Cell Mediated Immunity (II)

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Learning Objectives

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

① Understand the mechanisms of T cell activation

② Understand the mechanisms of T cell killing

③ Understand the mechanisms of NK cell killing

Cell-Mediated Immunity

- Immune response designed to detect and kill infected or diseased cells
- Antigen specific response:
  - Mediated by Cytotoxic T lymphocytes (CTL)
- Non-specific response:
  - Mediated by NK cells

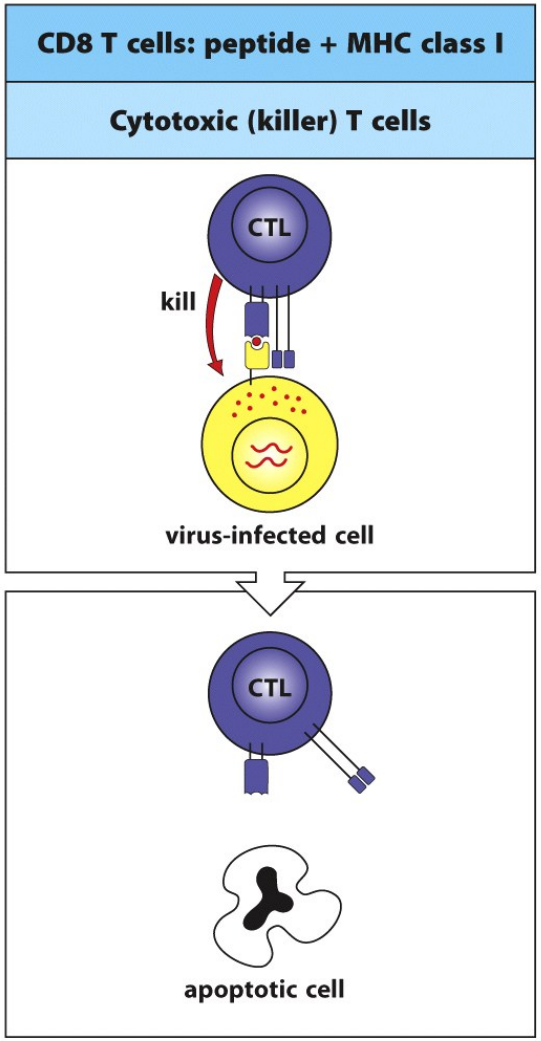


Figure 9.26 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Activation of CTL

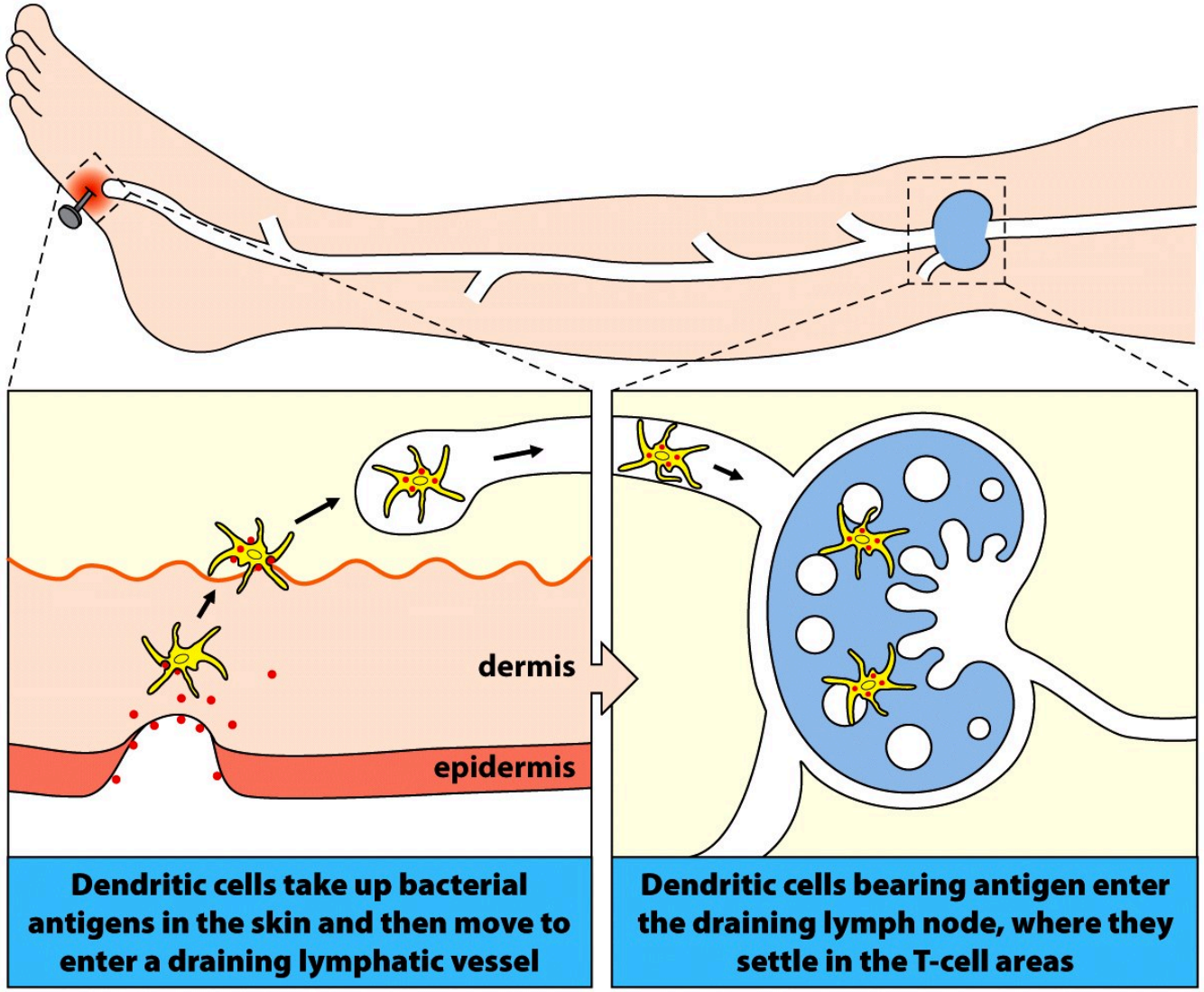


Figure 8.1 The Immune System, 3ed. (© Garland Science 2009)

Activation of CTL

- $CD8^+$ T cells encounter antigen presented by APCs on MHC-I
- Activated $CD8^+$ T cells by 3-signal model become CTL

