

**COURSE GOALS**

*Throughout the semester, students should be able to:*

1. Describe how the immune system is able to discriminate self vs. non-self.
2. Explain how the innate and adaptive immune systems work together to generate an effective immune response against a specific pathogen.
3. Explain how the immune system is able to respond to so many diverse antigens.
4. Describe the various steps and checkpoints involved in lymphocyte development.
5. Explain how and why certain immune cells change their phenotype following activation.
6. Given certain symptoms of a clinical disease or manipulation, predict the immunological cause of the disorder.

**PART I: AN INTRODUCTION TO IMMUNOBIOLOGY AND INNATE IMMUNITY****CHAPTER 1: BASIC CONCEPTS IN IMMUNOLOGY**Reading & Resources:

- Immunobiology: pg. 1-38
- Immunobiology videos
  - Phagocytosis
  - Dendritic Migration
  - The Immune Response
  - Chemotaxis

Vocabulary:

immunology	vaccination	memory cells	pathogens	primary immunization
secondary (booster) immunization	cellular immunity	antibodies	humoral immunity	adaptive immune response
protective immunity	innate immune response	effector functions	antigens	immunological memory
leukocytes	bone marrow	lymphatic system	lymph	hematopoietic stem cells
common myeloid progenitor	monocytes	granulocytes	common lymphoid progenitor	neutrophils
macrophage	eosinophils	basophils	mast cells	dendritic cells
inflammation	antigen presenting cells (APCs)	co-stimulatory molecules	natural killer (NK) cell	lipopolysaccharide (LPS)
memory cells	B lymphocytes (B cells)	T lymphocytes (T cells)	B-cell receptor (BCR)	T-cell receptor (TCR)
plasma cells	immunoglobulins (Ig)	cytotoxic T cells	helper T cells	regulatory T cells
antigen-binding sites	mucosal lymphoid tissue	primary lymphoid organs	secondary lymphoid organs	thymus
lymph nodes	spleen	Peyer's patch	cytokine	chemokine
clonal deletion	clonal expansion	clonal selection theory	lymphocyte receptor repertoire	marginal zone B cells
antigenic determinant (epitope)	major histocompatibility complex (MHC)	self antigens	programmed cell death (apoptosis)	draining lymph nodes
T-cell zones	afferent lymphatic vessels	germinal centers	follicles	cortex
paracortical areas	white pulp	red pulp	pattern recognition receptors (PRR)	pathogen associated molecular patterns (PAMP)

Students should be able to:

1. Describe the general functions of the immune system (immunological recognition, containment, immune regulation, immunological memory).

2. Compare and contrast the cells of the immune system in terms of: (Figure 1-3, 4)
  - a. System (innate vs. acquired)
  - b. Precursor (progenitor) cell
  - c. Location within body (tissue, blood, primary lymphoid organ, secondary lymphoid organ)
  - d. Types/subtypes
  - e. Receptors (pattern recognition receptor, B cell receptor, T cell receptor)
  - f. Effector function
3. Lymphatic system & organs
  - a. Compare the function of primary (bone marrow, thymus) and secondary lymphoid organs (lymph nodes, spleen, Peyer's patches) and describe what happens to B and T lymphocytes in these organs. (Figure 1-7)
  - b. Diagram the anatomy of secondary lymphoid organs including major regions and locations of antigen presenting cells (APCs), B lymphocytes, and T lymphocytes. (Figure 1-18, 19, 20)
  - c. Compare and contrast the different routes used by APCs, lymphocytes, and antigens to enter and/or exit secondary lymphoid organs.
4. Inflammation
  - a. Describe the characteristics commonly associated with inflammation (heat, pain, redness, swelling) and explain what causes these characteristics. (Figure 2-11)
  - b. Describe the beneficial effects of inflammation. (Figure 1-8)
5. Describe the role of APCs in activation of lymphocytes and induction of the adaptive immune response. (Figure 1-9)
6. Describe the 2 signals required for lymphocyte activation. (Figure 1-21, 2-23)
  - a. 1<sup>st</sup> signal: antigen (B cells); MHC + antigen (T cells)
  - b. 2<sup>nd</sup> signal: co-stimulation by helper T cells or APC
7. Distinguish between innate and adaptive immunity in terms of the following characteristics: (Figure 2-13)
  - a. Level of specificity
  - b. Time course of action
  - c. Ability to discriminate between self and non-self
  - d. Receptor diversity
8. Explain the 5 postulates of the clonal selection hypothesis. (Figure 1-11, 12)
9. Explain how the immune system is able to respond to so many diverse antigens (Antigen diversity problem).
  - a. Instructional hypothesis
  - b. Receptor diversity (Combinatorial diversity, Somatic gene rearrangement)

