

Basic Immunology

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Learning Objectives

- To understand adaptive immunity vs innate immunity
- To describe the different type of immune cells
- To understand antigen presentation
- To understand tolerance

What does the immune system do?

It protects us from infections with:

- 208 viruses

- 538 bacteria

- 317 fungi

- 287 worms

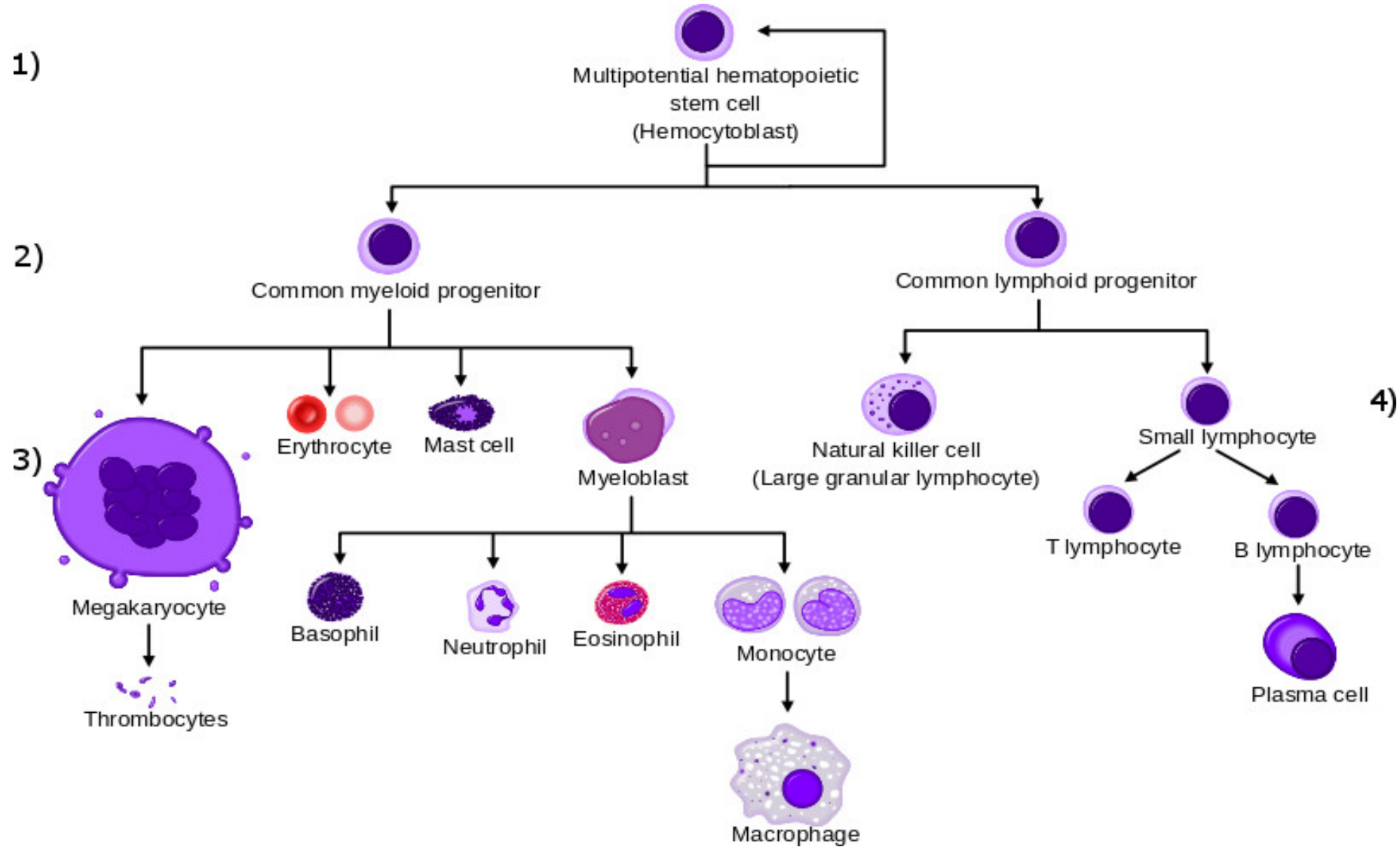
- 57 parasitic protozoa (CDC numbers)

It promotes normal functioning of the body (tissue cleanup, wound repair)

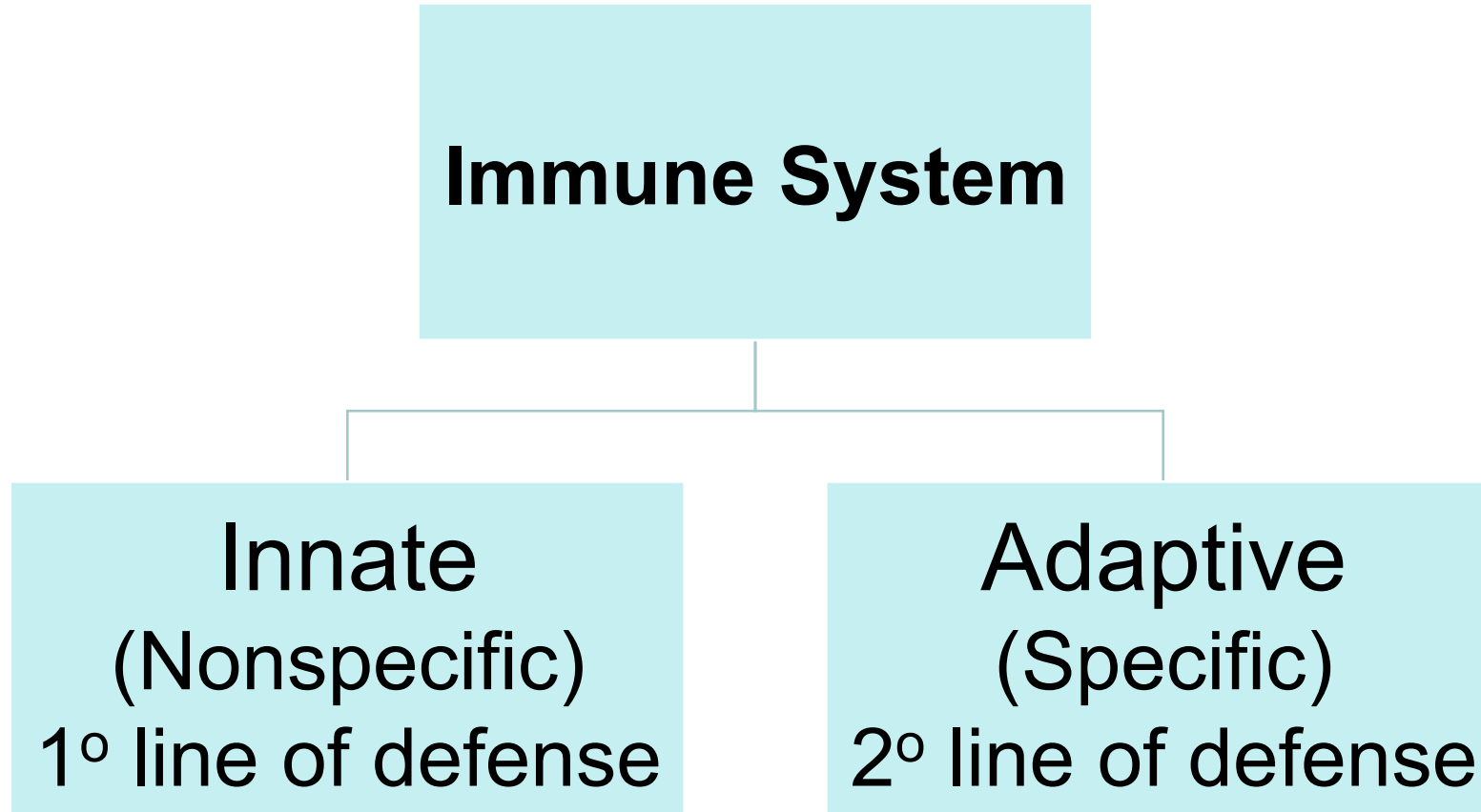
It removes abnormal cells including malignant ones

But the immune system can also cause disease when it is not doing the right thing (allergies, autoimmunity, transplant rejection, etc.)

