment maintain the equilibrium between stem cell quiescence, proliferation, and differentiation.

Clinical Correlations

Disruptions in haematopoiesis lead to a variety of **hematologic disorders**, many of which are diagnosed through laboratory investigations:

- **Aplastic anemia:** Failure of bone marrow stem cells, leading to pancytopenia.
- **Leukemia:** Malignant transformation of progenitor cells causing uncontrolled proliferation and accumulation of immature blasts.
- **Myelodysplastic syndromes:** Ineffective hematopoiesis with abnormal cell morphology.
- **Polycythemia vera:** Overproduction of erythrocytes due to JAK2 mutation.
- **Bone marrow suppression:** May result from chemotherapy, radiation, or toxic exposure.

Laboratory professionals play a key role in evaluating haematopoietic function through **complete blood counts (CBCs)**, **bone marrow aspirates and biopsies**, **flow cytometry**, and **cytogenetic testing**.