Cells of the Immune System

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Learning Objectives

By the end of this lecture you will be able to:

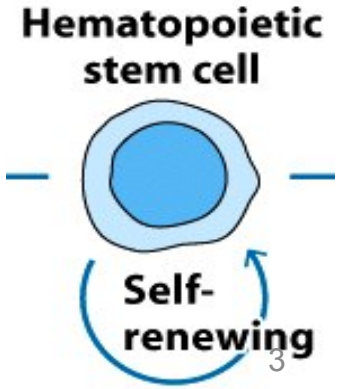
① Describe the structure and function of major immune cells

② Appreciate the collaborative relationship between innate and adaptive immune cells

Hematopoiesis

- Hematopoiesis is the process of formation and development of red and white blood cells.

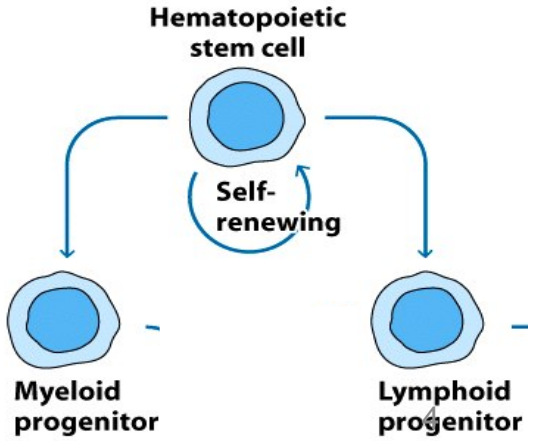
- All blood cells arise from a multipotent stem cell called **hematopoietic stem cell (HSC)**, which has the ability of **self renewal** and **differentiation** into other cell types.



Myeloid and Lymphoid Progenitors

- HSC differentiates along one of two pathways giving rise to either a **myeloid progenitor** or **lymphoid progenitor**

- Progenitor cells have lost the capability for self renewal and are committed to a particular cell lineage



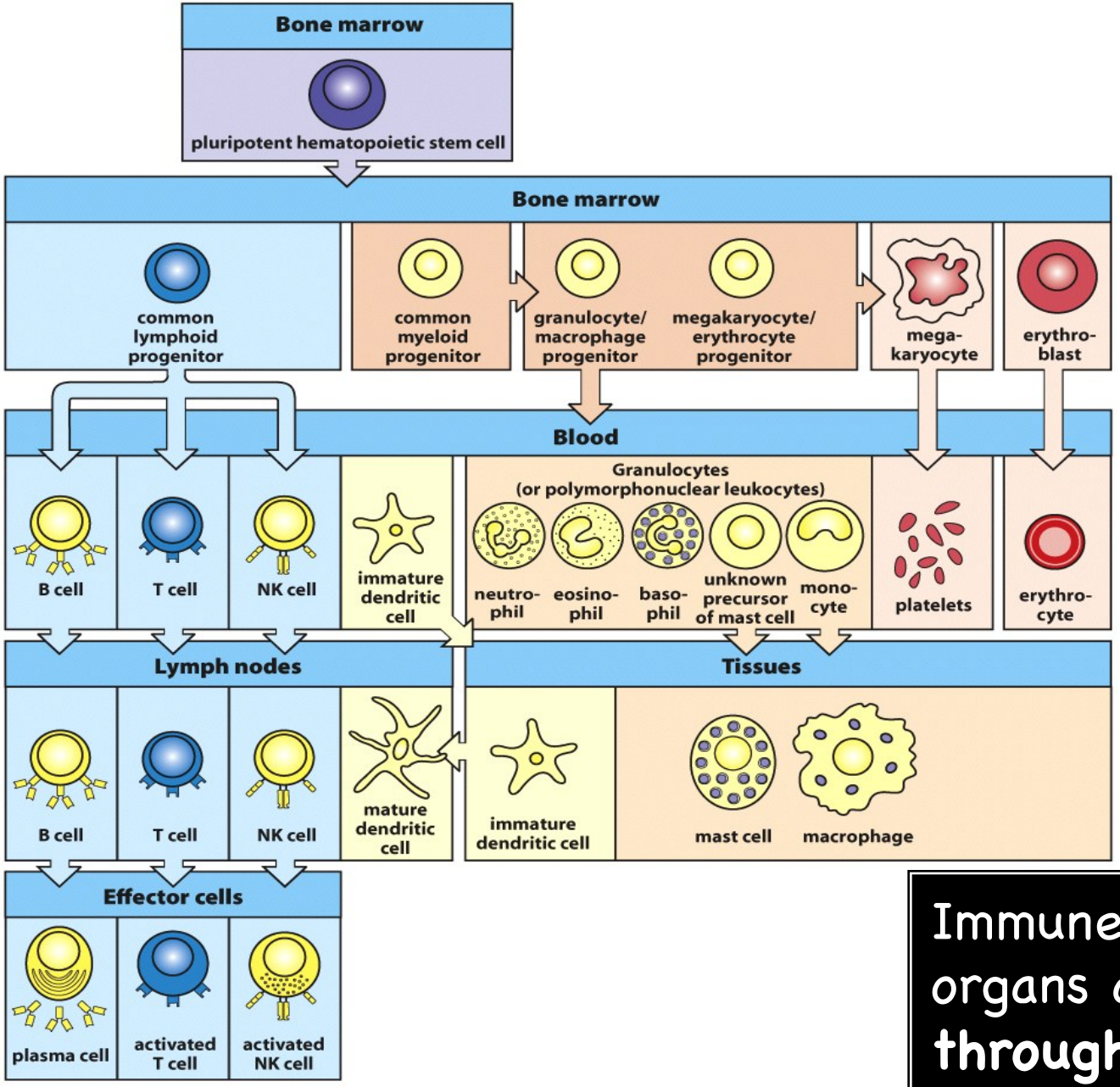


Figure 1.3 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Immune cells and organs are found **throughout** the body

Myeloid Cells

- Cells originated from the **common myeloid progenitor**
- They include:
  - **Mononuclear phagocytes** (monocytes and macrophages)
  - **Granulocytes** (neutrophils, eosinophils, basophils)
  - **Mast cells**
  - **Dendritic cells**

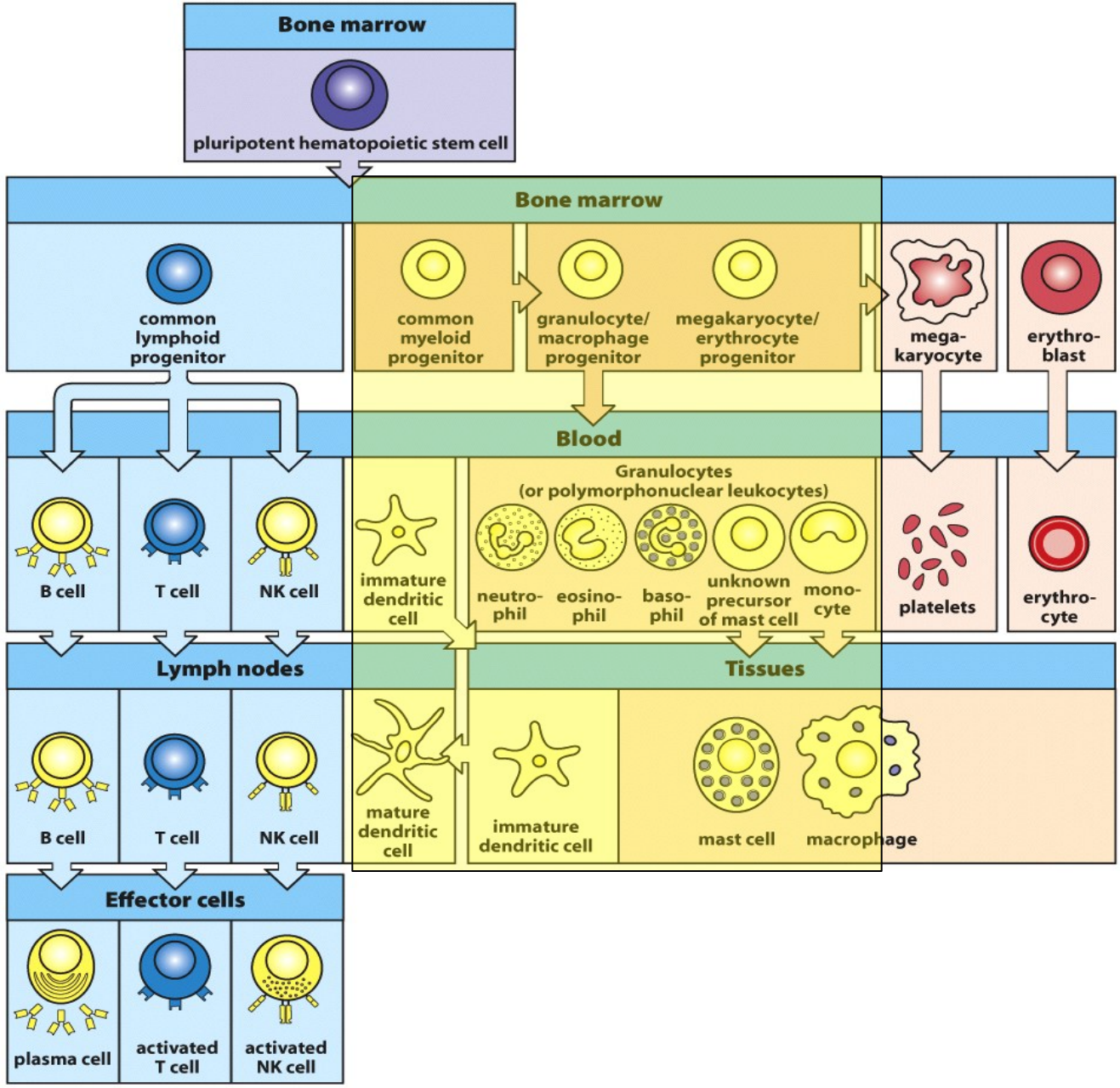


Figure 1.3 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Mononuclear Phagocytes

