Cell Mediated Immunity (I)

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Learning Objectives

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

① Understand the process of thymic selection

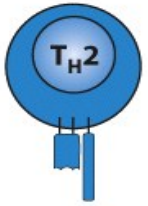
② Recognize the difference between T_H1 and T_H2 responses

③ Understand the signal 1 signal 2 signal 3 model

T lymphocytes

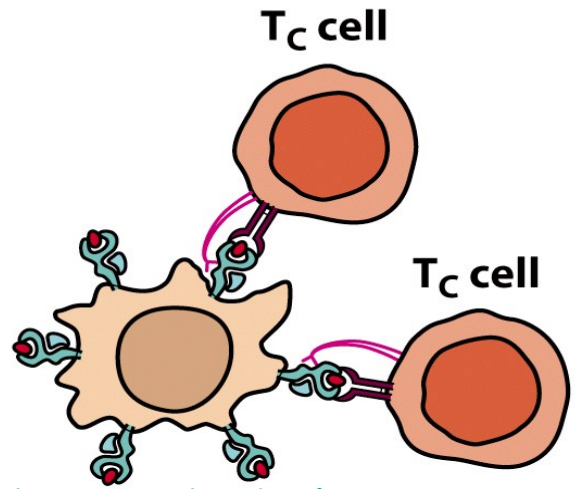
- Derived the letter T from its site of maturation (thymus)

- 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

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)



Any nucleated cell

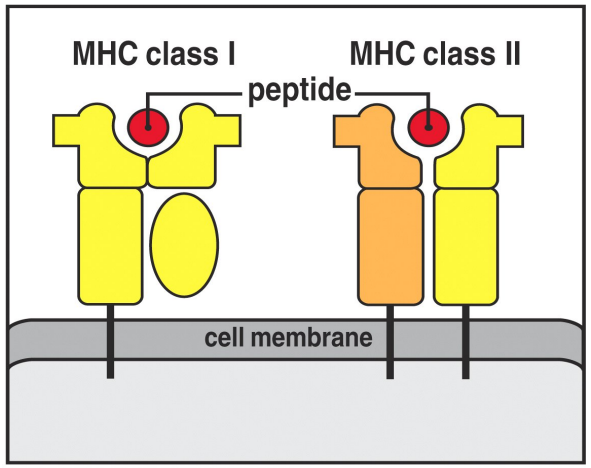
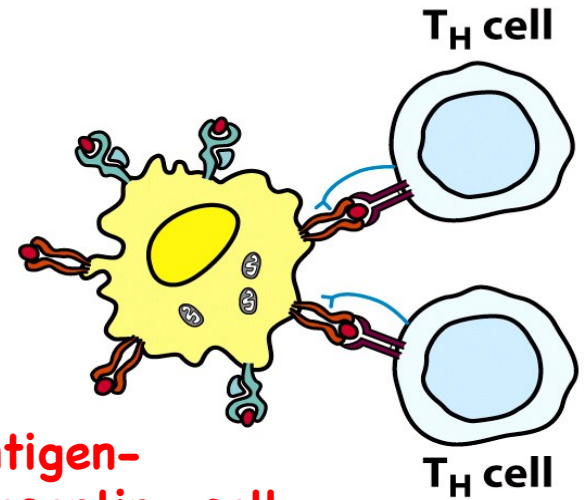


Figure 1-25 The Immune System, 2/e (© Garland Science 2005)



Antigen-presenting cell

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

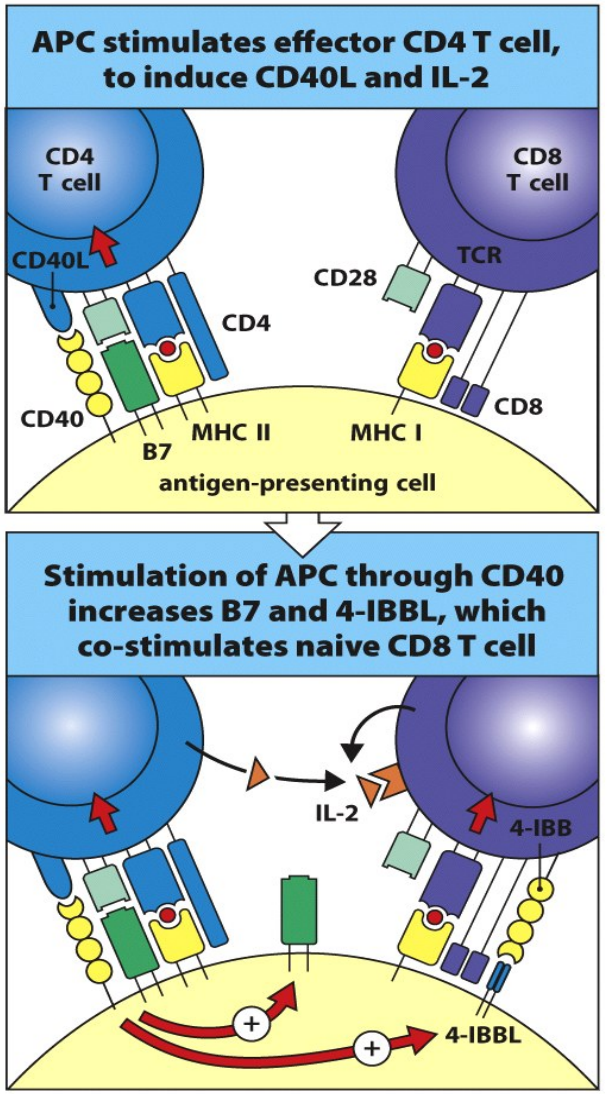
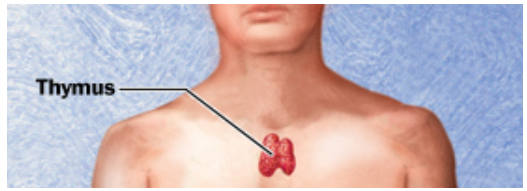


Figure 9.27 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Thymus



- Site of T cell maturation
- Bilobed organ situated above the heart
- Surrounded by capsule and divided into lobules
- Each lobule is organized into

