陳炳宏老師

bhchen@kmu.edu.tw
校內分機2676
http://allergy.kmu.edu.tw

MICROBIOLOGY

WITH DISEASES BY TAXONOMY, THIRD EDITION

Chapter 16 Adaptive Immunity

適應性免疫

學習目標

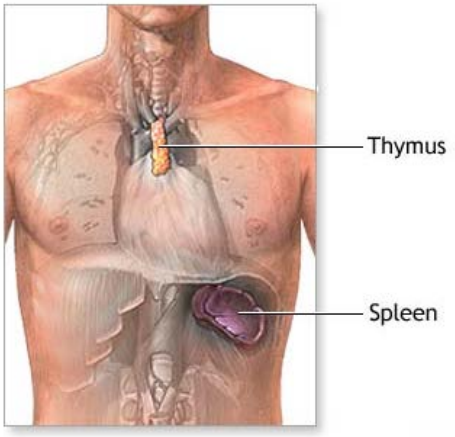
- Understand the nature and elements of adaptive immunity.
- Understand the process as how an adaptive immune response is prepared and initiated.
- Understand the characteristics of various responses in adaptive immunity
  - Cell-mediated response
  - Humoral response

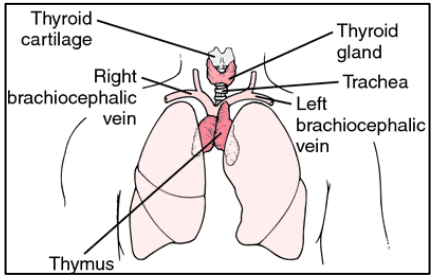
Overview of Adaptive Immunity

- Adaptive immunity is the body's ability to recognize and defend itself against distinct invaders and their products
- Five attributes of adaptive immunity
  - Specificity
  - Inducibility
  - Clonality
  - Unresponsiveness to self (tolerance)
  - Memory

Overview of Adaptive Immunity

- Involves activity of lymphocytes
- Two main types of lymphocytes
  - B lymphocytes (B cells)
    - Mature in the bone marrow
  - T lymphocytes (T cells)
    - Mature in the thymus
- Two types of adaptive immune responses
  - Humoral immune responses
  - Cell-mediated immune responses





Lymphocytes play a central role in adaptive immunity

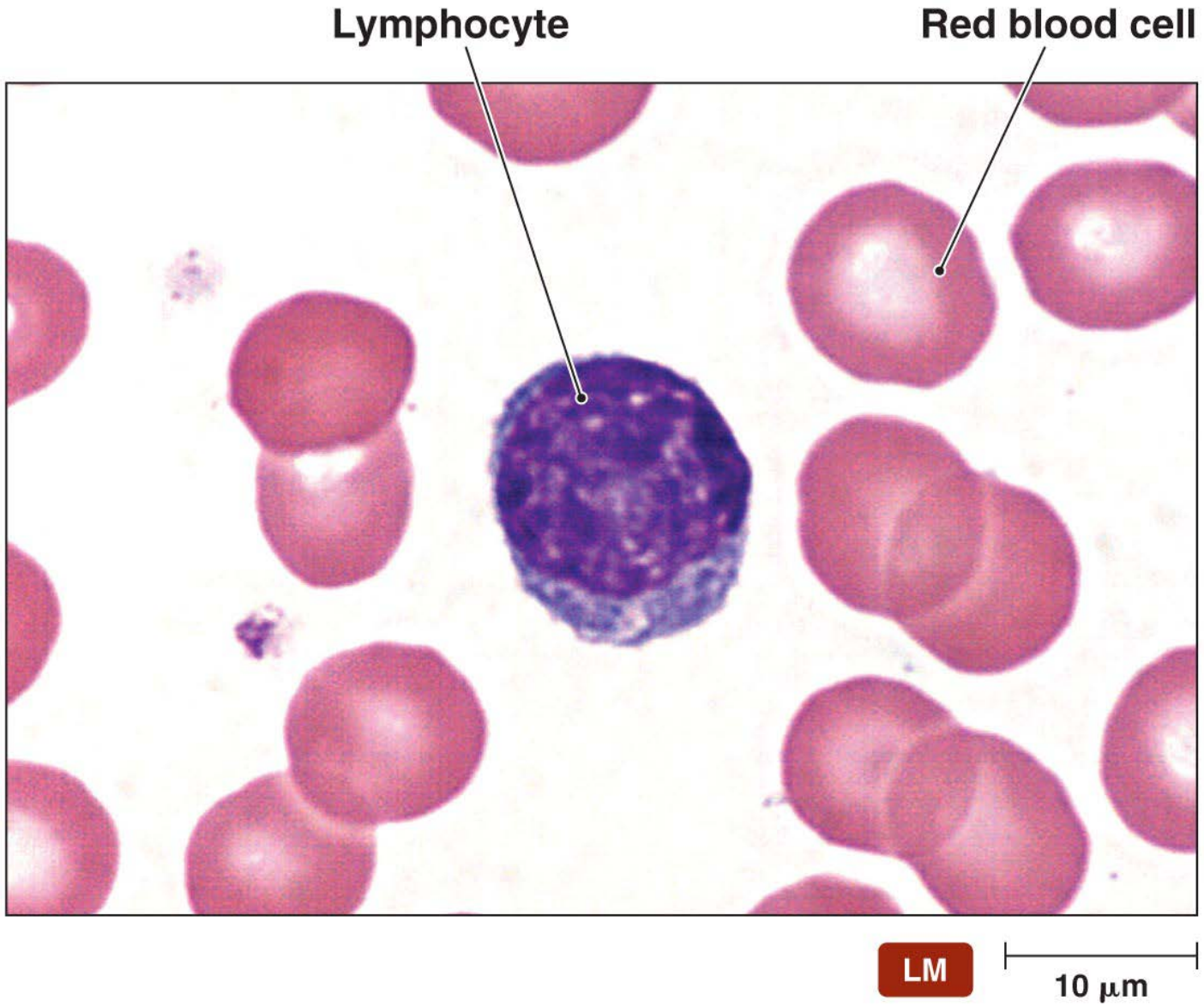
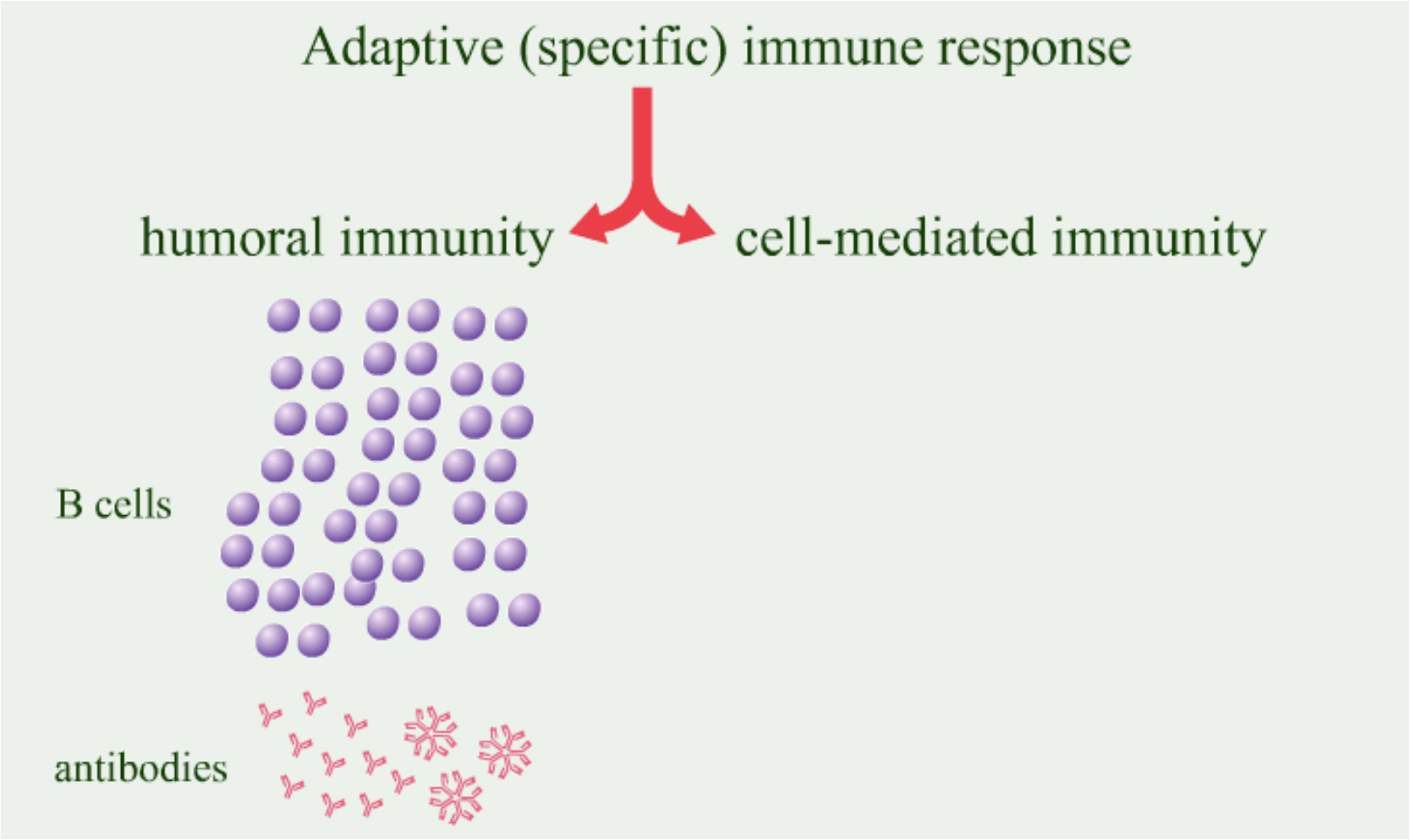


