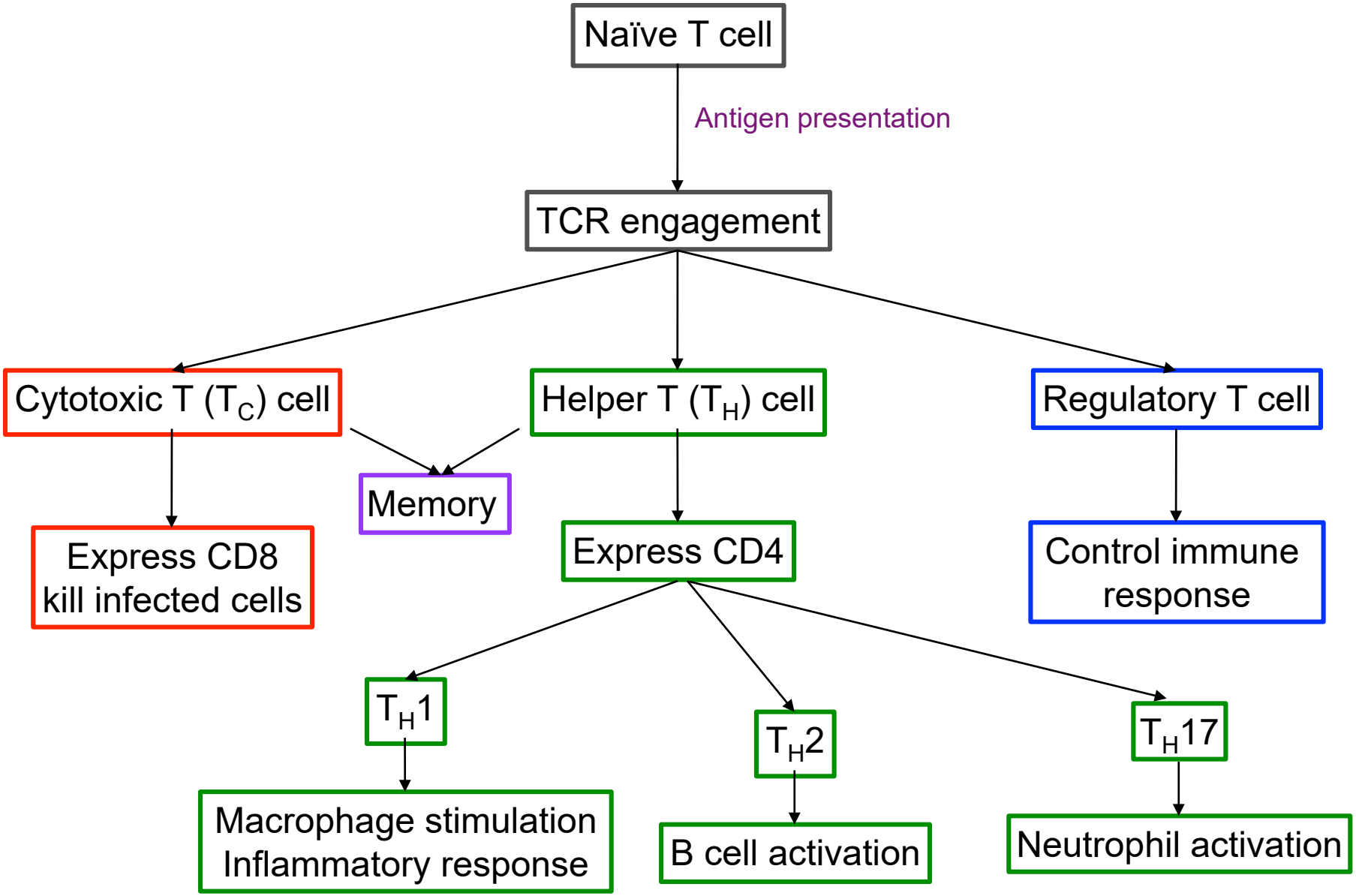
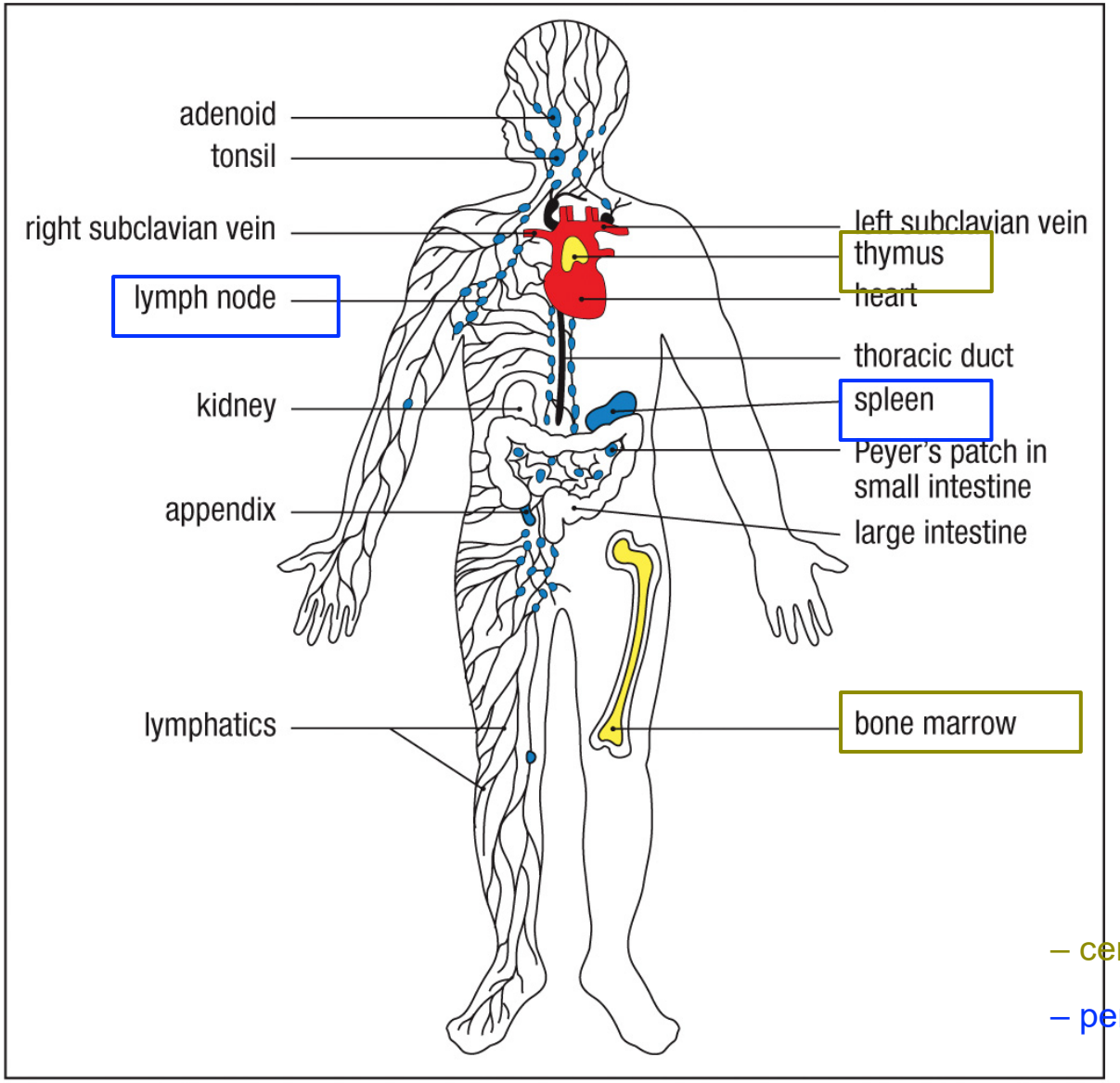
Outline

- T cell mediated immunity
  - T cell recruitment
  - Antigen presentation
  - T cell priming
- T cell signaling

T Lymphocyte Differentiation



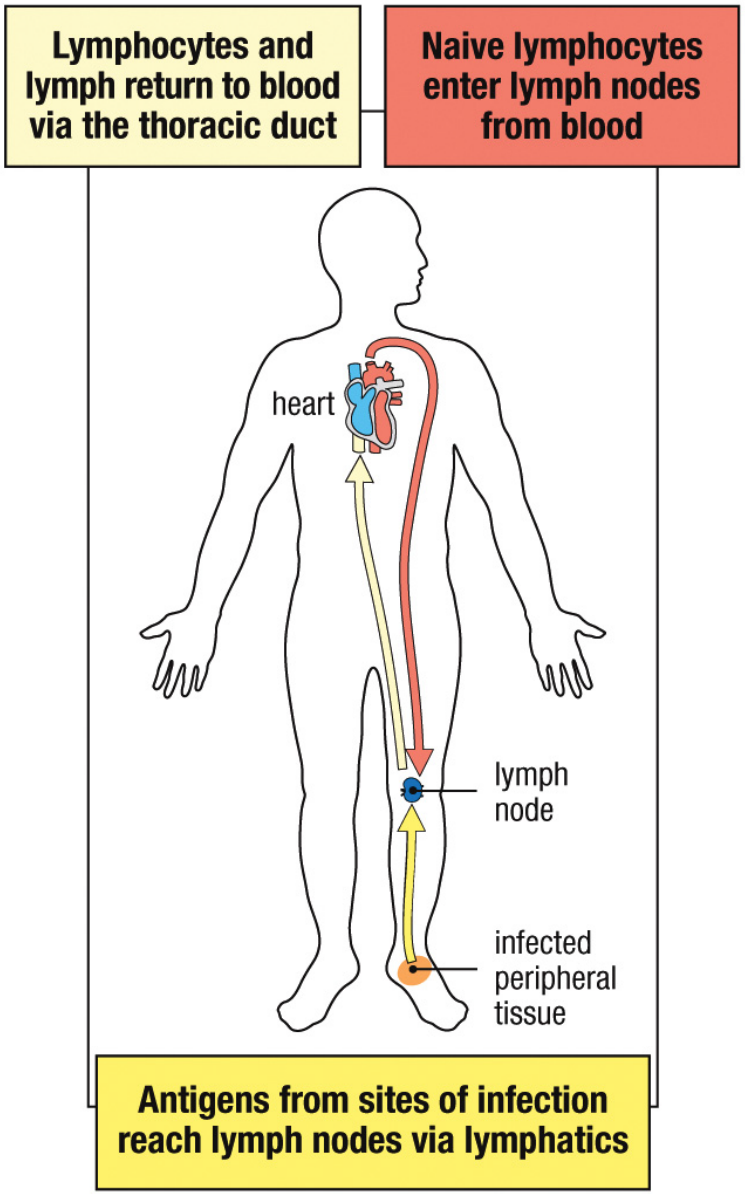
Lymphoid Tissue



– central lymphoid organ

– peripheral lymphoid organ

Lymphoid Organs: Sites of Antigen Encounter



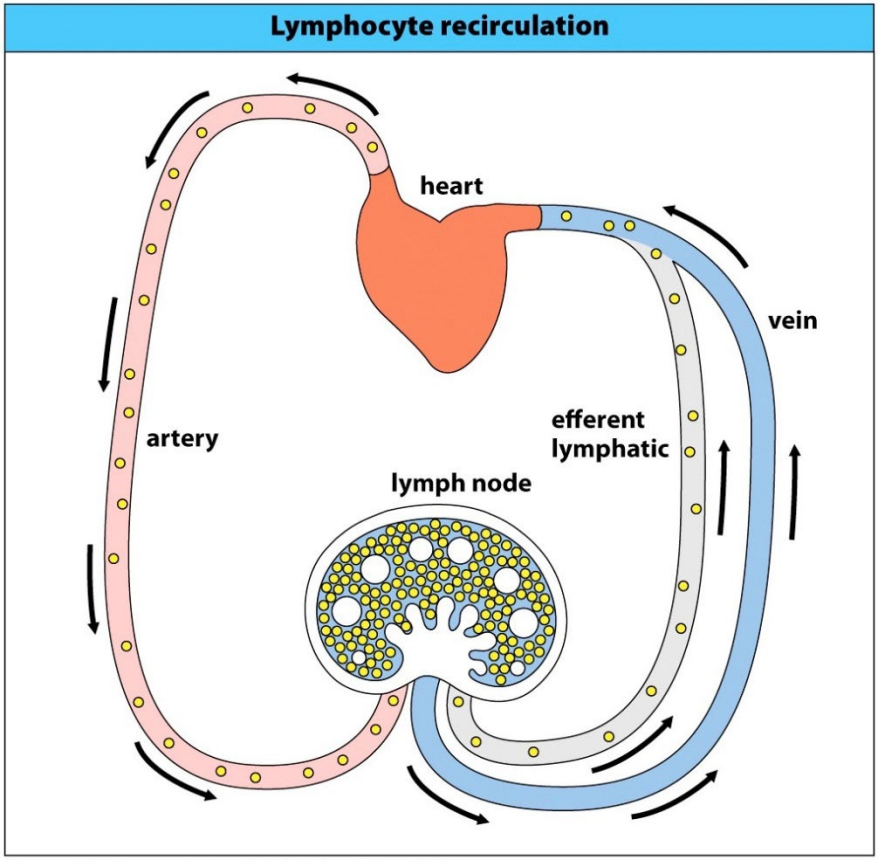
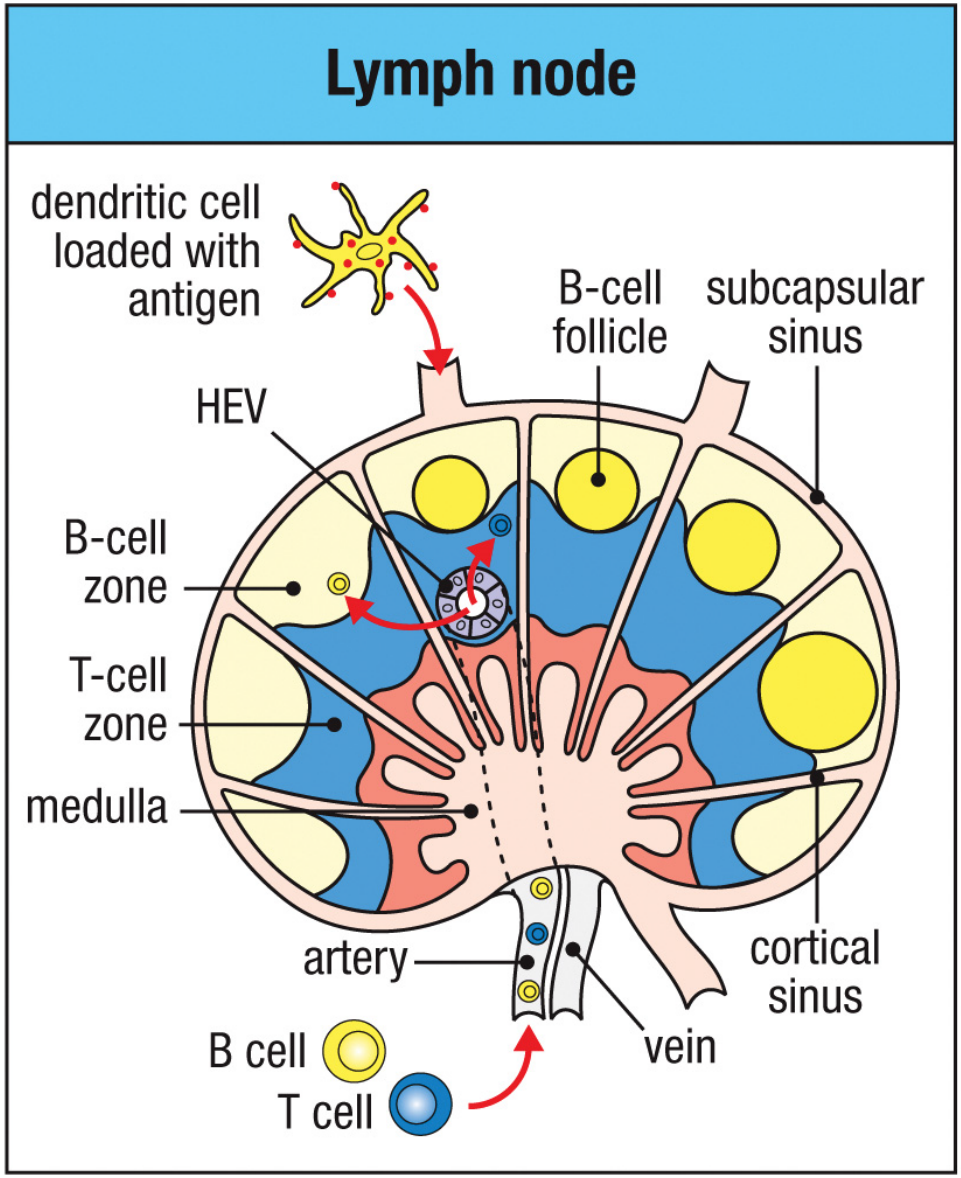
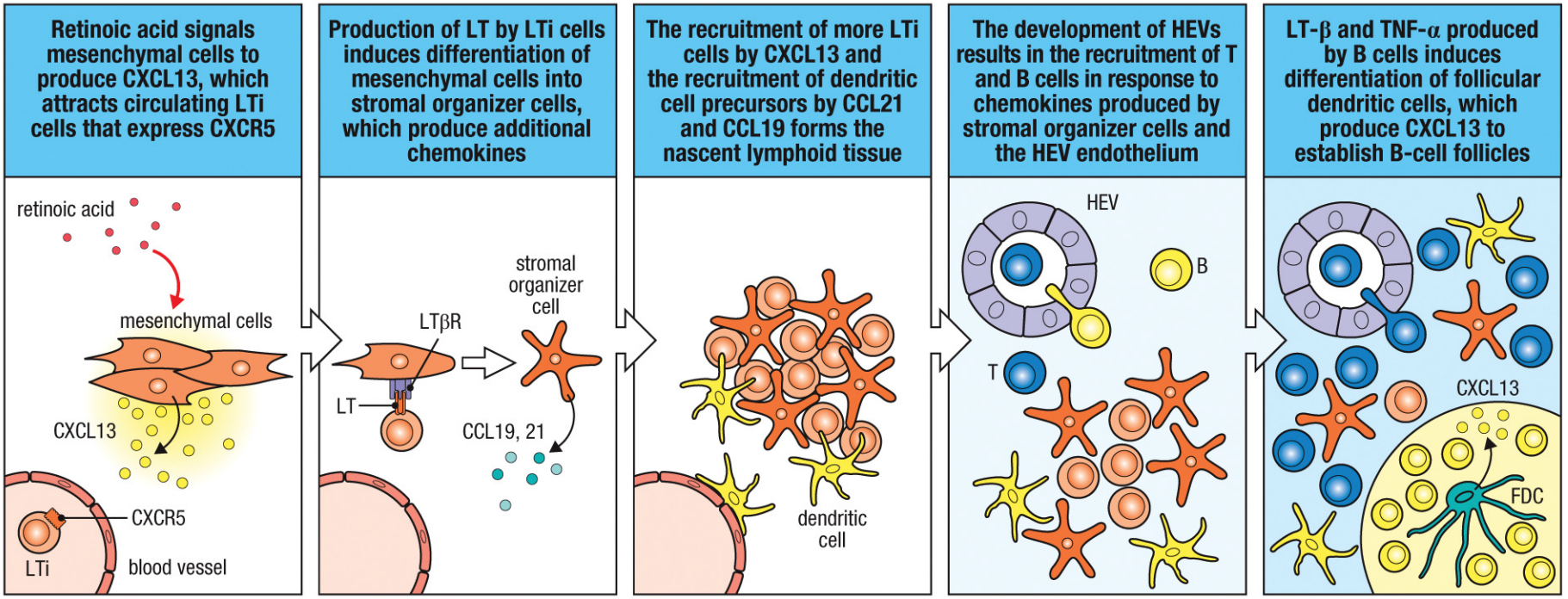


