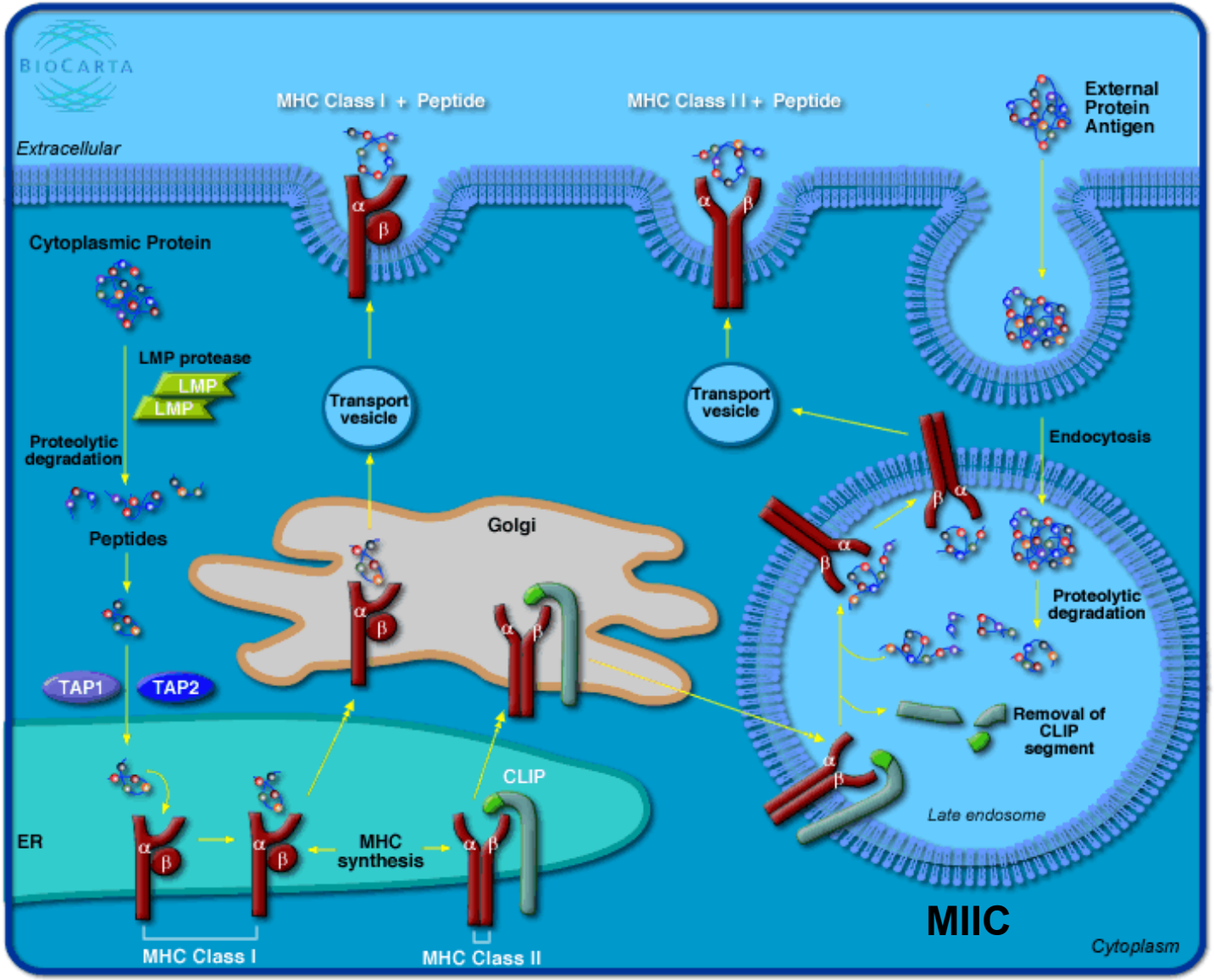
MHC Class I and II Life Cycle



http://dri-constant.slavoljubpenkala.hr/wp-content/uploads/2009/09/h_mhcPathway-BETTER-ONE.gif

Cross-presentation

The **presentation** of exogenous antigens on MHC class I molecules

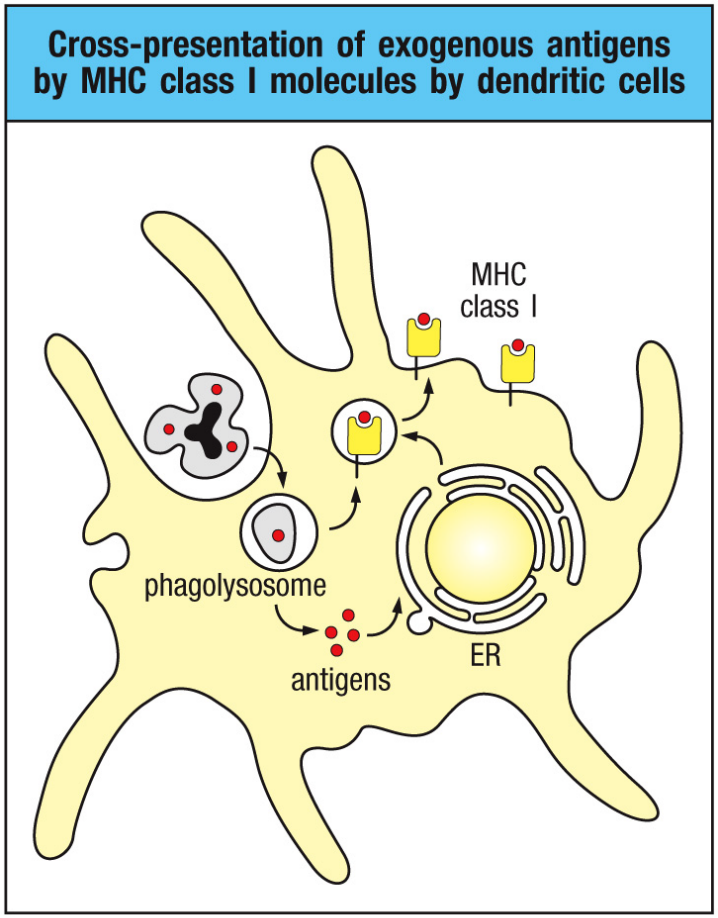


Figure 6.3 Janeway's Immunobiology, 9th ed. (© Garland Science 2017)

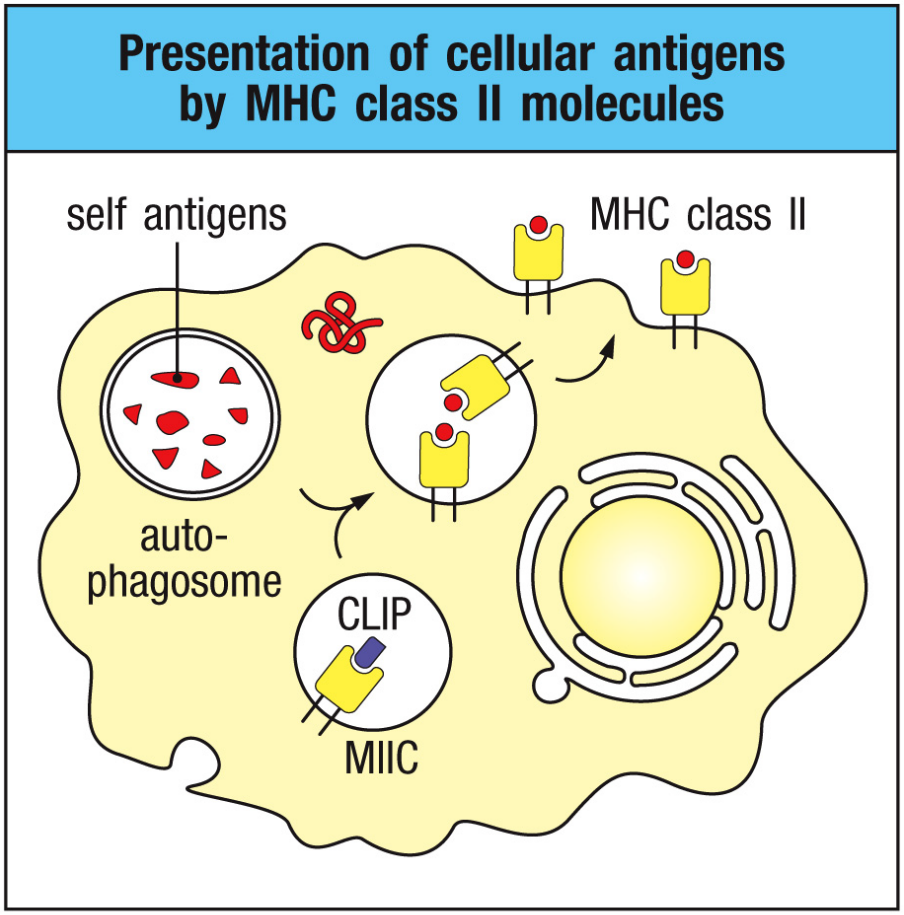


Figure 6.4 Janeway's Immunobiology, 9th ed. (© Garland Science 2017)