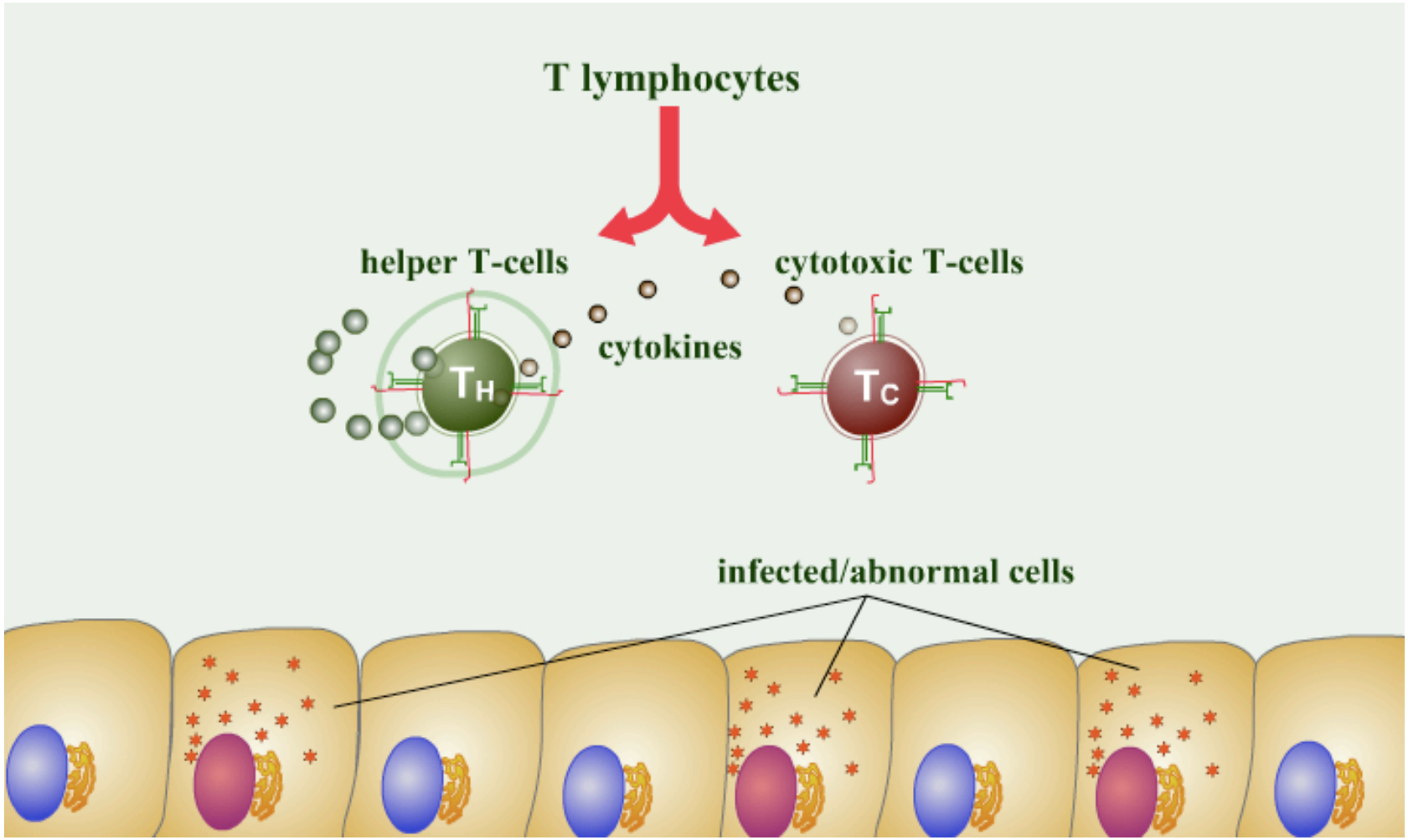
Figure 16.1

Overview of Adaptive Immunity



PLAY Animation: Humoral Immunity: Overview

Overview of Adaptive Immunity



PLAY Animation: Cell-Mediated Immunity: Overview

Elements of Adaptive Immunity

- The Tissues and Organs of the Lymphatic System
  - Screen the tissues of the body for foreign antigens
  - Composed of lymphatic vessels and lymphatic cells, tissues, and organs

Elements of Adaptive Immunity

- The Tissues and Organs of the Lymphatic System
  - Lymphatic vessels and the flow of lymph
    - One-way system that conducts lymph from tissues and returns it to the circulatory system
      - Lymph 淋巴液
        - Liquid with similar composition to blood plasma
        - Arises from fluid leaked from blood vessels into surrounding tissues

The lymphatic system

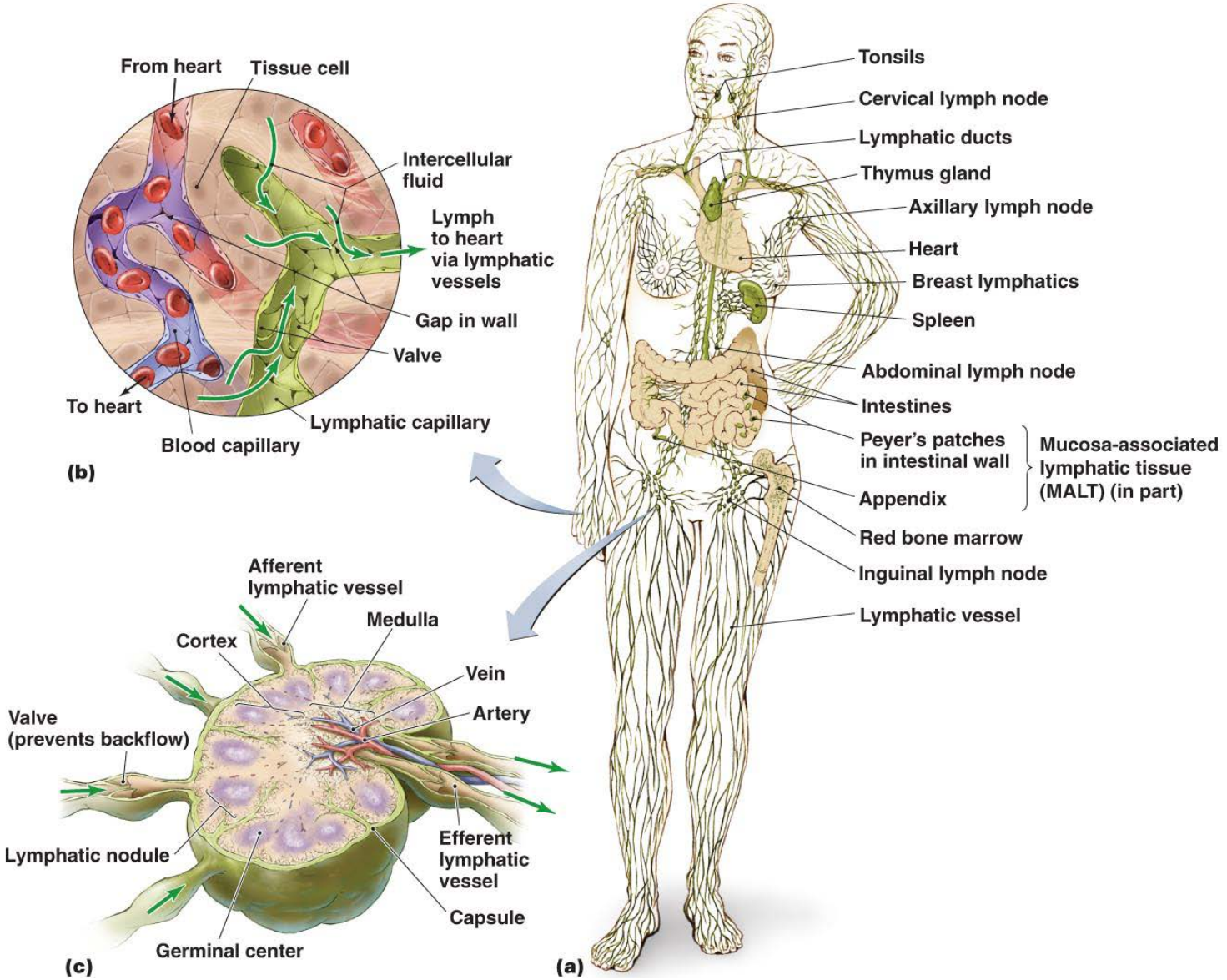


Figure 16.2

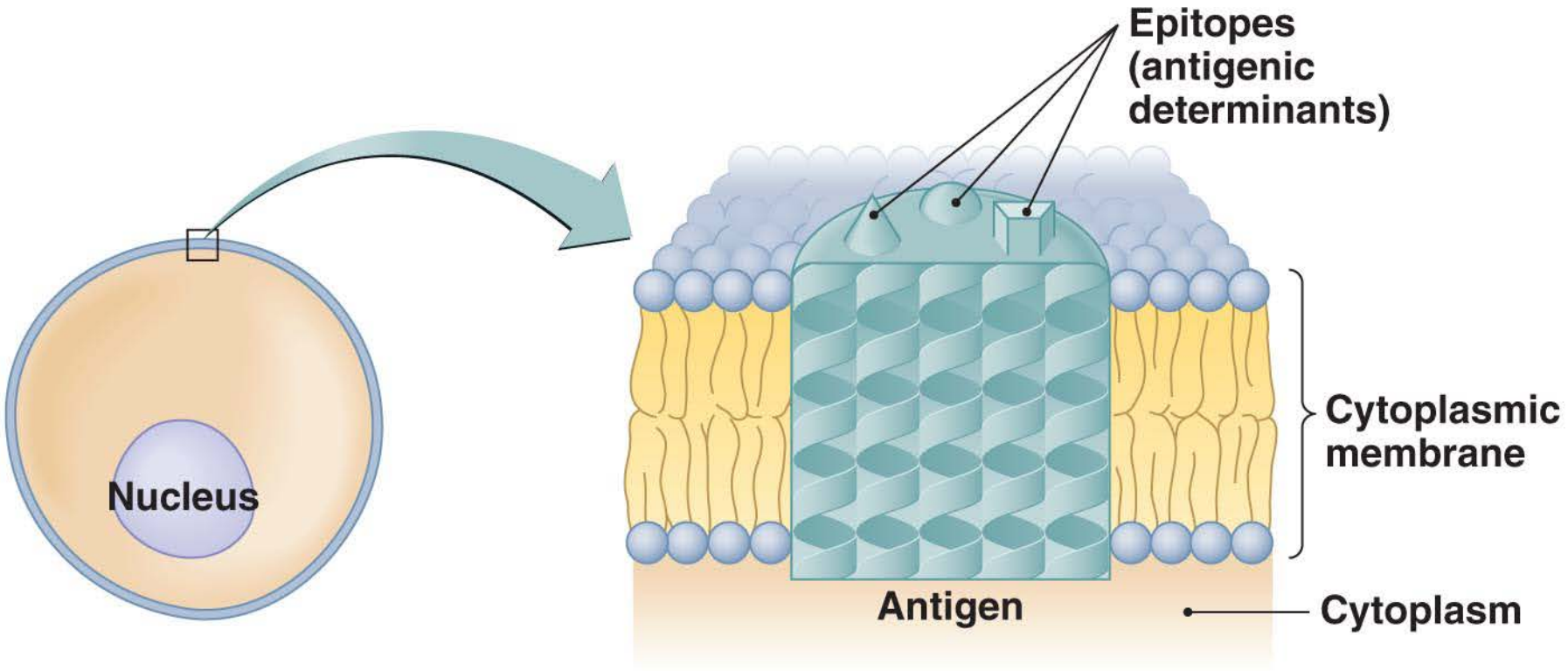
Elements of Adaptive Immunity

- The Tissues and Organs of the Lymphatic System
  - Lymphoid organs
    - Primary lymphoid organs
      - Red bone marrow
      - Thymus
    - Secondary lymphoid organs
      - Lymph nodes
      - Spleen
      - Tonsils
      - Mucosa-associated lymphatic tissue (MALT)

Elements of Adaptive Immunity

- Antigens
  - Properties of antigens
    - Molecules the body recognizes as foreign and worthy of attack
    - Recognized by three-dimensional regions called epitopes
    - Include various bacterial components as well as proteins of viruses, fungi, and protozoa
    - Food and dust can also contain antigenic particles

Antigens provoke a specific immune response



(a) Epitopes (antigenic determinants)

Figure 16.3a

3 Classes of Antigens

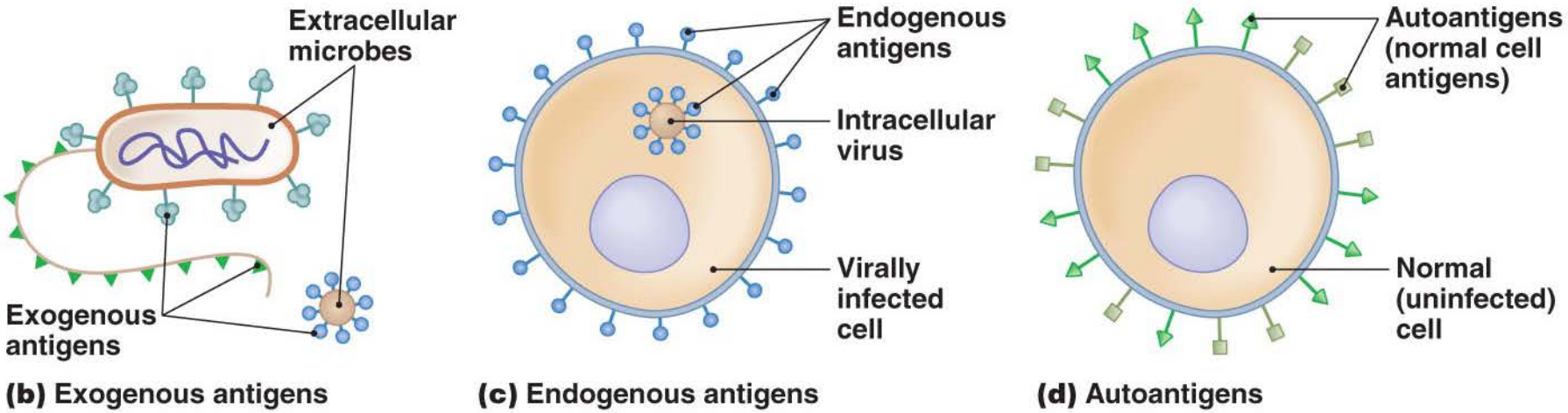


Figure 16.3b-d

Elements of Adaptive Immunity

- B Lymphocytes (B Cells) and Antibodies
  - Arise and mature in the red bone marrow
  - Found primarily in the spleen, lymph nodes, and MALT
  - Small percentage of B cells circulate in the blood
  - Major function is the secretion of antibodies

