Organs 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 primary and secondary lymphoid organs

② Appreciate the collaborative relationship between innate and adaptive immune cells

Organs of the Immune System

- Immune organs can be classified **functionally** into two main groups:
  ① **Primary lymphoid organs**: which provide appropriate microenvironment for the **development** and **maturation** of lymphocytes
  ② **Secondary lymphoid organs**: which trap antigens from nearby tissues and at which mature lymphocytes can interact with antigens

Organs of the Immune System

- **Primary lymphoid organs:**
  - Place of **maturation of lymphocytes**
- **Lymphatic system**
  - Interstitial fluid is returned to circulatory system by lymphatic vessels
  - **Antigen is carried by lymph** to lymph nodes
- **Secondary lymphoid organs:**
  - Mature **lymphocytes interact with antigen**

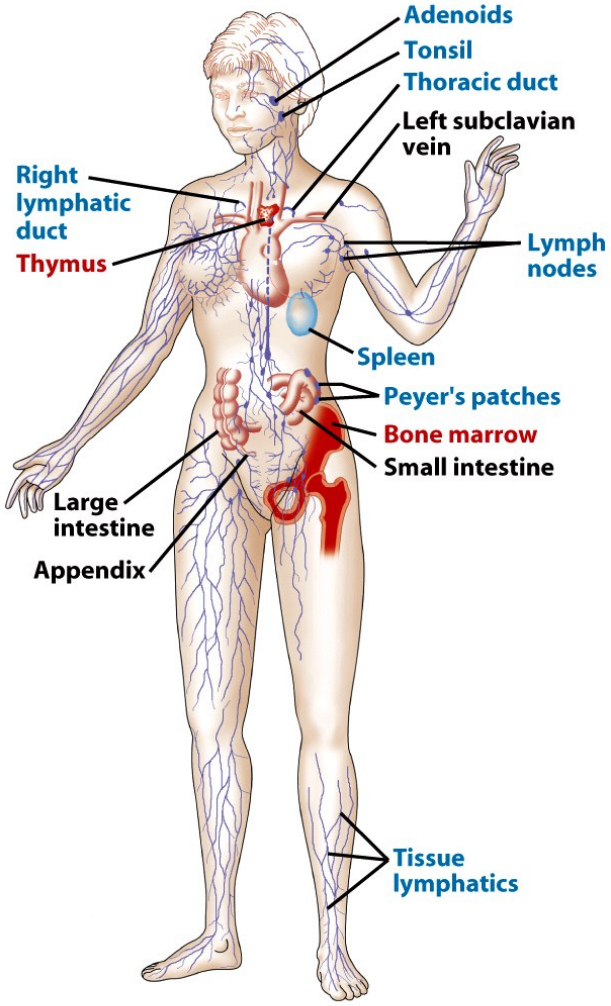

Figure 2-11
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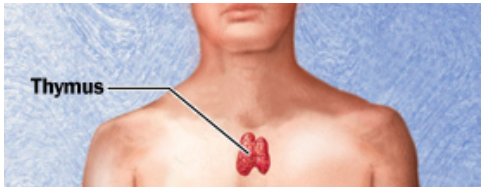
Primary Lymphoid Organs

- Sites for maturation of immature lymphocytes and educated to become **immunocompetent** i.e. capable of mounting immune response.

Thymus



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

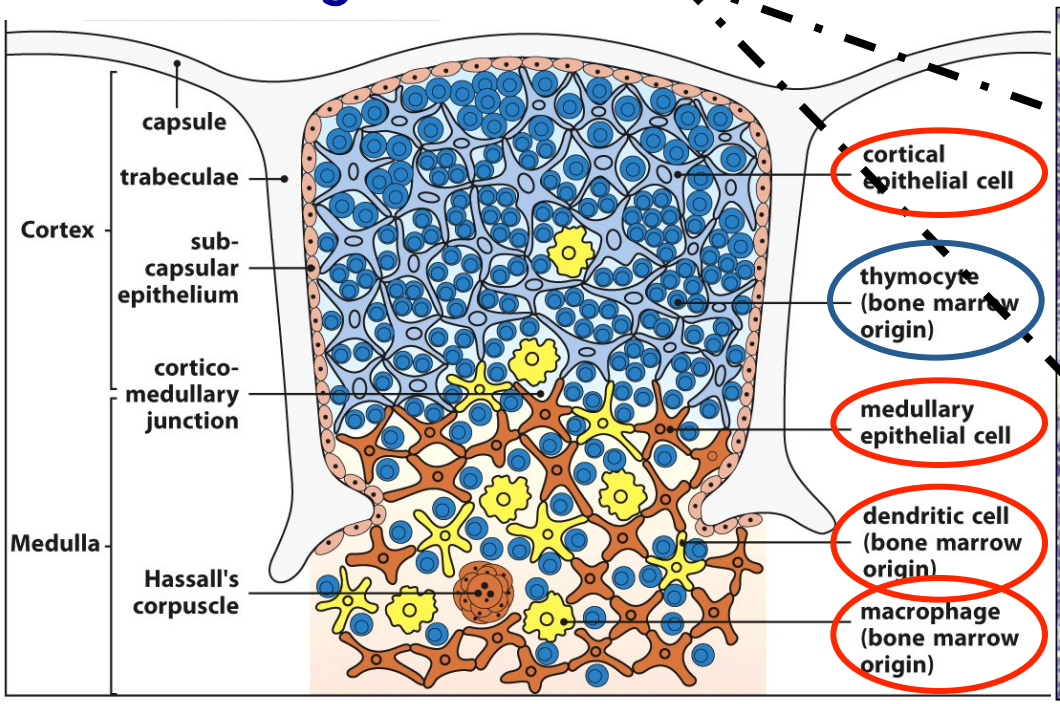


Figure 8.15 part 1 of 2 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

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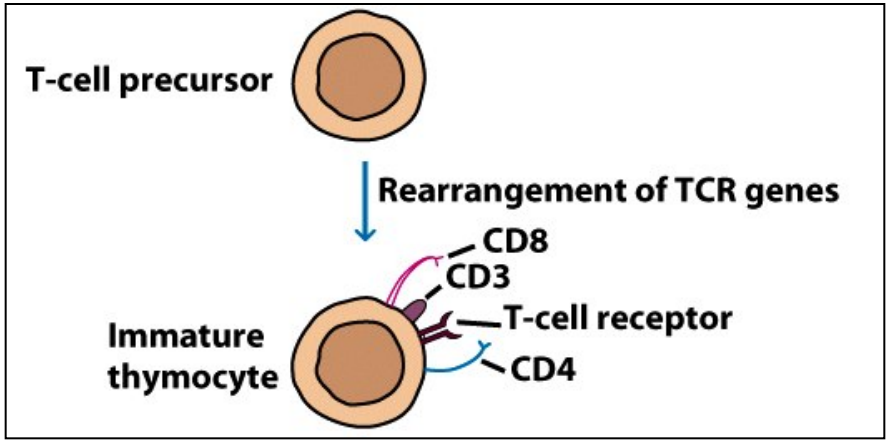
T Cell Maturation

- 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

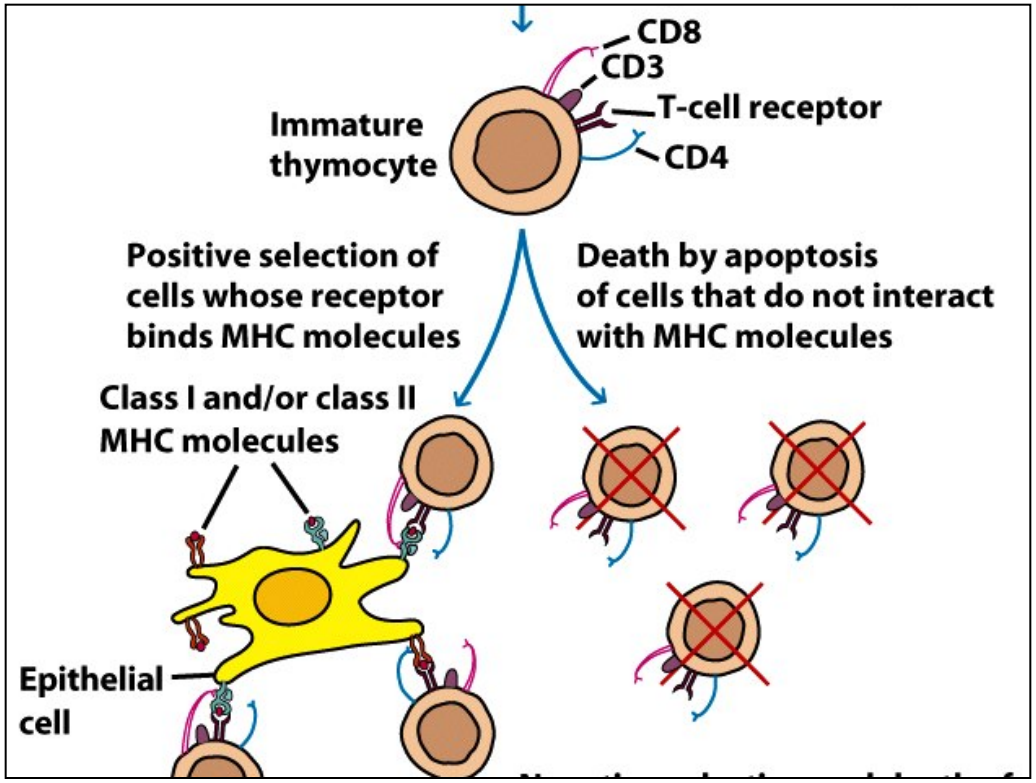
- TCR is generated by gene rearrangement. This is a random process that produces receptors of different specificity and reactivity
- Remember that TCRs must have two properties:
  ① Recognizes self MHC-I and MHC-II
  ② DO NOT react with self antigens



