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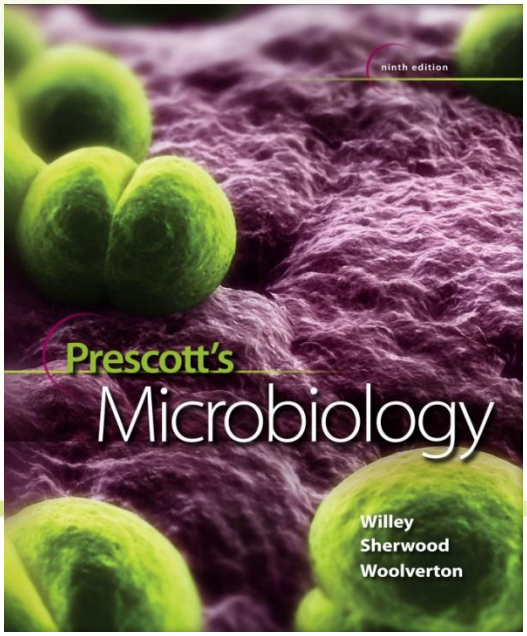


Adaptive Immunity

34.1 Overview of Adaptive Immunity

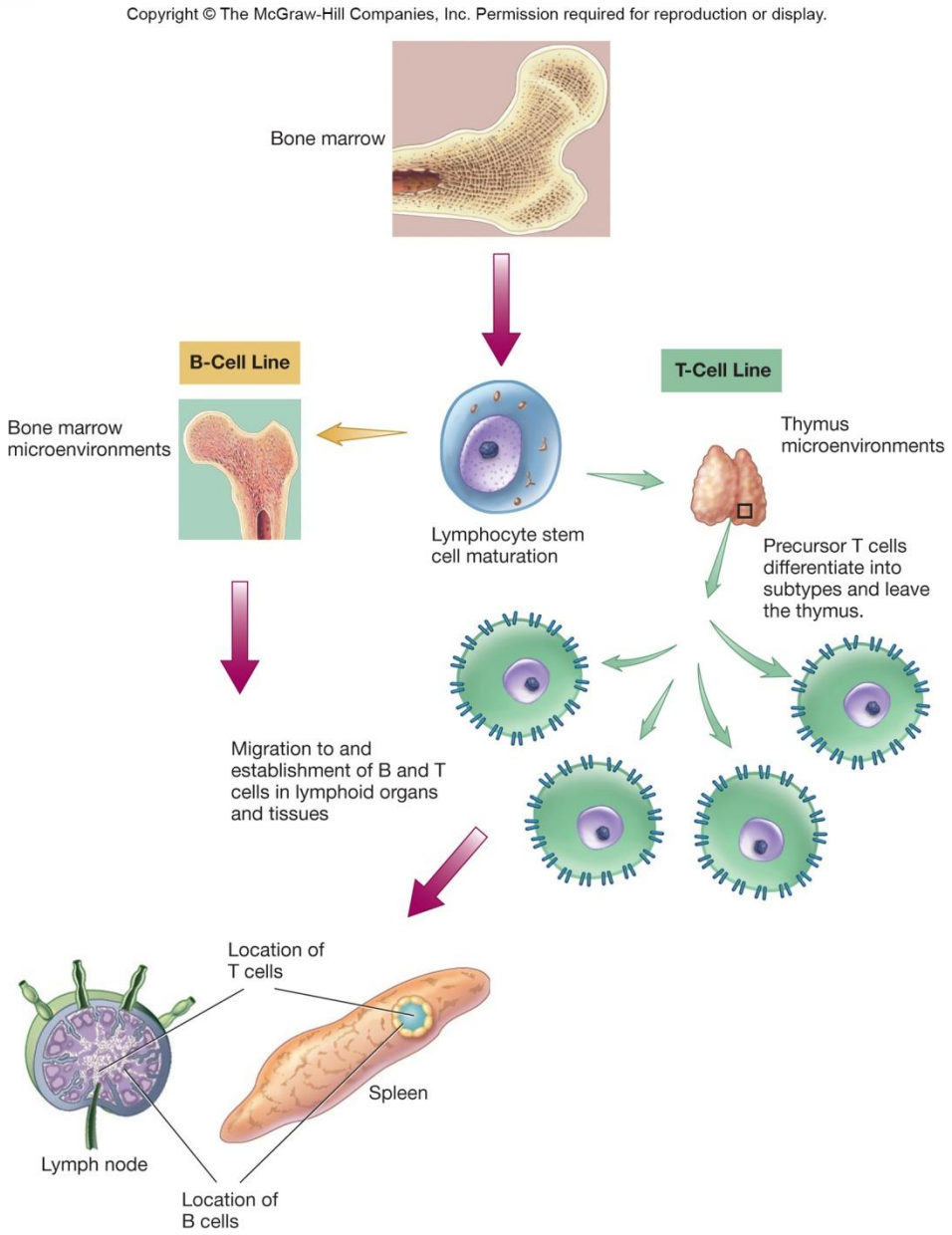
1. Contrast host innate resistance with adaptive immunity
2. Outline the localization of B and T cells during development

Overview of Specific (Adaptive) Immunity

- Three major functions
  - recognize nonself
  - respond to nonself
    - effector response
      - eliminates or renders foreign material harmless
    - anamnestic response
      - upon second encounter with same pathogen immune system mounts a faster and more intense response
  - remember nonself

Acquired Immune System Development

- B and T cells initially arise in the bone marrow
  - B cells continue to mature there
  - T cells are moved to the thymus for further maturation
- Both cell types go through extensive screening to avoid self-reactivity

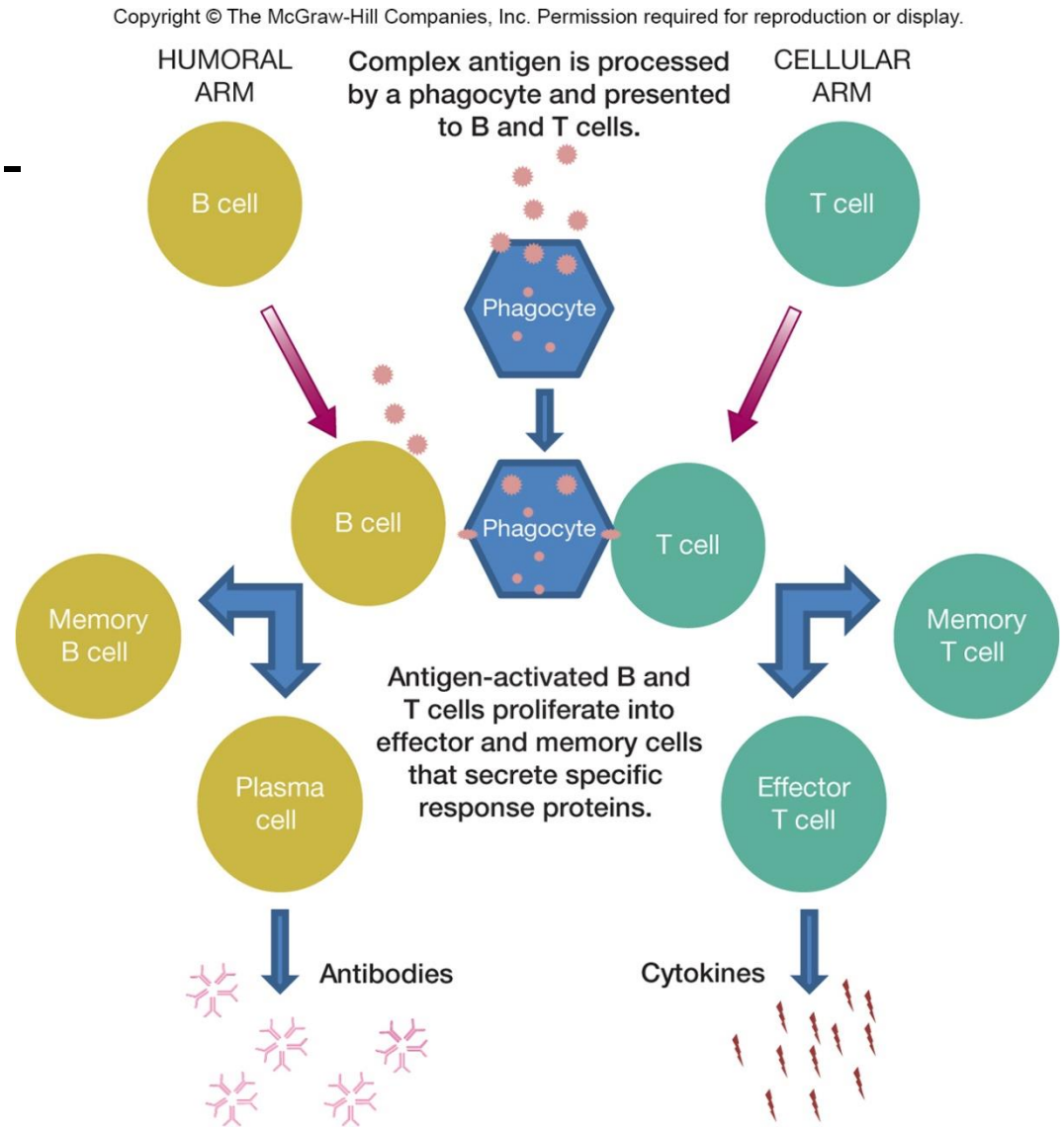


Four Characteristics of Specific Immunity

- Discrimination between self and non-self
  - usually responds selectively to non-self, producing specific responses against the stimulus
- Diversity
  - generates enormous diversity of molecules
- Specificity
  - can be directed against one specific pathogen or foreign substance among trillions
- Memory
  - response to a second exposure to a pathogen is so fast that there is no noticeable pathogenesis

