



Tikrit University
College of Veterinary Medicine

Lecture 4: Lymphocytes

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(Theoretical)

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Lecture Link

Lymphocytes

1) What are lymphocytes?

- **Definition & role:** Lymphocytes are the key immune cells that recognize foreign antigens and arrange or perform immune responses.
- **Basic morphology:** Small, round cells (7–15 μm) with a large, deeply stained nucleus (e.g., hematoxylin) and a thin border of cytoplasm containing mitochondria, free ribosomes, and a small Golgi apparatus.
- **Where they live:** Circulate in blood and populate lymphoid organs (lymph nodes, thymus, spleen, Peyer's patches).
- **Origin & maturation:** Derived from bone-marrow stem cells.
 - **B cells** mature primarily in bone marrow (and bursa of Fabricius in birds).
 - **T cells** mature in the thymus.
- **Mobility:** Among the most mobile cells—continually recirculate between blood, tissues, and lymph.

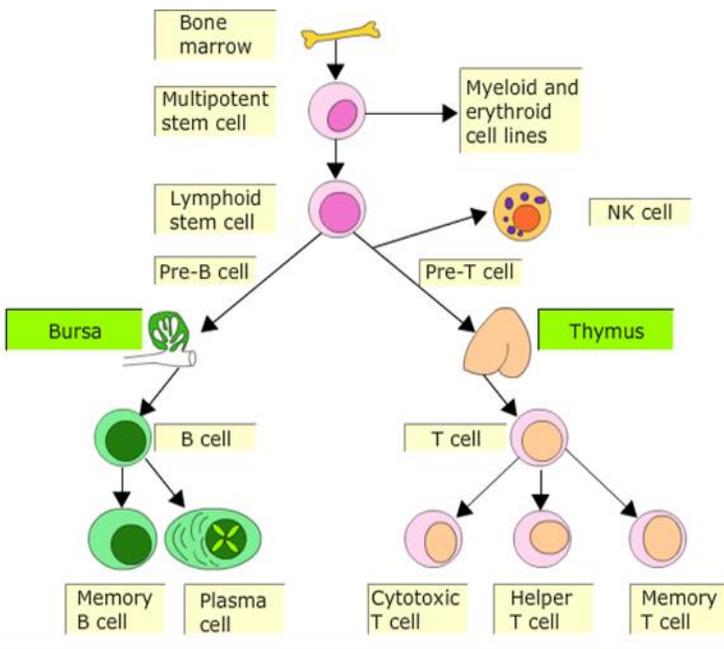


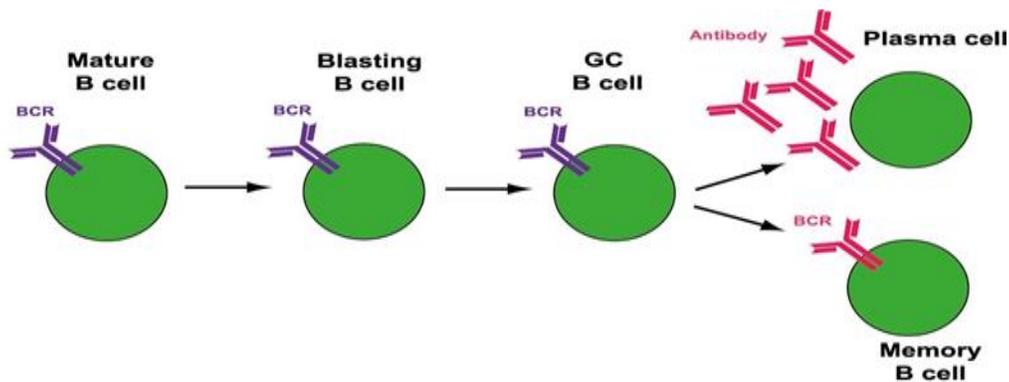
Figure 1 Origin and Lineage of B Cells, T Cells, and NK Cells

2) B lymphocytes (B cells)

- **Maturation:** From multipotent bone-marrow stem cells; in mammals, fetal liver supports early development, then bone marrow/Peyer's patches postnatally (refers to the period after hatching or birth)(bursa in birds).
- **Function:** Antibody production **after activation and differentiation** (naïve B cells are not antibody-secreting).