10. Diagram and explain the time course of a typical antibody and effector T cell response. (Figure 1-24)
  - a. Primary response
  - b. Secondary response (affinity maturation; immunological memory)
  - c. Explain how vaccinations help control infectious diseases. (Figure 1-35)
11. Distinguish between humoral and cell-mediated (cellular) immunity and the location of the pathogens they target (extracellular, intracellular). (Figure 1-26, 27, 28)
12. Explain what happens when there are defects in the immune system (i.e., autoimmune diseases, allergy, organ/tissue rejection).

**CHAPTER 2: INNATE IMMUNITY**

Reading & Resources:

- Immunobiology: pg. 39-108
- Immunobiology videos: Innate Immunity
  - Innate recognition of pathogens
  - Phagocytosis
  - Pathogen recognition receptors
  - Complement system
  - Rolling adhesion
  - Leukocyte rolling (video)
  - Leukocyte extravasation

Vocabulary:

innate immunity	pathogens	macrophage	mast cells	neutrophils
phagocytosis	phagosome	lysosome	phagolysosome	respiratory burst
pus	edema	dendritic cells	inflammation	cell-adhesion molecules
platelet-activating factor (PAF)	tumor necrosis factor-alpha (TNF-alpha)	extravasation	complement system	lectin pathway
coagulation system	pathogen-associated molecular patterns (PAMPs)	pattern recognition receptors (PRRs)	mannose-binding lectin (MBL)	classical pathway
surfactant proteins	mannose receptor	scavenger receptors	Toll-like receptors (TLRs)	bacterial lipopolysaccharide (LPS)
shock	sepsis	nuclear factor kappa-light-chain-enhancer of activated B cells (NFkB)	NOD	co-stimulatory molecules
alternative pathway	C3 convertase	C3b	C5 convertase	C5a
C5b	membrane-attack complex (MAC)	B-1 cells	adjuvants	C1 complex
complement receptors		anaphylatoxins	interferons	natural killer (NK) cells
cytokines	interleukin (IL)		chemokines	
selectins	intracellular adhesion molecules (ICAMs)	integrin	diapedesis	neutropenia
pyrogen	acute-phase response	acute-phase proteins	C-reactive protein	RIG-I
interferon receptor	NK T cells	natural killer (NK) cells	innate-like lymphocytes (ILLs)	gamma:delta T cells

Students should be able to:

1. Explain the different stages involved in the removal of an infectious agent. (Figure 2-1, 6)

2. Describe the key characteristics of the common types of pathogens that attack our bodies.
  - a. Types of disease-provoking pathogens (virus, bacteria, fungi, parasites) (Figure 2-2)
  - b. Site of infection (intracellular vs. extracellular) (Figure 2-3)
  - c. Route of entry/invasive strategy (Figure 2-5)
  - d. Mechanism of tissue damage (direct vs. indirect) (Figure 2-4)
3. Describe the various defense (effector) functions used by the innate system to prevent microorganisms from establishing an infection.
  - a. Pathogen barriers (mechanical, chemical, microbial) (Figure 2-7)
  - b. Phagocytosis by macrophage or neutrophils (Figure 2-8)
  - c. Secretion of antimicrobial enzymes/peptides (respiratory burst)(Figures 2-9, 10)
  - d. NFkB activation and expression of pro-inflammatory cytokines (Figure 2-44, 50, 51)
  - e. Vascular adaptations leading to changes in migration (Figure 2-12, 47, 49)
  - f. Migration of dendritic cells to lymph nodes to initiate adaptive immune response (Figure 2-22)
  - g. Upregulation of co-stimulatory molecules (Figure 2-23)
  - h. Fever (Figure 2-44)
  - i. Acute phase response
4. Compare and contrast the various pattern recognition receptors (PRR) in terms of:
  - a. Pathogen-associated molecular pattern (PAMP) (Figure 2-15, 16, 19, 20)
  - b. Location of receptor (membrane-associated, cytosolic; Figure 2-17)
  - c. Steps to NFkB activation
  - d. Effector functions
5. Diagram the classical and lectin complement cascades from beginning to end. (Figures 2-25, 28, 29, 36, 41)
6. Compare and contrast the initiation signals involved in activation of the 3 complement cascades (classical, lectin, alternative) and explain why these pathways must be tightly regulated. (Figure 2-24, 25, 43)
7. Discuss the 3 main consequences of complement activation (opsonization, recruitment, direct killing). (Figure 2-38, 39, 41)
8. Explain the local and systemic effects of cytokines released from activated macrophage. (Figure 2-44, 50, 51)
9. Diagram the steps involved in leukocyte (i.e., neutrophil) migration towards sites of infection. (Figure 2-12, 47, 49)
10. Discuss the role of interferons and natural killer (NK) cells in viral host defense. (Figure 2-53, 54, 55, 56)