Types of Specific Immunity

- Humoral immunity
  - also called antibody-mediated immunity
  - based on antibody activity
- Cellular immunity
  - also called cell-mediated immunity
  - based on action of specific kinds of T lymphocytes



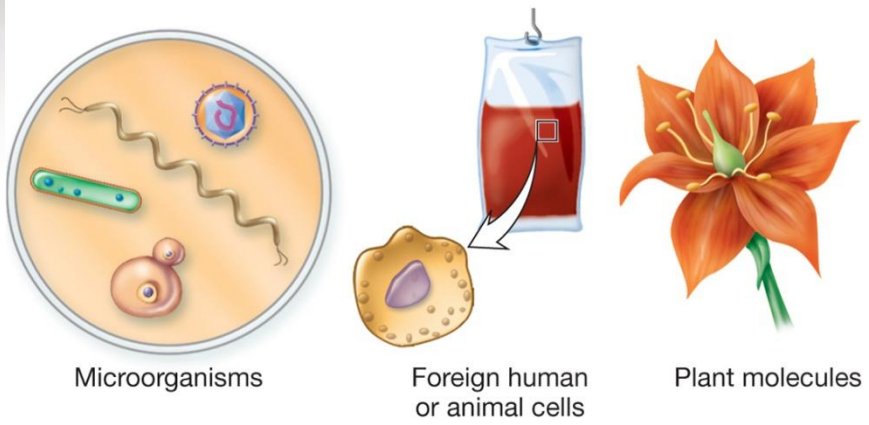
34.2 Antigens

1. Predict the types of molecules that can serve as antigens
2. Compare haptens and true antigens

Antigens

- Self and nonself substances that elicit an immune response and react with products of that response
- Most are large, complex molecules
- Antigenic determinant sites (***epitopes***)
  - site on antigen that reacts with specific antibody or T cell receptor
  - valence is number of epitopes on an antigen
- Antibody ***affinity***
  - strength with which antibody binds to its antigen at a given antigen-binding site
- ***Avidity*** of antibody
  - overall antigen-binding at all antigen binding sites

Haptens



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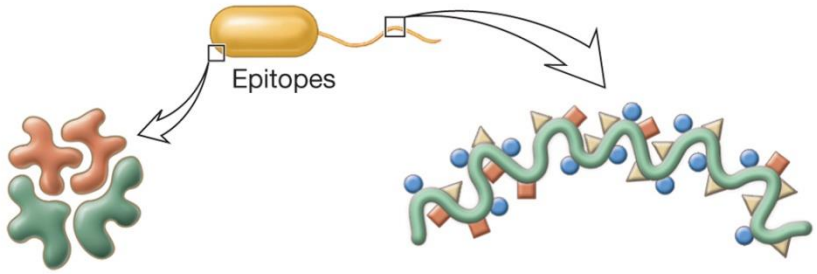

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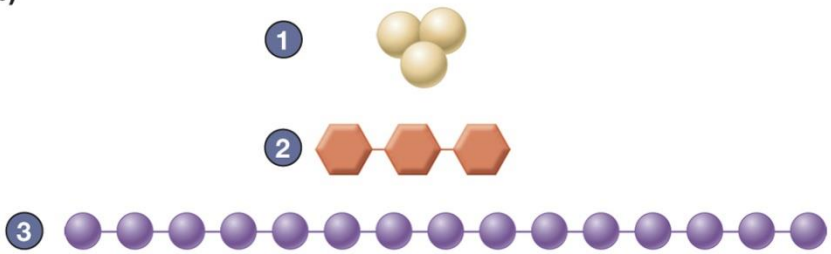

(c)

- Small organic molecules
- Not antigenic but may become antigenic when bound to larger carrier molecule
  - e.g., penicillin
  - may elicit hapten specific and carrier specific responses

34.3 Types of Adaptive Immunity

1. Report the methods by which immunity occurs by natural and artificial means
2. Distinguish between the active and passive forms of natural and artificial immunity

Types of Specific Immunity

- Naturally acquired active immunity
  - type of specific immunity a host develops after exposure to foreign substance
- Naturally acquired passive immunity
  - transfer of antibodies, e.g., mother to fetus across placenta, mother to infant in breast milk
- Artificially acquired active immunity (vaccination)
  - intentional exposure to a foreign material
- Artificially acquired passive immunity
  - preformed antibodies or lymphocytes produced by one host are introduced into another host

Acquired Immunity

Natural immunity
is acquired through the normal life experiences of a human and is not induced through medical means.

Artificial immunity
is that produced purposefully through medical procedures (also called immunization).

Active immunity
is the consequence of a person developing his or her own immune response to a microbe.

Passive immunity
is the consequence of one person receiving preformed immunity made by another person.

Active immunity
is the consequence of a person developing his or her own immune response to a microbe.

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Infection

Maternal antibody

Vaccination

Immune globulin therapy

34.4 Recognition of Foreignness

1. Define the method by which a host distinguishes itself from nonself (foreign) materials
2. Diagram the host cell receptors that distinguish self from nonself
3. Compare the processes by which MHC class I and class II receptors recognize foreignness
4. Identify cells that can function as antigen-presenting cells (APCs)
5. Explain the use of “cluster of differentiation” (CD) molecules to name cells

Recognition of Foreignness

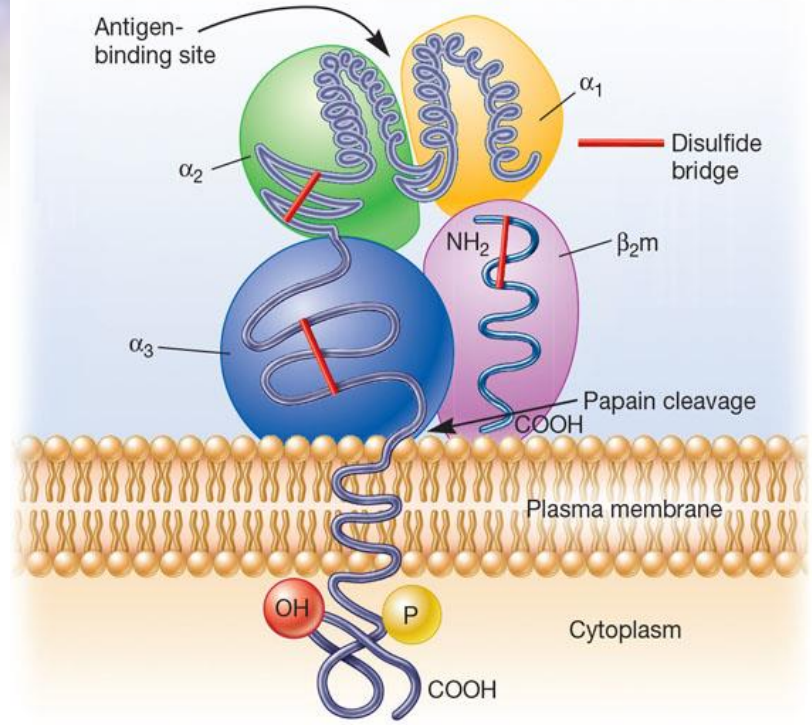
- Distinguishing between self and non-self is essential for the proper functioning of the immune system
  - this allows for selective destruction of invading pathogens without destruction of host tissues
  - involves major histocompatibility complex

Major Histocompatibility Complex (MHC)

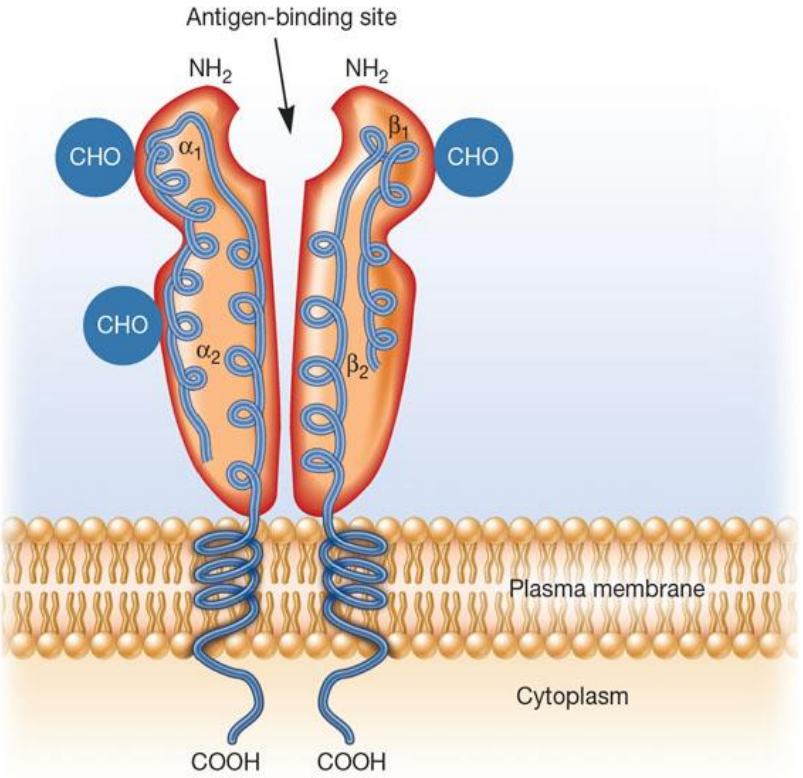
- Collection of genes that code for self/nonself recognition potential of a vertebrate
- In humans, called human leukocyte antigen (HLA) complex
  - on chromosome 6
  - three classes of MHC molecules
  - one paternal allele and one maternal allele