Figure 1.19 The Immune System, 3ed. (© Garland Science 2009)

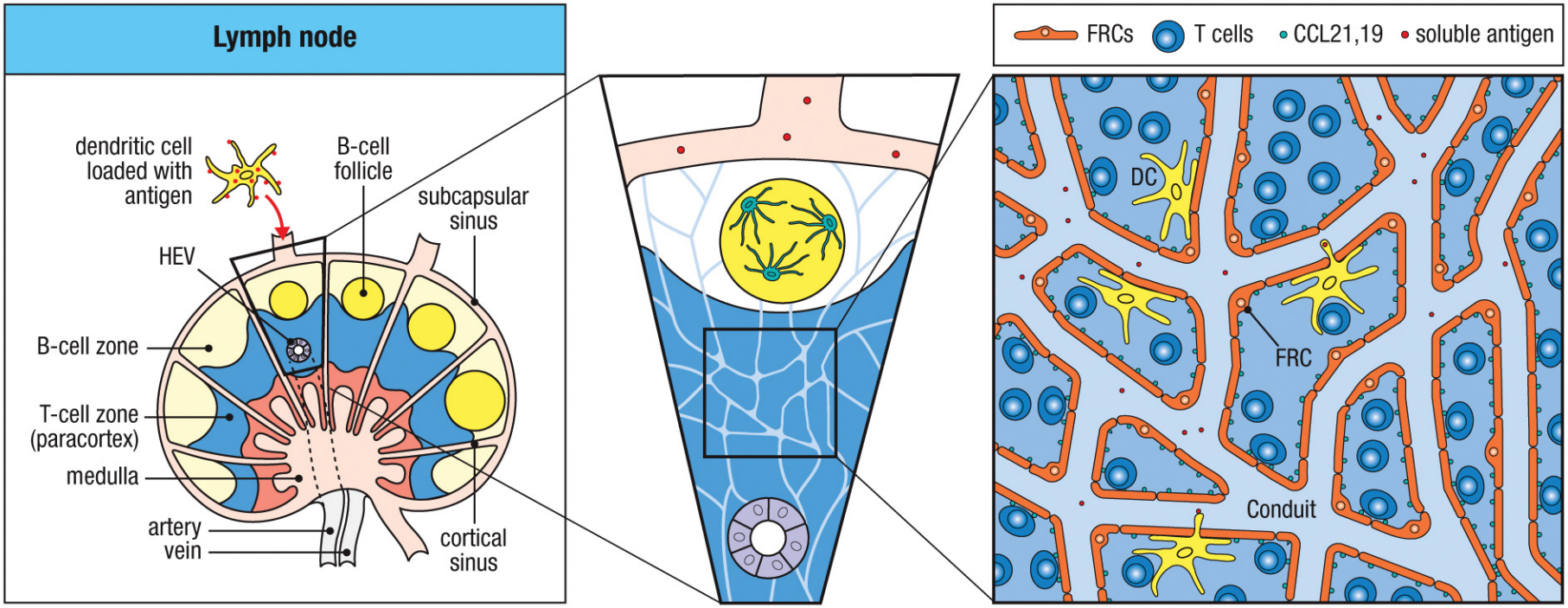
Organization of a Lymph Node



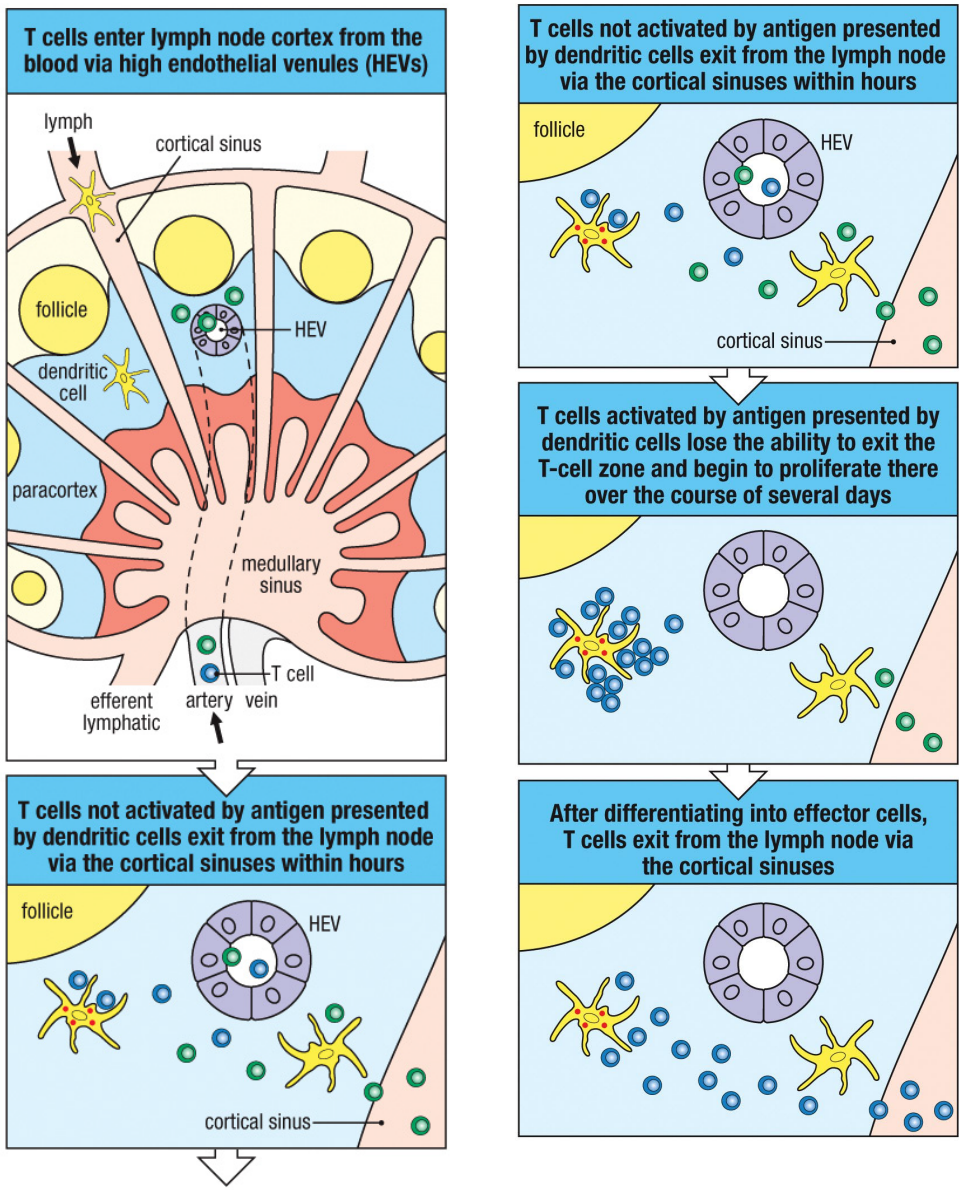
Lymphoid Tissue Inducer (LTi) Cells and Stromal Cells



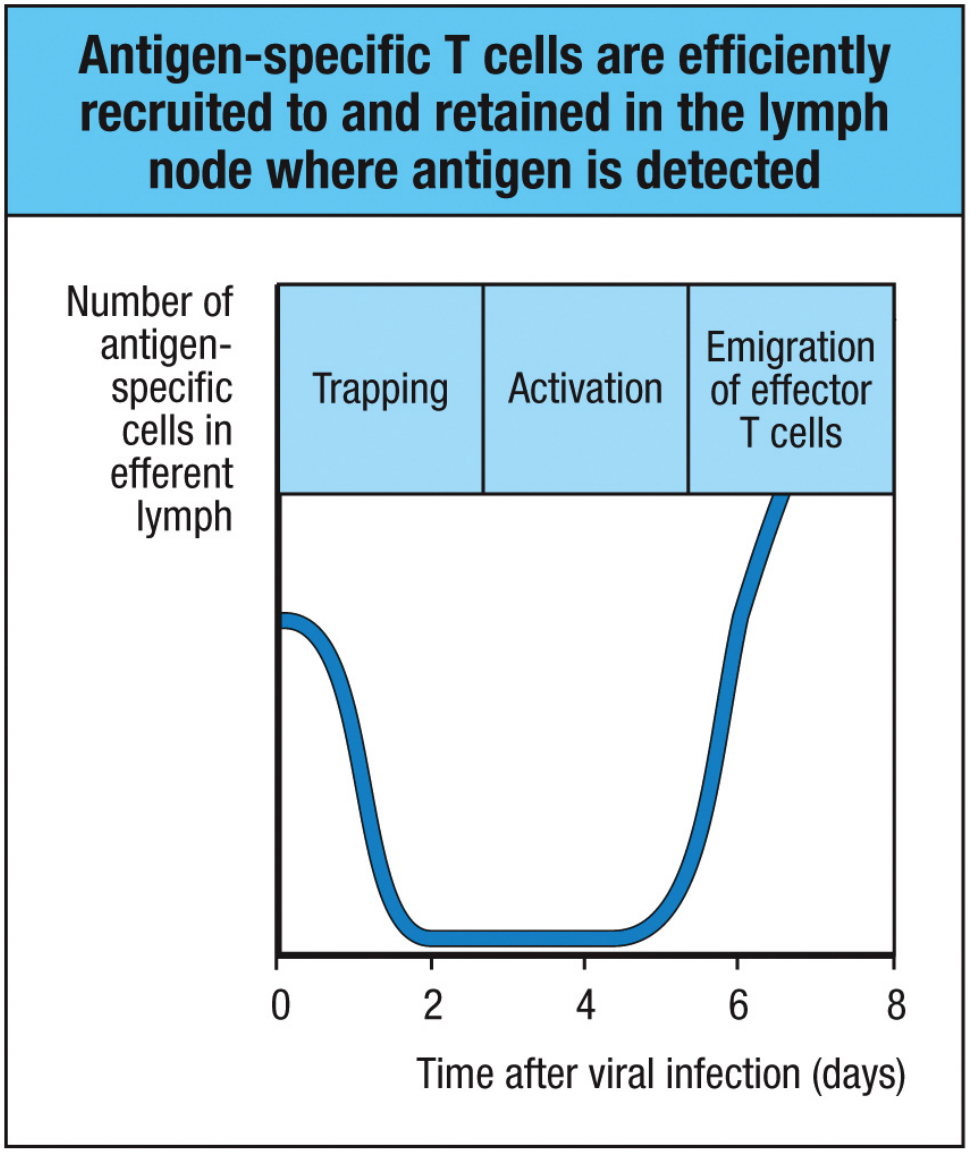
Fibroblast Reticular Cells Facilitate Interactions