Immune cells

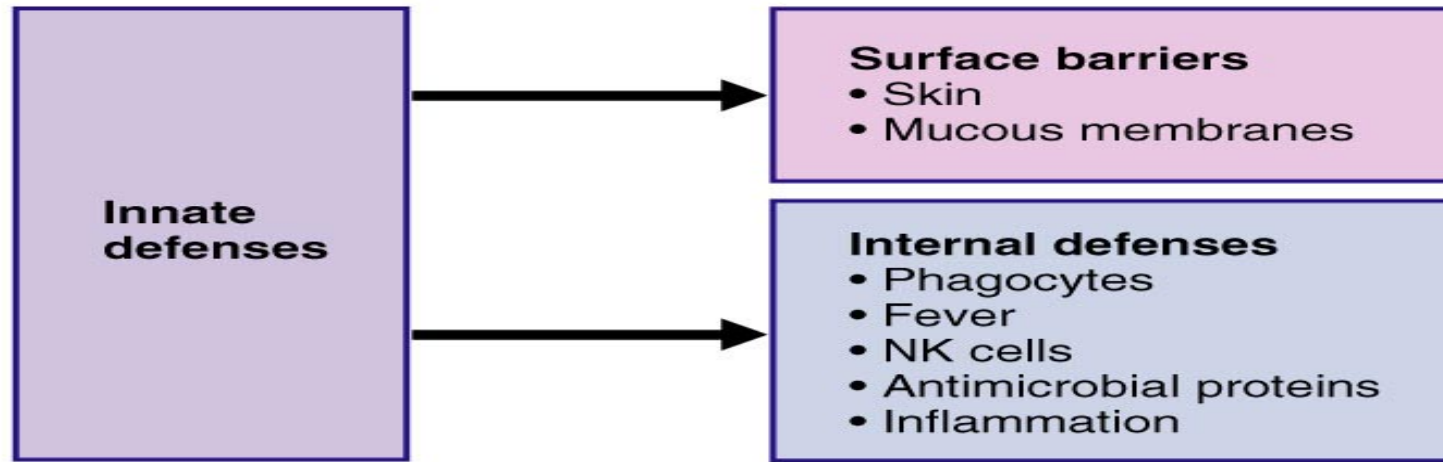


Overview of the Immune System

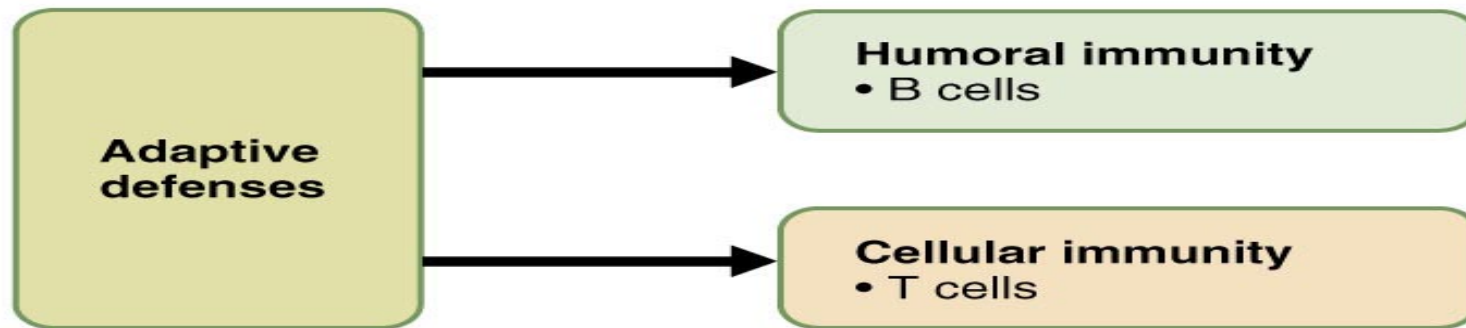


Interactions between the two systems

Overview of the Immune System



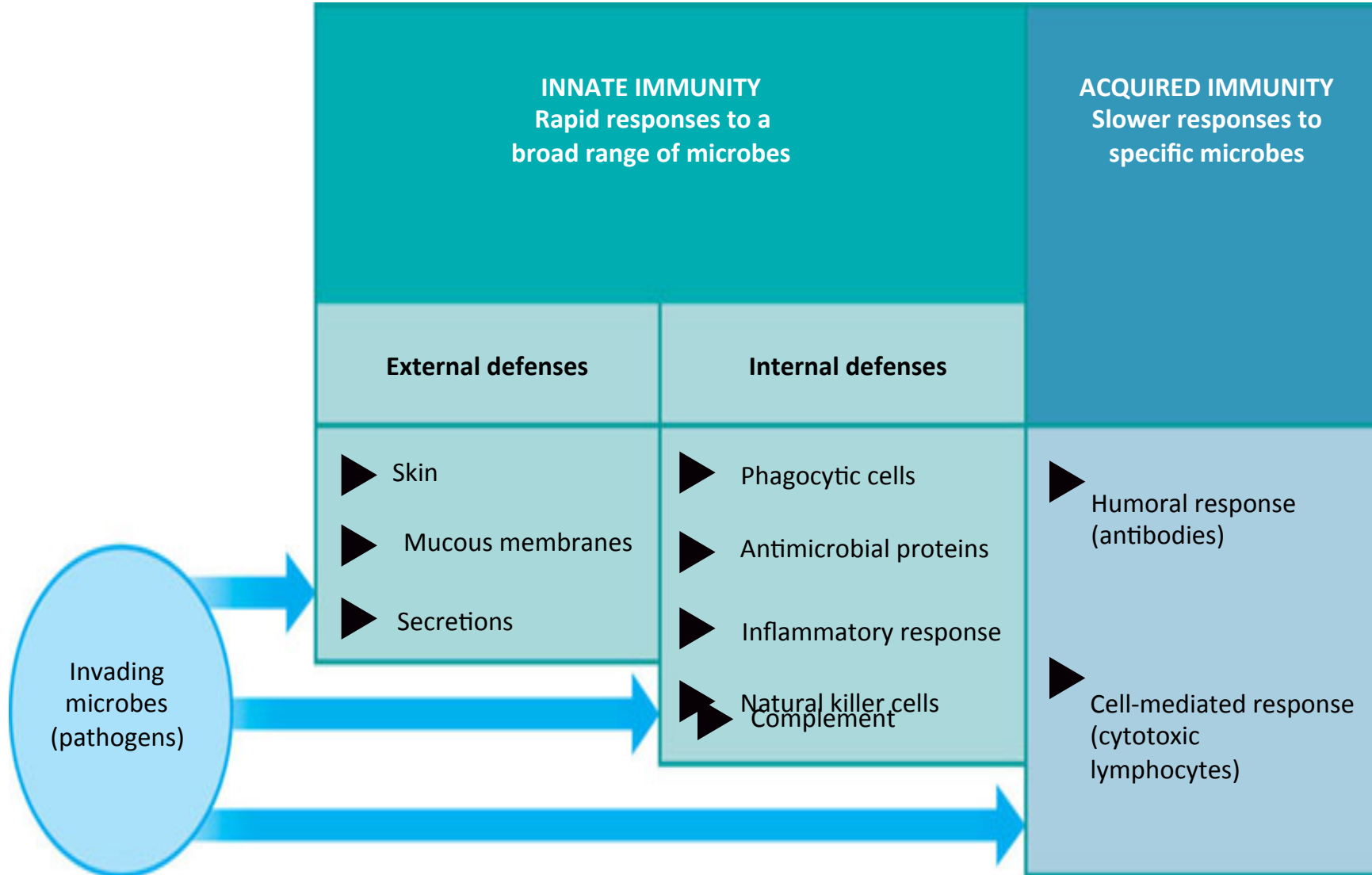
(a)



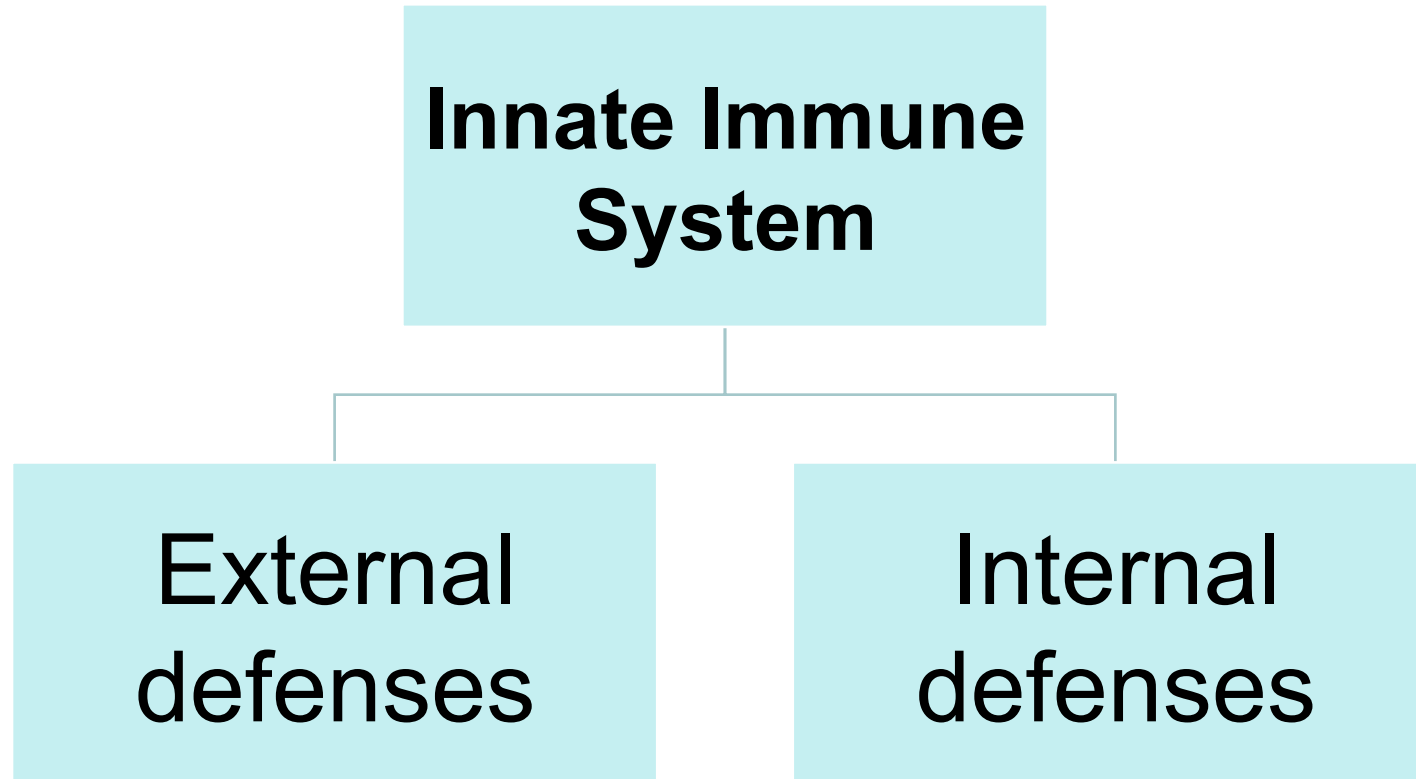
(b)