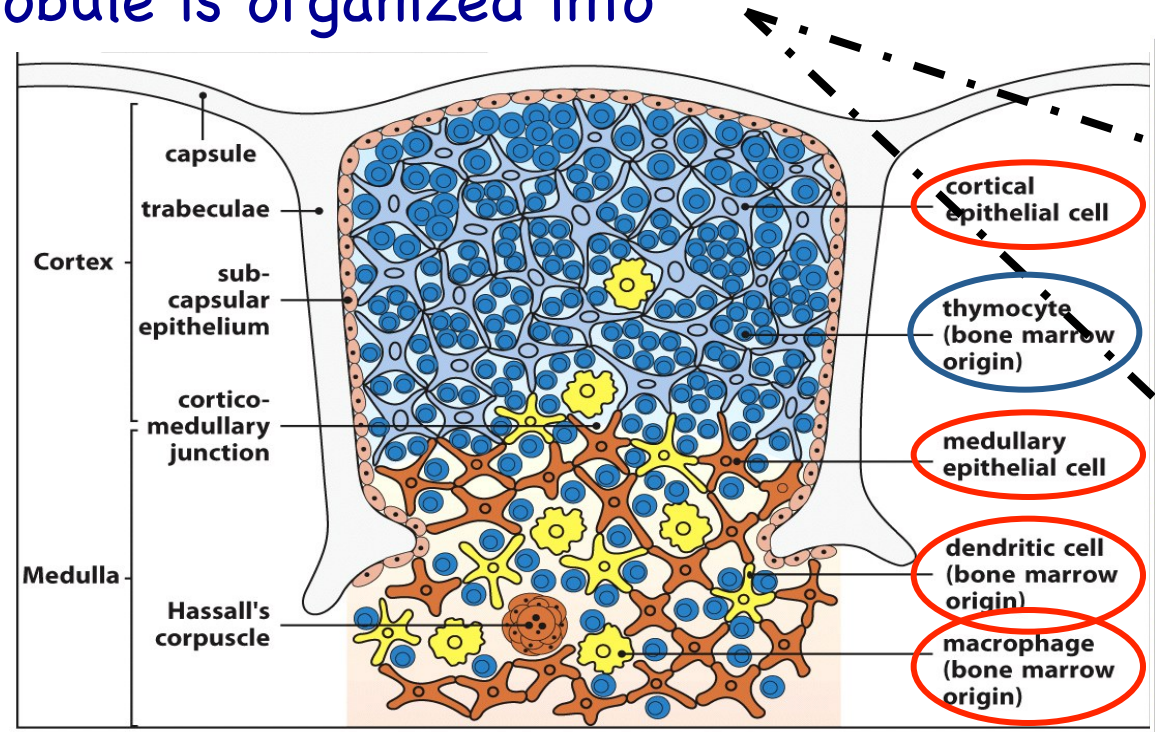


Figure 8.15 part 1 of 2 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

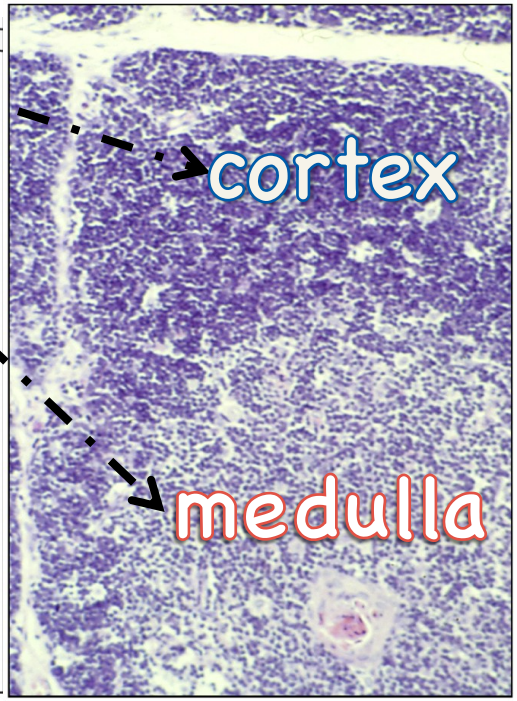


Figure 8.15 part 2 of 2 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

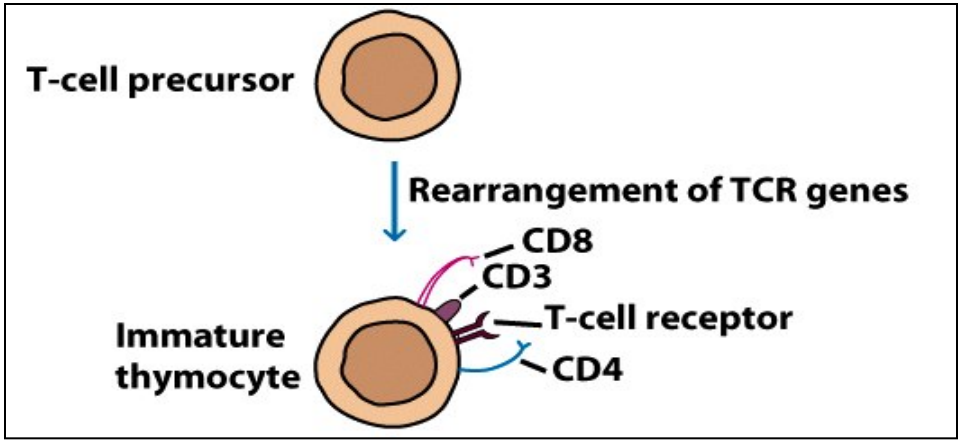
T Cell Maturation

- The function of the thymus is to **generate** and **select** a repertoire of T cells the will **protect** the body from infections and **do not be harmful** to body tissues

- Thymocytes undergo **positive** and **negative** selection processes on the basis of their reactivity with self antigens and self MHC molecules expressed in the thymus