- **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**

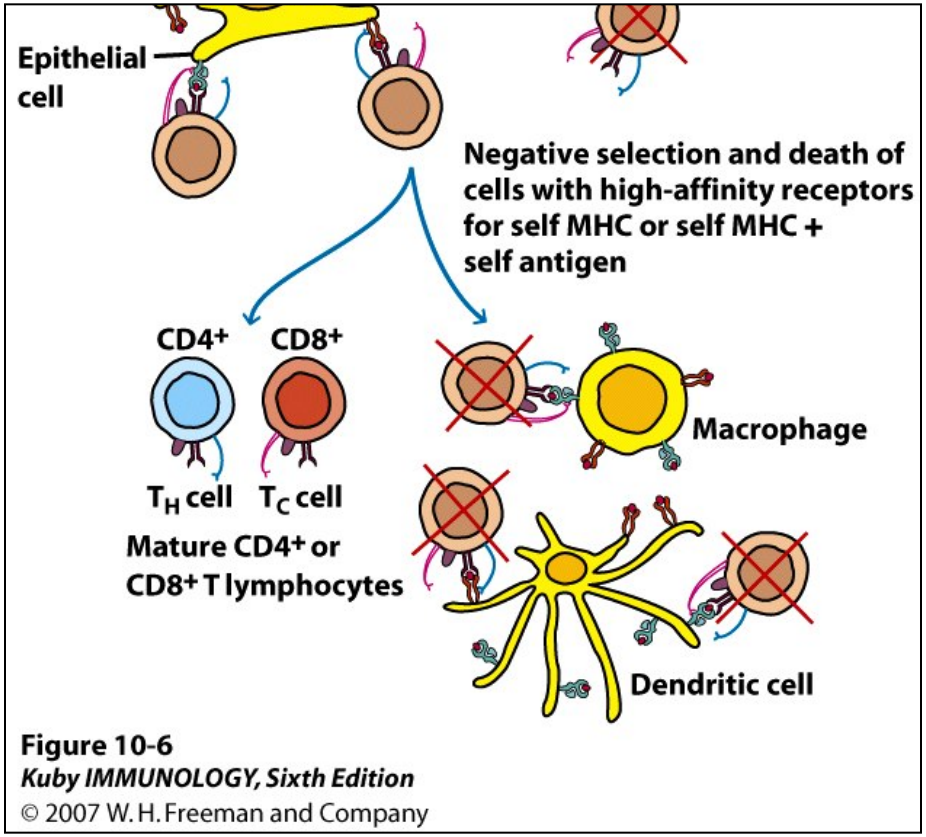


Figure 10-6
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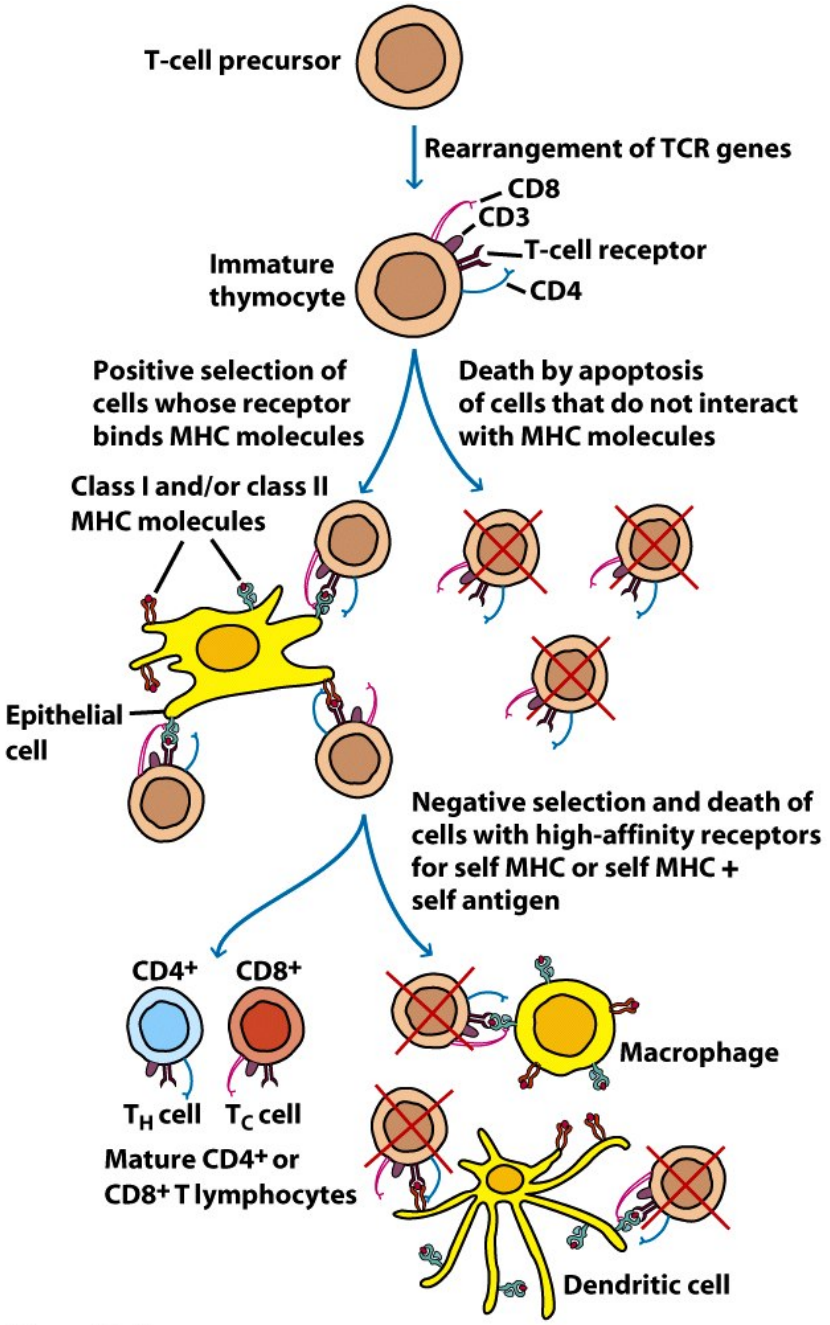

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Paradoxical Signaling Pathways in Developing Thymocytes

