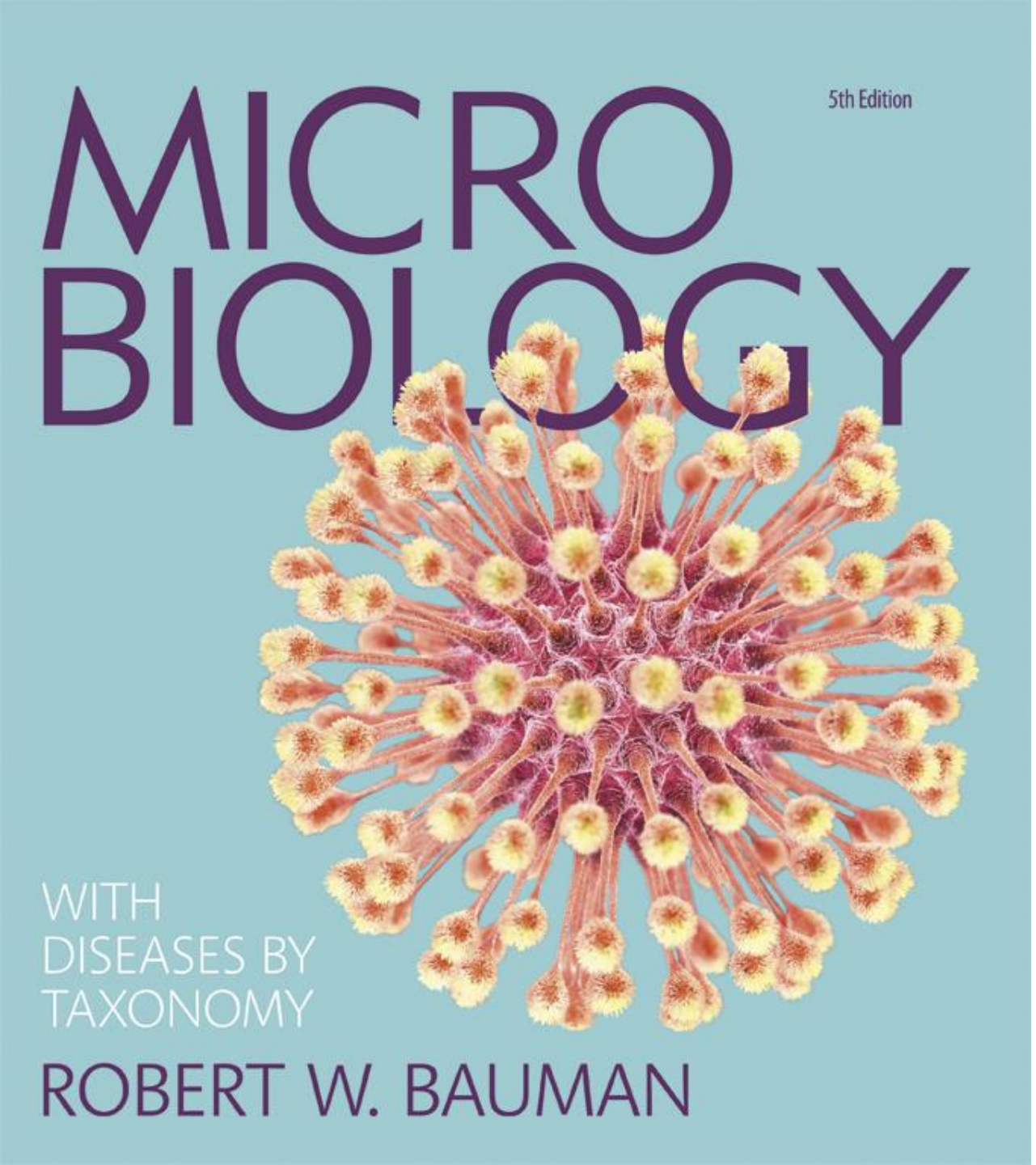



PowerPoint® Lecture Presentations prepared by Mindy Miller-Kittrell, North Carolina State University

CHAPTER **16**

# Adaptive Immunity

# Elements of Adaptive Immunity

- **Preparation for an Adaptive Immune Response**
  - The Roles of the Major Histocompatibility Complex (MHC) and Antigen-Presenting Cells
    - 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
    - Antigens on the surface of cells known as major histocompatibility antigens are how the body can distinguish “self” from “non-self.”
    - **Hold and position antigenic epitopes for presentation** to immune cells

# Elements of Adaptive Immunity

- **Preparation for an Adaptive Immune Response**
  - The Roles of the **Major Histocompatibility Complex (MHC)** and Antigen-Presenting Cells
    - Antigens bind in the antigen-binding groove of MHC molecules
    - Two classes of MHC proteins:
      - MHC class I
        - Present on all cells except red blood cells
      - MHC class II
        - Present on antigen-presenting cells (APCs)
        - Include macrophages and dendritic cells (aka Professional Antigen Presenting Cells)
        - Nonprofessional antigen-presenting cells: microglia and stellate macrophages

Figure 16.4 The two classes of major histocompatibility complex (MHC) proteins.

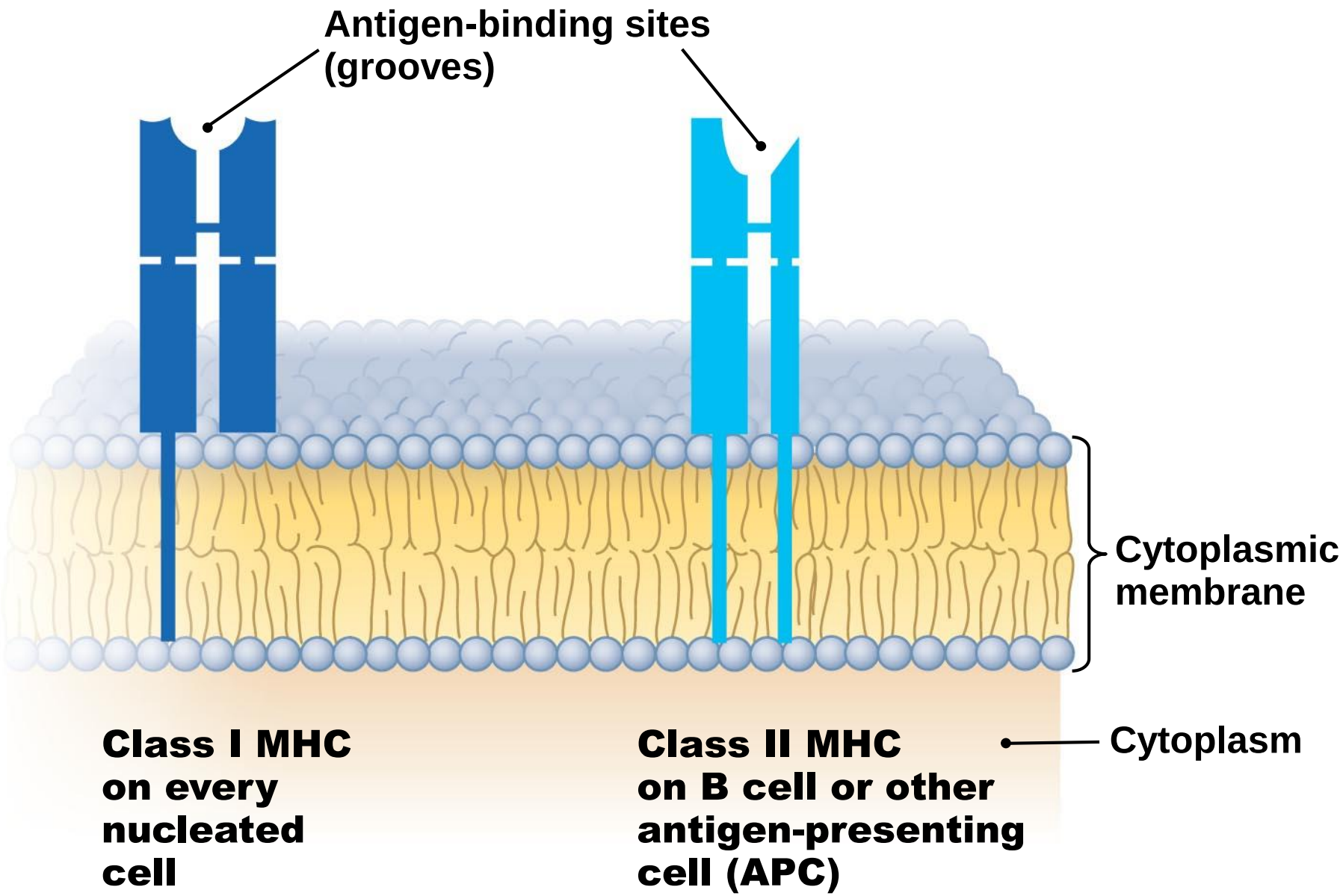
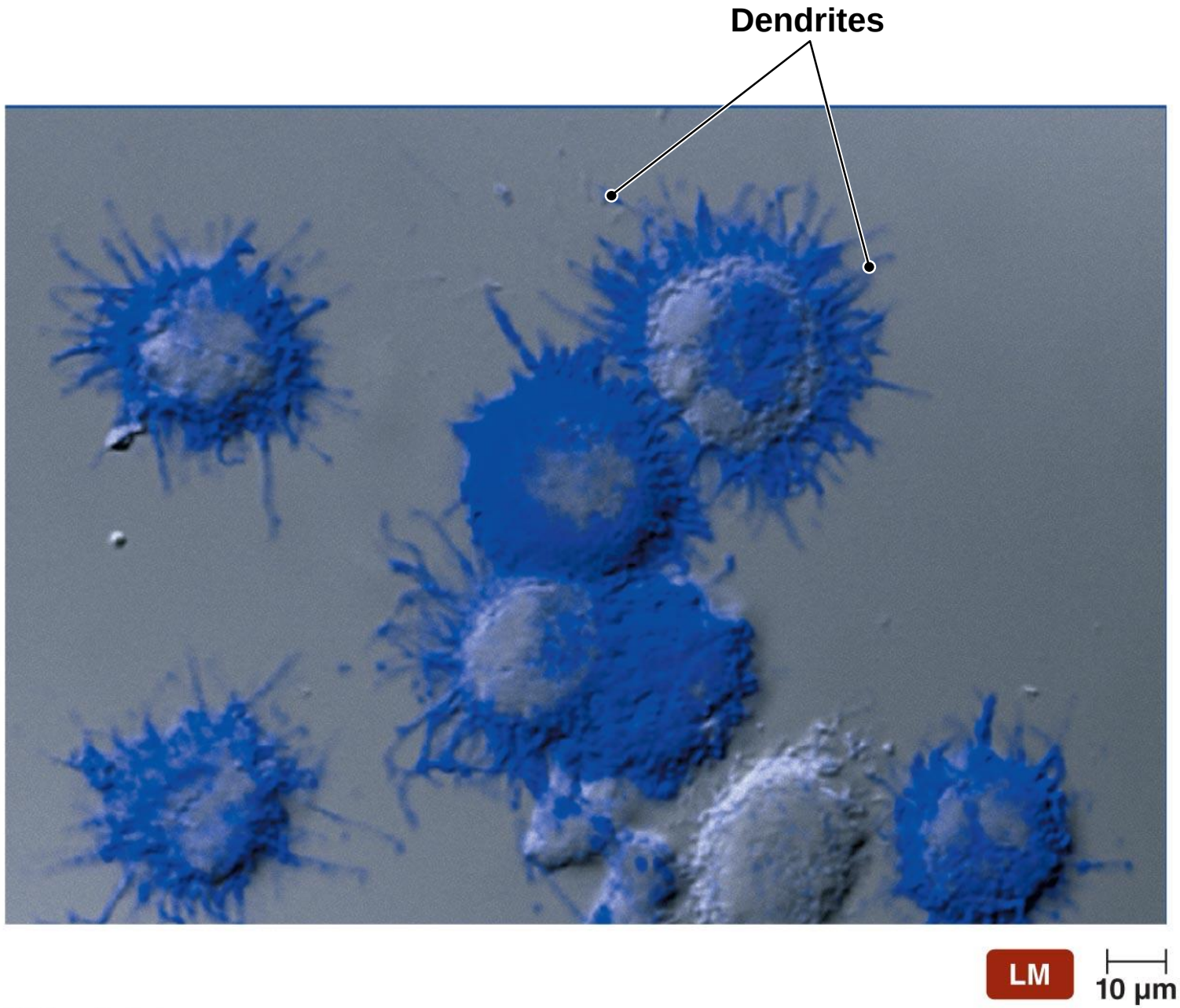