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A typical immune response



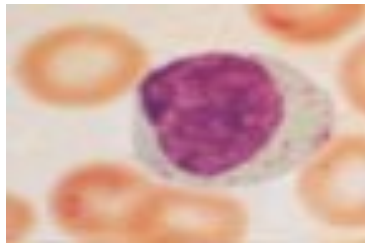
The innate immune System



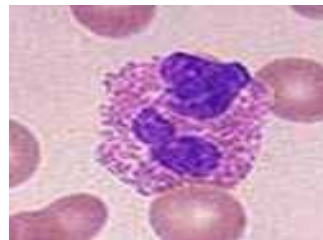
Interactions between the two systems

Innate immunity: mechanisms

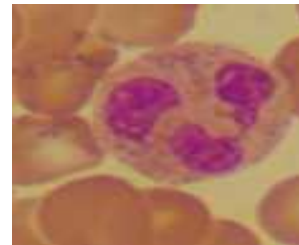
- Mechanical barriers / surface secretion
 - skin, acidic pH in stomach, cilia
- Humoral mechanisms
 - lysozymes, basic proteins, complement, interferons
- Cellular defense mechanisms
 - natural killer cells neutrophils, macrophages,, mast cells, basophils, eosinophils



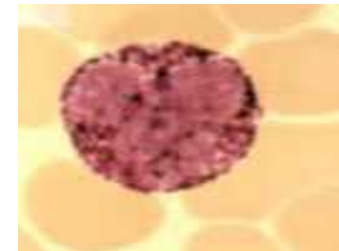
NK Cell



Eosinophils



Neutrophil



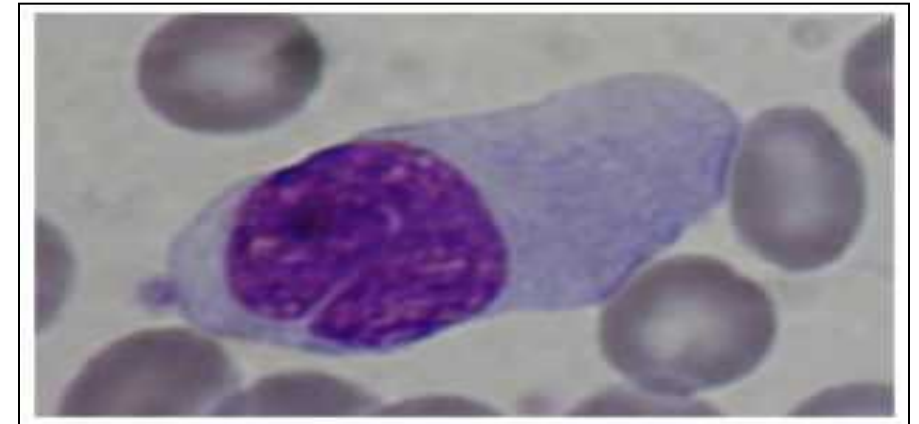
**Basophils & Mast
cells**



**Monocyte
Macrophage**

Adaptive immunity: mechanisms

- Cell-mediated immune response (CMIR)
 - T-lymphocytes
 - eliminate intracellular microbes that survive within phagocytes or other infected cells
- Humoral immune response (HIR)
 - B-lymphocytes
 - mediated by antibodies
 - eliminate extra-cellular microbes and their toxins



Plasma cell
(Derived from B-lymphocyte, produces antibodies)

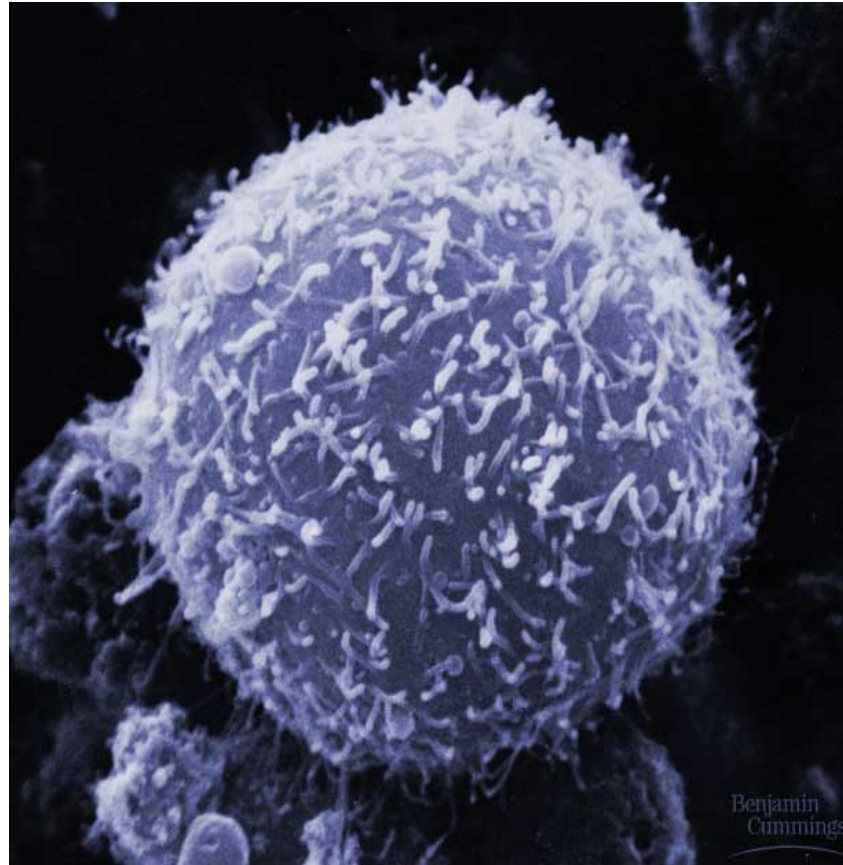
Humoral Immunity

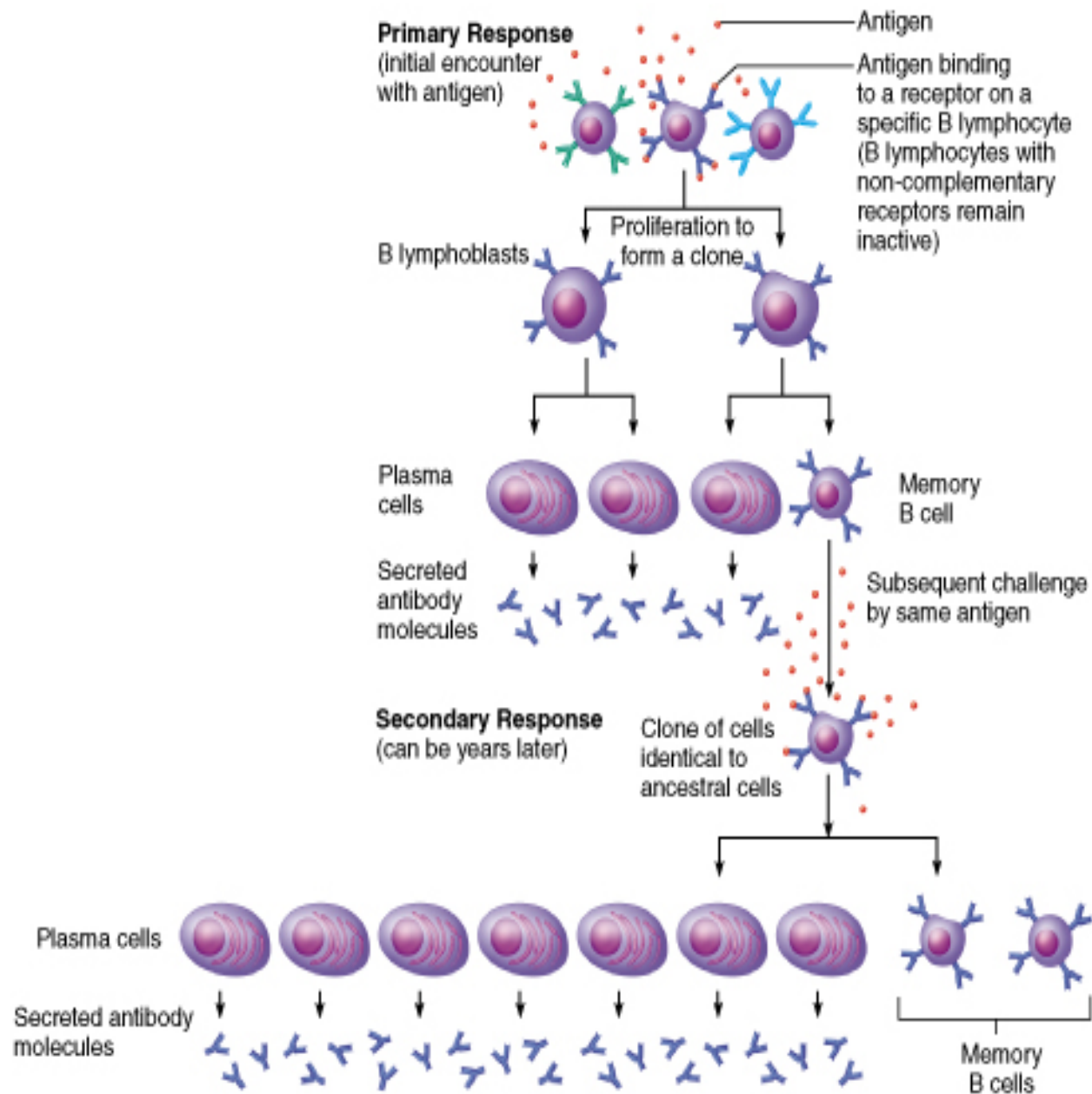
Also known as antibody-mediated immunity