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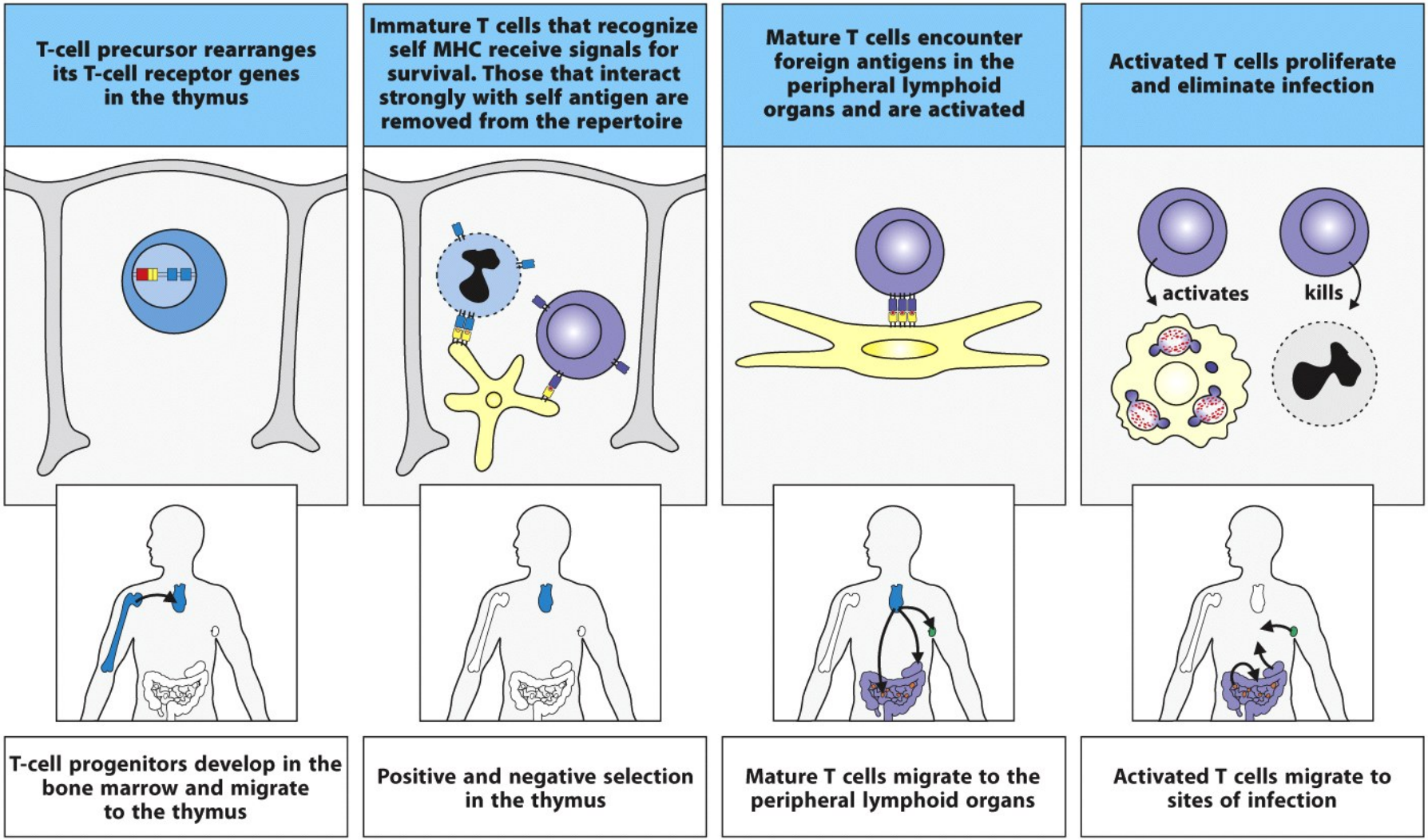
ABSTRACT- Thymocytes are subjected to processes of selection during their life in the thymus; negative selection for autoreactive thymocytes and positive selection for self-MHC restricted self-tolerant cells. Interestingly, signals for positive or negative selection originate from the same receptor. 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



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B Cell Maturation

- The bone marrow **generate** and **select** a repertoire of B cells the will **protect** the body from infections and **do not be harmful** to body tissues

- B cells also undergo **negative** and **positive** selection processes on the basis of their reactivity with self and foreign antigens

Bone Marrow

- Generation of mature B cells first occurs in the embryonic stages (in yolk sac, fetal liver, and fetal bone marrow)
- After birth, generation of mature B cells occurs in the bone marrow
- Site of hematopoiesis
- Site of B cell maturation
- **Bone Marrow Stromal Cells** are essential for B cell maturation by:
  ① Direct interacts
  ② Secretion of cytokines mainly **IL-7**