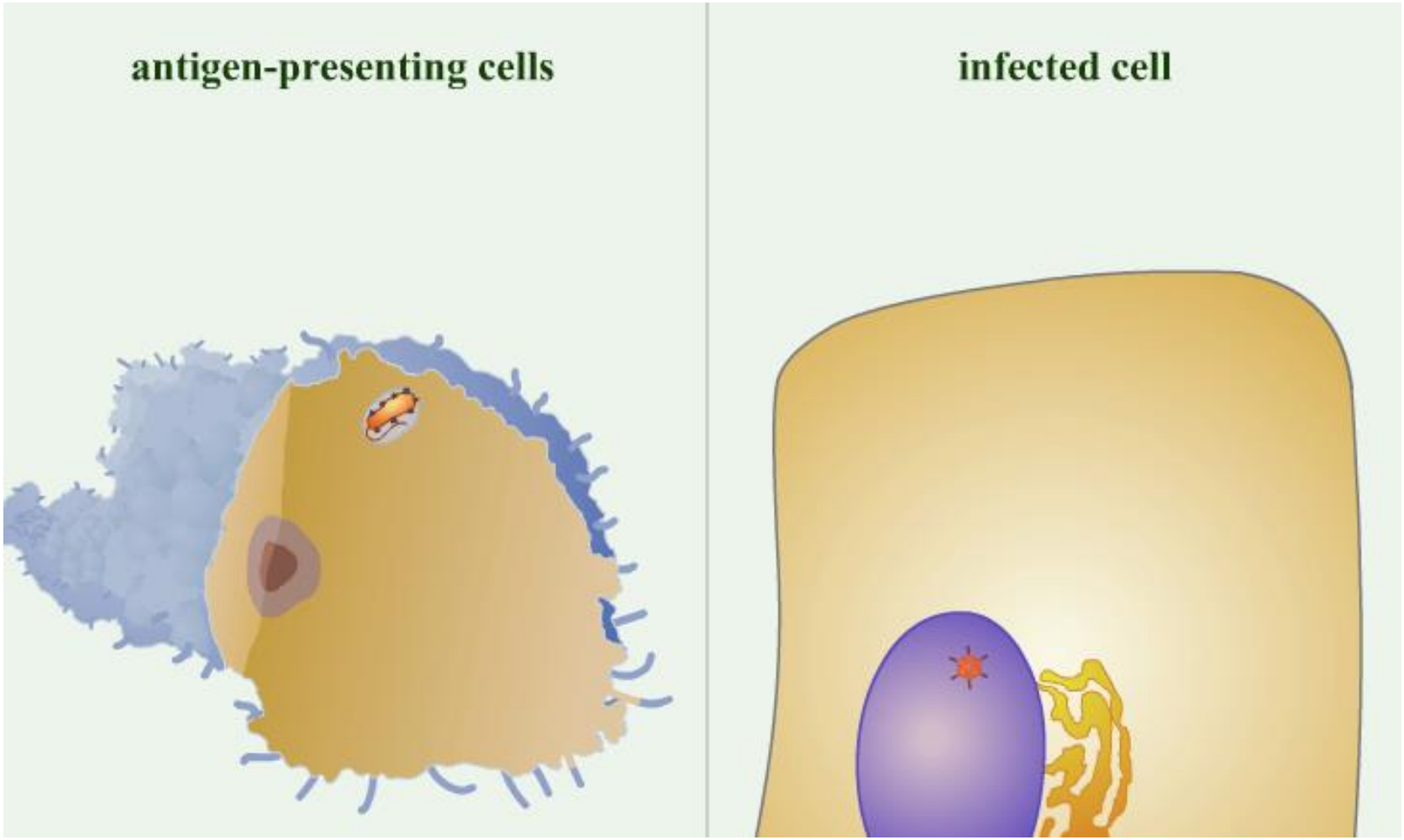
Figure 16.5 Dendritic cells.



# Elements of Adaptive Immunity

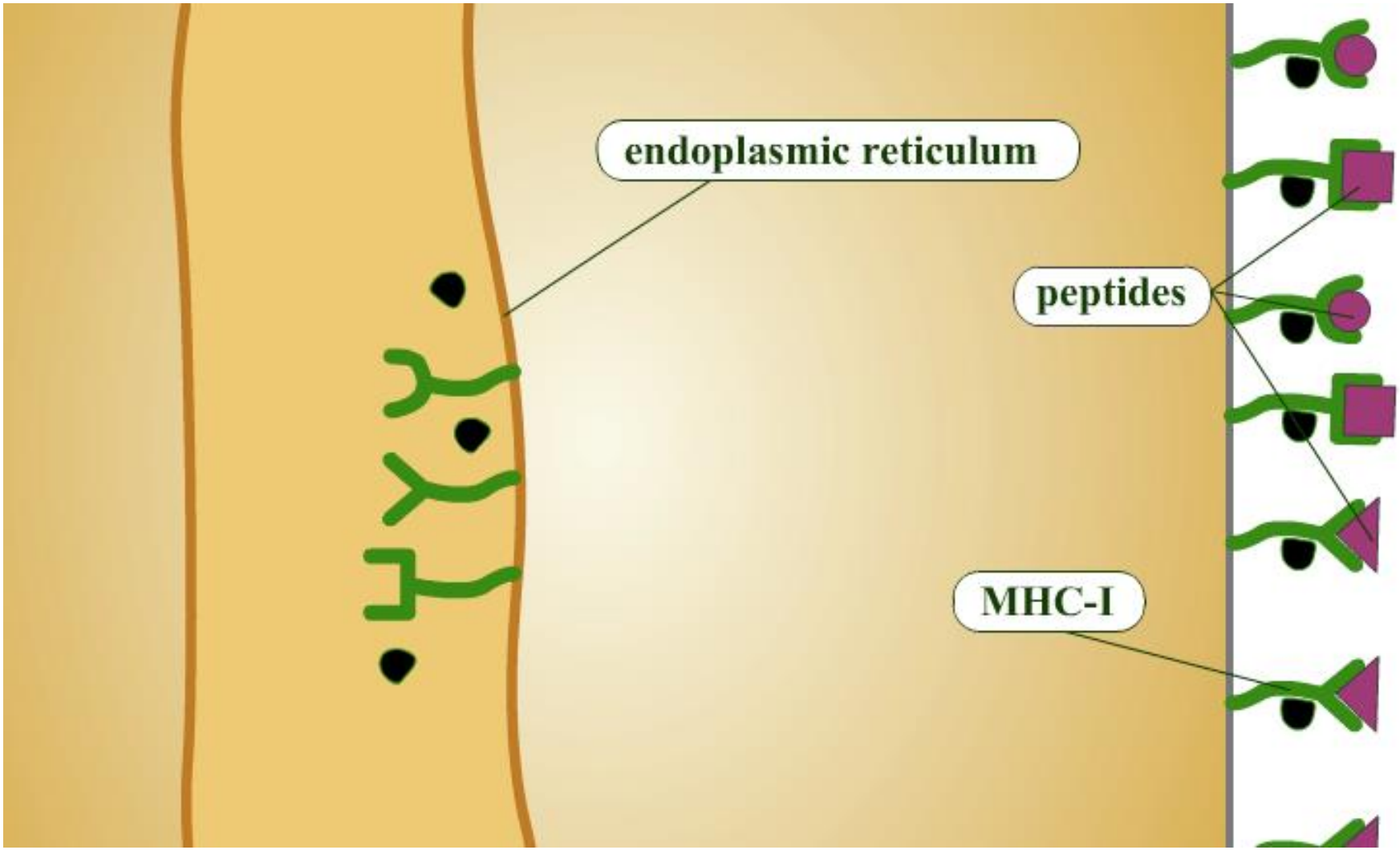
- **Preparation for an Adaptive Immune Response**
  - Antigen Processing
    - Antigens must be processed before MHC proteins can display epitopes
    - Different processes for endogenous and exogenous antigens