Outline

- T cell development
  - Thymus
  - Stages of T-cell development

T Cells Migrate to Thymus to Mature

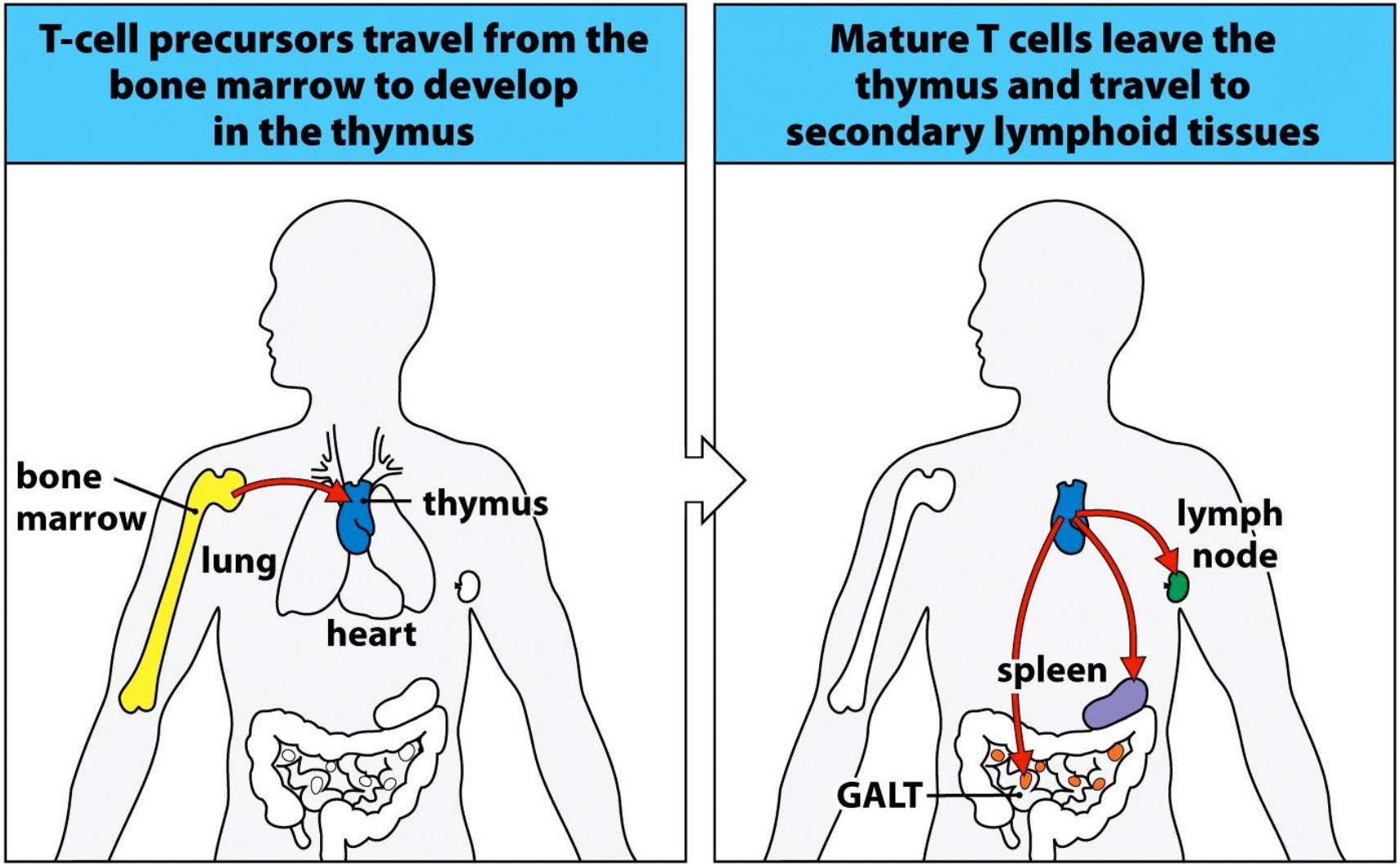
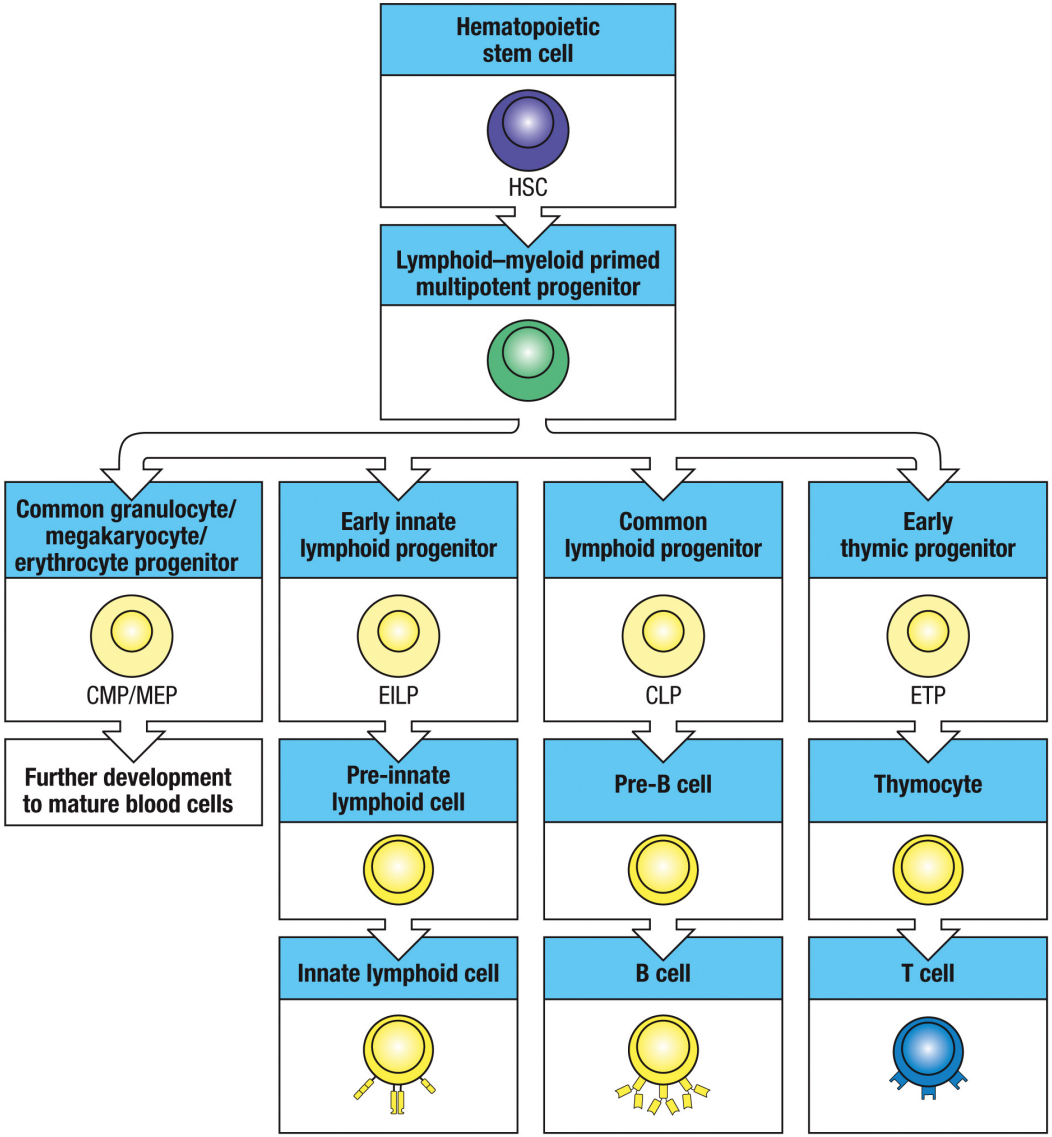
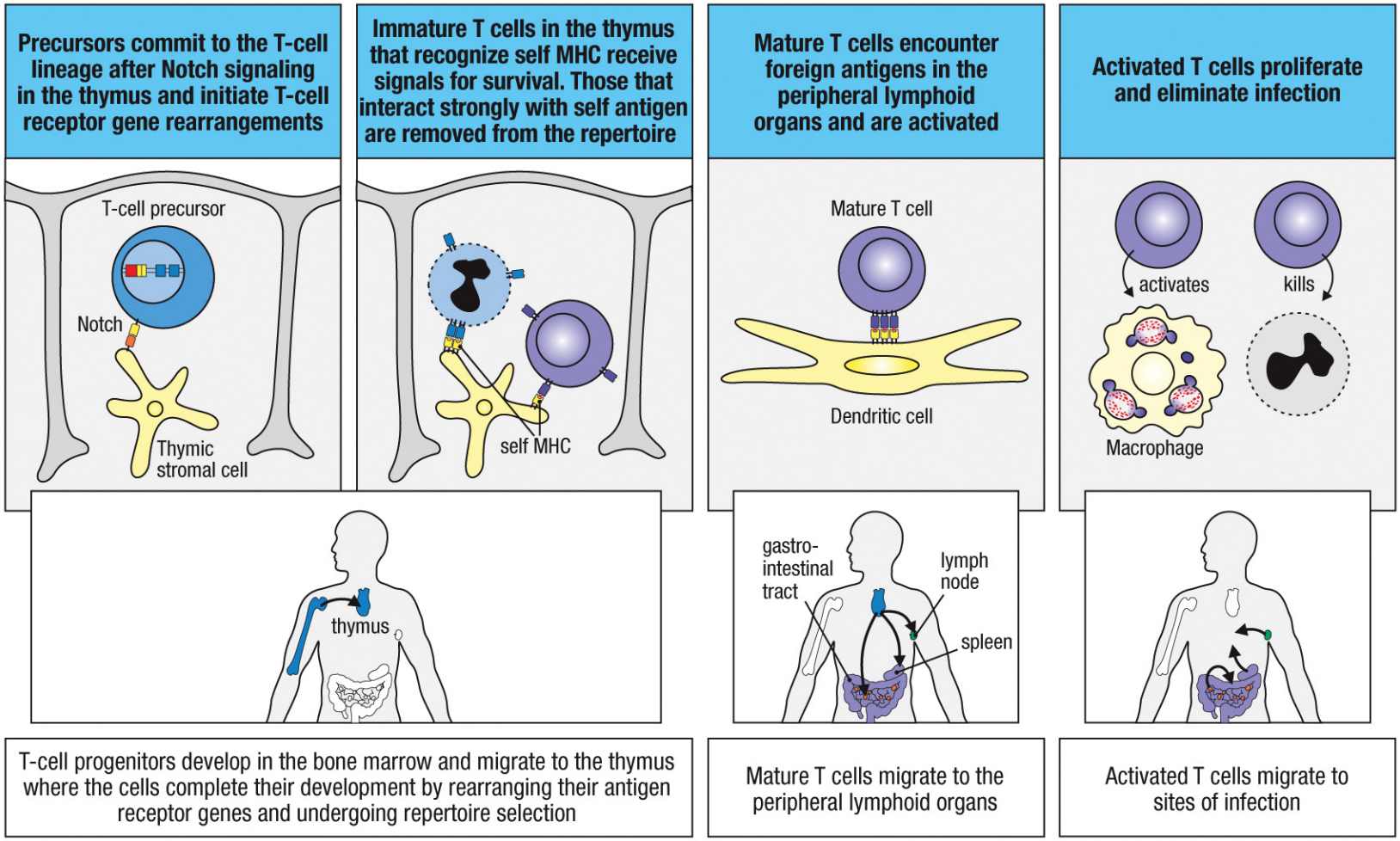


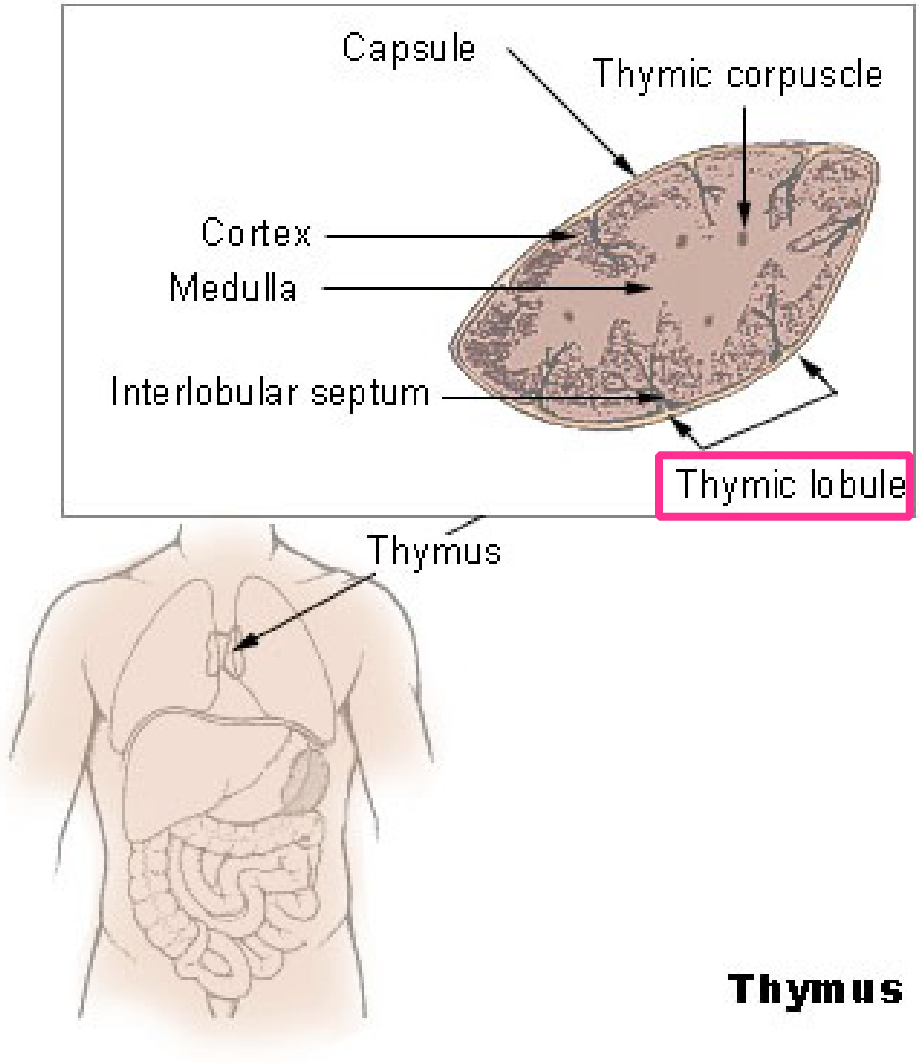
Figure 7.1 The Immune System, 3ed. (© Garland Science 2009)


Hematopoietic stem cell
HSC
Lymphoid–myeloid primed multipotent progenitor
Common granulocyte/ megakaryocyte/ erythrocyte progenitor
CMP/MEP
Early innate lymphoid progenitor
EILP
Common lymphoid progenitor
CLP
Early thymic progenitor
ETP
Further development to mature blood cells
Pre-innate lymphoid cell
Pre-B cell
Thymocyte
Innate lymphoid cell
B cell
T cell