**PART II: THE RECOGNITION OF ANTIGEN****CHAPTER 3: ANTIGEN RECOGNITION BY B-CELL AND T-CELL RECEPTORS****CHAPTER 4: THE GENERATION OF LYMPHOCYTE ANTIGEN RECEPTORS**Reading & Resources:

- Immunobiology: pg. 111-179

Vocabulary:

immunoglobulins (Ig)	B-cell receptor (BCR)	antibody	variable (V) region	constant (C) region
T-cell receptors (TCR)	MHC restriction	heavy (H) chain	light (L) chain	lambda chain
kappa chain	isotypes	IgM	IgD	IgG
IgA	IgE	hinge regions	Fab fragments	Fc fragment
hypervariable regions	antigen-binding site	combinatorial diversity	antigen-binding sites	epitope
alpha chain	beta chain	beta2-microglobulin	peptide-binding cleft (groove)	CD4
CD8	co-receptors		affinity	antibody repertoire
germline theory	somatic gene rearrangement	joining (J) segment	diversity (D) segment	somatic hypermutation
severe combined immune deficiency (SCID)	nonproductive rearrangements	gene conversion	class (isotype) switching	affinity maturation
avidity	affinity			

Students should be able to:

1. Diagram the characteristics of an antibody molecule and explain how this structure enables it to bind to a specific antigen. (Figures 3-1, 3-2)
2. Compare and contrast the main processes that generate diversity of the B and T lymphocyte repertoire in terms of where they occur, when they occur, and what subunits are affected (heavy/light, beta/alpha, variable/constant). (Figures 4-2, 6, 10, 21, 28)
  - a. Somatic gene rearrangement (VJ-VDJ shuffle)
  - b. Combinatorial diversity (heavy/light vs. beta/alpha chains)
  - c. Isotype switching (only B cells)
  - d. Somatic hypermutation & affinity maturation (only B cells)
3. Discuss the structural differences between an antibody and a B-cell receptor. (Figure 4-19)
4. Diagram and label the MHC molecules and their interactions with respective co-receptors. (Figures 3-15, 16, 24, 25)
5. Explain how T cells functionally distinguish between antigens presented by MHC class I and class II molecules.

6. Compare and contrast the structural and functional properties of the BCR and TCR in terms of: (Figures 3-11, 12)
  - a. V region
  - b. C region
  - c. Antigen-binding site
  - d. Antigen recognition (direct binding vs. peptide fragments)



**CHAPTER 5: ANTIGEN PRESENTATION TO T LYMPHOCYTES**Reading & Resources:

- Immunobiology: pg. 181-217
- Immunobiology Interactive CD: Antigen Recognition
  - MHC Class I Processing
  - MHC Class II Processing
  - Viral Evasins