Utilizes B-lymphocytes

Recognizes antigen directly

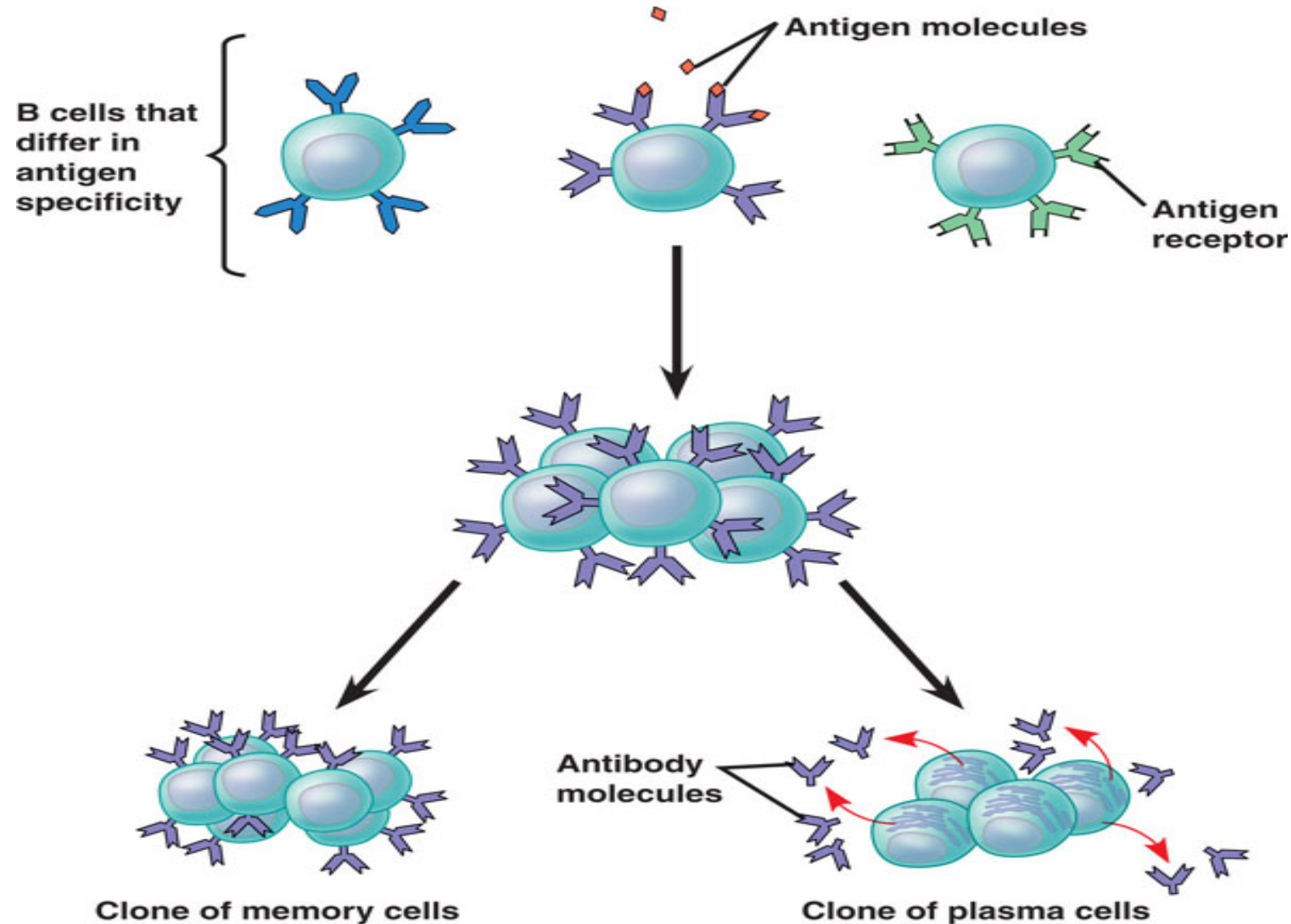
Made in the bone marrow



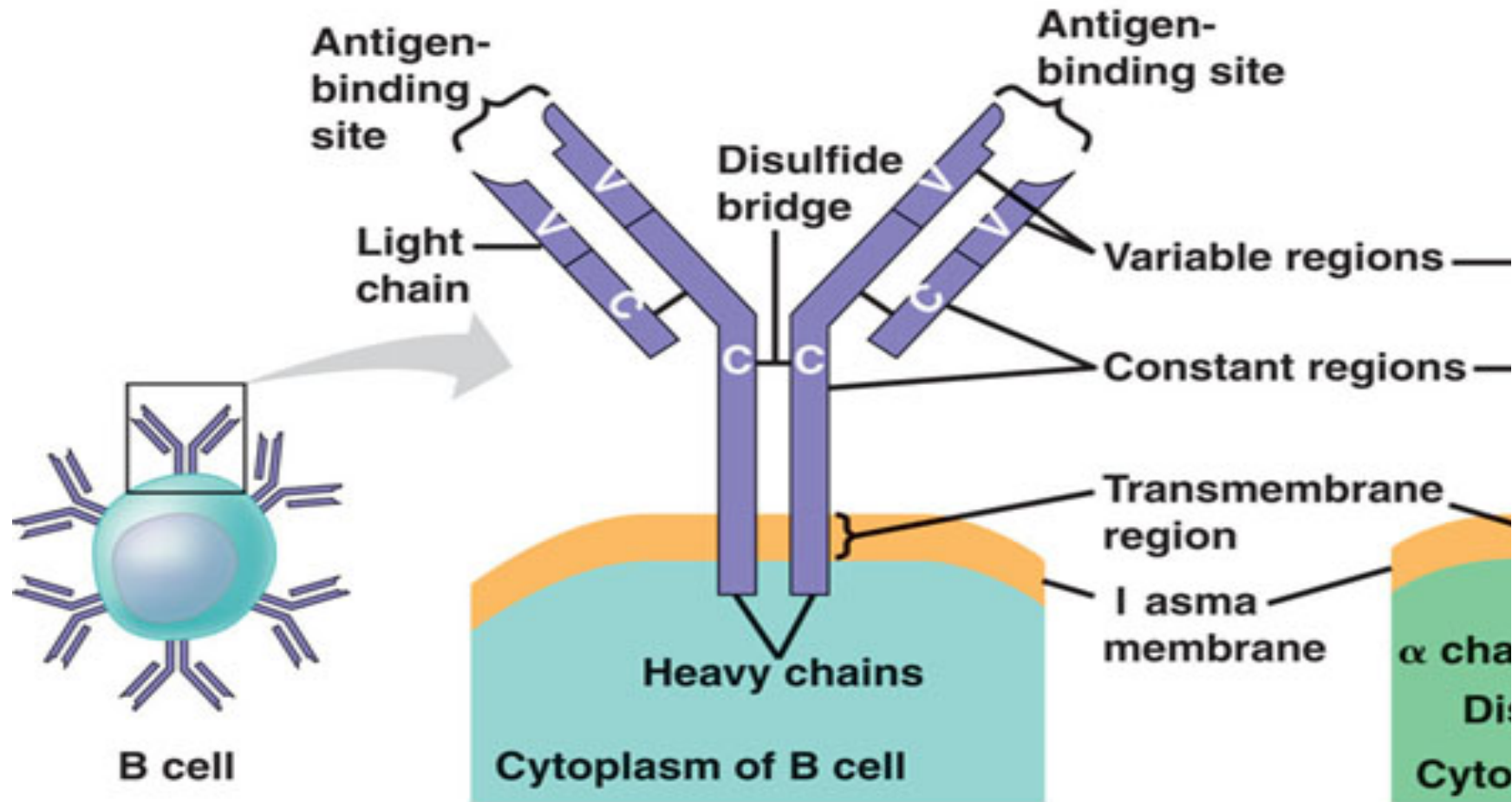


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Clonal Selection and Proliferation



Antibody Structure



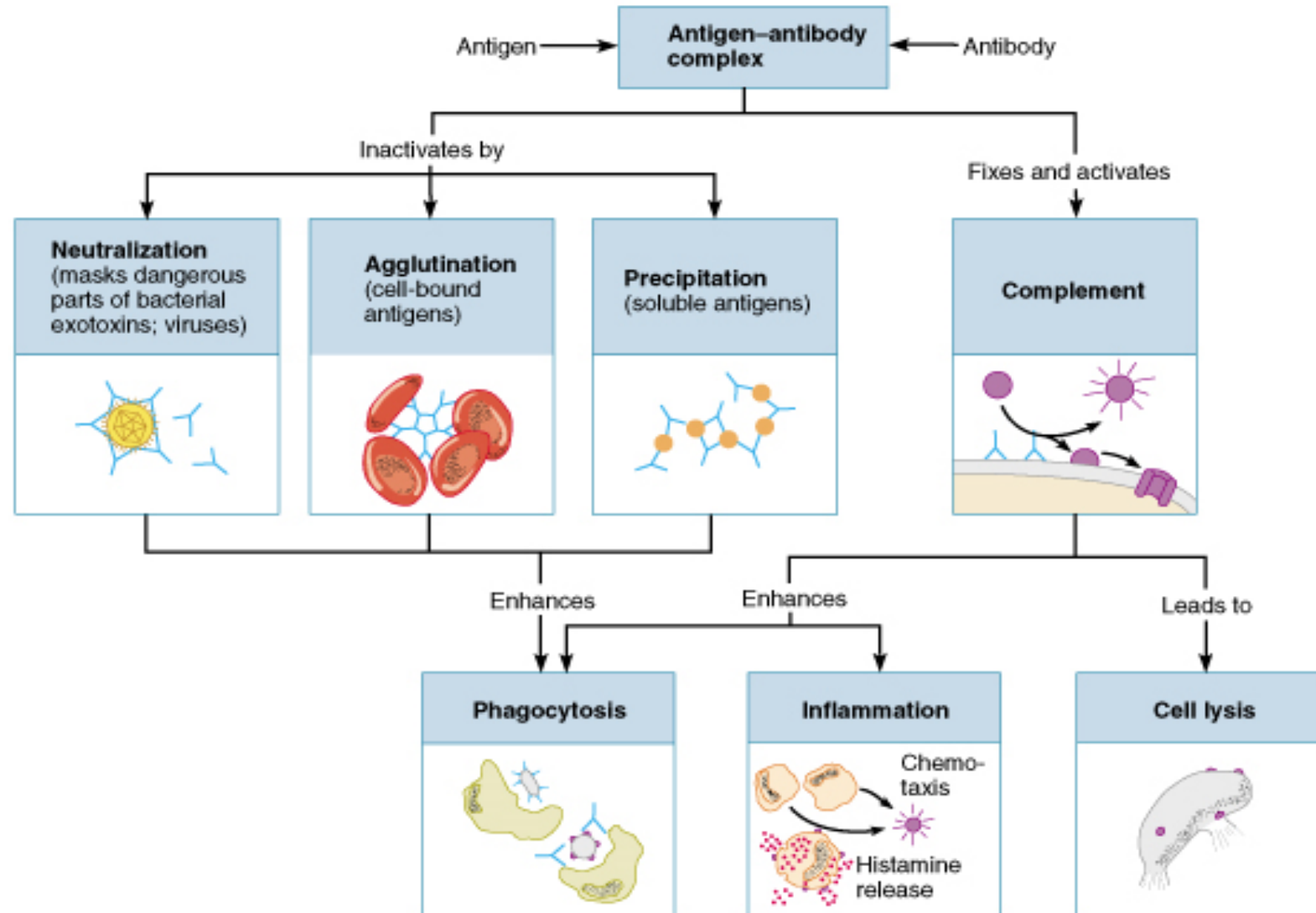
a A B cell receptor consists of two identical heavy chains and two identical light chains linked by several disulfide bridges