# Antigen Processing and Presentation: Overview



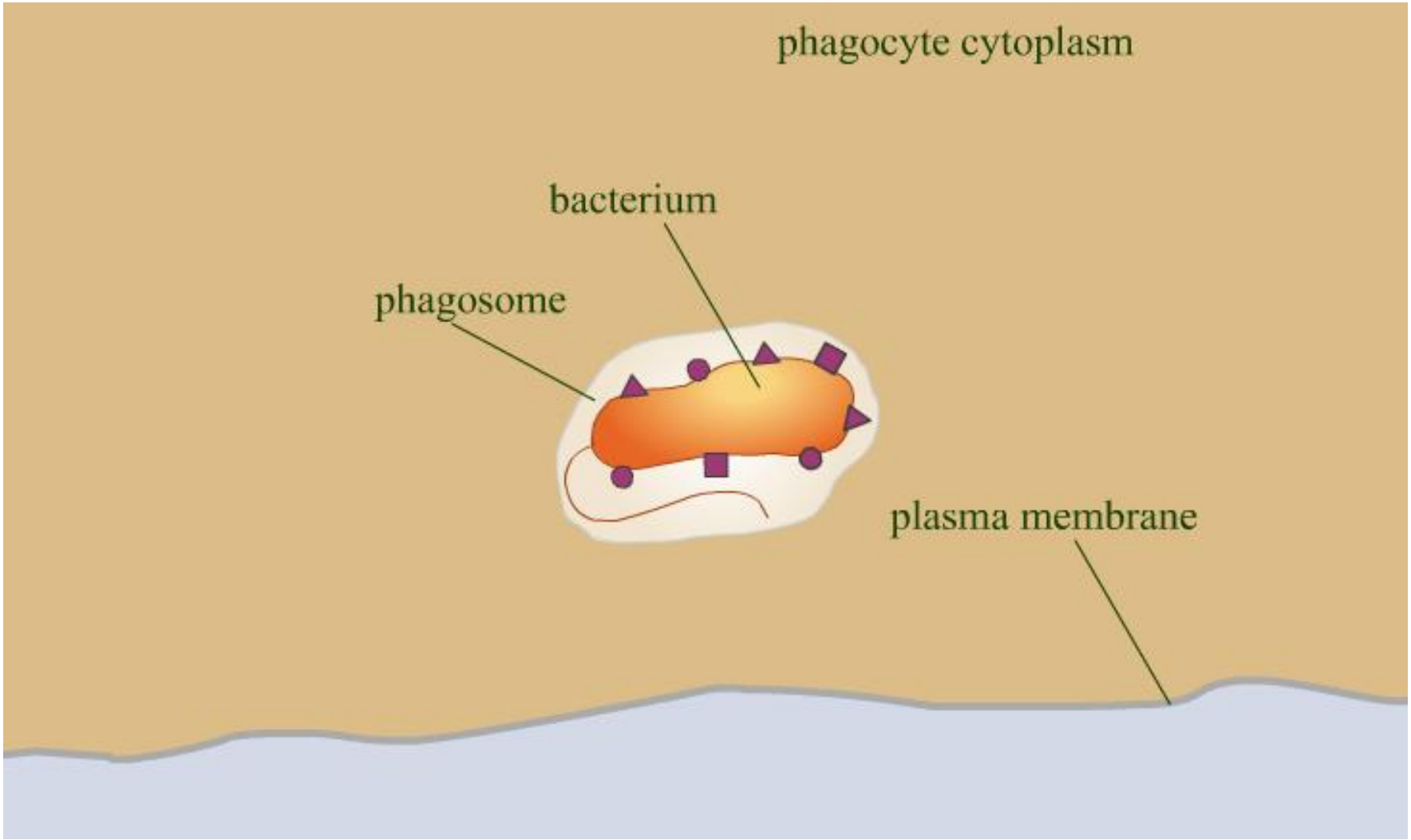

PLAY **Antigen Processing and Presentation: Overview**

# Antigen Processing and Presentation: Steps




PLAY **Antigen Processing and Presentation: Steps**

# Antigen Processing and Presentation: MHC




PLAY **Antigen Processing and Presentation: MHC**

# Elements of Adaptive Immunity

- **T Lymphocytes (T Cells)**
  - Produced in the red bone marrow and mature in the thymus
  - Act against endogenous antigens, producing cell-mediated immune responses
  - Circulate in the lymph and blood
  - Migrate to the lymph nodes, spleen, and Peyer's patches
  - Have T cell receptors (TCRs) on their cytoplasmic membrane for every possible epitope

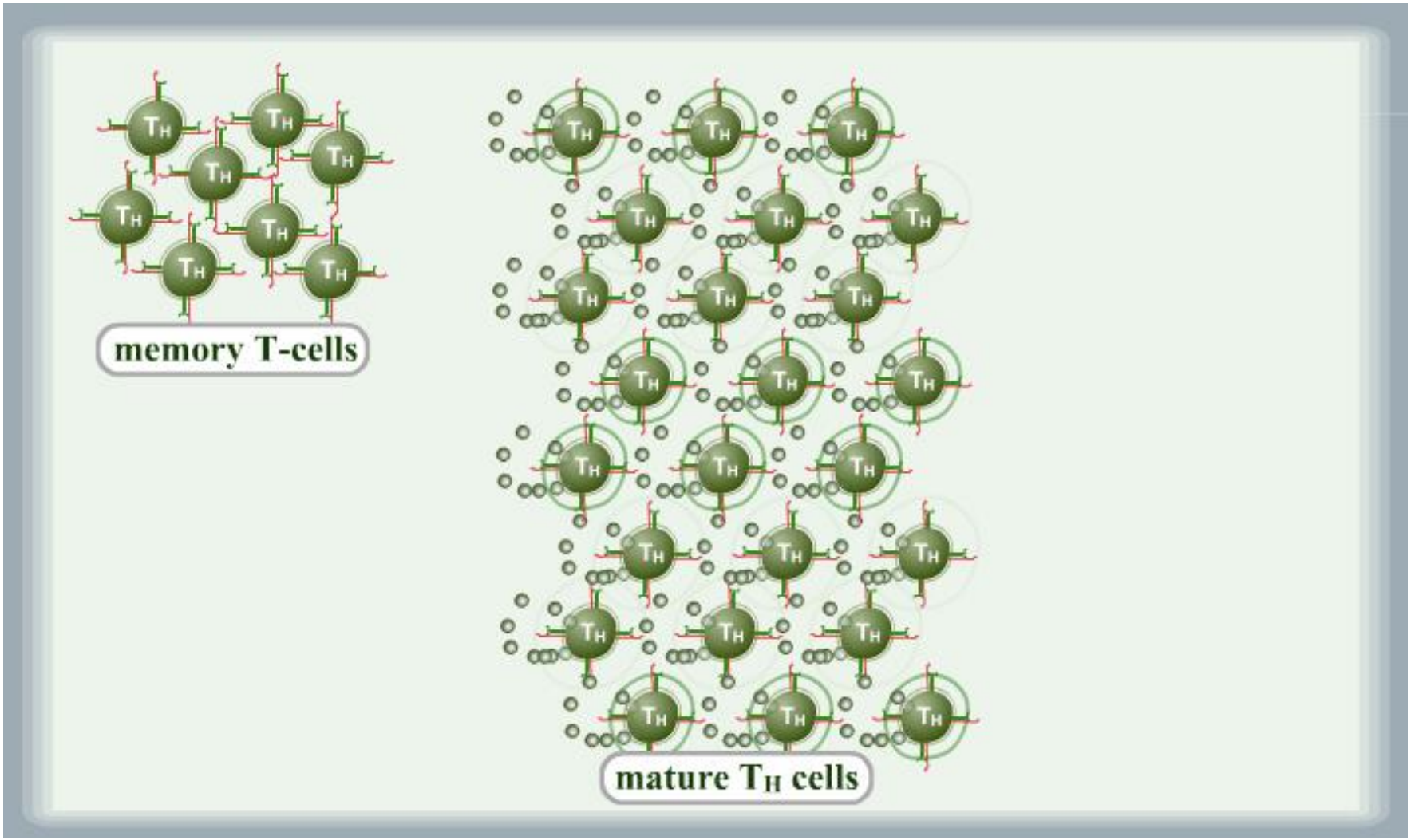
# Elements of Adaptive Immunity

- **T Lymphocytes (T Cells)**
  - Specificity of the T Cell Receptor (TCR)
    - TCRs do not recognize epitopes directly
    - TCRs only bind epitopes associated with an MHC protein
    - T cells act primarily against cells that harbor intracellular pathogens
    - Some T cells act against body cells that produce abnormal cell-surface proteins

# Elements of Adaptive Immunity

- **T Lymphocytes (T Cells)**
  - Types of T Lymphocytes
    - Based on surface glycoproteins and characteristic functions, three types:
      - **Cytotoxic T lymphocyte 9 (Tc or CD8 cells)**
        - Kill infected cells, as well as abnormal body cells such as cancer cells.
      - **Helper T lymphocyte (Th or CD4 cells)**
        - Helps regulate B cells and cytotoxic T cells
        - Includes type 1 and type 2 helper T cells
      - **Regulatory T lymphocyte (Tr cells or suppressor T cells)**
        - Represses adaptive immune responses

# Cell-Mediated Immunity: Helper T Cells




PLAY **Cell-Mediated Immunity: Helper T Cells**

# Elements of Adaptive Immunity

- **T Lymphocytes (T Cells)**
  - **Clonal Deletion of T Cells**
    - Vital that immune responses not be directed against autoantigens
    - Body eliminates self-reactive lymphocytes
    - Cells with receptors that respond to autoantigens are selectively eliminated via **apoptosis** in a process known as **clonal deletion** (because potential offspring—clones—are deleted)

