

# Johns Hopkins Engineering

## Immunoengineering

**Allergy and Autoimmunity**

**Distinguishing Foreign From Self**



**JOHNS HOPKINS**  
WHITING SCHOOL  
*of* ENGINEERING

# Mechanisms of Distinguishing Self from Non-self

- Central Tolerance
- Antigen Segregation
- Peripheral Tolerance
- Regulatory T cells
- Functional Deviation
- Activation-induced Cell Death

# Central T cell tolerance occurs in the thymus

- T cell receptor developed through genetic recombination
- CD4 and CD8 expression change
- Exposure to autoantigen regulates survival

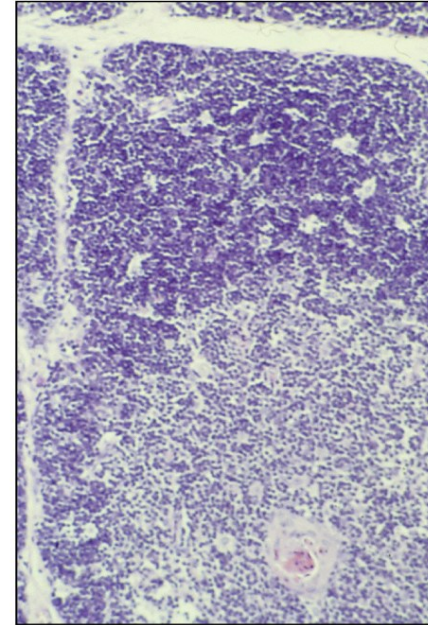
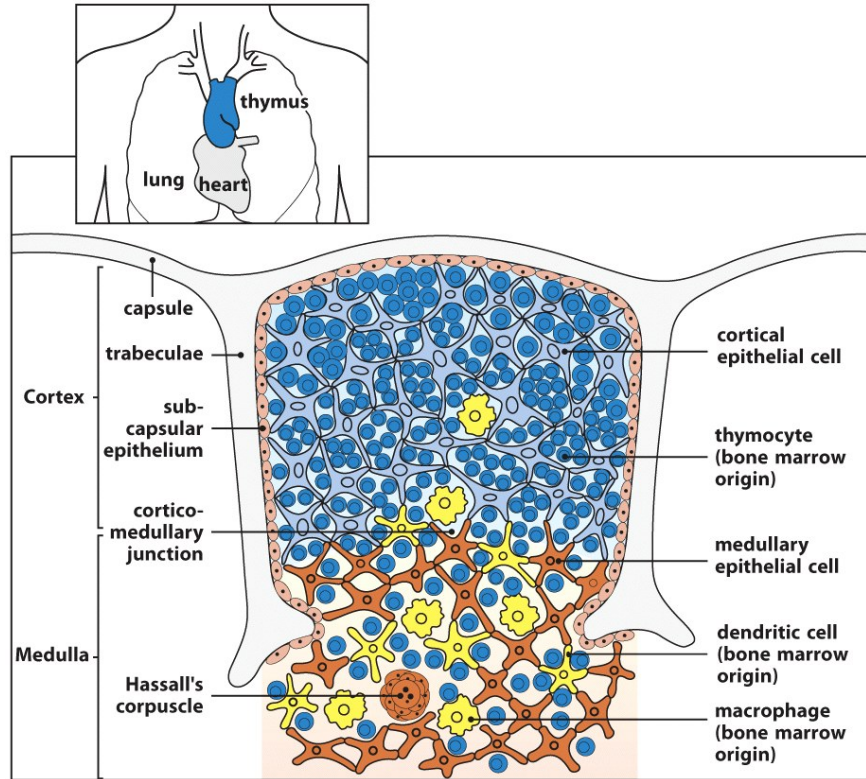