- The mononuclear phagocytic system consists of **monocytes** circulating in the blood and **macrophages** in the tissues

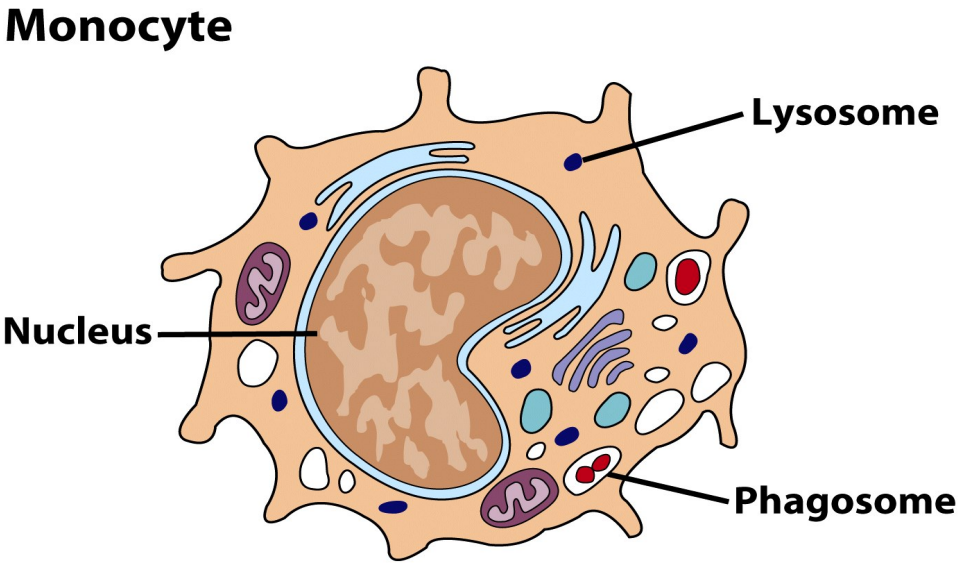


Figure 2-7a
Kuby IMMUNOLOGY, Sixth Edition

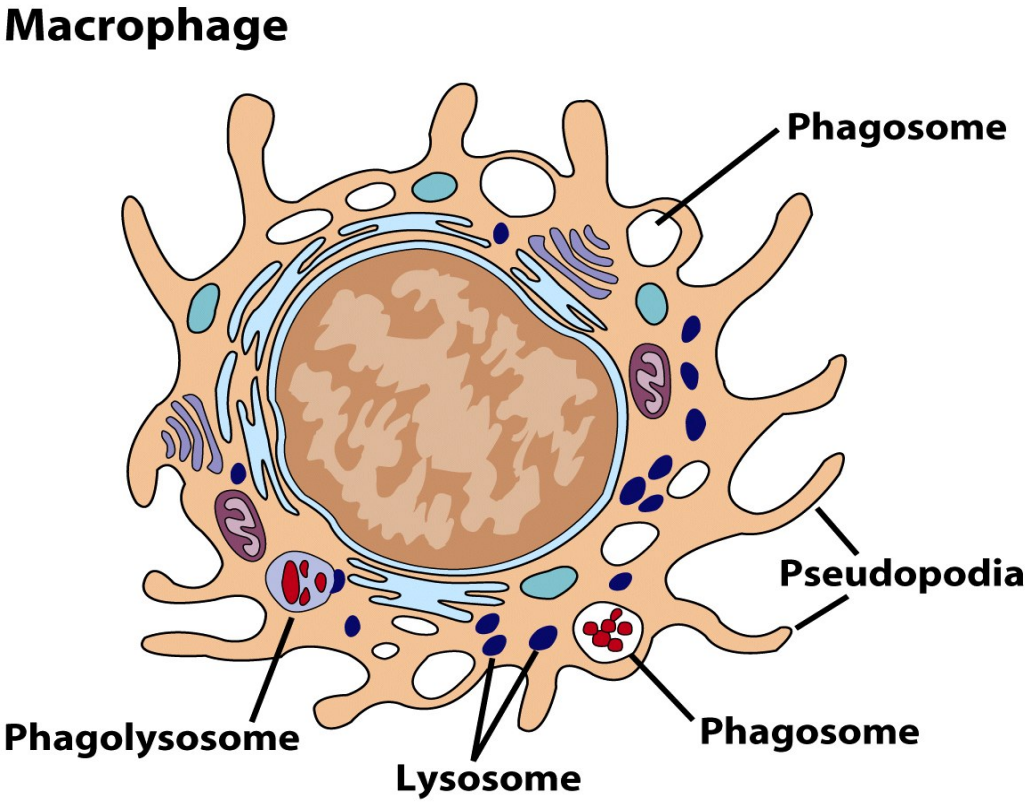


Figure 2-7b
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Mononuclear Phagocytes

- Monocytes enlarge while circulating in the blood then migrate to tissues where they are named according to their tissue location:
  - **Intestinal macrophages** in gut
  - **Alveolar macrophages** in lung
  - **Histiocytes** in connective tissue
  - **Kupffer cells** in the liver
  - **Mesangial cells** in the kidney
  - **Microglial cells** in the brain
  - **Osteoclasts** in bone

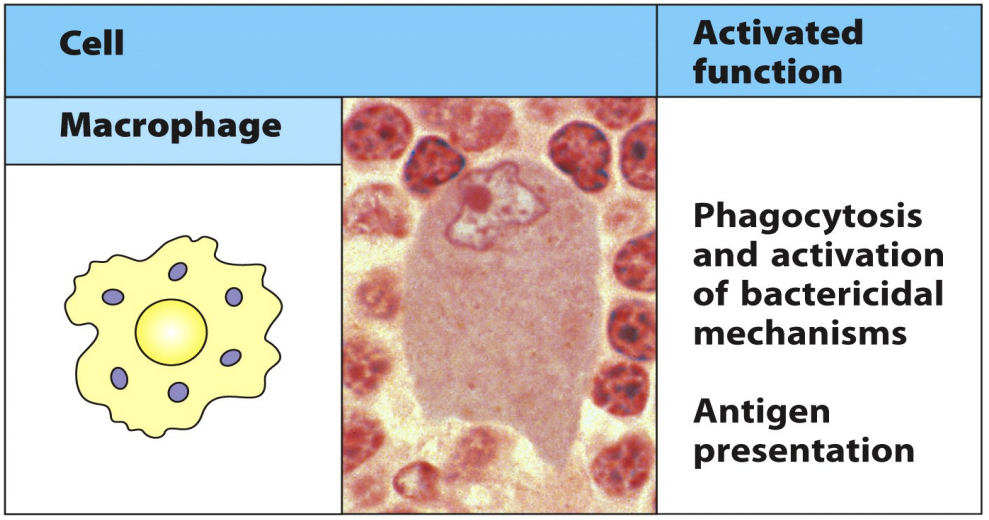

Figure 1.4 part 1 of 6 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Monocytes vs. Macrophages

- Differentiation of monocytes into macrophages involves many changes:

① The cell enlarges 5 to 10 times

② Intracellular organelles increase in number and complexity

③ Production of higher levels of hydrolytic enzymes

④ Secretion of many soluble factor

⑤ **Increased phagocytic ability and antigen presentation**

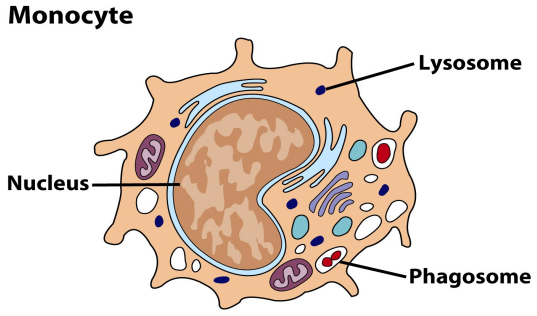

Figure 2-7a
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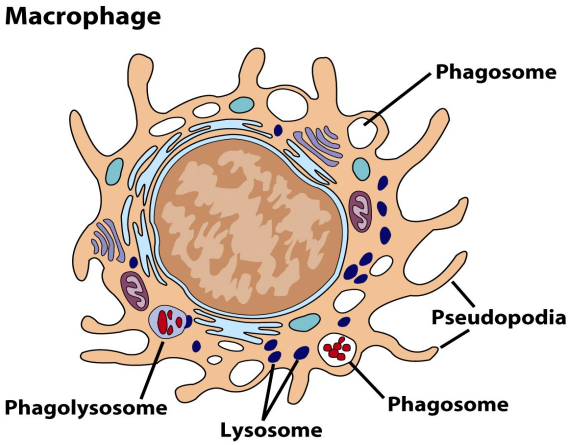

Figure 2-7b
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Macrophage Phagocytosis

① Macrophages engulf complex antigens such as bacteria by **phagocytosis**

② The **phagosome** moves toward the cell interior and fuses with a **lysosome** to form a **phagolysosome**

③ The lysosome contains digestive enzymes

④ The digested contents are eliminated by **exocytosis** and some get presented by **MHC-II** molecules