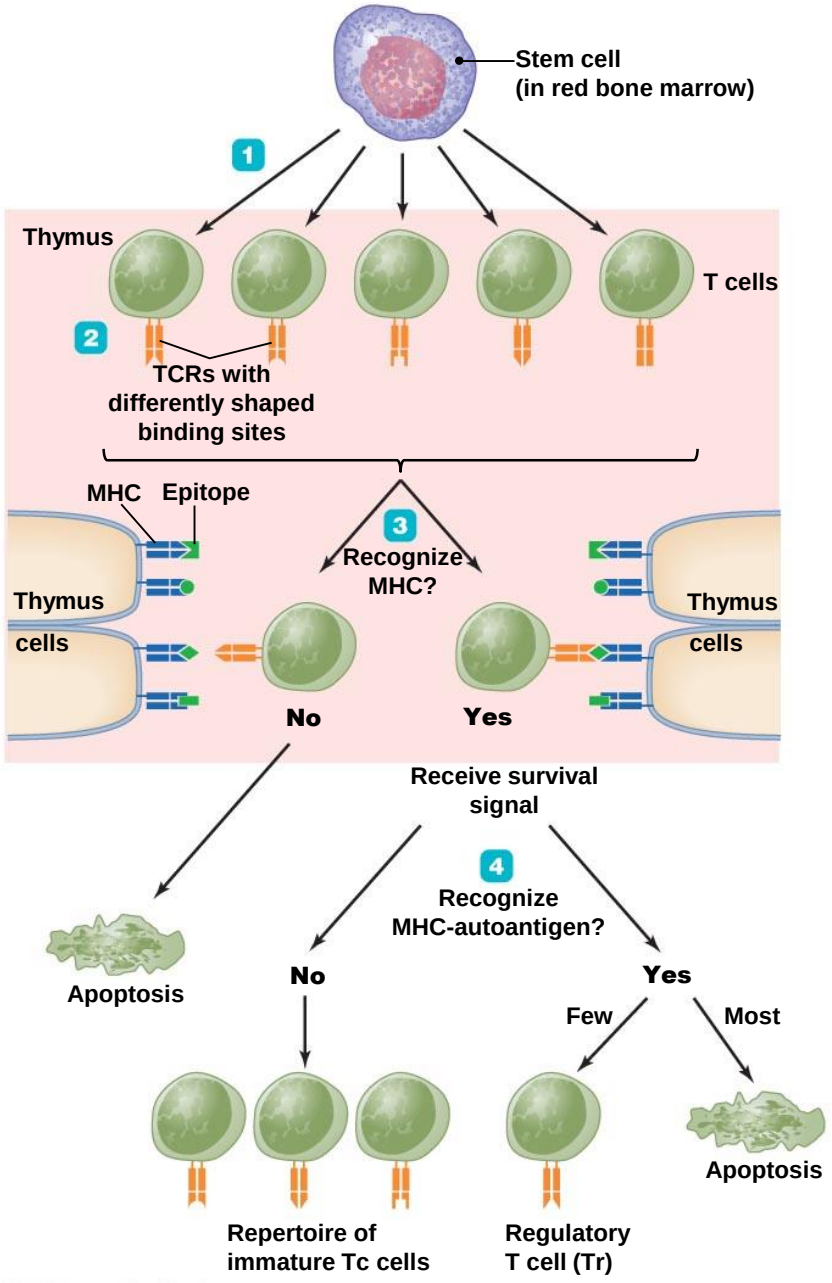
# Elements of Adaptive Immunity

- **T Lymphocytes (T Cells)**
  - **Clonal Deletion of T Cells**
    - Clonal deletion of T cells occurs in the thymus, where thymus cells process and present all the body's autoantigens to young T cells
    - T cells that do not recognize MHC are also deleted
    - Surviving lymphocytes and their descendants respond only to foreign antigens (except for a small number of regulatory T cells).
    - When self-tolerance is impaired, the result is an *autoimmune disease*

# Elements of Adaptive Immunity

- **T Lymphocytes (T Cells)**
  - **Clonal Deletion of T Cells: Summary**
    - Immature T cells undergo one of four fates
      - T cells that do not recognize body's MHC protein undergo **apoptosis**
      - T cells that recognize autoantigen die by apoptosis
      - Some "self-recognizing" T cells become regulatory T cells
      - T cells that recognize MHC protein and foreign epitopes become repertoire of protective T cells

## Figure 16.9 Clonal deletion of T cells.



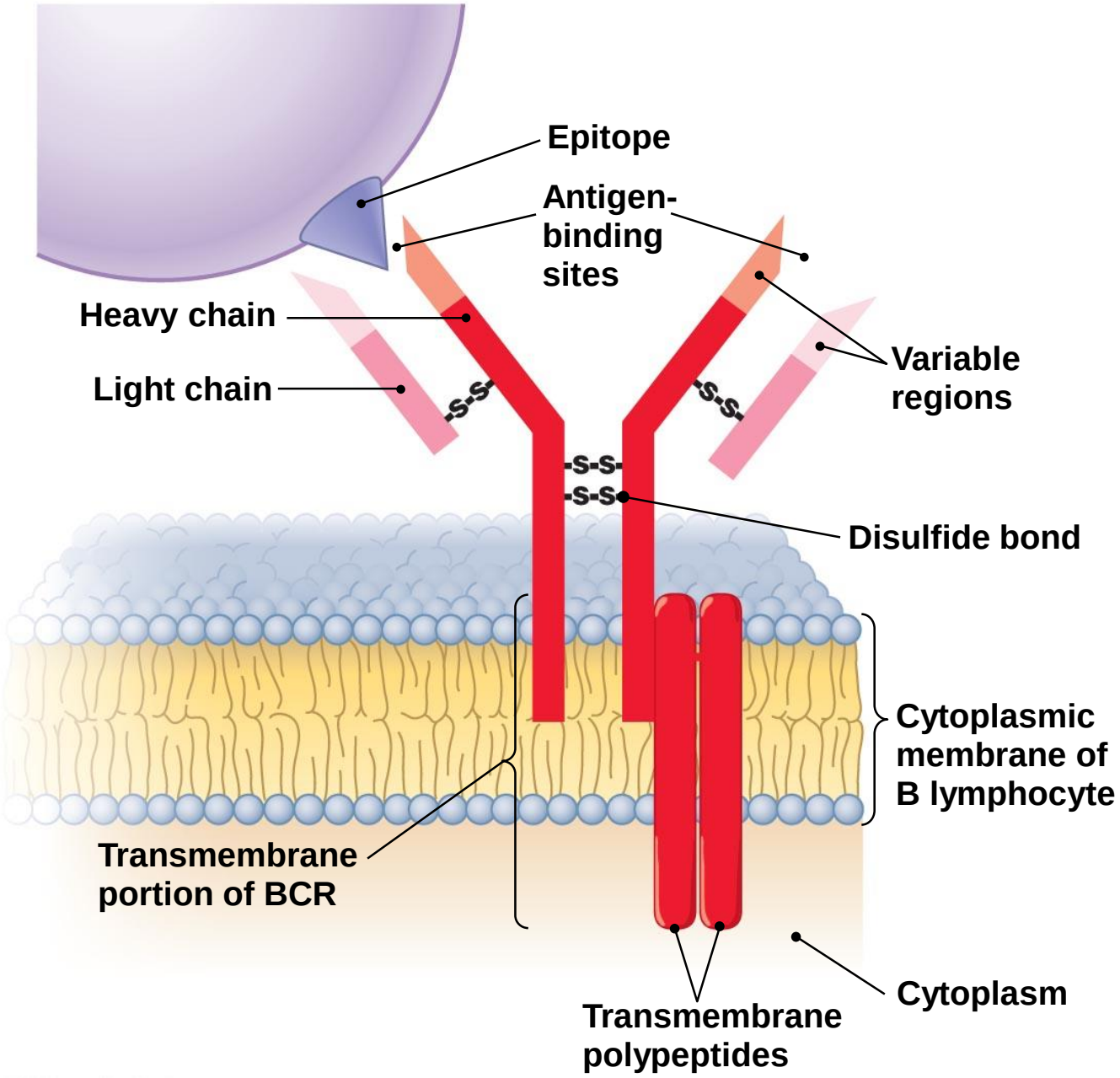
# Elements of Adaptive Immunity

- **B Lymphocytes (B Cells) and Antibodies**
  - 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
  - The specificity of B cell function comes from the membrane proteins called *B cell receptors*

# Elements of Adaptive Immunity

- **B Lymphocytes (B Cells) and Antibodies**
  - Specificity of the **B Cell Receptor (BCR)**
    - Each B lymphocyte has multiple copies of the BCR
    - Each B cell generates a single BCR
    - 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