Vocabulary:

major histocompatibility complex (MHC)	antigen processing	antigen presentation	cross-presentation	transporters associated with antigen processing (TAP)
proteasome	defective ribosomal products (DRiPs)	retrograde translocation	calnexin	calreticulin
tapasin	immunoevasins	dislocation	endosomes	invariant chain (Ii)
class II-associated invariant-chain peptide (CLIP)	MHC class II-compartment (MIIC)	HLA-DM	peptide editing	human leukocyte antigen (HLA) genes
polygeny	polymorphism	heterozygous	MHC haplotype	monomorphic
gene conversion	allogenic	mixed lymphocyte reaction	alloreactivity	superantigens
toxic shock syndrome toxin-1 (TSST-1)	MHC class Ib	MIC gene family	Erp57	acid activated proteases

Students should be able to:

1. Explain the role of major histocompatibility complex (MHC) proteins in antigen presentation. (Figure 5-2)
2. Describe the steps involved for normal antigen-processing and presentation on MHC class I molecules. (Figures 5-3, 5)
  - a. TAP, calnexin, Erp57, calreticulin, tapasin, DRiP, immunoproteasome, proteasome
3. Describe the steps involved for normal antigen-processing and presentation on MHC class II molecules. (Figures 5-8, 9, 11)
  - a. Acid activated proteases, HLA-DM, endosome, invariant chain, CLIP
4. Discuss some of the proteins that might prevent the display of MHC class I and class II molecules. (Figures 5-6, 7)

5. Discuss the two properties of MHC (polymorphism, polygeny) that allow it to bind to a wide variety of antigens. (Figures 5-14, 15, 16)
6. Describe what happens when antigen processing fails to produce a peptide that can bind with high affinity to MHC.
7. Discuss the relationship between alloreactivity and MHC restriction of the T-cell repertoire. (Figure 5-21)

**PART III: THE DEVELOPMENT OF MATURE LYMPHOCYTE RECEPTOR REPERTOIRES****CHAPTER 7: THE DEVELOPMENT AND SURVIVAL OF LYMPHOCYTES**Reading & Resources:

- Immunobiology: pg. 257-313
- Immunobiology Interactive CD: Lymphocyte Development
  - T cell development

Vocabulary:

central lymphoid tissues	peripheral lymphoid tissues	positive selection	negative selection	hematopoietic stem cells
stromal cells	multipotent progenitor cells (MPP)	common lymphoid progenitor (CLP)	early lymphoid progenitor (ELP)	pro-B cell
pre-B cell	mature B cell	pre-B-cell receptor	VpreB	$\lambda 5$
isotypic exclusion	central tolerance	clonal deletion	receptor editing	anergy
immunological ignorance	thymic cortex	thymic stroma	DiGeorge's syndrome	nude mutation
double-negative thymocytes	NK T cells	double-negative thymocytes	pre-T-cell receptor	double-positive thymocytes
single-positive thymocytes	bone marrow chimeras	regulatory T cells (Treg)	marginal zone	germinal centers
follicular dendritic cells (FDCs)	B-2 cells	lymphoma	oncogenes	passive cell death

Students should be able to:

1. Explain the role of the thymus and Notch-1 signaling in T cell education.
2. Discuss the ordered steps and location of B and T cell development, drawing the parallels between the two cell types. (Figures 7-5, 6, 10, 19, 20, 21, 24, 25, 45, 46)
3. Explain the function of the pre-B-cell receptor and the pre-T-cell receptor. (Figures 7-7, 8, 9, 20, 22)
4. Explain why lymphocyte development is notable for huge cell losses at several steps. (Figure 7-11)
5. Diagram the cellular organization of the thymus. (Figure 7-15)
6. Discuss the processes of positive selection, negative selection, and passive cell death. (Figures 7-27, 29, 30, 32)
7. Predict what may happen if some self-reactive B or T cells survive negative selection. (Figure 7-35, 36)

**PART IV: THE ADAPTIVE IMMUNE RESPONSE****CHAPTER 8: T-CELL MEDIATED IMMUNITY**Reading & Resources:

- Immunobiology: pg. 323 - 372
- Immunobiology Interactive CD: The Adaptive Immune Response
  - Activated T cell
  - T-cell killing
  - Dendritic cell migration
  - TCR-APC interaction
  - Immunological synapse
  - T-cell granule release
  - Lymphocyte trafficking
  - Lymphocyte homing