Figure 8.15 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

# Central Tolerance and Clonal Deletion

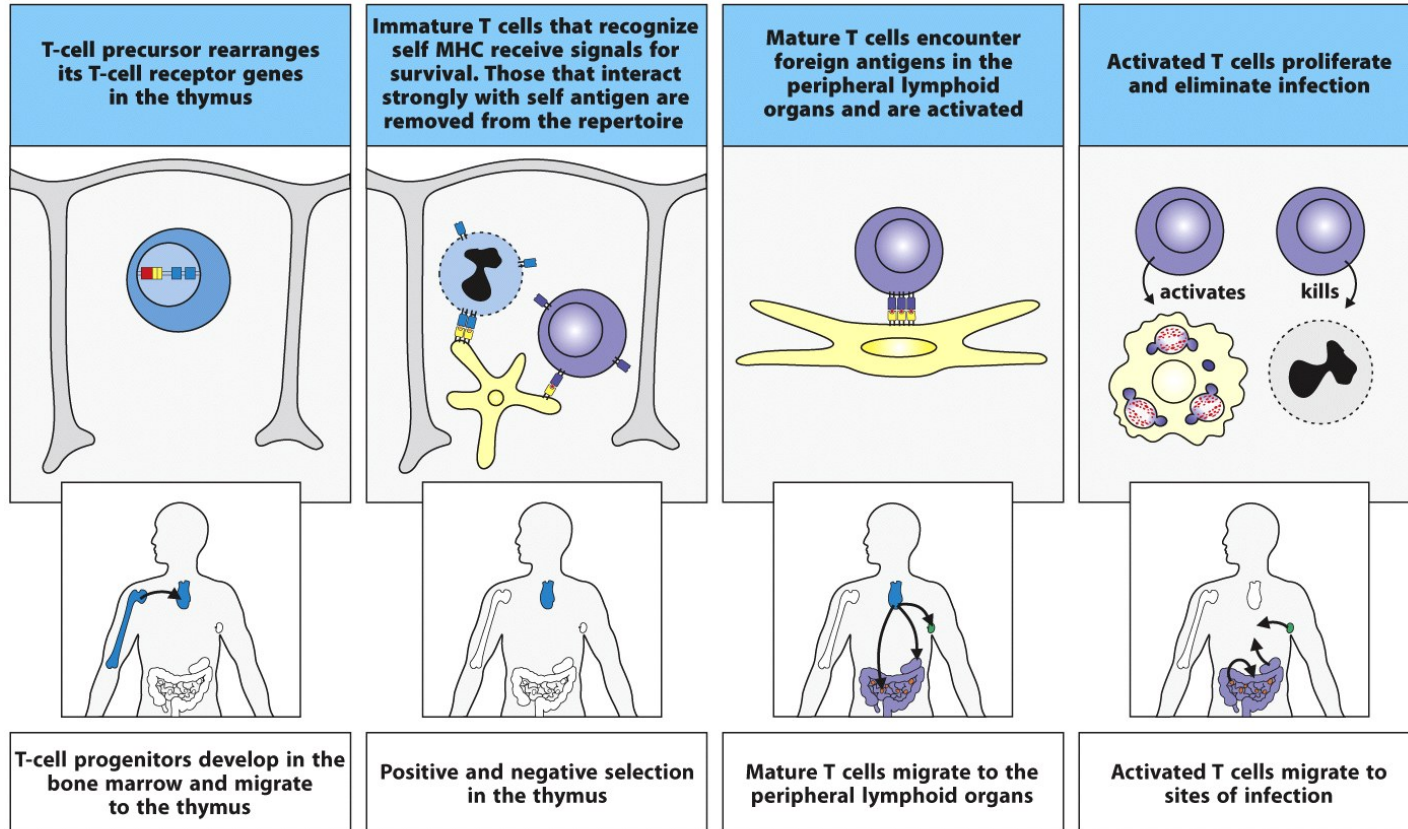


Figure 8.14 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

# The Importance of AIRE Expression

- Autoimmune Regulator
- Expressed in medullary thymic epithelial cells
- Turns on peripheral genes in thymus
- Example: Insulin

## AIRE expression in the thymus

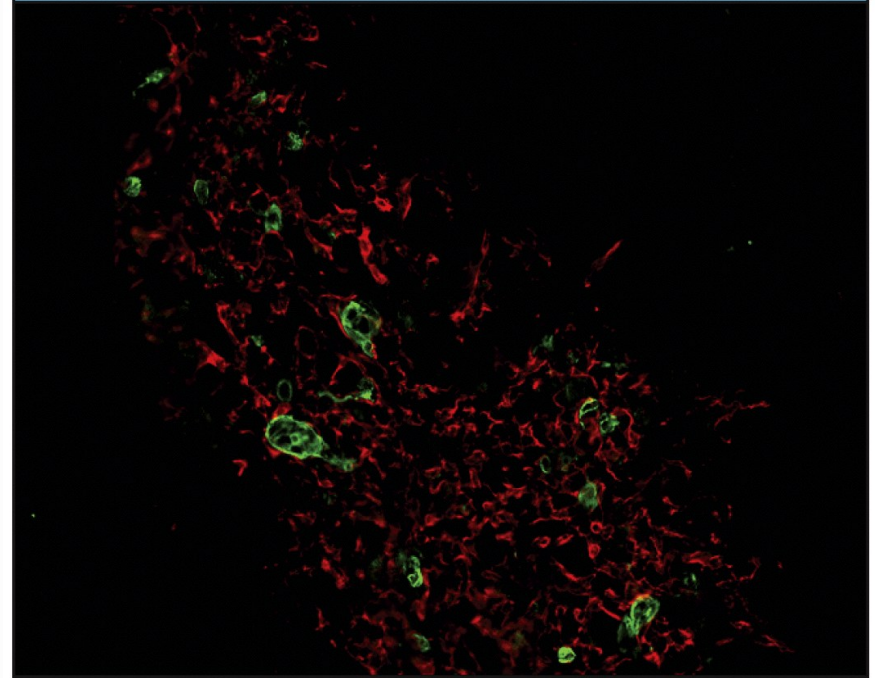


Figure 8.34 Janeway's Immunobiology, 8ed. (© Garland Science 2012)