Life Cycle of a T Cell



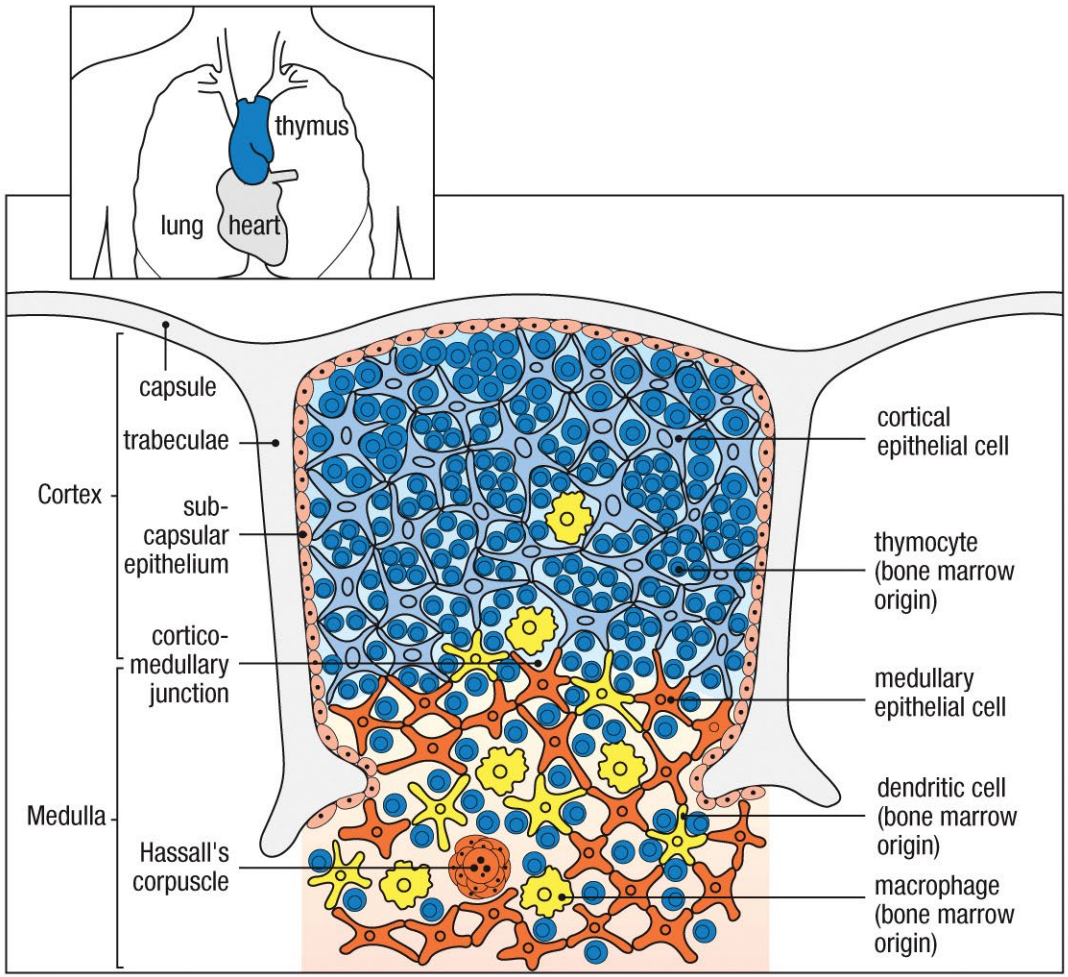
Thymus

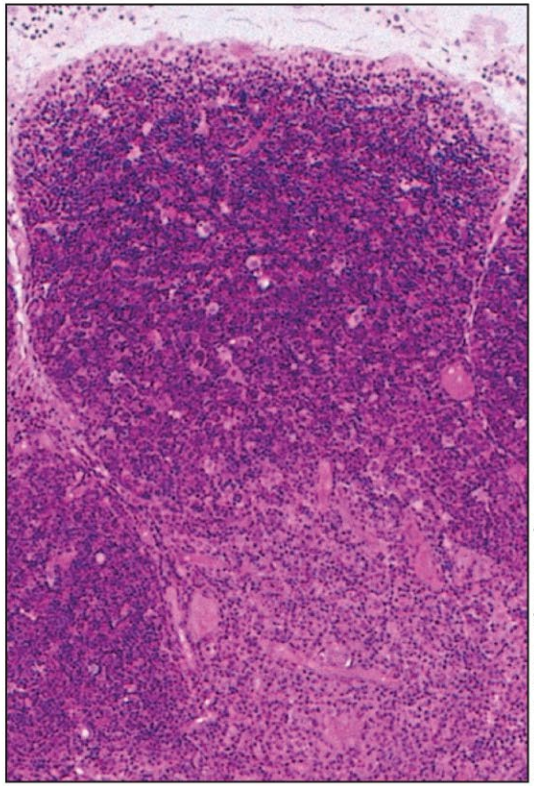


Thymus

http://www.rechargebiomedical.com/immunehealth.html

Cellular Organization of the Thymus





Michael Abbey/Science Source

Cortex of the Thymus

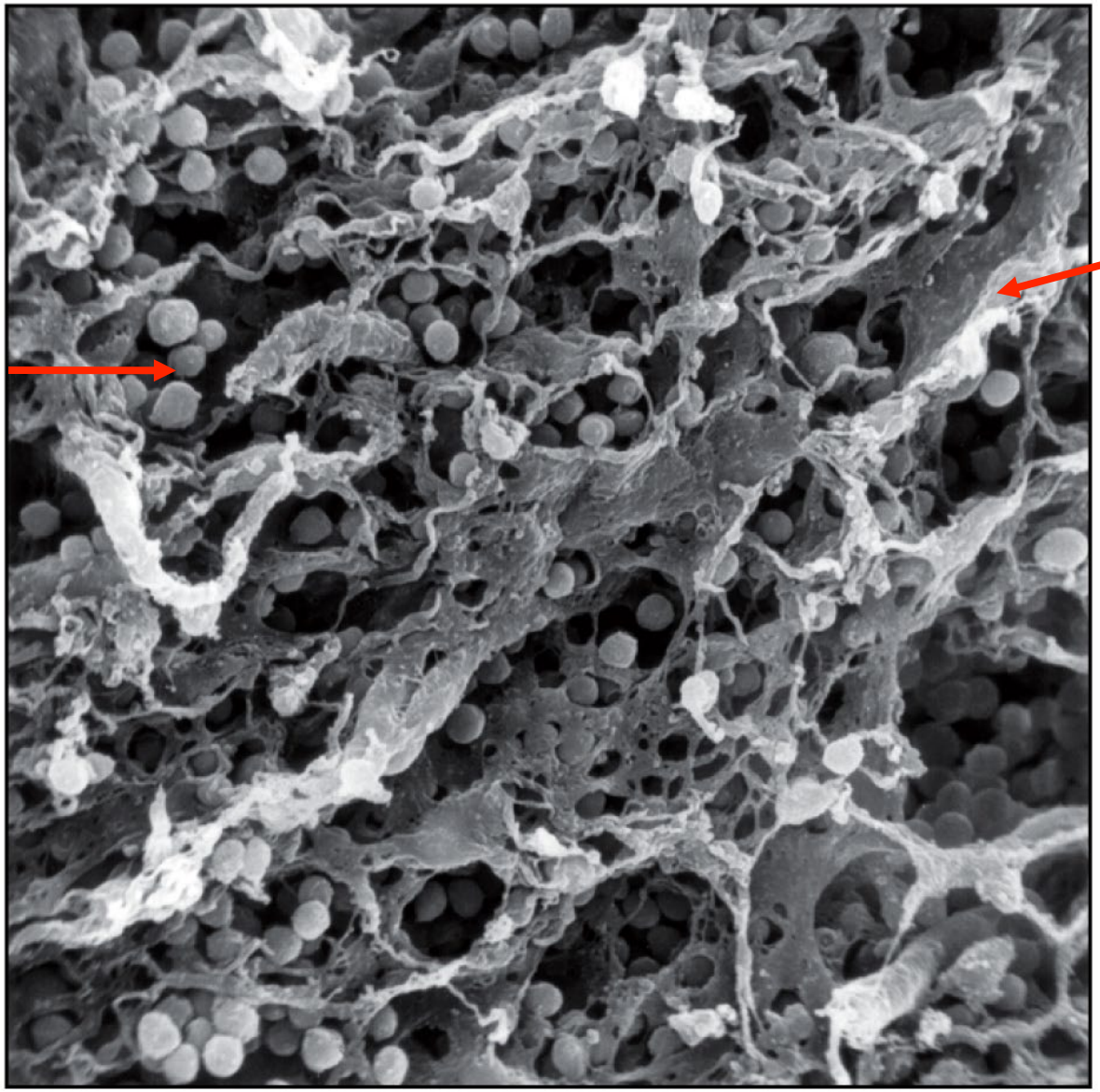


Figure 8.17 Janeway's Immunobiology, 9th ed. (© Garland Science 2017)

Notch Signaling Commits the Progenitor to T-Cell Lineage

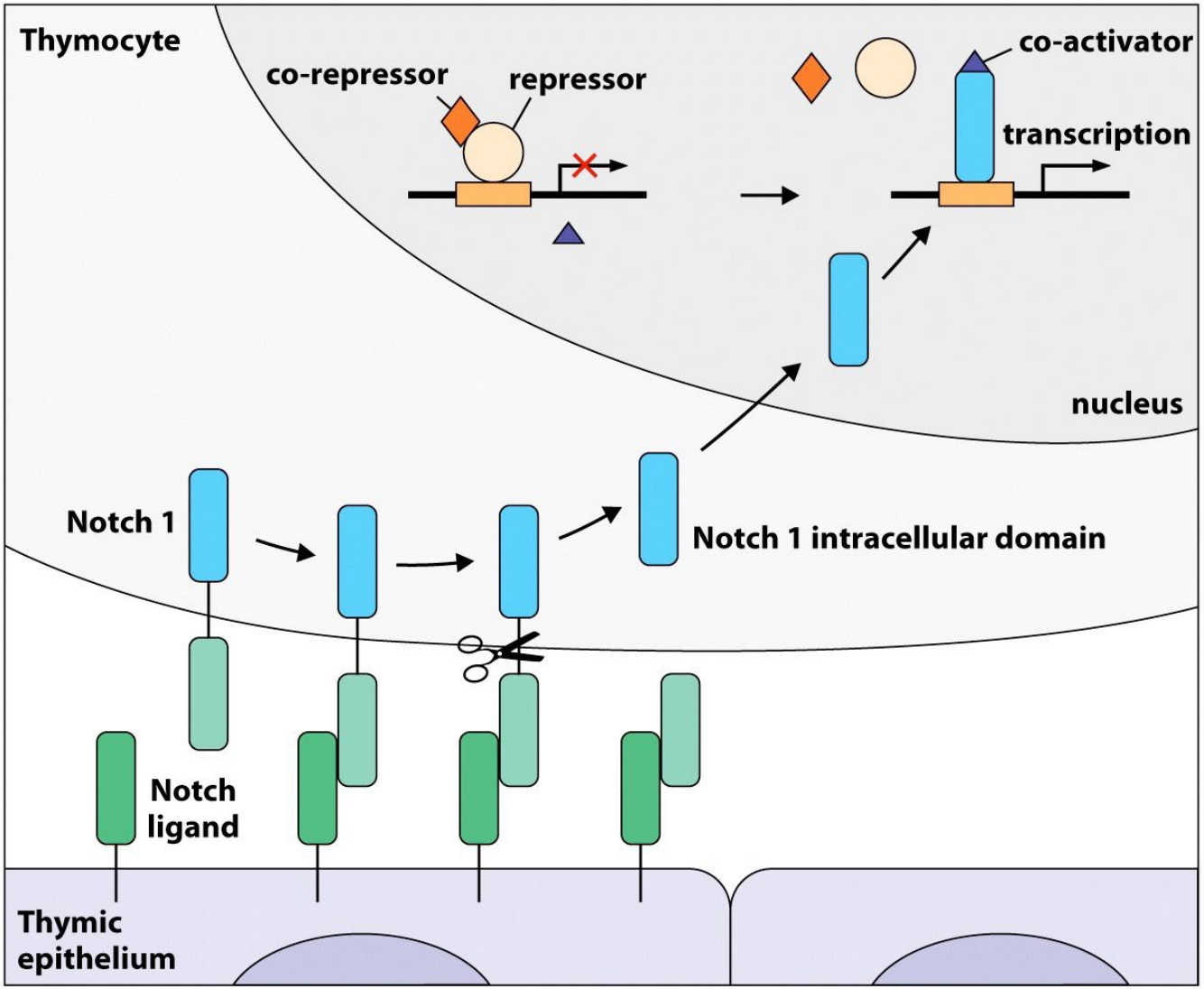


Figure 7.6 The Immune System, 3ed. (© Garland Science 2009)

Changes in Thymic Weight and Composition with Age

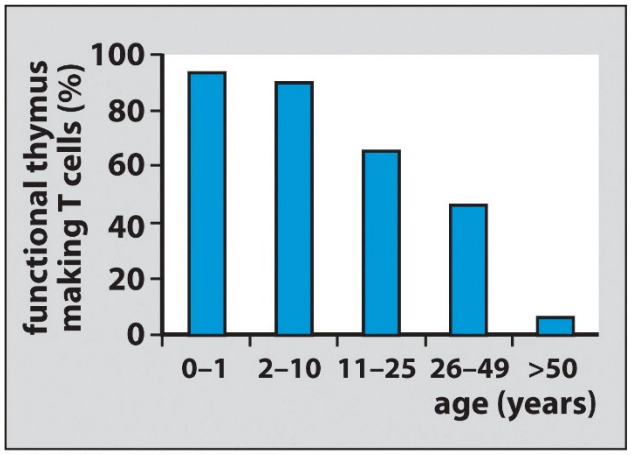
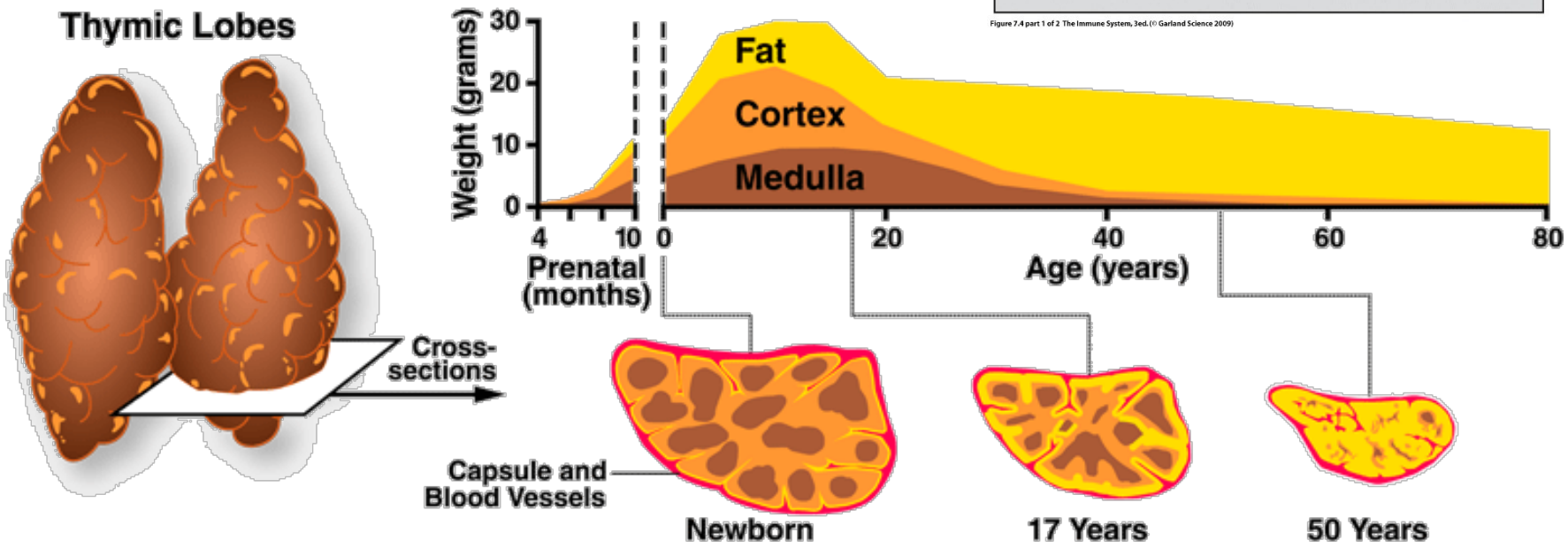
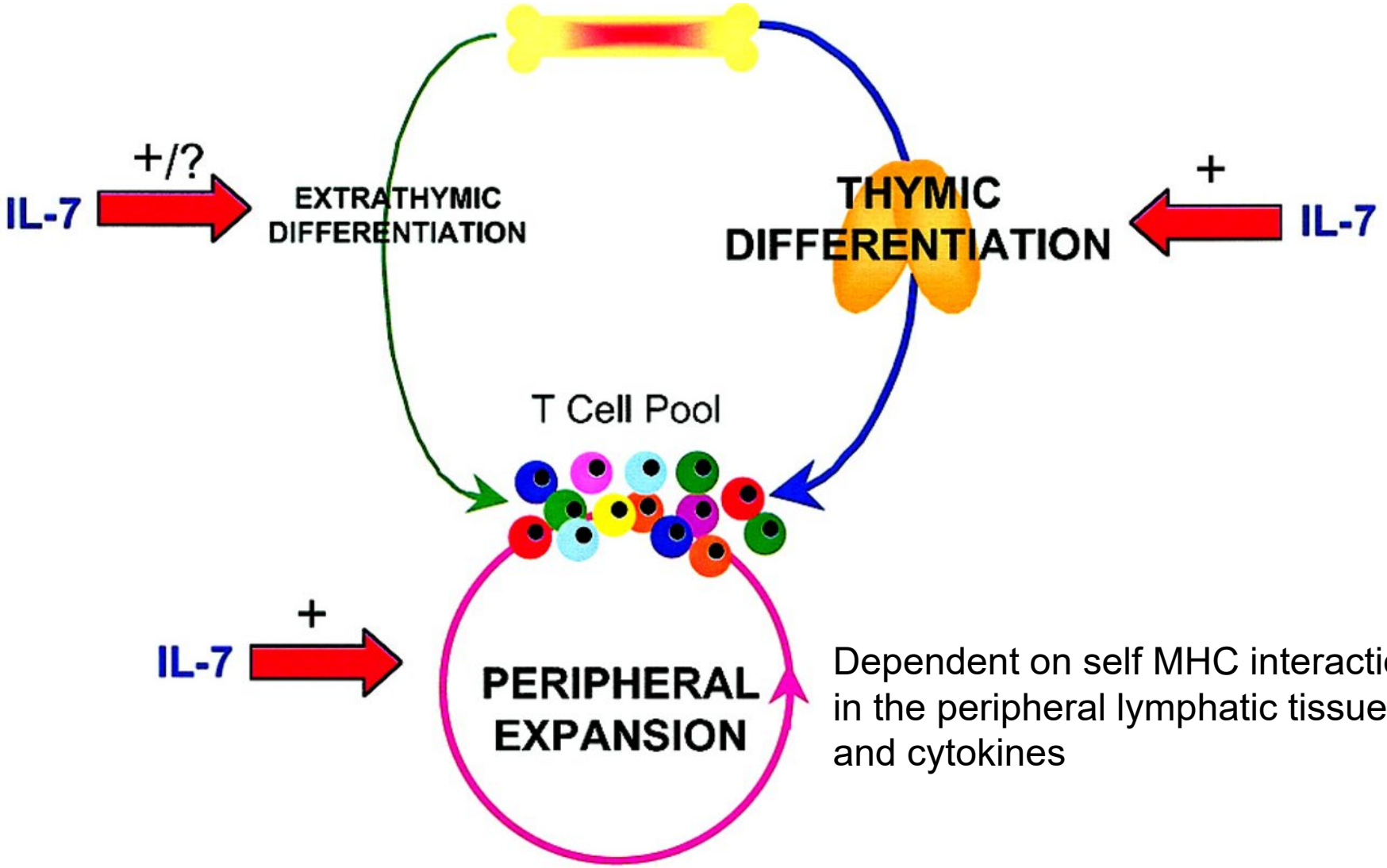