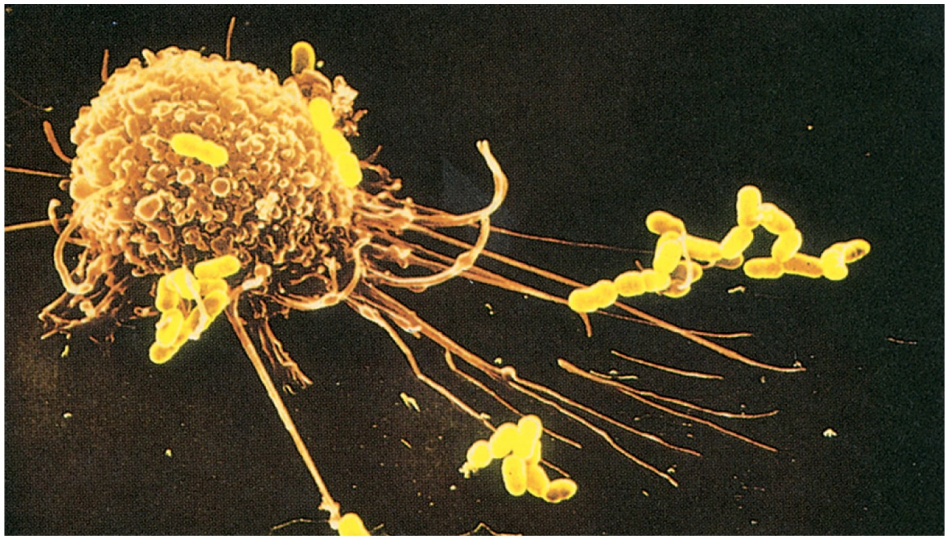

Figure 2-8a
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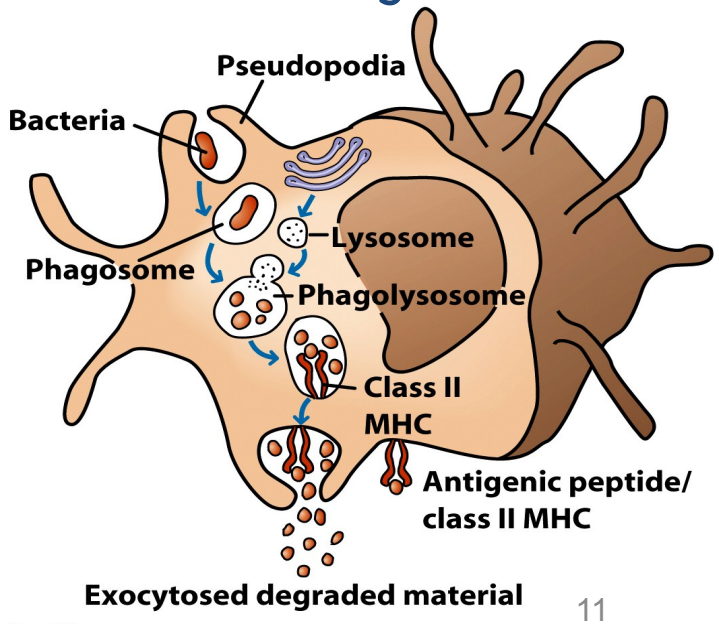

Figure 2-8b
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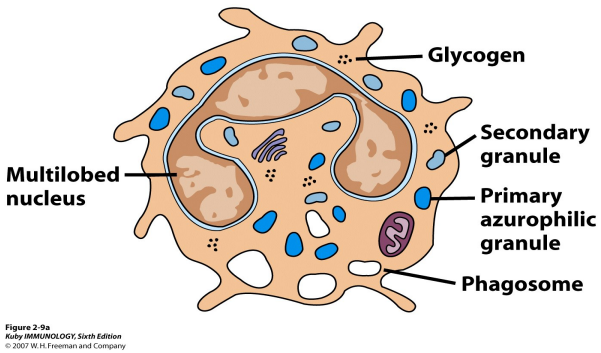
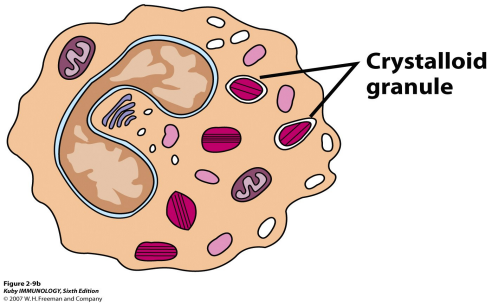
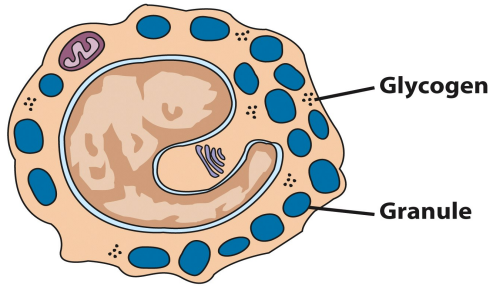
Granulocytes

- Classified on the basis of cellular morphology and cytoplasmic staining characteristics into:

Neutrophil	Eosinophil	Basophil
		
50% - 70% of WBC	1% - 3% of WBC	<1% of WBC
Highly Phagocytic	Phagocytic	Non-Phagocytic
General antimicrobial agents	Anti-parasitic immunity	Role in allergic reactions
1st to arrive at inflammation		Augment anti-parasitic
# increases with infection		immunity

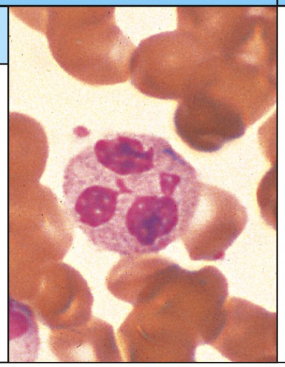
Cell		Activated function
Neutrophil		Phagocytosis and activation of bactericidal mechanisms

Figure 1.4 part 3 of 6 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

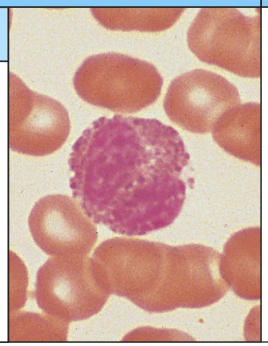
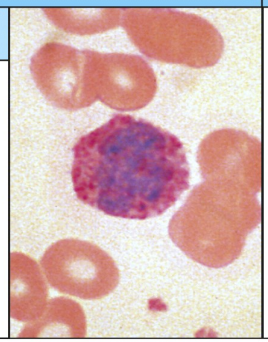
Cell		Activated function
Eosinophil		Killing of antibody-coated parasites

Figure 1.4 part 4 of 6 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Cell		Activated function
Basophil		Promotion of allergic responses and augmentation of anti-parasitic immunity

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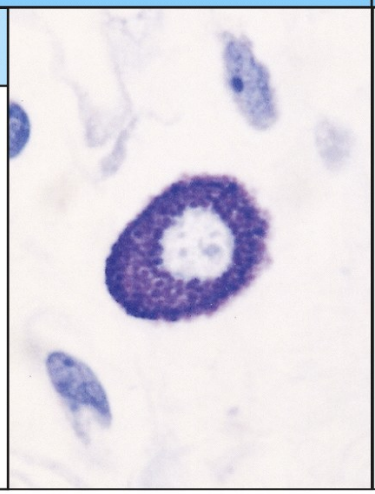
All granulocytes are called **polymorphnuclear leukocytes (PMN)**. However, this term is mainly used for Neutrophils because of their multilobed nucleous

Mast Cells

- Mast cells differentiate only after they leave the blood and enter the tissues
- They can be found in the skin, connective tissues, mucosal epithelial tissues (respiratory, genitouritary, and digestive tracts)
- Play important role in the development of allergies

Cell		Activated function
Mast cell		Release of granules containing histamine and active agents

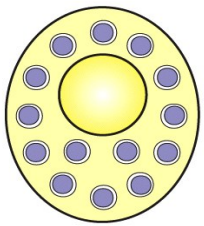


Figure 1.4 part 6 of 6 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Dendritic Cells

- The 4 major types of Dendritic Cells are:

① **Langerhans DC**
  - In the epidermal layer

② **Interstitial DC**
  - In the interstitial space of all organs except the brain