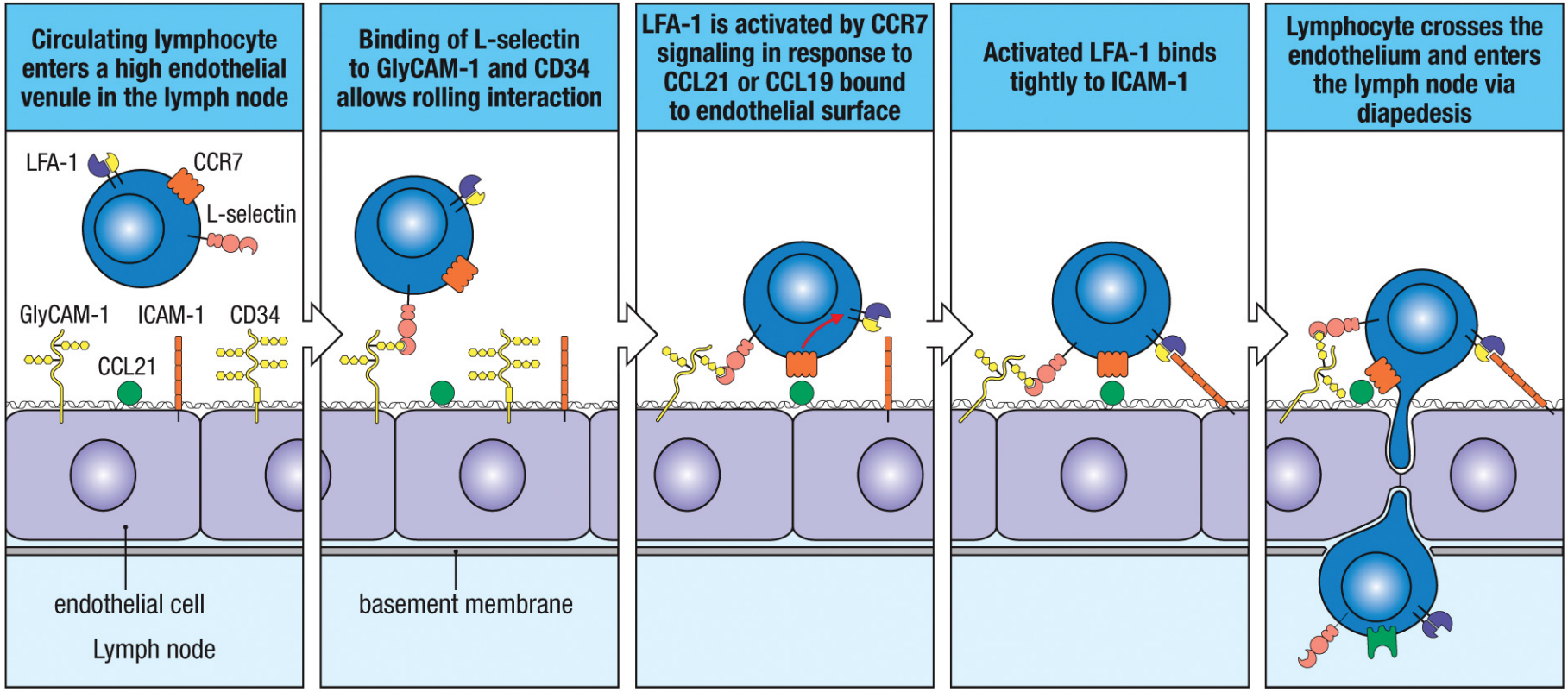
Naïve T-Cells Encounter Antigen During Recirculation Through Peripheral Lymphoid Organs



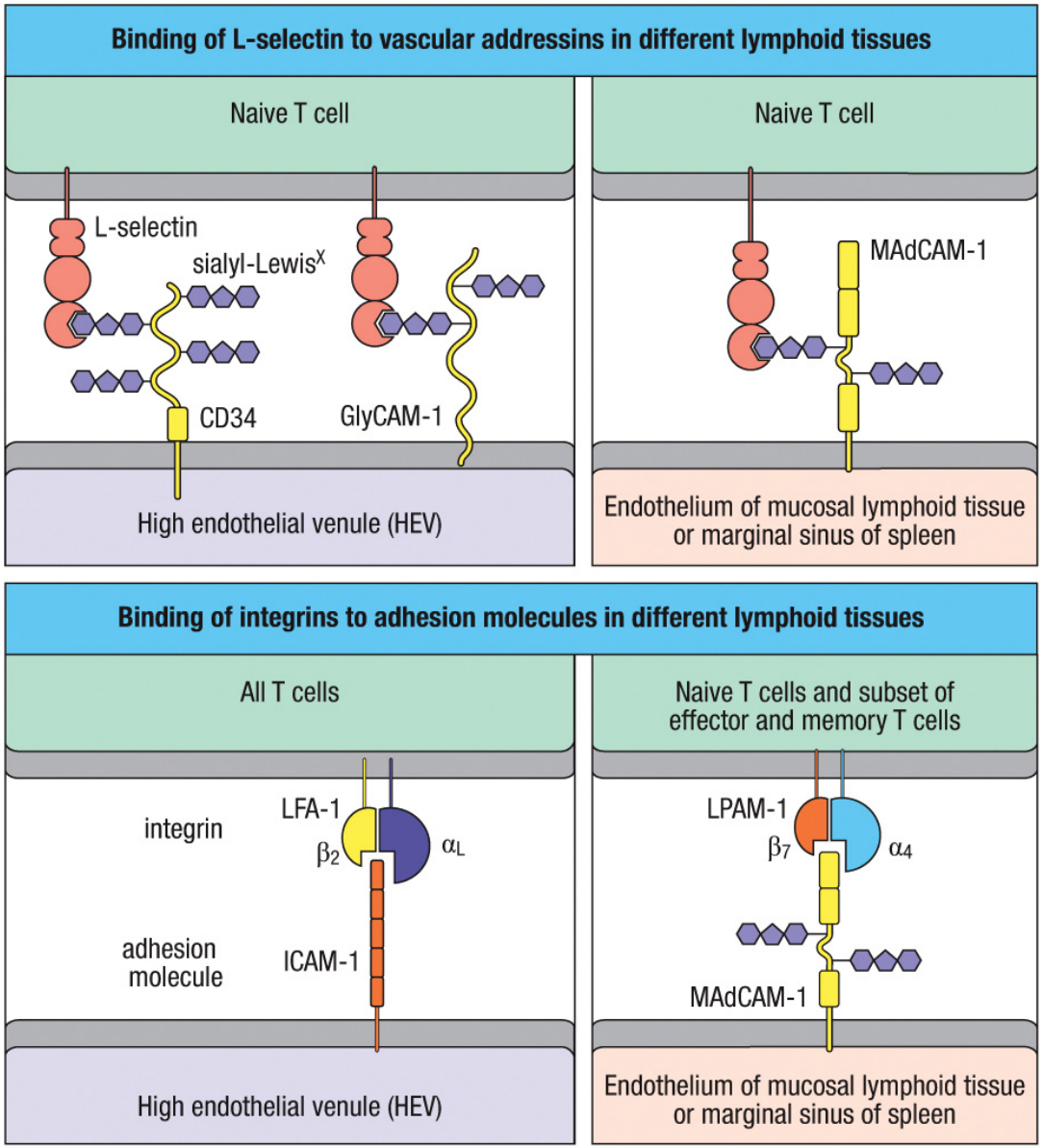
Antigen-Specific T-Cells Are Trapped in Lymphoid Tissues



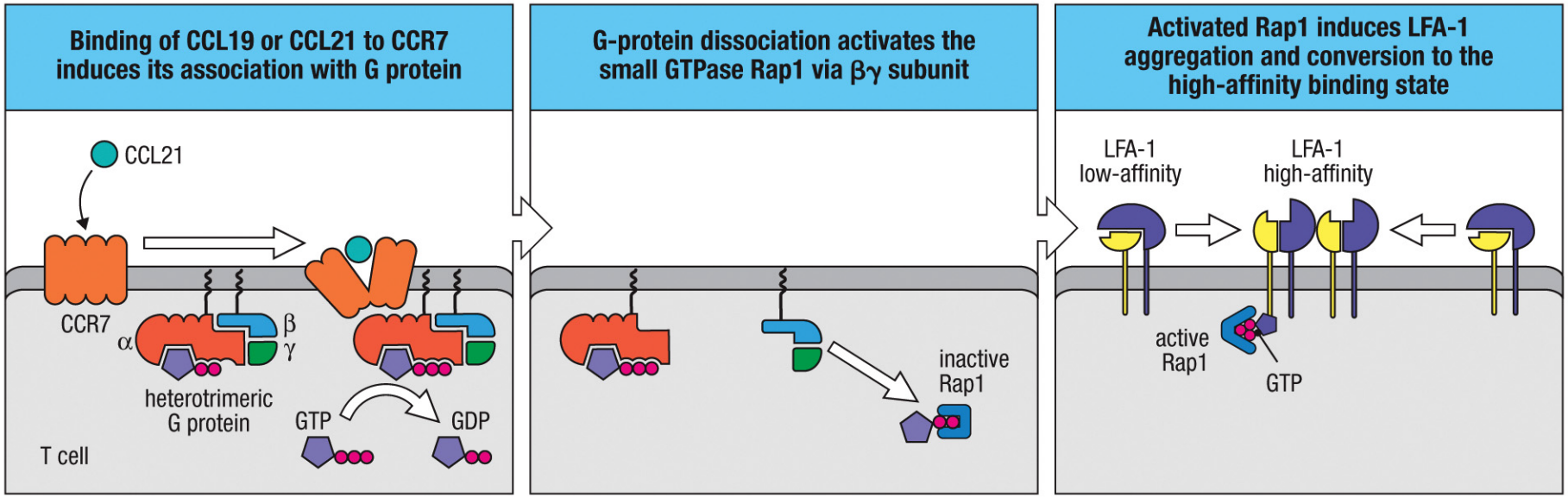
Lymphocytes Enter the Tissues Through HEVs



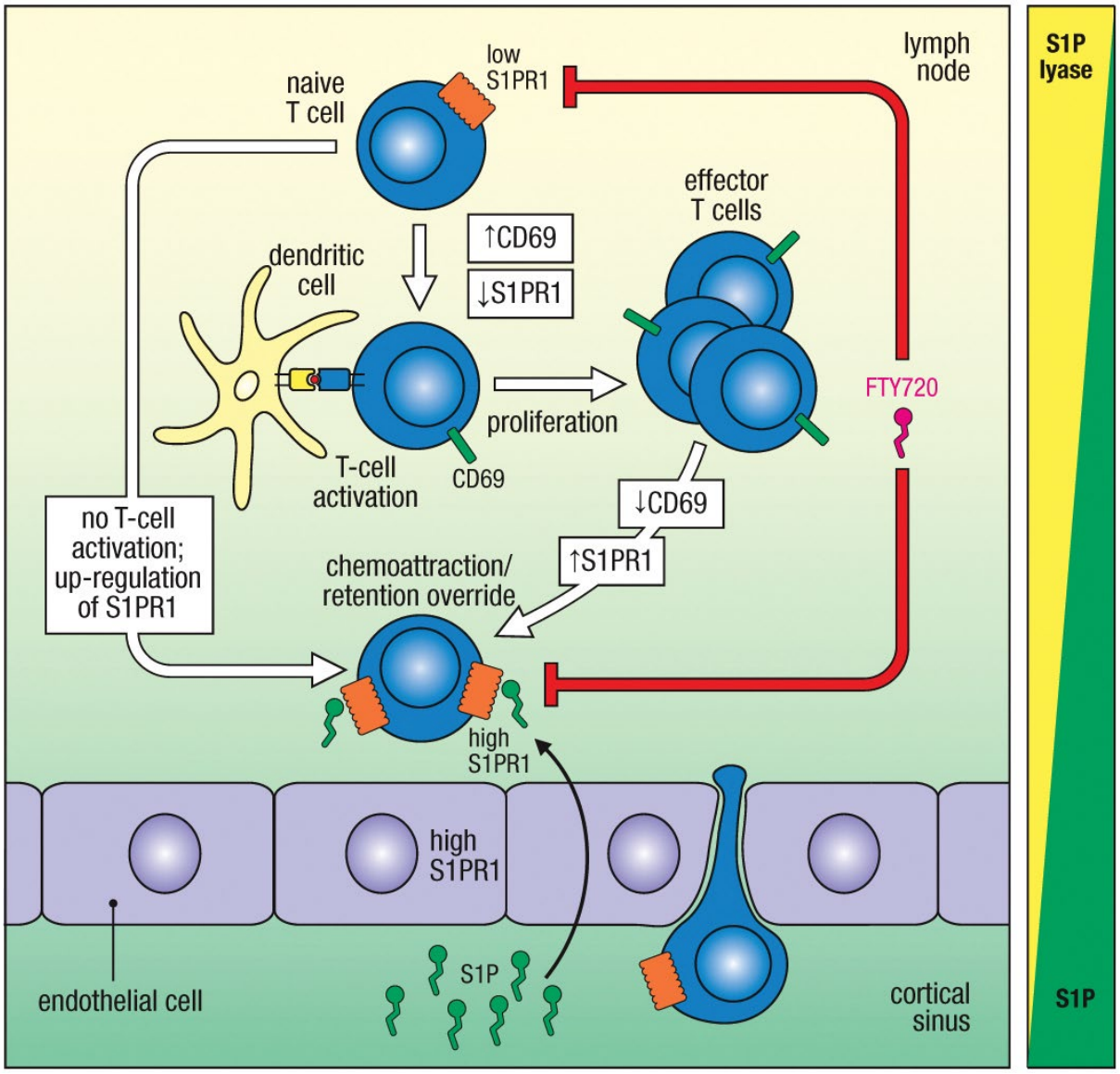
Activation of integrins by chemokines is responsible for the entry of naive T cells into lymph nodes



Activation of Integrins by Chemokines



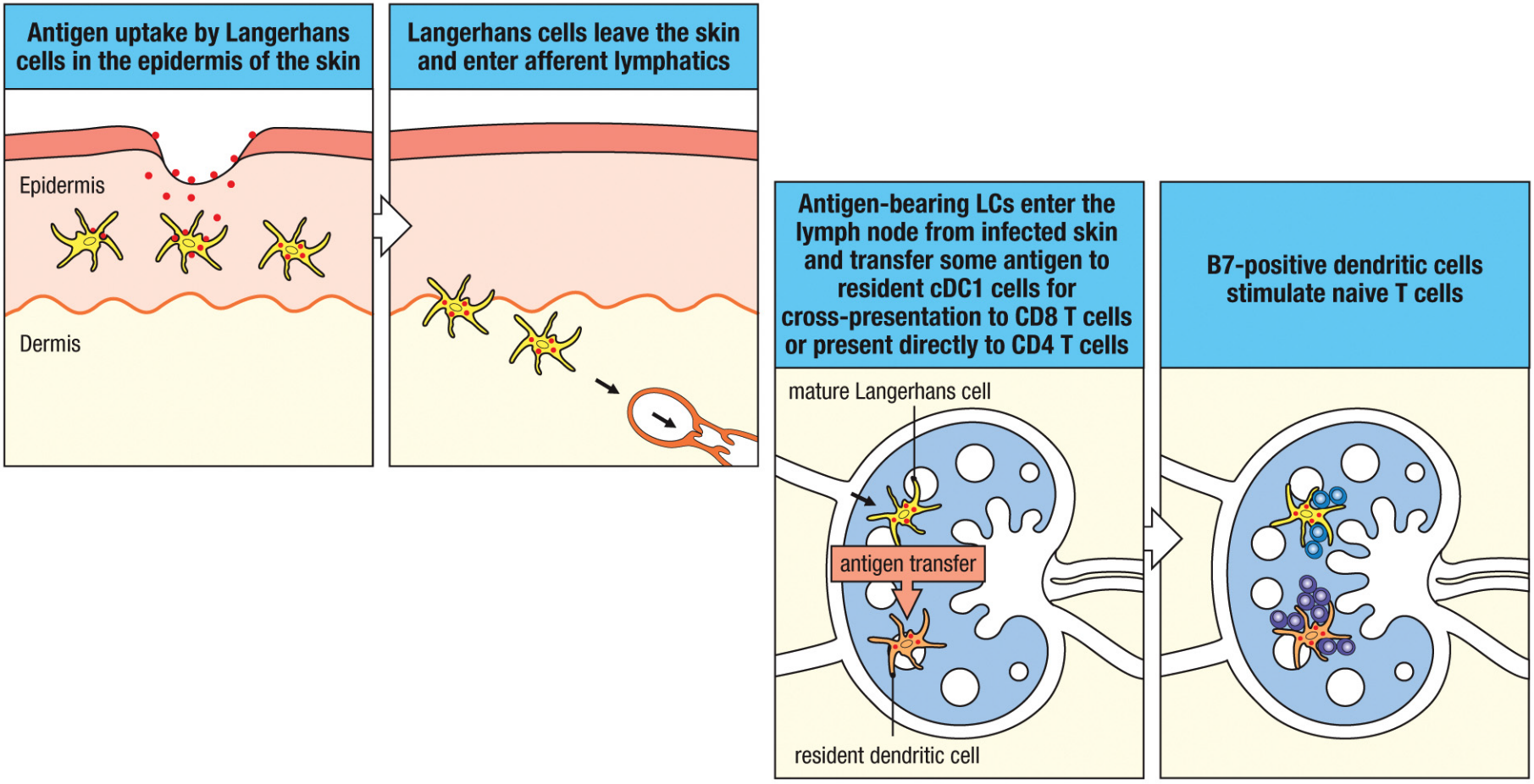
Egress of Lymphocytes



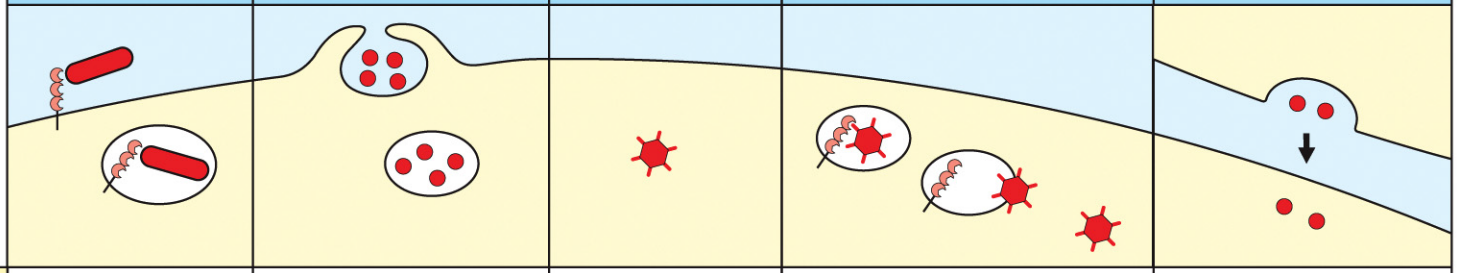
Outline

- T cell mediated immunity
  - T cell recruitment
  - Antigen presentation
  - T cell priming
- T cell signaling