Vocabulary:

effector T cell	target cells	memory T cells	priming	co-stimulatory molecules
conventional dendritic cells	clonal expansion	diapedesis	homing	L-selectin
vascular addressins	leukocyte integrins	CCL21	CCR7	conventional dendritic cells (cDC)
plasmacytoid dendritic cells (pDC)	CD28	interleukin-2	helper T cells: Th1, Th2, Th17, Treg	cytotoxic T cells
immunological synapse	antigen trapping	granzymes	cytotoxic granules	perforin

Students should be able to:

1. Compare and contrast the different subsets of effector T cells [CD8+, CD4+ (Th1, Th2, Th17, Treg)] in terms of: (Figures 8-1, 27)
  - a. Activation signals (MHC molecule, co-stimulatory pairs)
  - b. Effector functions
  - c. Cytokines released
  - d. Pathogens targeted (intracellular, extracellular)
2. Describe the 4 steps of entry (rolling, activation, adhesion, diapedesis) of naïve T cells into peripheral lymphoid organs. (Figure 8-2, 4, 5, 6, 8)
  - a. Explain how this process differs from leukocyte migration into tissues. (Figure 2-12)
3. Diagram the time course of antigen trapping and activation of antigen-specific naïve T cells in lymphoid tissues following infection. (Figure 8-3)
4. Explain the interaction of naïve T cells with antigen presenting cells, and predict the consequences of a disruption to this interaction. (Figure 8-9, 18)

5. Describe how dendritic cells identify the presence of infection in peripheral tissues and initiate an immune response to it in the lymph nodes or secondary lymphoid tissues. (Figure 8-10, 12, 13, 14)
6. Compare and contrast the 3 types of antigen presenting cells (dendritic cells, B cell, macrophage) in terms of: (Figure 8-10, 16)
  - a. Distribution within the lymph node
  - b. Mechanisms for antigen uptake
  - c. Types of antigen presented
  - d. Types of MHC molecules loaded
  - e. Type of naïve T cell activated
  - f. Location throughout the body
7. Describe the 3 signals involved in activation, survival, and differentiation of naïve T cells. (Figure 8-19, 29)
8. Explain the role of IL-2 and IL-2R in T cell activation. (Figure 8-20, 21)
9. Explain how signal 2 (co-stimulation) can be modified. (T-cell:APC dialogue)
10. Predict what happens to antigen recognition in the absence of co-stimulation. (Figure 8-23, 24, 25)
11. Diagram and label the appropriate cell types, components, and location of an immunological synapse. (Figure 8-31)
12. Describe mechanisms and time course of T-cell mediated cytotoxicity. (Figures 8-36, 39, 40)
13. Describe how Th1 cells facilitate macrophage activation. (Figure 8-41, 42)

**CHAPTER 9: THE HUMORAL IMMUNE RESPONSE**Reading & Resources:

- Immunobiology: pg. 379-420
- Immunobiology Interactive CD: The Adaptive Immune Response
  - Germinal Centers

Vocabulary:

humoral immune response	plasma cells	neutralization	B-cell receptor (BCR)	linked recognition
primary lymphoid follicles	germinal center	secondary follicle	affinity maturation	Fc receptors
antibody-dependent cell-mediated cytotoxicity (ADCC)	mast cell	thymus-dependent antigen	thymus-independent antigen	plasmablasts
transcytosis	cross-linking	opsonization	somatic hypermutation	isotype (class) switching
plasma cell	complement			

Students should be able to:

1. Review: Explain how antibodies contribute to immunity. (Figure 9-1)
  - a. Neutralization (Figure 9-24, 25)
  - b. Opsonization (cross-linking Fc receptors) (Figure 9-26)
  - c. Complement activation (IgM, IgG) (Figure 9-28)
2. Describe the requirements for the activation of naïve B cells by thymus-dependent or thymus-independent antigens. (Figure 9-2)
3. Explain the significance of linked recognition in promoting the adaptive immune response. (Figures 9-4, 5)
4. Compare and contrast mature B cells, plasmablasts, and plasma cells (Figure 9-8)
5. Describe the process of somatic hypermutation and affinity maturation of the antibody response. (Figure 9-11)
6. Discuss the roles of Th cytokines in determining B cell isotypes (class switching & “3<sup>rd</sup> signal”). (Figure 9-13)
7. Compare and contrast the properties and effector functions of the 5 different isotypes of antibody. (Figure 9-19, 22)
8. Explain how antibodies cross epithelial barriers (transcytosis). (Figure 9-20)