b A
ch
dis

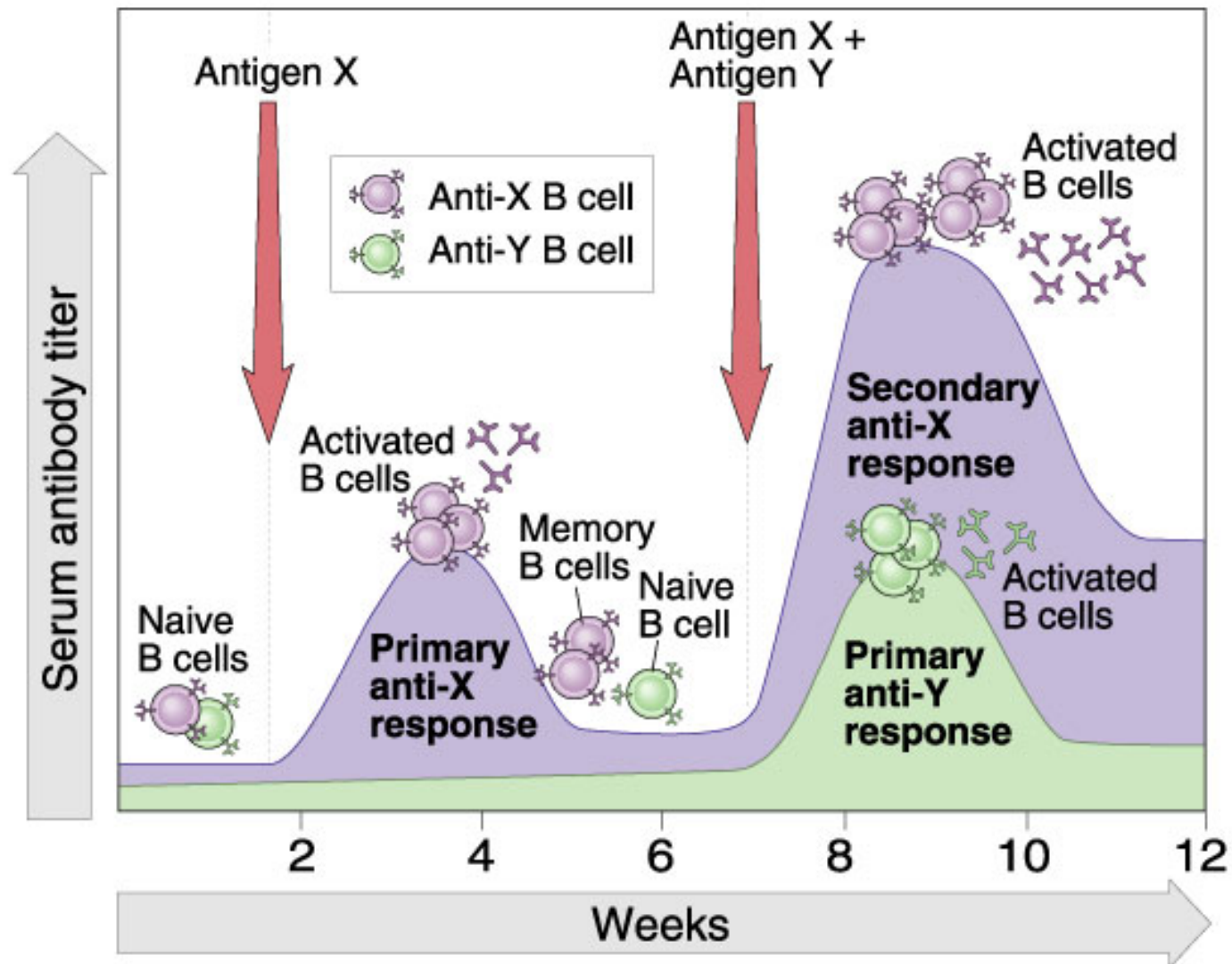
Classes of Antibodies (Immunoglobulins)

Class/ subclass	Heavy chain	Light chain	Molecular weight (kDa)	Structure	Function
IgA ₁ IgA ₂	α ₁ α ₂	λ or κ	150 to 600	Monomer to tetramer	Most produced Ig; protects mucosal surfaces; Resistant to digestion; secreted in milk
IgD	δ	λ or κ	150	Monomer	Function unclear; Works with IgM in B-cell development; mostly B cell bound
IgE	ε	λ or κ	190	Monomer	Defends against parasites; causes allergic reactions
IgG ₁ IgG _{2a} IgG _{2b} IgG ₃ IgG ₄	γ ₁ γ ₂ γ ₂ γ ₃ γ ₄	λ or κ	150	Monomer	Major Ig in serum; good opsonizer; moderate complement fixer (IgG ₃); can cross placenta
IgM	μ	λ or κ	900	Pentamer	First response antibody; Strong complement fixer; Good opsonizer

Antibody Functions



Specificity and memory in adaptive immunity, illustrated by primary and secondary immune responses.



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Cell-mediated immune response

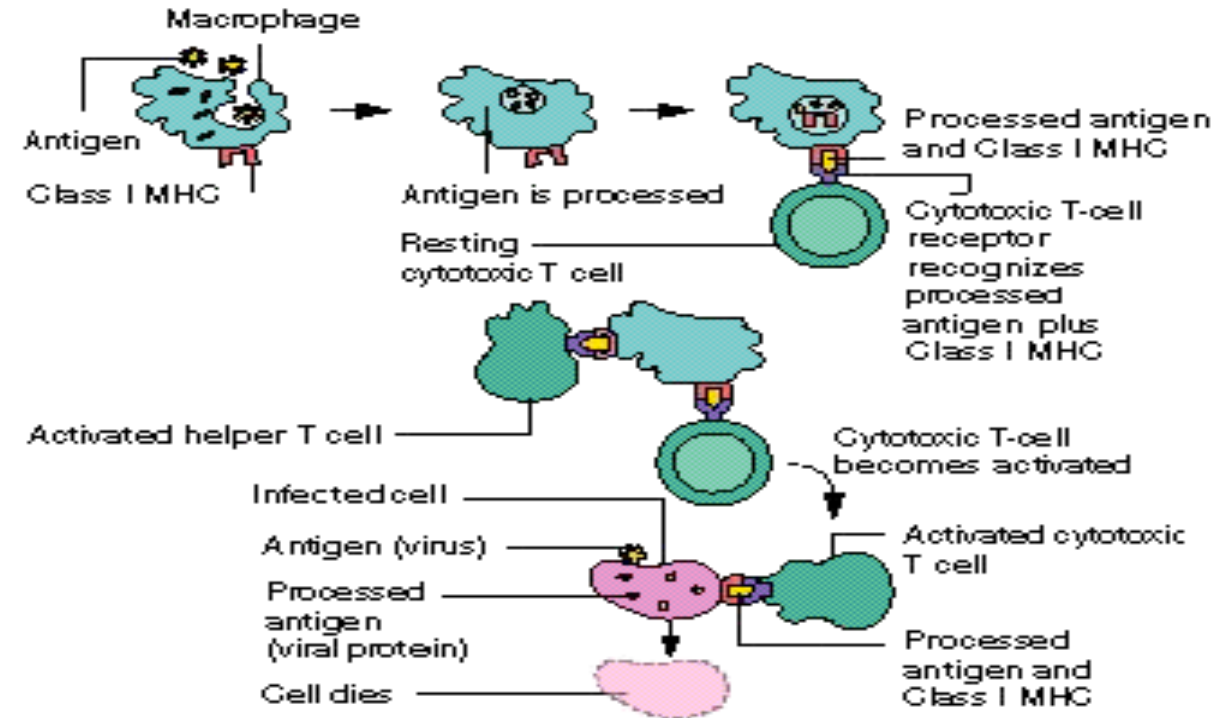
1. T-cell

recognizes peptide antigen on macrophage in association with major histo-compatibility complex (MHC) class