B Cell Maturation

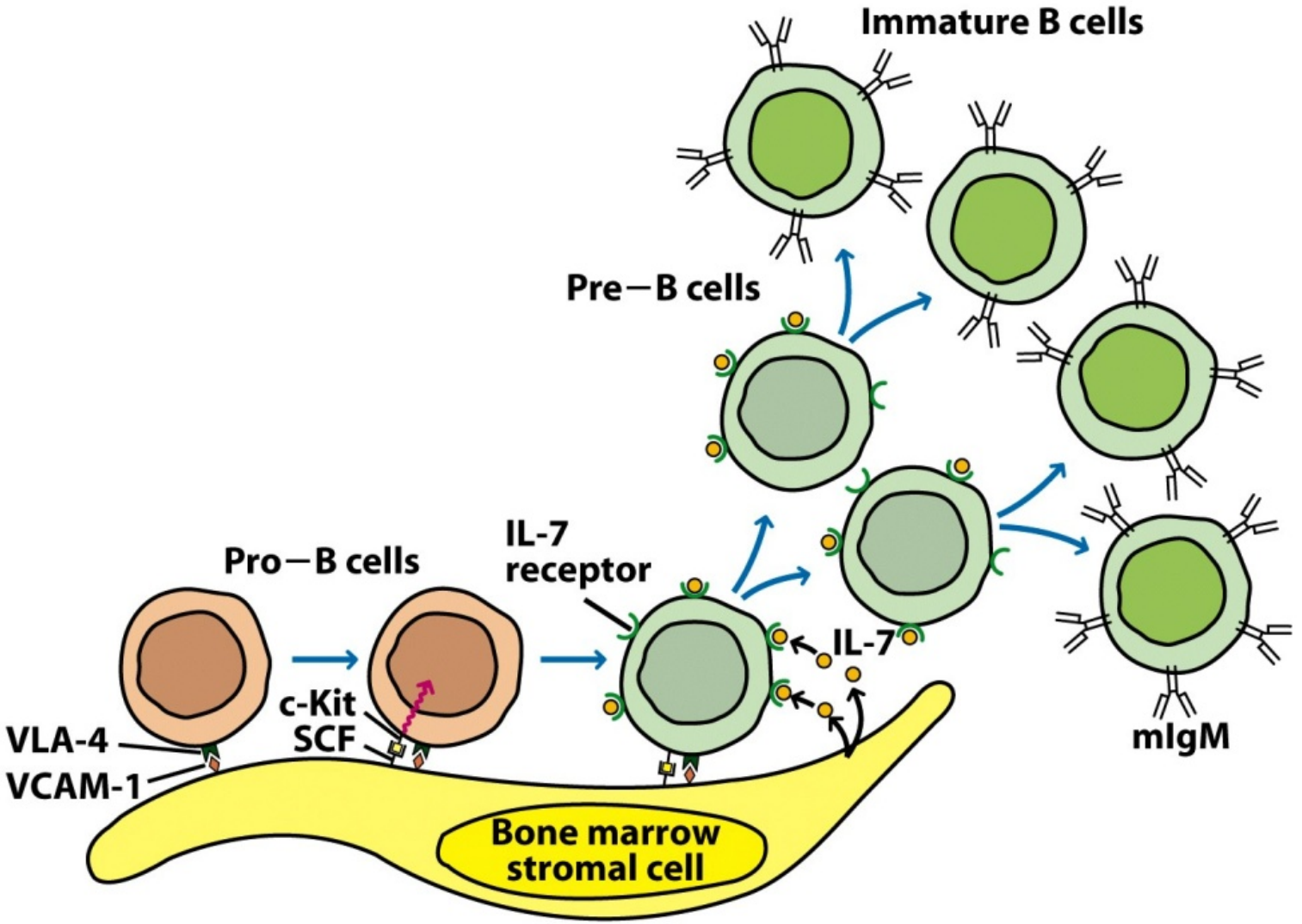

Figure 11-2
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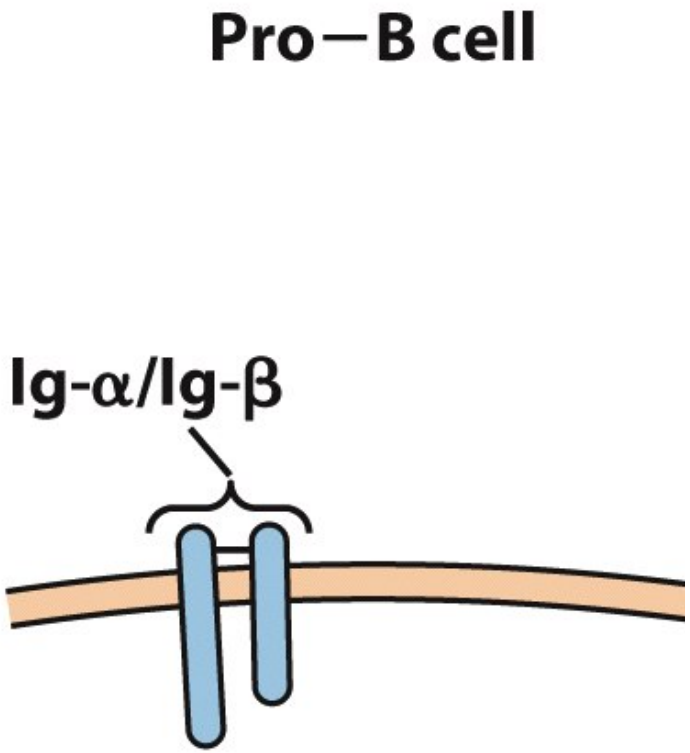
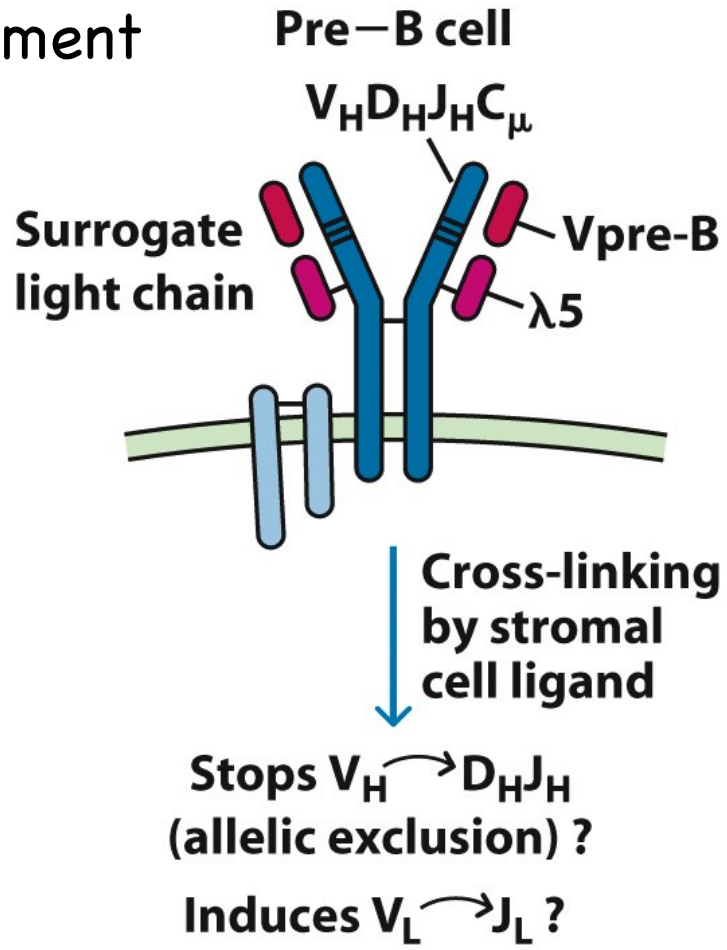
Ig-Gene Rearrangement

- Pro-B Cell
  - Heavy chain rearrangement



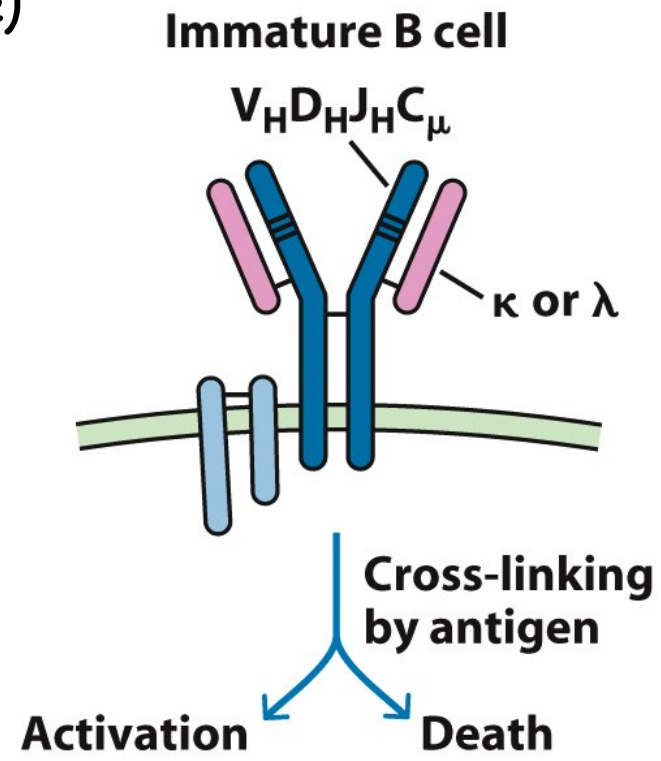
Ig-Gene Rearrangement

- Pre-B cell
  - Light chain rearrangement

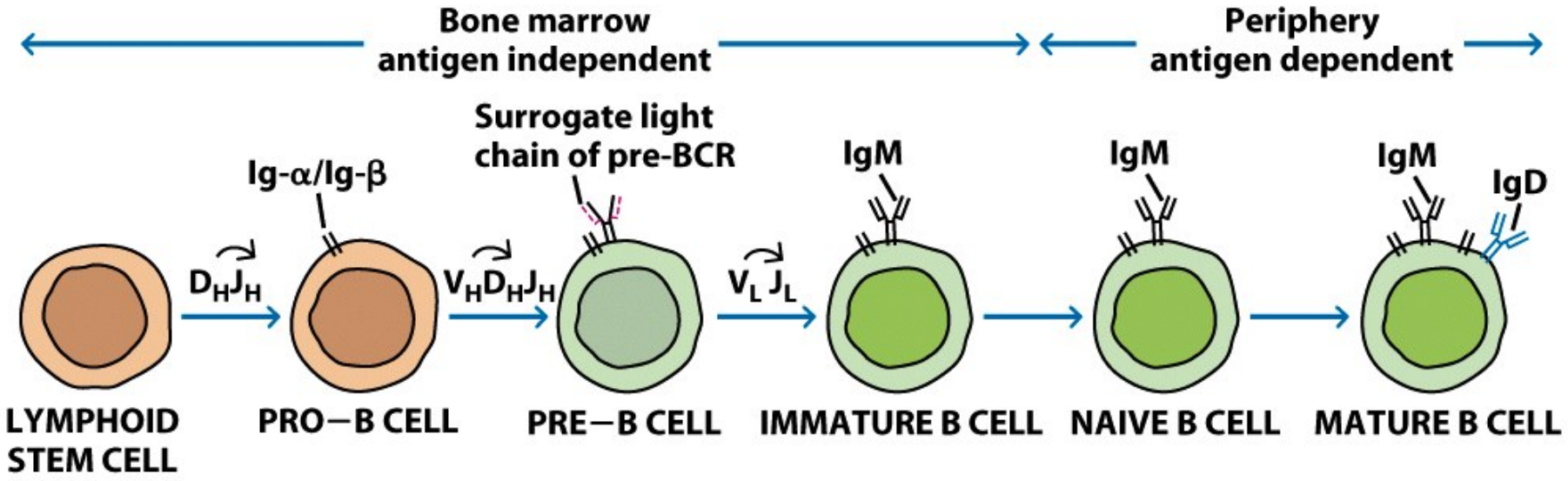


Ig-Gene Rearrangement

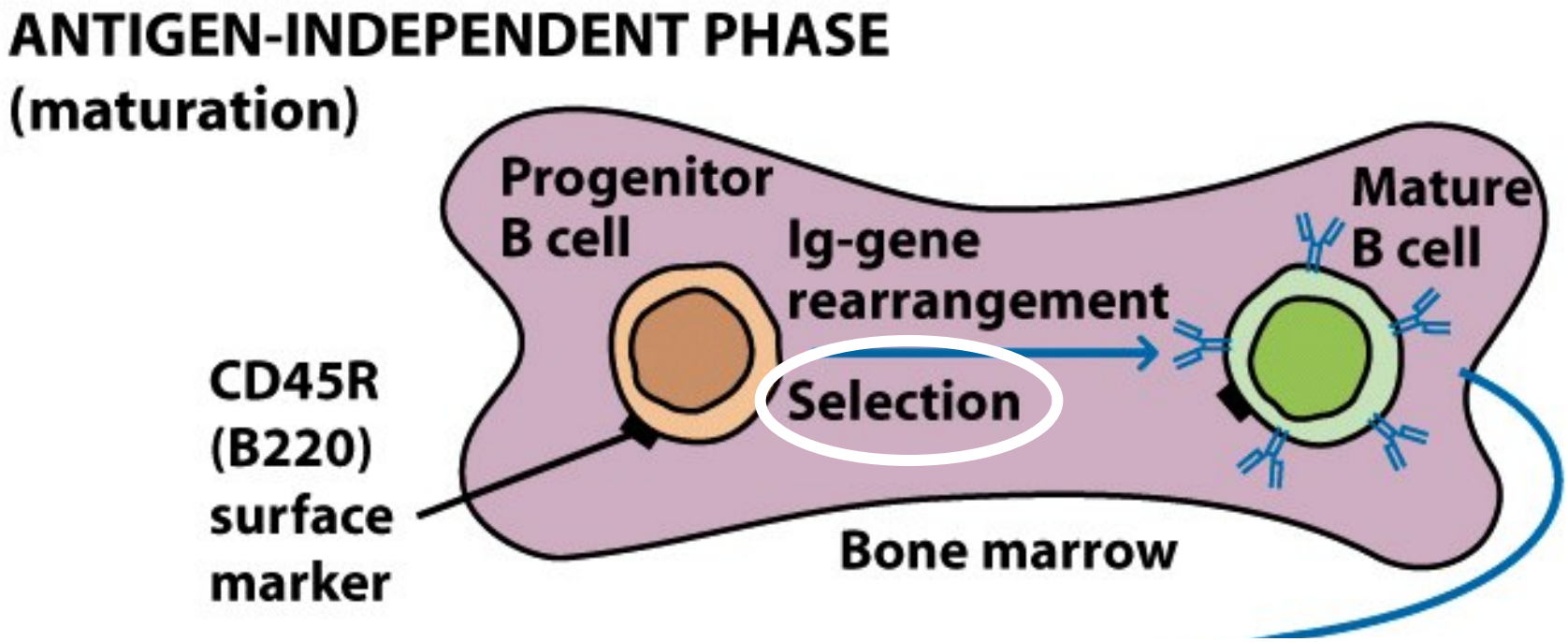
- Immature B cell
  - Committed to antigenic specificity and produces IgM (functional B cell must express both **IgM AND IgD** on membrane)