9. Explain the role of cross-linking Fc receptors in the destruction of antibody-coated pathogens. (Figures 9-31, 32, 34, 35)

**CHAPTER 10: DYNAMICS OF ADAPTIVE IMMUNITY**Reading & Resources:

- Immunobiology: pg. 421-458
  - Pg. 425 Section 10-2
- Immunobiology Interactive CD
  - The Immune Response
  - Chemotaxis
  - Lymphocyte Trafficking
  - Lymphocyte Homing
  - Germinal Centers

Vocabulary:

primary immune response	immunological memory	homing receptors	cutaneous lymphocyte antigen (CLA)	secondary immune response
memory B cells	memory T cells	effector memory cell	central memory cell	original antigenic sin

Students should be able to:

1. Diagram the time course of a typical infection that is cleared by adaptive immunity. (Figures 10-1, 2)
2. Explain how the nonspecific responses of innate immunity are necessary for the initiation of adaptive immune responses.
3. Discuss the driving factors that mold the different Th phenotypes. (Figures 10-4, 5, 8)
  - a. Co-stimulatory factors (T-cell: APC dialogue)
  - b. Cytokines (Reciprocal inhibition)
  - c. Nature of pathogen & concentration of ligand
  - d. TLR signals (MyD88)
4. Explain the advantage of having different subsets of effector T cells regulate each other's development. (Figure 10-7)
5. Discuss how effector T cells are guided to sites of infection by chemokines and adhesion molecules. (Figure 10-10)
6. Describe the advantages and disadvantages of differentiated T cells requiring continued signals to maintain their function. (Figures 10-11, 12)
7. Explain how memory responses differ from primary immune responses, and describe the underlying mechanisms involved in each case. (Figures 10-16, 17)
8. Describe the advantages of immunological memory.



9. Explain how memory cells are different from antigen-naïve and effector cells. (Figure 10-22)
10. Discuss the relative role of cytokines in the survival and function of memory T cells. (Figures 10-23, 24)
11. Explain “original antigenic sin.” (Figure 10-27)

**CHAPTER 11: THE MUCOSAL IMMUNE SYSTEM**Reading & Resources:

- Immunobiology: pg. 459-495
- InterActive Physiology CD (Silverthorn Human Physiology text): Immune System
  - Anatomy Review (pg. 16-22)

Vocabulary:

mucosal immune system	commensal	lamina propria	transcytosis	tonsils
Peyer's patches	appendix	intraepithelial lymphocytes (IEL)	microfold (M) cells	MadCAM-1
nasal-associated lymphoid tissues (NALT)	mucosa-associated lymphoid tissues (MALT)	mesenteric lymph nodes	gut-associated lymphoid tissues (GALT)	bronchus-associated lymphoid tissues (BALT)
poly-Ig receptor	secretory IgA	lymphoid follicles	oral tolerance	

Students should be able to:

1. Describe the distinctive anatomical features of the mucosal immune system. (Figures 11-1, 3, 4, 5, 6)
2. Describe the specialized mechanisms of antigen uptake by M cells in Peyer's patches or dendritic cells in the lamina propria. (Figures 11-3, 8, 9)
3. Describe what populations of T lymphocytes and other leukocytes are found in the intestinal mucosa and explain what roles they play in host defense. (Figures 11-10, 16, 17)
4. Describe the processes that allow specific CD4 T cells to be primed against antigen in the intestine and discuss how the resulting effector T cells can return to the intestinal surface. (Figure 11-11)
5. Discuss how IgA antibodies gain access to the intestinal lumen and outline how these antibodies might contribute to defense against infection. (Figures 11-13, 14, 15)
6. Compare and contrast the host response to commensal and invasive bacteria in the intestine, indicating the immunological consequences of these different effects. (Figures 11-20, 21)
7. Explain how the immune system distinguishes between food antigens and antigens that are potentially harmful (Oral tolerance). (Figure 11-22, 25)
8. Describe how different aspects of the host immune response may produce either protective immunity or tissue damage during infection by intestinal helminths. (Figures 11-26, 27)