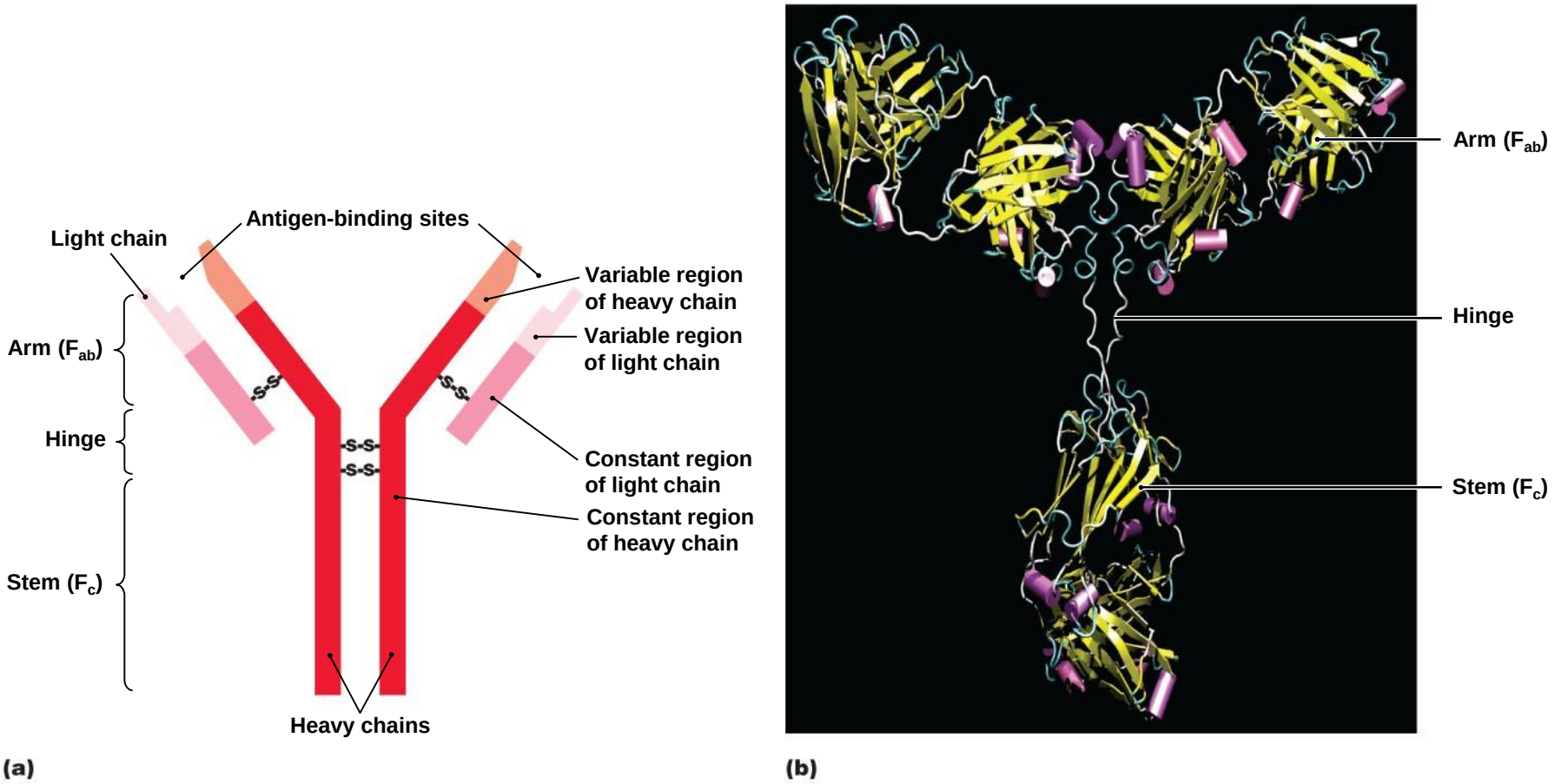
Figure 16.10 B cell receptor (BCR).



# Elements of Adaptive Immunity

- **B Lymphocytes (B Cells) and Antibodies**
  - Specificity and Antibody Structure
    - **Antibodies** are immunoglobulins similar to BCRs
    - Secreted by activated B cells called plasma cells
    - Have antigen-binding sites and antigen specificity identical to the BCR of the activated B cell

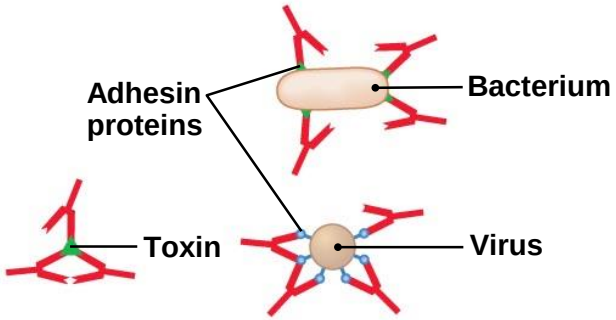
## Figure 16.12 Basic antibody structure.



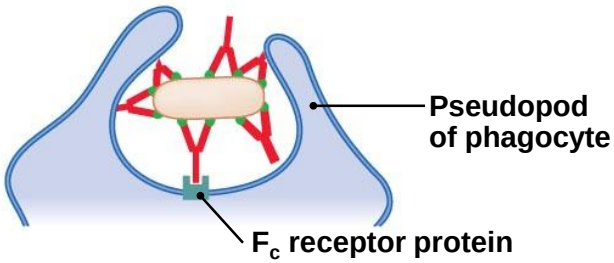
# Elements of Adaptive Immunity

- **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)

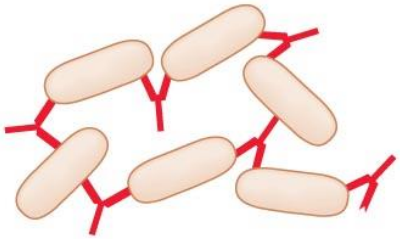
**Figure 16.13 Five functions of antibodies.**



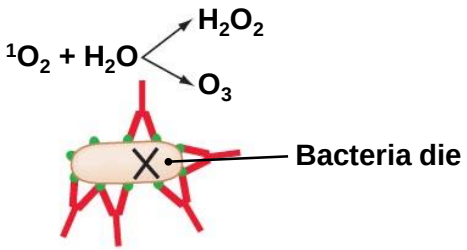

(a) **Neutralization**



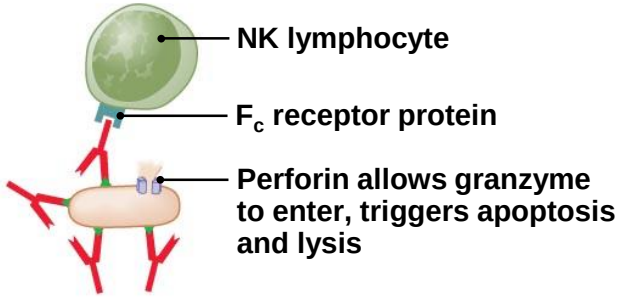

(b) **Opsonization**



(d) **Agglutination**

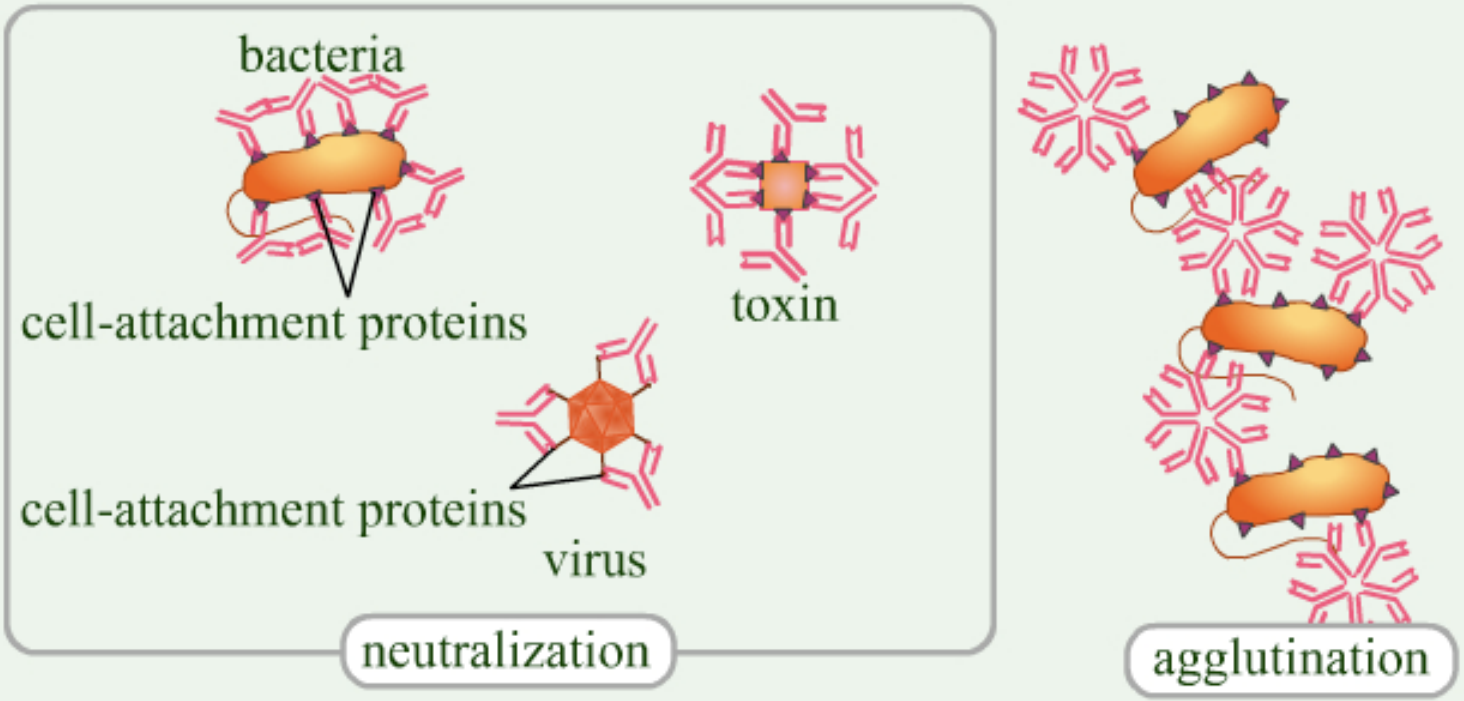



(c) **Oxidation**




(e) **Antibody-dependent cell-mediated cytotoxicity (ADCC)**

# Humoral Immunity: Antibody Function




PLAY **Humoral Immunity: Antibody Function**

# Elements of Adaptive Immunity

- **B Lymphocytes (B Cells) and Antibodies**
  - Classes of Antibodies
    - Threats confronting the immune system are variable
    - Antibody class involved in the immune response varies
      - Type of antigen
      - Portal of entry
      - Antibody function needed
    - Five different classes of antibodies