③ **Monocyte-derived DC**
  - Derived from migrated monocytes

④ **Plasmacytoid-derived DC**
  - Play role in innate immune defence

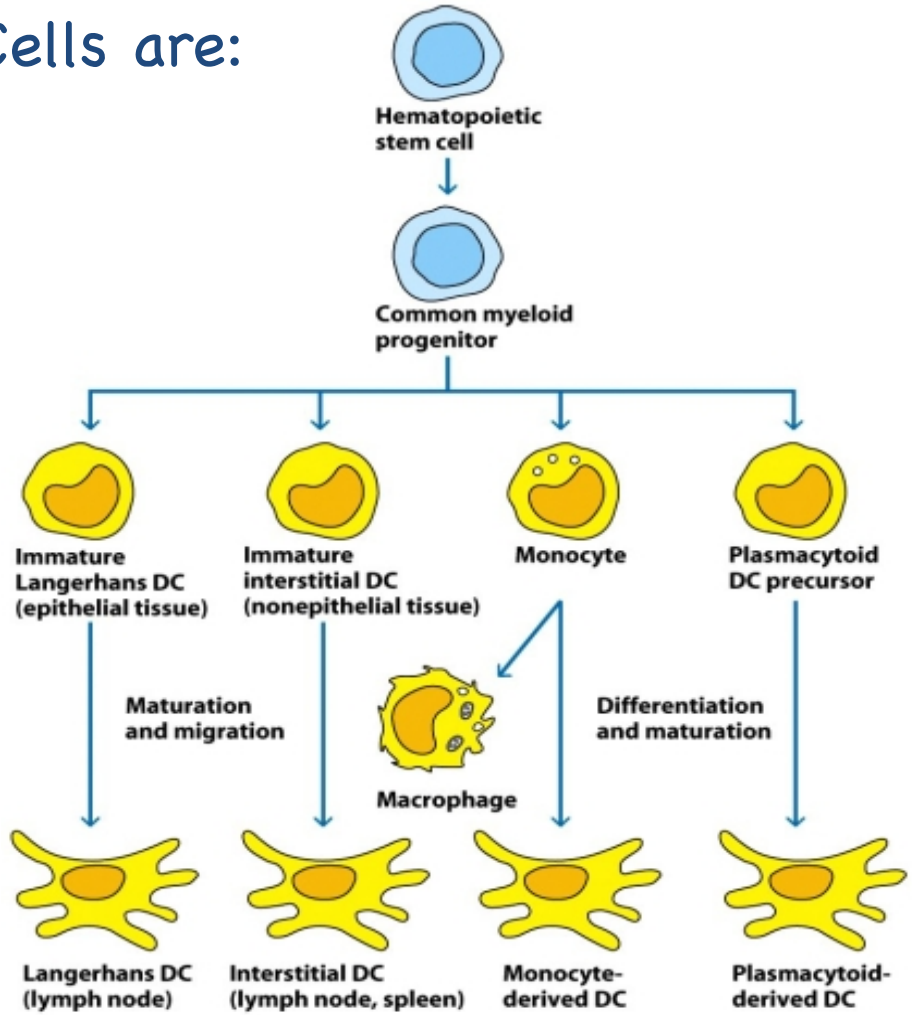


Figure 2-10
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Dendritic Cells

- Dendritic cells are important to mount robust adaptive immune response

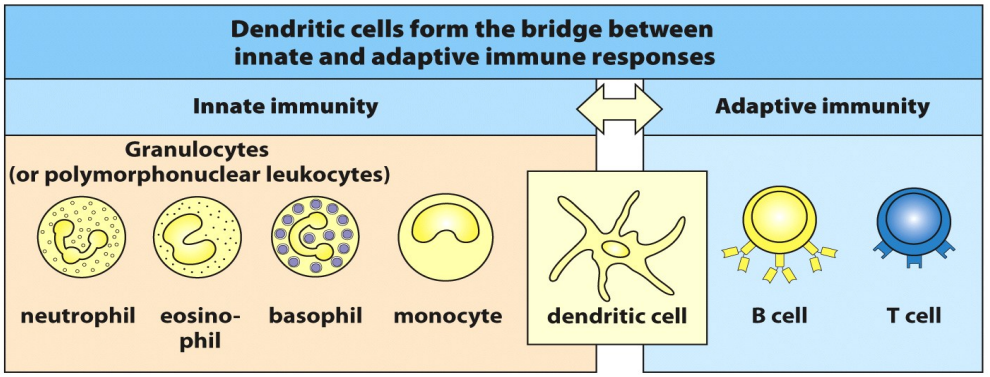


Figure 1.5 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

- They express molecules special for **antigen presentation**

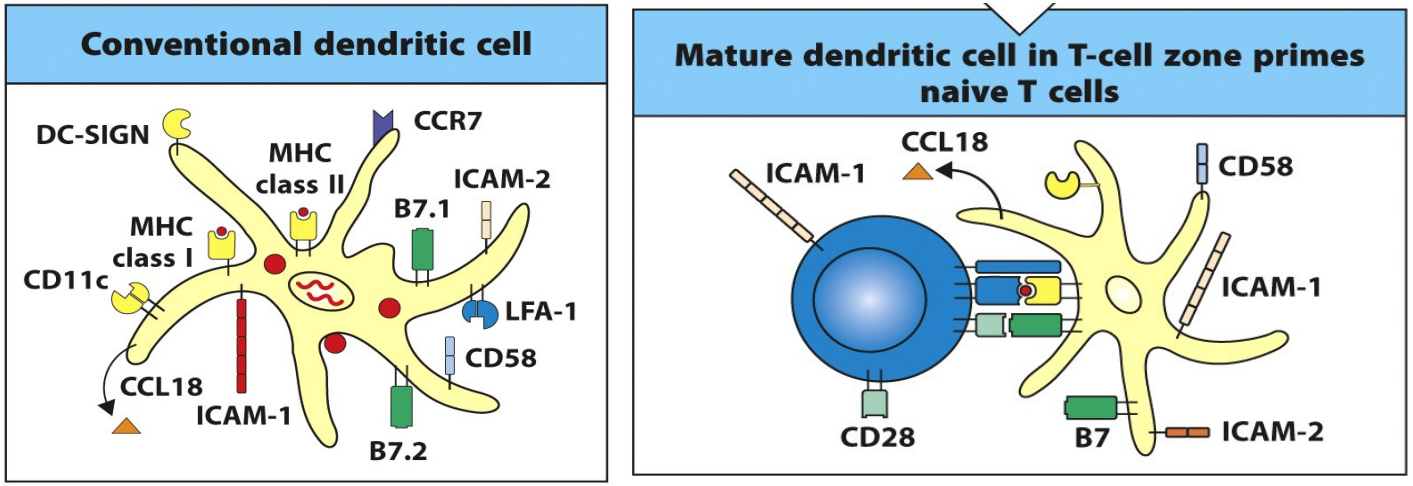
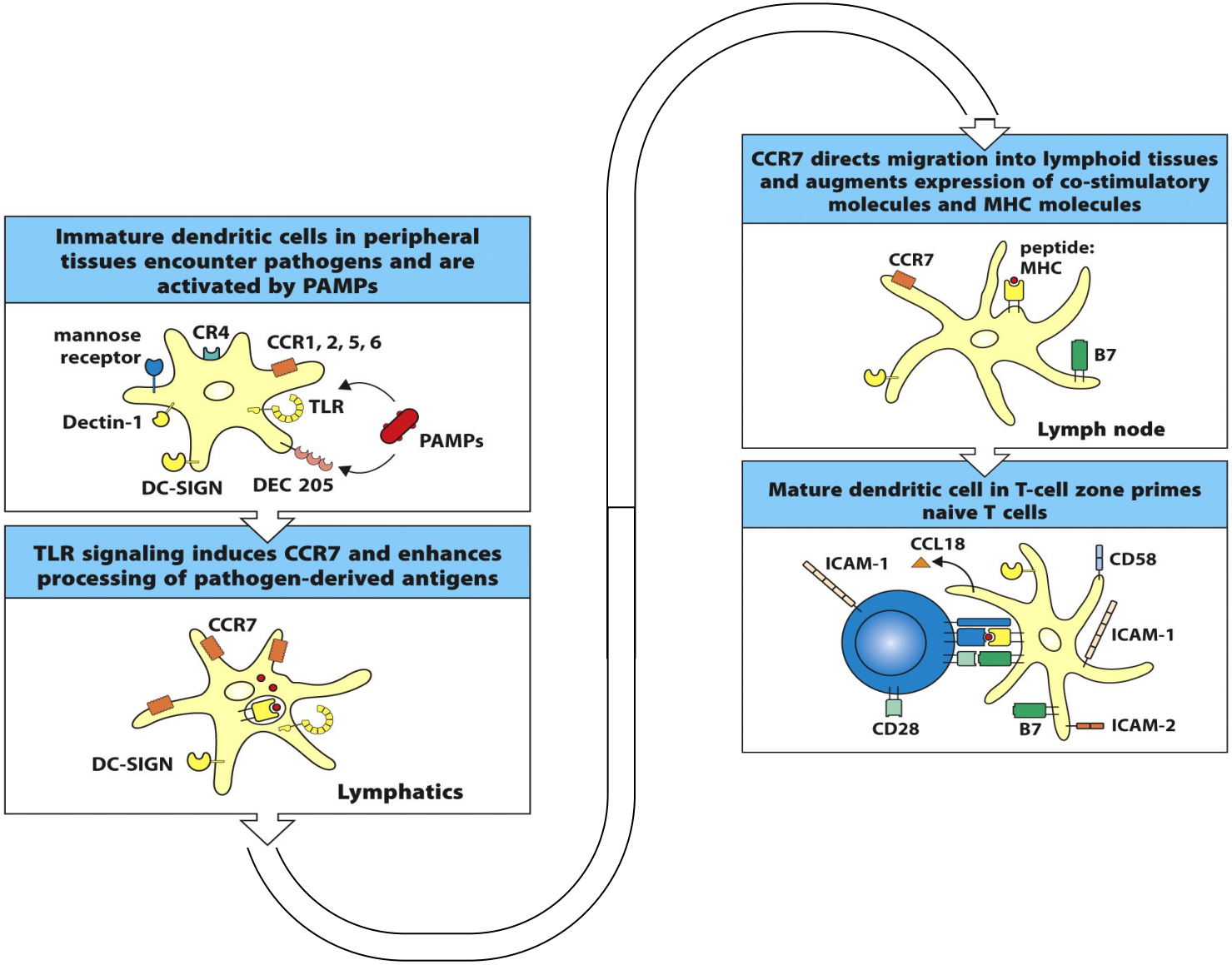
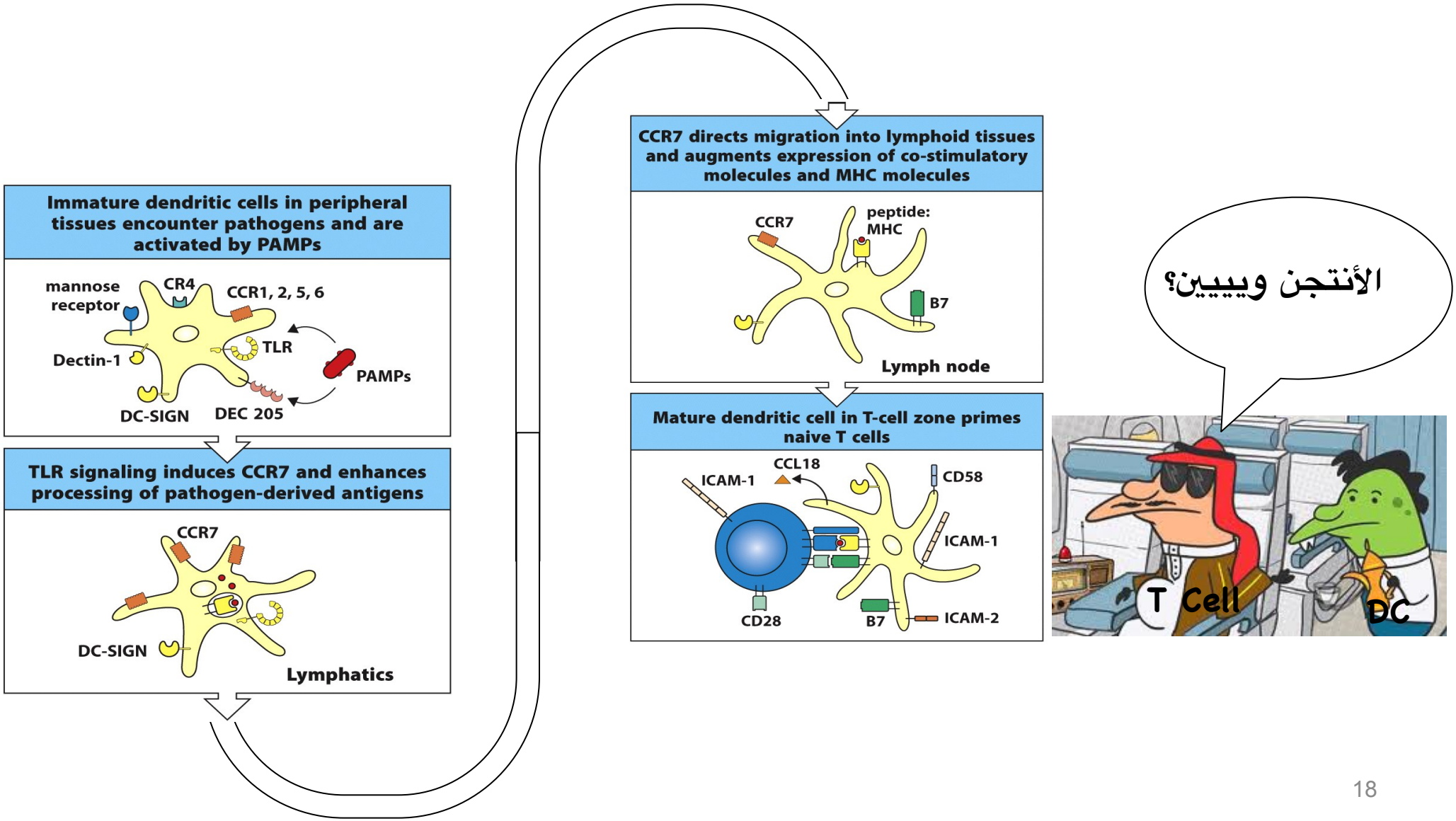