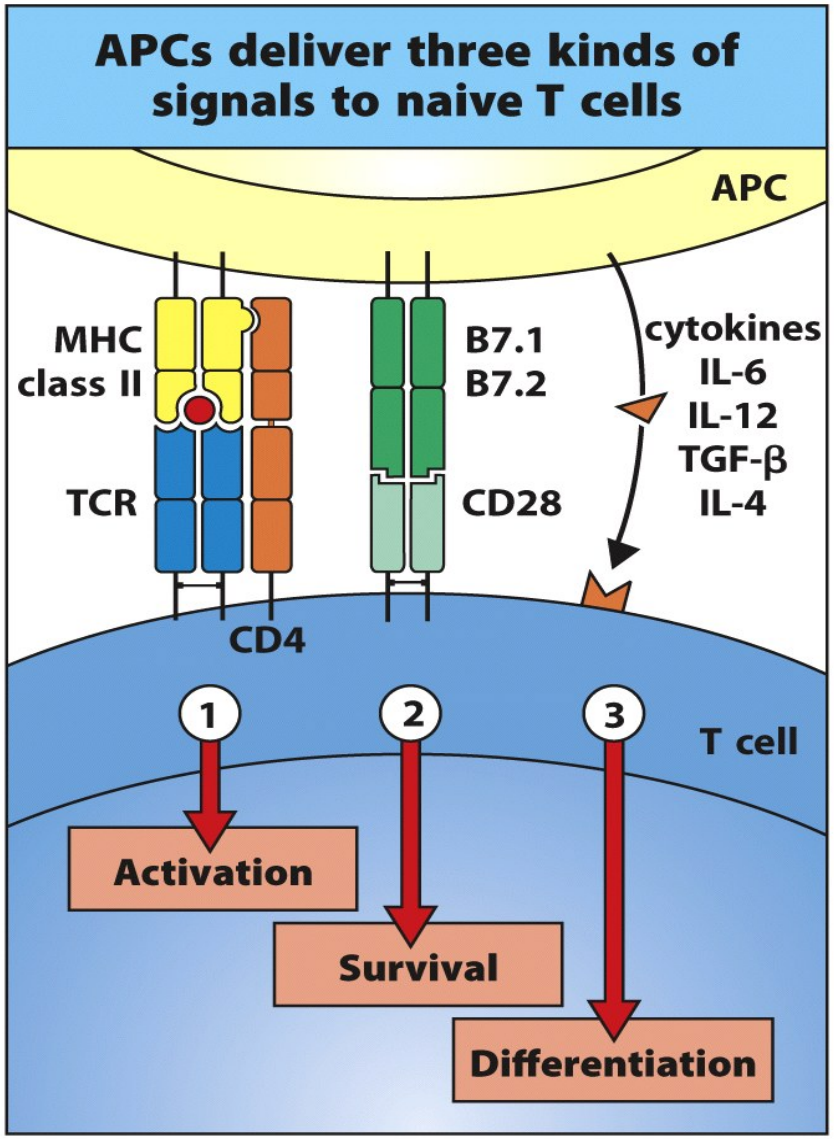


Figure 9.19 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Activation of CTL

- $CD4^+$ T cells stimulate APCs to express co-stimulatory molecules to enhance CTL activation

- $CD4^+$ T cells (T_H1) are crucial to induce CTL proliferation

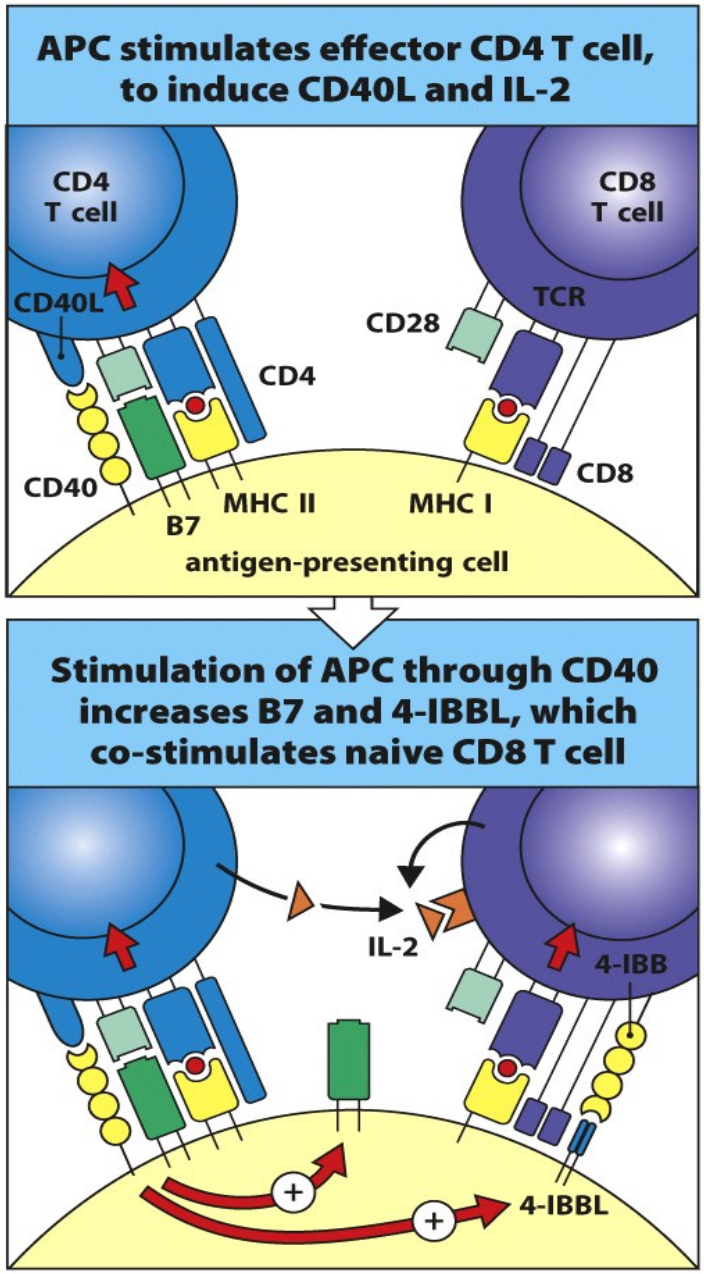
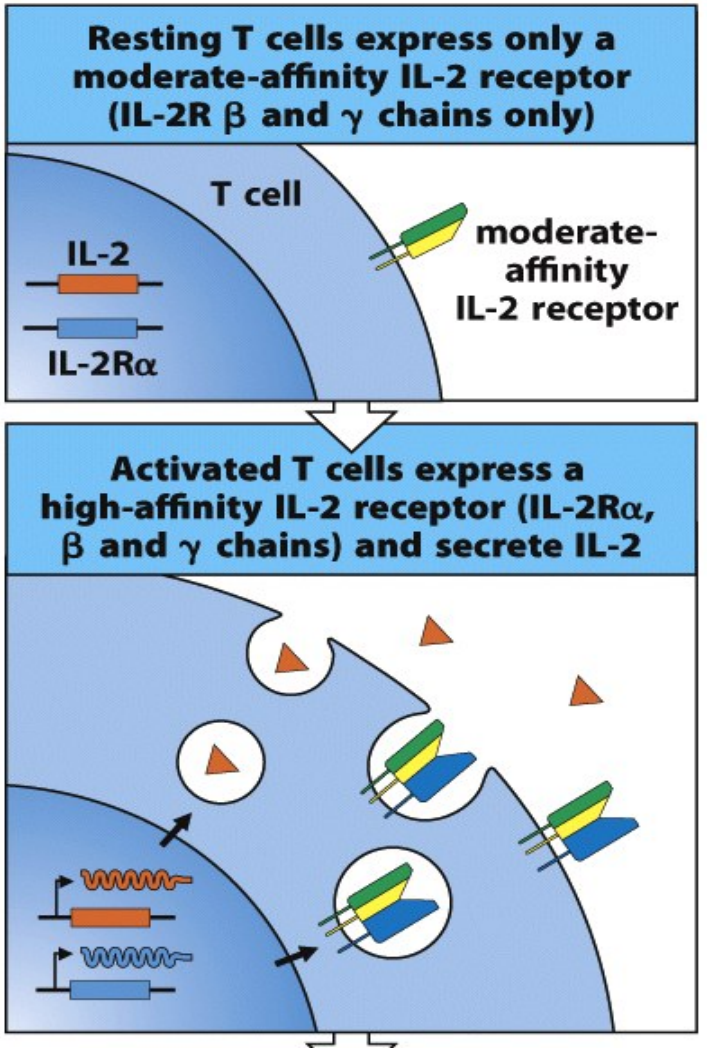


Figure 9.27 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Activation of CTL

- Naïve T cells express moderate-affinity IL-2R
- Activated T cells express high-affinity IL-2R
- Stimulation of IL-2R by IL-2 induces the expression of IL-2 and IL-2R