# AIRE Aids in Generating Organism-wide Tolerance

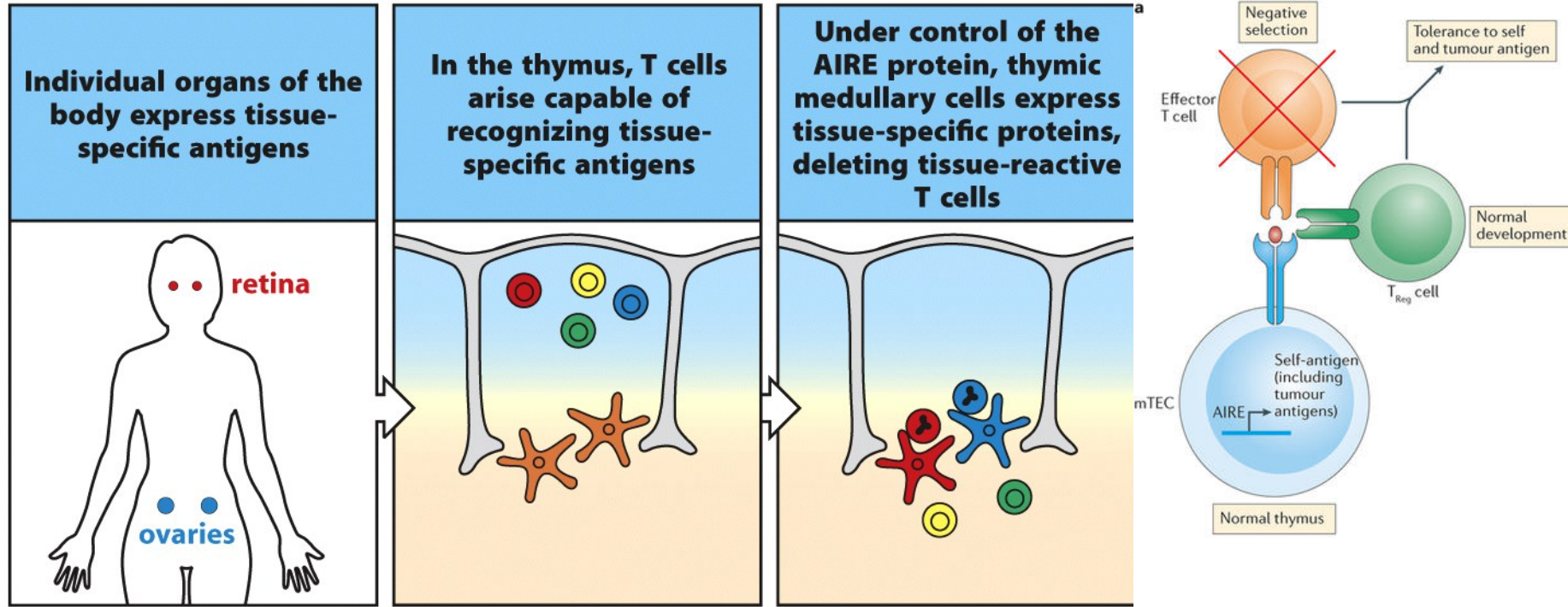


Figure 15.4 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

# Central Tolerance and Clonal Deletion

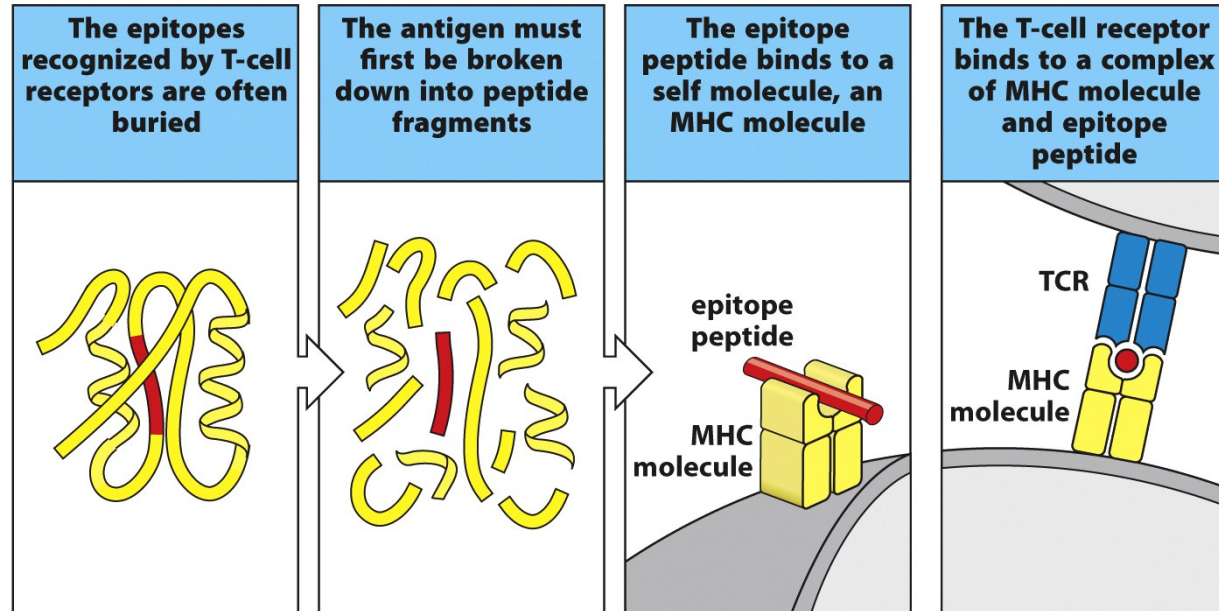