Figure 7.4 part 1 of 2 The Immune System, 3ed. (© Garland Science 2009)



http://www.gladstone.ucsf.edu/gladstone/files/publicaffairs/Napolitanofig2LG.gif

T Cell Homeostasis in the Periphery

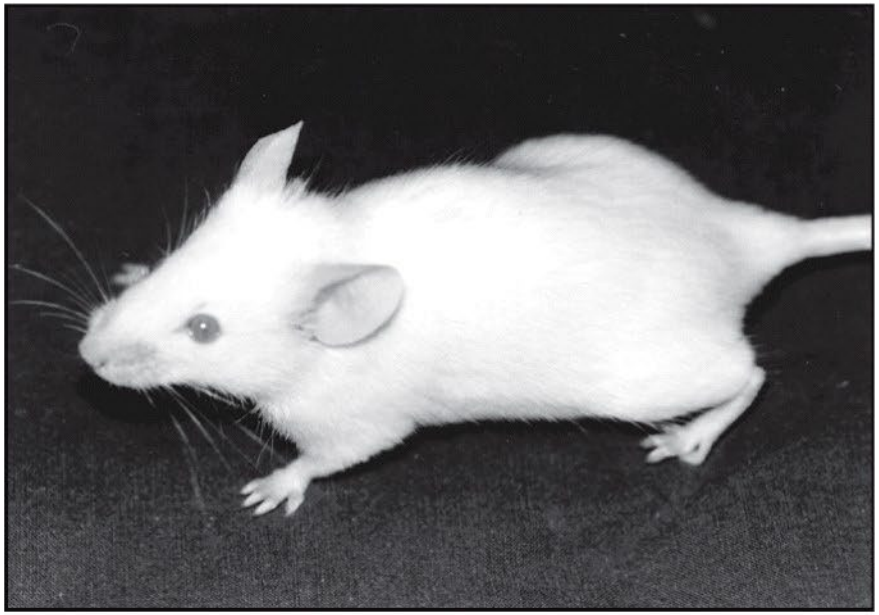


Dependent on self MHC interaction in the peripheral lymphatic tissue and cytokines

http://www.bloodjournal.org/content/99/11/3892

Thymus Is Required for T-Cell Maturation

BCR and TCR rearrangement defect



***scid/scid* mouse**

Thymic epithelium fails to differentiate

***nu/nu* mouse**

Figure 8.17 part 1 of 3 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Thymus Is Required for T-Cell Maturation

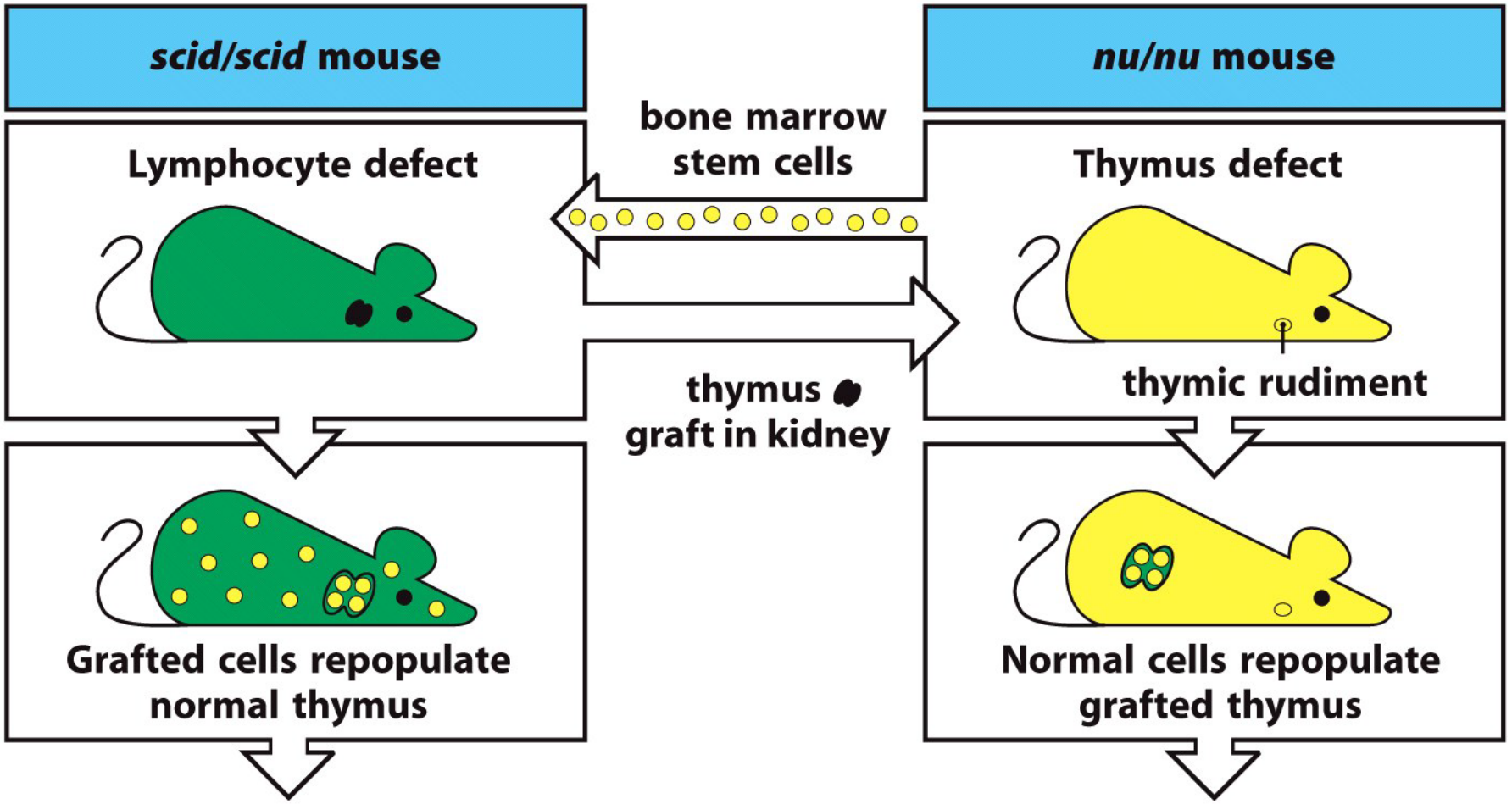


Figure 8.17 part 2 of 3 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Thymus Is Required for T-Cell Maturation

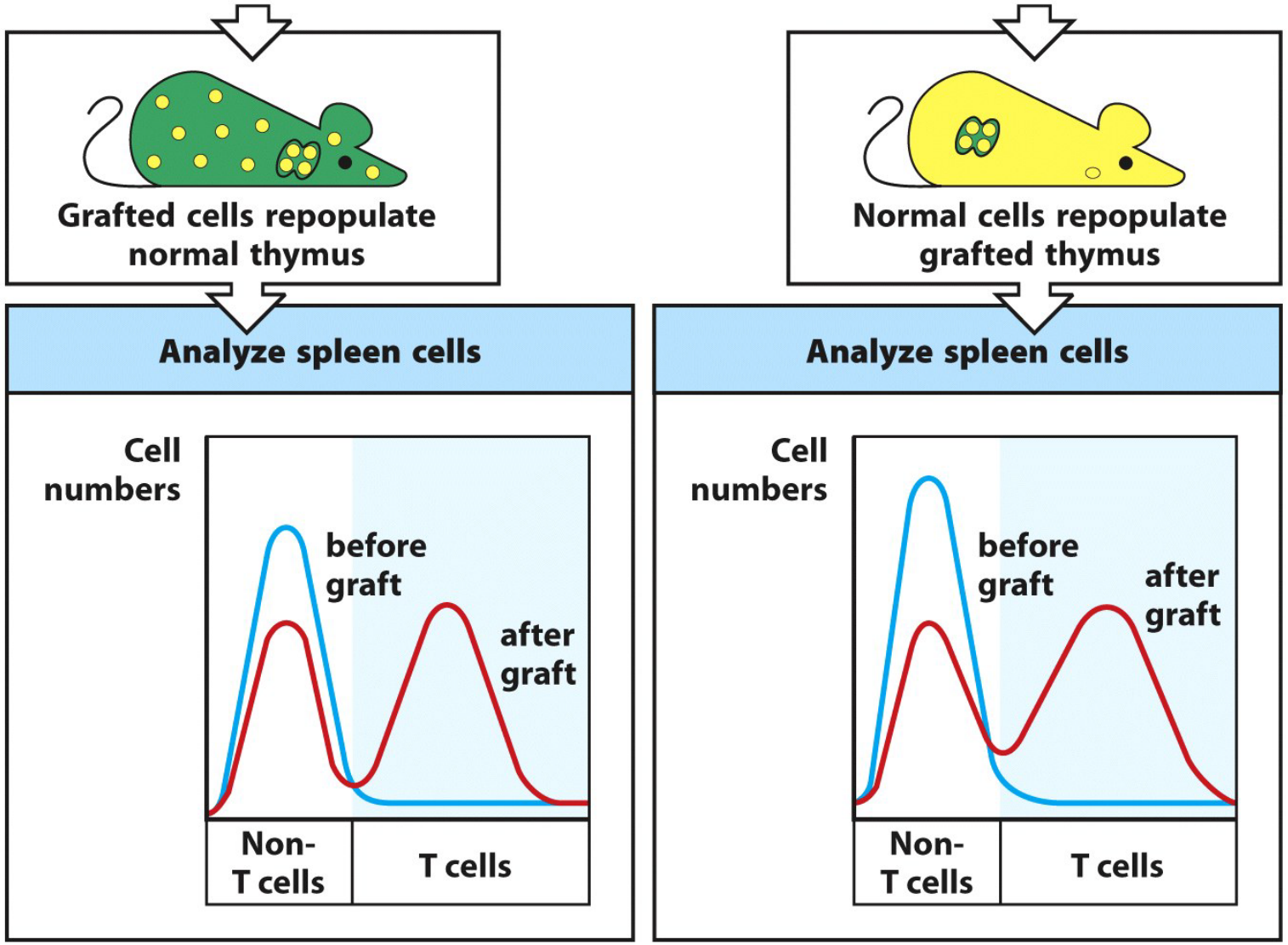


Figure 8.17 part 3 of 3 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

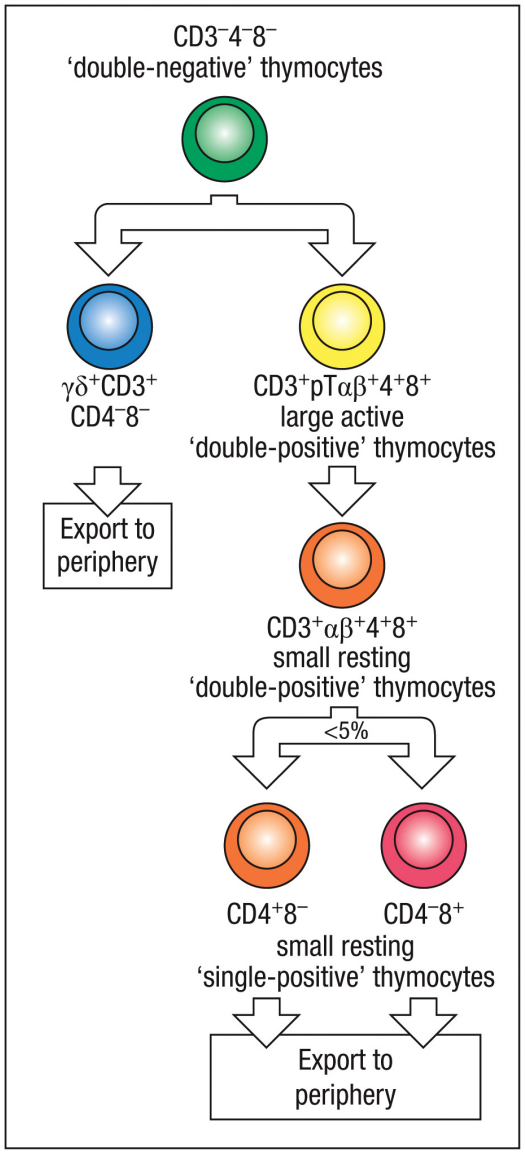
Question

- Why are people with defects in thymic epithelium immune deficient?