Figure 9.11 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Antigen Presentation



Antigen Presentation



Follicular Dendritic Cells

- **DO NOT** arise from bone marrow
- **DO NOT** express MHC-II
- **DO NOT** act as antigen presenting cell for T_H

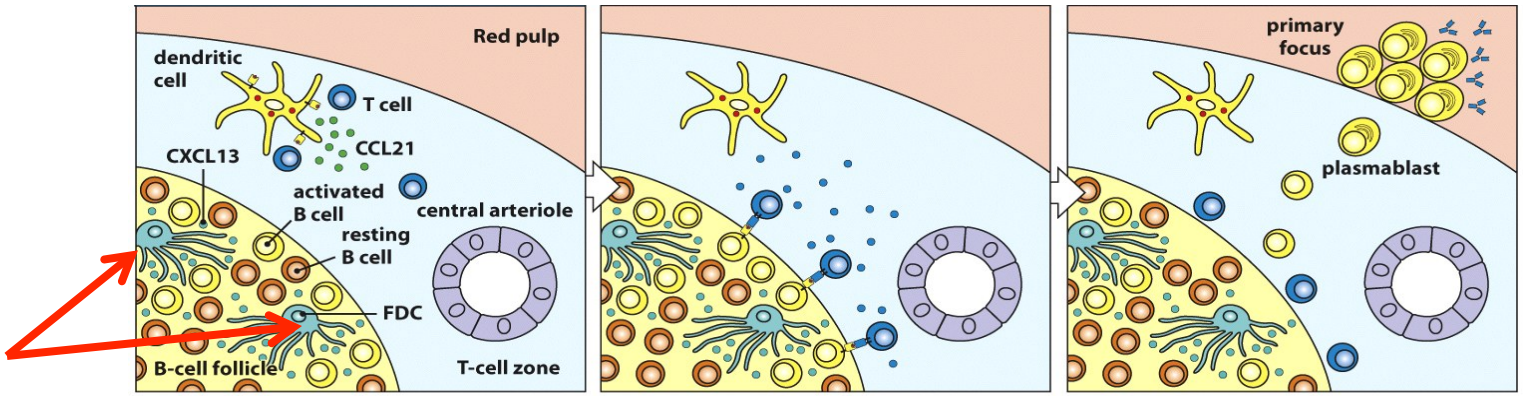


Figure 10.7 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

- Present in lymph follicles rich in B cells
- Express receptors for antibodies
- Important for maturation and diversification of B cells

Lymphoid Cells

- AKA **lymphocytes**
- They circulate continuously in the blood and lymph and are capable of **migrating** into the **tissue spaces** and **lymphoid organs**
- Lymphocytes comprise 20-40% of total WBC
- Consist of 3 cell populations: **B cells**, **T cells** and **natural killer (NK) cells**.

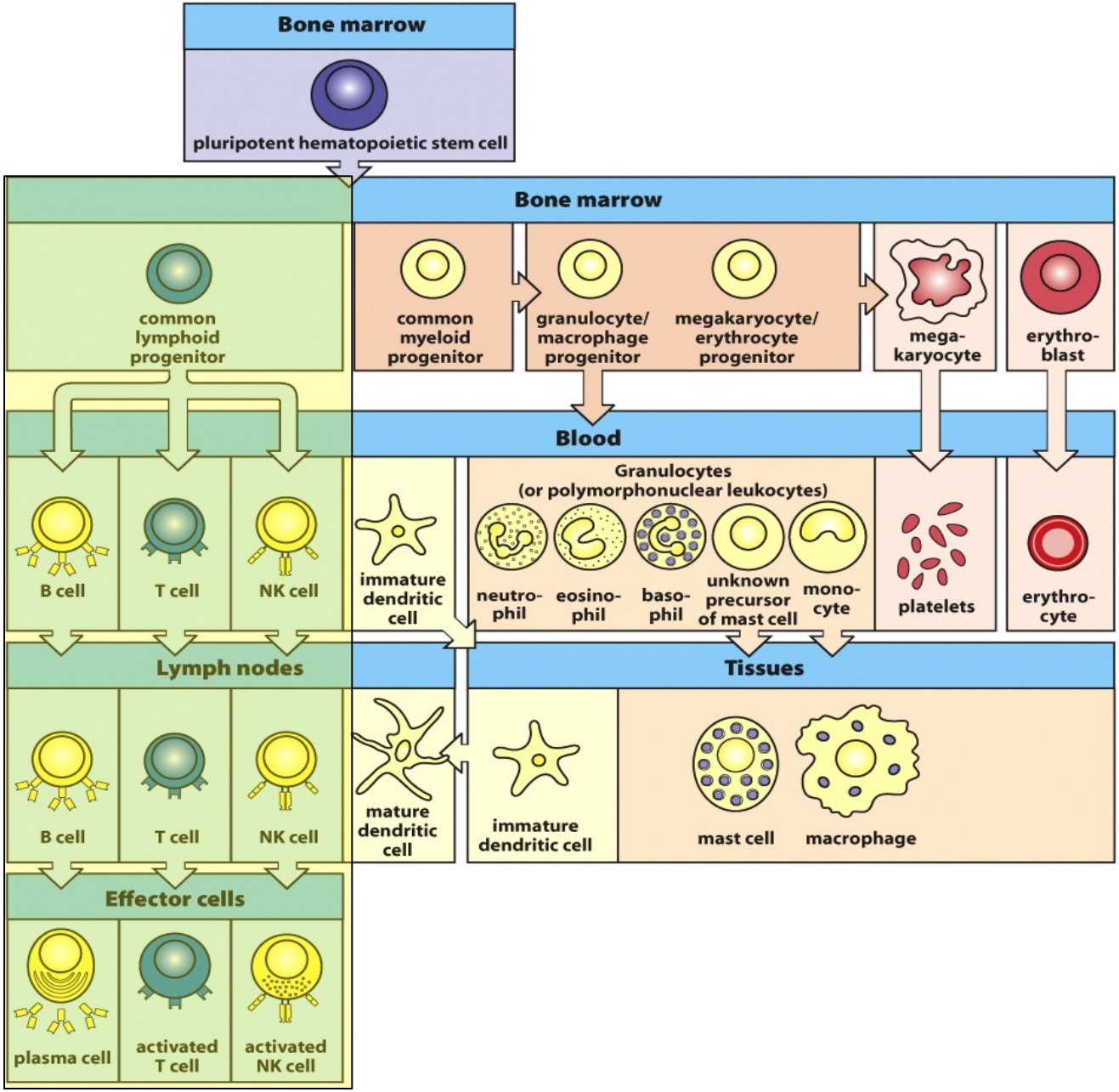
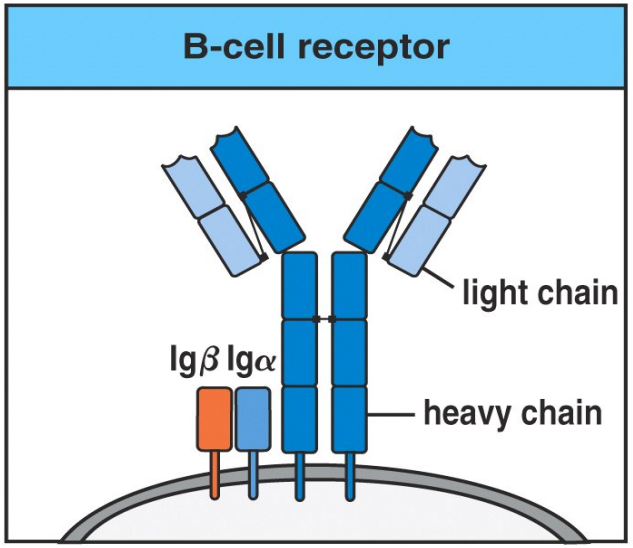


Figure 1.3 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

B lymphocytes

- Derived the letter **B** from its site of maturation (**b**ursa of Fabricius in birds or **b**one marrow in mammalian species)
- B cells display a membrane bound antibody **(Ab)**, which serves as a receptor for antigens



Plasma Cells

- Upon antigen encounter, naïve B cell differentiate into effector cells called **plasma cells**.