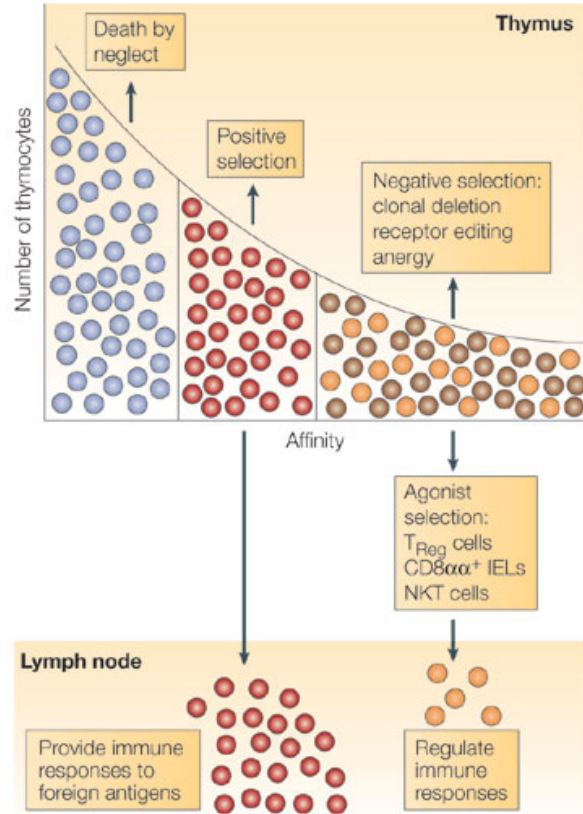


Figure 1.16 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

(Hogquist, Kristin A., Troy A. Baldwin, and Stephen C. Jameson. "Central tolerance: learning self-control in the thymus." *Nature Reviews Immunology* 5.10 (2005): 772-782.)