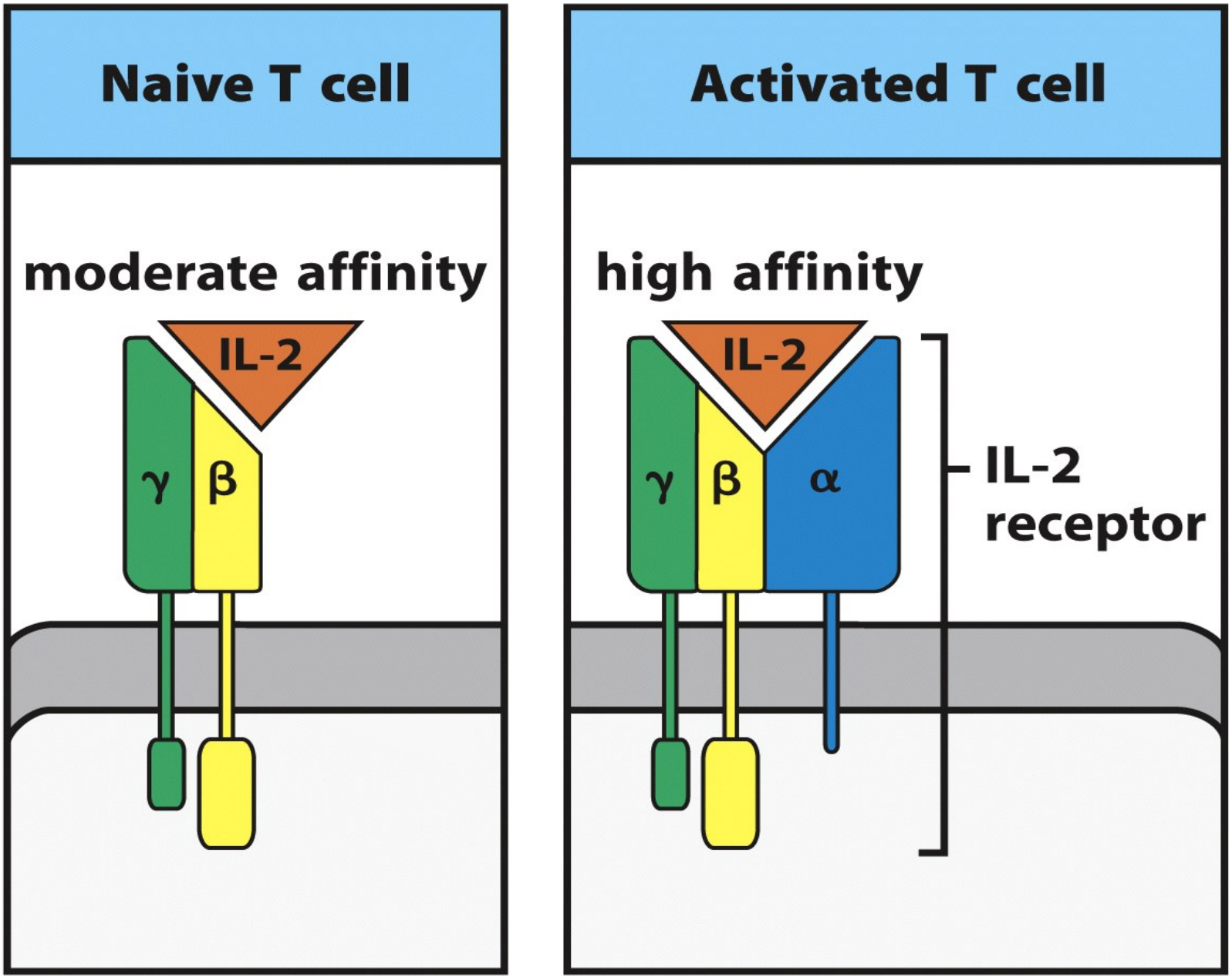
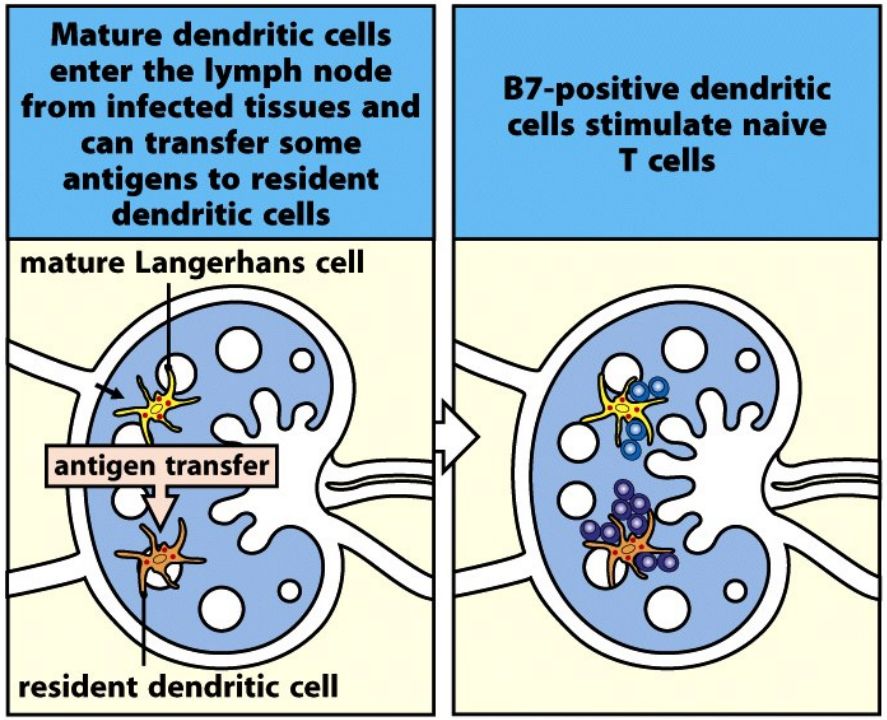


Figure 9.20 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Activation of CTL