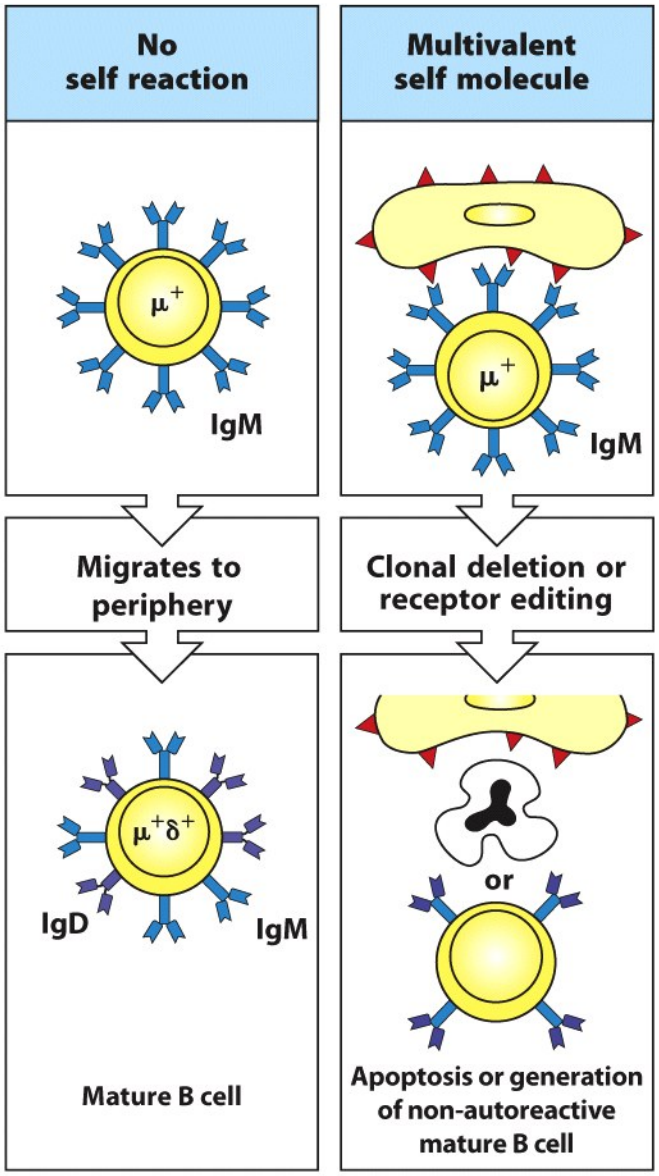
B Cell Maturation



Antigen-Independent Phase



Antigen-Independent Phase



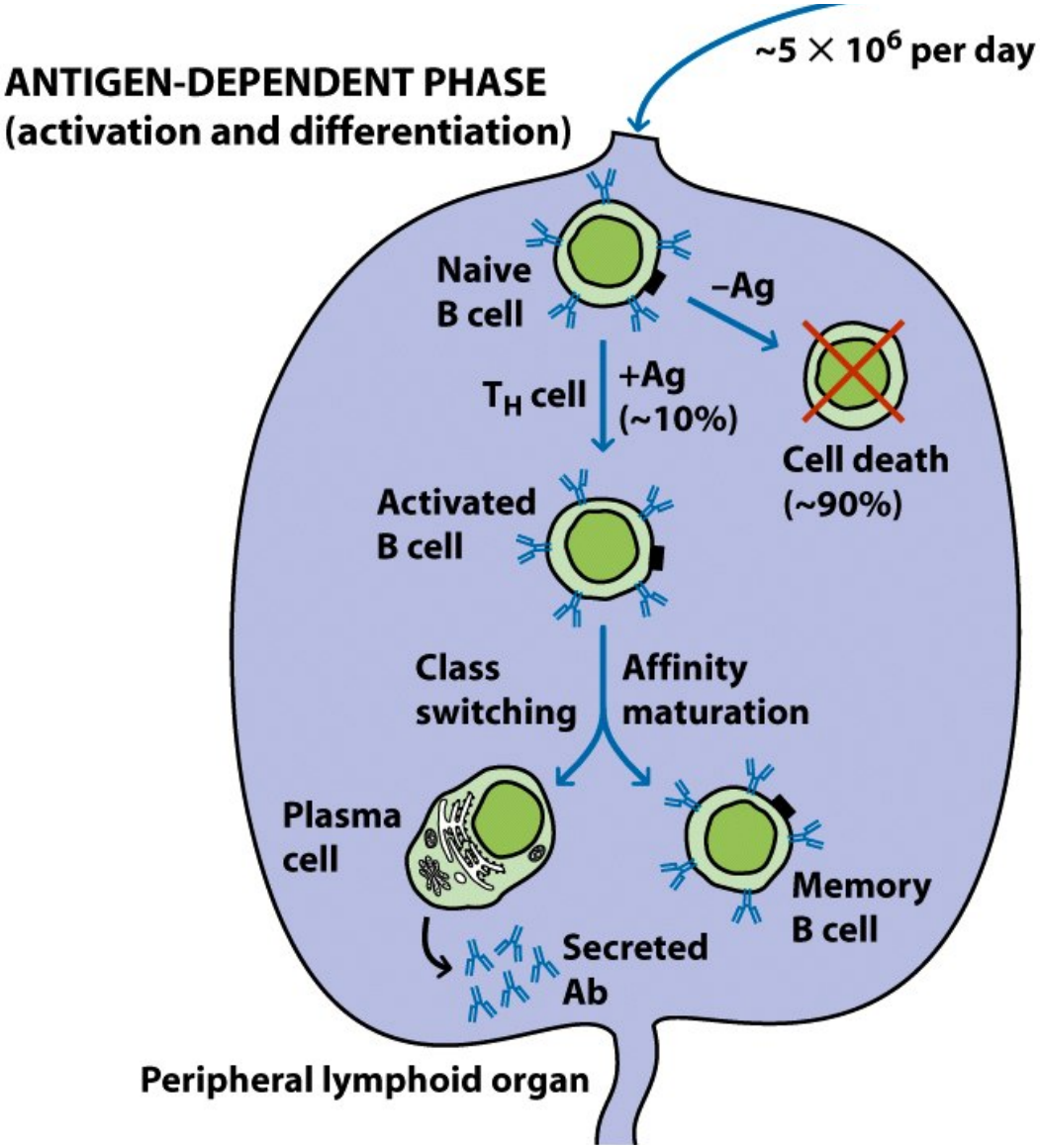
Negative Selection

Bone Marrow

Antigen-Dependent Phase

Positive Selection

Secondary lymphoid organ



B Cell Development

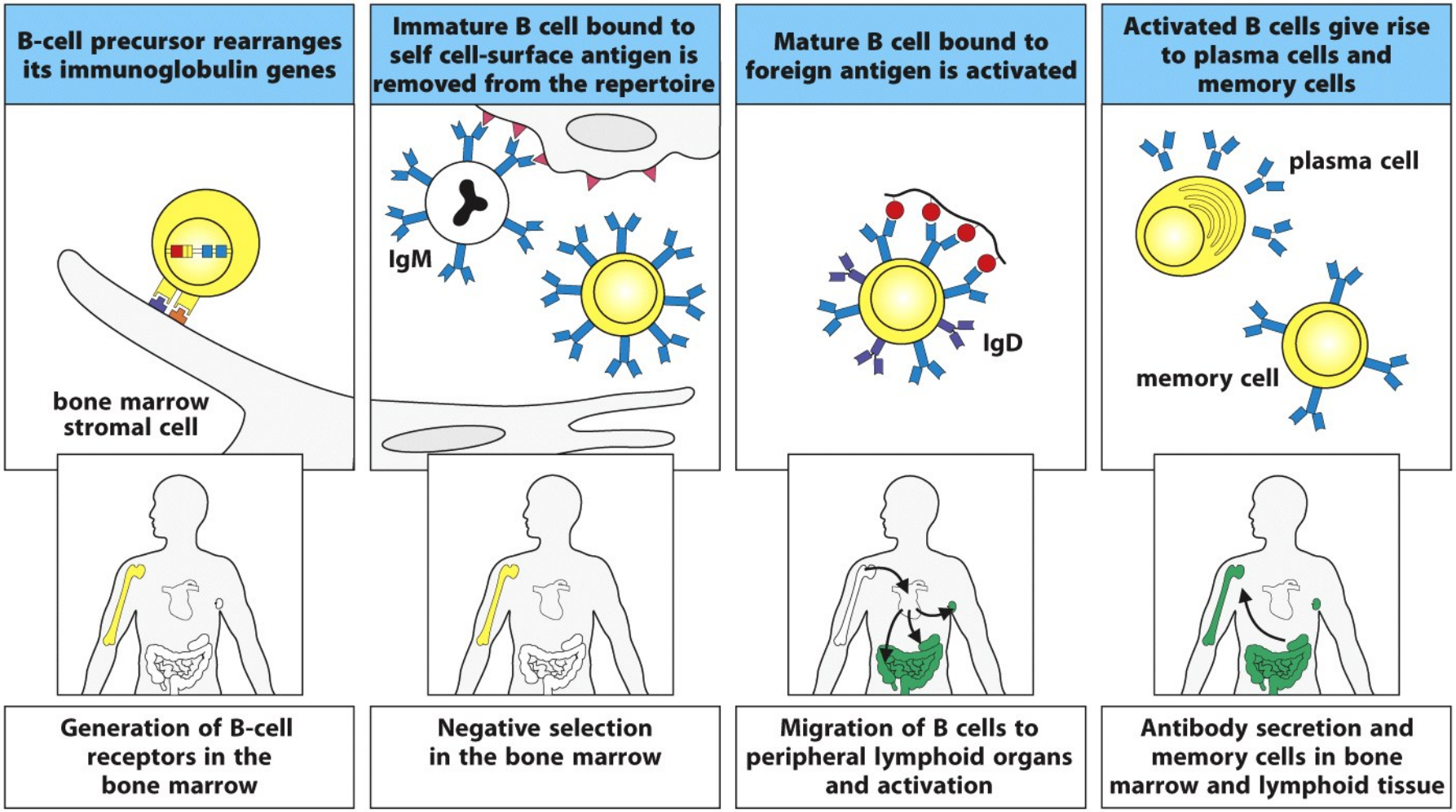


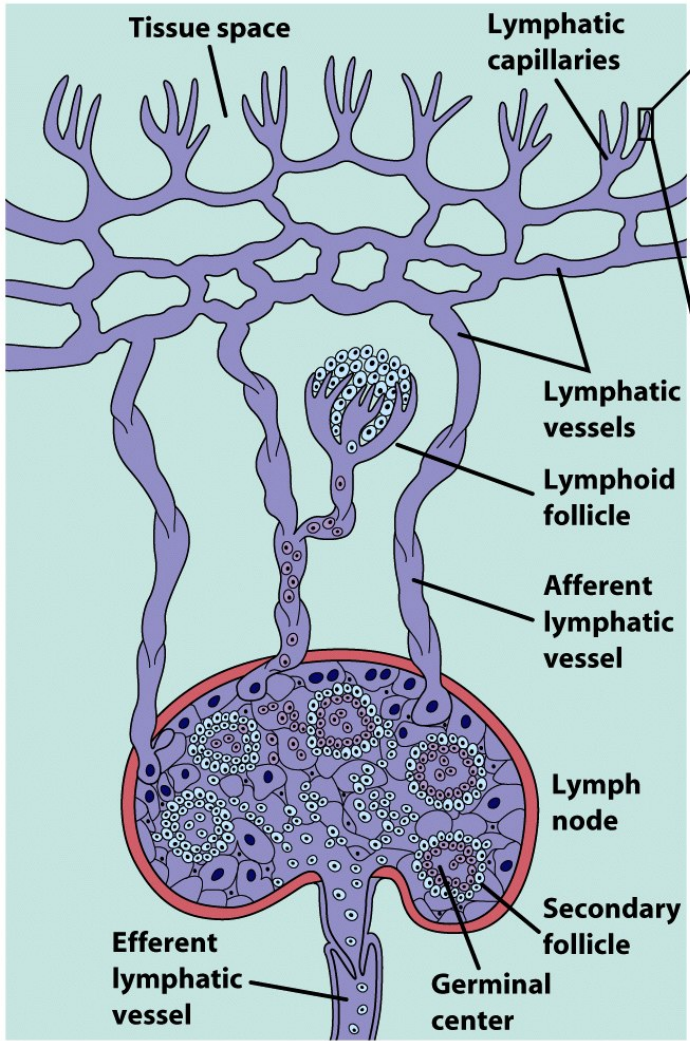
Figure 8.1 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Secondary Lymphoid Organs

- Situated along the vessels of the lymphatic system
- Sites where immune responses are mounted to antigens
- Involves **lymph nodes**, **spleen**, and **mucosa-associated lymphoid tissue (MALT)**

Secondary Lymphoid Organs

- **Primary follicle**
  - Not activated lymphoid follicle