DCs Carry Antigens From the Site of Infection to Secondary Lymphoid Tissues

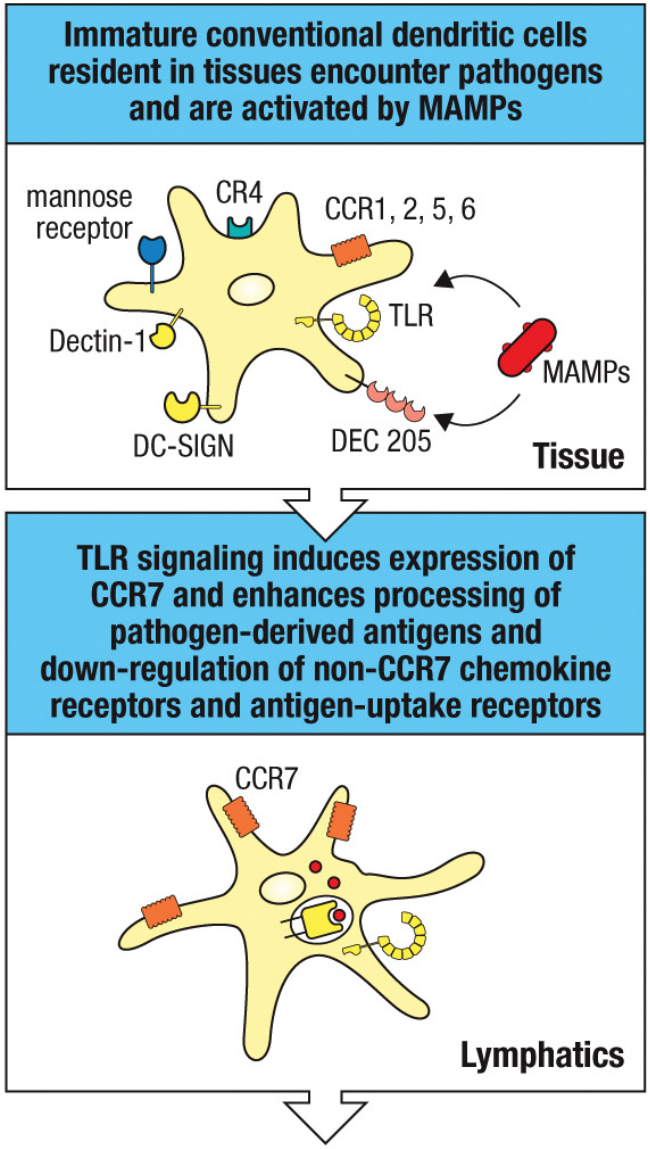


Dendritic Cells Present Protein Antigen

	Routes of antigen processing and presentation by dendritic cells				
	Receptor-mediated phagocytosis	**Macropinocytosis**	**Viral infection**	**Cross-presentation after phagocytic or macropinocytic uptake**	**Transfer from incoming dendritic acell to resident dendritic cell**
					
Type of pathogen presented	Extracellular bacteria, fungi	Extracellular bacteria, soluble antigens, virus particles	Viruses	Viruses	Viruses
MHC molecules loaded	MHC class II	MHC class II	MHC class I	MHC class I	MHC class I, MHC class II
Type of naive T cell activated	CD4 T cells	CD4 T cells	CD8 T cells	CD8 T cells	CD8 T cells, CD4 T cellls

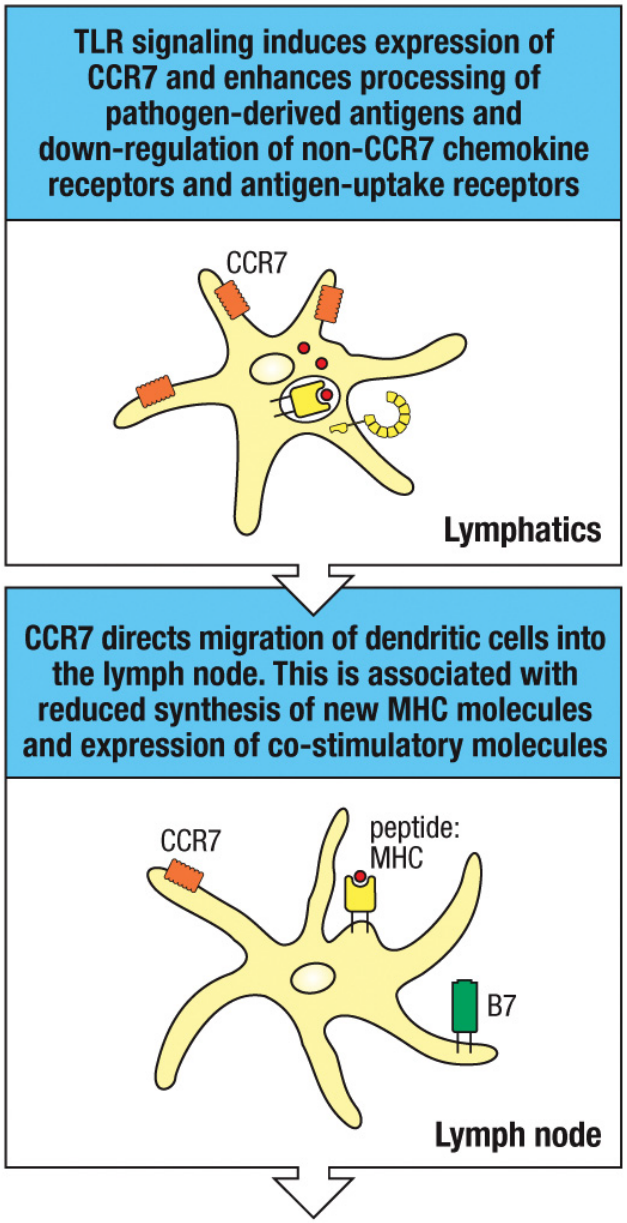
Dendritic cells are not necessarily infected, but they need to display viral antigen

Stages of Dendritic Cell Maturation



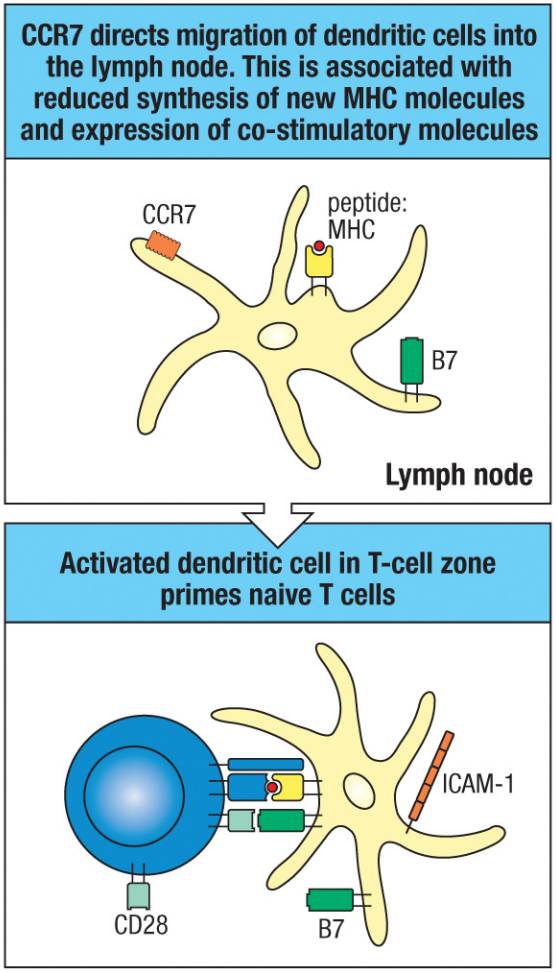
Licensing
CCR7: a chemokine receptor

Stages of Dendritic Cell Maturation



B7: co-stimulation

Stages of Dendritic Cell Maturation



Stages of DC Maturation

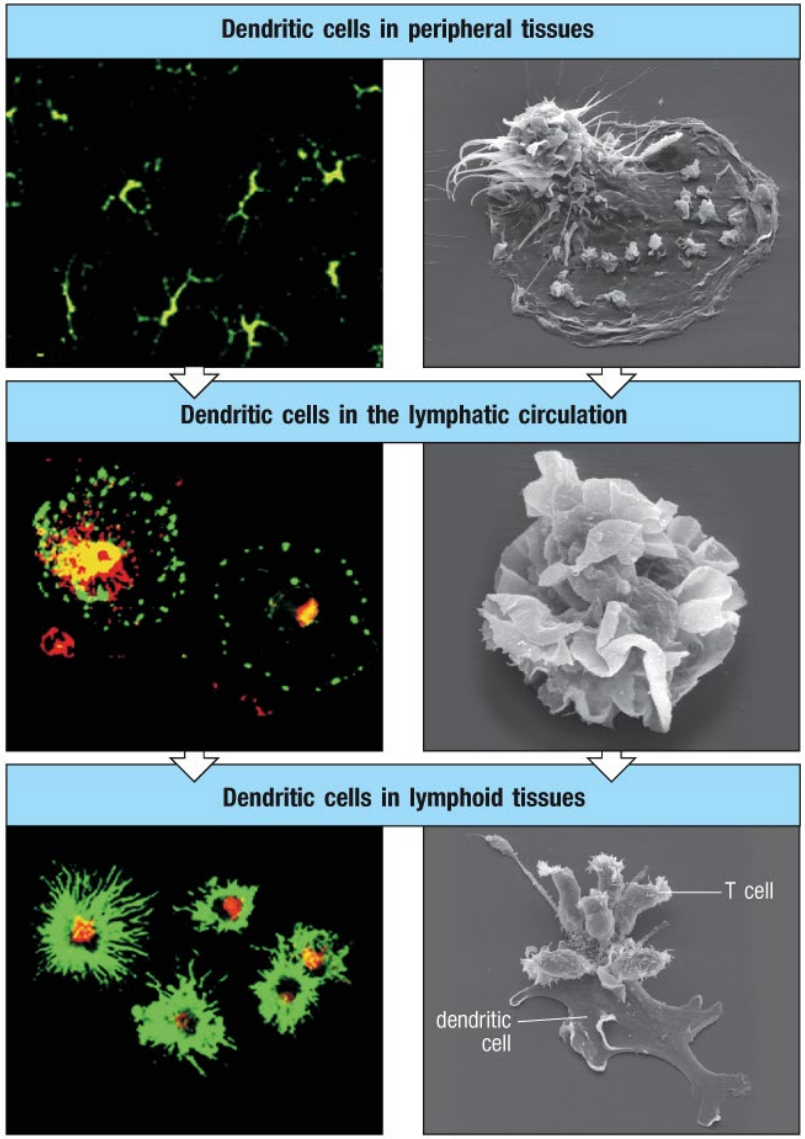


Figure 9.12 Janeway's Immunobiology, 9th ed. (© Garland Science 2017)

Green: MHC II
Red: Lysosomes

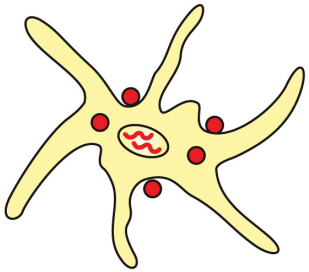
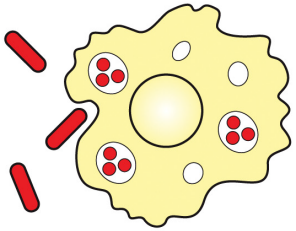
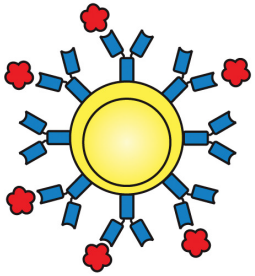
CCR7+

B7 and MHC

Question

- What are the three major surface changes of dendritic cells after antigen encounter? What are their functions?