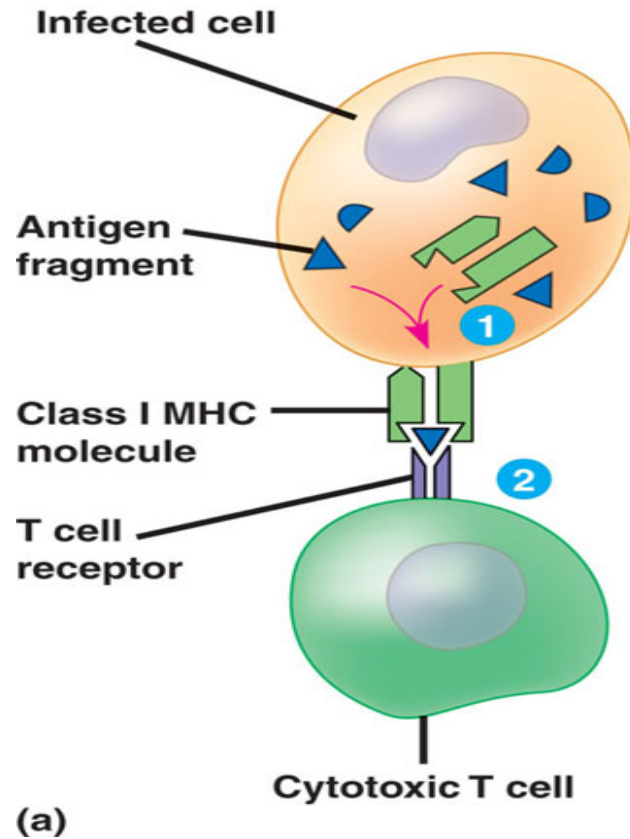
identifies molecules on cell surfaces

helps body distinguish self from non-self

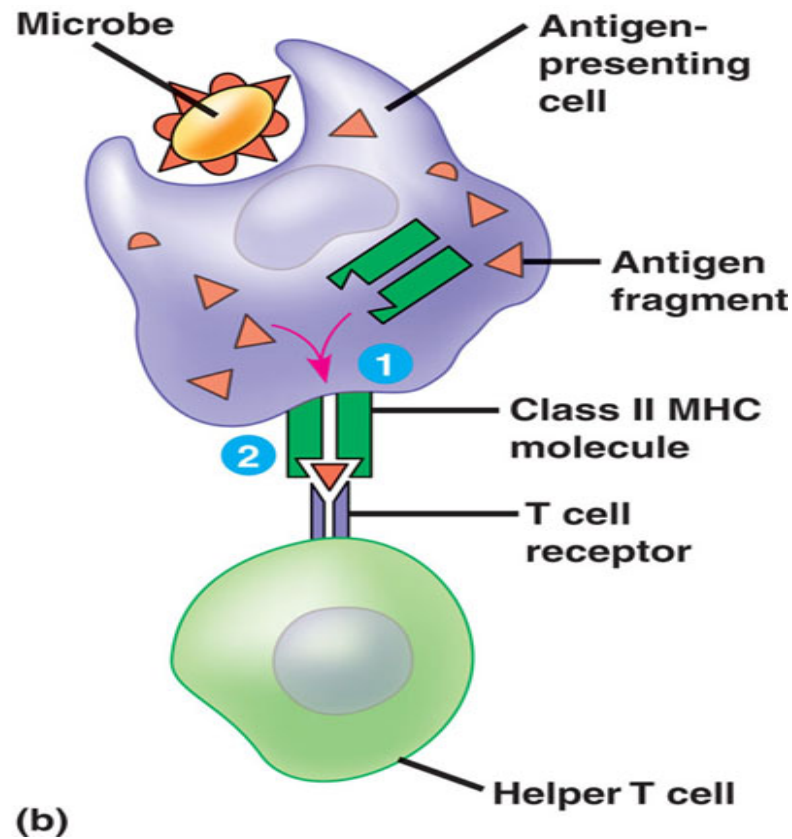
2. T-cell goes into effectors cells stage that is able to kill infected cells



Cell-Mediated Immunity

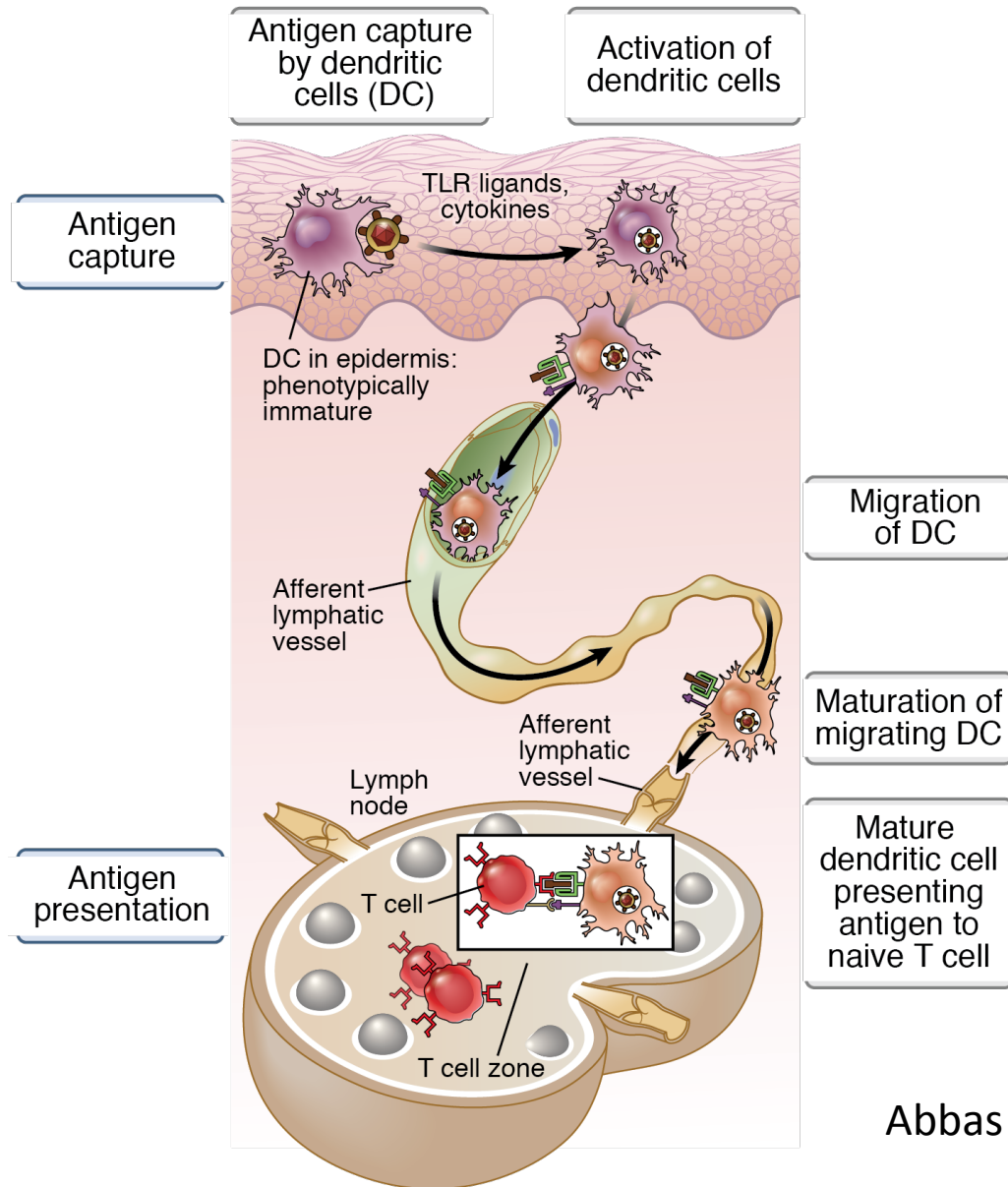


CLASS I MHC PROTEIN



CLASS II MHC PROTEIN

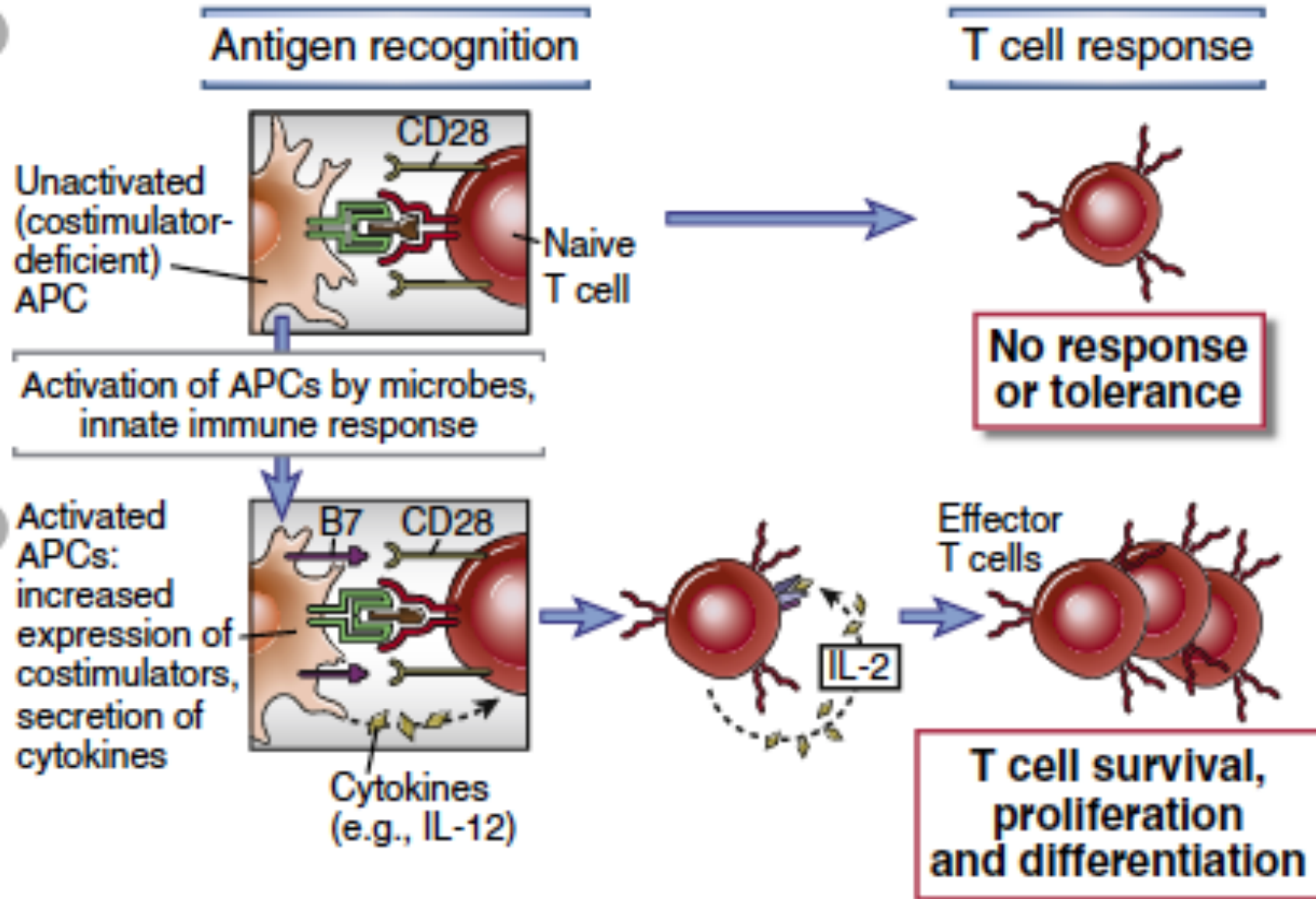
Capture and presentation of antigens by dendritic cells