Major Histocompatibility Complex (MHC)

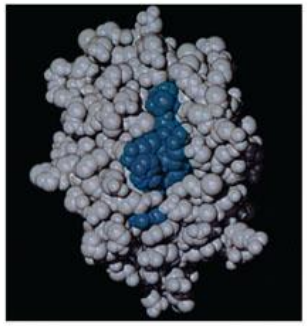
- Class I molecules found on almost all types of nucleated cells
  - important for organ transplantation
- Class II molecules found only on antigen presenting cells
  - required for T cell communication to macrophages, dendritic cells, B cells
- Class III molecules include secreted proteins not required for self/nonself recognition



(a) Class I MHC



(b) Class II MHC



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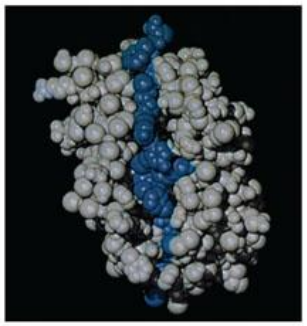
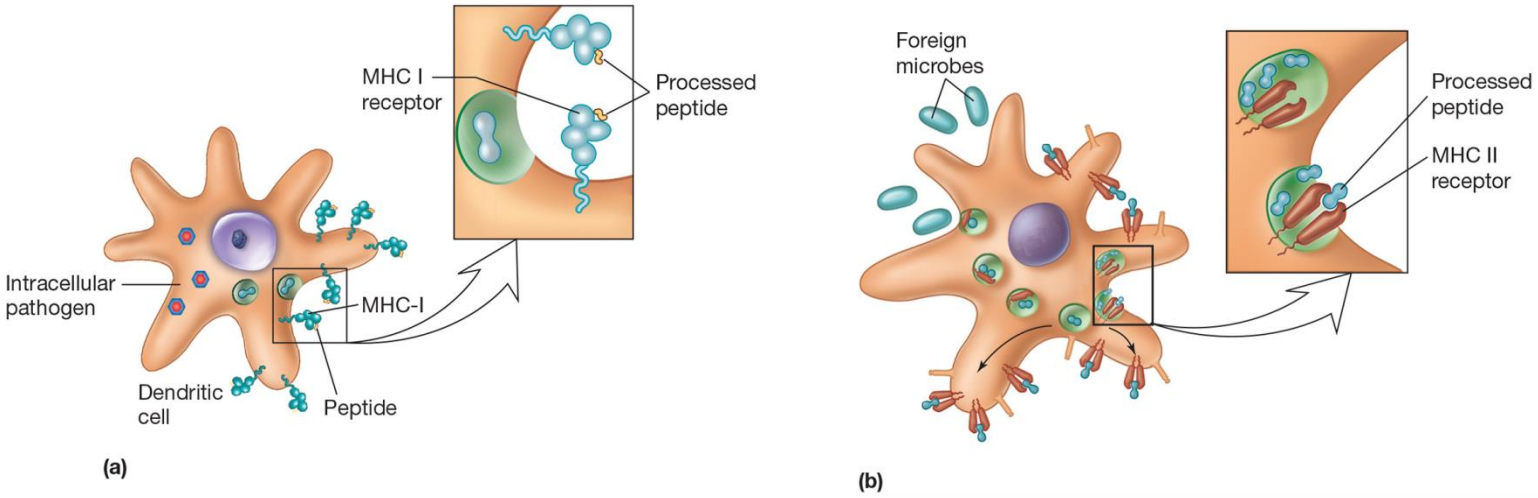


(d)

Courtesy of Dr. Paul Travers

MHC and Antigen Processing

- Class I and Class II bind to antigens in the cell
  - endogenous antigen processing
    - class I binds to antigen peptides that originate in the cytoplasm and present antigen to CD8+ T cells
  - exogenous antigen processing
    - class II binds to antigen fragments that come from outside the cell and present to CD4+ T helper cells



Cluster of Differentiation Molecules (CDs)

Table 34.1 Functions of Some Cluster of Differentiation (CD) Molecules

Molecule	Function
CD1 a, b, c	MHC class I–like receptor used for lipid antigen presentation
CD3 δ, ε, γ	T-cell antigen receptor
CD4	MHC class II coreceptor on T cells, monocytes, and macrophages; HIV-1 and HIV-2 (gp120) receptor
CD8	MHC class I coreceptor on cytotoxic T cells
CD11 a, b, c, d	α-subunits of integrin found on various myeloid and lymphoid cells; used for binding to cell adhesion molecules
CD19	B-cell antigen coreceptor
CD34	Stem cell protein that binds to sialic acid residues
CD45	Tyrosine phosphatase common to all hematopoietic cells
CD56	NK cell and neural cell adhesion molecule

- Membrane proteins on lymphocytes and other cells
  - have specific roles in intercellular communication
  - used to identify and differentiate between leukocyte subpopulations
    - e.g., CD4 is the cell surface receptor for HIV

34.5 T-cell Biology

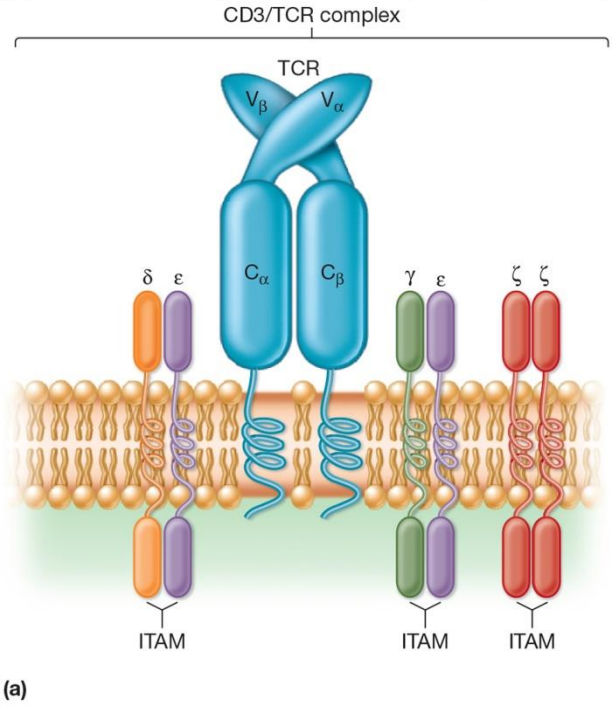
1. Categorize T cells based on their CD designation
2. Contrast the biological functions of T-cell subsets
3. Describe T-cell receptor structure and function
4. Illustrate the T-cell developmental process
5. Connect antigen presentation within MHC receptors and T-cell subset recognition
6. Build a model of the molecular events resulting in T-cell activation

T-Cell Biology

- Major players in cell-mediated immune response
- Originate from CD34+ stem cells in the bone marrow but mature in thymus
- Have major role in B cell activation
- Immunologically specific and function in a variety of regulatory and effector ways

T-Cell Receptors (TCRs)

- Reside in the plasma membrane surface
- Recognize and bind fragments of antigens
- Antigen fragments must be presented by antigen-presenting cells (APCs) on the ends of MHC molecules



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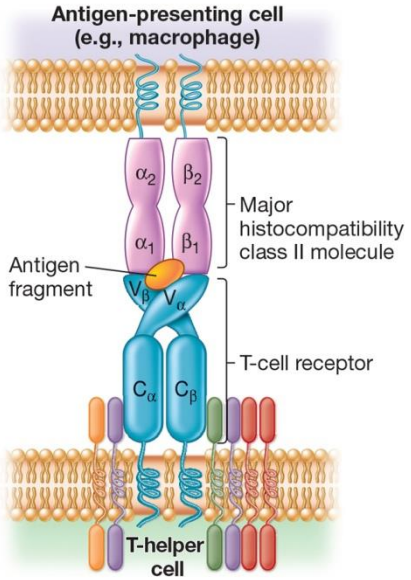

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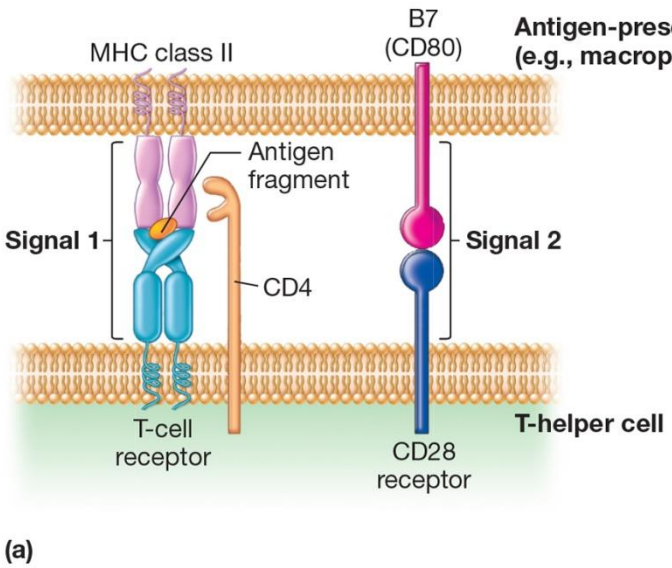
T Cell Activation