Elements of Adaptive Immunity

BCR = membrane-bound Ab on B cell

- B Lymphocytes (B Cells) and Antibodies
  - Specificity of the B cell receptor (BCR)
    - Each B lymphocyte has multiple copies of the B cell receptor
    - Each B cell generates a single BCR (= single Ab specificity)
    - Two variable regions of the BCR form the antigen-binding sites
    - Each BCR recognizes only one epitope
    - The entire repertoire of an individual's BCRs is capable of recognizing millions of different epitopes

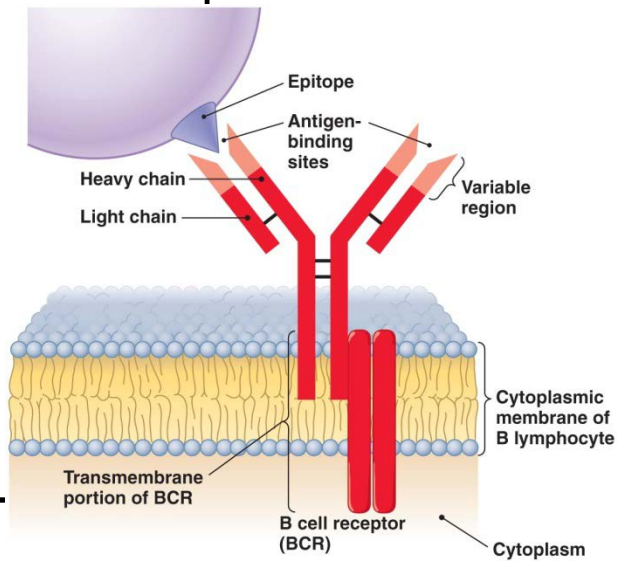
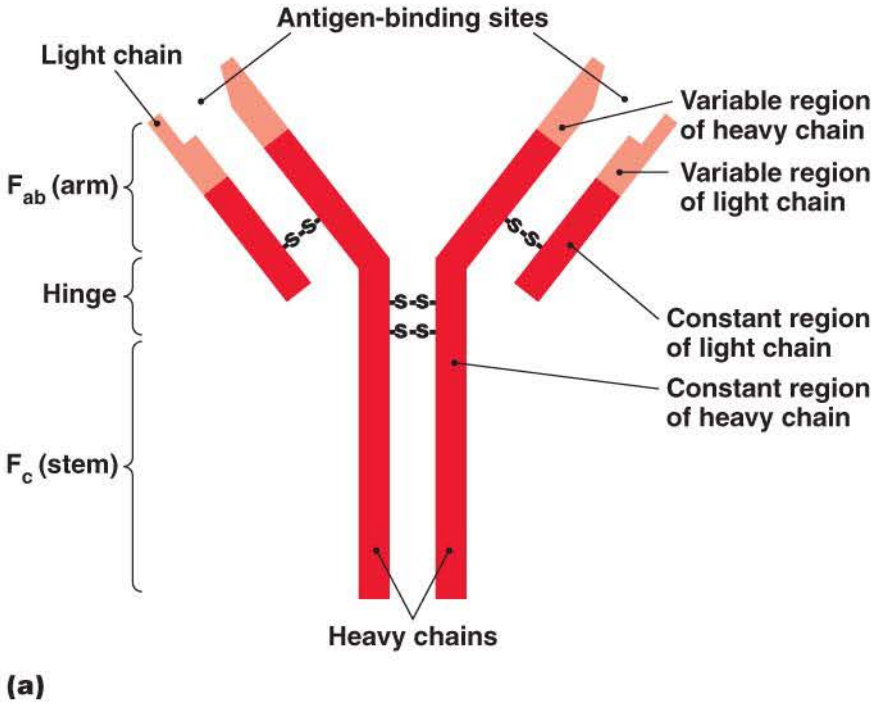


Figure 16.4

Elements of Adaptive Immunity

- B Lymphocytes (B Cells) and Antibodies
  - Specificity and antibody structure
    - Antibodies are immunoglobulins *similar* to BCRs
      - Antibodies: secreted form, no transmembrane domain
      - BCR: membrane-bound form, with transmembrane domain
    - Secreted by activated B cells called plasma cells
    - Have identical antigen-binding sites and antigen specificity as the BCR of the activated B cell

Basic antibody structure



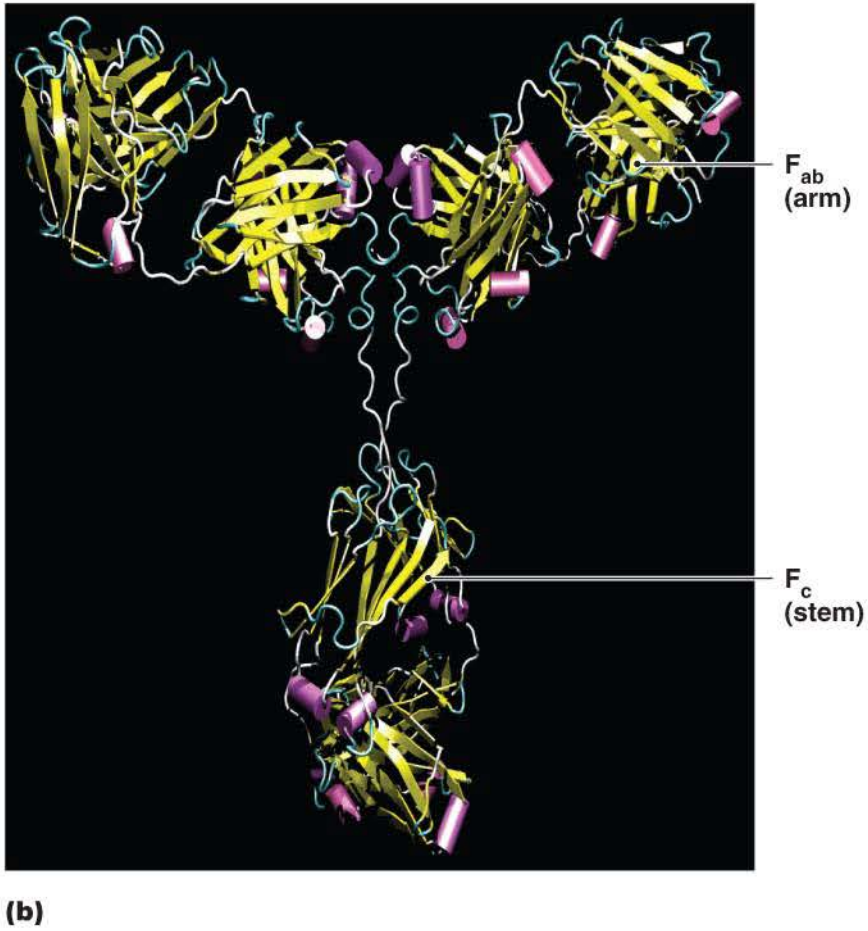
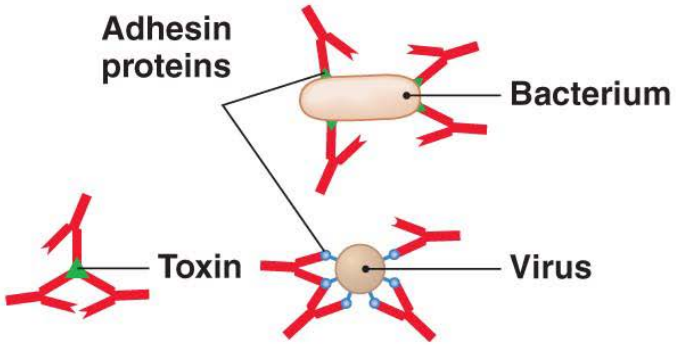


Figure 16.5

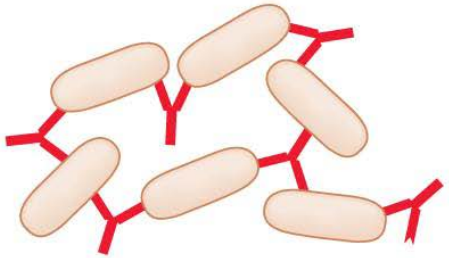
Elements of Adaptive Immunity

- B Lymphocytes (B Cells) and Antibodies
- Antibody function
  - Antigen-binding sites are *complementary* to epitopes
  - Antibodies function in several ways
    - Activation of complement and inflammation
    - Neutralization
    - Opsonization
    - Killing by oxidation
    - Agglutination
    - Antibody-dependent cellular cytotoxicity (ADCC)

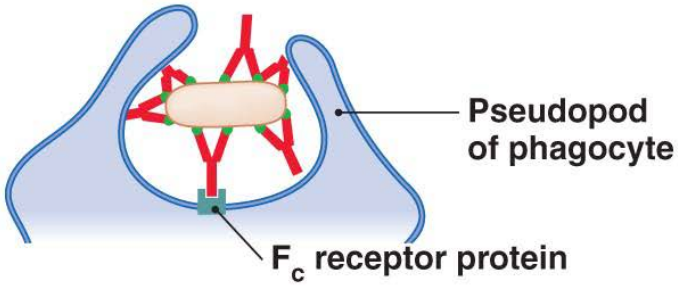
Four functions of antibodies



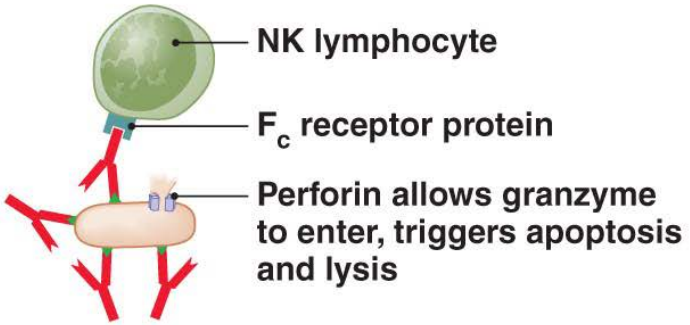
(a) Neutralization



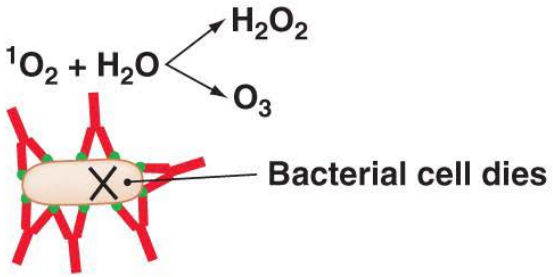
(d) Agglutination



(b) Opsonization



(e) Antibody-dependent cellular cytotoxicity (ADCC)



(c) Oxidation

Figure 16.6

Elements of Adaptive Immunity

- B Lymphocytes (B Cells) and Antibodies
  - Classes of antibodies
    - Threats confronting the immune system are variable
    - Class involved in the immune response depends on the type of antigen, portal of entry, and antibody function needed
    - Five different classes of antibodies

Elements of Adaptive Immunity

- B Lymphocytes (B Cells) and Antibodies
  - Classes of antibodies
    - IgM : first antibody produced
    - IgG : most common and longest-lasting antibody
    - IgA : associated with body secretions (e.g. guts, mucosal surfaces)
    - IgE : involved in response to parasitic infections and allergies
    - IgD : exact function is not known