- Stimulation of IL-2R by IL-2 induces T cell proliferation in the lymph node



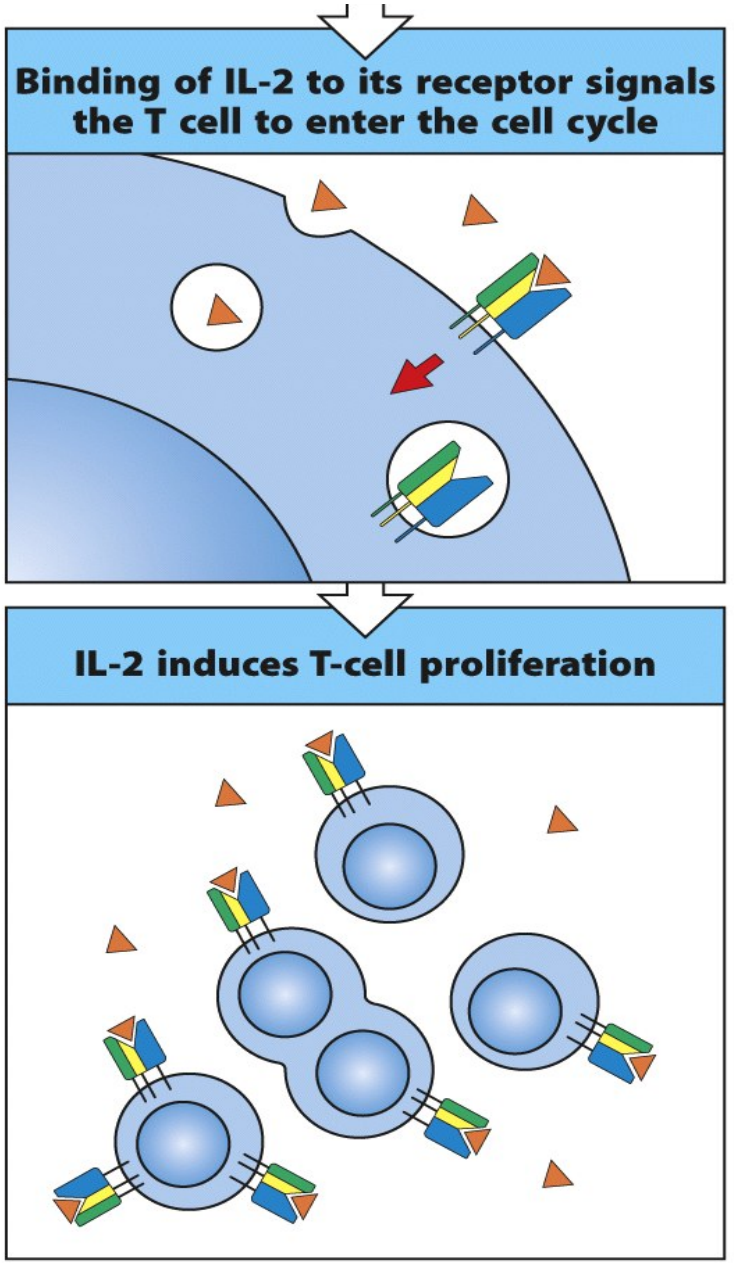


Figure 9.21 part 2 of 2 Janeway's Immunobiology, 8ed. (© Garlan

Cytotoxic T Cell Killing

Activated CTLs do not require co-stimulatory signal

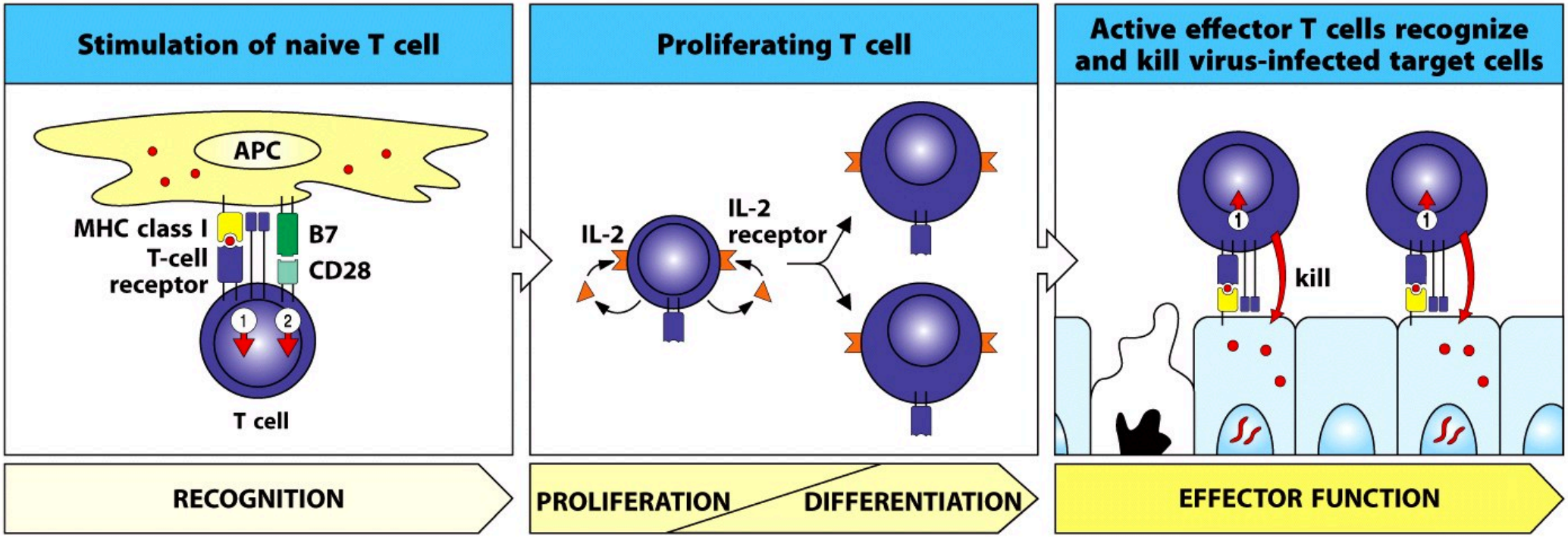


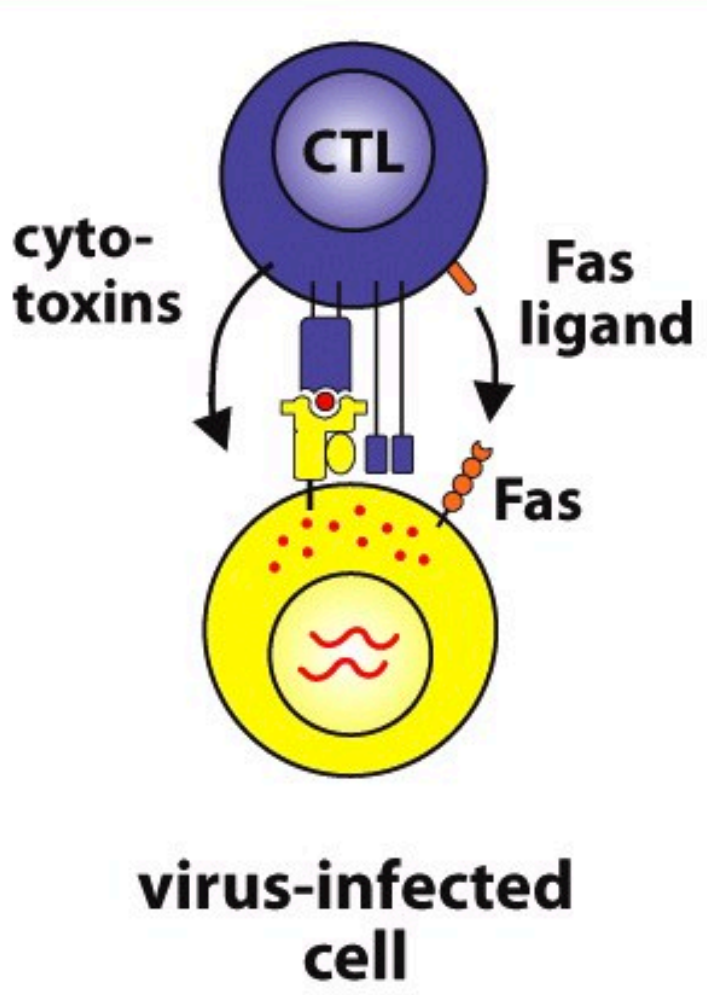
Figure 8.23 The Immune System, 3ed. (© Garland Science 2009)

Cytotoxic T Cell Killing

- Cytotoxic T cells kill their target cells by inducing apoptosis

① Apoptosis from the release of cytotoxins (perforins and granzymes)

② Apoptosis from cell-surface signalling through Fas-Fas ligand interaction



Cytotoxins release

- T cell organelles rearrange and orient toward target cell killing
- Degranulation of CTL leads to the release of perforins and granzymes