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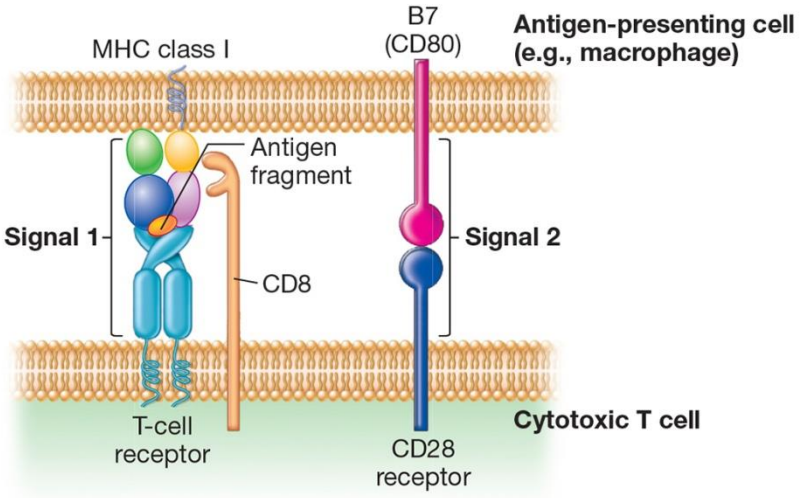
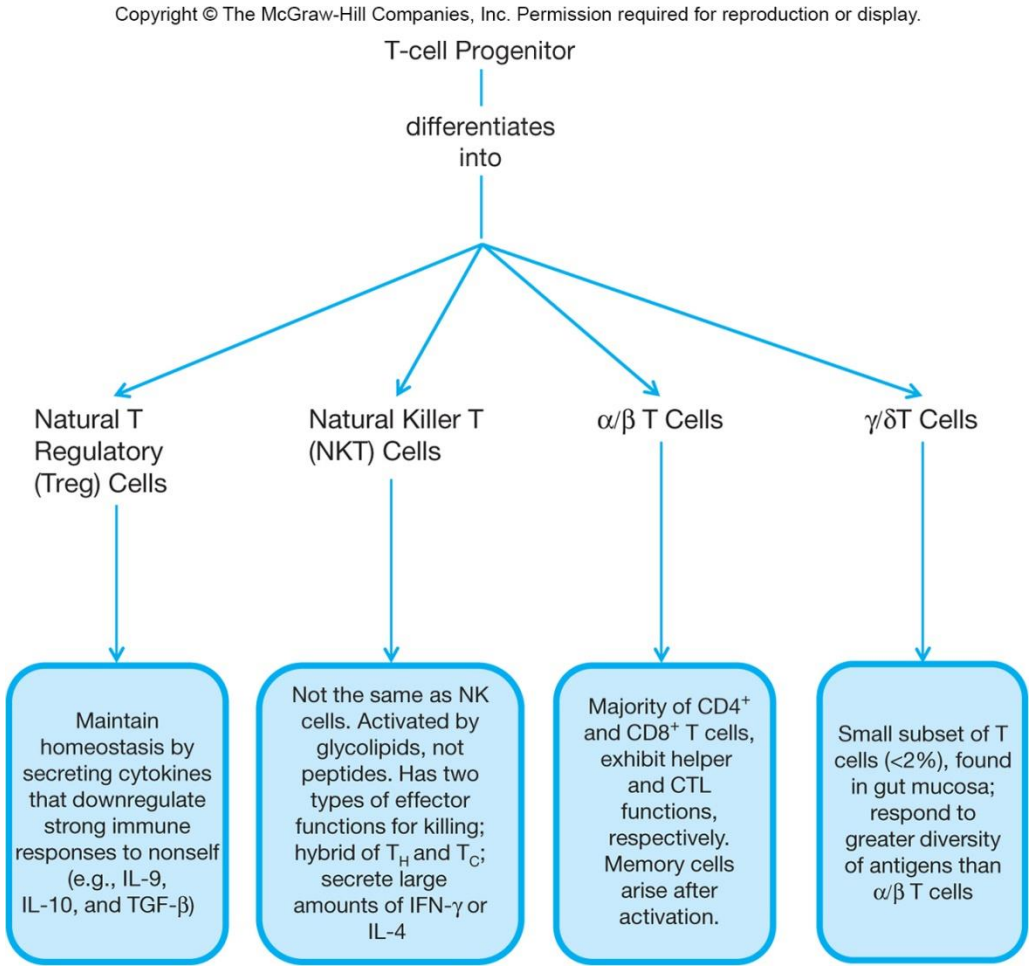


(b)

- Requires binding a specific antigen
  - occurs through antigen presentation bridging MHC class II on the APC to the TCR on the T cell
  - initiates signaling cascade involving other membrane-bound proteins and intracellular messengers
  - second signal required for lymphocyte proliferation, differentiation, and expression of specific cytokine genes

Types of T Cells

- Mature T cells are naïve until activated by antigen presentation
- Once activated they proliferate into effector cells and memory cells
  - effector cells carry out specific functions to protect host
  - three types
    - T helper (T_H), cytotoxic T lymphocytes (T_Cs), and regulatory T cells



T-Helper Cells

- Also known as CD4+ T cells
- Activated by antigen presentation with class II MHC
- Subdivisions of T helper cells
  - T_H0 – undifferentiated T cells
  - T_H1 – help activate macrophages
  - T_H2 – help B cells produce antibodies
  - T_H17 – assist in antibacterial responses
  - Treg – help control lymphocyte responses

T Helper Cells

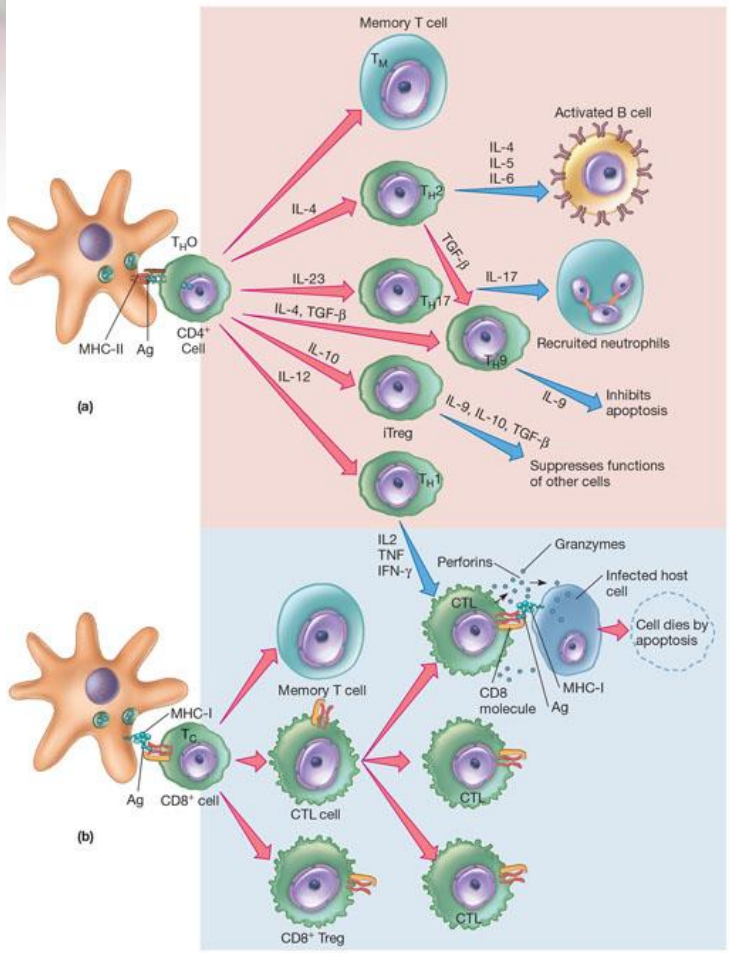
- T_H1 cells
  - promote cytotoxic T cell activity and activate macrophages
  - mediate inflammation and delayed hypersensitivity by producing a specific set of cytokines
    - IL-2, IFN-γ, tumor necrosis factor (TNF)-β
- T_H2 cells
  - stimulate antibody responses and defend against helminth parasites
  - involved in promoting allergic reactions
  - produce a specific set of cytokines
    - IL-5, IL-6, IL-10, and IL-13

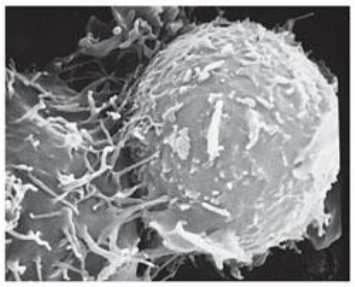
Cytotoxic T Cells (T_Cs)

