

Adaptive Immune System

- Unlike the **Innate** immune system, the adaptive/ acquired Immune system exhibits 2 specific characteristics:

SPECIFICITY - Antigenic Specificity

Diversity

Self/Non-Self Recognition

MEMORY

Specificity:

- The exquisite specificity of the immune system allows it to selectively recognize billions of different foreign antigens, while maintaining tolerance to an equally diverse panel of self antigens
- Failure of this system results in increased susceptibility to disease, or autoimmune disorders.

Memory

- This is the basis of vaccination. The Acquired/Specific/ Adaptive Immune system will respond more effectively, and more vigorously to a secondary exposure of any given antigen. Normally, this results in a protective response.

The adaptive immune system can be subdivided into antibody-based (**humoral**) and cell based (**cellular**) immunity.

Humoral Immunity

- Humoral immunity is generated by ANTIBODY RESPONSES. Antibodies bind to foreign antigens and assist in their destruction/elimination by the innate immune system
- Humoral immunity targets **extracellular** antigens, including viruses, bacteria, protozoa, parasites.

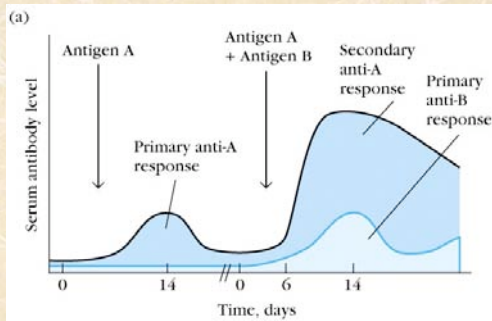
Cellular Immunity

- Cellular Immunity serves 2(3) basic purposes:
 - *To assist the humoral response by secretion of cytokines*
 - *To kill foreign eukaryotic cells, or altered self cells.*
 - Virally infected cells
 - Organ grafts
 - Cancer
 - *(To suppress specific immune responses)*

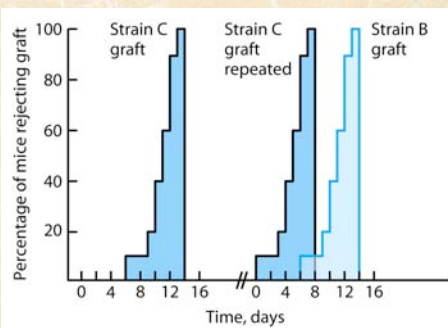
Cellular Immunity 2

- Cellular Immunity targets **intracellular antigens**, through the interaction of specific cell surface molecules on T cells with complementary molecules on target or antigen-presenting cells (MHC molecules).

ANTIBODY MEMORY RESPONSE



CELLULAR MEMORY RESPONSE



Cells of the Immune System

- The cells which give the immune system its specificity are the lymphocytes (a subset of leukocytes).
- Lymphocytes are assisted in their function by specialized accessory cells called **Antigen Presenting Cells (APCs)**

Cells and Organs of the Immune System

- Cells of the Acquired Immune System
- Cells of the Innate Immune System
- Hemopoiesis
 - Stem Cells
 - Regulation of Differentiation

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B versus T Lymphocytes

- Both B and T lymphocytes possess antigen-specific cell surface receptors
 - B Cells - Antibody
 - T Cells - T Cell Receptor
- Each lymphocyte expresses only a **SINGLE SPECIFICITY** or **TYPE OF RECEPTOR**. Therefore, a B or T cell must exist which specifically recognizes each individual foreign antigen.

Lymphocytes

- Make up roughly 20-40% of peripheral blood leukocyte pool.
- Many migrate continually between the blood and the tissues via the lymph (details to follow in migration lecture).

TABLE 2-4 Normal adult blood-cell counts

Cell type	Cells/mm ³	%
Red blood cells	5.0×10^6	
Platelets	2.5×10^5	
Leukocytes	7.3×10^3	
Neutrophil		50–70
Lymphocyte		20–40
Monocyte		1–6
Eosinophil		1–3
Basophil		<1

B Lymphocytes

B cell - in birds, develops in the Bursa of Fabricius

- mature B cells possess surface antibody
- on stimulation, B cells differentiate into
 - a) Plasma cells - secrete antibody
 - b) Memory cells

RECOGNIZE WHOLE/UNPROCESSED ANTIGEN

Surface Markers of B Cells

- Antibody or Surface Immunoglobulin (sIg)
- B220/CD45R (220Kd surface protein)
- CD19 - part of the surface B cell receptor, THE lineage-specific marker
- CD40 - important signalling receptor on B cells.

T cells

T cells - develop in the Thymus

- possess a surface receptor, (TcR), which shows some similarity in molecular structure to antibody
- recognizes foreign antigen which must be PROCESSED and PRESENTED by auxiliary cells.

T Cell Subsets

- ALL T cells possess a T cell receptor, and the signalling CD3 complex.
- CD3+ T cells are further subdivided into:
 - CD4+ T cells - "Helper" T cells which regulate immune responses by cytokine secretion, B cell interaction
 - CD8+ T cells - "Cytotoxic" T cells which kill foreign cells (allogeneic), virally infected self cells, or "altered" self cells.

Other T cell Subsets

- Suppressor T cells - The nature of these cells is still unclear. A population of CD8+ T cells MAY have this characteristic.
- $\gamma\delta$ -T cells (Gamma-Delta T cells). Possess a "different" T cell receptor
 - They are a small population in humans, mice, but a LARGE population in ruminants.
 - Their function remains unclear, but MAY be involved in protecting epithelial surfaces.

Null Cells

- Null cells lack the specific lineage markers associated with B and T cells, but morphologically resemble lymphocytes
- Natural Killer Cells (NK- cells)
 - Appear to play a role in tumor immunity
 - Express **CD16**.