TCR Generation

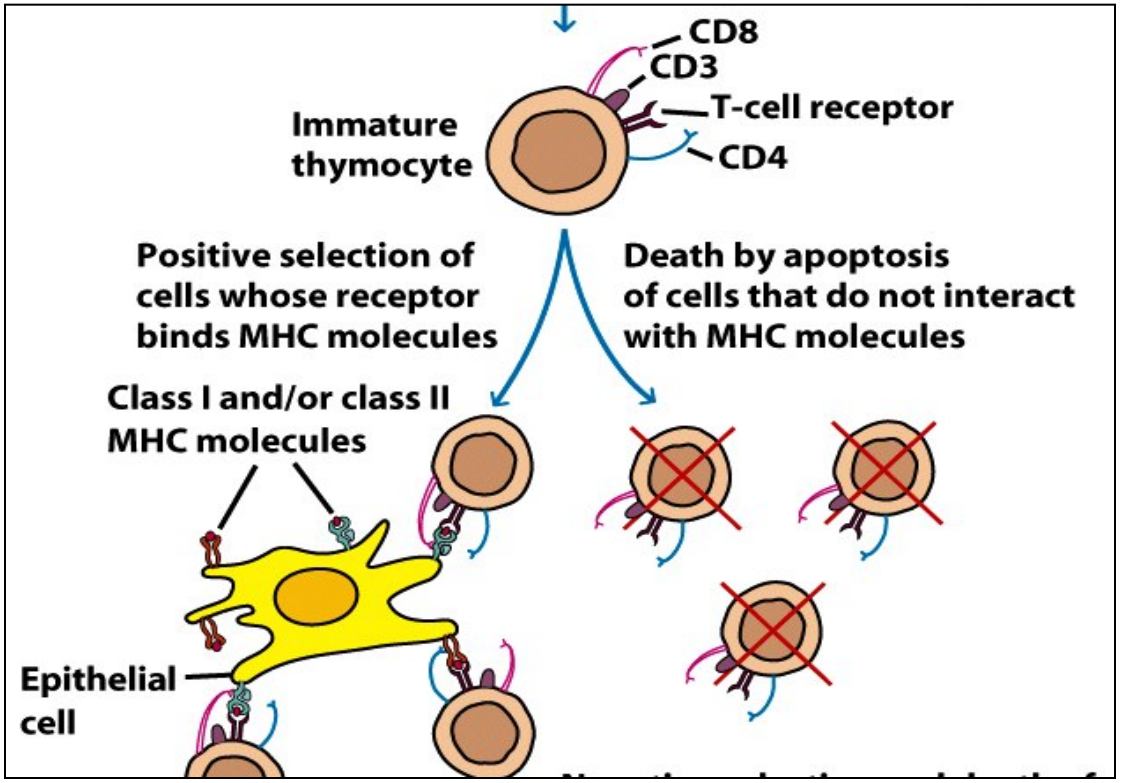
- TCR is generated by gene rearrangement. This is a random process that produces receptors of different specificity and reactivity
- Remember that TCRs must have two properties:
  ① Recognizes self MHC-I and MHC-II
  ② DO NOT react with self antigens



- **At this point, thymocytes express both CD4 and CD8 molecules i.e. called double-positive**

Positive Selection

- Small portion of TCR react with combination of self-antigen/MHC complexes



- **The thymus induces death of T cells that cannot recognize self-antigen/MHC complexes**

Negative Selection

- The thymus induces death of T cells that react with self-antigen/MHC complexes strongly enough to cause autoimmune disease