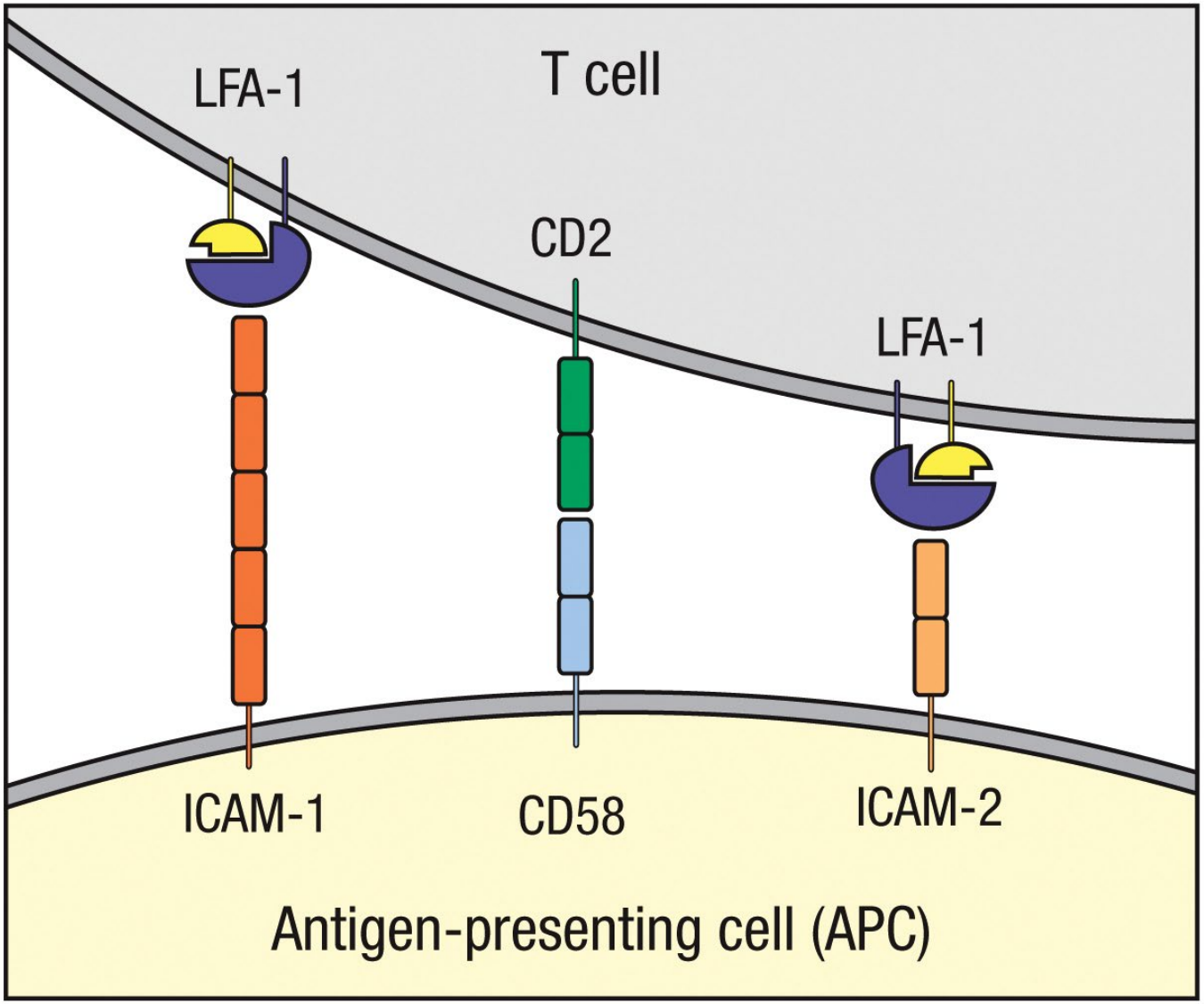
Properties of Antigen Presenting Cells

	Dendritic cells	Macrophages	B cells
			
Antigen uptake	+++ Macropinocytosis and phagocytosis by tissue dendritic cells	+++ Macropinocytosis +++ Phagocytosis	Antigen-specific receptor (Ig) ++++
MHC expression	Low on immature dendritic cells High on dendritic cells in lymphoid tissues	Inducible by bacteria and cytokines – to +++	Constitutive Increases on activation +++ to ++++
Co-stimulation delivery	Constitutive by mature, nonphagocytic lymphoid dendritic cells ++++	Inducible – to +++	Inducible – to +++
Location	Ubiquitous throughout the body	Lymphoid tissue Connective tissue Body cavities	Lymphoid tissue Peripheral blood
Effect	Results in activation of naive T cells	Results in activation of macrophages by effector and memory T cells	Results in delivery of help to B cell by T_{FH} cells

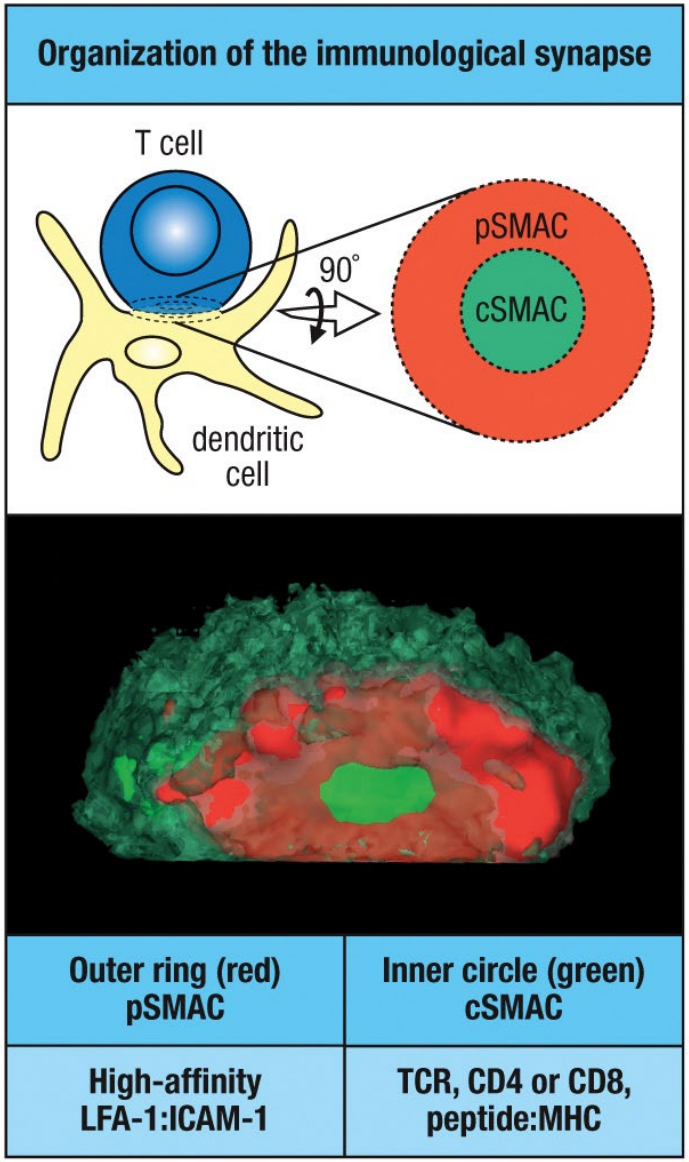
Outline

- T cell mediated immunity
  - T cell recruitment
  - Antigen presentation
  - T cell priming
- T cell signaling

T Cell Activation Requires Prolonged Interaction with APC

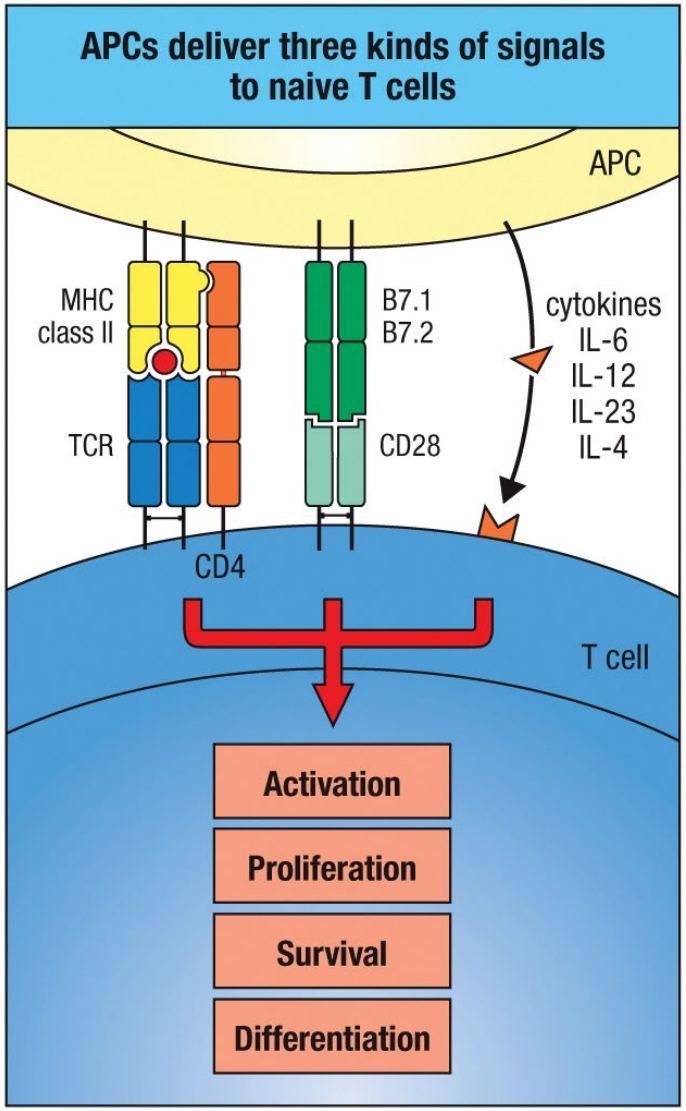


Immunological Synapse



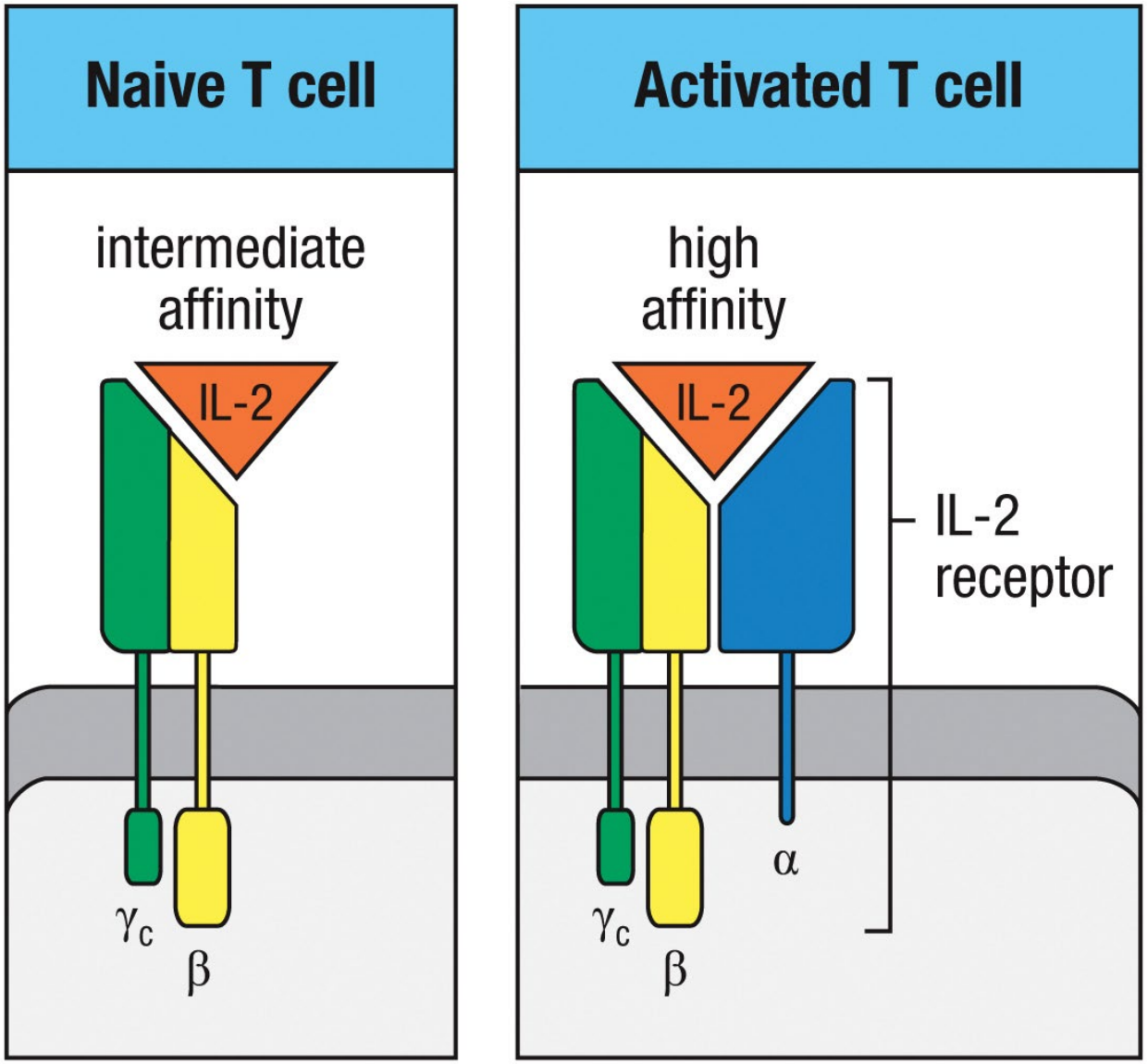
Photograph courtesy of Avi Kupfer

Activation of Naïve T Cells

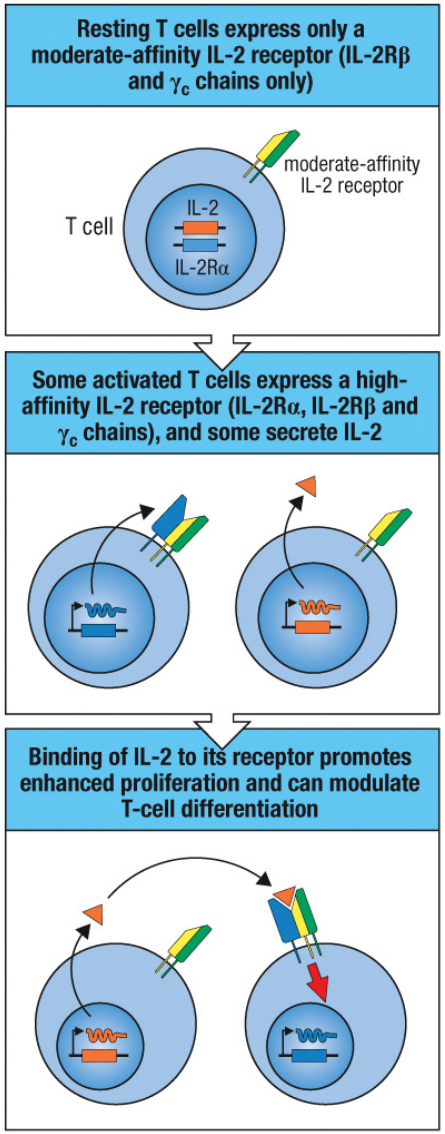


The cytokines are extremely important in T cell subtype development

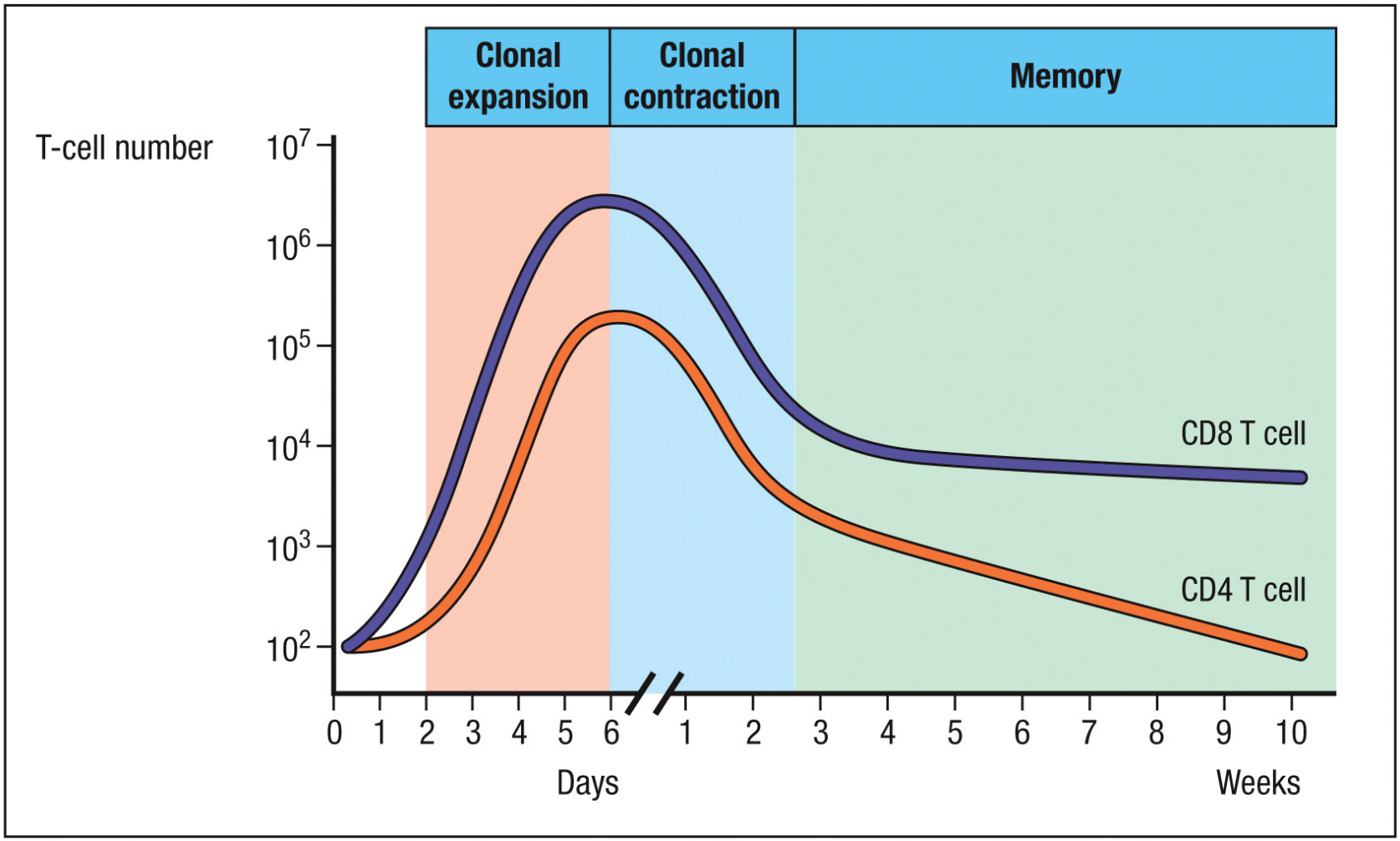
IL-2 Promotes Cell Growth and Differentiation



Activated T Cells Secret and Respond to IL-2



Clonal Expansion and Contraction



Question

- What are the three signals for T cell priming?
- Can you draw it?