- **Secondary follicle**
  - Follicle that is activated by antigen
  - Ring of B cells that surround **germinal center**
    - Proliferating B cells and T helper cells



Lymph Nodes

- Encapsulated bean-shaped structures packed with **lymphocytes**, **macrophages**, and **dendritic cells**

- Traps any particulate antigen that is brought in with the lymph

Lymph Nodes

① Cortex

- B cells, macrophages, dendritic cells
- Primary and secobdary follicles

② Paracortex

- Mostly T cells, dendritic cells

③ Medulla

- Macrophages Plasma cells

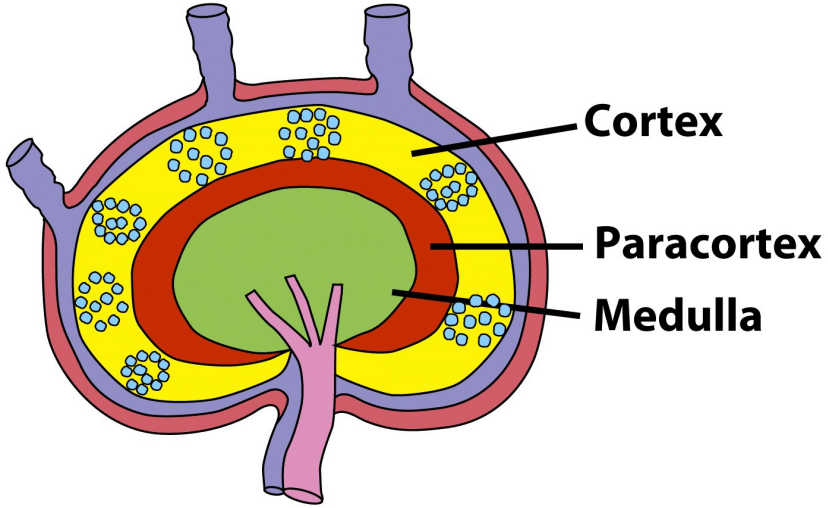


Figure 2-16a
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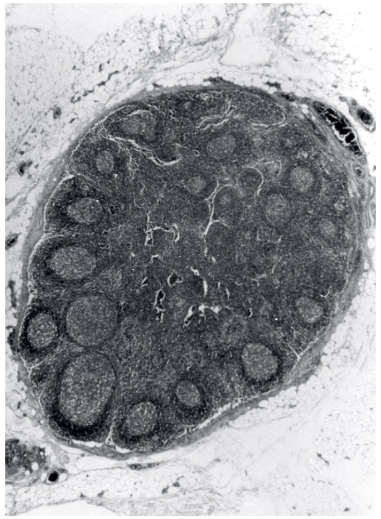

Figure 1.18 part 2 of 2 Janeway's Immunobiology, 8ed.