Abbas et al. Basic Immunology

Antigens and naïve T cells come together in lymphoid organs

T cell activation



Class I MHC Pathway

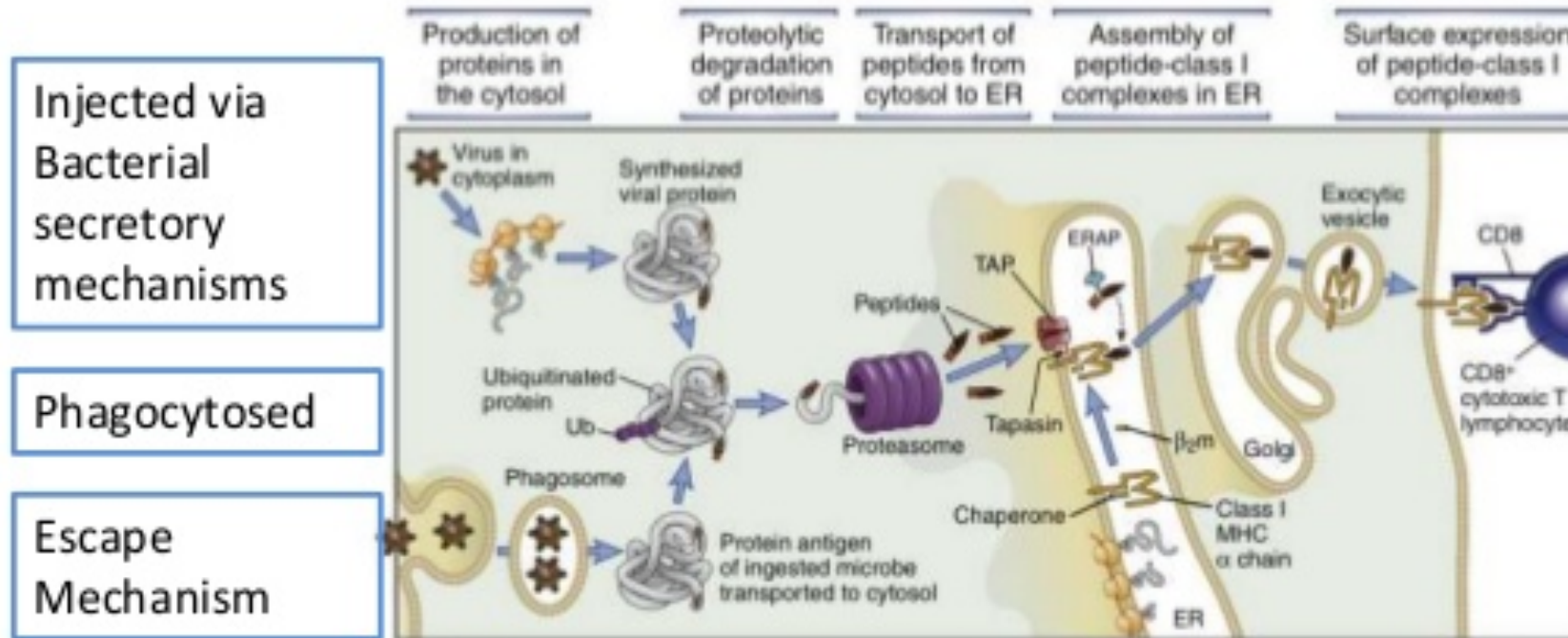


FIGURE 6-16 The class I MHC pathway of antigen presentation. The stages in the processing of cytosolic proteins are described in the text. ERAP, endoplasmic reticulum associated peptidase; ER, endoplasmic reticulum; β_2m , β_2 -microglobulin; TAP, transporter associated with antigen processing; Ub, ubiquitin.

Cellular and Molecular Immunology 8th Ed. (2015) by Abbas et al.

Class II MHC Pathway

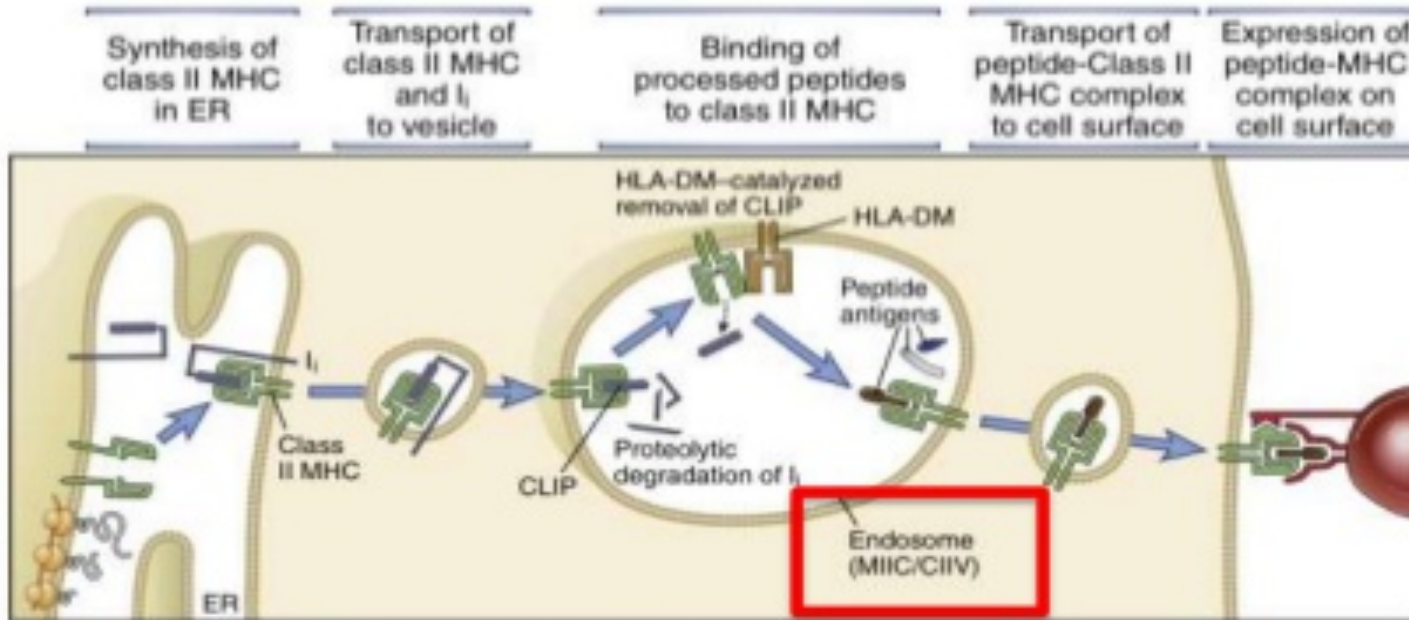
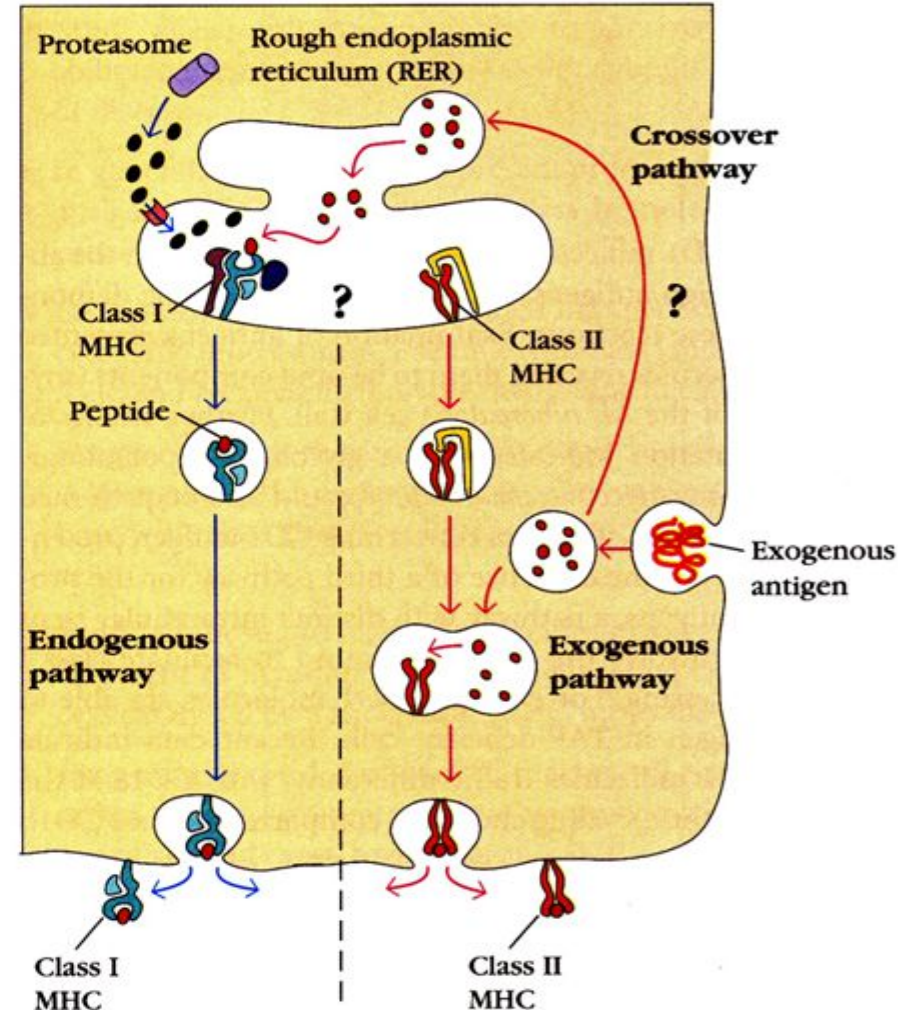


FIGURE 6-19 The functions of class II MHC-associated invariant chain and HLA-DM. Class II molecules with bound invariant chain, or CLIP, are transported into vesicles, where the I_i is degraded and the remaining CLIP is removed by the action of DM. Antigenic peptides generated in the vesicles are then able to bind to the class II molecules. Another class II-like protein, called HLA-DQ, may regulate the DM-catalyzed removal of CLIP (not shown). CIIV, class II vesicle.