- **Effector fates (refers to the developmental paths)**

- **Plasma cells:** Large, rER-rich(rough endoplasmic reticulum), non-dividing, short-lived; secrete large quantities of immunoglobulins.
- **Memory B cells:** Long-lived antigen-specific cells that rapidly differentiate into plasma cells upon re-exposure; can be stratified by the immunoglobulin class they carry (e.g., IgM⁺, IgG⁺).



3) T lymphocytes (T cells)

- **Maturation:** Thymus-derived (hence “T” cells).
- **TCR (T-cell receptor) recognition:** T-cell receptors recognize antigenic peptides **only** when presented by MHC molecules.
- **MHC restriction:**
 - **MHC I** on most nucleated cells → recognized by **CD8⁺ T cells** (endogenous antigens, e.g., viral).

- **MHC II** on professional antigen-presenting cells (dendritic cells, macrophages, B cells) → recognized by **CD4⁺ T cells** (exogenous antigens).
- **Major T-cell subsets:**
 - **CD4⁺ helper T cells (Th):** Arrange immunity via cytokines (Th1—cell-mediated; Th2—humoral; Th17—**inflammatory**; Tfh—**B-cell help**).
 - **CD8⁺ cytotoxic T lymphocytes (CTLs):** Execute targeted killing of infected and malignant cells.
 - **Regulatory T cells (Treg):** Maintain tolerance and prevent excessive inflammation.
 - **Memory T cells:** Long-term antigen-experienced cells that respond rapidly upon re-exposure.
 - **γδ T cells:** Bridge innate and adaptive features; enriched at epithelial barriers.

They are called **γδ T cells** because their T-cell receptor (TCR) is made of **gamma (γ) and delta (δ) chains** instead of the usual alpha (α) and beta (β) chains found on conventional T cells (αβ T cells)

- **Natural Killer T (NKT) cells:** Hybrid properties—TCR-bearing but recognize lipid antigens.

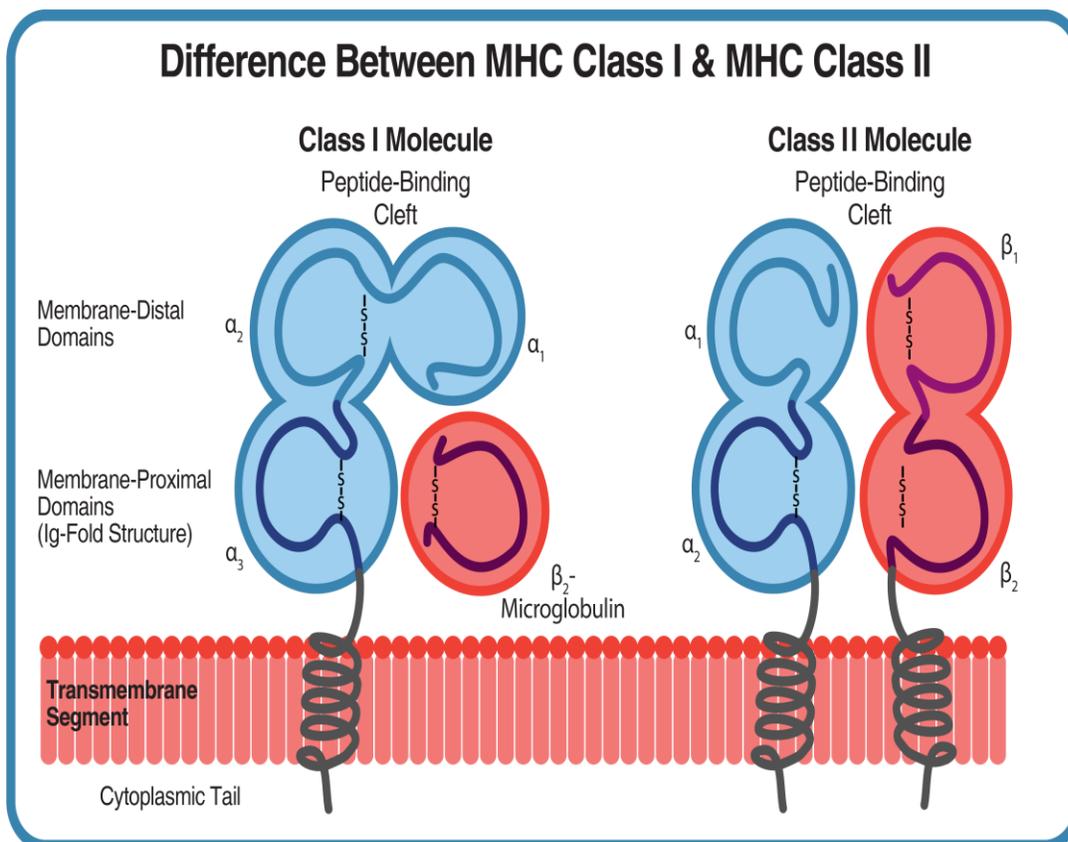
4) Surface markers as identifiers (phenotyping)