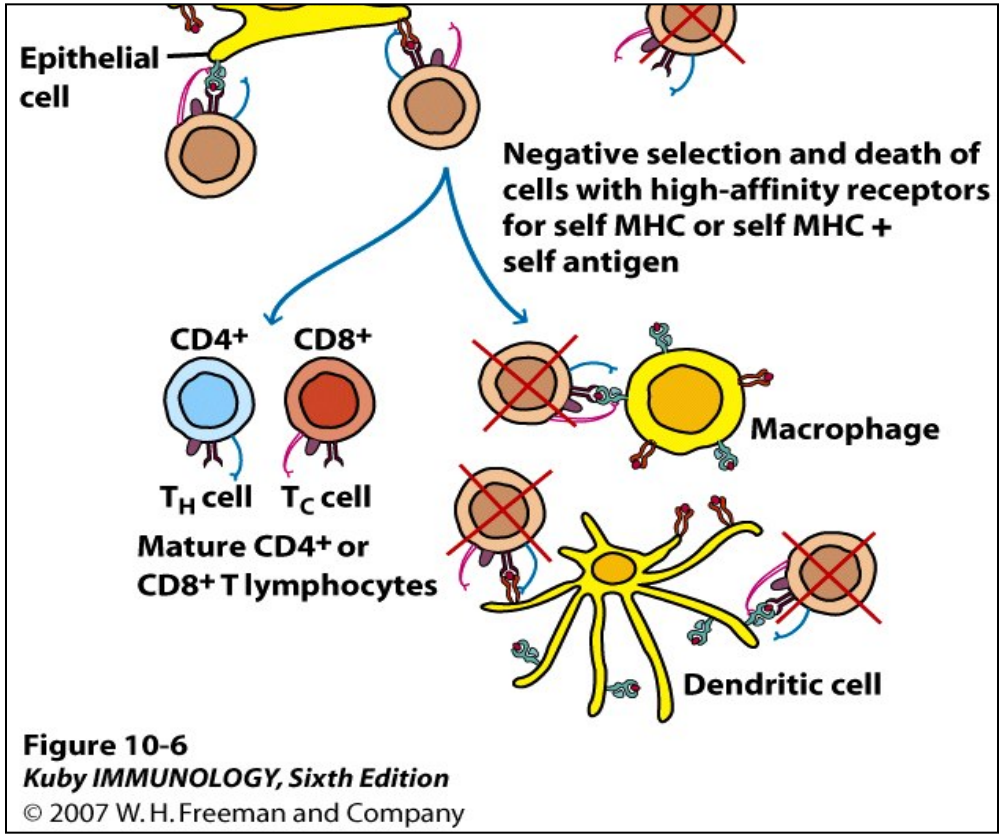


Figure 10-6
Kuby IMMUNOLOGY, Sixth Edition

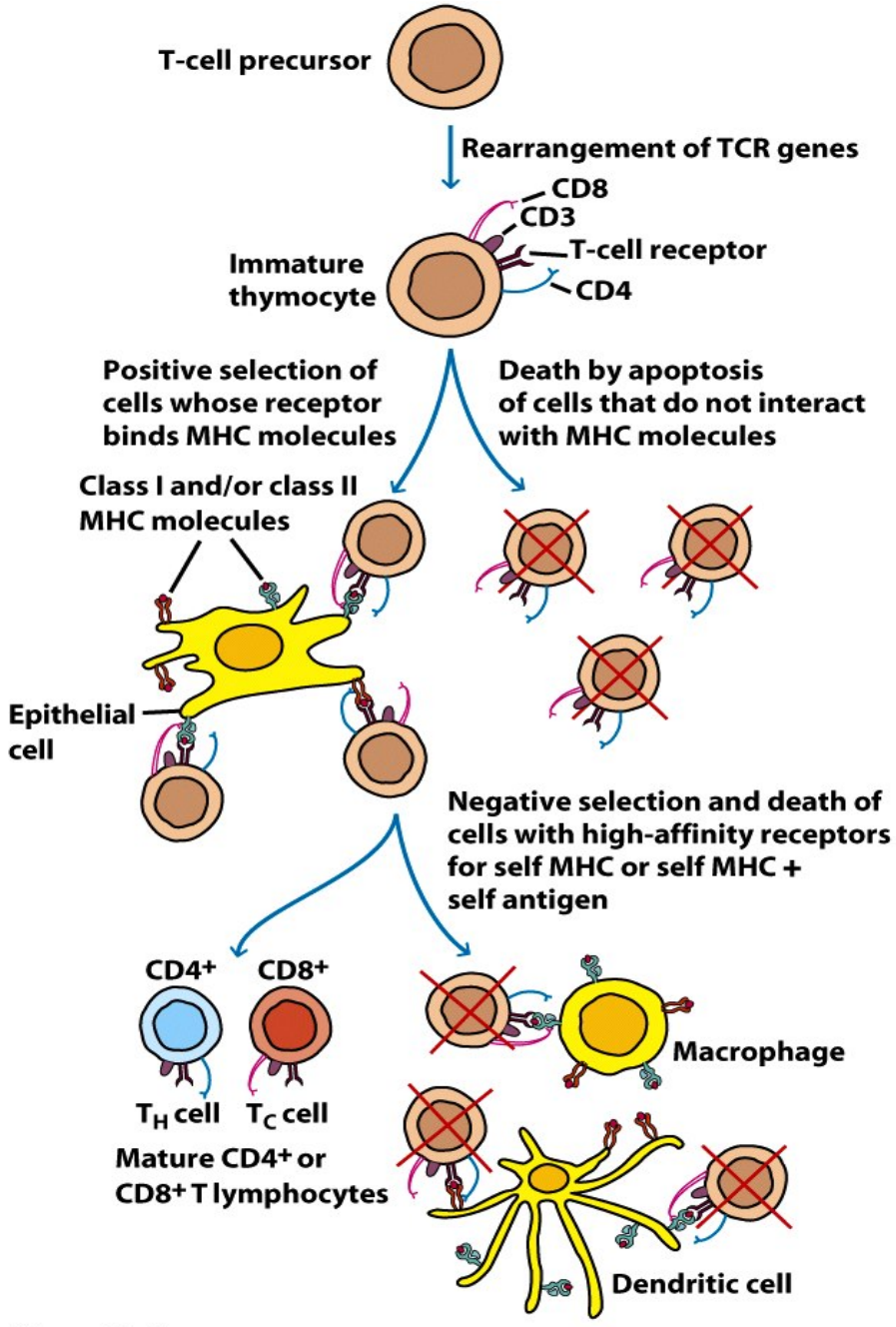


Figure 10-6
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Paradoxical Signaling Pathways in Developing Thymocytes

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Table of Contents

ABSTRACT- Thymocytes are subjected to processes of selection during their life in the thymus; negative selection for autoreactive thymocytes and positive selection for self-MHC restricted self-tolerant cells. Interestingly, signals for positive or negative selection originate from the same receptor. More importantly, evidence showed that both death and survival signals are mediated by the MAPK pathway. The degree and order of ERK activation, but not other MAPK proteins, has been found to be different in either cases of cell fate. Therefore, it is suspected that the kinetics of ERK after activation may dictate cell death or survival. There are two important GEF proteins that are involved in Ras/ERK activation, RasGRP and SOS. It is thought that the level, order and kinetics of ERK are influenced upstream by the type of GEF. This review discusses the role of both GEF proteins in positive and negative selection and how this reflects on ERK activation.