Dendritic Cells

- The Principal Antigen Presenting Cell in the Immune System.
- Identified morphologically by a large number of cellular processes resembling neurological dendrites.
- Occur in many tissues, and named according to which tissue they are found in.
- Some are derived from similar precursors to macrophages (myeloid), others from lymphoid precursors

Summary 1

- The Adaptive Immune System demonstrates SPECIFICITY and MEMORY.
- LYMPHOCYTES are the cells of the Adaptive Immune System
- B Lymphocytes express and secrete antibody (humoral arm)
- T Lymphocytes express surface receptors and kill altered self or foreign cells (cellular arm).
T cells may be "helper" or "cytotoxic"
- Dendritic Cells present antigen to T cells, and are therefore included in the Adaptive Immune System.

Cells of the Immune System

- Cells of the INNATE Immune System include: monocytes / macrophages, granulocytes-neutrophils, basophils, eosinophils.
- Cells of the ACQUIRED Immune System include: T lymphocytes, B lymphocytes, and dendritic cells.

Cells of the Innate Immune System

- Monocytes - Develop into tissue macrophages or dendritic cells, represent about 10% of PBL
- Neutrophils (PMNs) - Major phagocytic inflammatory cell, produces mediators, about 50% of PBL
- Eosinophils - contain eosinophilic granules (stain with certain dyes), play a role in allergy, immunity to parasites, rare
- Basophils - precursor of mast cells, play a role in inflammation, allergy. Rare.

Development

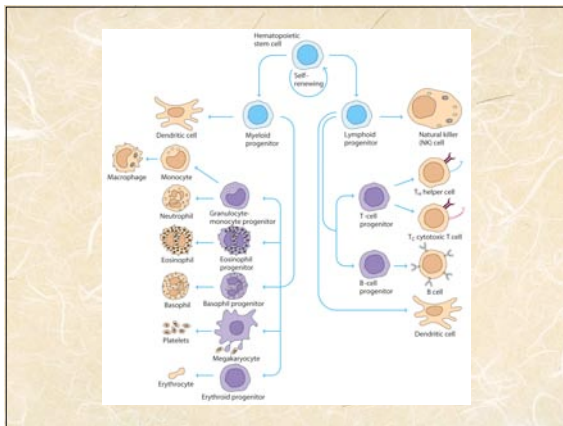
- The process whereby cells of the immune system are produced by the body is called HEMATOPOIESIS
- Cells of both the innate and the acquired immune system arise from a common progenitor cell:
 - The Hematopoietic Stem Cell (HSC)

Hematopoiesis

- Fetal/Neonatal Development
 - Begins in embryonic yolk sac
 - Differentiate from multipotential embryonic stem cells
 - Migrate from the Yolk Sac to the fetal liver, then to spleen.
 - Fetal hematopoiesis occurs in this way through the second trimester
 - 3rd Trimester on-occurs in Bone Marrow.

Adult Hematopoiesis

- Occurs in Bone Marrow from Multi/Pluripotential Stem Cells
- One stem cell (rare, <0.5% of BM) gives rise to all blood cells
- The MYELOID lineage consists of rbc's and cells of the innate immune system.
- The LYMPHOID lineage consists of T and B lymphocytes.



Myeloid Lineage

- HSC gives rise to Myeloid progenitor
- With appropriate cytokine stimulation, provided in most cases by the bone marrow STROMAL CELLS, the Myeloid progenitor gives rise to virtually all cells of the Innate Immune system

Myeloid Cytokines

- Most defined as growth factors from in vitro culture assays.
- Include: - **Multilineage CSF/IL-3**
 - **Macrophage CSF (M-CSF)**
 - **Granulocyte CSF (G-CSF)**
 - **Granulocyte-Macrophage CSF (GM-CSF)**
 - **Erythropoietin.**

Lymphoid Lineage

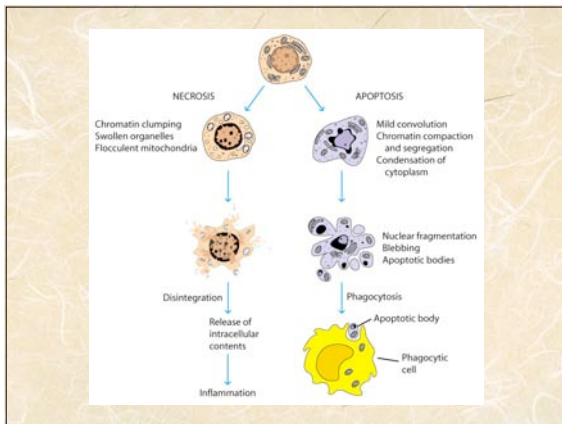
- HSC gives rise to Lymphoid Progenitor
- Stromal cell cytokines encourage development of B and T cells.
- Mostly regulated by INTERLEUKINS, including IL-7, IL-3, IL-4, etc.

Regulation of Hematopoiesis

- Amount, Type of cytokine produced locally by bone marrow stromal cells
- Inflammatory production of growth factors/ cytokines by other cell types
- Receptor expression by stem cells during development
- Induction of Cell Death

Genetic Regulation of Cell Development, Death

- Experiments have shown that differentiation can be controlled by transcription factor activation
 - *GATA-2* - regulates multilineage development
 - *Ikaros* - regulates LYMPHOID development
- Cell death generally occurs by apoptosis during hematopoiesis
 - Major genes of interest include *bcl-2* (downregulate), *fas/CD95* (upregulate) which regulate apoptosis



Next Lecture

- Organs of the Immune System
 - Primary Lymphoid Organs
 - Secondary Lymphoid Organs
 - Tertiary Lymphoid Tissue

Read Chapter 2, pp 47-57.