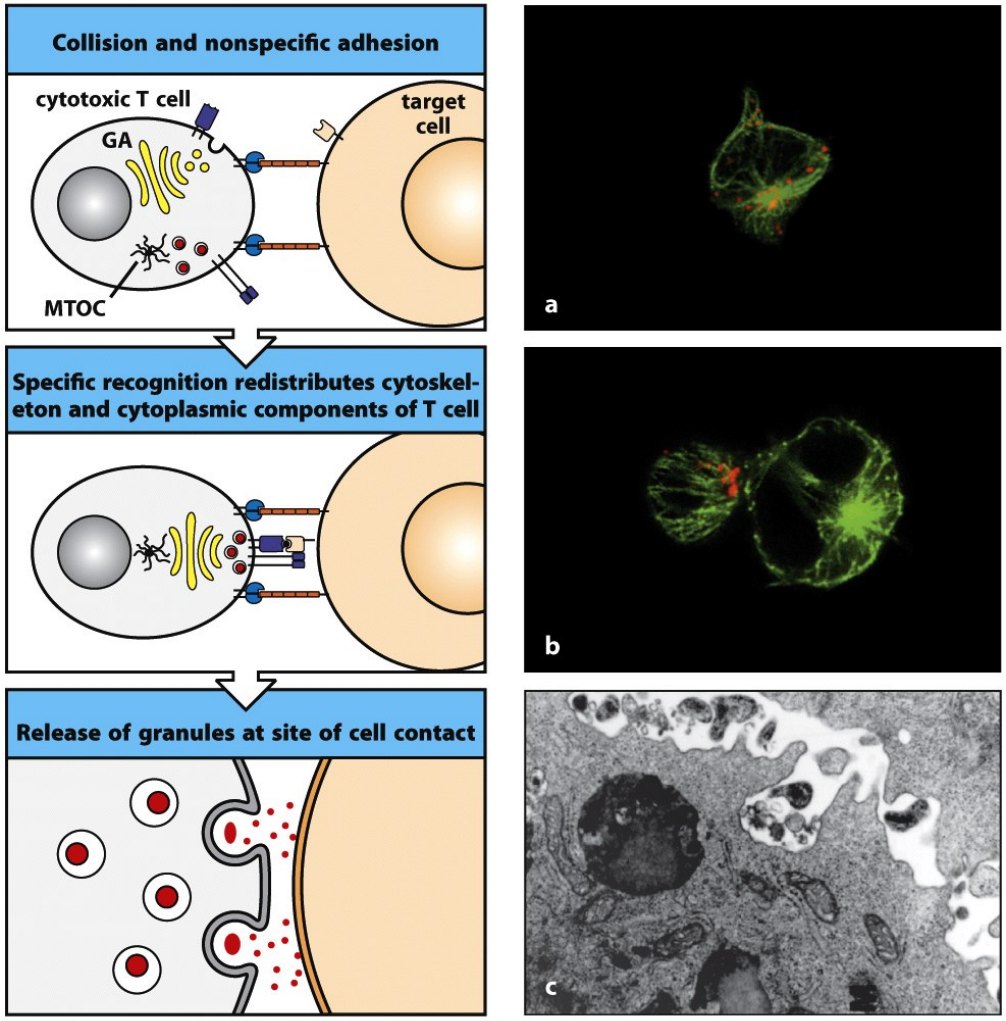
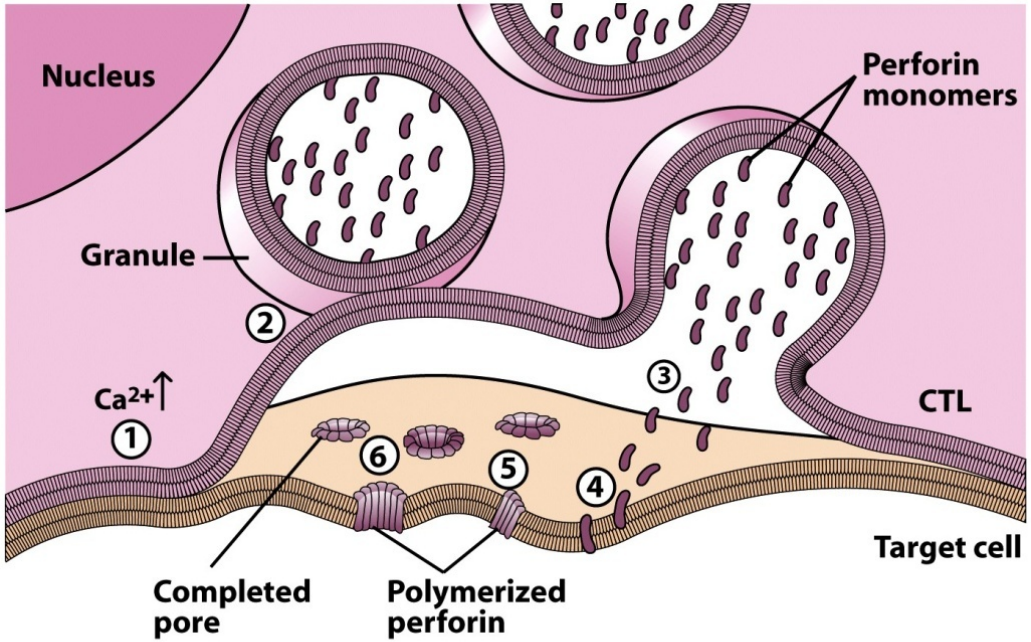


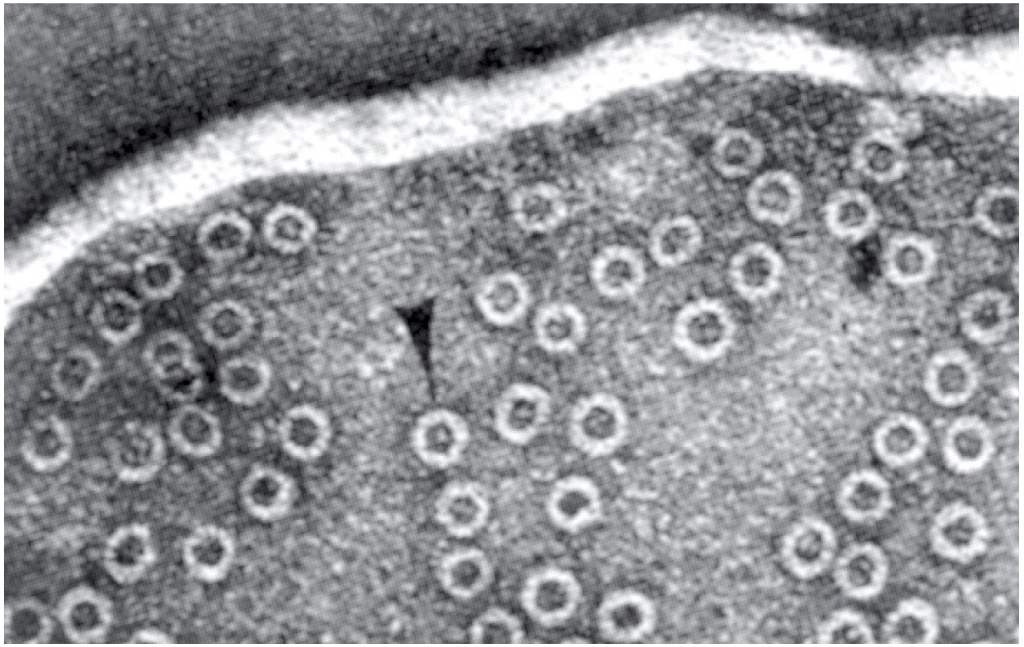
Figure 8-32 Immunobiology, 7ed. (© Garland Science 2008)

Perforin

- Perforins are proteins that get released upon conjugation of CTL with target infected cells

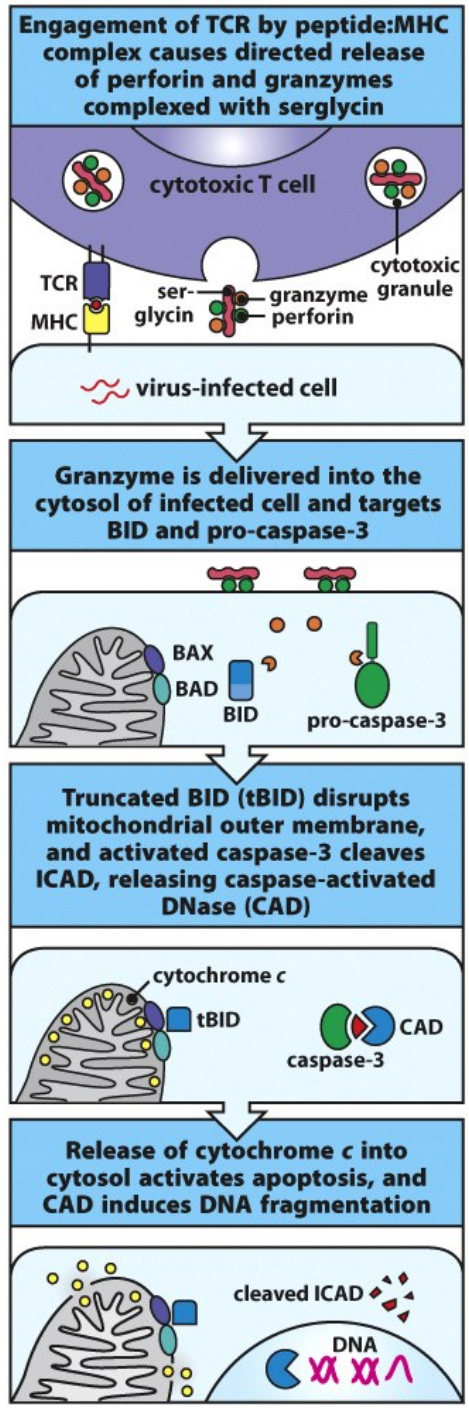
- Perforins polymerize on the surface of target cells, which will open holes to facilitate granzymes intracellular transfer