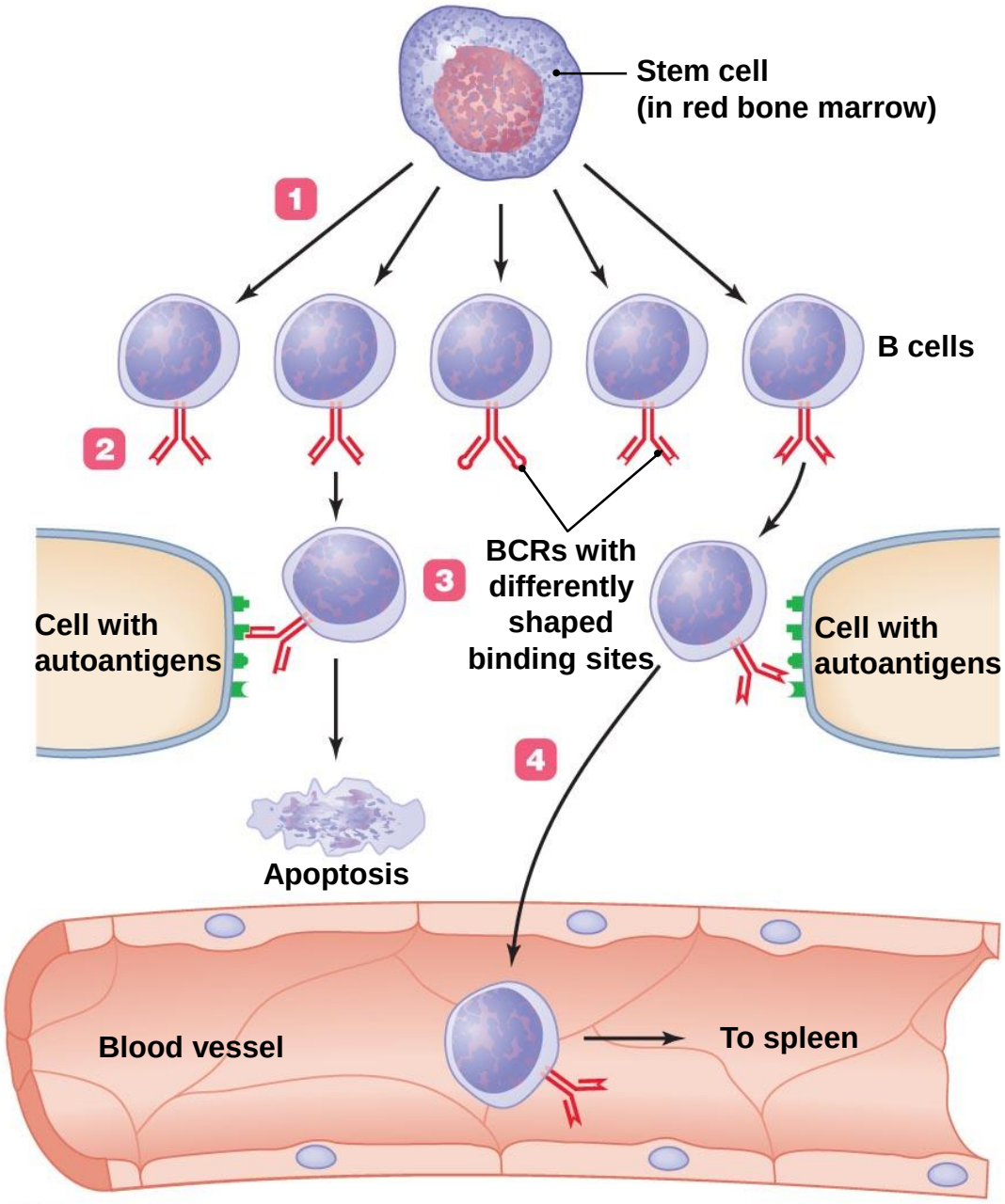
# Elements of Adaptive Immunity

- **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
    - IgE — involved in response to parasitic infections and allergies
    - IgD — exact function is not known

# Elements of Adaptive Immunity

- **B Lymphocytes (B Cells) and Antibodies**
  - Clonal Deletion of B Cells
    - Occurs in the bone marrow in a manner similar to deletion of T cells
    - Self-reactive B cells may become inactive or change their BCR rather than undergo apoptosis

Figure 16.14 Clonal deletion of B cells.



# Elements of Adaptive Immunity

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

# Elements of Adaptive Immunity

- **Immune Response Cytokines**
  - **Interleukins (ILs)**
    - Signal among leukocytes
  - **Interferons (IFNs)**
    - Antiviral proteins that may act as cytokines
  - **Growth factors**
    - Proteins that stimulate stem cells to divide
  - **Tumor necrosis factor (TNF)**
    - Secreted by macrophages and T cells to kill tumor cells and regulate immune responses and inflammation
  - **Chemokines**
    - Chemotactic cytokines that signal leukocytes to move

# Cell-Mediated Immune Responses

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

# Cell-Mediated Immune Responses

- **Activation of Cytotoxic T Cell Clones and Their Functions**
  - Adaptive immune responses initiated in lymphoid organs
  - Steps involved in activation of cytotoxic T cells:
    1. **Antigen presentation**
    2. **Helper T cell differentiation**
    3. **Clonal expansion**
    4. **Self-stimulation**

Figure 16.15 Activation of a clone of cytotoxic T (Tc) cells.

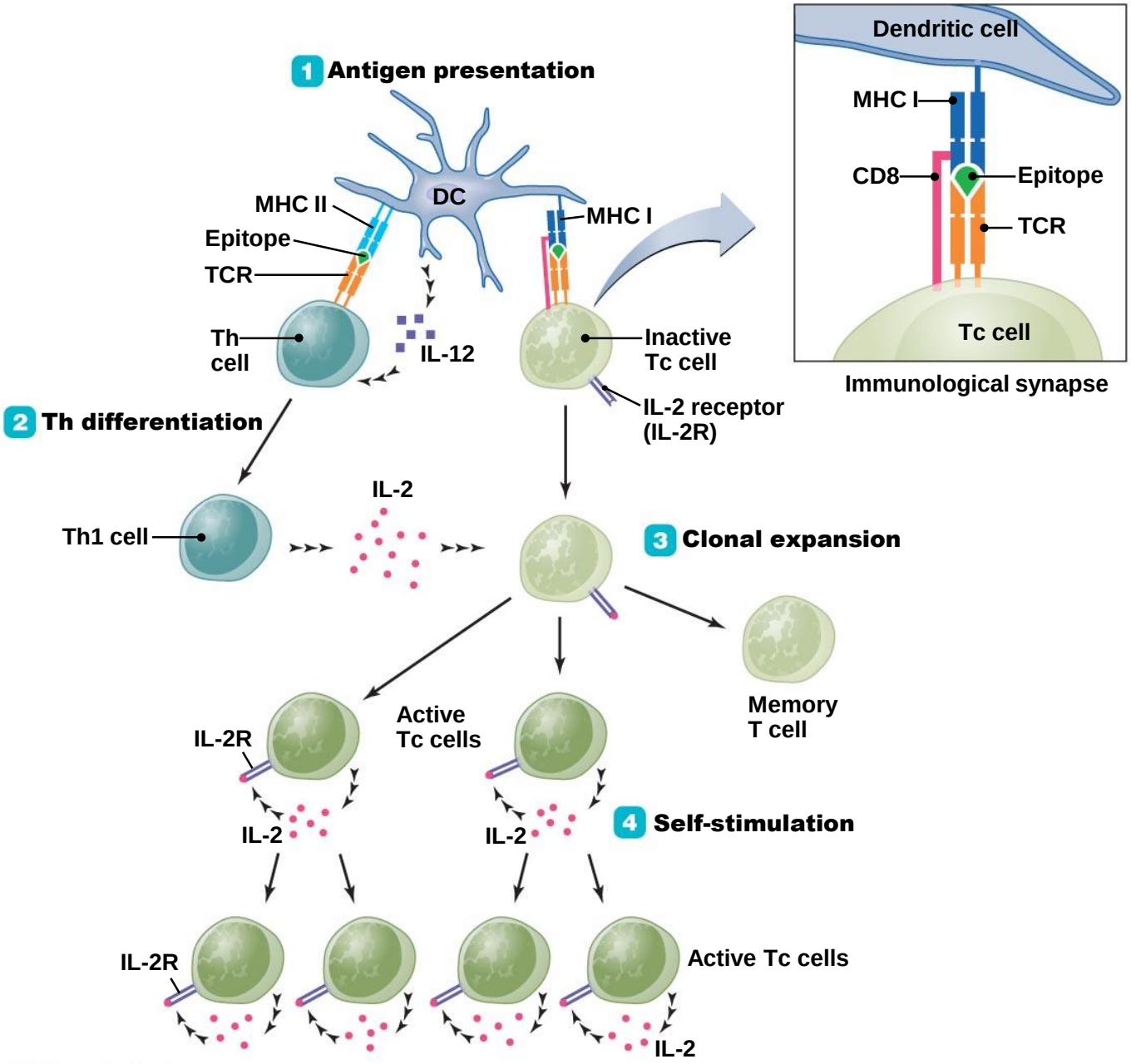
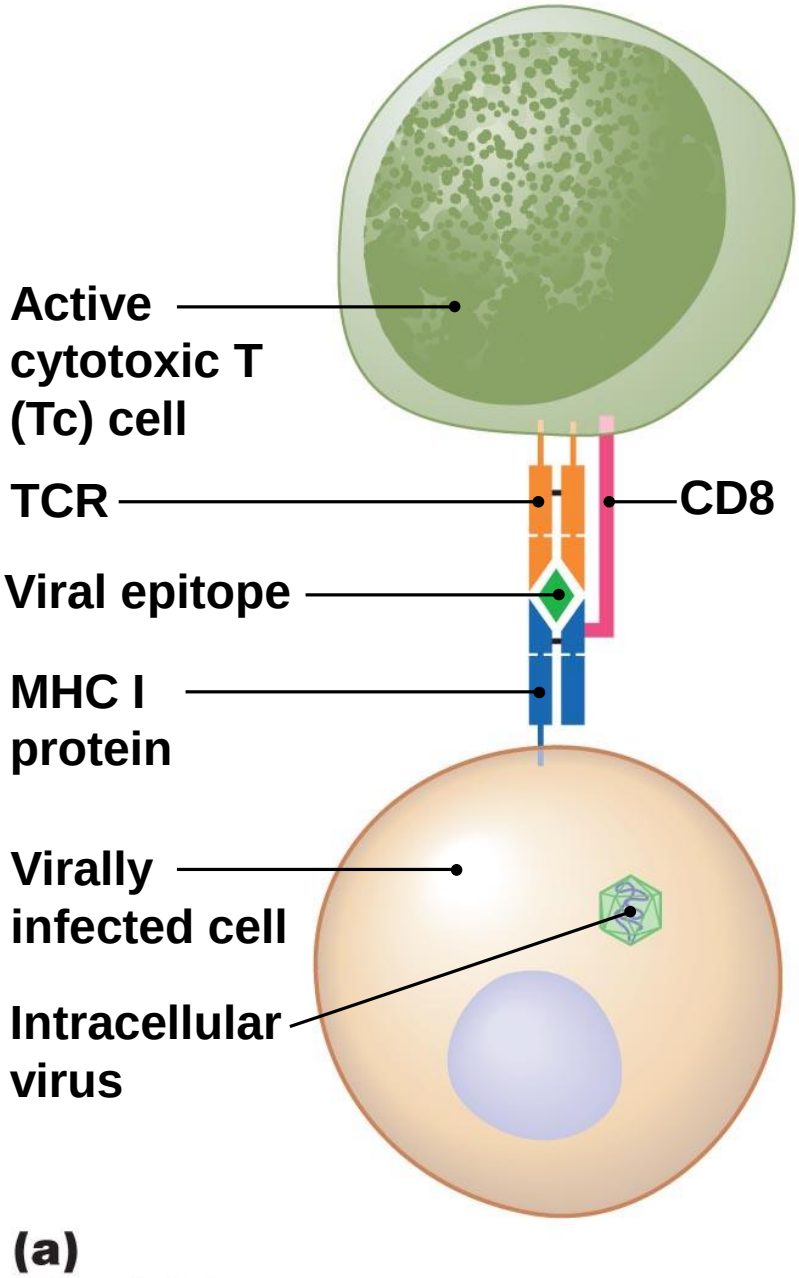
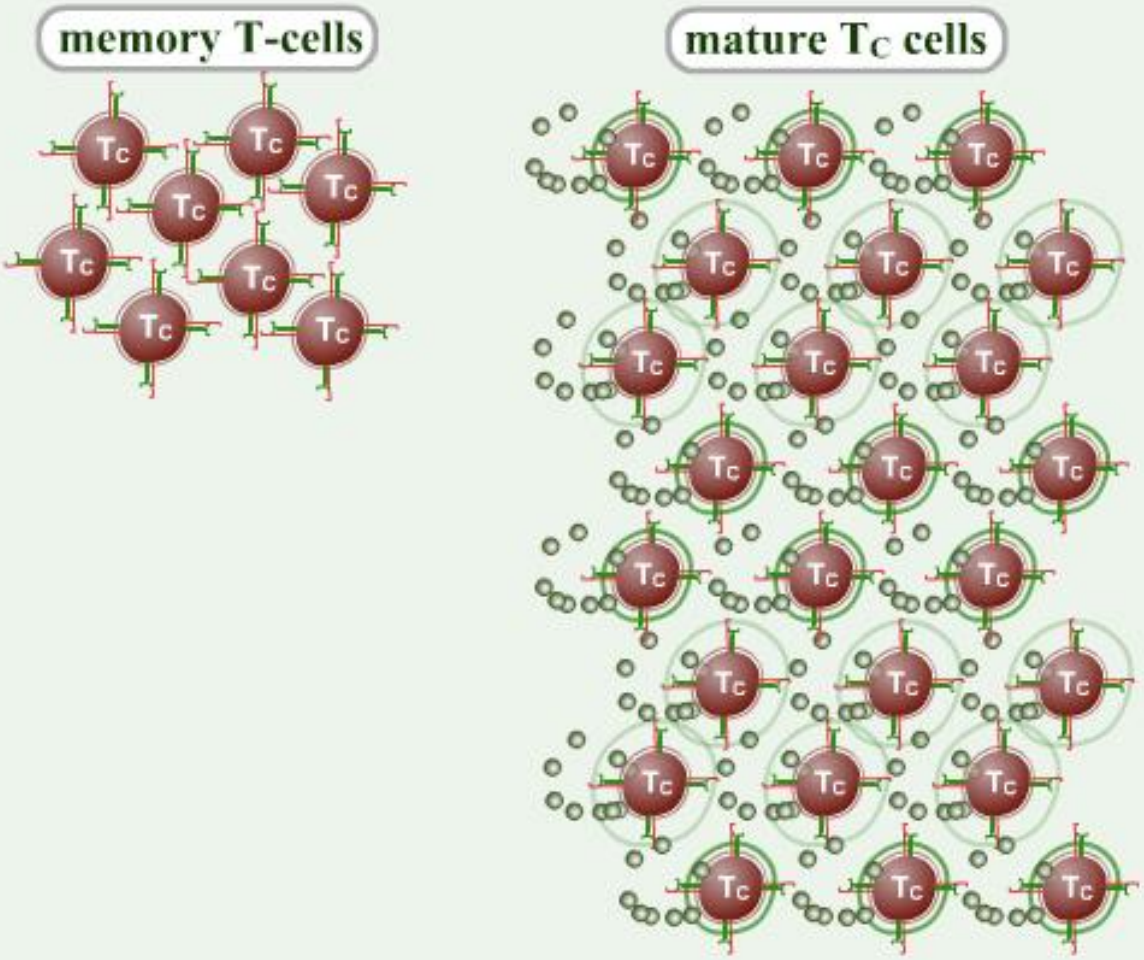