T Cell Development

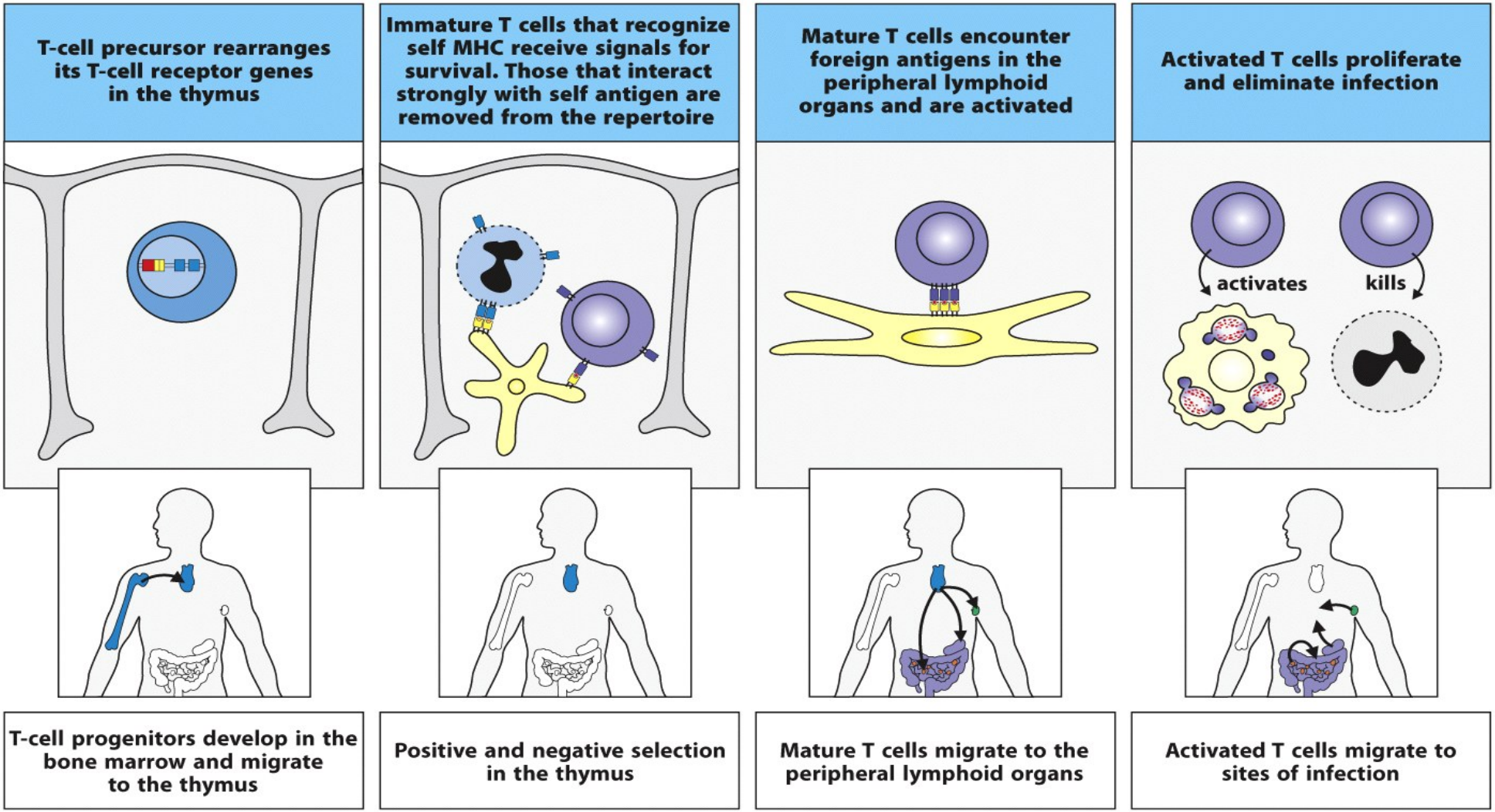


Figure 8.14 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

T_H Cells

- $CD4^+$ T_H cells exert most of helper functions through secreted cytokines

- 2 populations based on secreted cytokines:
  - T_H1 mediates Cell-mediated immunity
  - T_H2 provides help to B cells, promotes production of large amounts of antibodies

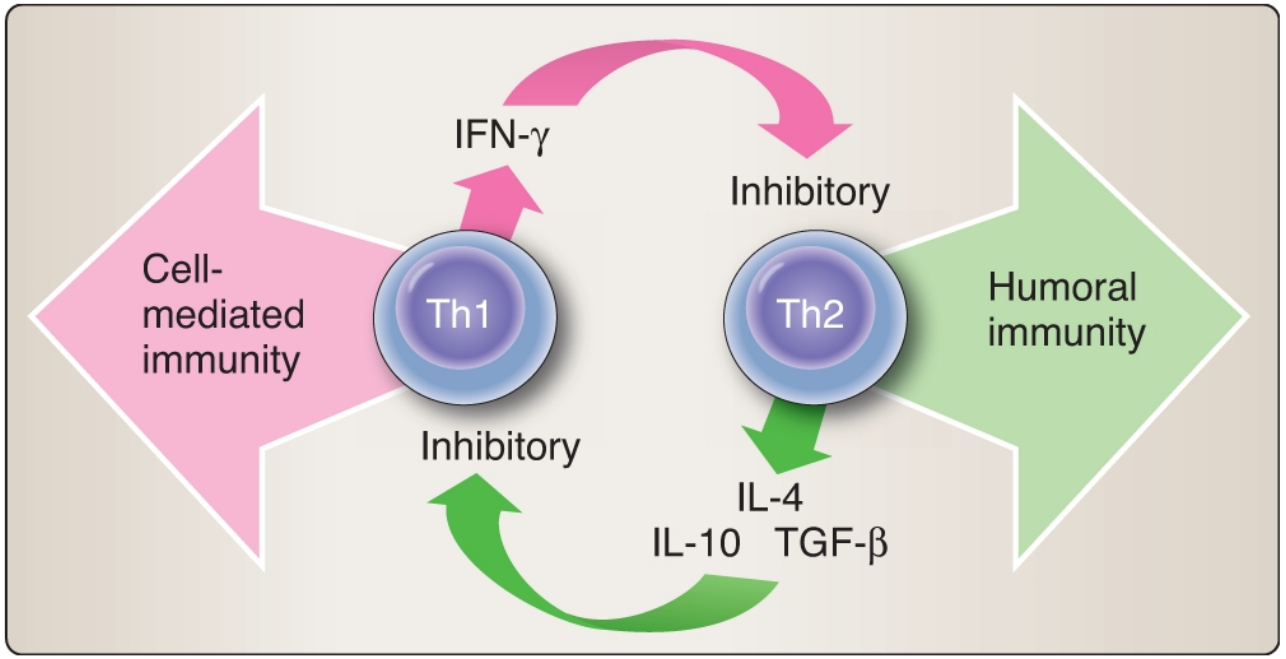
- Some T_H cells do not show T_H1 or T_H2 profiles

TABLE 12-4 Cytokine secretion and principal functions of mouse T_H1 and T_H2 subsets

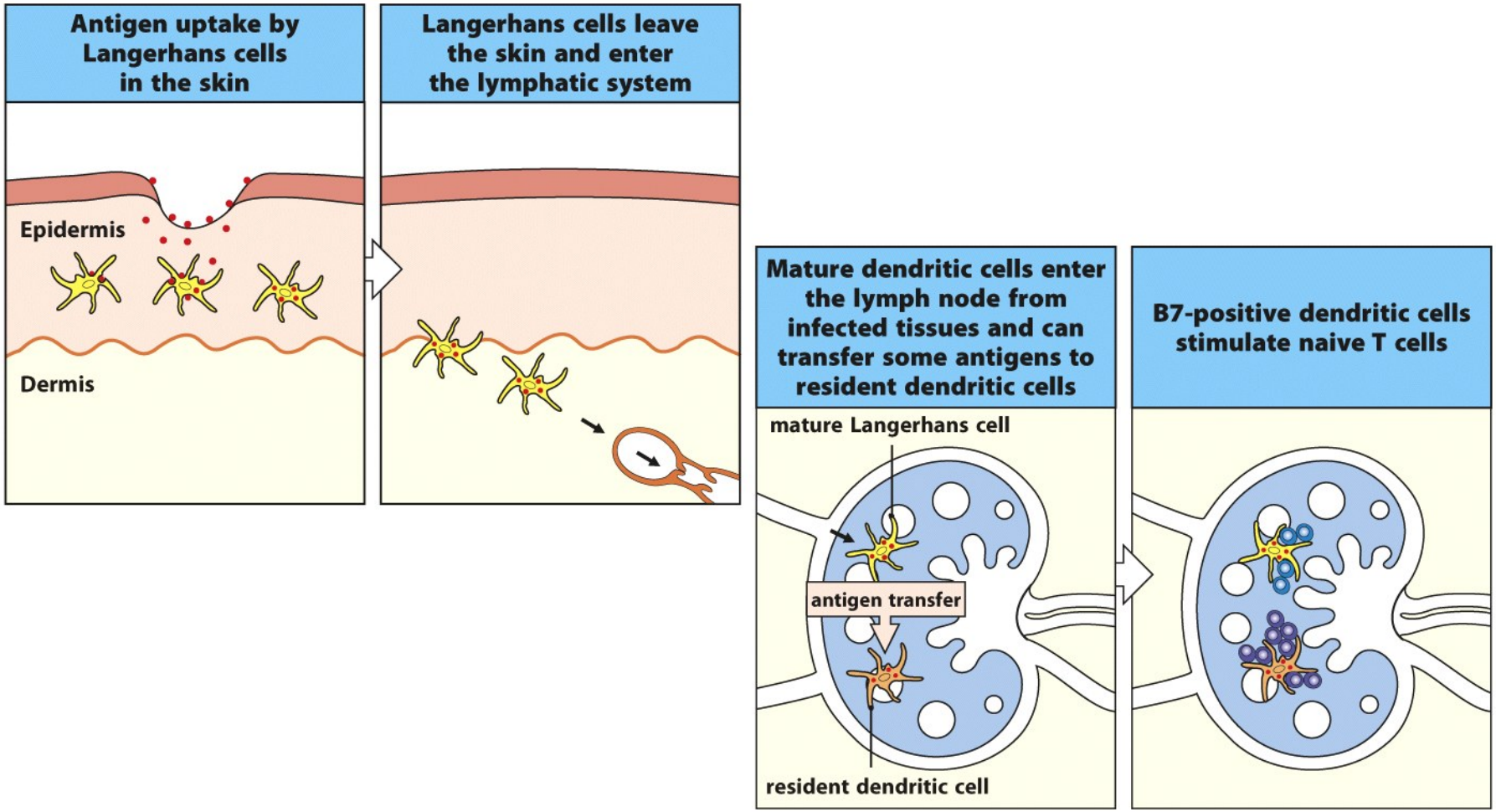
	T_H1	T_H2
CYTOKINE SECRETION		
IL-2	+	–
IFN-γ	++	–
TNF-β	++	–
GM-CSF	++	+
IL-3	++	++
IL-4	–	++
IL-5	–	++
IL-10	–	++
IL-13	–	++