Granzymes

- Granzymes are enZYMES found in the GRANules of $CD8^+$ T cells
- Granzyme A causes the release of cytochrome C which activates caspase 9
- Granzyme B causes the activation of caspase 3



Fas-Fas Ligand Interaction

- Fas (CD95)-FasL interaction leads to the activation of caspase 8
- Important for Activation-Induced Cell Death (AICD)

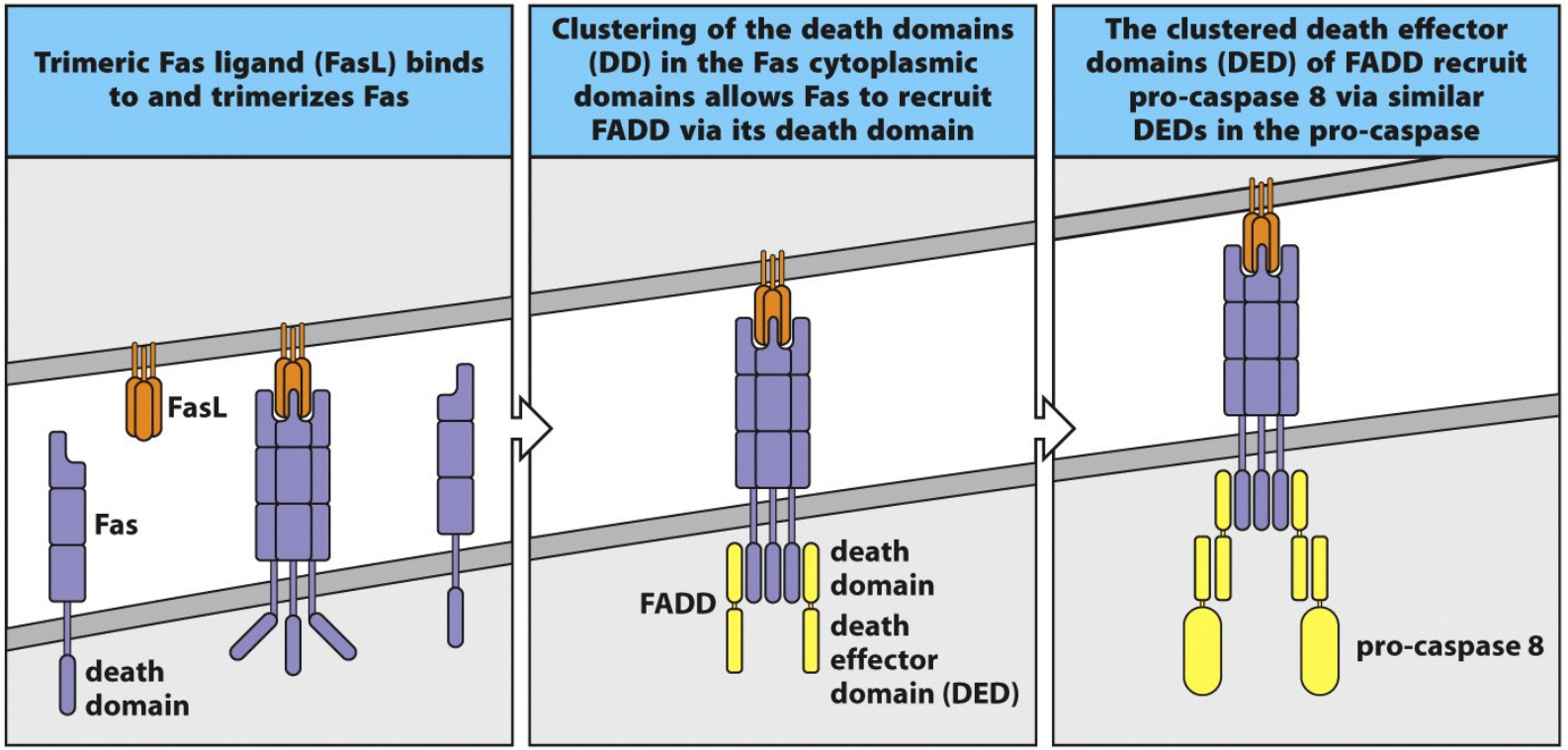


Figure 7.30 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Effector Phase of CTL

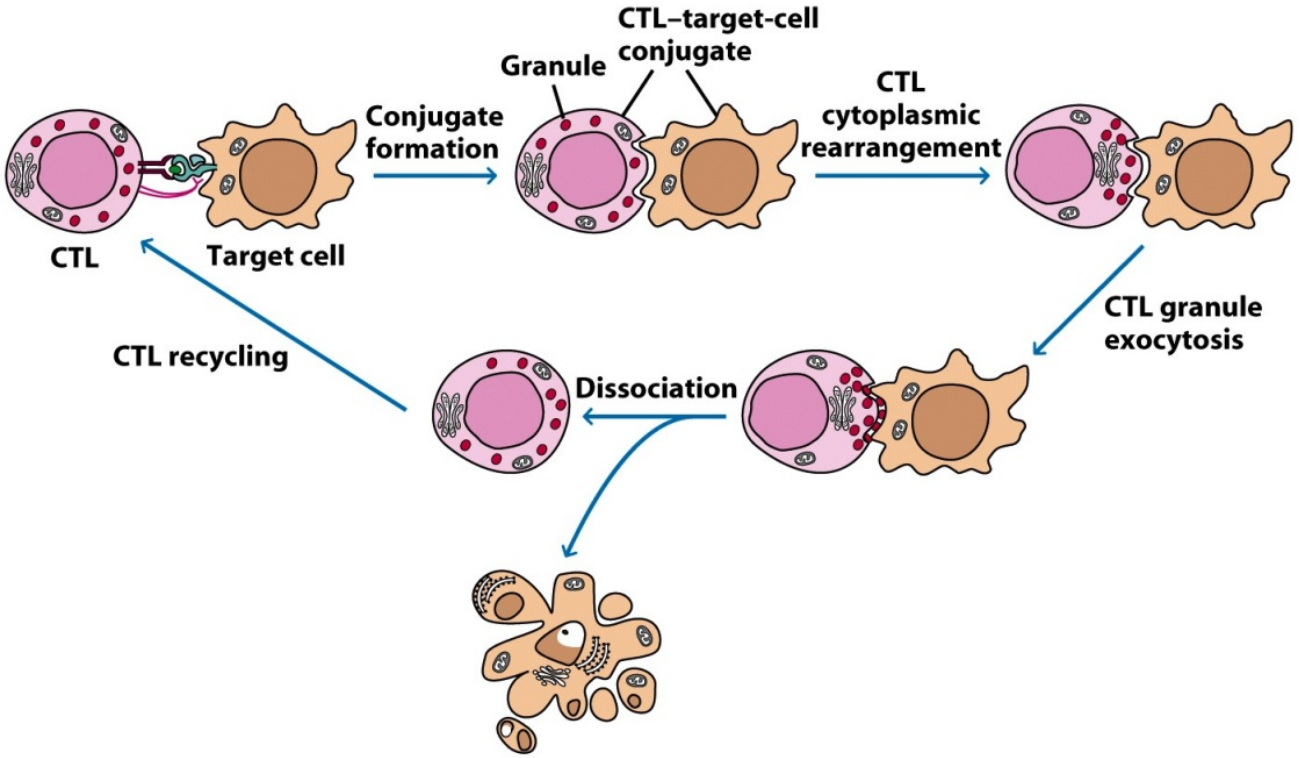
- Cell-mediated killing comprises 4 steps:

1-Conjugate formation

2-Membrane attack

3-CTL dissociation

4-Target cell destruction



Cytotoxic T Cell Killing

- One CTL kills more than one infected cell
- Activated CTLs do not require co-stimulatory signal