Outline

- T cell development
  - Thymus
  - Stages of T-cell development

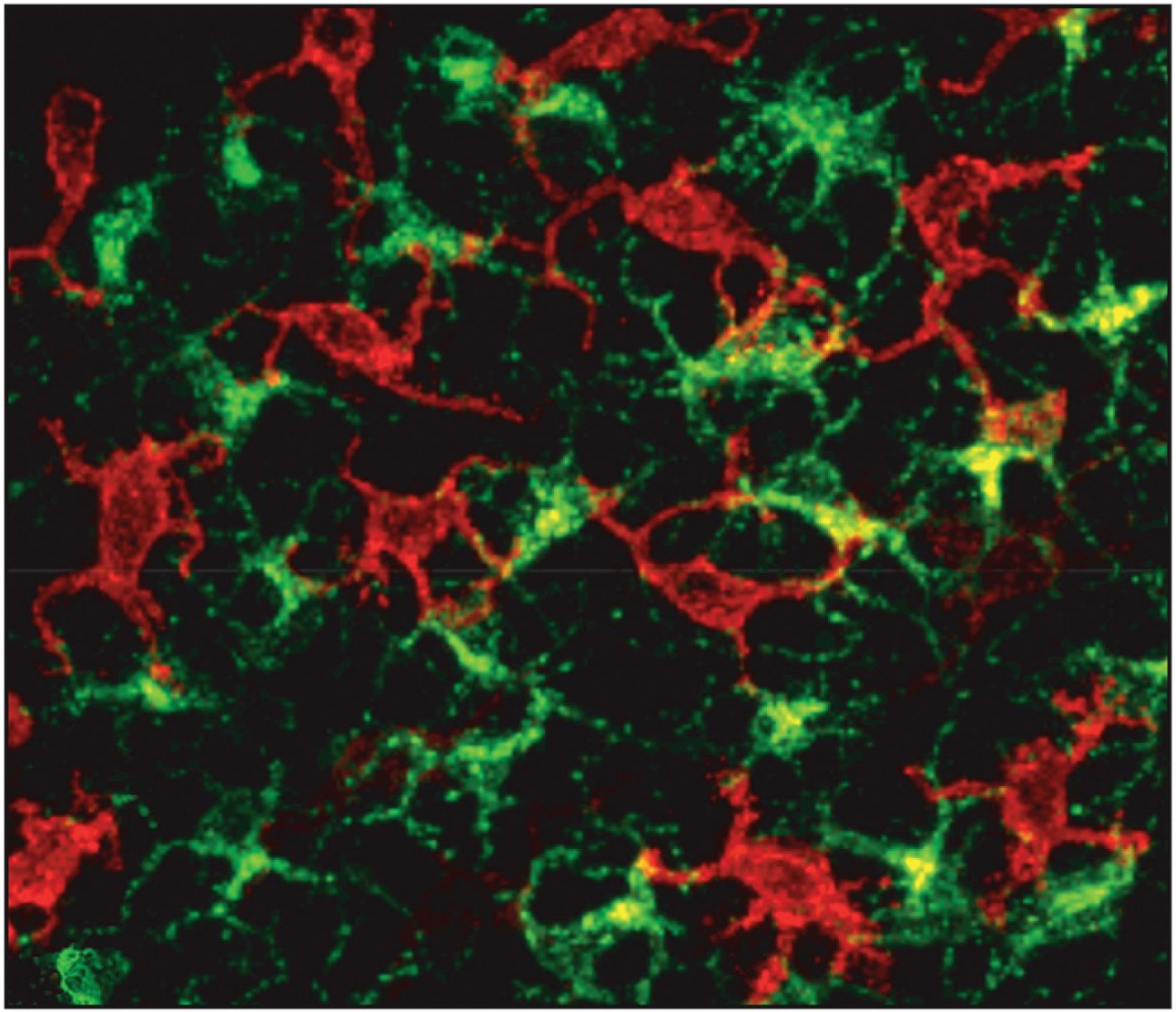
T Cell Development



About 1-2 million good T cells every day

2-4 % success rate

Dendritic Epidermal T Cells



Courtesy of Adrian Hayday

Generation of γ:δ T Cells

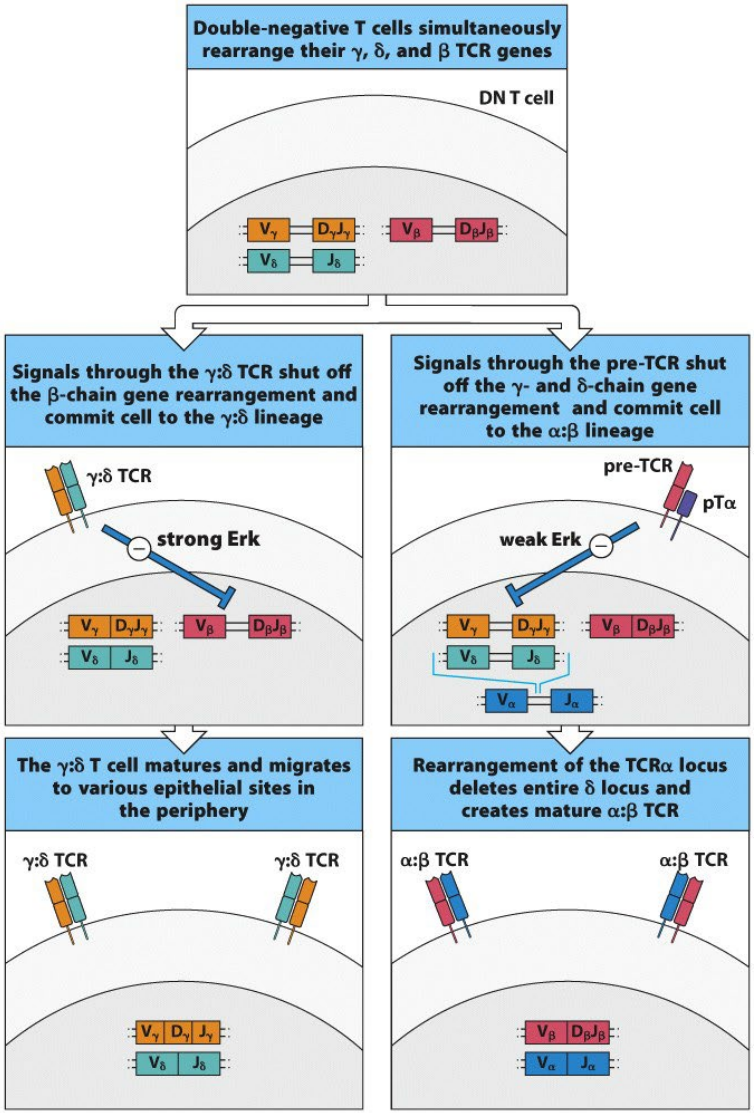
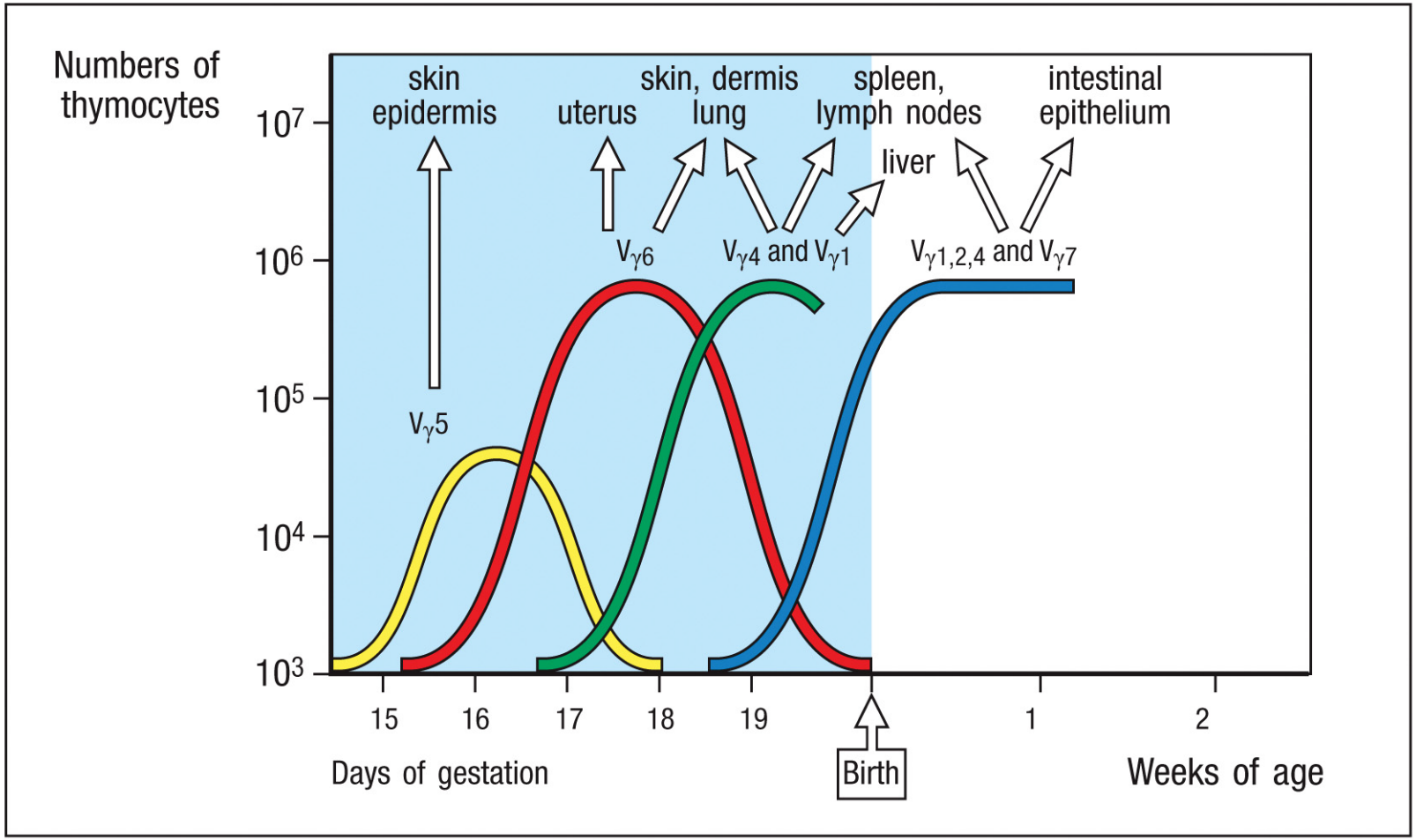
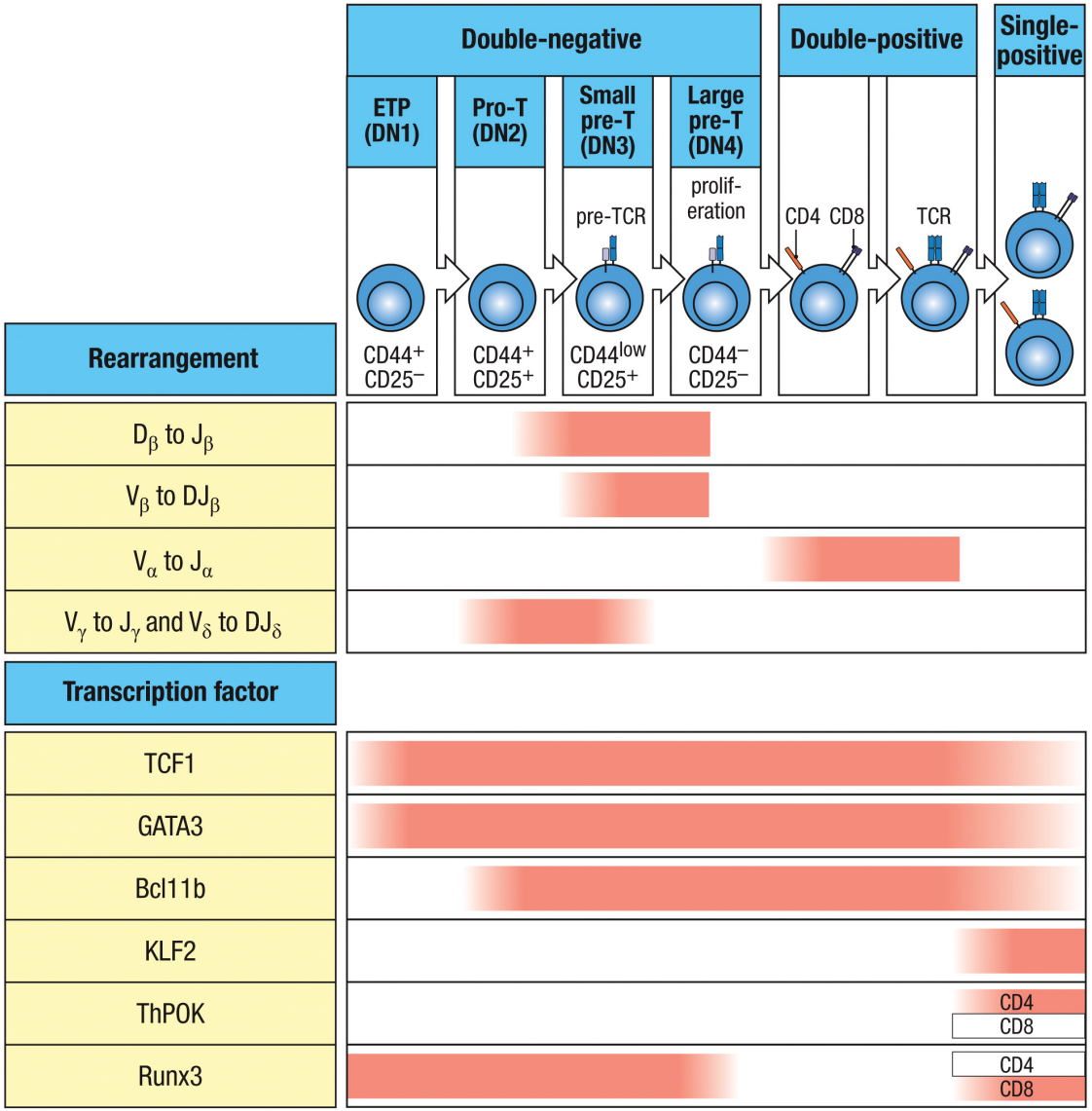