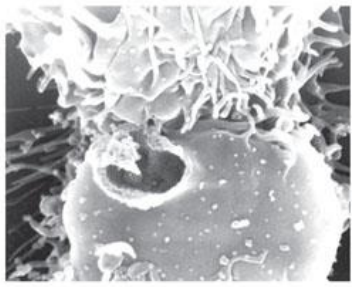
- Are $CD8^+$ T cells that have been activated by antigen presented on MHC-1 molecules of nucleated cells
- Once activated these CTLs can kill target cells that have the same antigen-MHC-1 combination that originally activated the CTL
- After bind target, CTL kills target cell via the perforin pathway and CD95 pathway

Regulatory T Cells

- Treg cells
  - derived from approximately 10% of CD4+ T cells and 2% of CD8+ T cells
  - IL-10 induces regulatory function by inhibiting T helper cell function
    - Activates transcription factor Foxp3
    - Foxp3 upregulated CD25 and CTLA-4
    - CTLA-4 binds to B7 on APCs, blocking the 2nd signal required for lymphocyte activation
  - Tregs also suppress/regulate functions by secretion of IL-9 and TGF-β







Courtesy of Dr. Gilla Kaplan, PHRI, UMDNJ

Superantigens

- Bacterial and viral proteins
  - staphylococcal enterotoxin B
  - the toxin that causes toxic shock syndrome
  - mouse tumor virus superantigen
  - putative proteins from Epstein-Barr and rabies viruses
- Stimulate stronger immune response than normal antigens by “tricking” T cells into activation although they have not been triggered by a specific antigen
- Stimulate T cells to proliferate nonspecifically
- Contribute to microbial pathogenicity
- stimulate release of massive quantities of cytokines from T cells
  - may result in circulatory shock and multiorgan failure

Contrast host innate resistance with adaptive immunity

Outline the localization of B and T cells during development

34.1 OVERVIEW OF ADAPTIVE IMMUNITY

Overview of Specific (Adaptive) Immunity

- Three major functions
  - recognize nonself
  - respond to nonself
    - effector response
      - eliminates or renders foreign material harmless
    - anamnestic response
      - upon second encounter with same pathogen immune system mounts a faster and more intense response
  - remember nonself

Acquired Immune System Development

- B and T cells initially arise in the bone marrow
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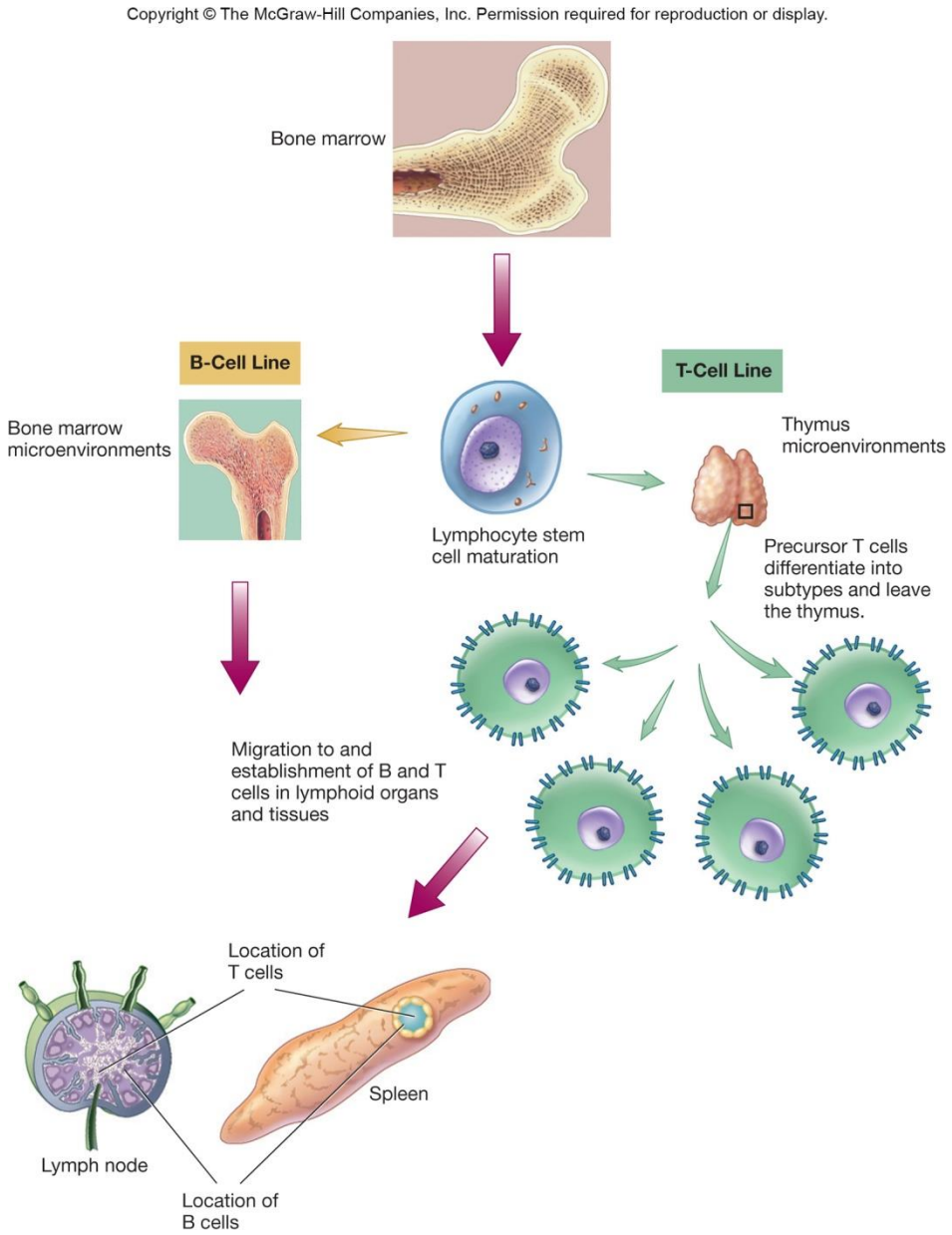

Four Characteristics of Specific Immunity

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  - generates enormous diversity of molecules
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  - can be directed against one specific pathogen or foreign substance among trillions
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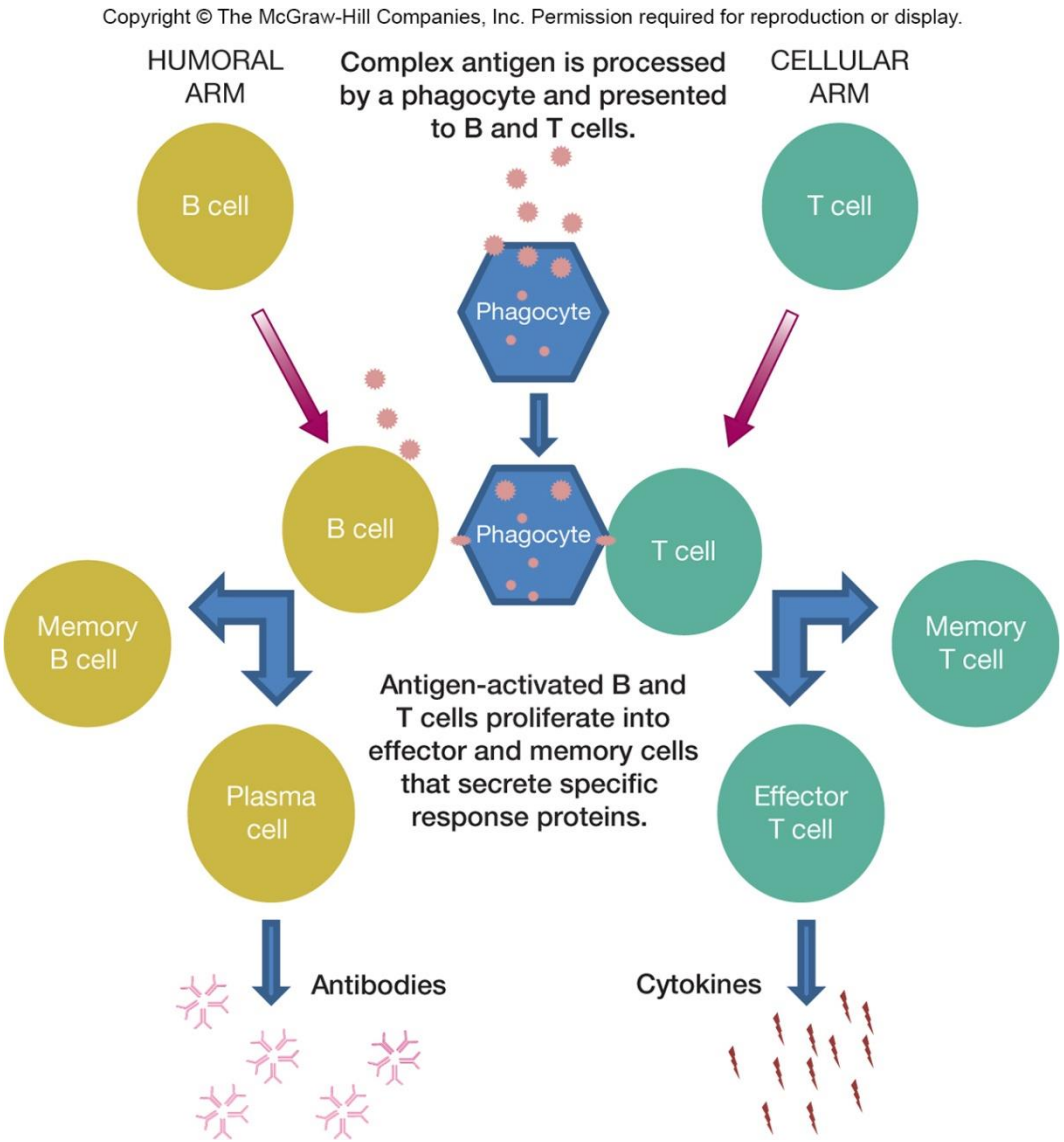