T_H Cells

- Cytokines produced by T_H1 and T_H2 subsets:
  - Promote growth of subset that produces them
  - Inhibit development and activity of the other subset
  - Progression of some diseases depends on balance between T_H1 and T_H2



Antigen presentation



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Antigen Presentation

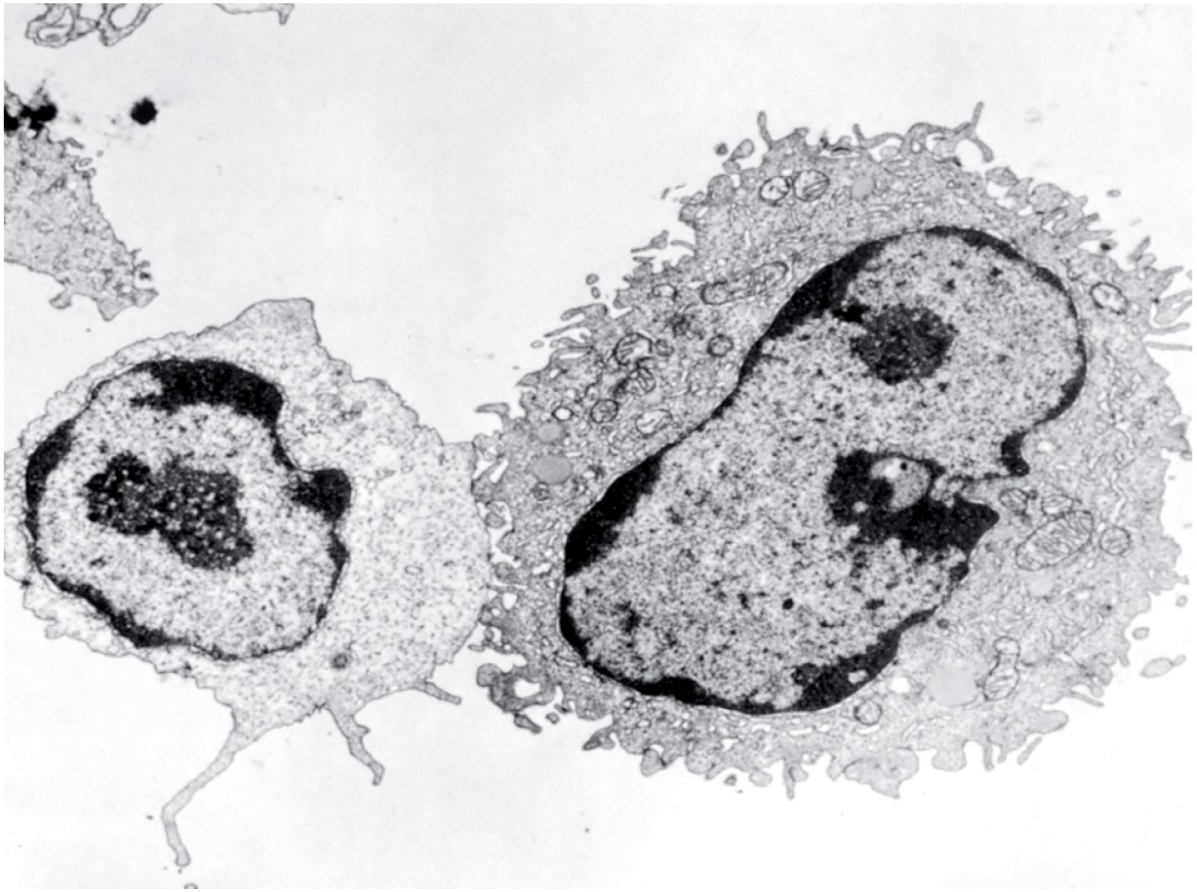

Figure 1-9