Figure 8.22 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

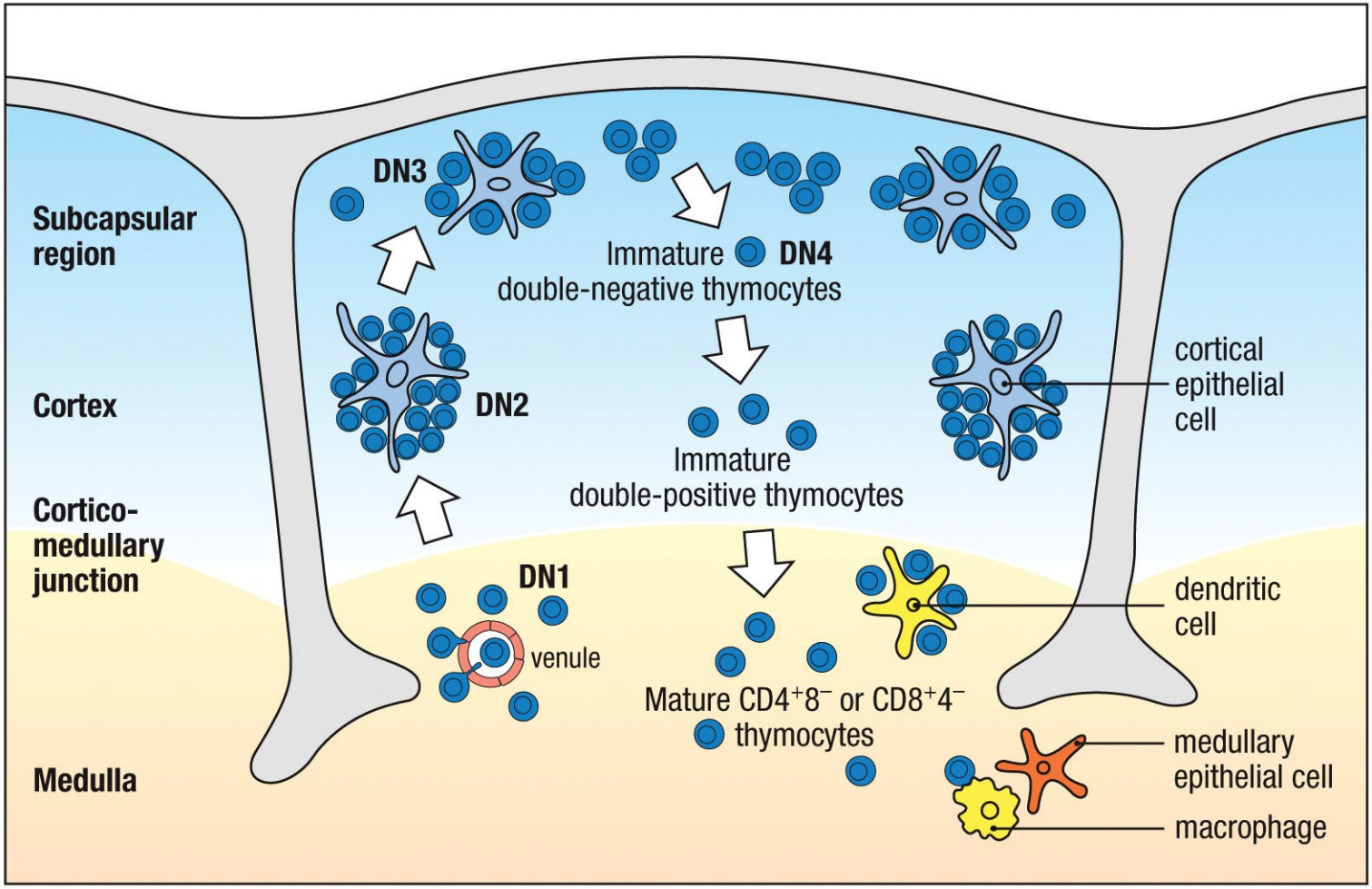
Generation of γ:δ T Cells



Gene Rearrangement During T-Cell Development



Thymocytes at Different Developmental Stages Are Found in Distinct Parts of the Thymus



Checkpoints During T-Cell Development

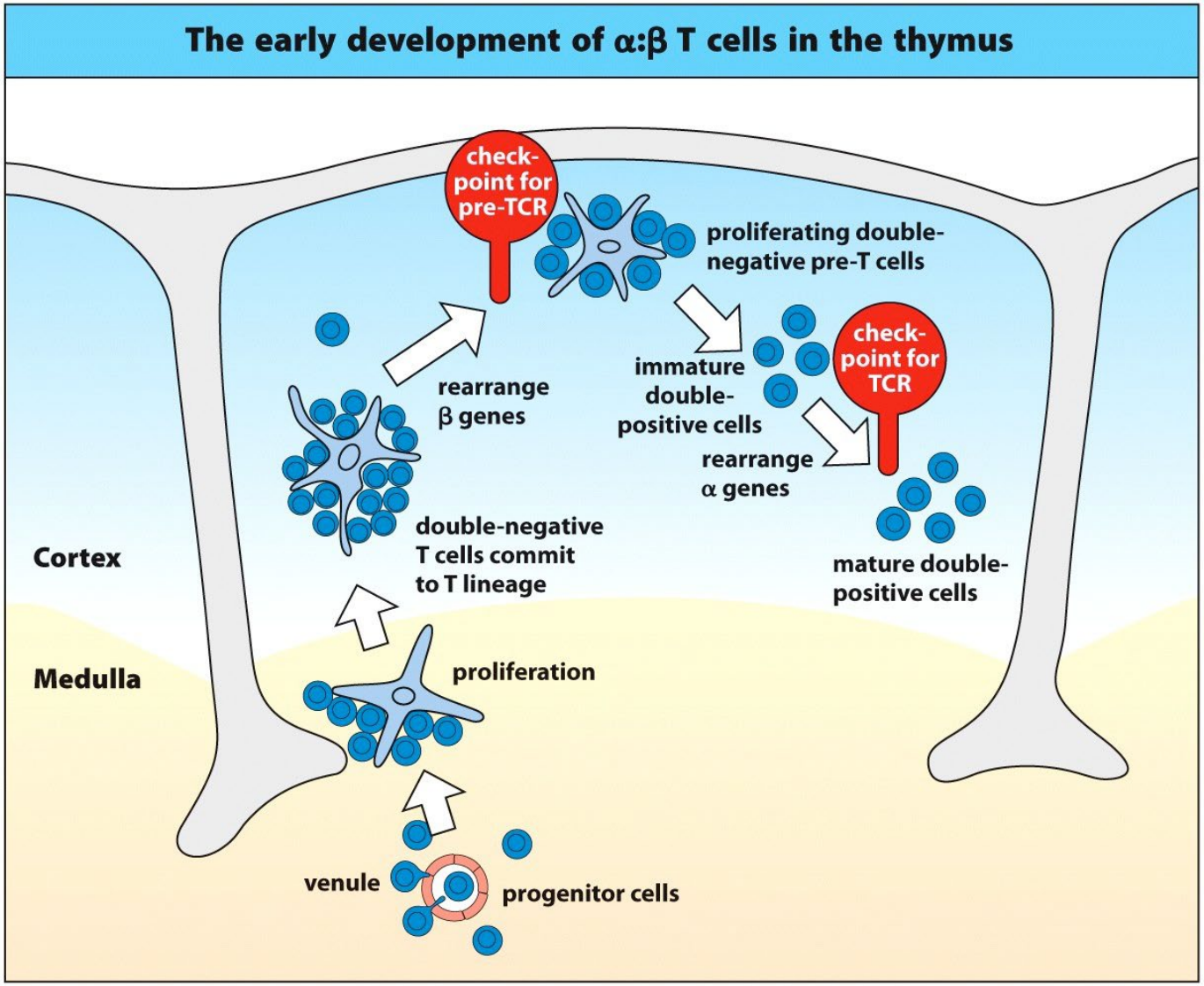


Figure 7.15 The Immune System, 3ed. (© Garland Science 2009)

Pre-TCR and TCR Signaling Complexes

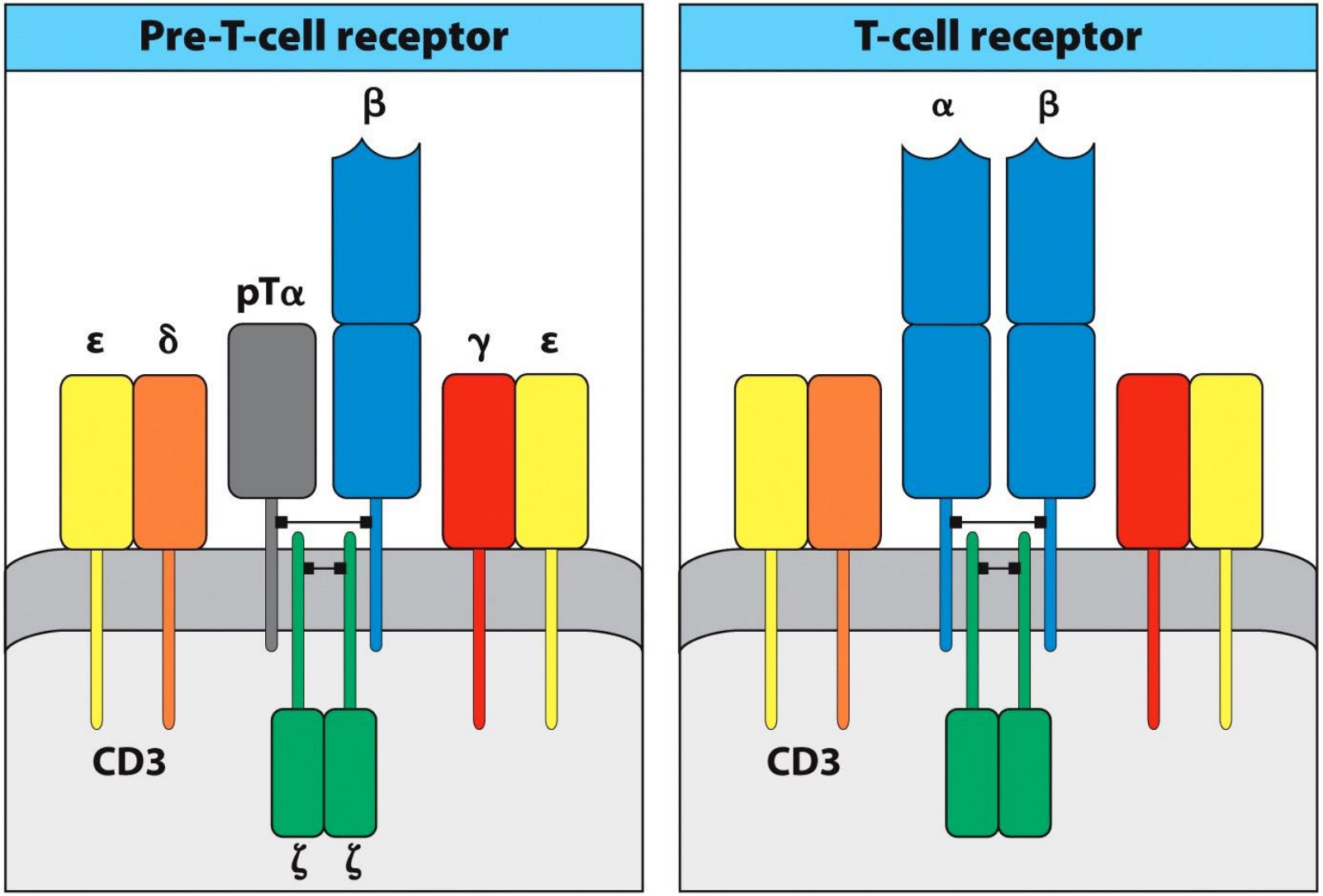
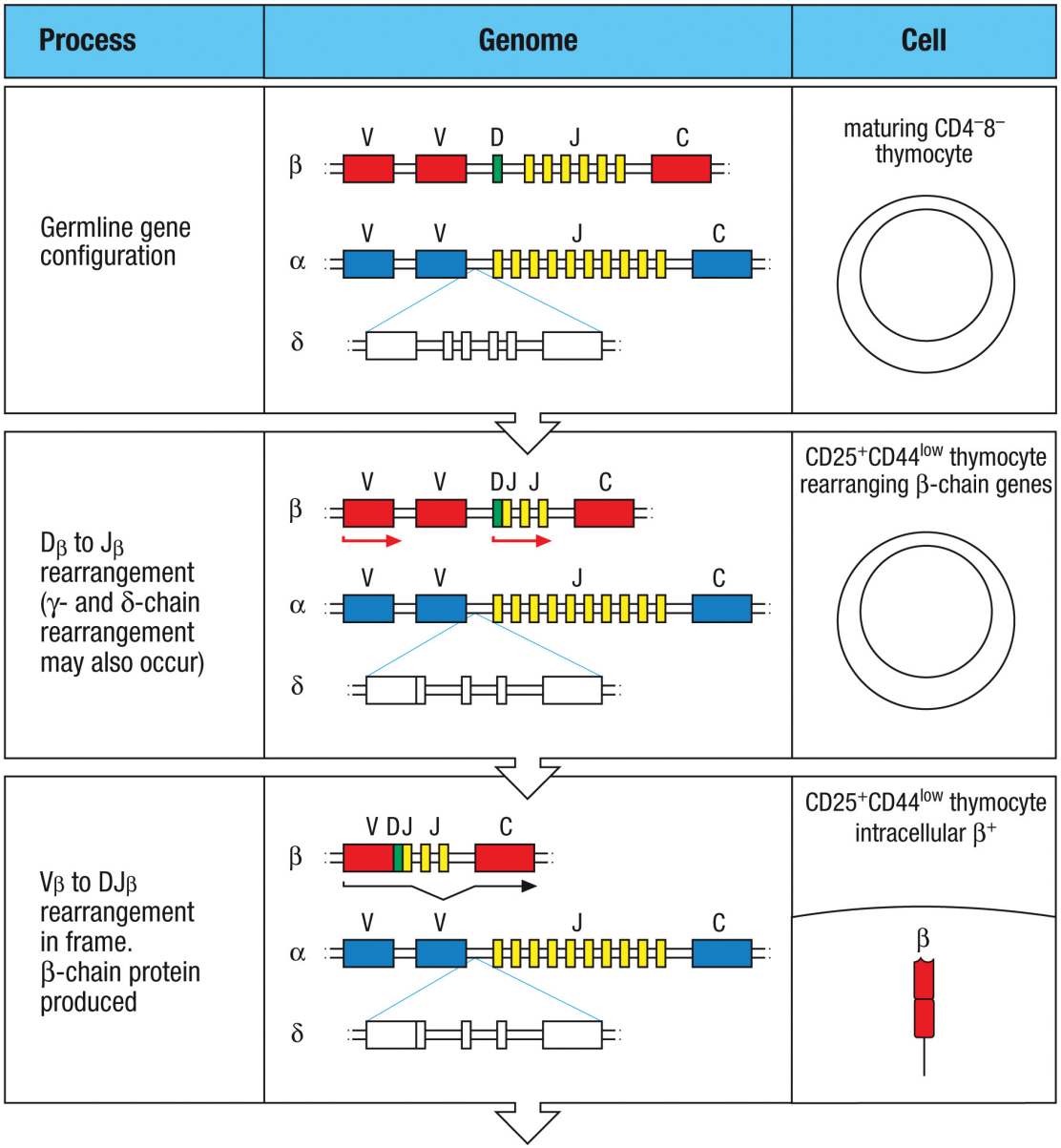