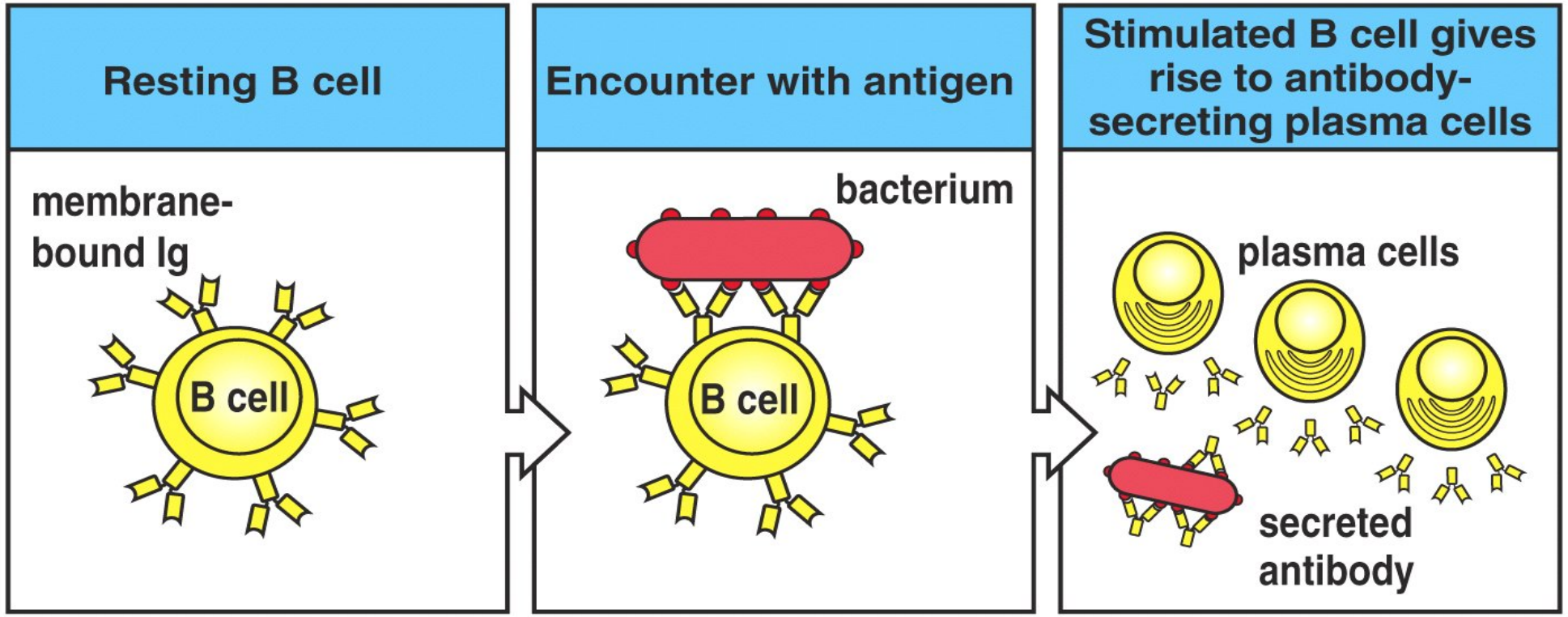


Figure 2-1 The Immune System, 2/e (© Garland Science 2005)

Plasma Cells

- Plasma cells exhibit the following attributes:
  ① They are end-stage cells i.e. do not divide
  ② They have almost no membrane-bound Ab
  ③ They die within 1 to 2 weeks
  ④ A single cell can secrete 100-1000 molecules of the same Ab per second

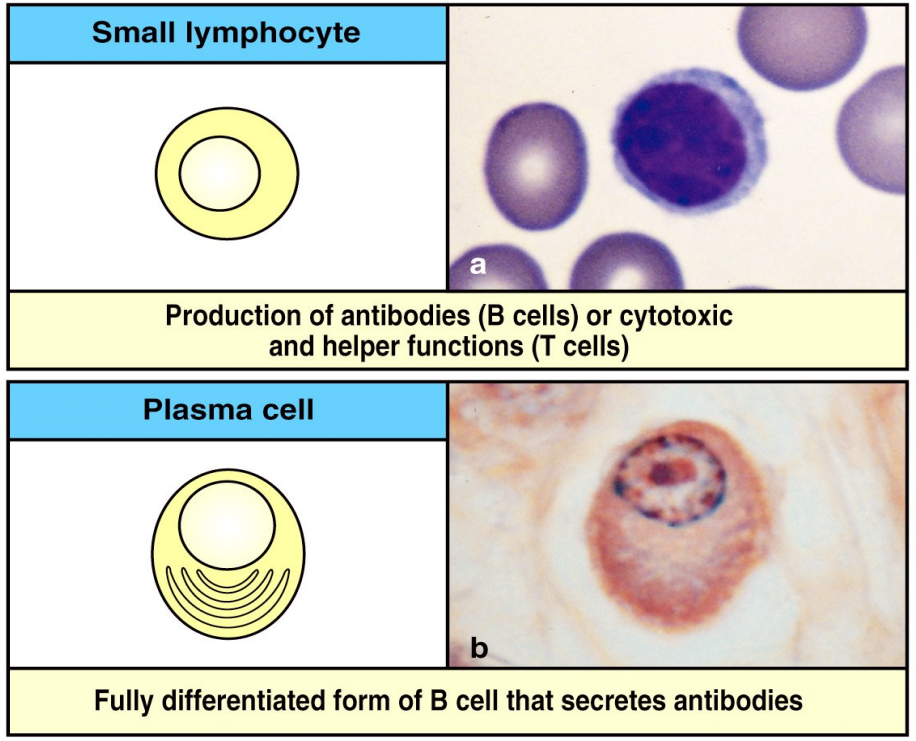


Figure 1-9 part 1 of 6 The Immune System, 2/e (© Garland Science 2005)

Memory B Cells

- Memory B cells exhibit the following attributes:
  - ① They express similar Ab to naïve B cells but different **isotype**
  - ② They can differentiate to plasma cells
  - ③ They respond to the second exposure of an antigen with faster and higher magnitude response
  - ④ They have longer life-span than naïve B cells

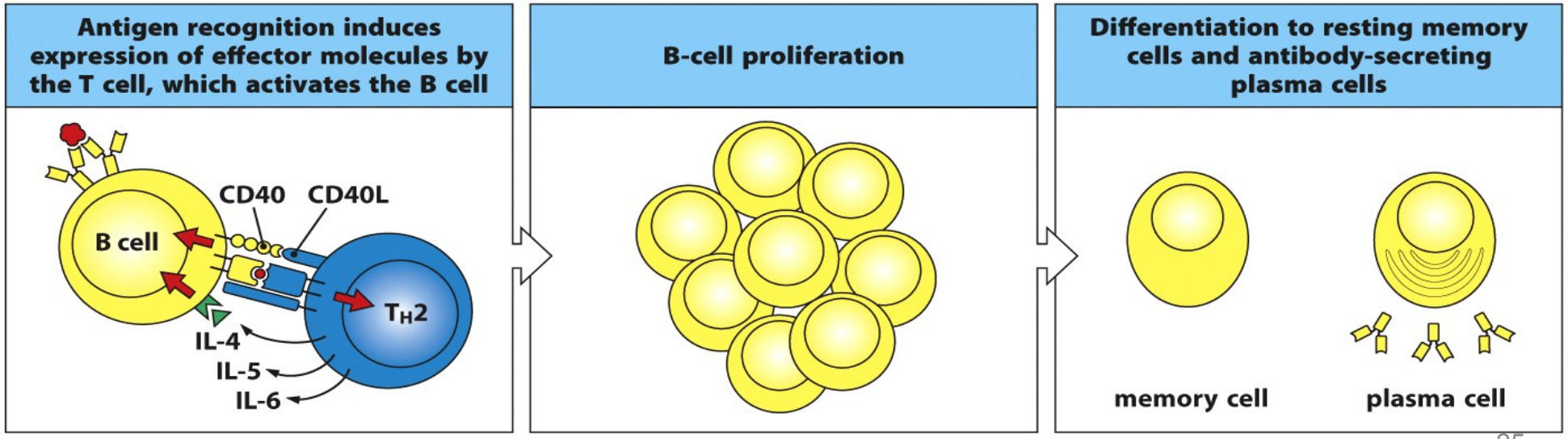
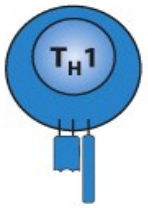
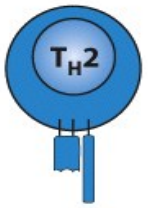
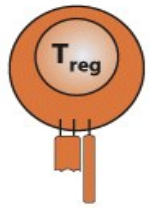


Figure 10.3 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

T lymphocytes

- Derived the letter **T** from its site of maturation (thymus)
- Based on their structural and functional differences, T cells are divided into 3 subpopulations: **T helper**, **T cytotoxic**, and **T regulatory**

	CD8 cytotoxic T cells	CD4 T_H1 cells	CD4 T_H2 cells	CD4 regulatory T cells (various types)
Types of effector T cell				
Main functions in adaptive immune response	Kill virus-infected cells	Activate infected macrophages Provide help to B cells for antibody production	Provide help to B cells for antibody production, especially switching to IgE	Suppress T-cell responses