Elements of Adaptive Immunity

- T Lymphocytes (T Cells)
  - Produced in the red bone marrow and mature in the thymus
  - Circulate in the lymph and blood and migrate to the lymph nodes, spleen, and Peyer's patches
  - Antigen-binding sites are complementary to epitopes
  - Have T cell receptors (TCRs) on their cytoplasmic membrane

Elements of Adaptive Immunity

- T Lymphocytes
  - Specificity of the T cell receptor (TCR)
    - TCRs *do not* recognize epitopes directly
    - TCRs only bind epitopes associated with a MHC protein
    - TCRs act primarily against cells that harbor intracellular pathogens

MHC = major histocompatability complex 主要組織相容性複合物

MHC-I: 表現在所有有核細胞細胞膜上
MHC-II: 主要表現在抗原呈現細胞(APCs – B cells, macrophages, DCs)細胞膜上

A T cell receptor (TCA)

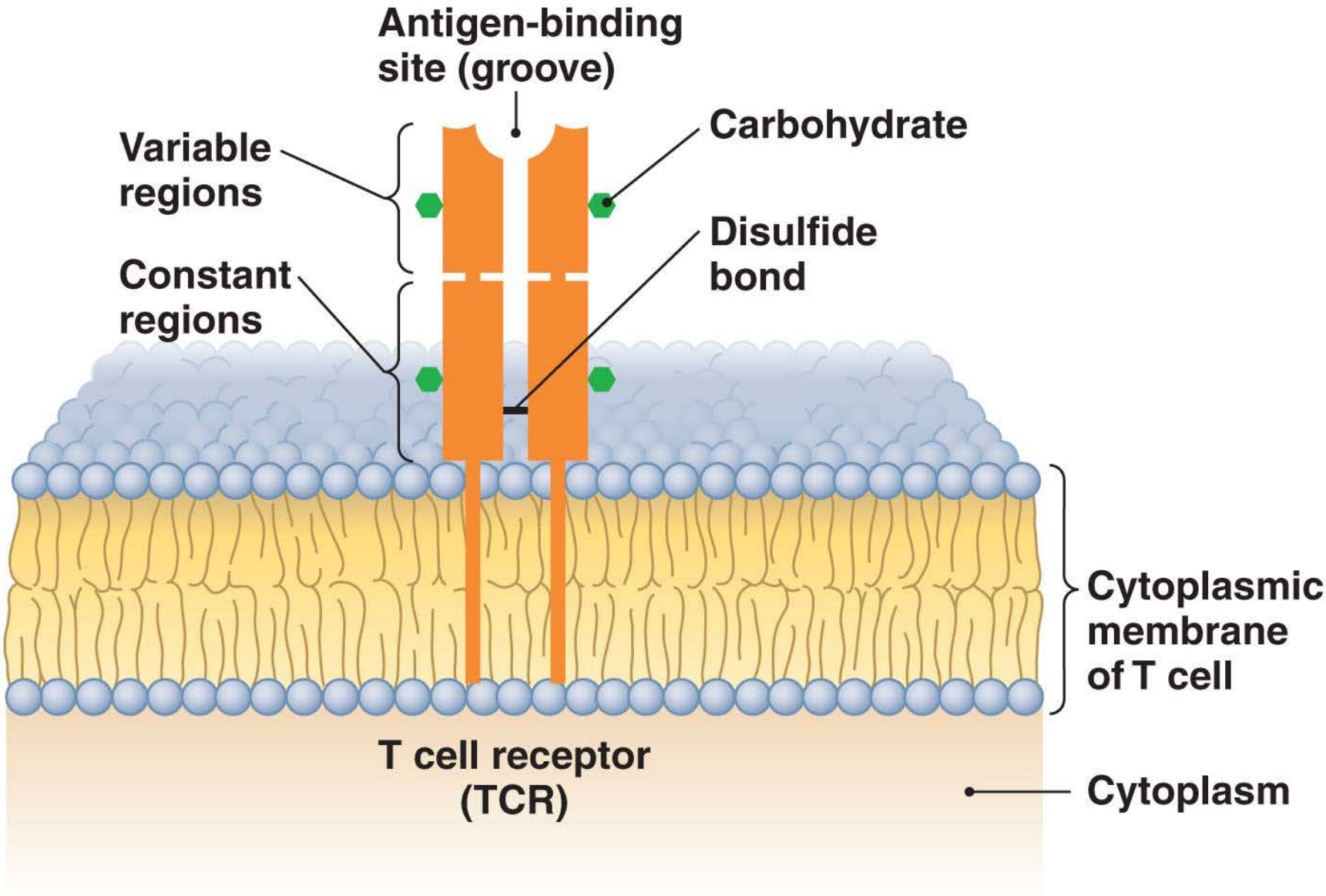


Figure 16.7

Elements of Adaptive Immunity

- T Lymphocytes
  - Types of T lymphocytes
    - Based on surface glycoproteins and characteristic functions
    - Three types
      - Cytotoxic T lymphocyte (Tc)
        - Directly kills other cells
      - Helper T lymphocyte (Th)
        - Helps regulate the activities of B cells and cytotoxic T cells
      - Regulatory T lymphocyte (Tr)
        - Represses adaptive immune responses

Elements of Adaptive Immunity

- Clonal Deletion 殖株刪除
  - Vital that immune responses not be directed against autoantigens
  - Body eliminates self-reactive lymphocytes
  - Lymphocytes that react to autoantigens undergo apoptosis

Clonal deletion of T cells

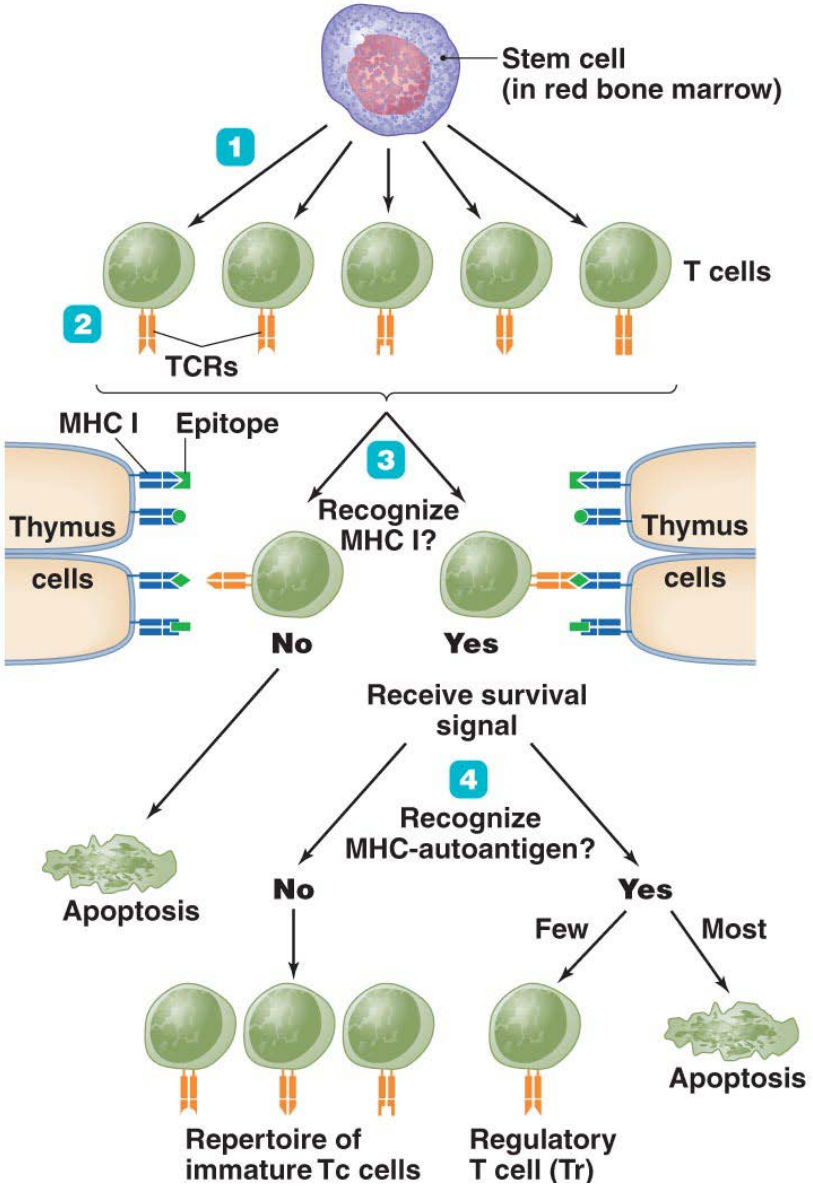


Figure 16.8

Clonal deletion of B cells

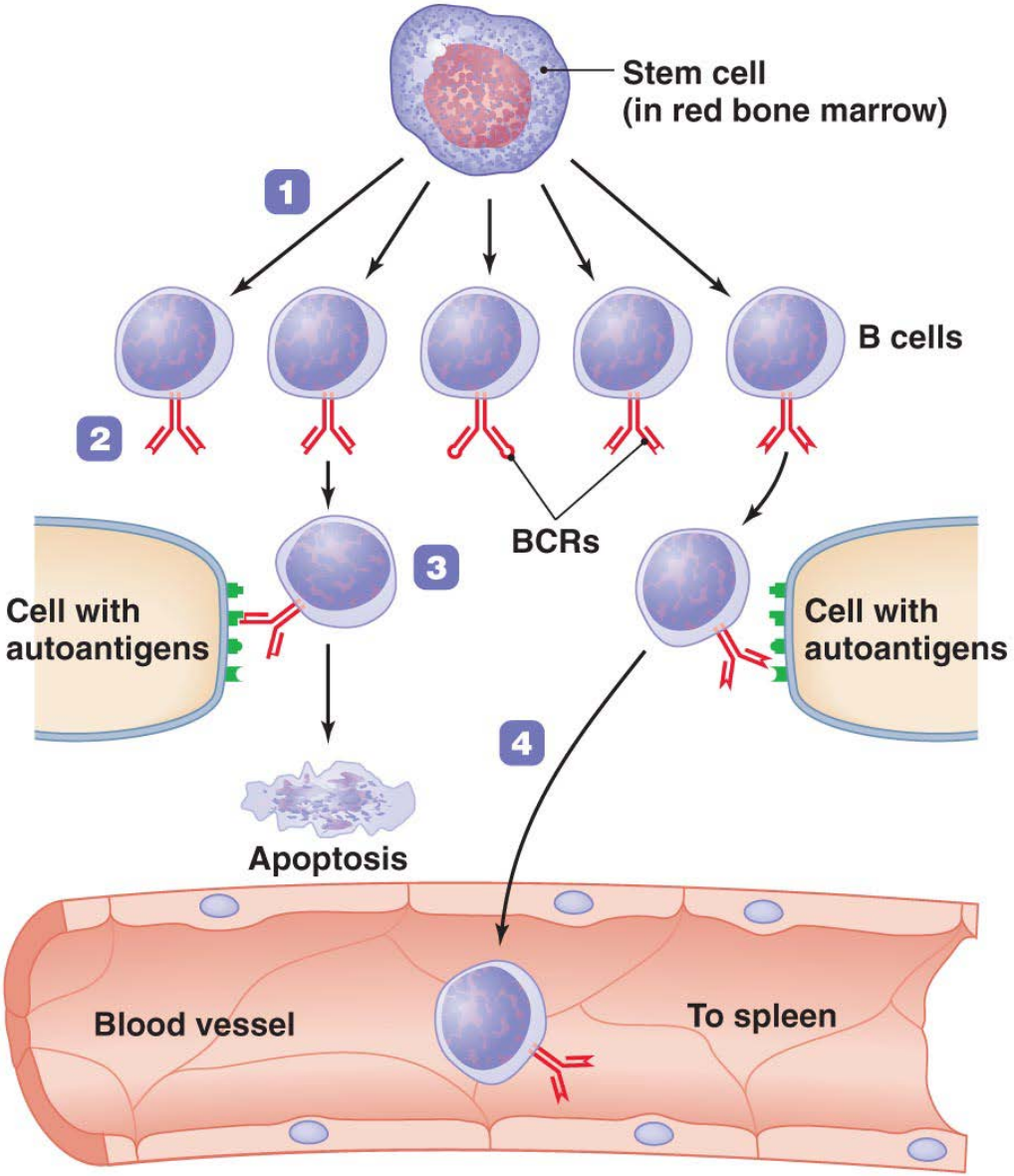


Figure 16.9

Elements of Adaptive Immunity

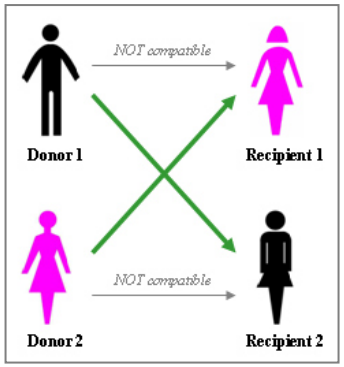
- Immune Response Cytokines
  - Soluble regulatory proteins that act as intercellular signals
  - Cytokines secreted by various leukocytes
  - Cytokine network
    - The complex web of signals among all the cells of the immune system