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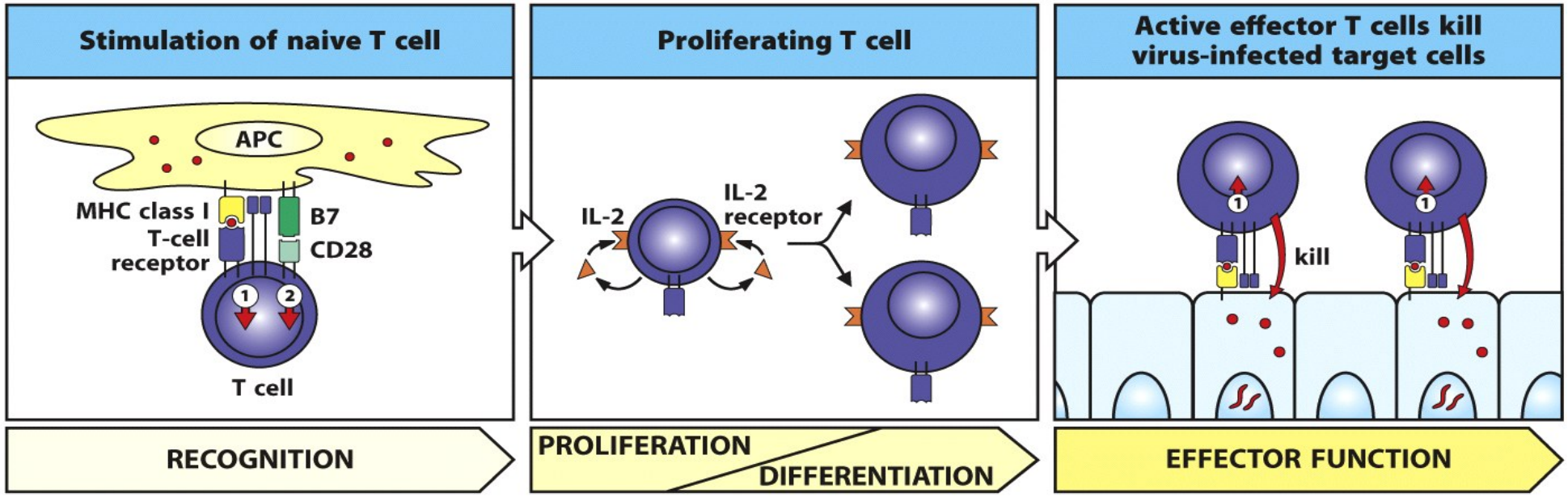
Electron micrograph of an antigen-presenting Mϕ (right) associating with a T lymphocyte (left)

T_H1 Cells

- T_H1 mediates Cell-mediated immunity



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T_H2 Cells

- T_H2 provides help to B cells, promotes production of large amounts of antibodies

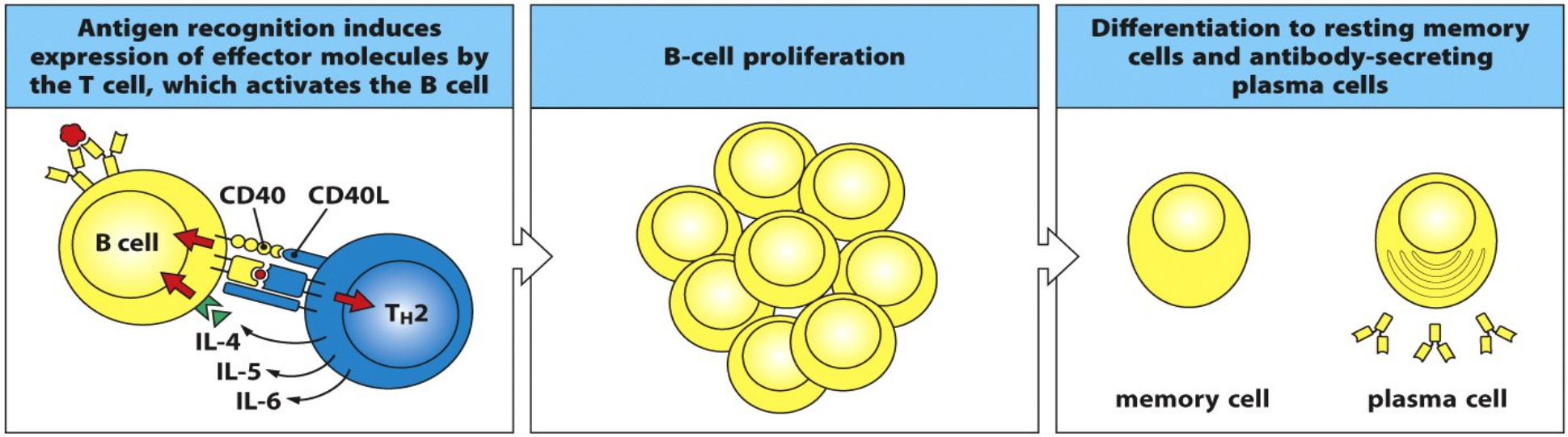
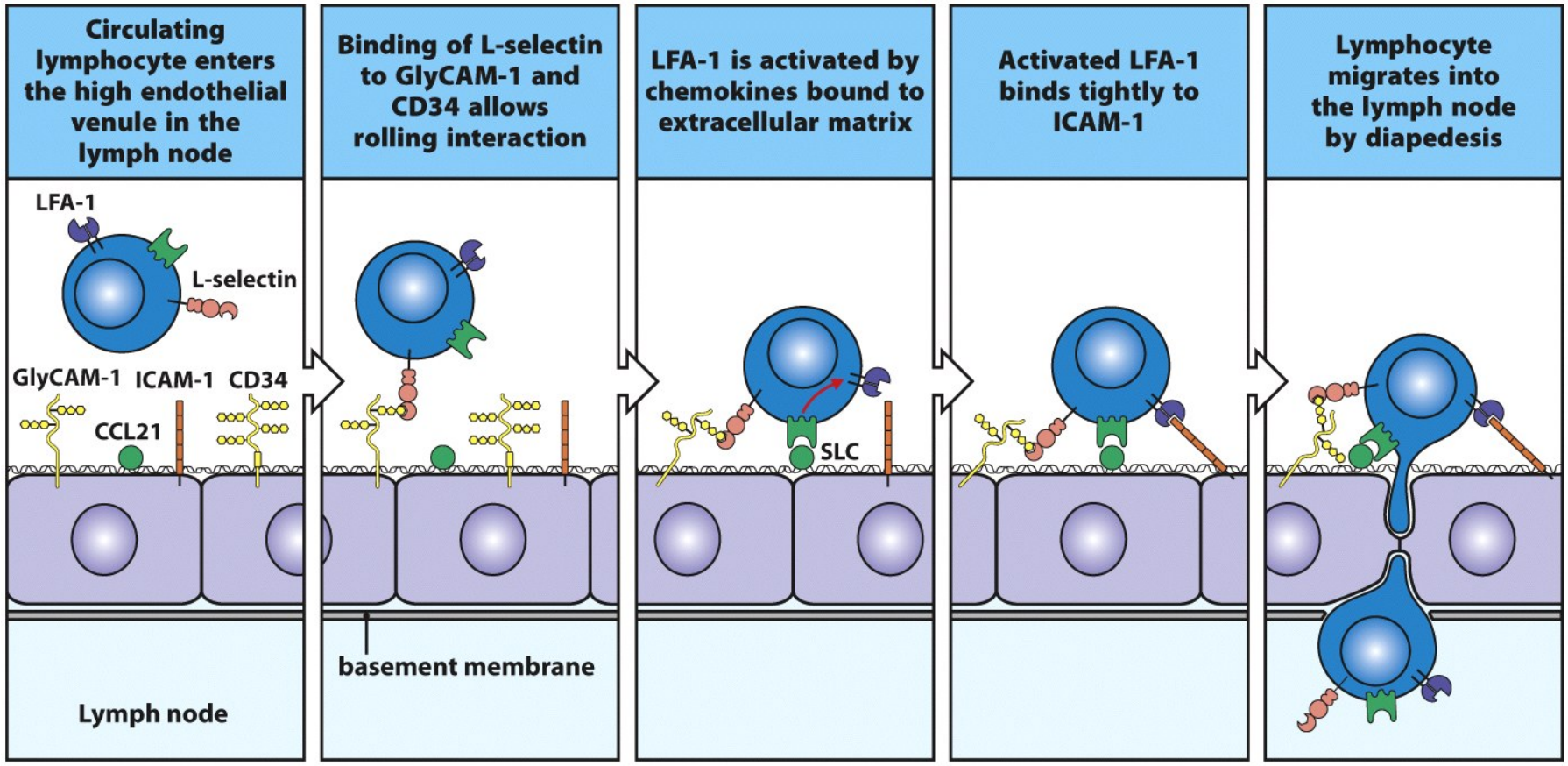