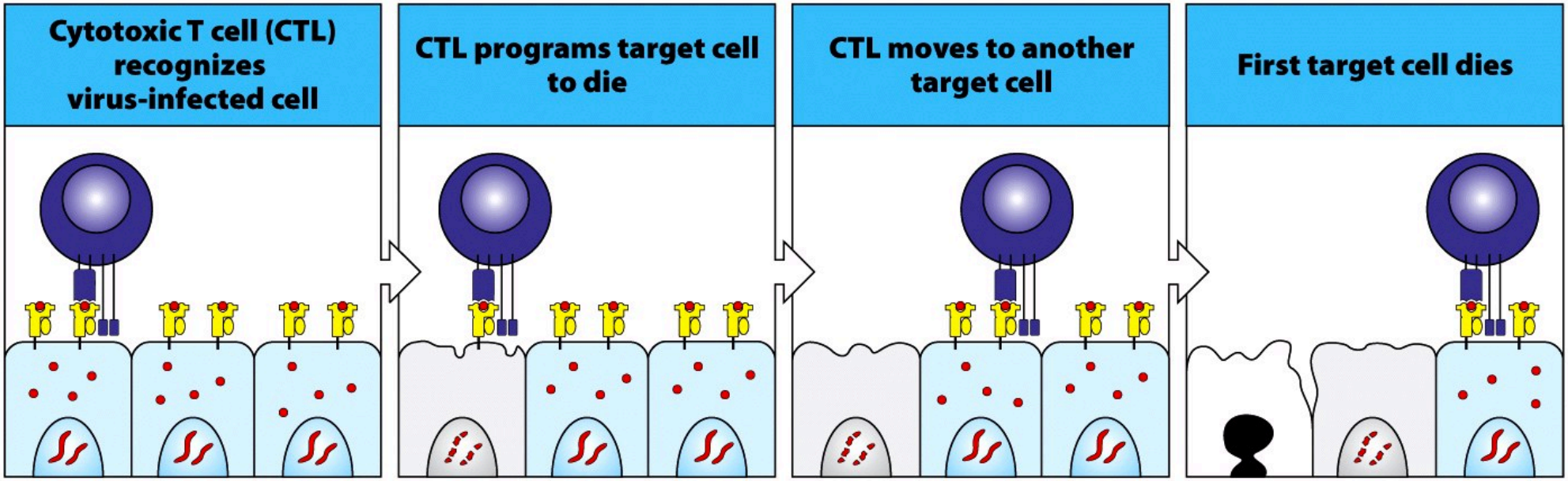


Figure 8.30 The Immune System, 3ed. (© Garland Science 2009)