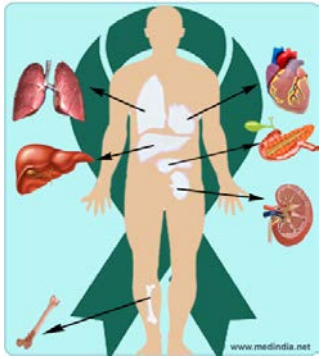
Elements of Adaptive Immunity

- Immune System Cytokines
  - Interleukins (ILs) 白血球間素
    - Signal among leukocytes
  - Interferons (IFNs) 干擾素
    - Antiviral proteins that may act as cytokines
  - Growth factors
    - Proteins that stimulate stem cells to divide
  - Tumor necrosis factor (TNF) 腫瘤壞死因子
    - Secreted by macrophages and T cells to kill tumor cells and regulate immune responses and inflammation
  - Chemokines 趨化激素
    - Chemotactic cytokines that signal leukocytes to move

Preparation for an Adaptive Immune Response

- The Roles of the Major Histocompatibility Complex
  - Group of antigens first identified in graft patients
  - Important in determining compatibility of tissues for tissue grafting
  - Major histocompatibility antigens are glycoproteins found in the membranes of most cells of vertebrate animals
  - Hold and position antigenic determinants for presentation to T cells





Preparation for an Adaptive Immune Response

- The Roles of the Major Histocompatibility Complex
  - Antigens bind in the antigen-binding groove of MHC molecules
  - Two classes of MHC proteins
    - MHC class I
    - MHC class II

MHC = major histocompatability complex 主要組織相容性複合物

MHC-I: 表現在所有有核細胞細胞膜上
MHC-II: 主要表現在抗原呈現細胞(APCs – B cells, macrophages, DCs)細胞膜上

The two classes of MHC proteins

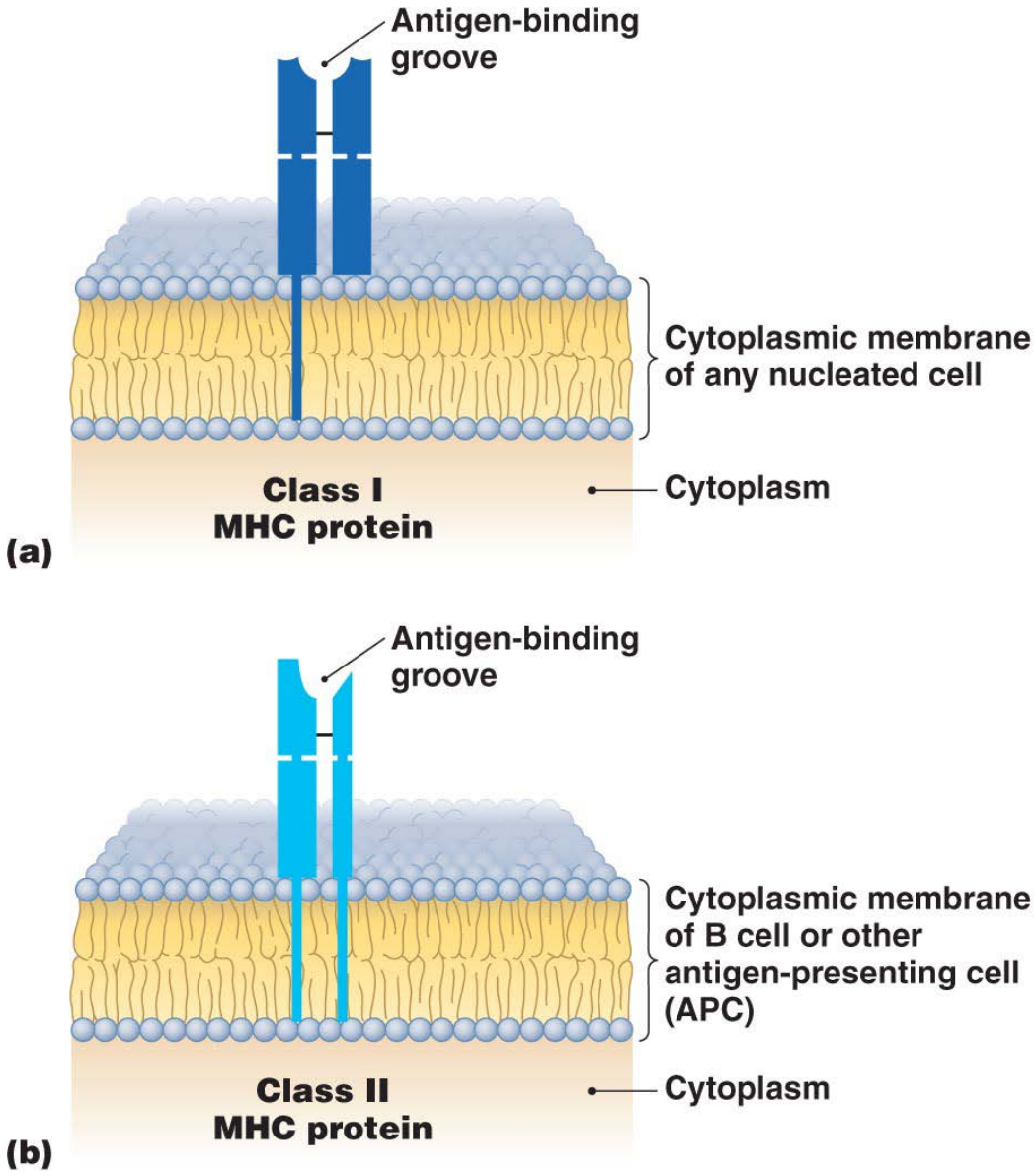


Figure 16.10

Dendritic cells

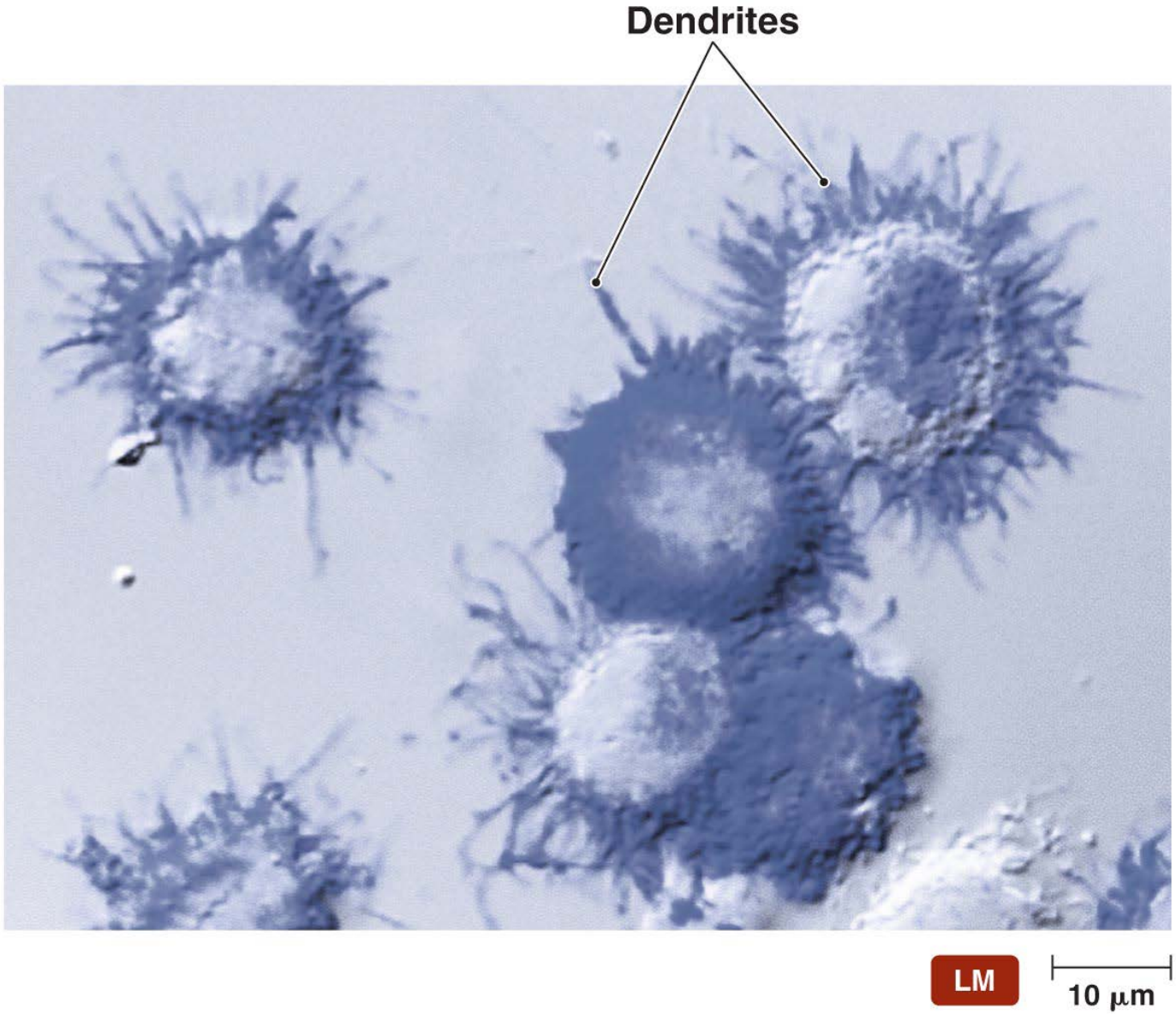


Figure 16.11

Preparation for an Adaptive Immune Response

- Antigen Processing
  - Antigens processed for MHC proteins to display epitopes
  - Different processes for endogenous and exogenous antigens
    - Endogenous antigen
      - Processed and presented via MHC-I
      - e.g. viral protein
    - Exogenous antigen
      - Processed and presented via HMC-II
      - e.g. engulfed bacteria by macrophages