Other T lymphocytes

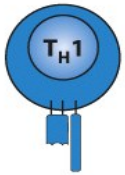
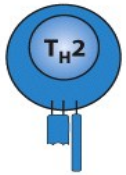
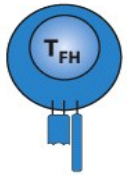
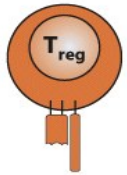
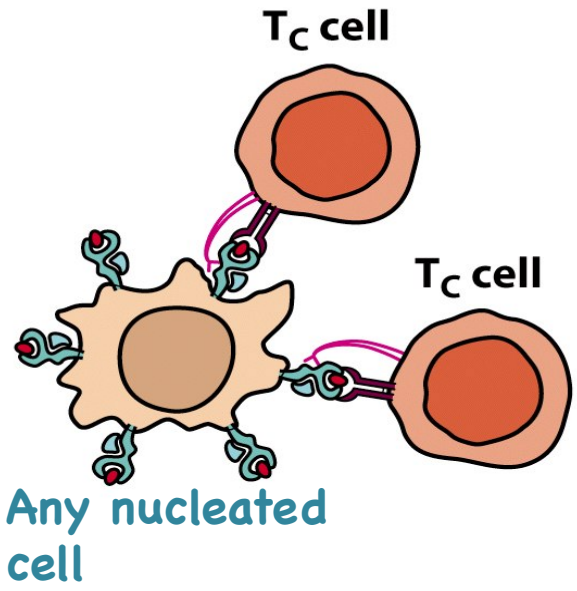
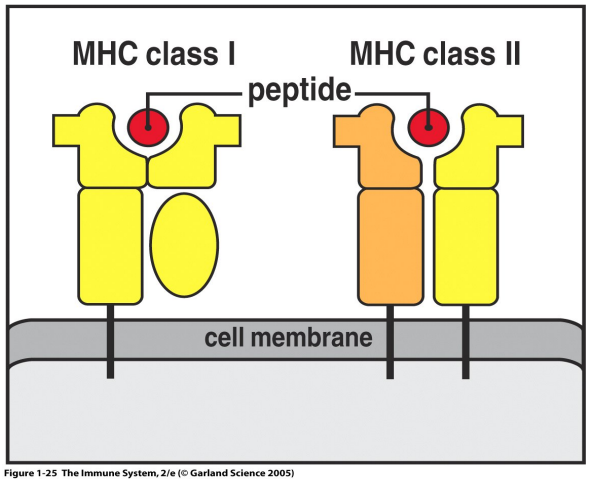
	CD8 cytotoxic T cells	CD4 T_H1 cells	CD4 T_H2 cells	CD4 T_H17 cells	T_{FH} cells	CD4 regulatory T cells (various types)
Types of effector T cell						
Main functions in adaptive immune response	Kill virus-infected cells	Activate infected macrophages Provide help to B cells for antibody production	Provide help to B cells for antibody production, especially switching to IgE	Enhance neutrophil response Promote barrier integrity (skin, intestine)	B-cell help Isotype switching Antibody production	Suppress T-cell responses
Pathogens targeted	Viruses (e.g. influenza, rabies, vaccinia) Some intracellular bacteria	Microbes that persist in macrophage vesicles (e.g. mycobacteria, *Listeria*, *Leishmania donovani*, *Pneumocystis carinii*) Extracellular bacteria	Helminth parasites	*Klebsiella pneumoniae* Fungi (*Candida albicans*)	All types	

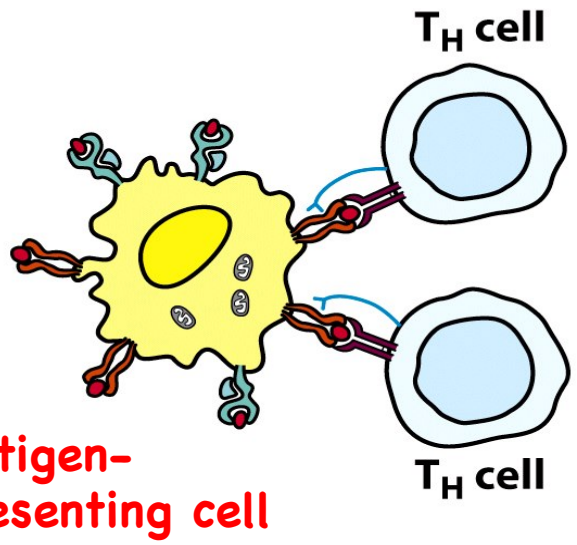
Figure 9.1 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

T Lymphocytes

- T cells display a unique antigen-binding molecule called T-cell receptor (TCR)
- TCR only recognizes antigen that is bound to a cell-membrane protein called Major Histocompatibility Complex (MHC)







T_H Cells

- T_H cells differentiate into effector and memory cells
- **Effector T_H** cells enables the activation of B cells, T_C, macrophages, and other immune cells

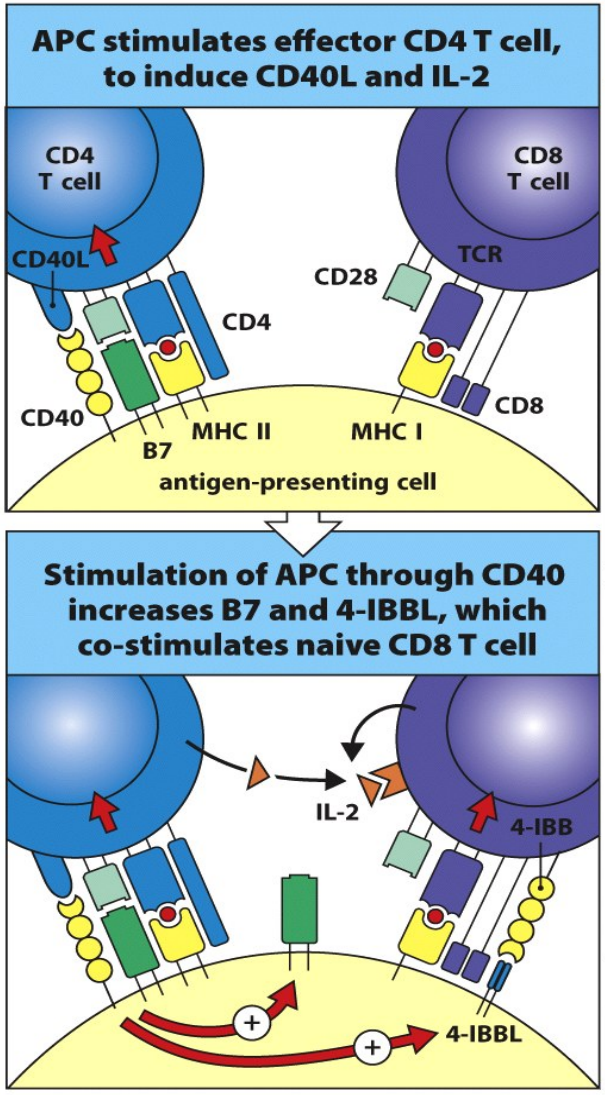


Figure 9.27 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

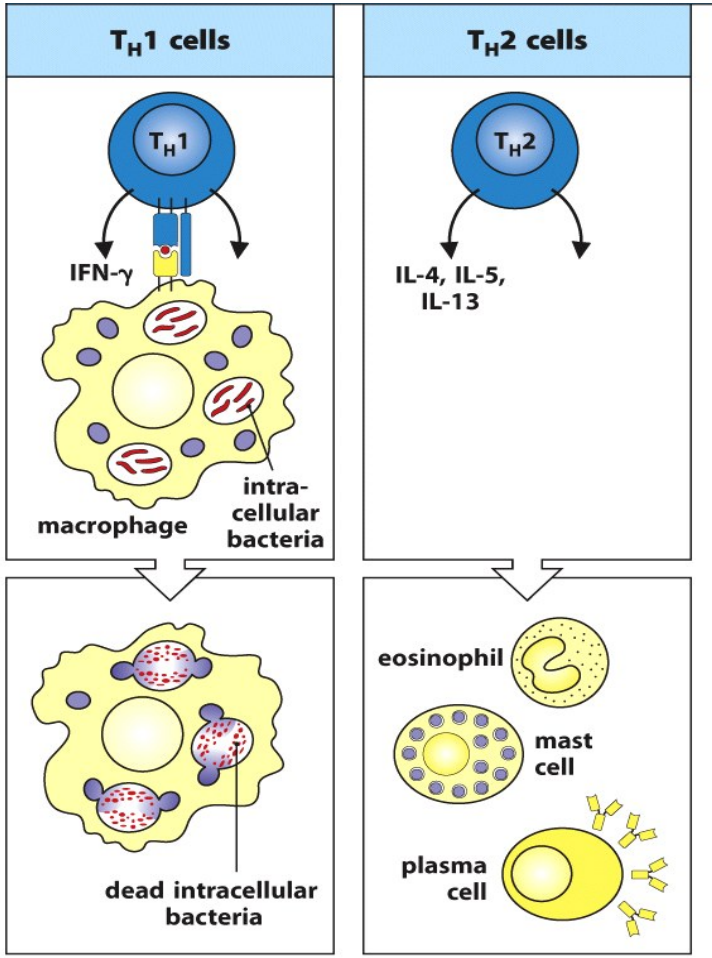


Figure 9.28 Janeway's Immunobiology, 8ed. (© Garland Science 201

Cytotoxic T Lymphocytes

- T_c cells differentiate into effector **Cytotoxic T lymphocytes (CTL)** and memory cells
- Eliminate (KILL) cells that display antigen on MHC-I molecules such as virus-infected cells, tumor cells, and cells of a foreign graft

