Introduction To Haemopoiesis

Cassandra Hobbs
CNC Apheresis
St George Hospital
Objectives

• Basic overview of haemopoiesis
• Stem cells & differentiation
• Myeloid & lymphoid lineages
• Role of immunoglobulins
Haemopoiesis

- Haemopoiesis is from Greek meaning “to make new blood”
- It refers to the formation of blood cellular components
- All blood cellular components are derived from a haematopoietic stem cells
- In a healthy adult approx $10^{11}$- $10^{12}$ new blood cells are produced daily
Cell hierarchy (Haemopoiesis schematic representation)

Key:
- Precursor cells or "blasts"
- Formed elements of circulating blood
- Tissue cells

Pluripotent stem cell

Myeloid stem cell

CFU-E
- Proerythroblast
- Nucleus ejected
- Reticulocyte
- Red blood cell

CFU-Meg
- Megakaryoblast
- Megakaryocyte
- Platelets

CFU-GM
- Monoblast
- Myeloblast
- Eosinophilic myeloblast
- Basophilic myeloblast
- Monocyte
- Neutrophil
- Eosinophil
- Basophil
- B lymphocyte
- T lymphocyte
- Plasma cell
- Macrophage

Lymphoid stem cell

Pre-B cells
- B lymphoblast
- B lymphocyte

Prothymocyte
- T lymphoblast
- T lymphocyte

Reference:
https://www.slideshare.net/rimbi_osraju/haemopoiesis-45250369
Haematopoietic Stem Cells

- Haematopoietic stem cells reside in the medulla of the bone (bone marrow).
- They are very unique as they have the ability to mature into all the different blood cell types and tissues.
- They are self-renewing cells.
- Daughter cells are cells that are the result from the division of a single parent cell. A single parent cell divides forming two daughter cells.
- Mitosis - stage of the cell cycle that involves division of cell nucleus and separation of chromosomes.
Daughter cells

Reference:
https://www.thoughtco.com/stages-of-mitosis-373534
Cell Cycle

Interphase

G1
Rapid growth and metabolic activity; centrioles replicate

S
Growth and DNA synthesis

G2
Growth and final preparations for division

Mitosis

Reference: https://raisedgardenbed.club/read/boundary-representation.html
Bone Marrow

- Found in the spongy gelatinous tissue found in hollow spaces in the interior of bones
- In children haemopoiesis occurs in long bones - femur & tibia
- In adults occurs in mostly pelvis, cranium, vertebra & sternum
- Extra medullary haematopoiesis - liver & spleen
Bone marrow

Reference: http://slideplayer.com/slide/3902325/
Life & Death in the Bone Marrow

• The stem cell has to mature, when it starts to mature it undergoes changes in its gene expression that “tells” the cell what type of cell it can become & it moves closer to a particular cell type (cell differentiation).

• The cell will have the presence of proteins on the cell so that it can be detected. I.e CD34, CD20

• Ultimately by regulating the balance between cell types, the bone marrow can alter the quantity of different cells to be produced.
Growth Factors

• Red & white blood cell production is a highly regulated production in healthy adult
• Self renewal & proliferation on all those cells depend on growth factors
• Most important is Stem Cell Factor-
• They are known as Colony- stimulating Factors(CSF)& cytokines
• There are many cytokines
Many cytokines

Reference:
http://www.sanidadanimal.info/cursos/inmun/images/6cells.jpg
The rate of new cell production is controlled by the body’s needs.

In response to an infection more white cells are produced & released.

When 02 is low in tissues erythropoietin is released by kidney that stimulates more red cells to be produced.

In response to bleeding- more platelets are produced.
Cell hierarchy (Haemopoiesis schematic representation)

Reference:
https://www.slideshare.net/rimbosraju/haemopoiesis-45250369
Lineages

• Lymphocytes: adaptive immune system. Lymphoid progenitors, T cells, B cells NK cells
• Myeloid lineage - immunity & blood clotting & red blood cells
• Red blood cells (erythrocytes) carry oxygen
Myeloid Cells

- Granulocytes & monocytes are differentiated cells derived from the pluripotent stem cell.
- Myeloid cells include macrophages, **neutrophils**, basophils, eosinophils, **erythrocytes**, dendritic cells & **platelets**
- Myeloid cells play a major role in immunity
Myeloid Cells