Question

- Which cytokine is most important in T-cell activation?

  A) IL-2

  B) IL-4

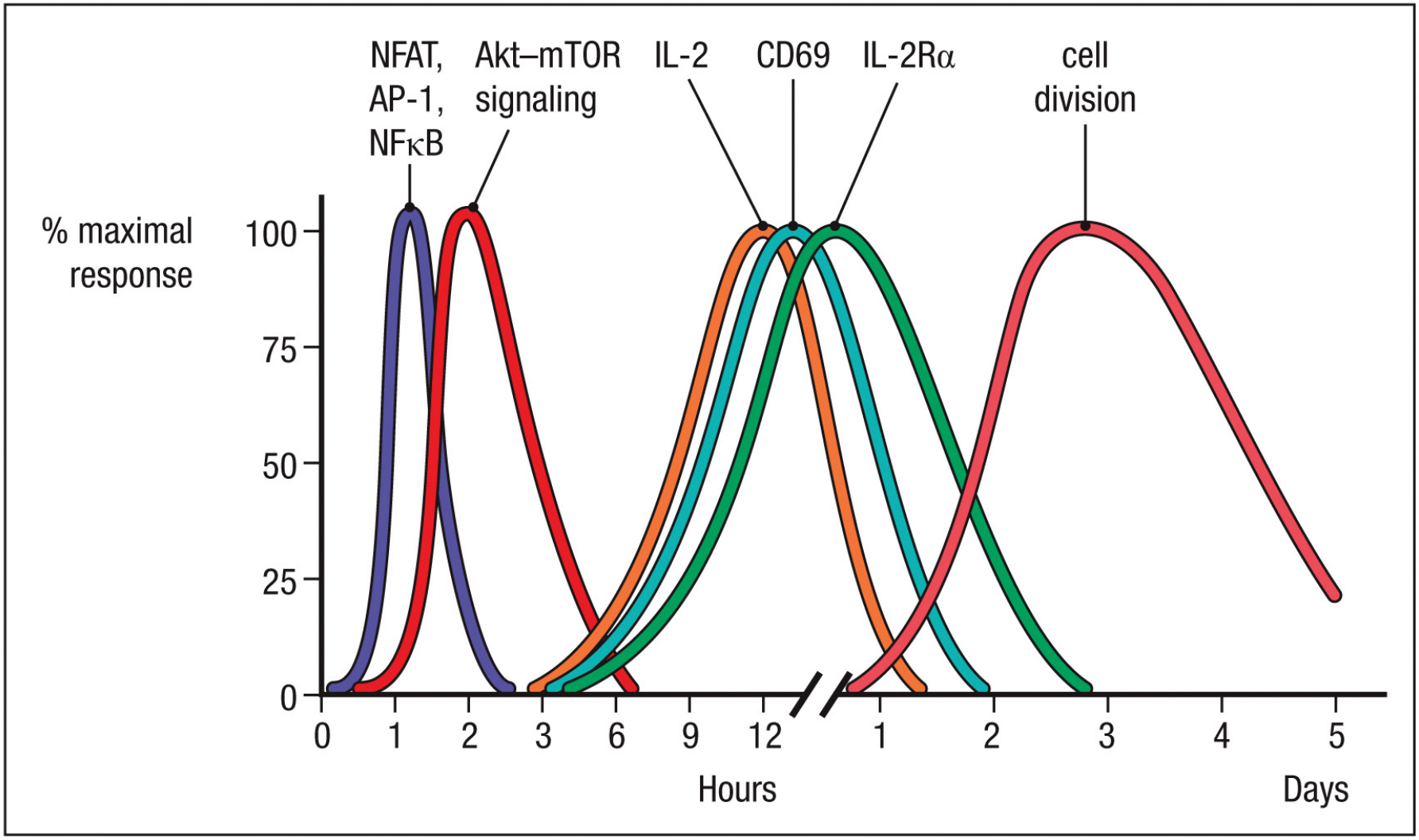
  C) IL-8

  D) IL-10

Outline

- T cell mediated immunity
  - T cell recruitment
  - Antigen presentation
  - T cell priming
- T cell signaling

Cell Signalling in Clonal Expansion



Requirement of Both Signals

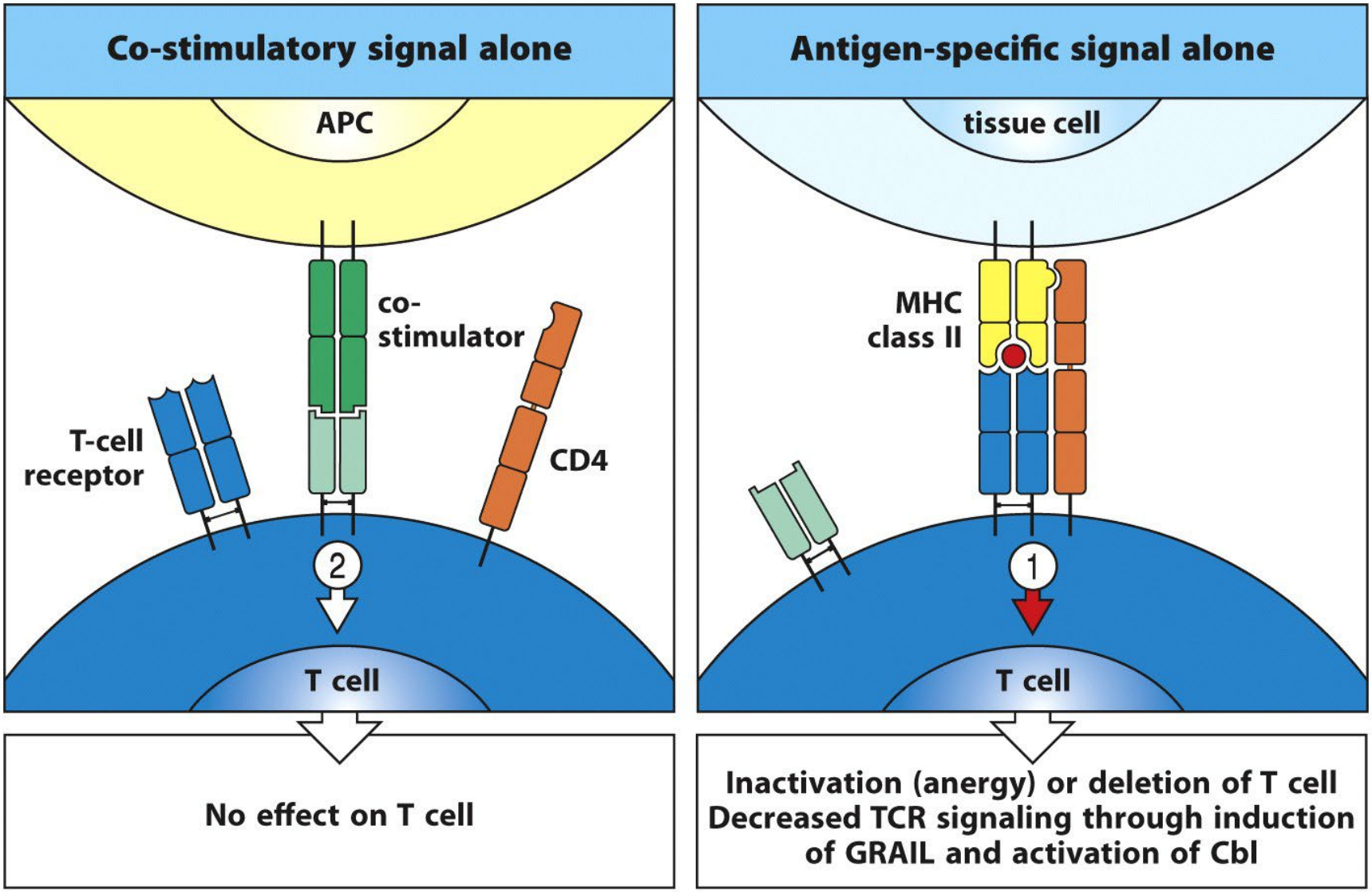
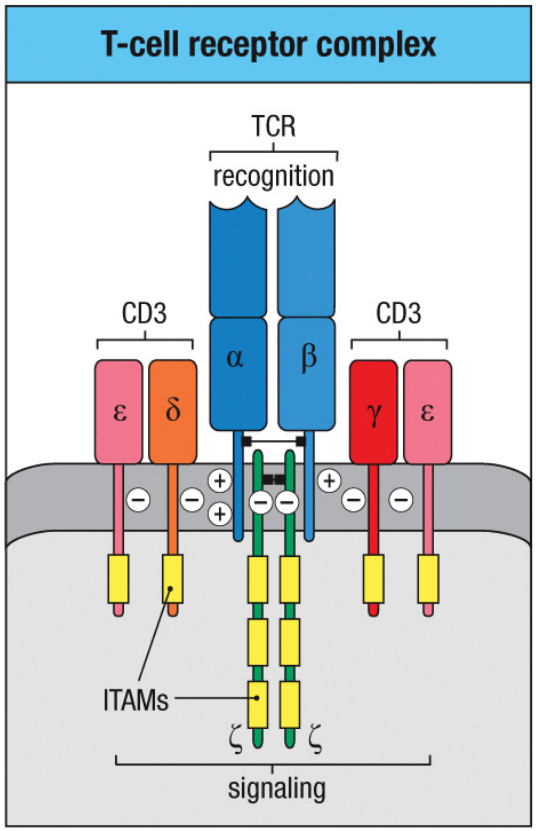
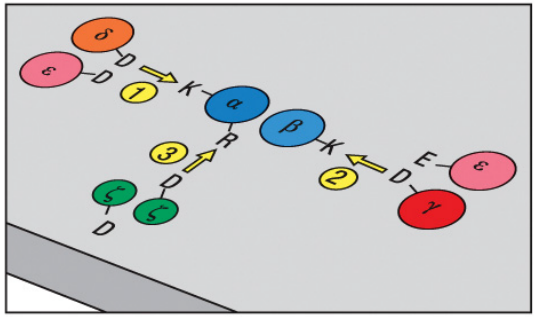