Figure 10.3 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

T cell motion



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Adaptive Immune System

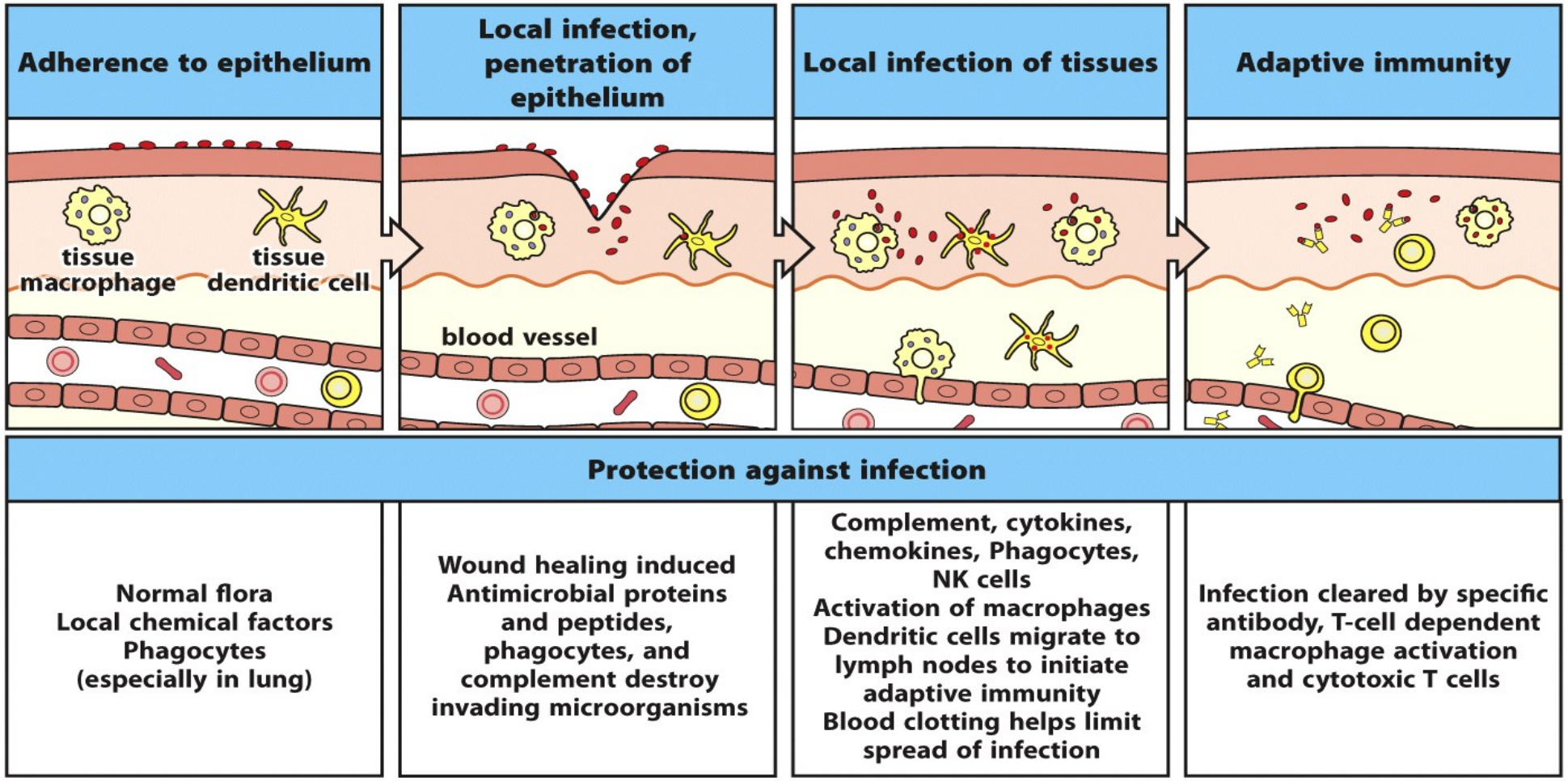

Figure 2.5 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Adaptive Immune System

- Displays 4 characteristic attributes:

① Antigenic specificity

- Distinguish subtle differences among antigens

② Diversity

- Recognitions of billions structures on foreign antigens

③ Immunologic memory

- Higher immune reactivity upon second encounter

④ Self-Nonself recognition

- Ability to respond only to foreign antigens

Adaptive Immune System

- Typically, it takes about 5 to 6 days to develop an adaptive immune response against an antigen after the initial exposure

- Future exposure to the same antigen results in a **memory response**: more quicker, stronger, and effective in clearing pathogens

You are now able to:

- ✓ Understand the process of thymic selection
- ✓ Recognize the difference between T_H1 and T_H2 responses