- **Neutrophils**: major role in innate immunity. 1st cells to migrate to site of infection. Kill invading organism
- **Dendritic Cells**: process antigen material and present it on to the cell surface to the T cell (messenger between innate & adaptive systems)
- **Basophil**: Inflammatory response, produce histamine, promote blood flow
- **Eosinophil**: inflammatory response. Bacteria & parasites
Lymphoid Cells

• Are differentiated cells derived from the pluripotent stem cell
• White blood cells
• Includes T-cells, B-cells & natural killer cells
• B-Cells: produce antibodies that fight bacterial, viral infections & toxins
• T-Cells: destroy bodies own cells that are infected or cancer cells
Myeloid Lineages

Myeloid

• Myeloid = tissue of bone marrow
• Are blood cells that have differentiated from the haematopoietic stem cell- then the myeloid progenitor cell (MPC)
• Associated with the *innate* (inborn, natural) immune system
• MPC differentiates in the bone marrow into RBC, megakaryocytes (platelets) & myelocytic – monocytes, macrophages and dendritic cells (innate immune system)
Innate Immunity

• Reaction is against foreign
• Response is immediate
• Response is mounted to wide variety of agents
• No memory, subsequent exposure to agents generate the same response
Lymphoid

Figure 1: Hematopoiesis in Bone Marrow

Lymphoid Lineage

- Composed of T-cells, B-cells & Natural killer (NK) cells
- Type of white cell produced by immune system to defend the body against cancer, pathogens & foreign matter.
- Circulate in blood & lymph fluid & found in body tissues - spleen, thymus, bone marrow & lymph nodes
B CELLS

• B cells become activated due to the presence of an antigen— they create antibodies that are specific to that antigen (pathogen)
• Antibodies are crucial to *humoral* immunity
• Also known as “antibody mediated system”
• B cells lock onto the surface of the pathogen & its marked for destruction
• B cells have ability to differentiate into plasma cells that secrete immunoglobulins
• Antibodies are produced in the spleen or lymph nodes
Adaptive Immunity

• Highly specialised, systemic cells & processes that eliminate pathogens & prevent growth
• Reaction is against foreign agent
• Response can take up to a few days
• The response is directed only to the agent that initiated it
• Wide range of antigen receptors
• Memory present- subsequent exposure to the same agent induce in amplified responses
Innate vs adaptative

Reference: http://slideplayer.com/slide/9019644/
Plasma cells

- White blood cells that secrete large volumes of antibodies
- Transported in blood & lymphatic system
- B cells differentiate into plasma cells that produce antibody molecules
- Plasma cell binds to the target antigen & starts destruction
B cells & plasma cells

Reference: http://iahealth.net/b-cells/
T Cells

• T cells mature in the thymus
• *Cell mediated immunity*- *adaptive immunity*
• Specific for a particular antigen
• Activated by antigen- presenting cells
• 2 main types: Helper & Killer
• Helper: assist other cells in immune process
T Cells

- T cells mature in the thymus
- *Cell mediated immunity*- *adaptive immunity*
- Specific for a particular antigen
- Activated by antigen- presenting cells
- 2 main types: Helper & Killer
- Helper: assist other cells in immune process
Immunoglobulins

- A class of proteins present in serum & cells which function as antibodies
- Critical part of immune system response by specifically recognizing & binding to particular antigens. i.e. bacteria or virus
- 5 classes:
Immunoglobulins

- IgG: bacterial & viral infections
- IgA: body surfaces, mucous membranes
- IgM: 1st antibody produced to fight infection
- IgE: parasites & allergic reactions
- IgD: not fully understood, may have something to do with activation of B cells in immune response
Anti body classification

How they work

A. Pathogens enter tissues through a wound.

B. Attacked by macrophages at the infection site

C. Antigens of the pathogen are displayed on the surface of the macrophage.

D. Helper T cells have receptor sites that recognize and bind to the antigens on the macrophage.

E. B cells can bind to antigens directly.

F. Helper T cells bind to antigens on B cells.

G. T cells release chemicals that cause B cells to produce clones of plasma cells.

H. Most plasma cells secrete antibodies that bind to antigens on infected cells.

I. Each plasma cell secretes more than 2000 antibodies per second in the blood. Memory B cells and antibodies remain in the blood and respond to future invasions by the same pathogen.

Reference: http://slideplayer.com/slide/9364369/
Why this is important

- An understanding makes us aware of disease process & potential problems pts will have
- Basis of how antineoplastic drugs work
- Basis of how immune modulators work
- How IVIG works
- Graft vs Host Disease
References

- 2018 ASFA annual conference. WWW. Apheresis.org