# B Cell Tolerance

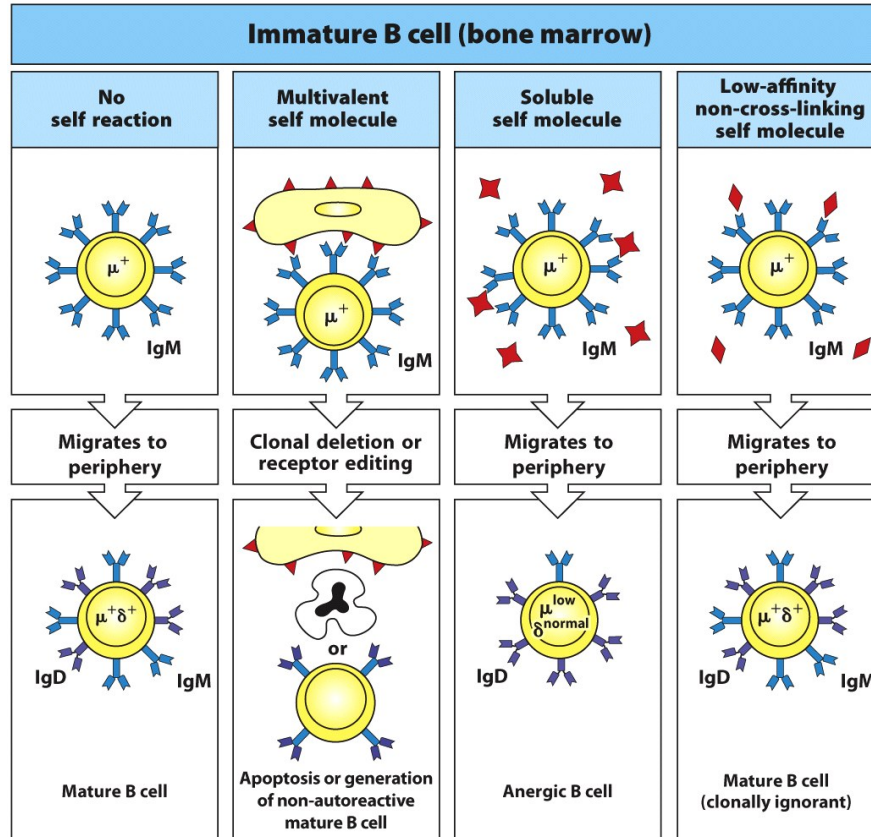


Figure 8.12 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

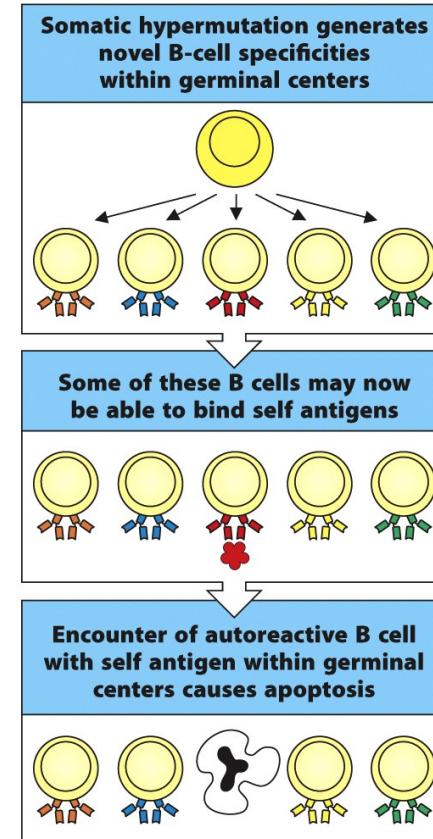
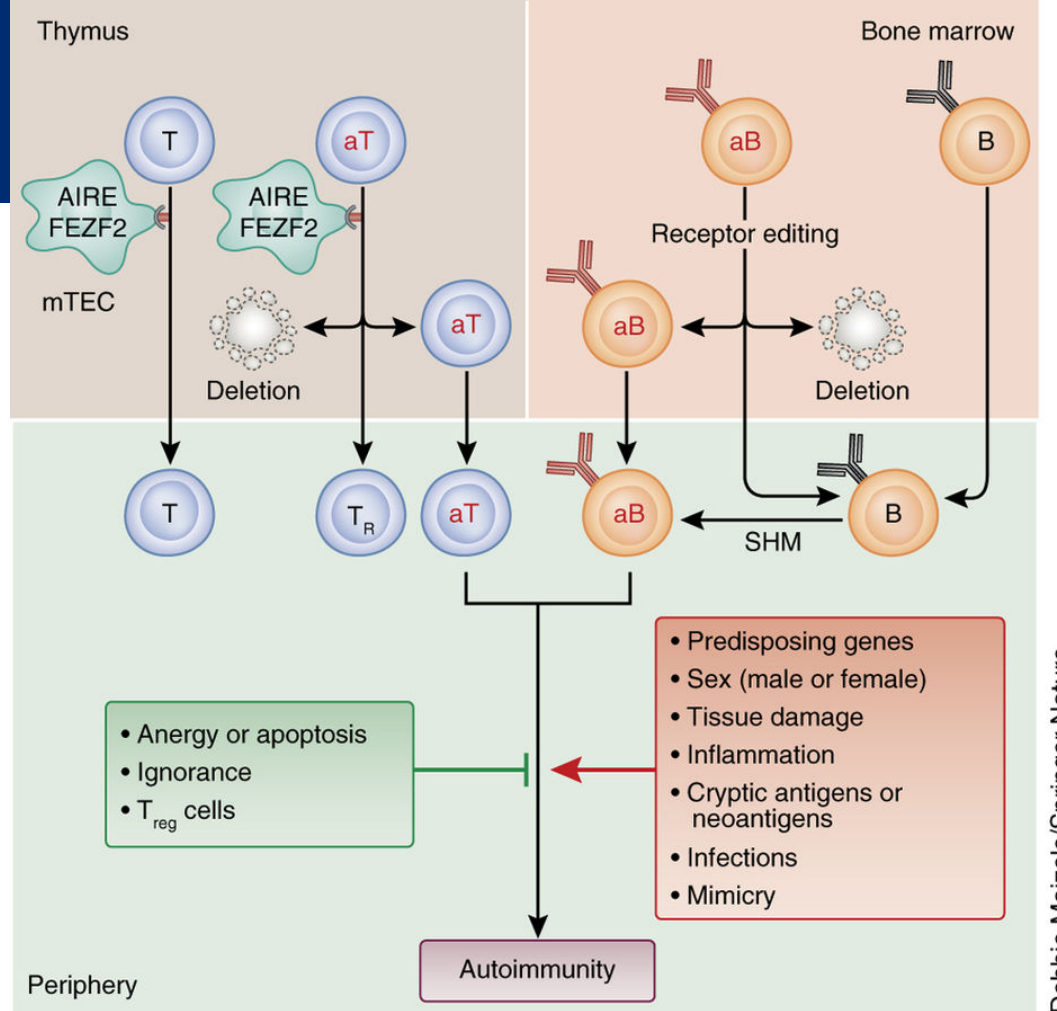