Figure 7.10 The Immune System, 3ed. (© Garland Science 2009)

Stages of Gene Rearrangement in α:β T-Cells

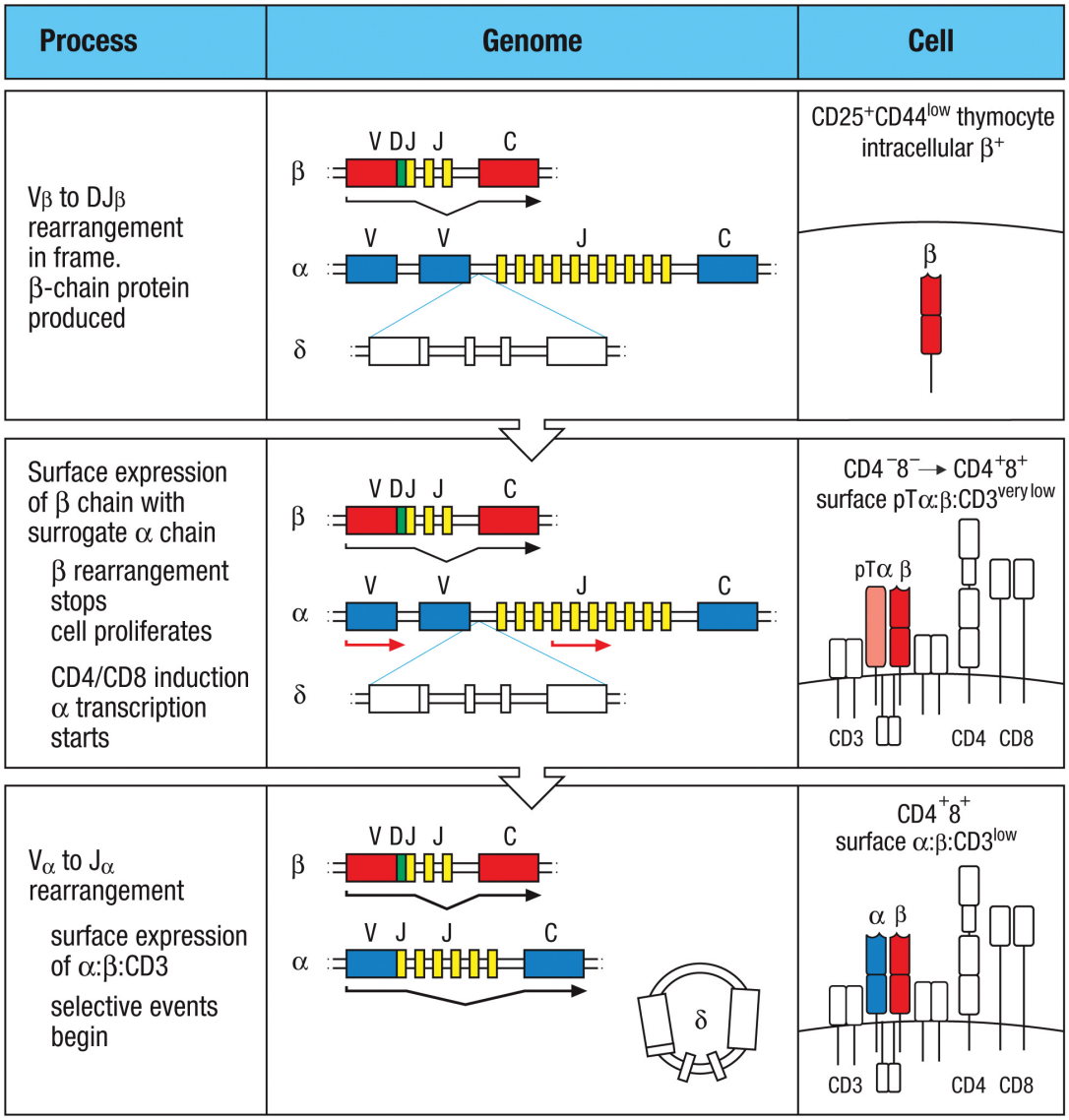


DN1&2

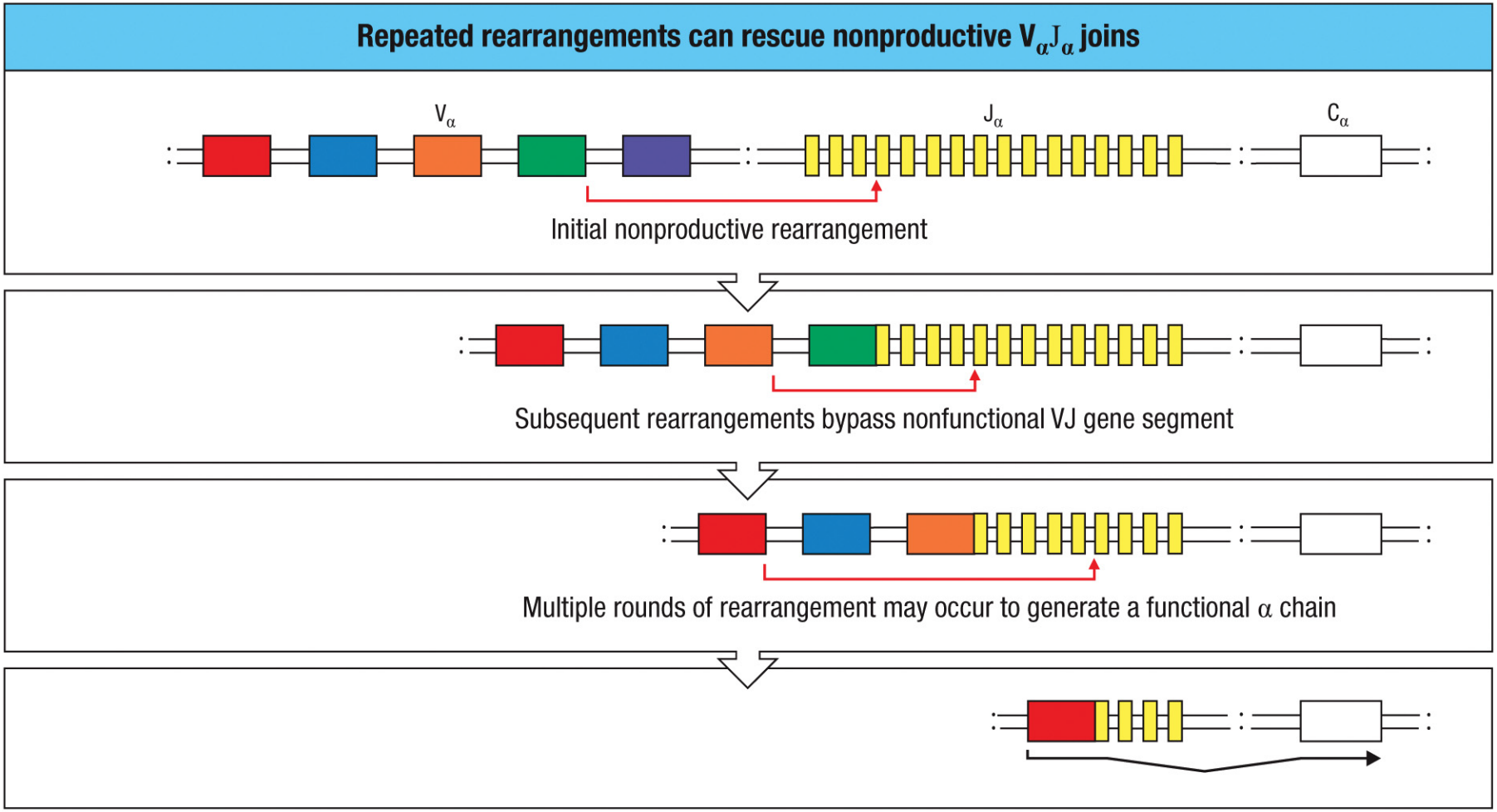
DN3

DN3

Stages of Gene Rearrangement in α:β T-Cells



TCR α-Chain Rearrangement Continues Until Positive Selection



Allelic Exclusion

- Successful beta rearrangement at one chromosome will stop the rearrangement at the other.
  - Beta chain and surrogate alpha chain
  - Degradation of RAG
  - Ensure that only one receptor is expressed on each cell.