Figure 16.16a A cell-mediated immune response.



# Cell-Mediated Immunity: Cytotoxic T Cells

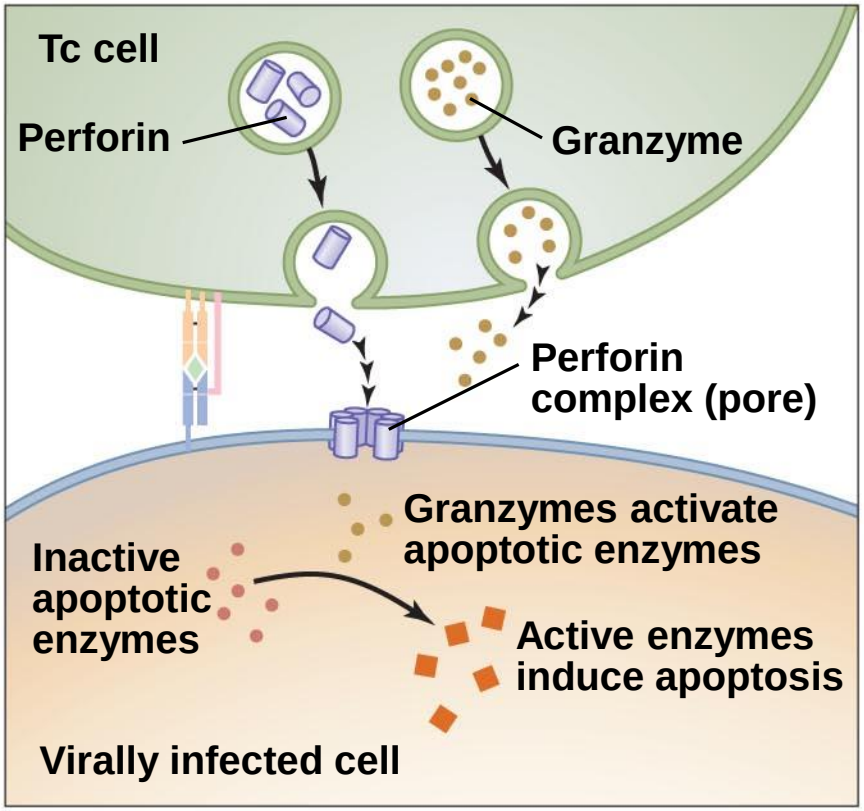



PLAY **Cell-Mediated Immunity: Cytotoxic T Cells**

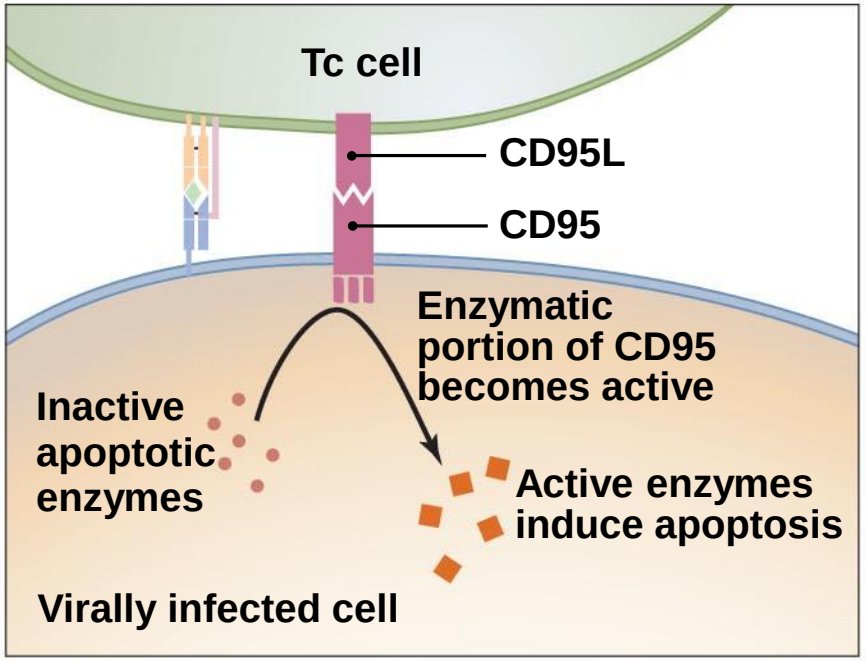
# Cell-Mediated Immune Responses

- **Activation of Cytotoxic T Cell Clones and Their Functions**
  - Cytotoxic T cells kill targets through one of two pathways:
    - *Perforin-granzyme pathway*
      - Involves synthesis of special killing proteins
    - *CD95 pathway*
      - Mediated through glycoprotein on body's cells

Figure 16.16b-c A cell-mediated immune response.