Predict the types of molecules that can serve as antigens

Compare haptens and true antigens

34.2 ANTIGENS

Antigens

- Self and nonself substances that elicit an immune response and react with products of that response
- Most are large, complex molecules
- Antigenic determinant sites (***epitopes***)
  - site on antigen that reacts with specific antibody or T cell receptor
  - valence is number of epitopes on an antigen
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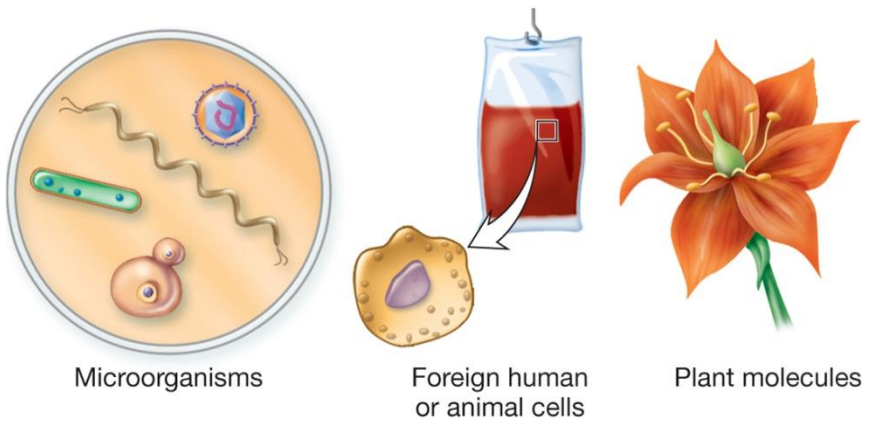
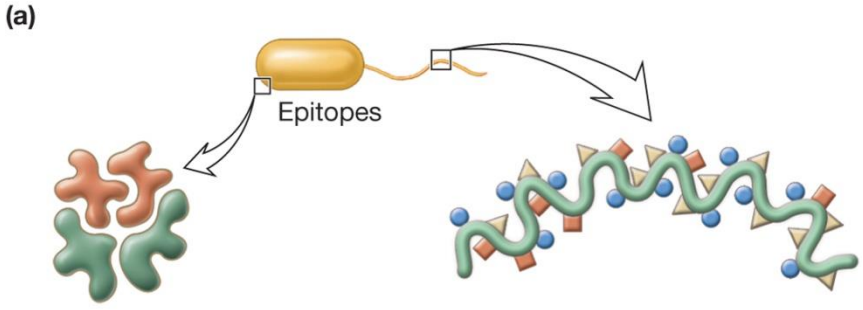
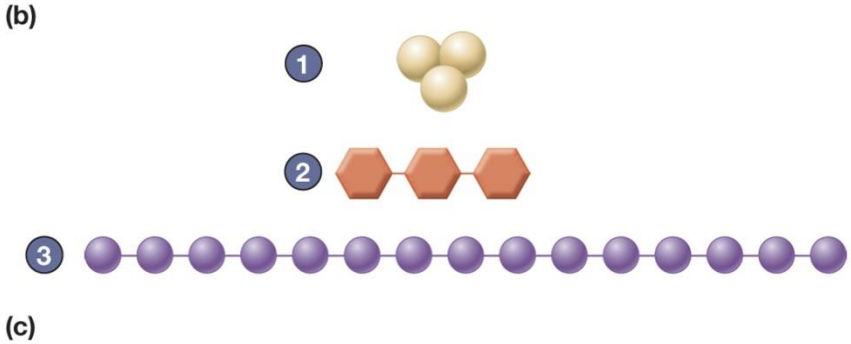
Haptens







- Small organic molecules
- Not antigenic but may become antigenic when bound to larger carrier molecule
  - e.g., penicillin
  - may elicit hapten specific and carrier specific responses

Report the methods by which immunity occurs by natural and artificial means

Distinguish between the active and passive forms of natural and artificial immunity

34.3 TYPES OF ADAPTIVE IMMUNITY

Types of Specific Immunity

- Naturally acquired active immunity
  - type of specific immunity a host develops after exposure to foreign substance
- Naturally acquired passive immunity
  - transfer of antibodies, e.g., mother to fetus across placenta, mother to infant in breast milk
- Artificially acquired active immunity (vaccination)
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Acquired Immunity

Natural immunity
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Active immunity
is the consequence of a person developing his or her own immune response to a microbe.

Infection

Passive immunity
is the consequence of one person receiving preformed immunity made by another person.

Maternal antibody

Artificial immunity
is that produced purposefully through medical procedures (also called immunization).

Active immunity
is the consequence of a person developing his or her own immune response to a microbe.

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Passive immunity
is the consequence of one person receiving preformed immunity made by another person.

Immune globulin therapy

Define the method by which a host distinguishes itself from nonself (foreign) materials
Diagram the host cell receptors that distinguish self from nonself
Compare the processes by which MHC class I and class II receptors recognize foreignness
Identify cells that can function as antigen-presenting cells (APCs)
Explain the use of “cluster of differentiation” (CD) molecules to name cells

34.4 RECOGNITION OF FOREIGNNESS

Recognition of Foreignness

- Distinguishing between self and non-self is essential for the proper functioning of the immune system
  - this allows for selective destruction of invading pathogens without destruction of host tissues
  - involves major histocompatibility complex

Major Histocompatibility Complex (MHC)

- Collection of genes that code for self/nonself recognition potential of a vertebrate
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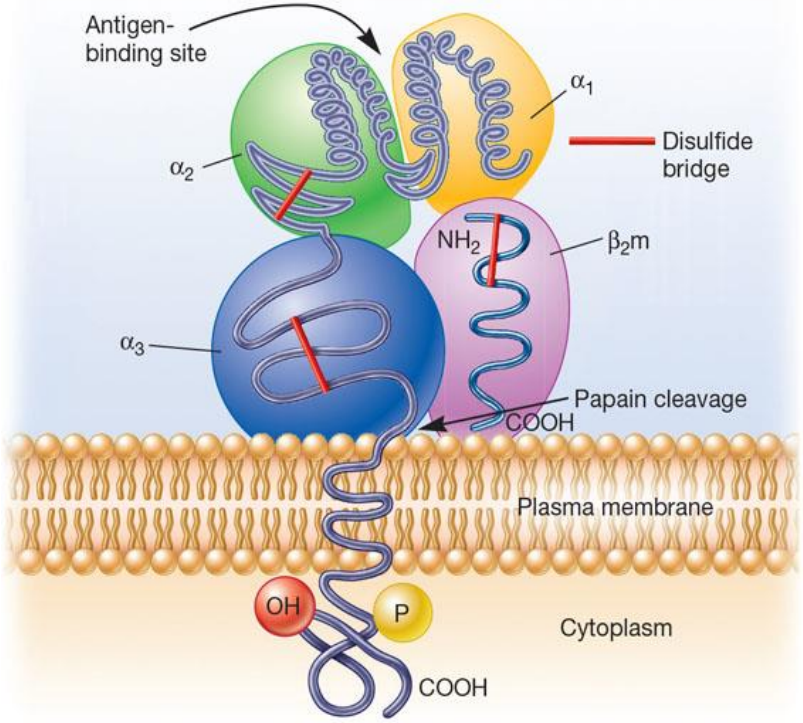
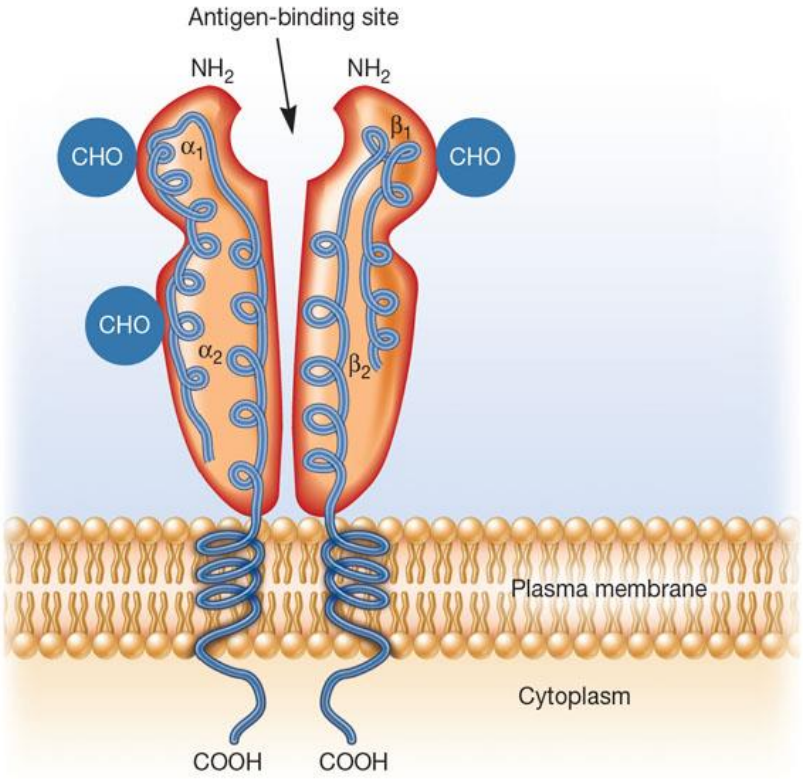
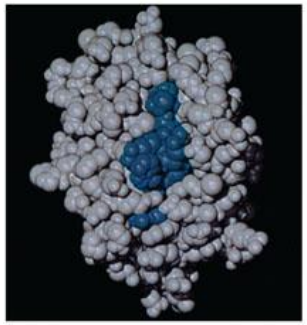