Other functions of T_H1 cells

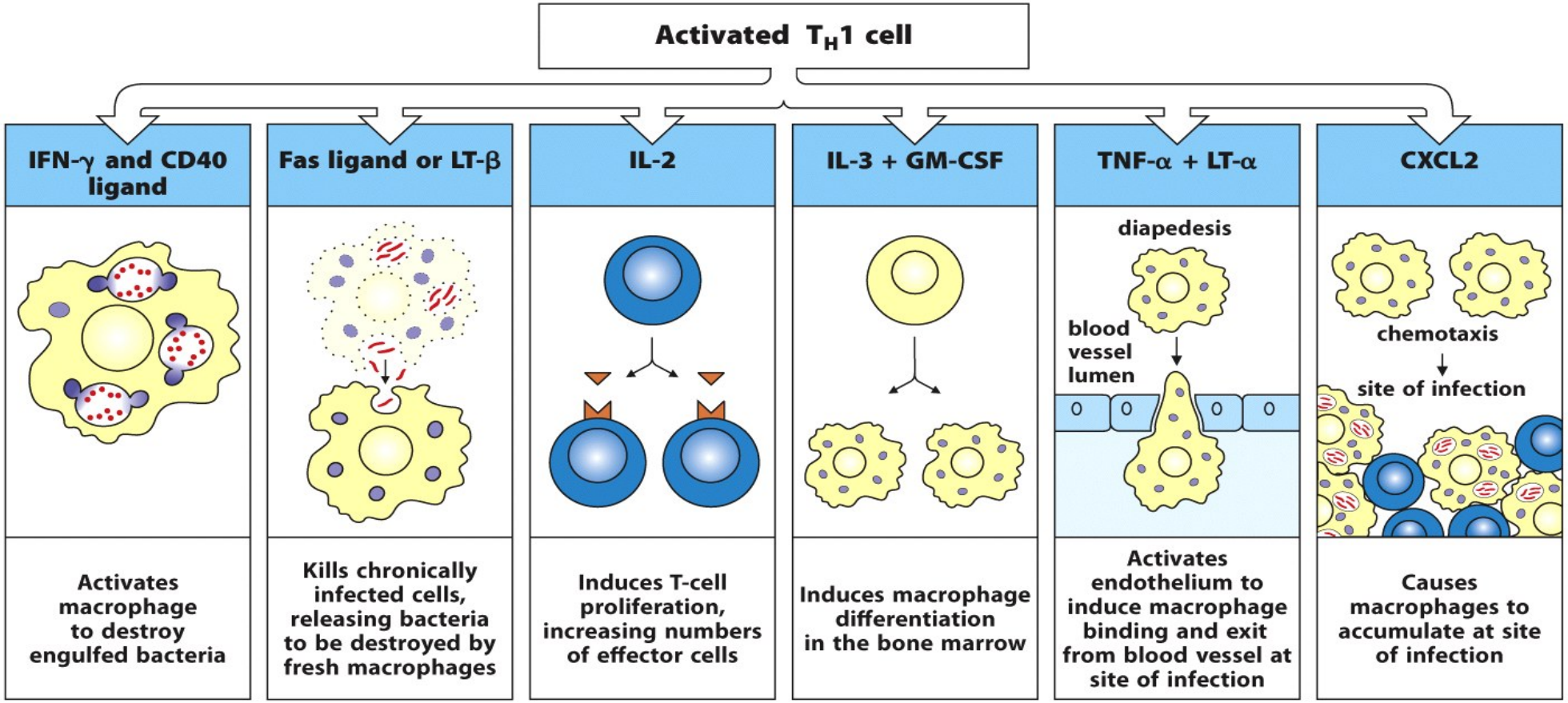


Figure 9.42 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

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

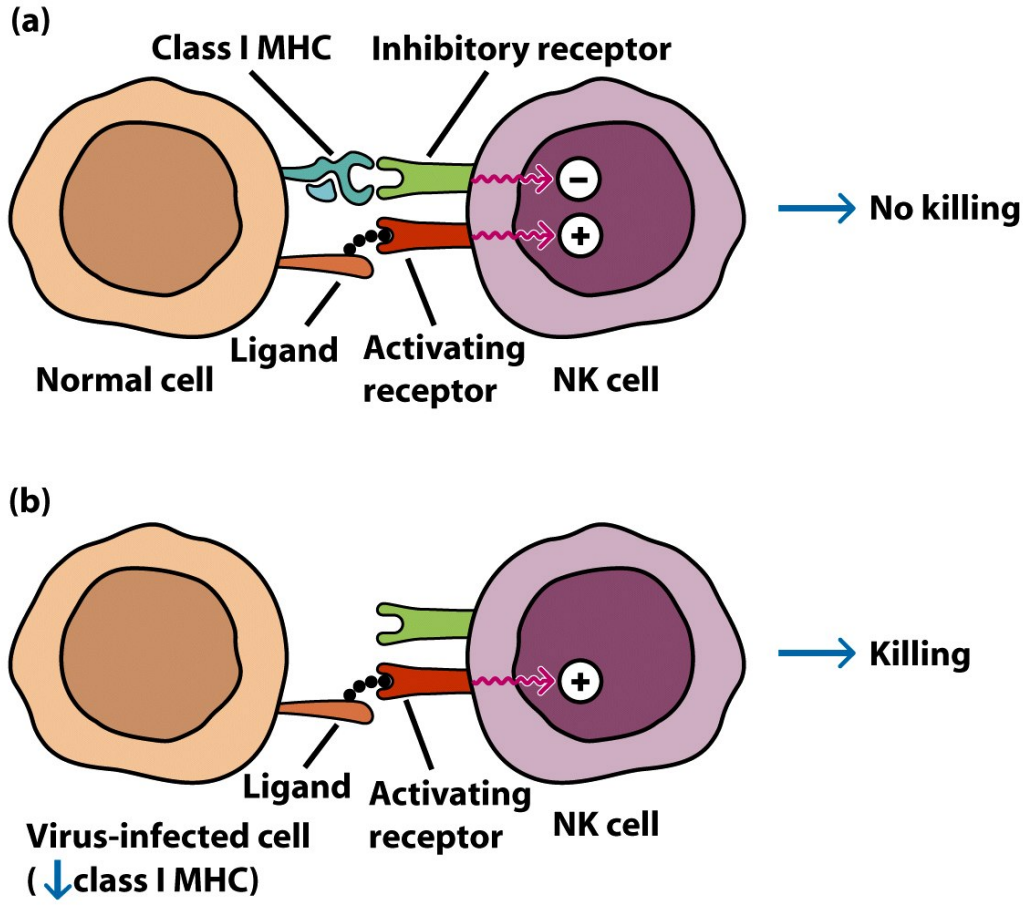


Figure 14-14
Kuby IMMUNOLOGY, Sixth Edition

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)**

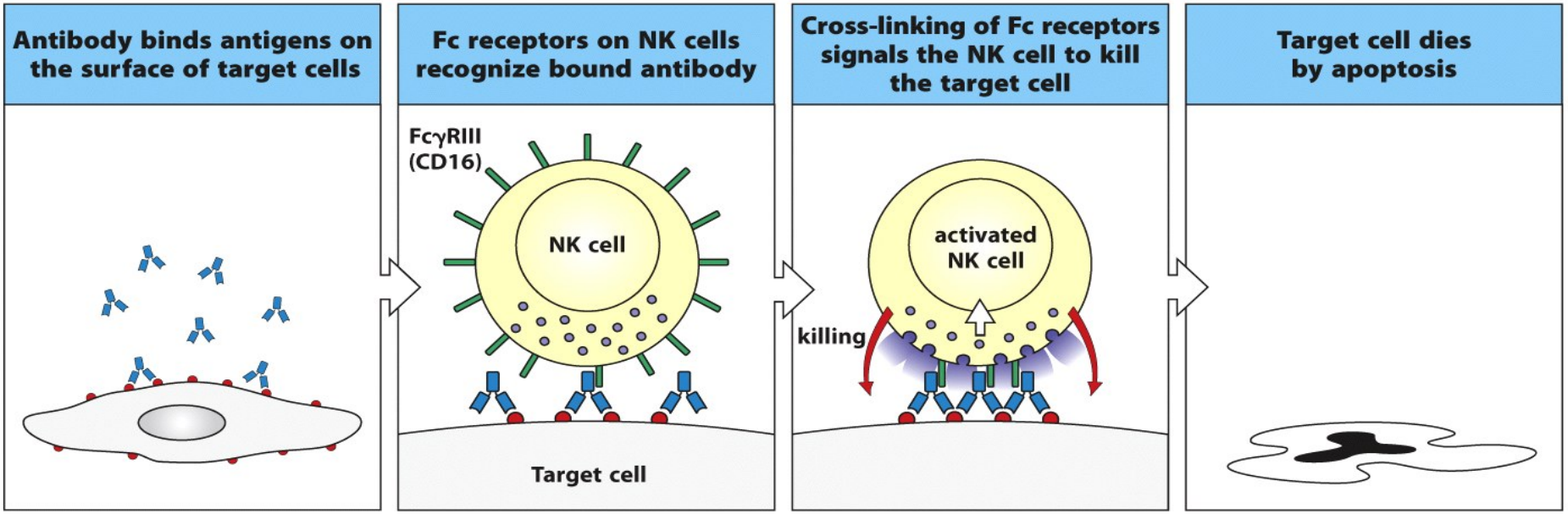


Figure 10.36 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Relationship between NK and CTL

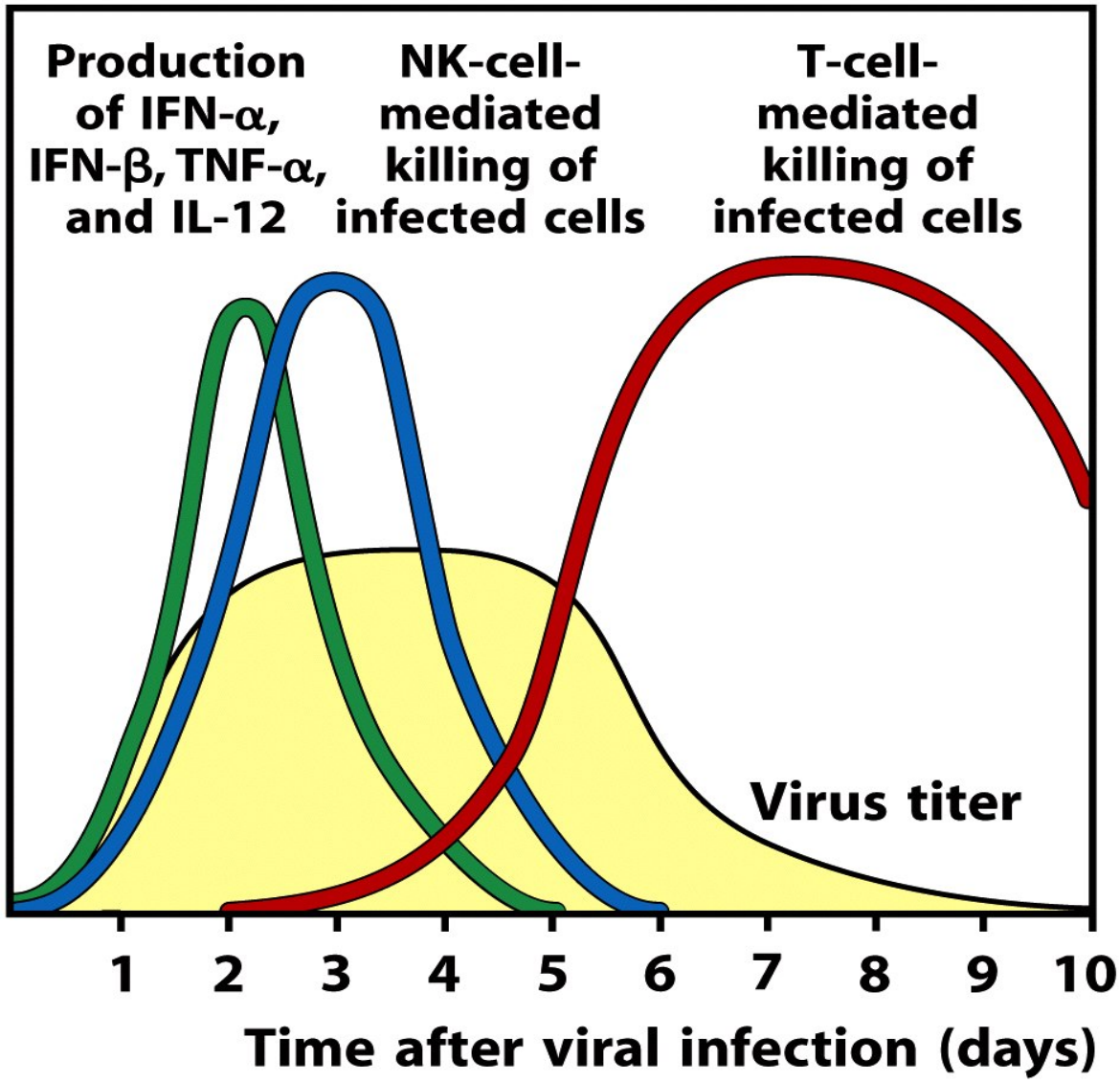


Figure 2-55 Immunobiology, 7ed. (© Garland Science 2008)

You are now able to:

- ✓ Understand the mechanisms of T cell activation
- ✓ Understand the mechanisms of T cell killing
- ✓ Understand the mechanisms of NK cell killing