(b)




(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-MHC complex specific to its TCR
  - Memory response is more effective than the primary response

# 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
  - Regulatory T cells also moderate cytotoxic T cell activity

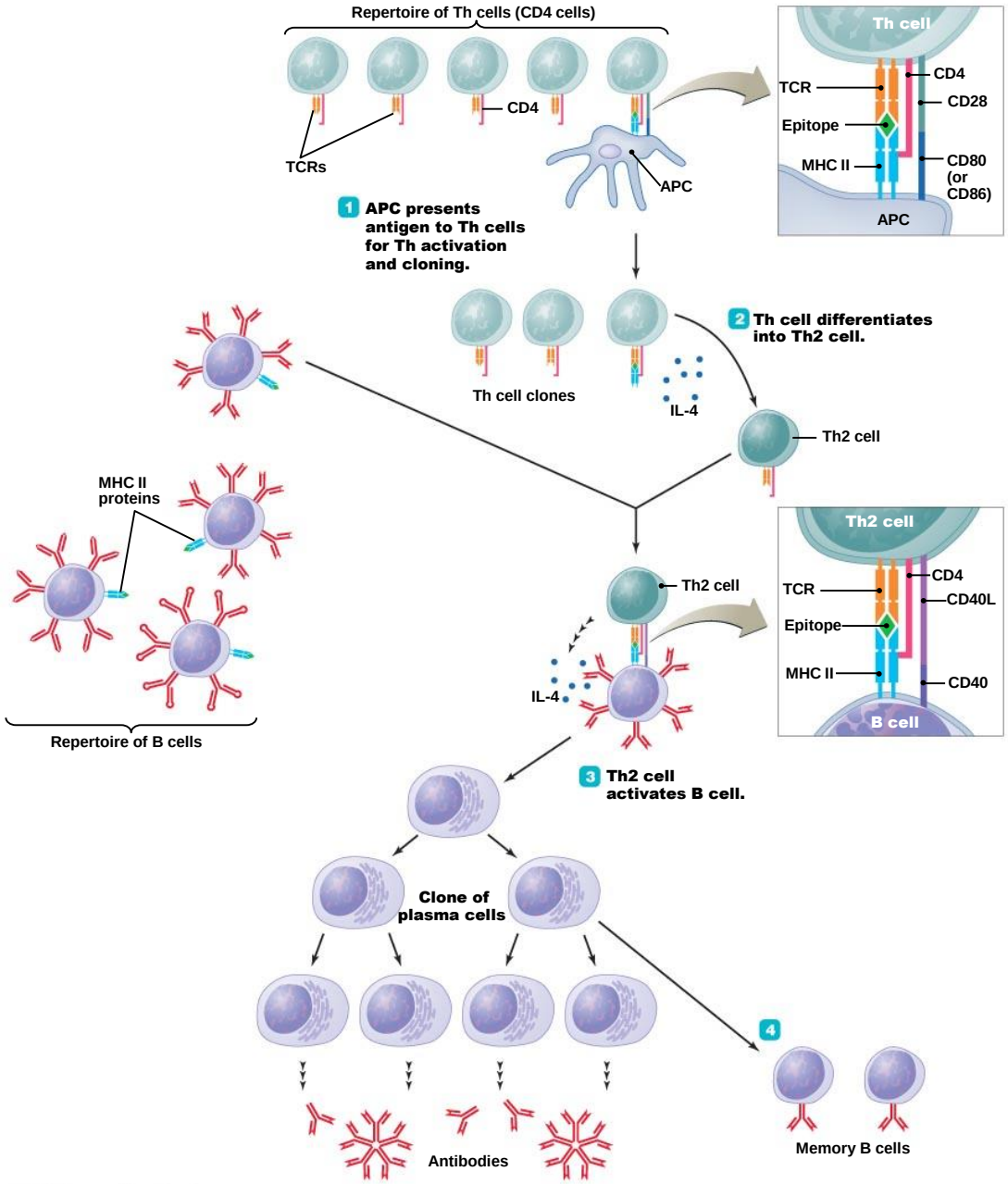
# Antibody Immune Responses

- Antibody immune responses mounted against **exogenous** pathogens and toxins
- Activates only in response to specific pathogens

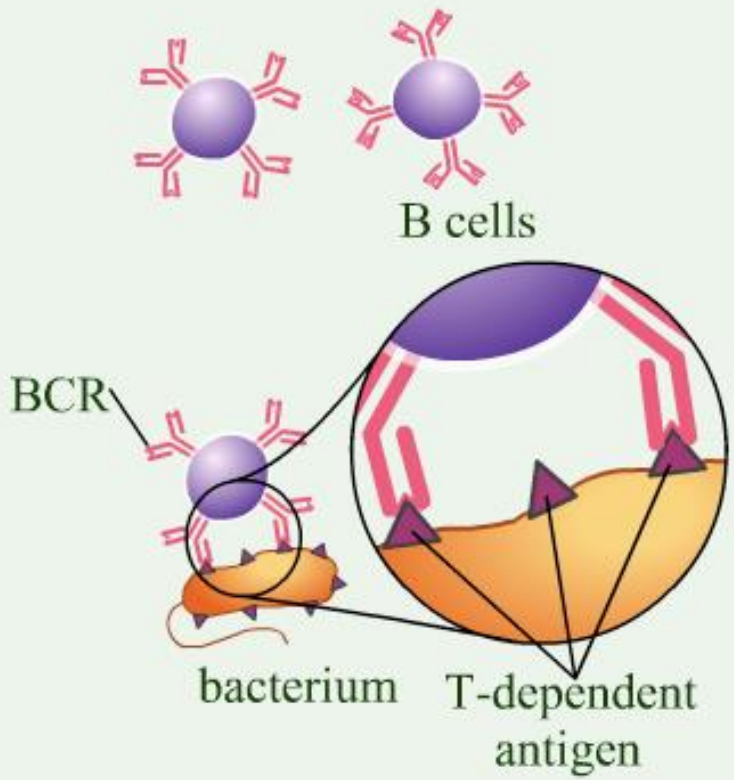
# Antibody Immune Responses

- **Inducement of T-Dependent Antibody Immunity with Clonal Selection**
  - T-dependent antibody immunity
    - Depend on the function of helper T cells
    - Four steps of this immune response:
      1. **Antigen presentation for Th activation and cloning**
      2. **Differentiation of helper T cells into Th2 cells**
      3. **Activation of B cells**
      4. **Proliferation of B cells**

## Figure 16.17 A T-dependent antibody immune response.



# Humoral Immunity: Clonal Selection and Expansion




PLAY **Humoral Immunity: Clonal Selection and Expansion**

# Antibody Immune Responses

- **Inducement of T-Dependent Antibody Immunity with Clonal Selection**
  - 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

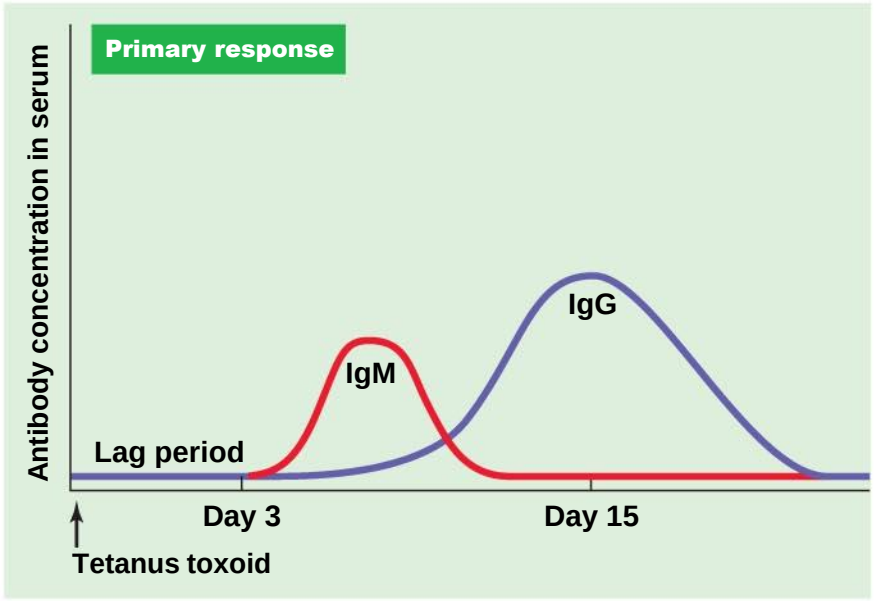
# Antibody Immune Responses

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

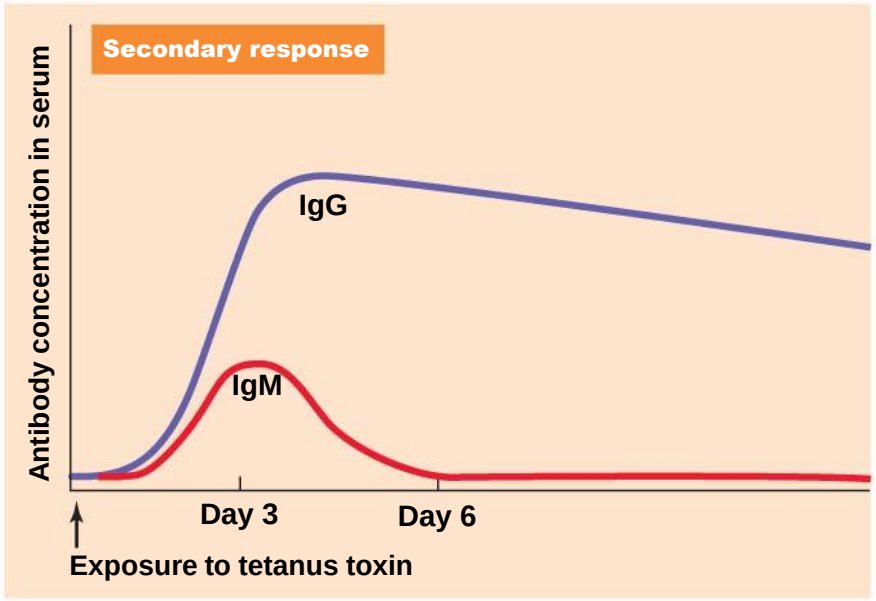
# Antibody Immune Responses

- **Memory Cells and the Establishment of Immunological Memory**
  - Primary immune response
    - Small amounts of antibodies produced
    - May take days to produce enough antibodies to eliminate the antigen from the body
  - Secondary immune response
    - Memory cells respond to another exposure to the antigen
    - Much faster than the primary response

**Figure 16.18 The production of primary and secondary antibody immune responses.**




(a)




(b)

# 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

## TABLE 16.4 A Comparison of the Types of Acquired Immunity

| | Active | Passive |
|---|---|---|
| **Naturally Acquired** |  The body responds to antigens that enter naturally, such as during infections. |  Antibodies are transferred from mother to offspring, either across the placenta (IgG) or in breast milk (secretory IgA). |
| **Artificially Acquired** |  Health care workers introduce antigens in vaccines; the body responds with antibody or cell-mediated immune responses, including the production of memory cells. |  Health care workers give patients antisera or antitoxins, which are preformed antibodies obtained from immune individuals or animals. |