- **CD4:** Co-receptor for MHC II; hallmark of helper T cells.
- **CD8:** Co-receptor for MHC I; hallmark of cytotoxic T cells (CTLs).
- These “markers” don’t just label subpopulations—they participate in recognition and signaling.

MHC class I and MHC class II are both types of major histocompatibility complex molecules that present antigens to the immune system, but they differ in their

cellular location, the source of the antigens they present, and the types of T cells they interact with.

MHC class I molecules are found on almost all nucleated cells and present intracellular antigens (like viral proteins) to CD8⁺ cytotoxic T cells, while MHC class II molecules are expressed on antigen-presenting cells (APCs) like macrophages and B cells, and present extracellular antigens (from pathogens) to CD4⁺ helper T cells



5) **Natural Killer (NK) Cells (The Body's First Line of Cellular Defense)**

Natural Killer (NK) cells are a special type of lymphocytes that belong to the **innate immune system**. Unlike B cells and T cells, NK cells can kill infected or cancerous cells **without needing prior exposure** to an antigen. This makes them one of the fastest responders during early infection.

Key Features of NK Cells

Feature	Explanation
Type of cell	<u>Large granular lymphocytes</u>
Immune system	<u>Innate immunity</u>
Location	Blood, spleen, liver, lungs, lymph nodes
Main targets	Virus-infected cells, tumor cells
Activation	Do not require antigen presentation

How Do NK Cells Know What to Kill?

NK cells use a **smart detection system** called the "**missing-self**" mechanism. Healthy cells show a molecule called **MHC class I** on their surface. But many virus-infected or cancer cells **reduce MHC I expression** to escape cytotoxic T cells. NK cells recognize this loss and **attack automatically**.

How Do NK Cells Kill?

NK cells use **two powerful killing mechanisms**:

1. **Perforin/Granzyme Pathway (main method):**

- Perforin punches holes in the target cell membrane.
- Granzyme enters and triggers apoptosis (programmed cell death).

2. **Death Receptor Pathway:**

- NK cells express **Fas Ligand (FasL)**.
- Binds to **Fas receptor** on target cells → activates apoptosis.

3. **Antibody-Dependent Cell-Mediated Cytotoxicity (ADCC)**

NK cells are also part of **humoral protection** even though they are innate.

They express **CD16**, which recognizes the tail of **IgG antibodies** attached to

infected cells.

→ This allows NK cells to kill **antibody-coated targets**.

This process is called **ADCC** – very important in antiviral and anti-tumor immunity.

5) Killer Cells — the core focus

A) CD8⁺ Cytotoxic T Lymphocytes (CTLs)

Identity: Antigen-specific “killer” T cells of the adaptive immune system.

B) Natural Killer (NK) Cells

Identity: Innate “killer” lymphocytes—**do not** require prior antigen sensitization via TCR.

Killing mechanisms:

- **Perforin–granzyme release and death receptors** (similar to CTLs).
- **ADCC (antibody-dependent cellular cytotoxicity):** NK cells express **CD16 (FcγRIIIa)**; they bind the Fc portion of IgG coating a target cell and kill it efficiently.

C) Natural Killer T (NKT) Cells

Identity: Hybrid lymphocytes—express a **TCR** yet recognize **lipid/glycolipid antigens** presented by **CD1d** (instead of classical MHC).