Figure 15.6 Janeway's Immunobiology, 8ed. (© Garland Science 2012)





Debbie Maizels/Springer Nature

# Antigen Segregation

- Antigen does not pass through conventional lymphatics
- Cytokines leave with antigens (e.g. TGF- $\beta$ )
- Expression of Fas ligand by tissues

## Immunologically privileged sites

**Brain**

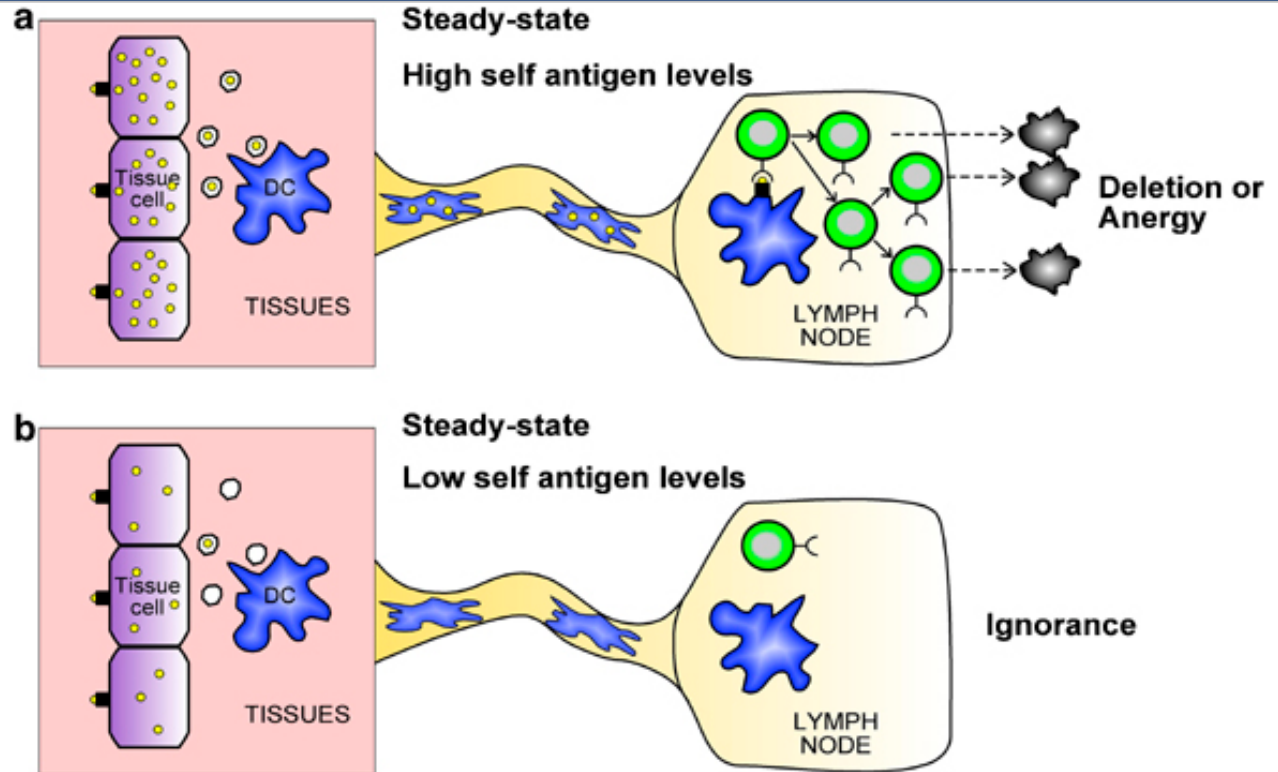
**Eye**

**Testis**

**Uterus (fetus)**

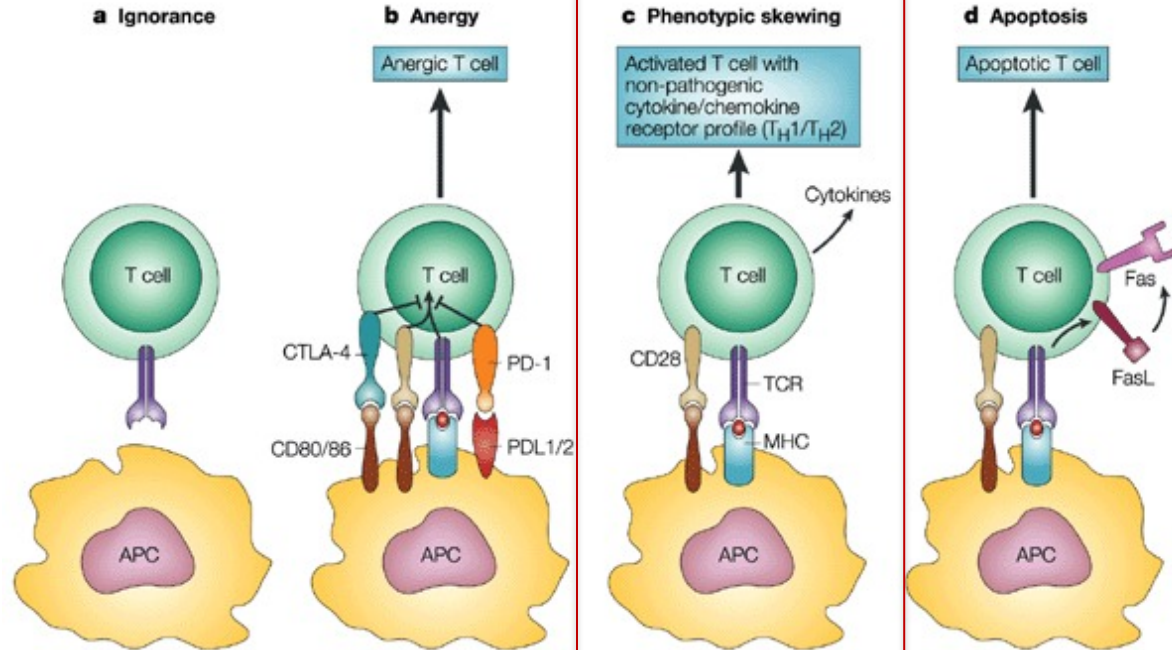
**Hamster cheek pouch**

# Peripheral Tolerance



(Parish, Ian A., and William R. Heath. "Too dangerous to ignore: self-tolerance and the control of ignorant autoreactive T cells." *Immunology and cell biology* 86.2 (2008): 146-152.)

# Peripheral Tolerance



Nature Reviews | Immunology

(Walker, Lucy SK, and Abul K. Abbas. "The enemy within: keeping self-reactive T cells at bay in the periphery." *Nature Reviews Immunology* 2.1 (2002): 11-19.)