Figure 9.23 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

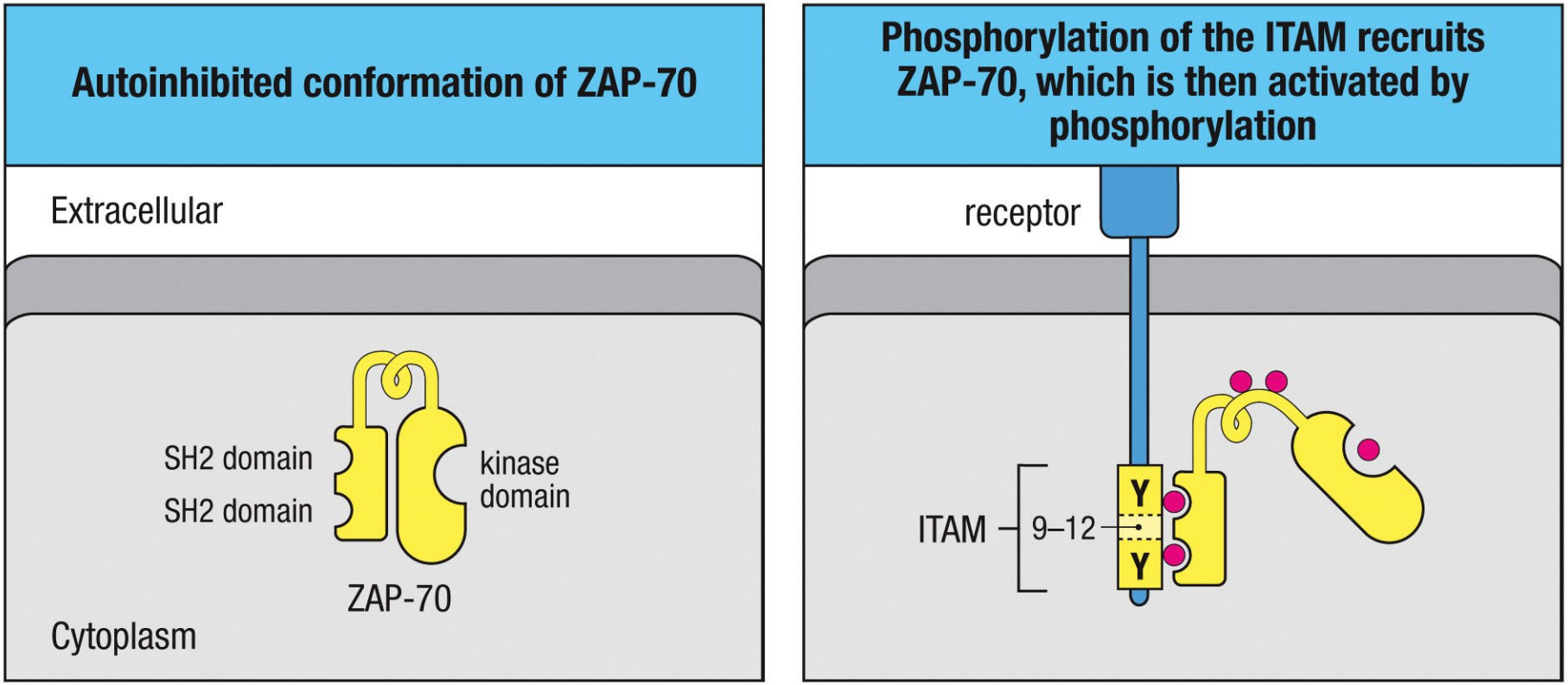
T Cell Receptor



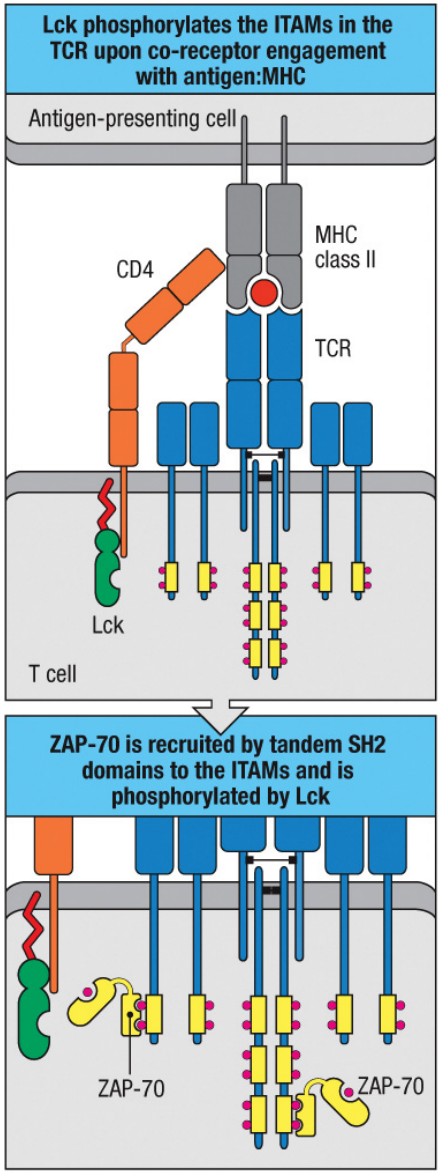


ITAMs: immuno-receptor tyrosine based activation motifs

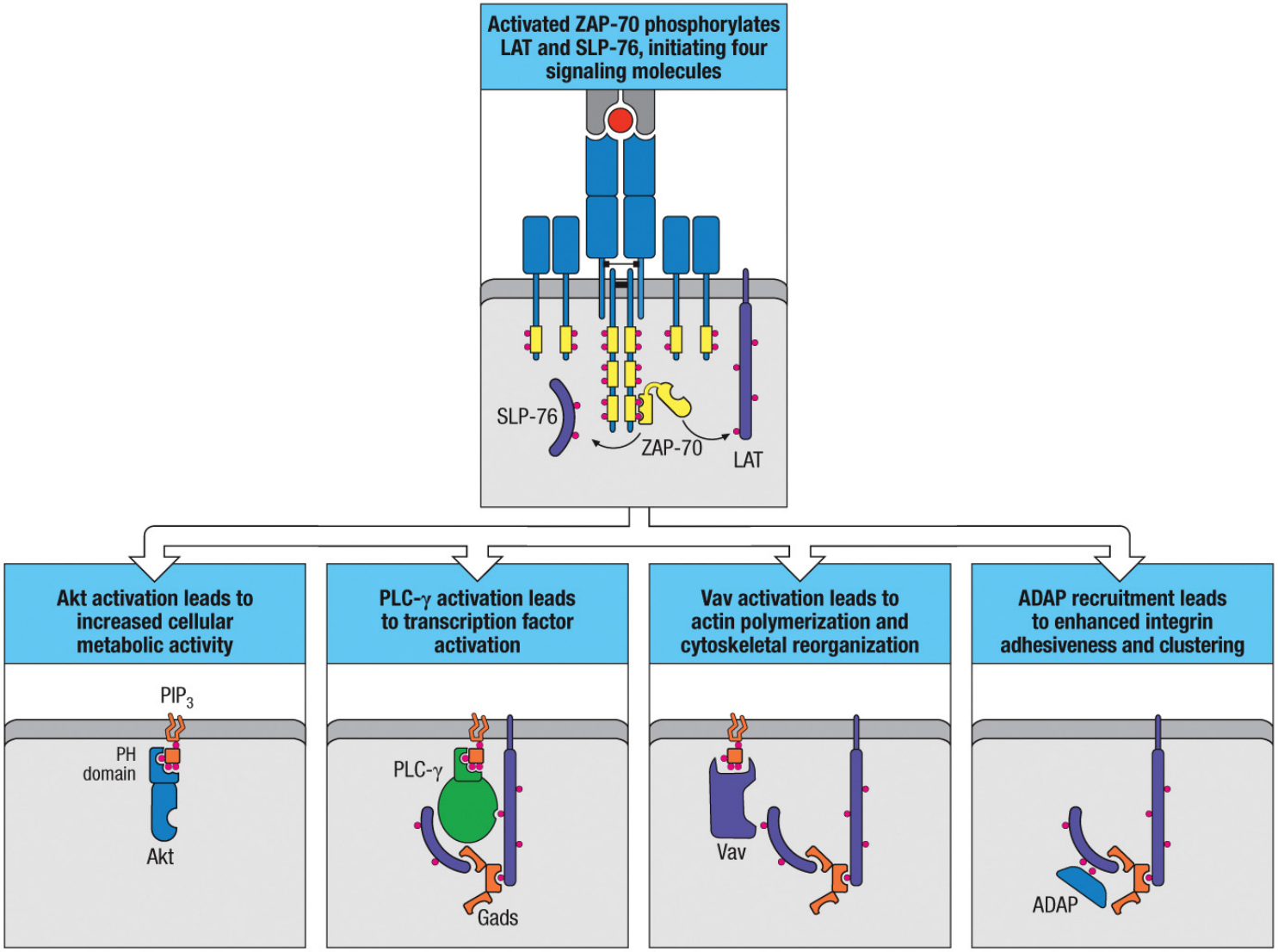
ITAMs Recruit ZAP-70



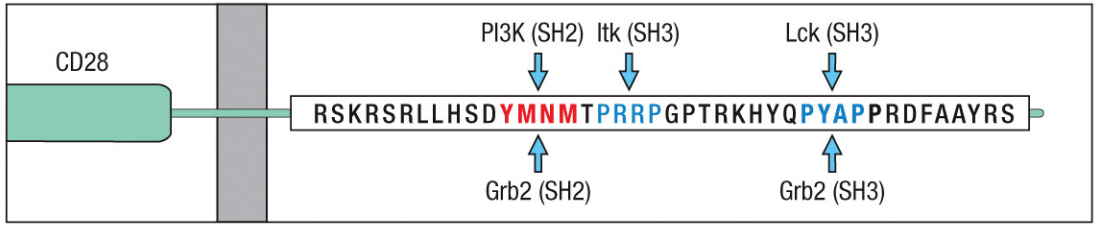
TCR Activates ZAP-70

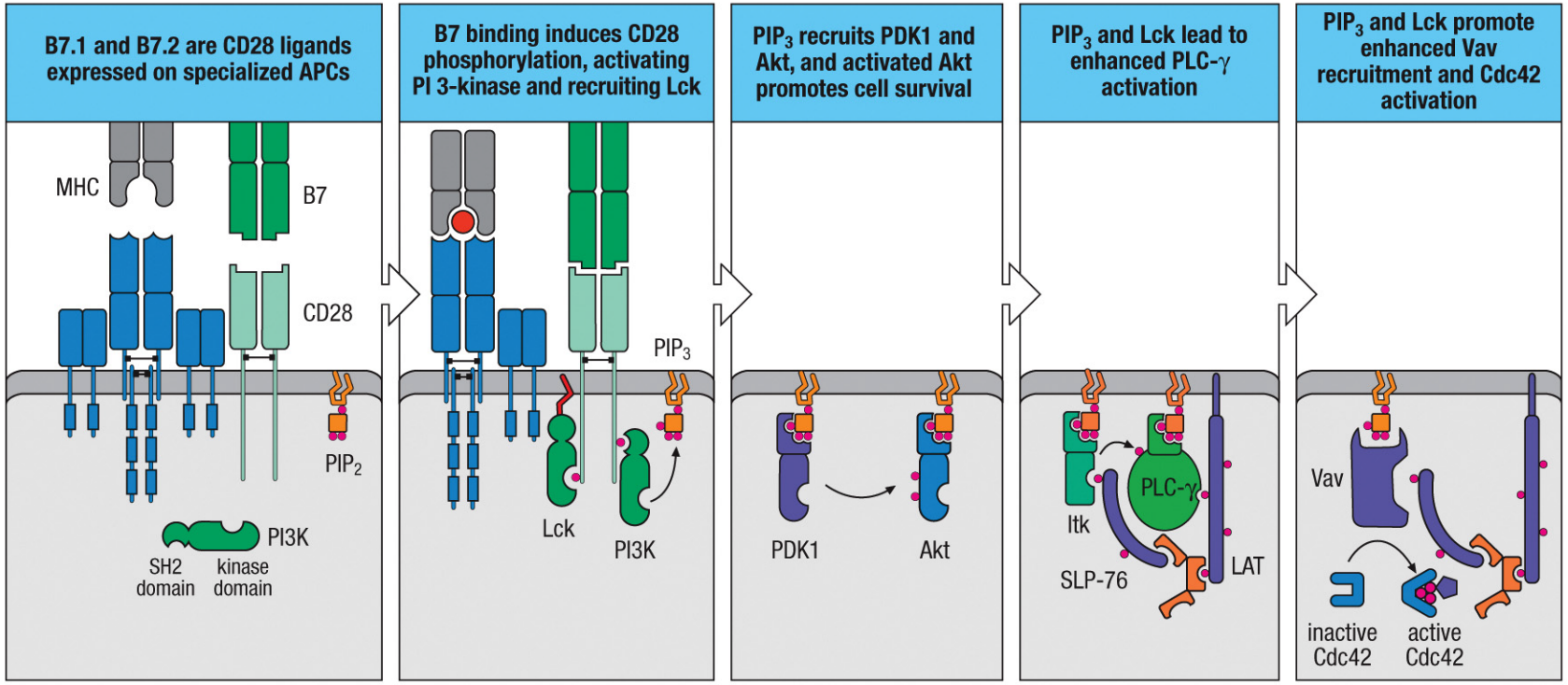


TCR Activates ZAP-70



Co-stimulation is Required for TCR Signaling





Complicated Signaling Cascades

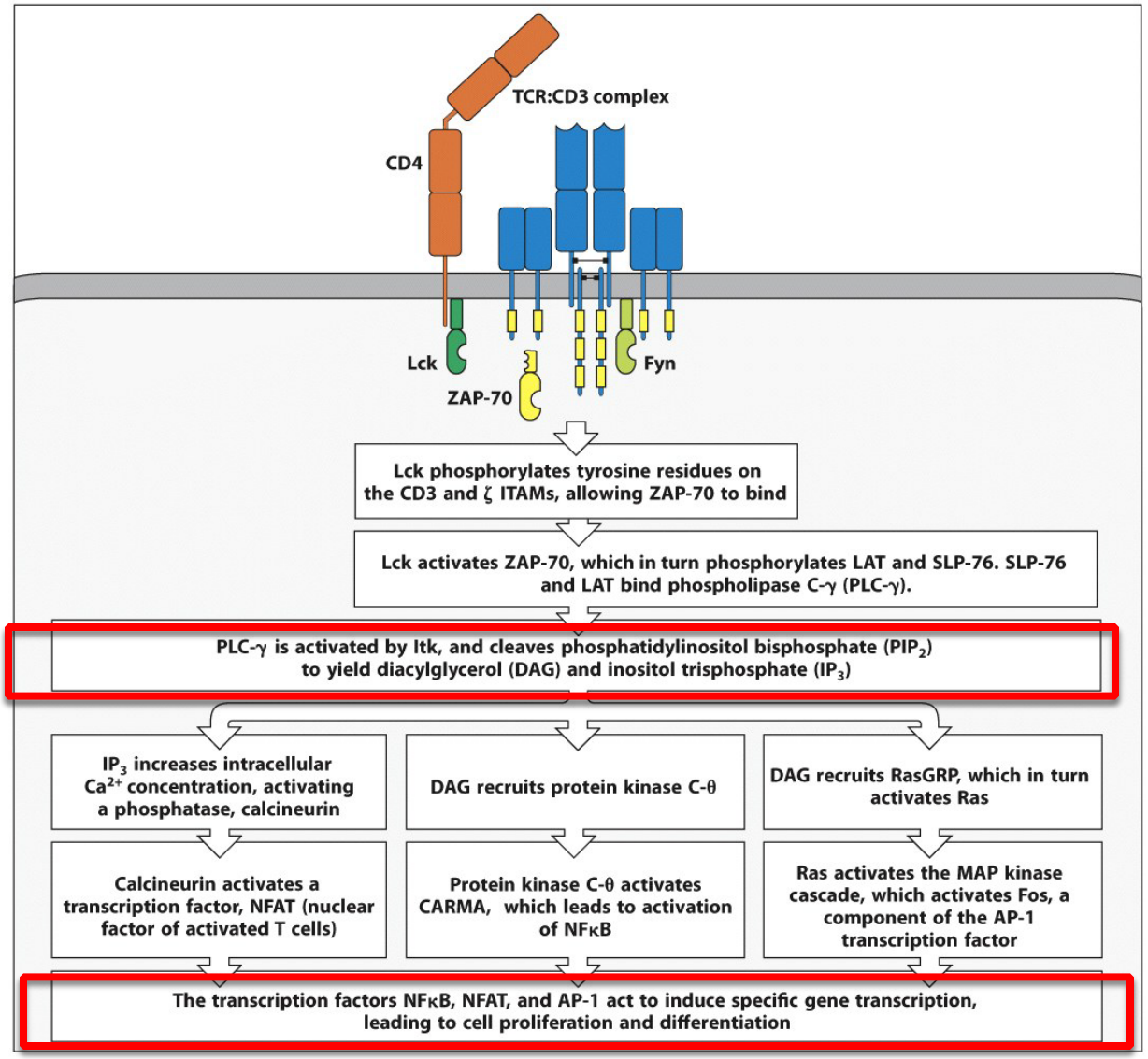
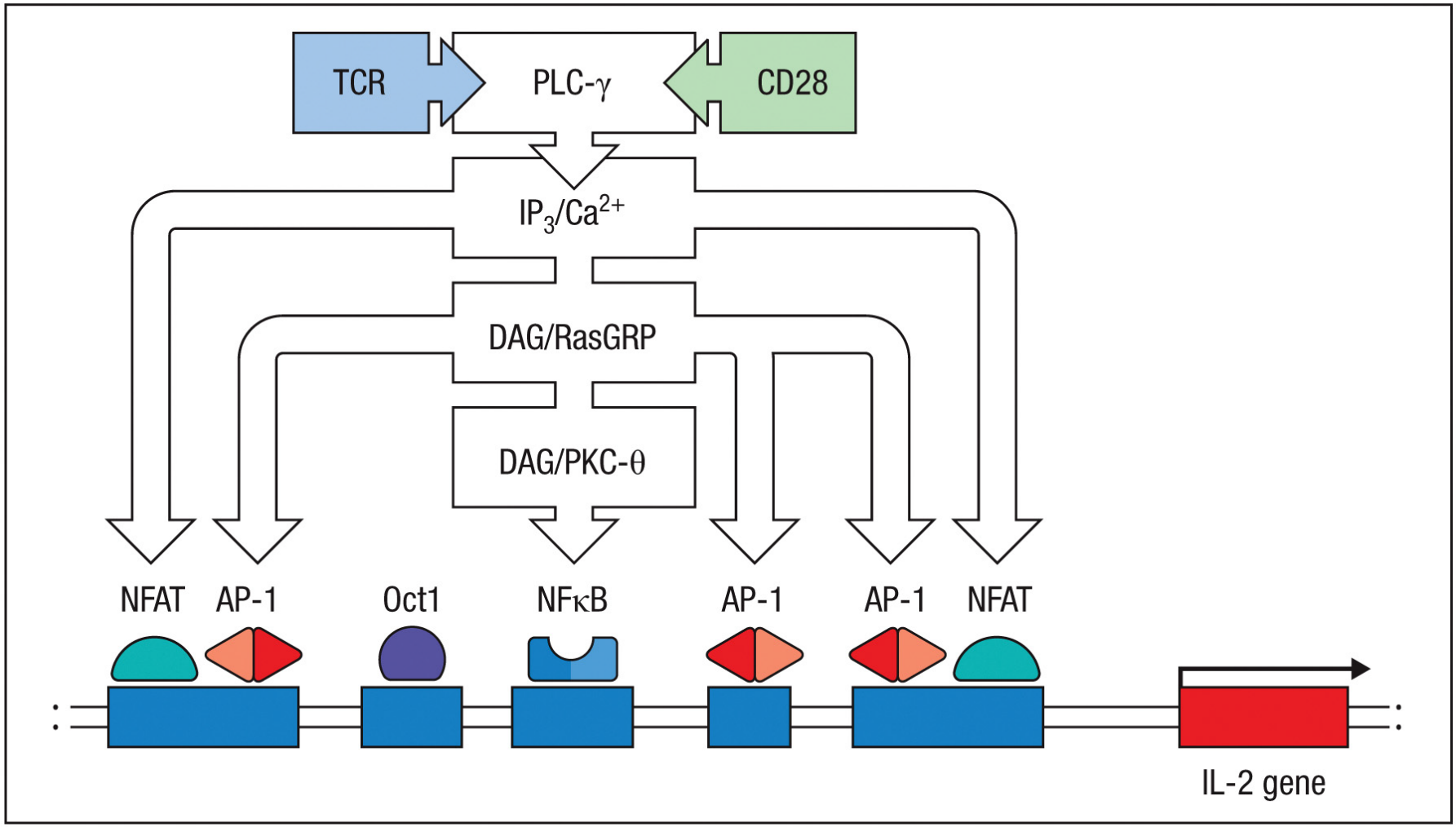
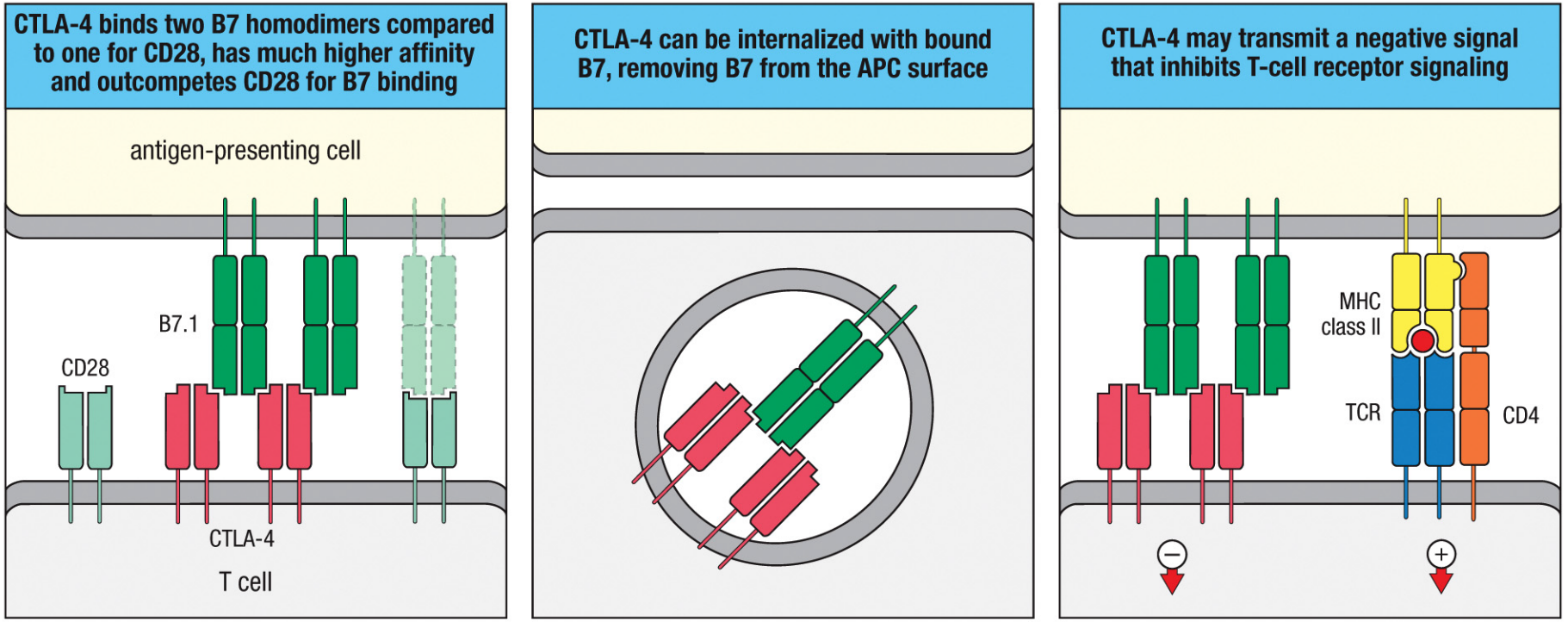