The processing of endogenous antigens

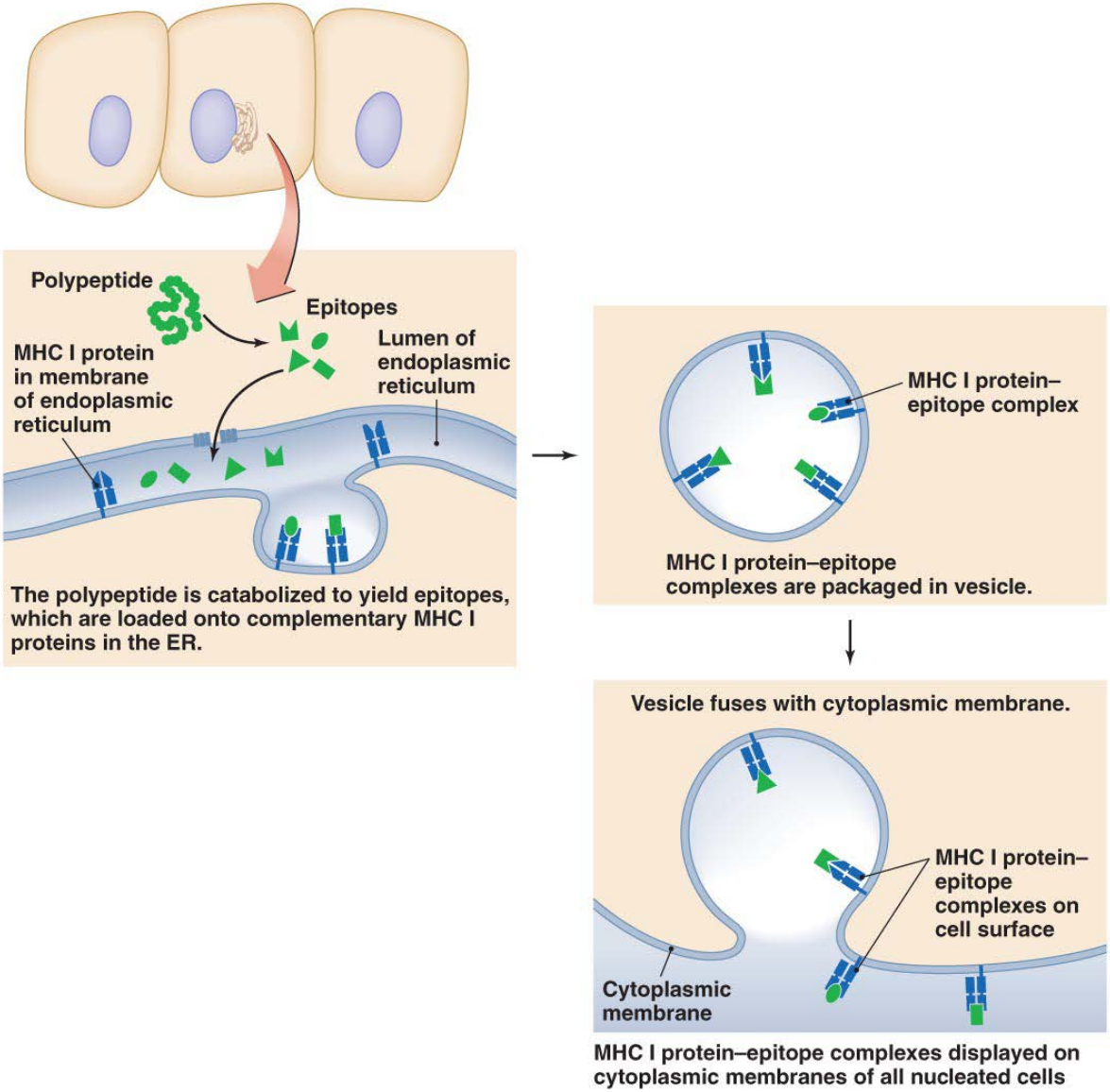


Figure 16.12

The processing of endogenous antigens

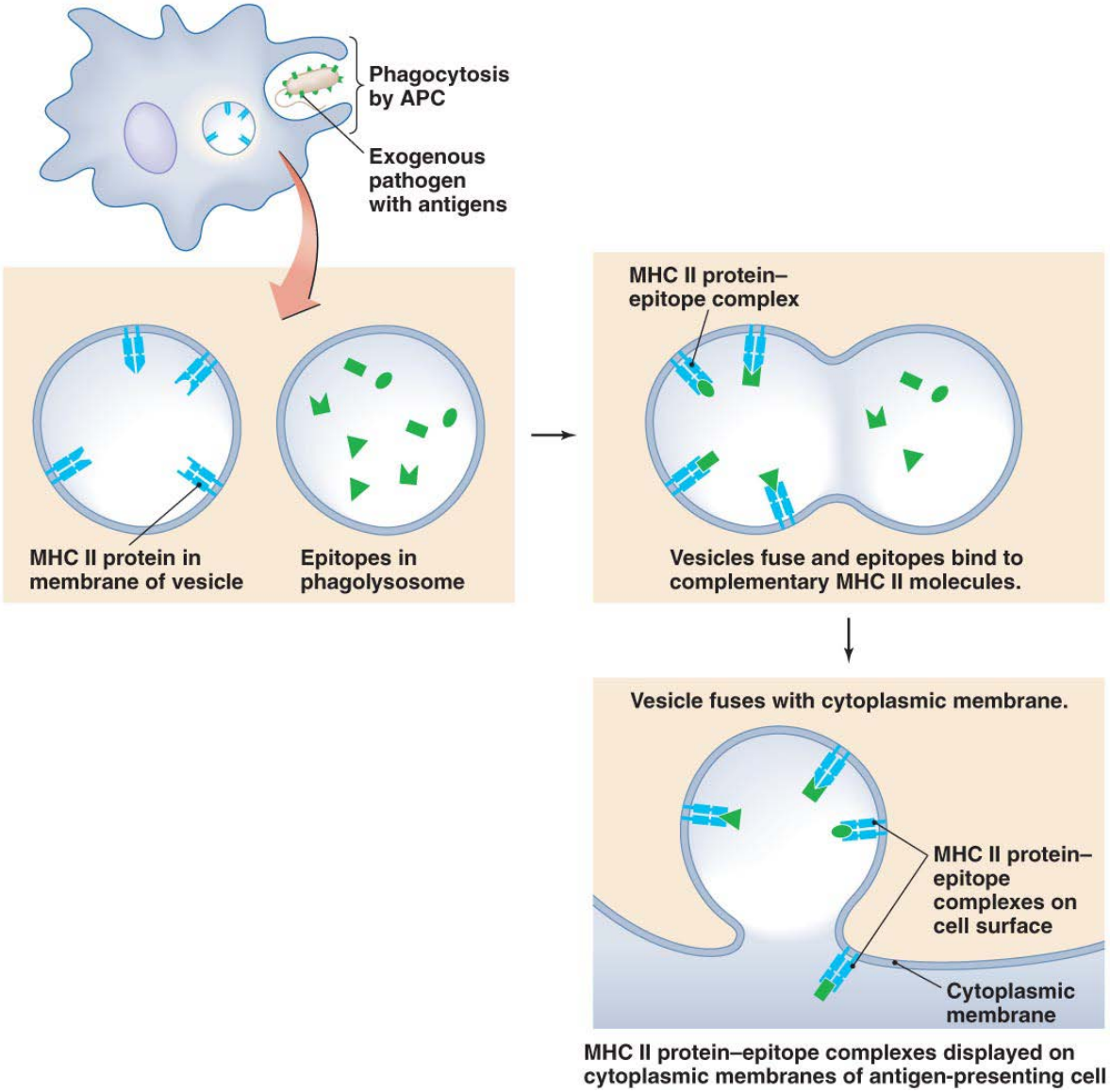


Figure 16.13

Cell-Mediated Immune Responses

- Respond to intracellular pathogens and abnormal body cells
- The most common intracellular pathogens are viruses
- The response is also effective against cancer cells, intracellular protozoa, and intracellular bacteria

Cell-Mediated Immune Responses

- Activation of T Cell Clones and Their Functions
  - Steps involved in activation of cytotoxic T cells
    - Antigen presentation
    - Helper T cell differentiation
    - Clonal expansion
    - Self-stimulation (via IL-2)