# Regulatory Tolerance

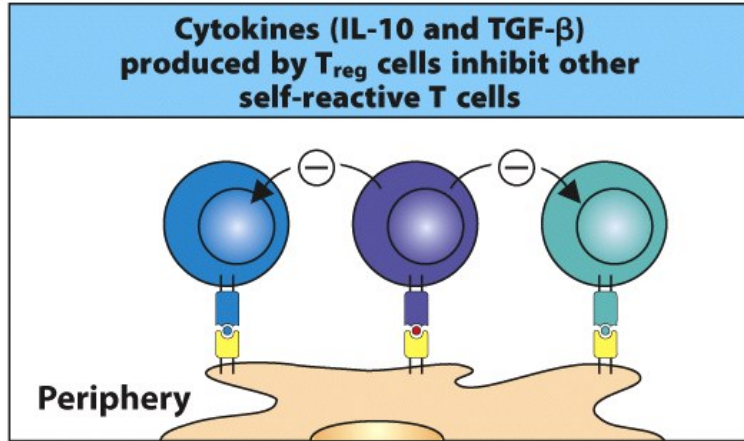
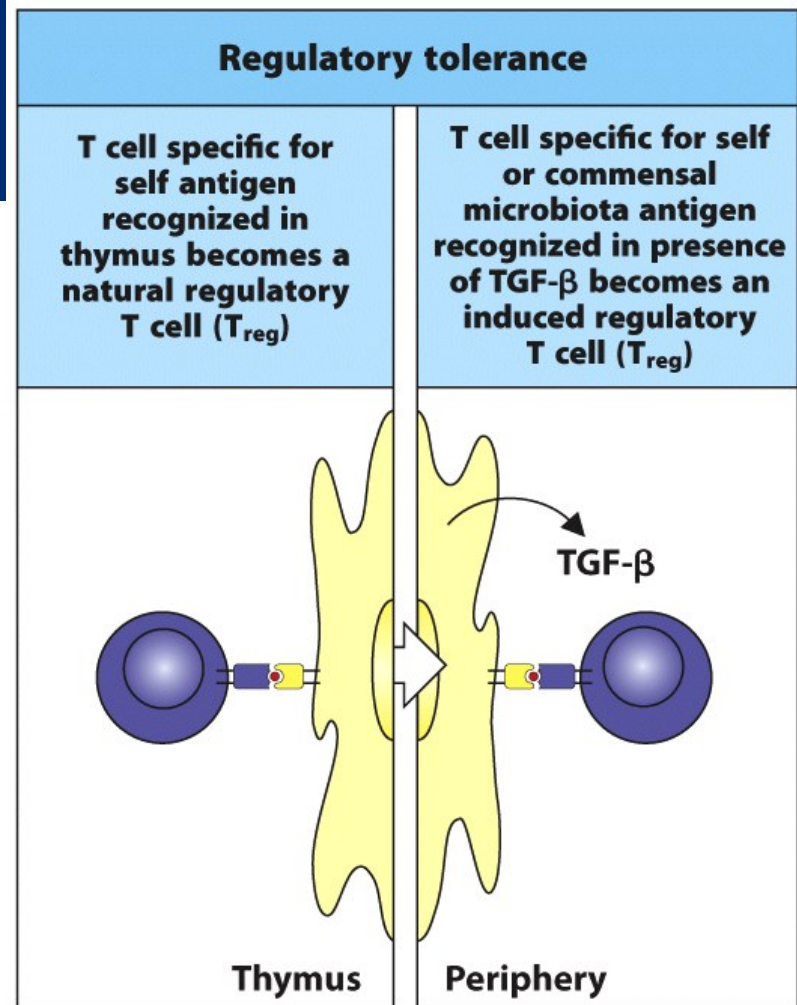