Checkpoints During T-Cell Development

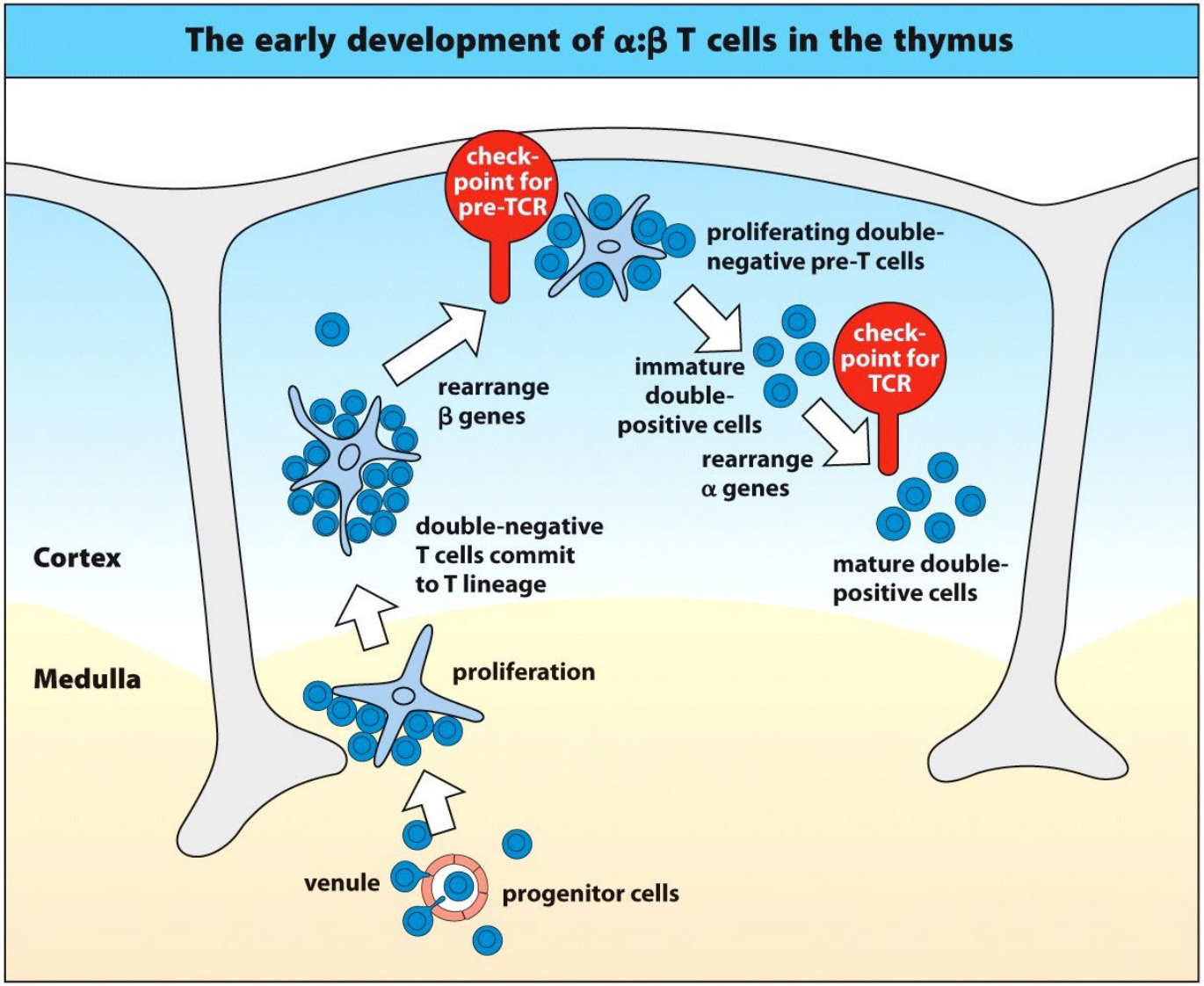
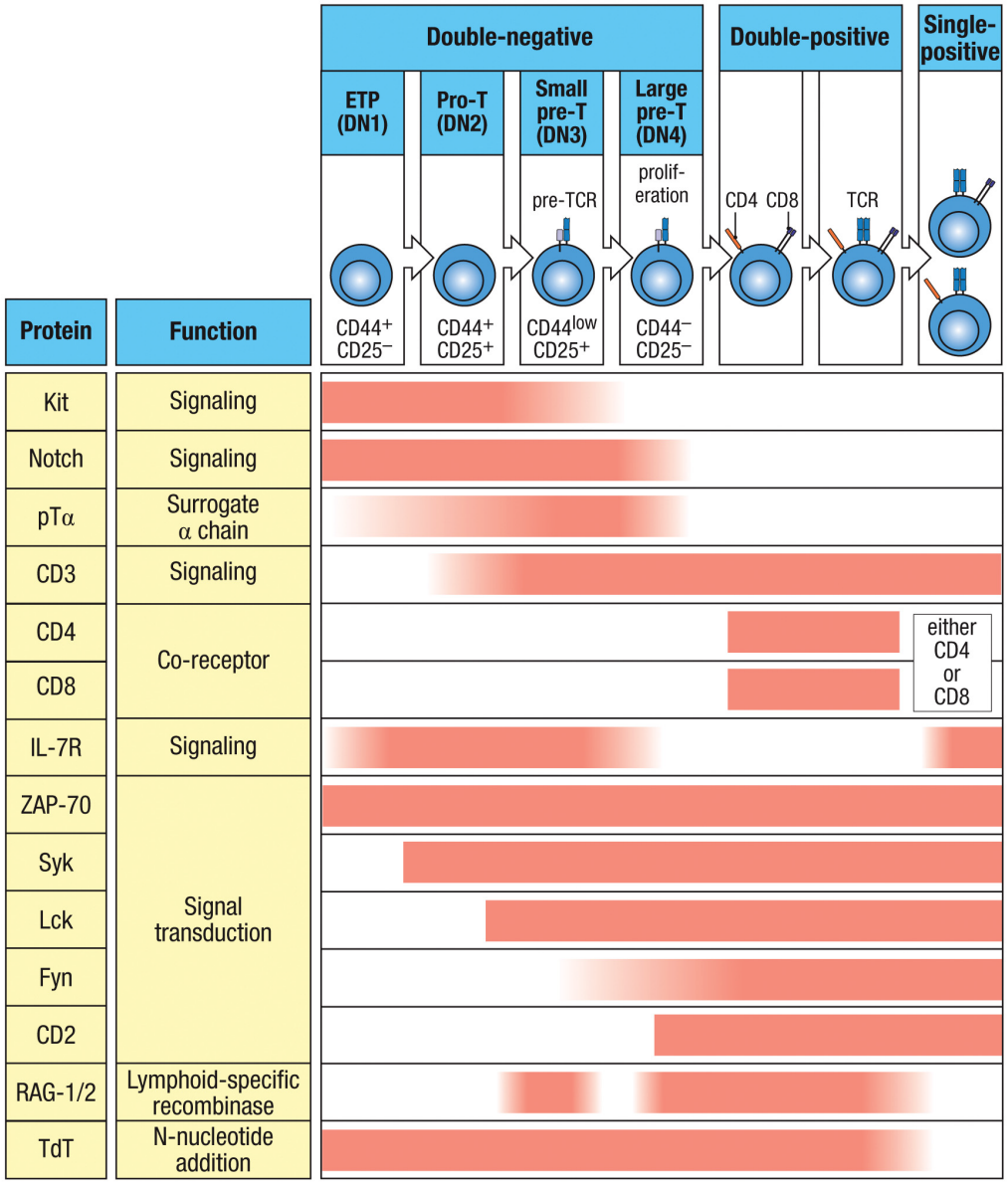


Figure 7.15 The Immune System, 3ed. (© Garland Science 2009)

Summary of T-Cell Development



Question

- What is the consequence if the patient is defect in pTα?

- A) Expression of two TCRs on each T cells
- B) Reduced T cell numbers
- C) Auto-immune
- D) All of the above

Question

- What are the two checkpoints in T cell development?
- How does an individual T cell avoid expressing two different TCRs?

Case Studies

- DiGeorge Syndrome
- Omenn syndrome

DiGeorge Syndrome

- Patient:

  New born with dysmorphic face feature, heart defect, seizures and hypocalcemia

  Severe T-cell lymphopenia

- Treatment:

  Thymic transplant-improved T cell count

DiGeorge Syndrome

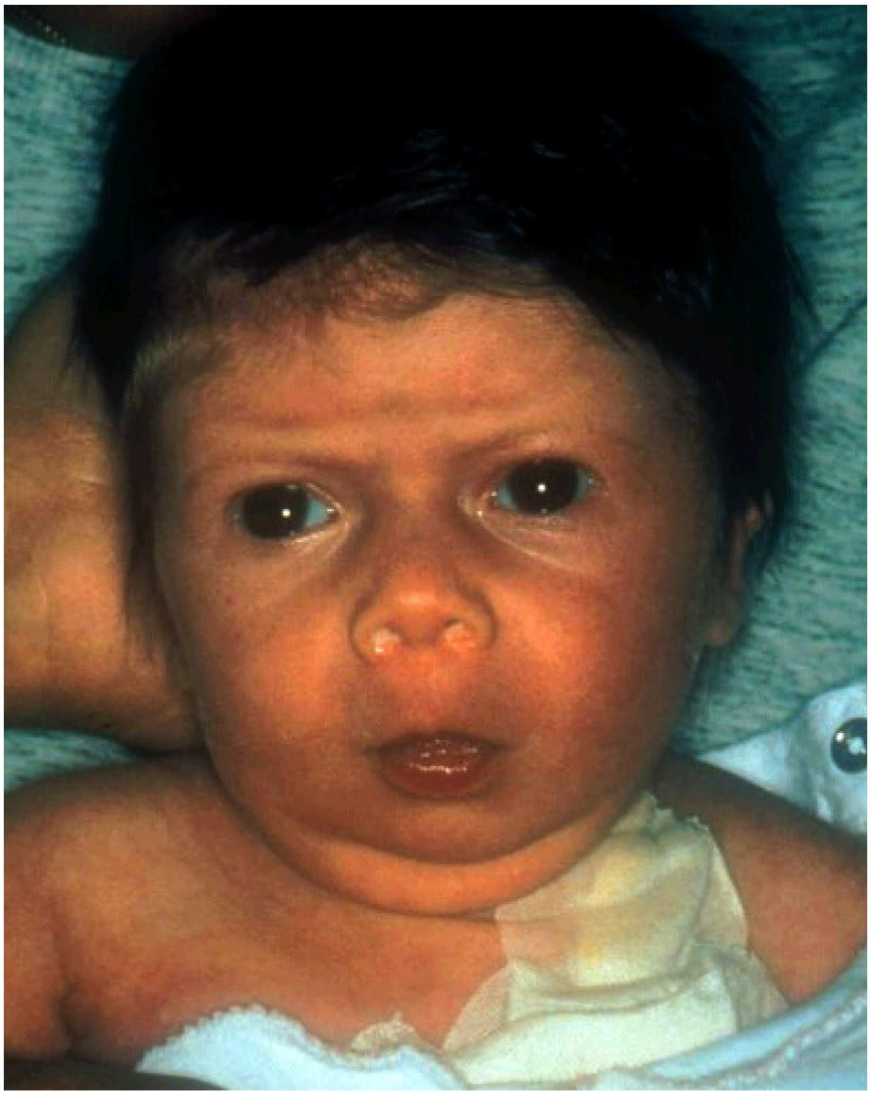


Figure 9.3 Case Studies in Immunology, 6ed. (© Garland Science 2012)

Defect in TBX1

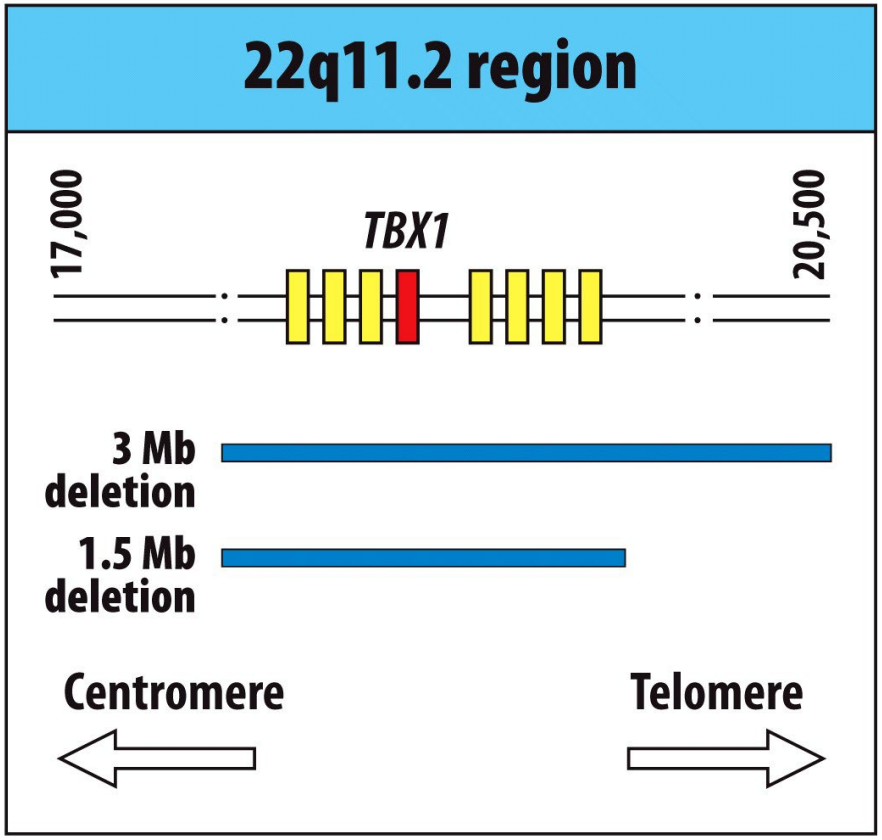


Figure 9.2 Case Studies in Immunology, 6ed. (© Garland Science 2012)

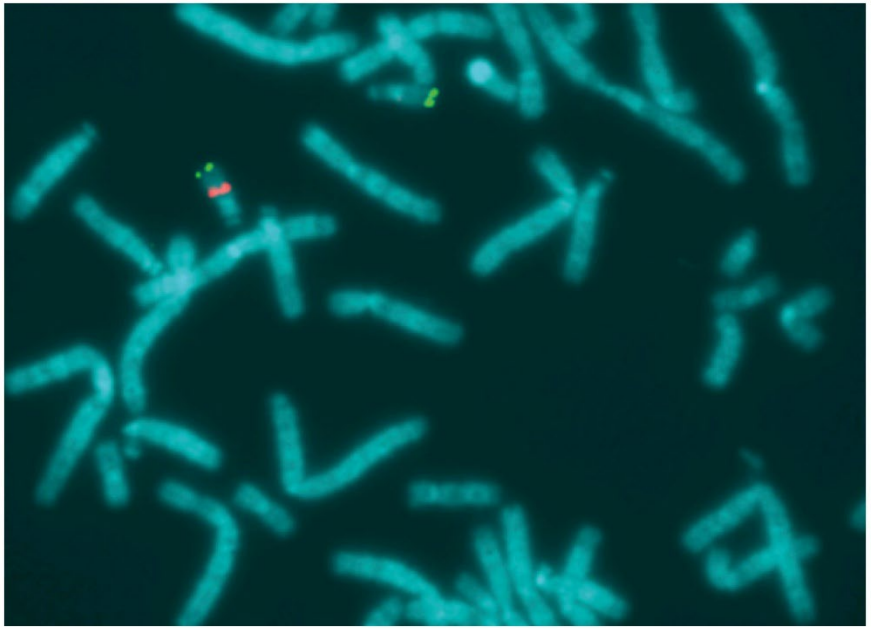


Figure 9.4 Case Studies in Immunology, 6ed. (© Garland Science 2012)

What's wrong with the patient?

- Defect in TBX1 gene, a transcription factor responsible for parathyroid gland, heart and thymus development.

- Impaired T cell development
  -immune deficiency

- Autoimmune Disease (platelets deficiency)
  -improper negative selection

Questions?

- Would Bone Marrow transplantation correct the immune deficiency with DiGeorge Syndrome—defect thymus development?

- A) Yes
- B) No

Omenn syndrome

- Patient:

  17 days after birth, rash

  low serum lymphocytes, high eosinophils

  no enlarged peripheral lymphatic organs

  Condition worse with multiple infections and enlarged lymph nodes

  Undetectable B cells and oligoclonal T cells

  Died of respiratory failure

What's wrong with the patient?

- RAG2 deficient.
  - Point mutation that reduced function

- Very few clonal T cells
  - Rapidly expand
  - Escape negative selection
  - Immune deficiency and auto-immune
  - A heightened Th2 response

- Can be treated with bone marrow transplantation.