Spleen

- Large encapsulate ovoid structure located high in the left abdominal cavity
- Major role in mounting immune response to **antigens in the blood**
- The spleen specializes in filtering blood and trapping blood-borne antigens

Spleen

① Red Pulp

- Macrophages, RBCs, and few lymphocytes

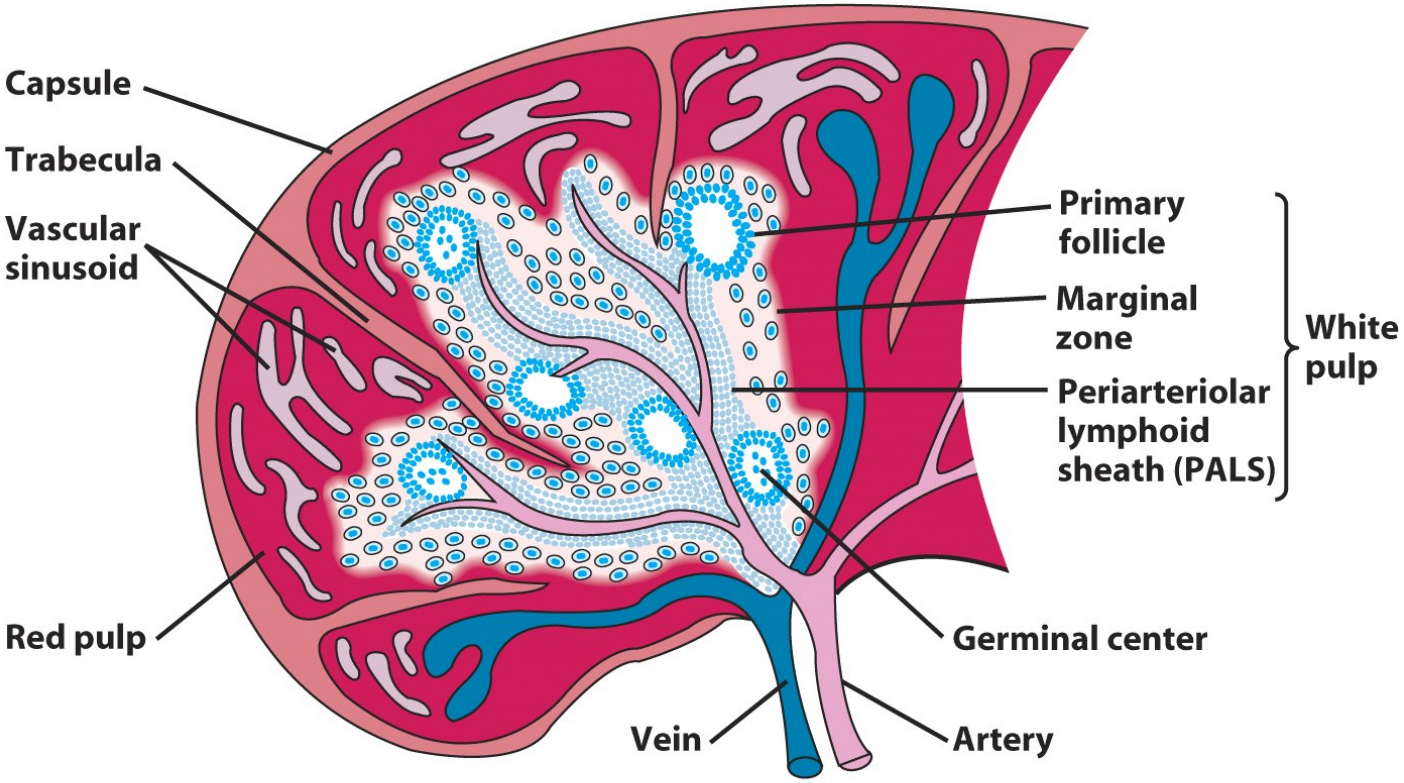

Figure 2-17b
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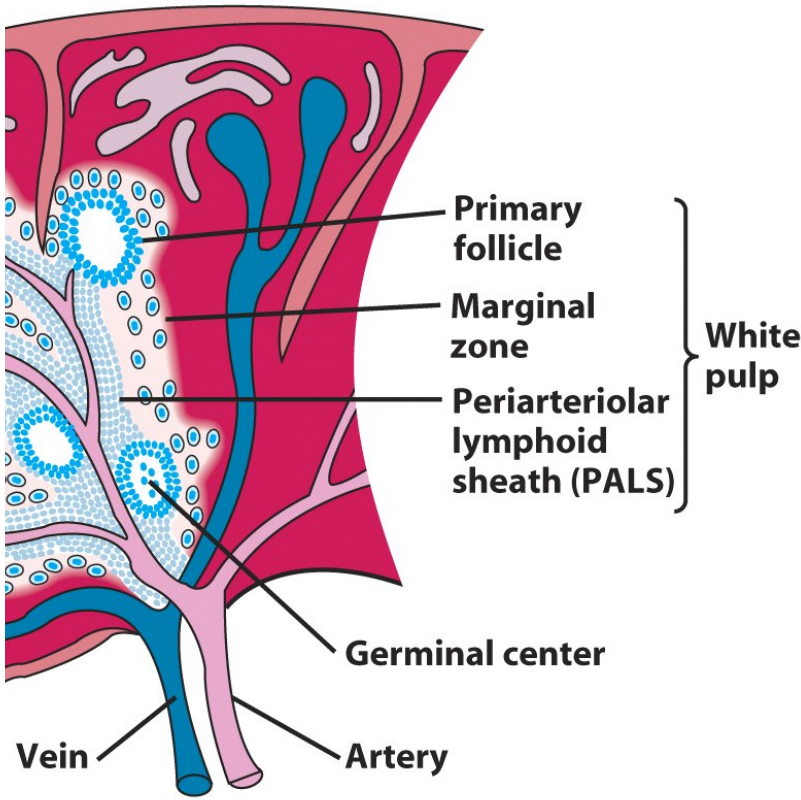
Spleen

② White Pulp

- Surrounds branches of splenic artery
- Forms periarteriolar lymphoid sheath (PALS)
  - ➢ Populated by T lymphocytes
- Primary lymphoid follicles
  - ➢ Rich in B cells and contain germinal center
- Marginal zone
  - ➢ Lymphocytes and macrophages



Splenic Lymphocyte Activation

- Initial activation of B and T cells in PALS where DC capture antigens and present them on MHC-II to T_H cells. Those T_H cells then activate B cells, which move to primary follicles in the marginal zone. Then the primary follicles develop into secondary follicles with germinal center