(a) Class I MHC



(b) Class II MHC



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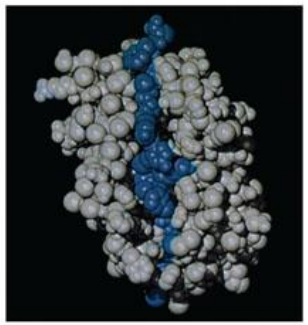

(d)

Courtesy of Dr. Paul Travers

MHC and Antigen Processing

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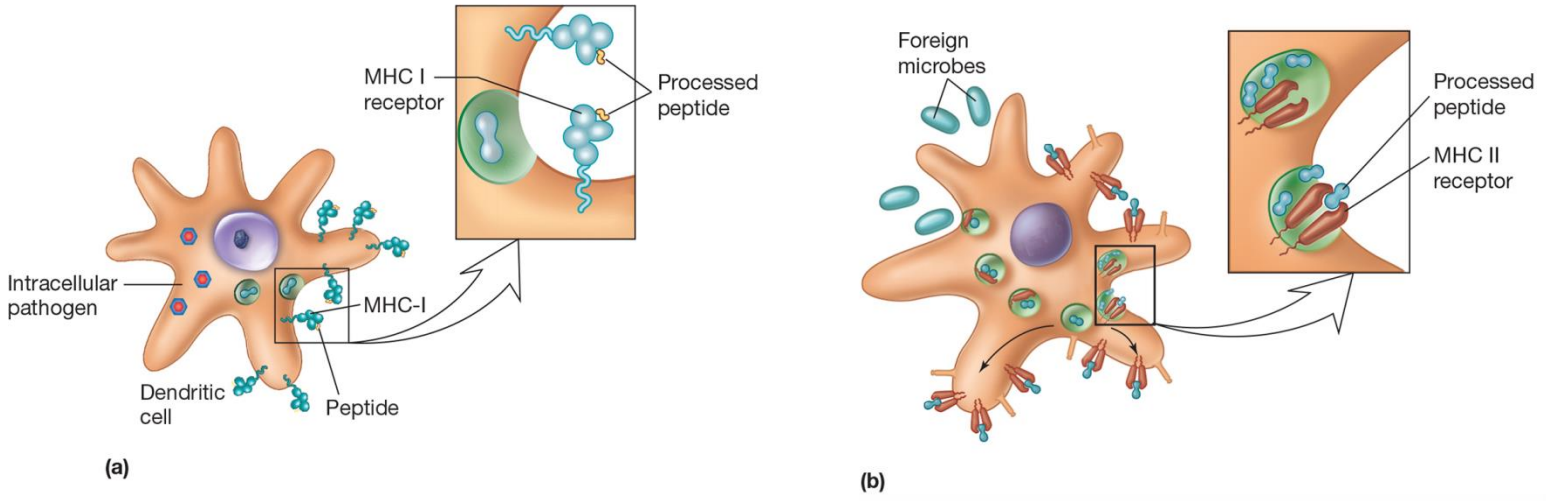

Cluster of Differentiation Molecules (CDs)

Table 34.1 Functions of Some Cluster of Differentiation (CD) Molecules

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  - have specific roles in intercellular communication
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Contrast the biological functions of T-cell subsets

Describe T-cell receptor structure and function

Illustrate the T-cell developmental process

Connect antigen presentation within MHC receptors and T-cell subset recognition

Build a model of the molecular events resulting in T-cell activation

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- Originate from CD34+ stem cells in the bone marrow but mature in thymus
- Have major role in B cell activation
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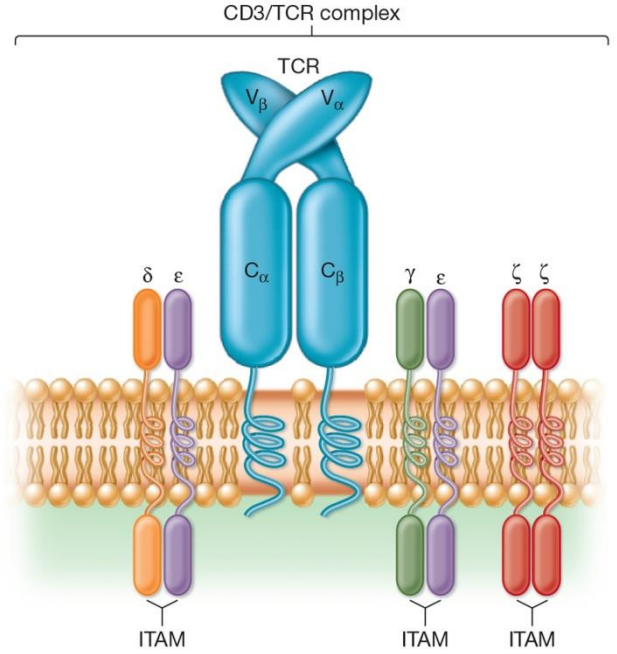
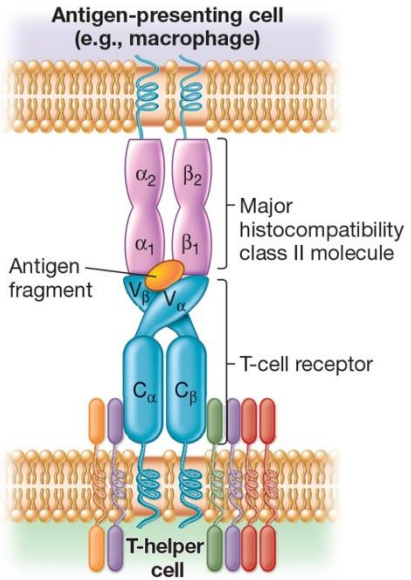
- Recognize and bind fragments of antigens
- Antigen fragments must be presented by antigen-presenting cells (APCs) on the ends of MHC molecules

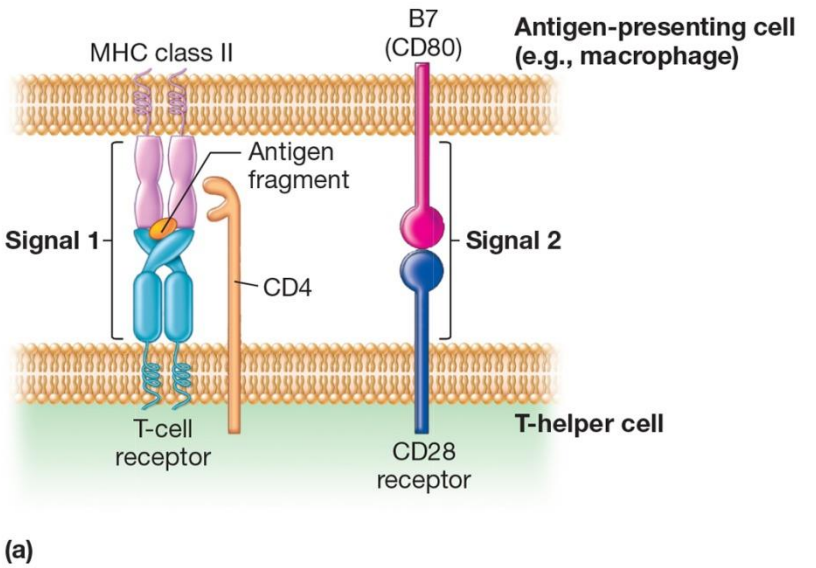


(a)

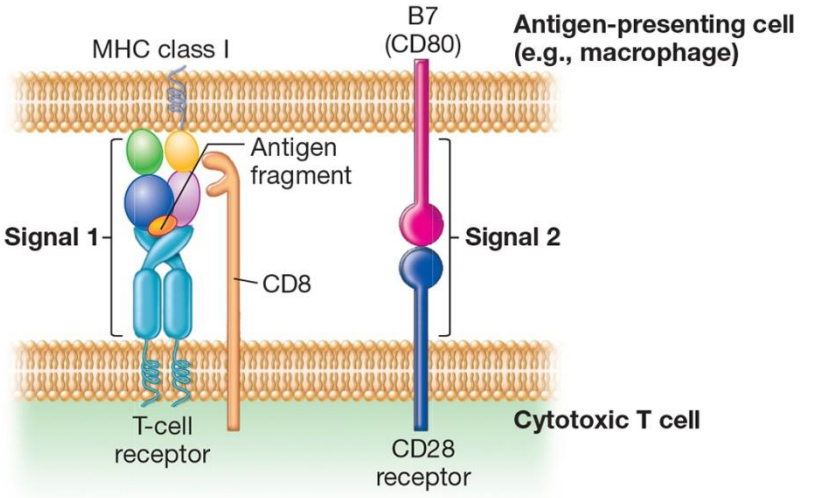


(b)

