

Diseases of Immunity

Introduction to T and B Cells

- The immune system is the body's defense mechanism against foreign invaders, including:
 - Pathogens (bacteria, viruses, fungi)
 - Cancer cells
 - Transplanted tissues
- It is composed of two major components:

A. Innate Immunity:

- First line of defense
- Non-specific, rapid response
- Includes neutrophils, macrophages, natural killer (NK) cells

B. Adaptive Immunity:

- Specific, slower response
- Has memory
- Mediated by **T lymphocytes (T cells)** and **B lymphocytes (B cells)**

Origin and Development of Lymphocytes

Feature	T Cells	B Cells
Origin	Bone marrow	Bone marrow
Maturation Site	Thymus	Bone marrow
Receptor	TCR (T-cell receptor)	BCR (B-cell receptor)
Main Function	Cell-mediated immunity	Antibody (humoral) immunity

- Both cell types originate from **hematopoietic stem cells** and differentiate based on their lineage and maturation signals.

T Cells in Detail

Subtypes of T Cells

1. CD4+ Helper T cells (Th cells)

- Coordinate immune responses.
- Activate B cells, cytotoxic T cells, and macrophages.
- Subsets include: Th1, Th2, Th17, Tfh.

- Secrete cytokines (e.g., ILs, IFN- γ).

2. CD8+ Cytotoxic T cells (CTLs)

- Destroy virus-infected, tumor, or foreign cells.
- Recognize antigens on **MHC Class I** molecules.
- Induce apoptosis in target cells.

3. Regulatory T cells (Tregs)

- Suppress overactive immune responses.
- Prevent autoimmunity.
- Express **FOXP3** gene.

Activation of T Cells

- **Antigen Presentation:** By **Antigen Presenting Cells** (APCs), mainly dendritic cells.
- **Signal 1:** TCR binds to antigen-MHC complex.
- **Signal 2:** Costimulatory signals (e.g., CD28-B7).
- **Signal 3:** Cytokines drive clonal expansion and differentiation.
- **Lack of co-stimulation:** Leads to T cell anergy (non-responsiveness).

Pathophysiological Relevance

1. Deficiencies:

- SCID: Loss of T cell function → severe infections.
- DiGeorge Syndrome: Thymic hypoplasia → T cell deficiency.

2. Overactivation:

- Multiple sclerosis, Type 1 diabetes, rheumatoid arthritis.

3. Viral susceptibility & cancers:

- CTL dysfunction impairs clearance.

B Cells in Detail

Subtypes of B Cells

1. **Naive B Cells:** Have not encountered antigen.
2. **Plasma Cells:** Effector B cells that secrete antibodies.
3. **Memory B Cells:** Persist long-term and rapidly respond to re-exposure.

B Cell Activation Mechanisms

T Cell-Dependent (most common):

- Requires CD4+ T cell help.
- Leads to class-switch recombination (IgM → IgG, IgA, IgE).
- Produces high-affinity, long-lasting antibodies.

T Cell-Independent:

- Triggered by repetitive structures (e.g., bacterial polysaccharides).
- Mostly produces IgM.
- Weak or no memory generation.

Functions of B Cells

- **Antibody production** (main role).
- **Antigen presentation** to helper T cells (APC role).
- Participate in immune regulation via cytokines.

Pathophysiological Relevance

Deficiency:

- X-linked agammaglobulinemia: Absence of B cells → severe bacterial infections.

Overactivity:

- Autoantibodies in diseases like **SLE, RA**.

Malignancies:

- Chronic lymphocytic leukemia (CLL), Multiple Myeloma.

Immunopathology Involving T and B Cells

A. Hypersensitivity Reactions

Type	Mechanism	Key Players	Example
I	Immediate	B cells (IgE), mast cells	Anaphylaxis, asthma
II	Antibody-mediated	B cells (IgG/IgM), complement	Autoimmune hemolytic anemia
III	Immune complex	B cells (IgG), complement	SLE, serum sickness
IV	Delayed	T cells (Th1/CTLs)	TB skin test, contact dermatitis

B. Autoimmune Diseases

- Failure of self-tolerance in T or B cells.
- **Examples:**

- **SLE:** B cells produce pathogenic autoantibodies.
- **RA:** Th1 and Th17 cells mediate chronic joint inflammation.

C. Immunodeficiencies

1. Primary (Congenital)

- **SCID:** Lack of both T and B cell function.
- **X-linked agammaglobulinemia:** Absent B cells.
- **DiGeorge syndrome:** T cell deficiency due to thymic absence.

2. Secondary (Acquired)

- **HIV/AIDS:** Targets and depletes CD4+ T cells → opportunistic infections.

D. Graft Rejection (Transplant Immunology)

- **T Cells:** Recognize and destroy graft tissue via CTLs.
- **B Cells:** Produce **alloantibodies** → complement activation → vascular rejection.

Clinical Applications and Relevance

- **Diagnosis:** Immune deficiencies (e.g., flow cytometry for CD markers).
- **Therapy:**
 - Immunosuppressants (e.g., steroids, biologics in autoimmunity).
 - Monoclonal antibodies (e.g., anti-CD20 for B-cell lymphomas).
- **Vaccination:** Relies on **memory T and B cells** for long-lasting immunity.
- **Allergy and Hypersensitivity:** IgE and mast cell involvement.
- **Transplant Medicine:** Targeting T/B cell responses to reduce rejection.

MHC Proteins (Transplantation Antigens)

Overview: What is MHC?

- Major Histocompatibility Complex (MHC) — also called Human Leukocyte Antigen (HLA) in humans — is a group of genes located on chromosome 6 that encode proteins responsible for presenting antigenic peptides to T cells.
- MHC plays a central role in:
 - Immune recognition:** Self vs. non-self-discrimination
 - Transplantation:** Major determinant of graft acceptance or rejection
 - Autoimmunity:** Certain MHC alleles are linked to autoimmune diseases

Types of MHC Molecules

MHC Class	Expressed On	Presents To	Peptide Origin
Class I	All nucleated cells	CD8+ T cells (CTLs)	Intracellular (e.g., viruses)
Class II	Antigen-presenting cells (APCs): Dendritic cells, macrophages, B cells	CD4+ T helper cells	Extracellular (e.g., bacteria)

Structure of MHC Molecules

A. MHC Class I

- Composed of:
 - **α chain** (domains: α1, α2, α3)
 - **β2-microglobulin**
- **Peptide-binding cleft:** Formed by α1 and α2 domains

B. MHC Class II

- Composed of:
 - **α chain** (α1, α2)
 - **β chain** (β1, β2)
- **Peptide-binding cleft:** Formed by α1 and β1 domains

Antigen Presentation Pathways (Pathophysiological Perspective)

A. Endogenous Pathway (MHC Class I)

- **Presented by:** All nucleated cells
- **Peptide origin:** Cytosolic proteins (e.g., viral proteins, tumor antigens)
- **Mechanism:**

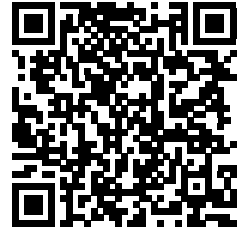


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