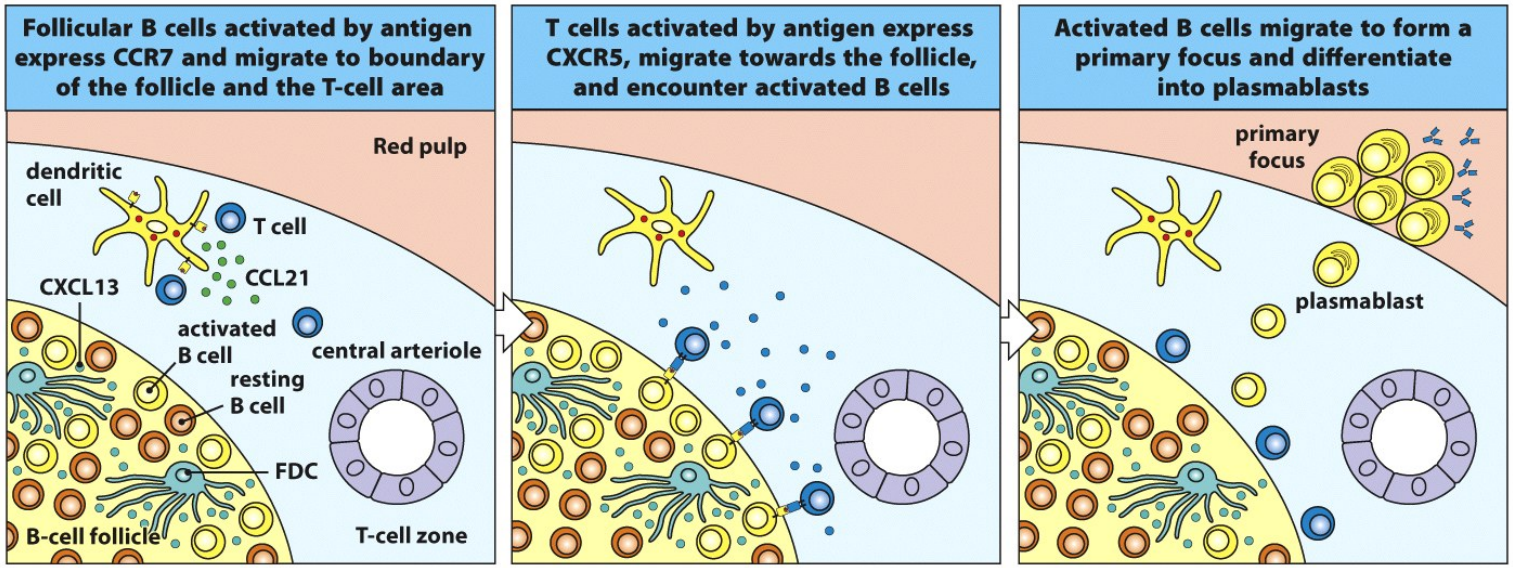


Figure 10.7 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

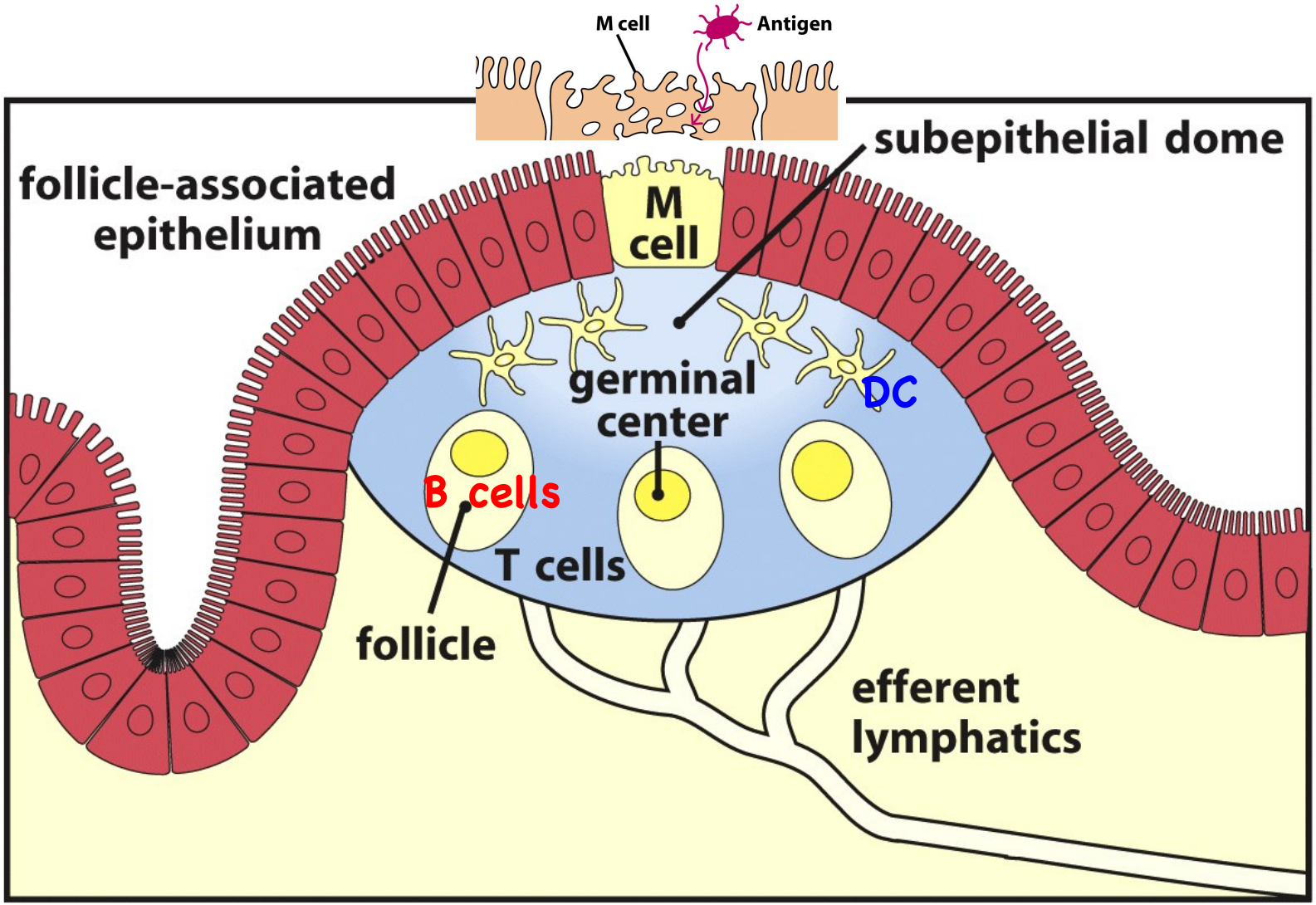
Mucosa-Associated Lymphoid Tissue

- Organized areas along **digestive (GALT)**, **respiratory (BALT)**, and **urogenital** tracts

- Very well organized areas in intestine are referred to as **Peyer's patches**

- Includes **tonsils** and **appendix**

Peyer's Patch



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Peyer's Patch

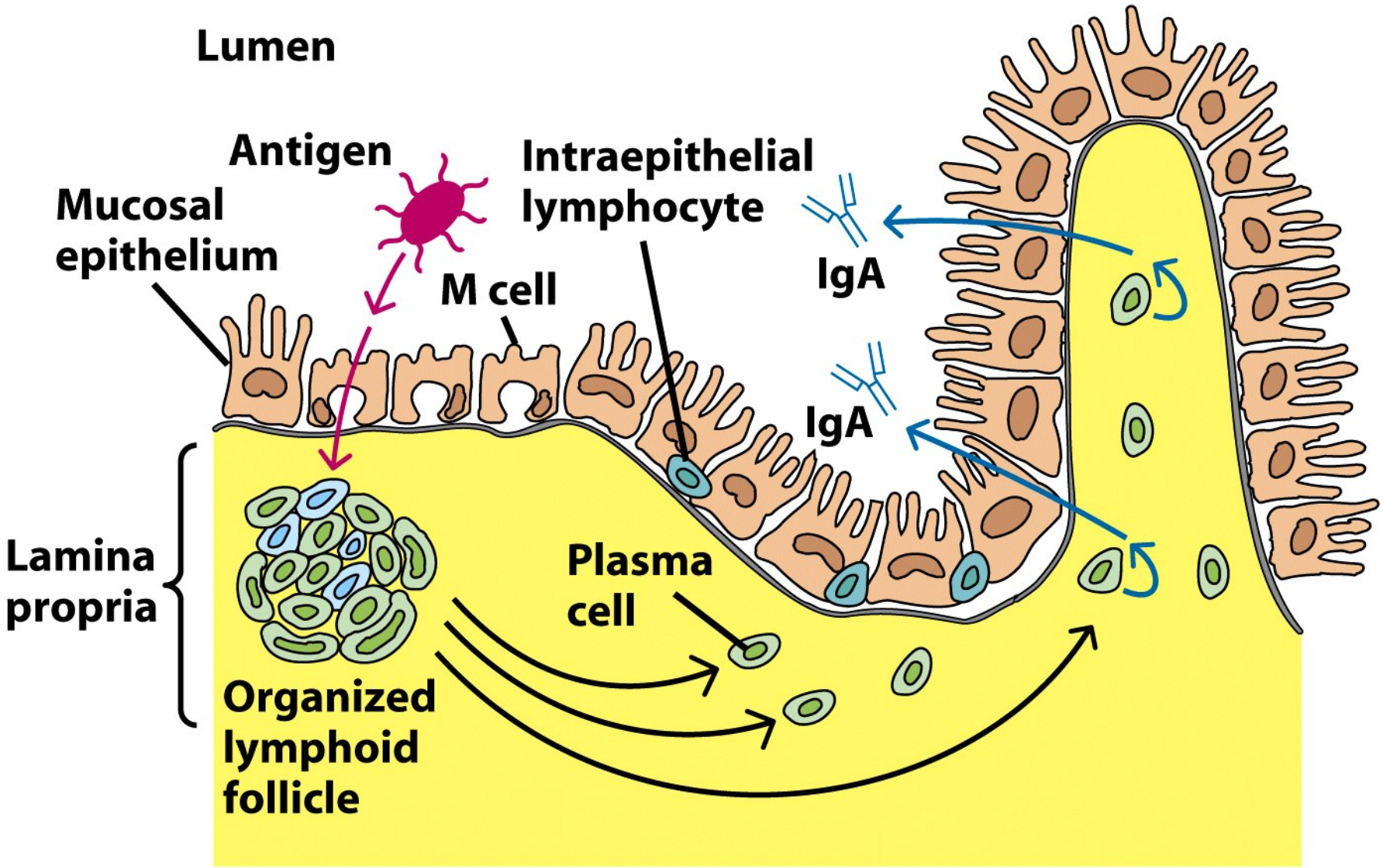

TABLE 3-1 Innate and adaptive immunity

Attribute	Innate immunity	Adaptive immunity
Response time	Minutes/hours	Days
Specificity	Specific for molecules and molecular patterns associated with pathogens	Highly specific; discriminates even minor differences in molecular structure; details of microbial or nonmicrobial structure recognized with high specificity
Diversity	A limited number of germ line–encoded receptors	Highly diverse; a very large number of receptors arising from genetic recombination of receptor genes
Memory responses	None	Persistent memory, with faster response of greater magnitude on subsequent infection
Self/nonself discrimination	Perfect; no microbe-specific patterns in host	Very good; occasional failures of self/nonself discrimination result in autoimmune disease
Soluble components of blood or tissue fluids	Many antimicrobial peptides and proteins	Antibodies
Major cell types	Phagocytes (monocytes, macrophages, neutrophils), natural killer (NK) cells, dendritic cells	T cells, B cells, antigen-presenting cells

Table 3-1
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You are now able to:

- ✓ Describe the structure and function of primary and secondary lymphoid organs
- ✓ Appreciate the collaborative relationship between innate and adaptive immune cells