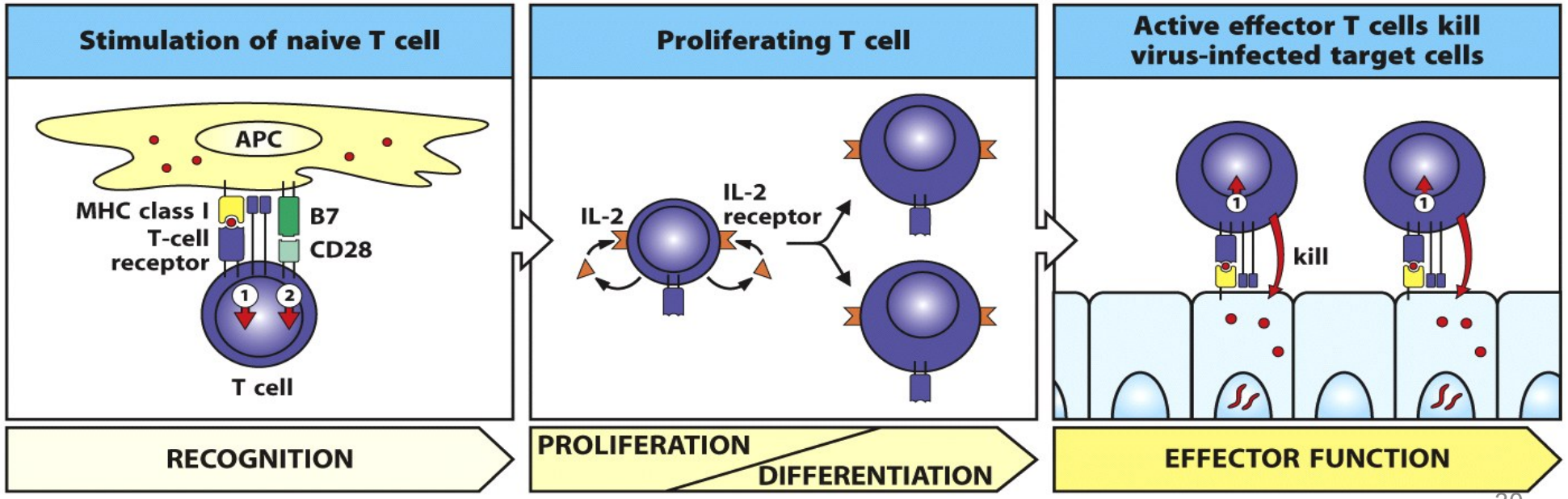
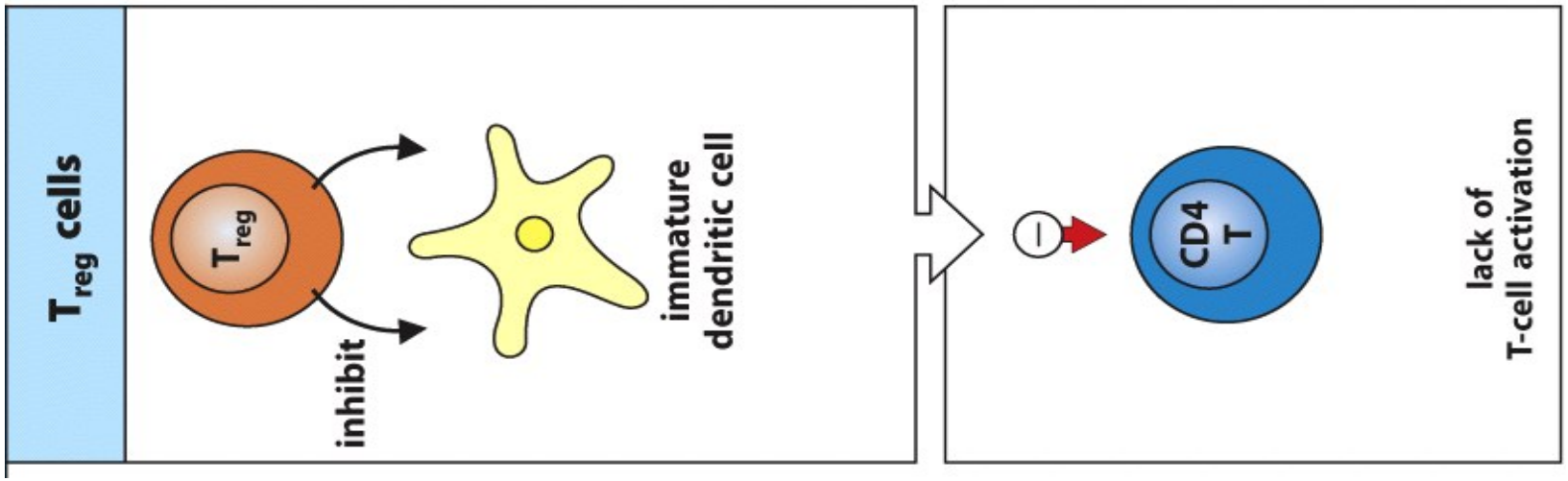


Figure 9.24 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Regulatory T Lymphocytes

- T_{reg} cells identified by the presence of CD4 and CD25 molecules on their membrane
- They suppress immune responses i.e. negative regulators of the immune system
- Members of T_{reg} cells may be progenitors of memory cells



Natural Killer Cells

- NK cells are part of the innate immune system
- They are large granular lymphocytes that display cytotoxic activity against tumors and some viruses

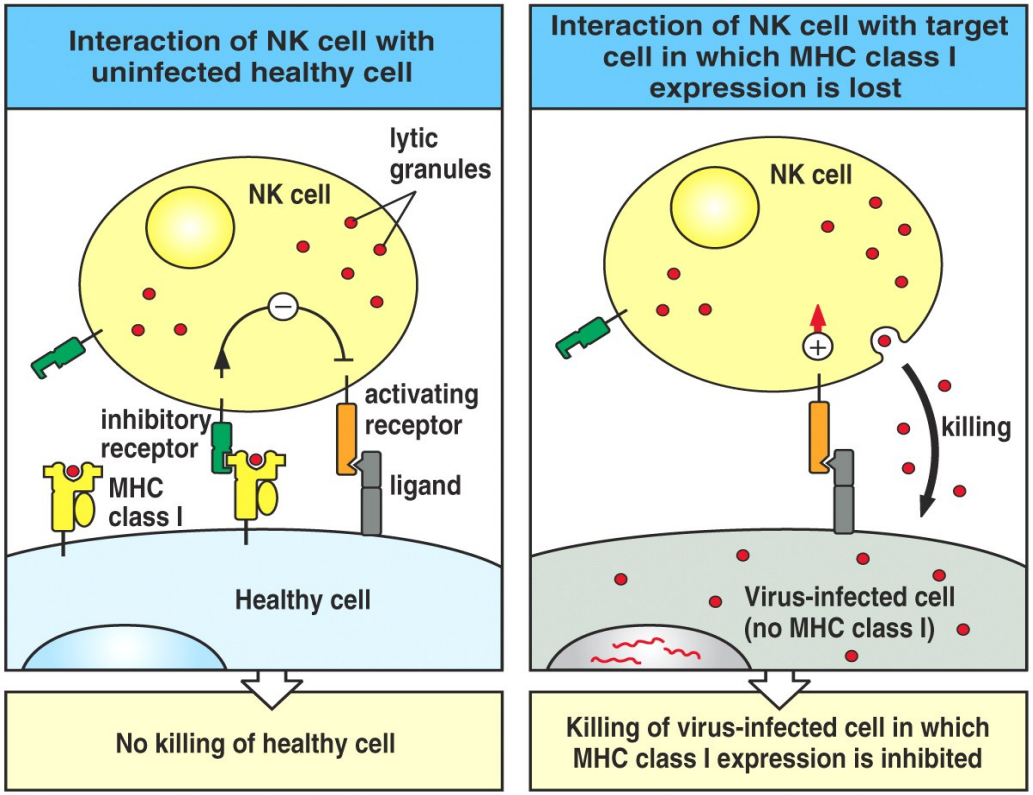


Figure 8-32 The Immune System, 2/e (© Garland Science 2005)

Natural Killer Cells

- NK cells express a receptor **(CD16)** that recognizes a specific region in the antibody molecule
- Antibodies can attach to this receptor and stimulate NK cell activity leading to a process known as **antibody-dependent cell-mediated toxicity (ADCC)**

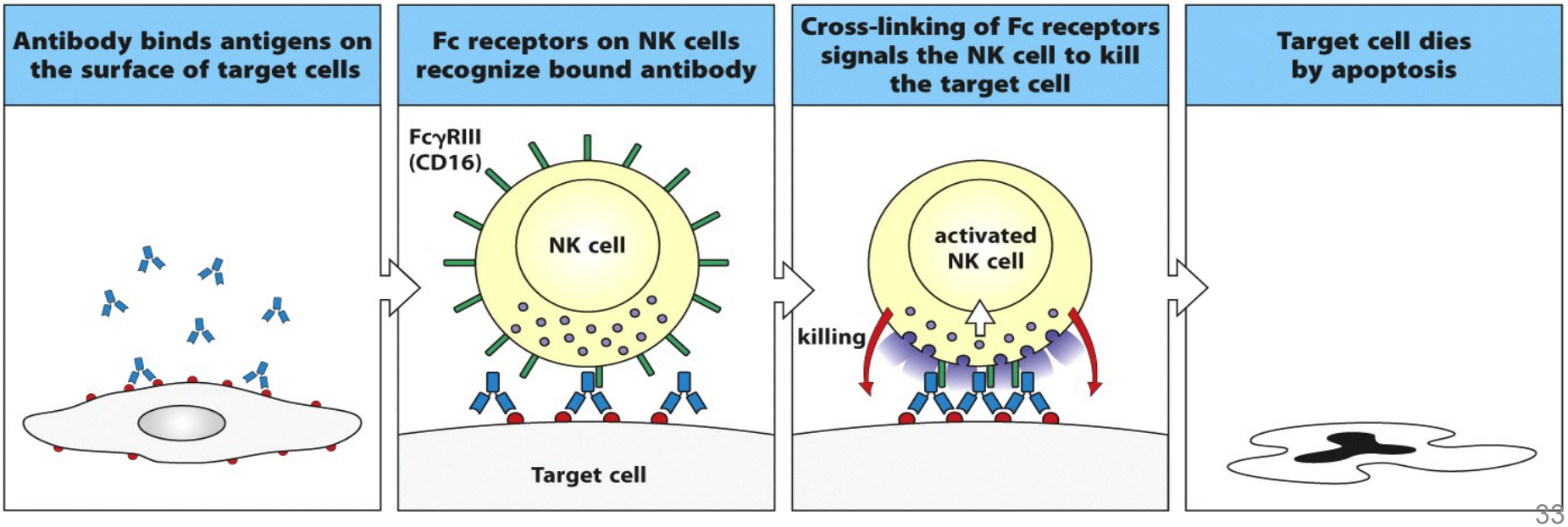


Figure 10.36 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

You are now able to:

- ✓ Describe the structure and function of major immune cells
- ✓ Appreciate the collaborative relationship between innate and adaptive immune cells