Cellular and Molecular Immunology 8th Ed. (2015) by Abbas et al.

Cross-Presentation of Exogenous Ag

- Sometimes APC present exogenous antigens bound to Class I molecules.
- This is not well understood but is believed to occur in the lumen of the RER.
- This may provide a selective advantage in that it would allow dendritic cells to phagocytose viruses and present viral antigens with Class I.
 - This causes the generation and activation of cytotoxic T cells that can kill virus-infected cells prior to the general spread of the infection.



Physical Triggers of Immune Response:

- **Infections**
 - Bacterial, viral
 - Fungal, parasitic
- **Toxins**
 - Exogenous
 - Endogenous
- **Food peptides**
- **Allergens**
- **Medications**
- **Auto antigens**

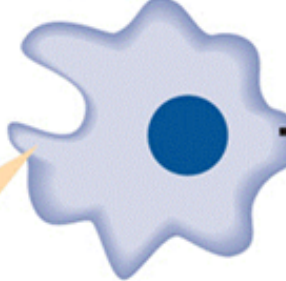
Th17

- Extracellular bacteria (skin, lining of intestine)
- Fungi
- Autoimmunity

Th17

IL-17
IL-21
IL-22

Antigen Presenting Cells



Naïve T cell

Th0

Th1

- Cell-mediated immunity and inflammation
- Intracellular pathogens
 - Viruses, bacteria
- Autoimmunity
- Inflammation

Th1

IL-2
IFN- γ
TNF- α

Th2

- Antibody-mediated immunity
- Extracellular parasites
- Asthma, allergy

Th2

IL-4
IL-5
IL-6
IL-10
IL-13

TGF- β
IL-35
IL-10

Treg

Treg

- Immune tolerance
- Lymphocyte homeostasis
- Regulation of immune responses

Th0: Naïve T cells

Th: Helper T cells

Treg: Regulatory T cells

IL: Interleukin

TNF- α : Tumor necrosis factor-alpha

IFN- γ : Interferon-gamma

TGF- β : Transforming growth factor-beta

Central vs Peripheral Tolerance

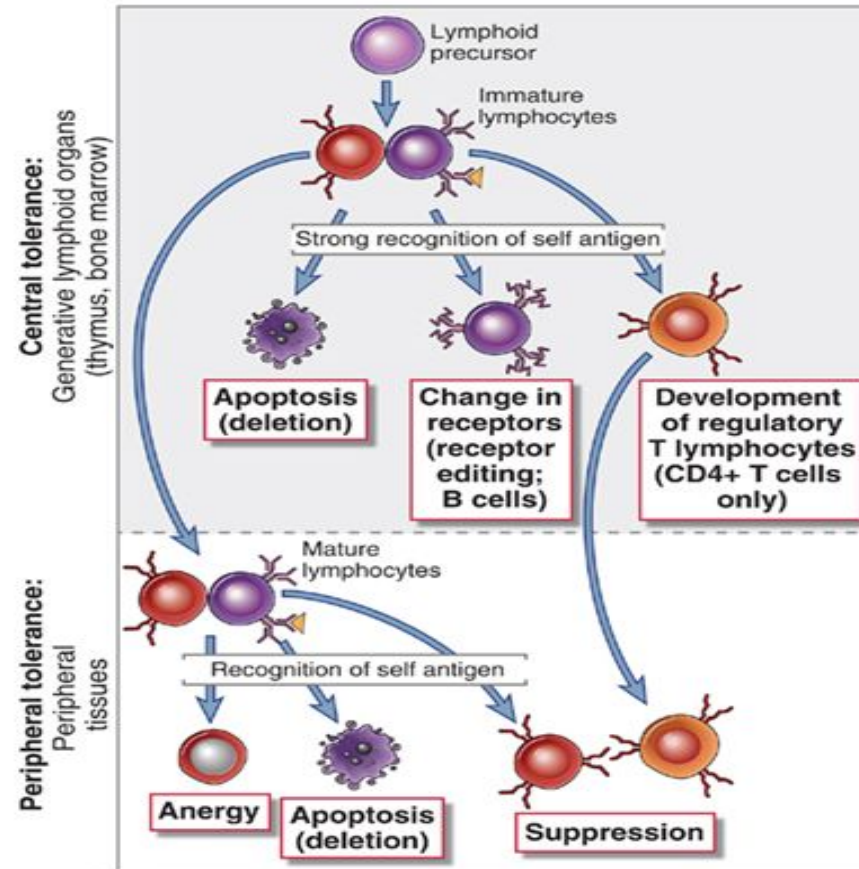
Self tolerance

■ Central tolerance

- ❑ Negative selection
- ❑ Receptor editing
- ❑ Generation of regulatory T cells

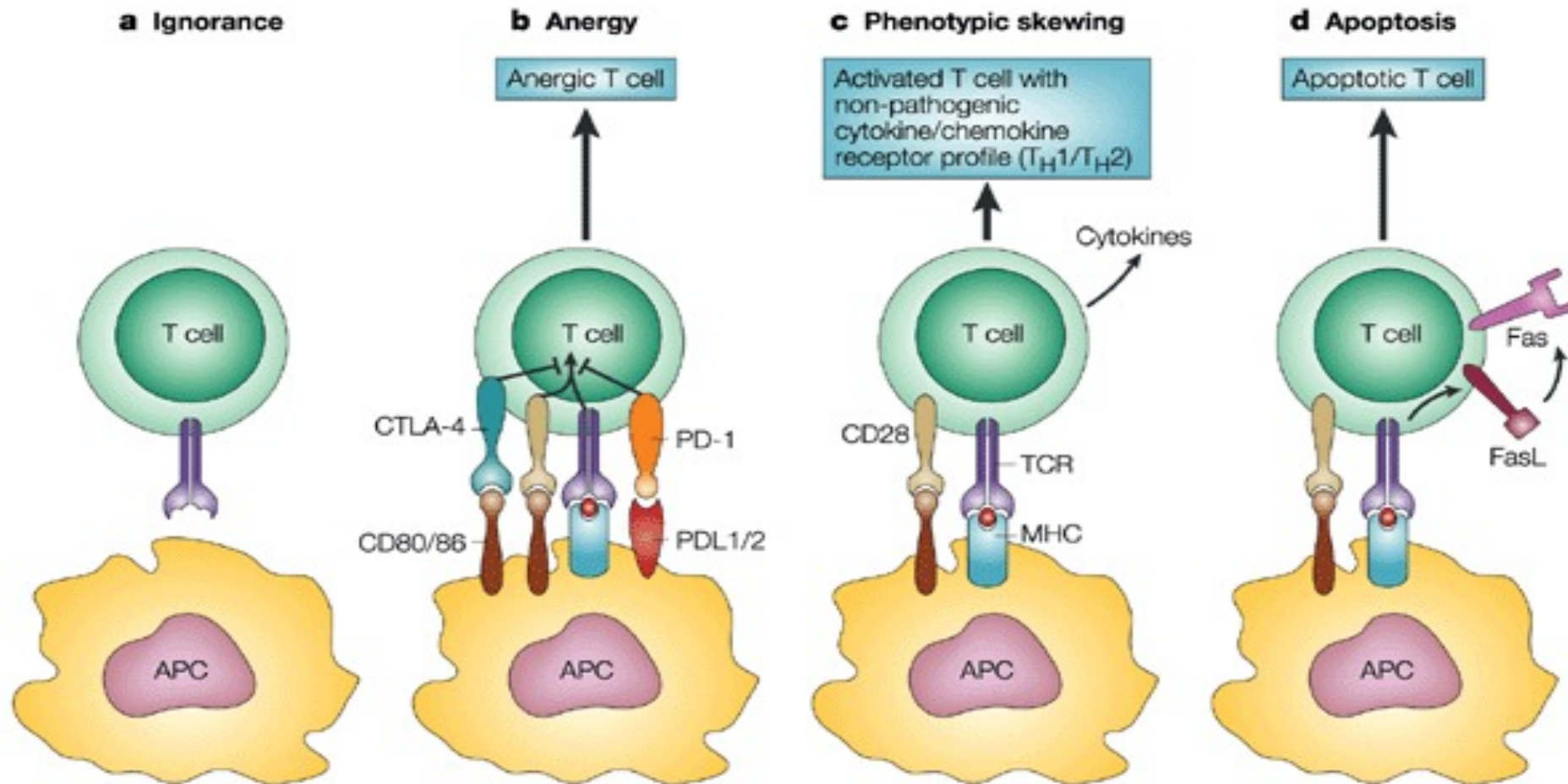
■ Peripheral tolerance

- ❑ Clonal anergy
- ❑ Clonal deletion
- ❑ Regulatory T cells
- ❑ T-T interaction



Abbas et al: Cellular and Molecular Immunology, 7e.
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Mechanism of Peripheral Tolerance



Problems with the Immune System

Blood Transfusion Reaction

Tissue Rejection

Allergies

Autoimmune disease

Immunodeficiencies