Figure 7.15 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

IL-2 Expression Requires Binding of All Transcription Factors



CTLA-4 Inhibits B7



Limit T cell proliferation after activation

Case Study: Wiskott-Aldrich Syndrome

- Patient:

  Male infant, Normally developed

  Recurrent infection

  Eczema, Asthma, Bloody diarrhea

  Autoimmmune hemolytic anemia

  Thrombocytomia with small platelets

  Poor antibody response

  Reduced T cell function
- Diagnosis:

  Wiskott-Aldrich Syndrome
- Treatment:

  Bone Marrow Transplantation and cured

Smaller Platelets

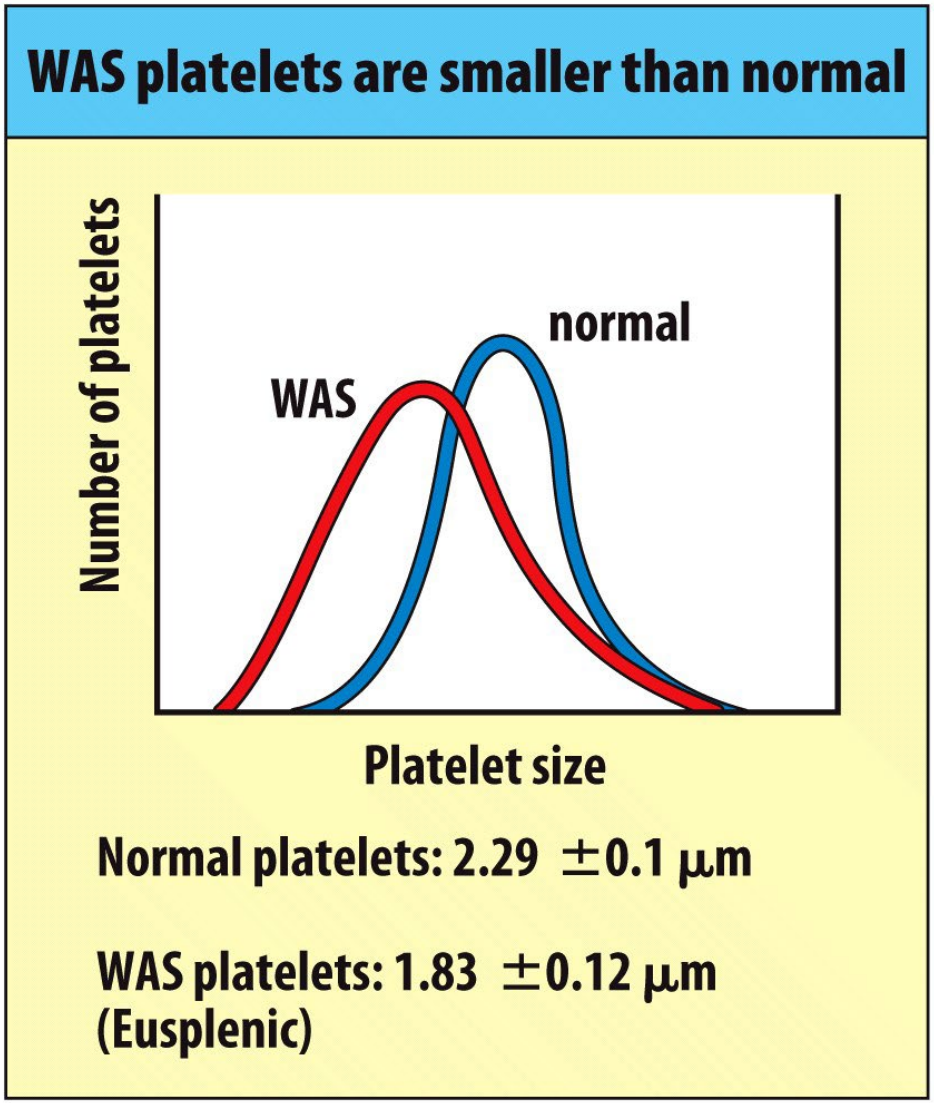


Figure 16.3 Case Studies in Immunology, 6ed. (© Garland Science 2012)

Impaired T-cell capping

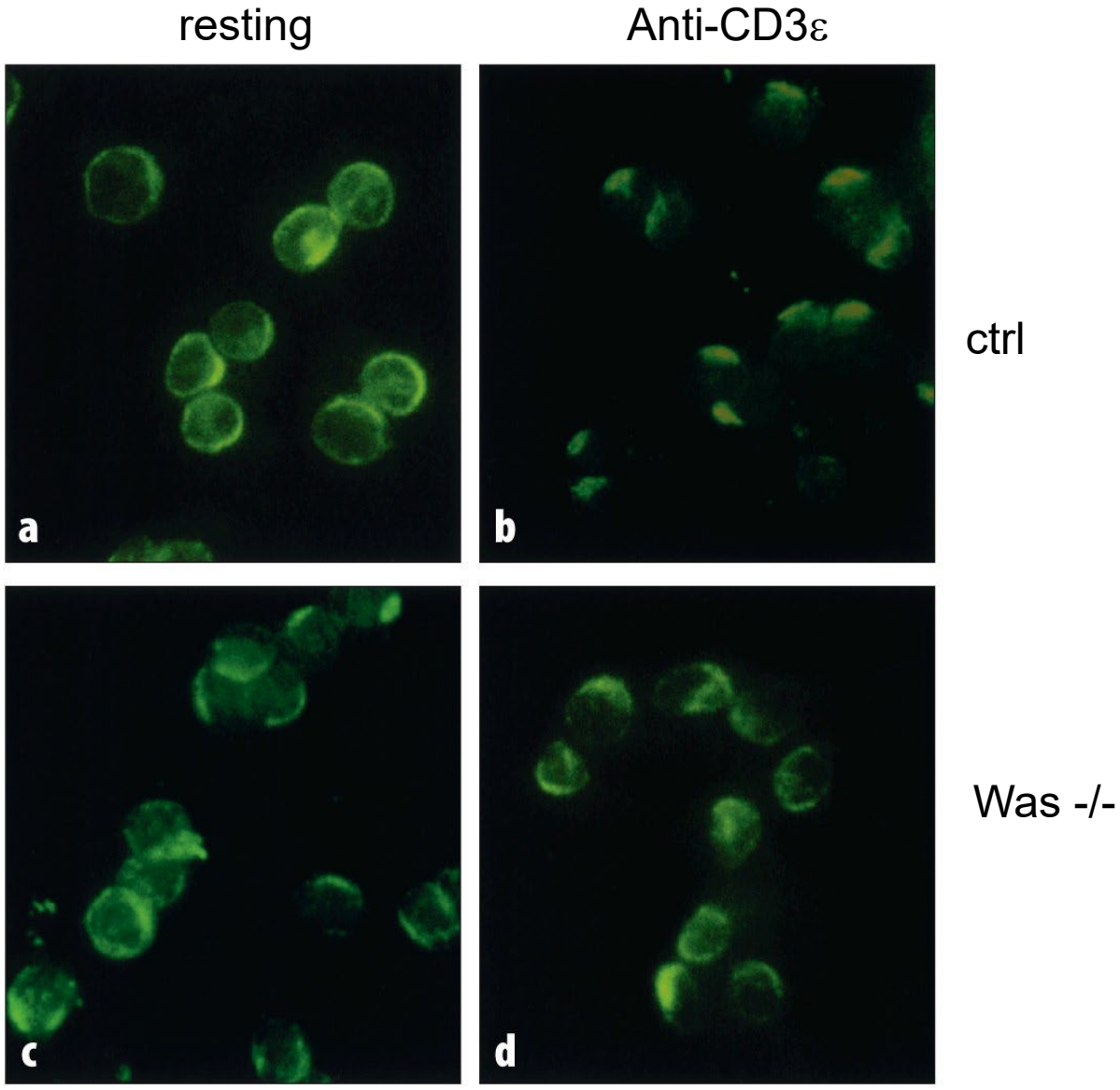


Figure 16.7 Case Studies in Immunology, 6ed. (© Garland Science 2012)

WASP is required for Actin Organization

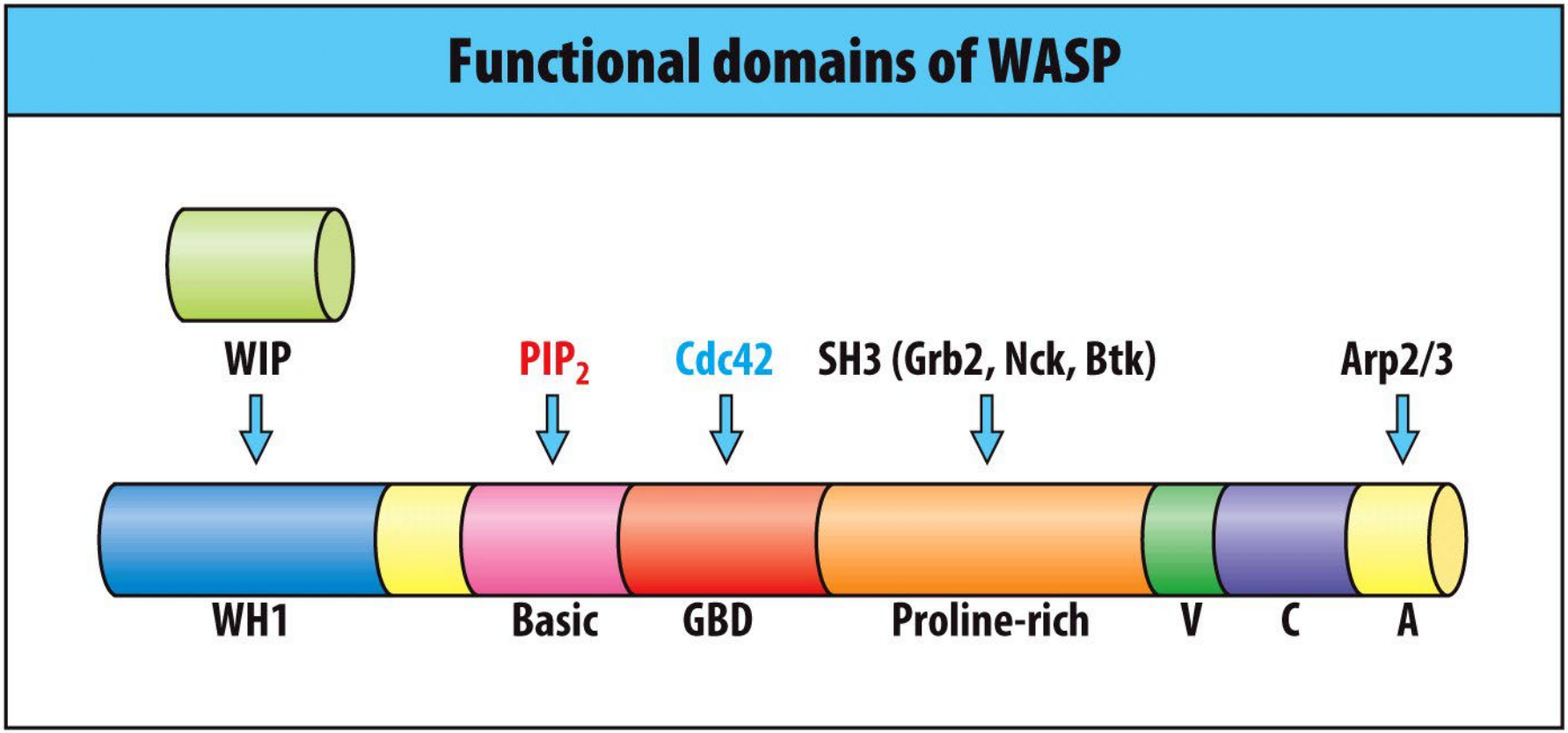


Figure 16.6 Case Studies in Immunology, 6ed. (© Garland Science 2012)

What's Wrong with the Patient?

- Deficient in WASP leads to defect in cell migration, immune synapse formation and cell division.
  - Impaired positive/negative selection
  - Impaired activation

- WASP is expressed in white blood cells and megakaryocytes (platelets precursor)