Activation of a clone of cytotoxic T cells

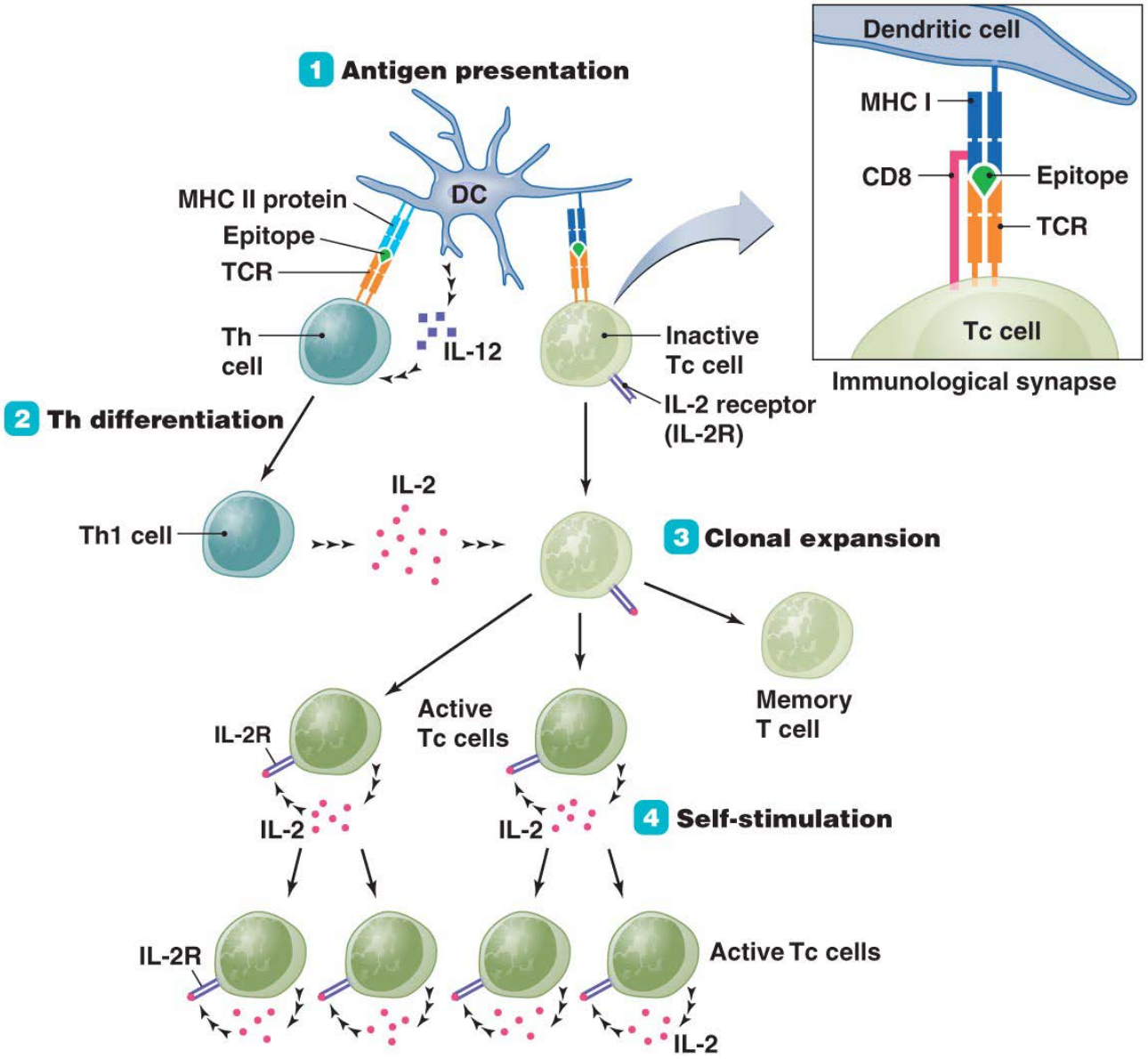


Figure 16.14

A cell-mediated immune response

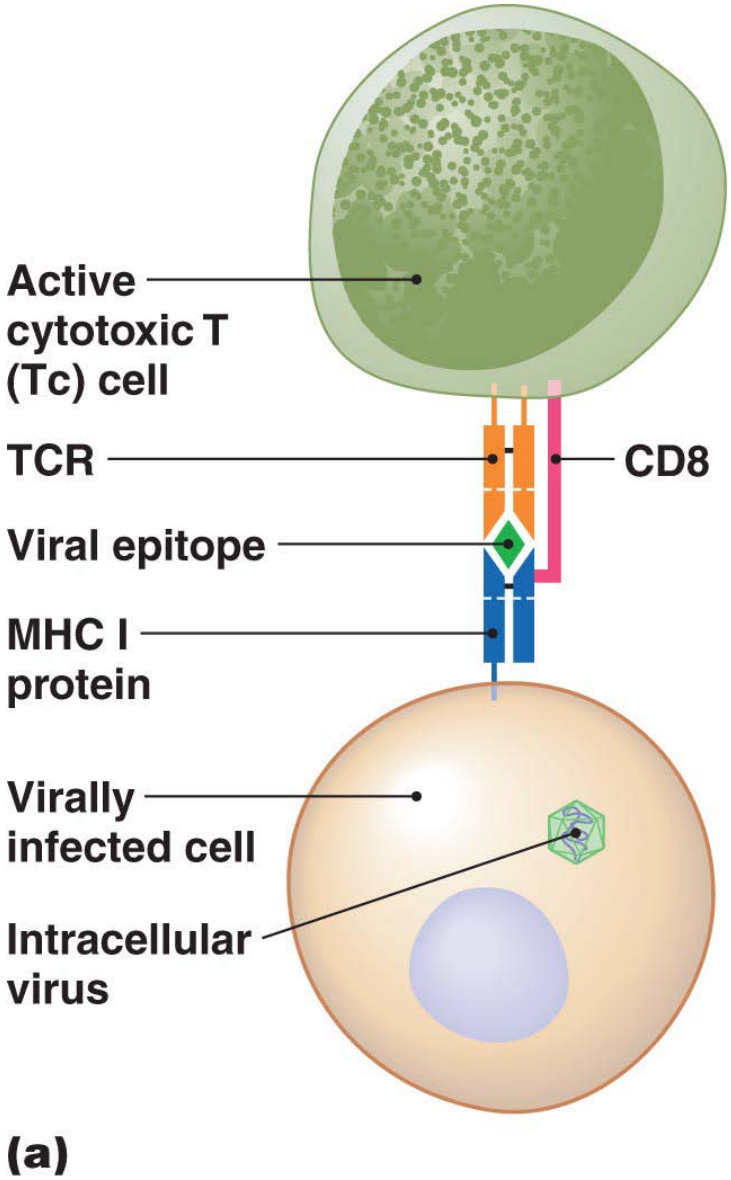
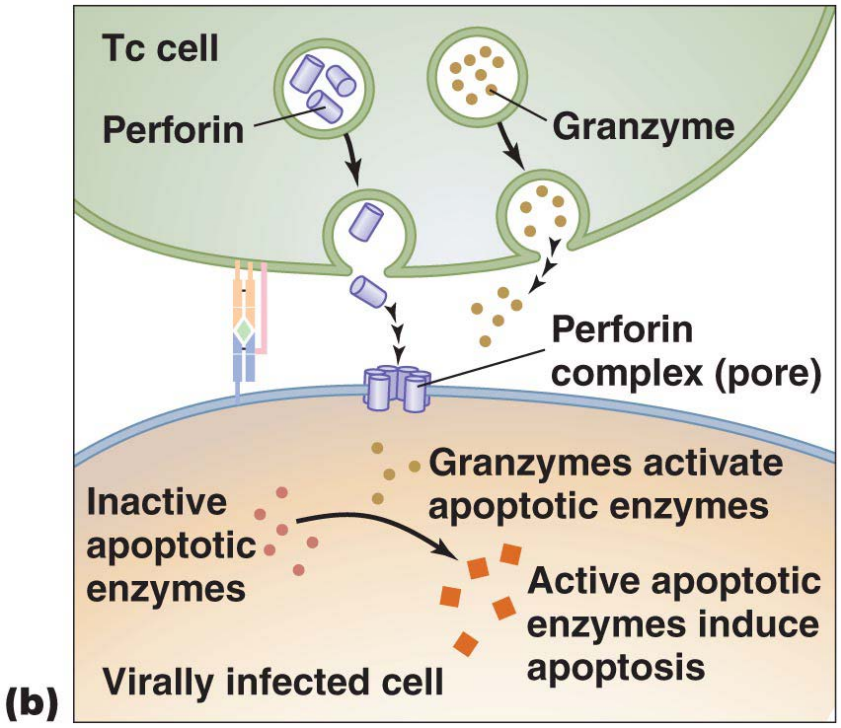


Figure 16.15a

A cell-mediated immune response



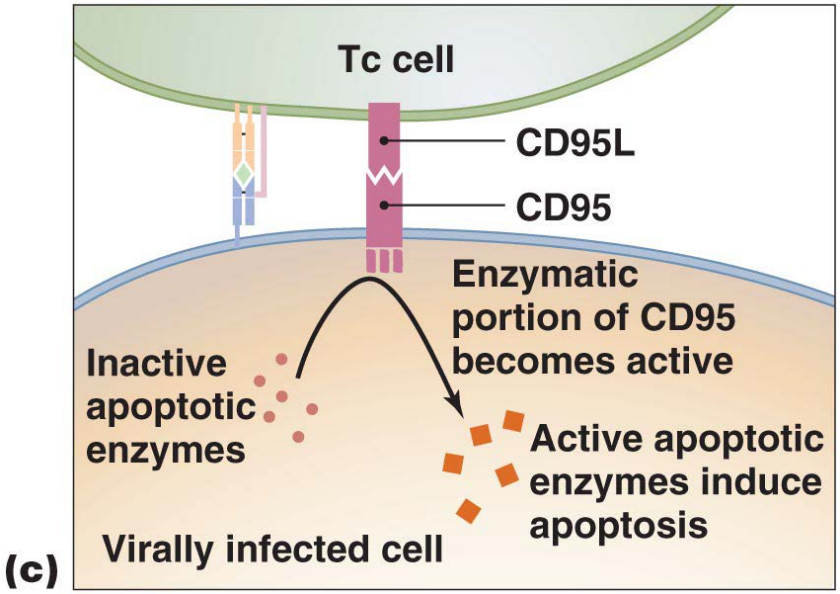


Figure 16.15b-c

Cell-Mediated Immune Responses

- Memory T Cells
  - Some activated T cells become memory T cells
  - Persist for months or years in lymphoid tissues
  - Immediately functional upon subsequent contacts with epitope specific to its TCR

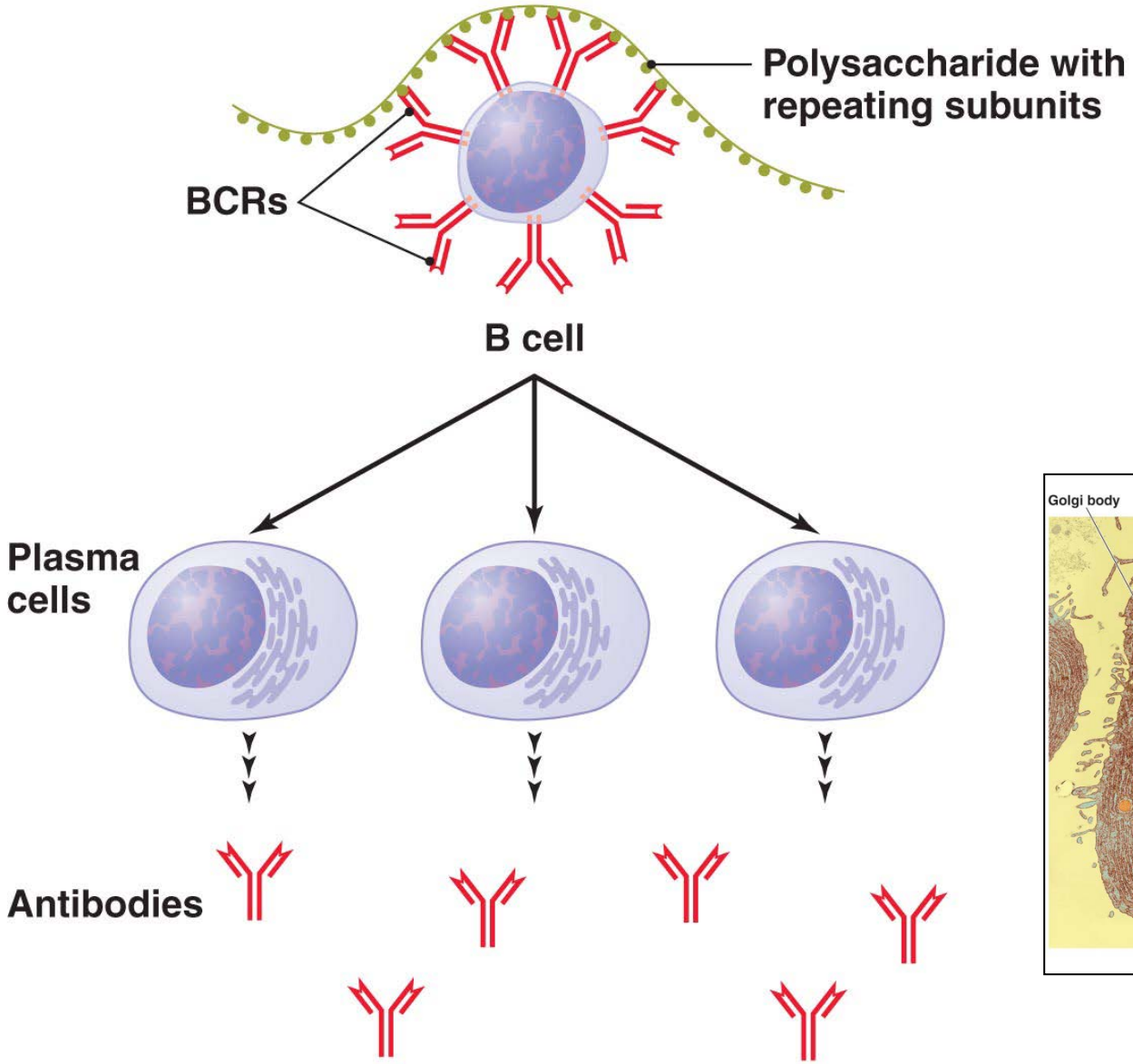
Cell-Mediated Immune Responses

- T Cell Regulation
  - Regulation needed to prevent T cell response to autoantigens
  - T cells require additional signals from an antigen-presenting cell
    - Interaction of the T cell and antigen-presenting cell stimulates the T cell to respond to the antigen

Humoral Immune Responses

- Humoral immune responses mounted against exogenous pathogens
- Activates only in response to specific pathogens