T Cell Activation



(a)

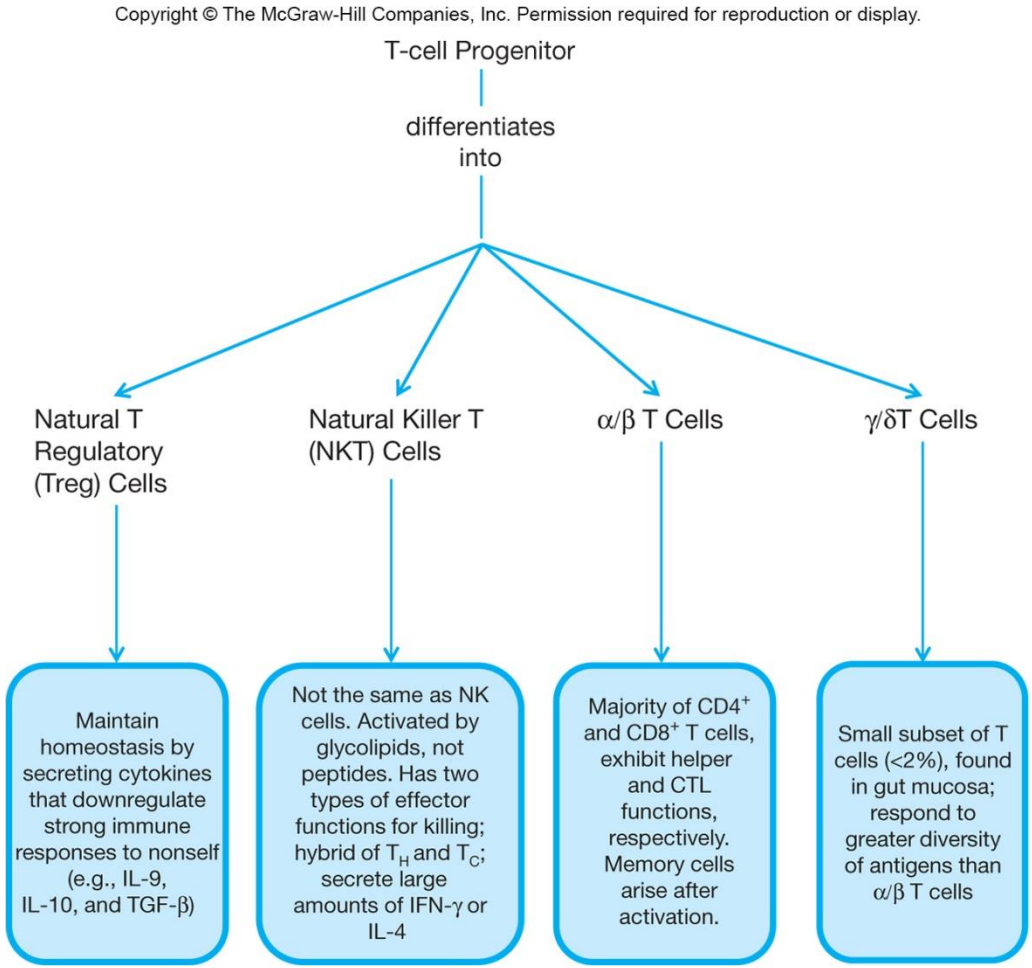


(b)

- Requires binding a specific antigen
  - occurs through antigen presentation bridging MHC class II on the APC to the TCR on the T cell
  - initiates signaling cascade involving other membrane-bound proteins and intracellular messengers
  - second signal required for lymphocyte proliferation, differentiation, and expression of specific cytokine genes

Types of T Cells

- Mature T cells are naïve until activated by antigen presentation
- Once activated they proliferate into effector cells and memory cells
  - effector cells carry out specific functions to protect host
  - three types
    - T helper (T_H), cytotoxic T lymphocytes (T_Cs), and regulatory T cells



T-Helper Cells

- Also known as CD4+ T cells
- Activated by antigen presentation with class II MHC
- Subdivisions of T helper cells
  - T_H0 – undifferentiated T cells
  - T_H1 – help activate macrophages
  - T_H2 – help B cells produce antibodies
  - T_H17 – assist in antibacterial responses
  - Treg – help control lymphocyte responses

T Helper Cells

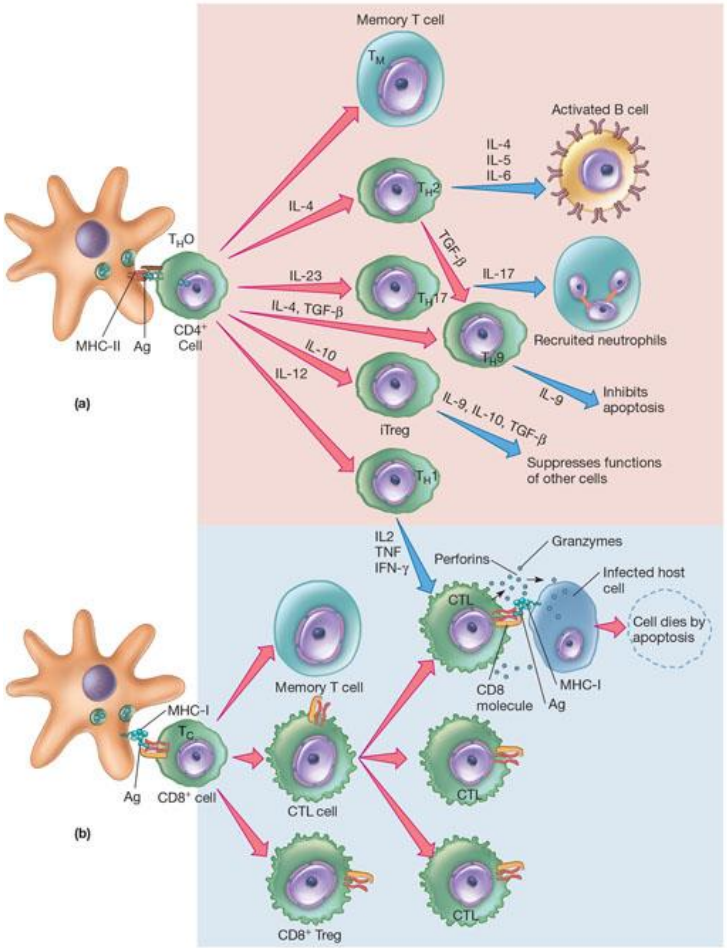
- T_H1 cells
  - promote cytotoxic T cell activity and activate macrophages
  - mediate inflammation and delayed hypersensitivity by producing a specific set of cytokines
    - IL-2, IFN-γ, tumor necrosis factor (TNF)-β
- T_H2 cells
  - stimulate antibody responses and defend against helminth parasites
  - involved in promoting allergic reactions
  - produce a specific set of cytokines
    - IL-5, IL-6, IL-10, and IL-13

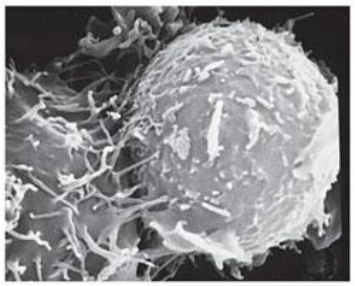
Cytotoxic T Cells (T_Cs)

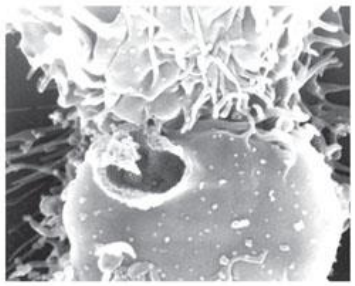
- Are $CD8^+$ T cells that have been activated by antigen presented on MHC-1 molecules of nucleated cells
- Once activated these CTLs can kill target cells that have the same antigen-MHC-1 combination that originally activated the CTL
- After bind target, CTL kills target cell via the perforin pathway and CD95 pathway

Regulatory T Cells

- Treg cells
  - derived from approximately 10% of CD4+ T cells and 2% of CD8+ T cells
  - IL-10 induces regulatory function by inhibiting T helper cell function
    - Activates transcription factor Foxp3
    - Foxp3 upregulated CD25 and CTLA-4
    - CTLA-4 binds to B7 on APCs, blocking the 2nd signal required for lymphocyte activation
  - Tregs also suppress/regulate functions by secretion of IL-9 and TGF-β







Courtesy of Dr. Gilla Kaplan, PHRI, UMDNJ

Superantigens

- Bacterial and viral proteins
  - staphylococcal enterotoxin B
  - the toxin that causes toxic shock syndrome
  - mouse tumor virus superantigen
  - putative proteins from Epstein-Barr and rabies viruses
- Stimulate stronger immune response than normal antigens by “tricking” T cells into activation although they have not been triggered by a specific antigen
- Stimulate T cells to proliferate nonspecifically
- Contribute to microbial pathogenicity
- stimulate release of massive quantities of cytokines from T cells
  - may result in circulatory shock and multiorgan failure