The binding of a T-independent antigen by a B cell



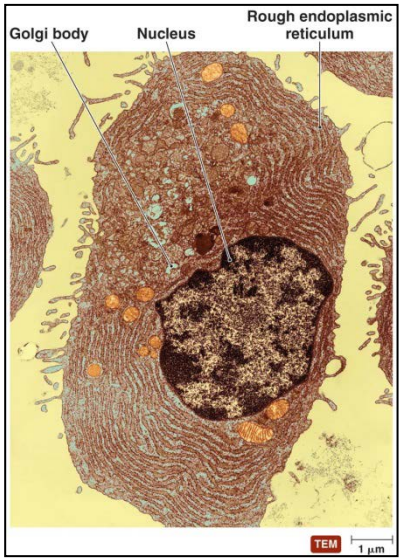


Figure 16.16

A T-dependent humoral immune response

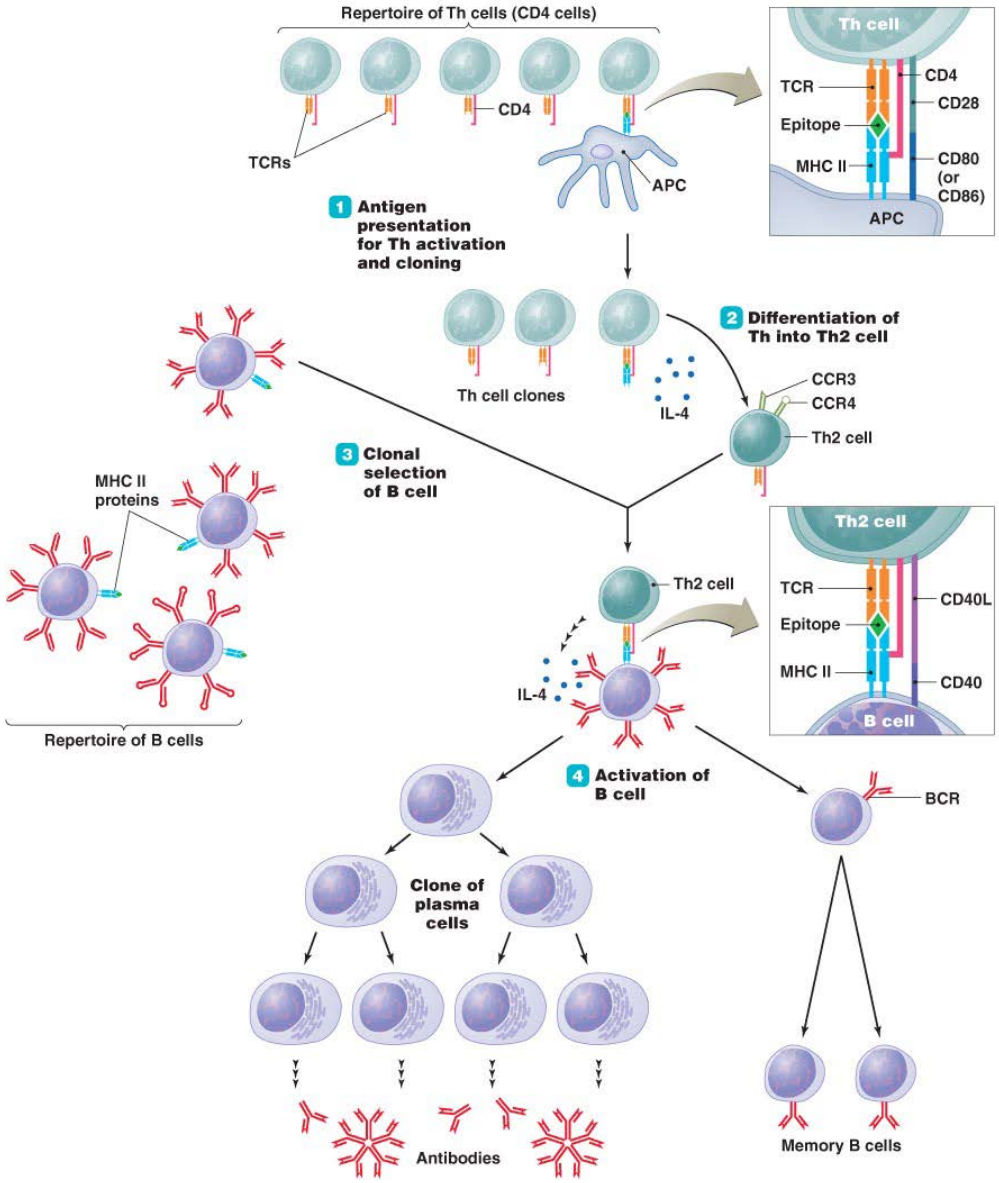


Figure 16.18

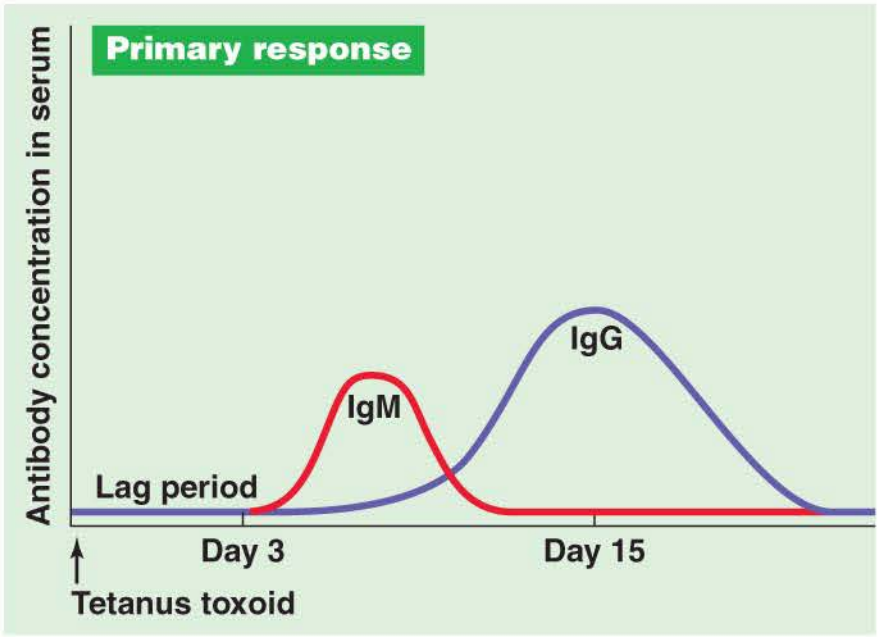
Humoral Immune Responses

- Inducement of T-Dependent Humoral Immunity
  - Plasma cells
    - Majority of cells produced during B cell proliferation
    - Only secrete antibody molecules complementary to the specific antigen
    - Short-lived cells that die within a few days of activation
      - Their antibodies and progeny can persist

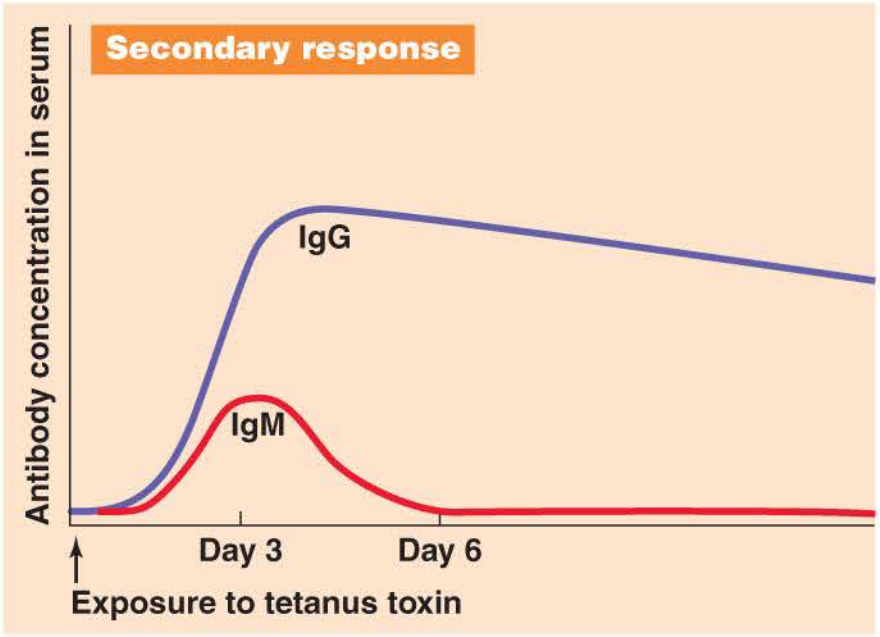
Humoral Immune Responses

- Memory B Cells and the Establishment of Immunological Memory
  - Produced by B cell proliferation but do not secrete antibodies
  - Have BCRs complementary to the antigenic determinant that triggered their production
  - Long-lived cells that persist in the lymphoid tissue
  - Initiates antibody production if antigen is encountered again

The production of humoral immune responses



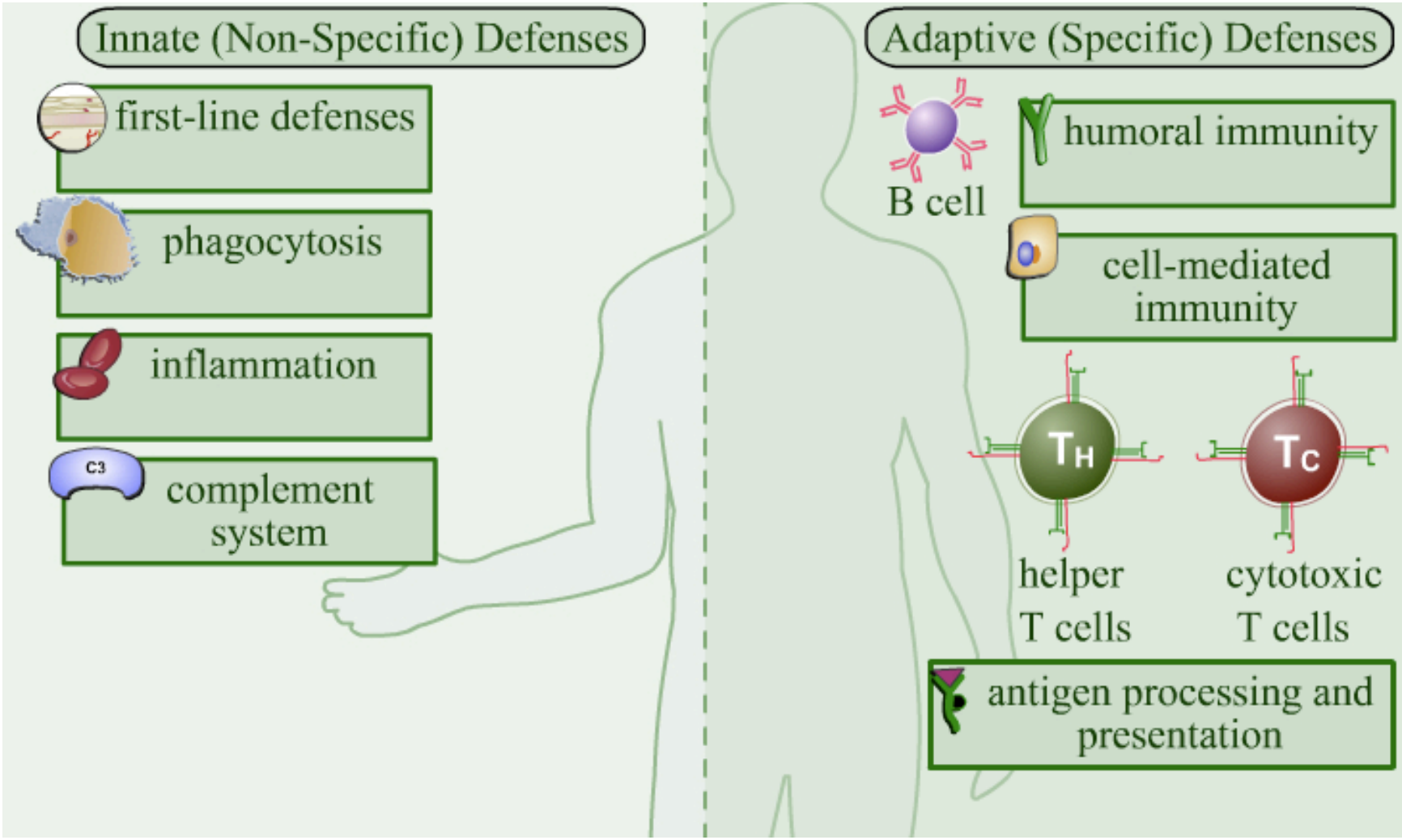
(a)



(b)

Figure 16.19

Humoral Immune Responses



PLAY Animation: Host Defenses: The Big Picture

Types of Acquired Immunity

- Specific immunity acquired during an individual's life
- Two types
  - Naturally acquired
    - Response against antigens encountered in daily life
  - Artificially acquired
    - Response to antigens introduced via a vaccine
- Distinguished as either active or passive
  - Active
  - Passive
    - Passively receive antibodies from another individual

End of Chapter