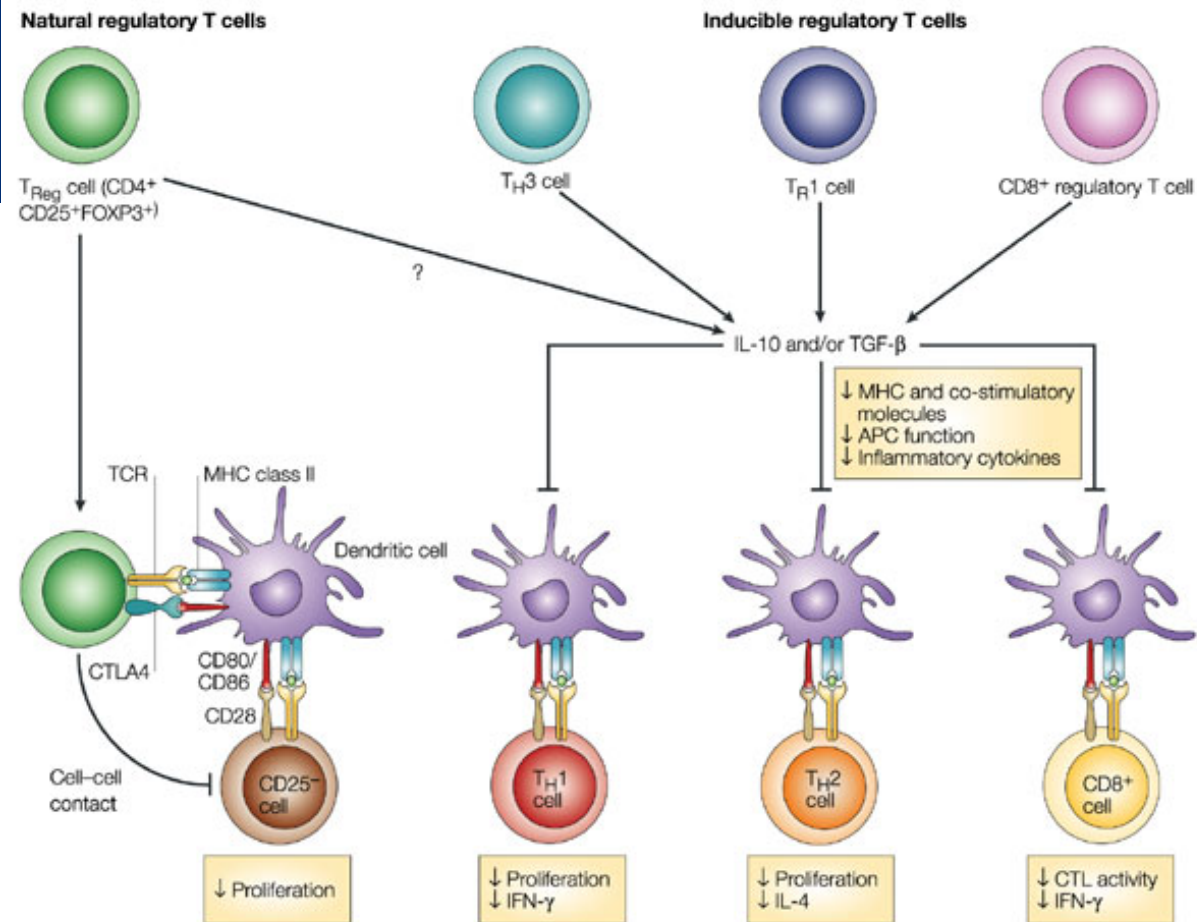


Figure 15.9 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

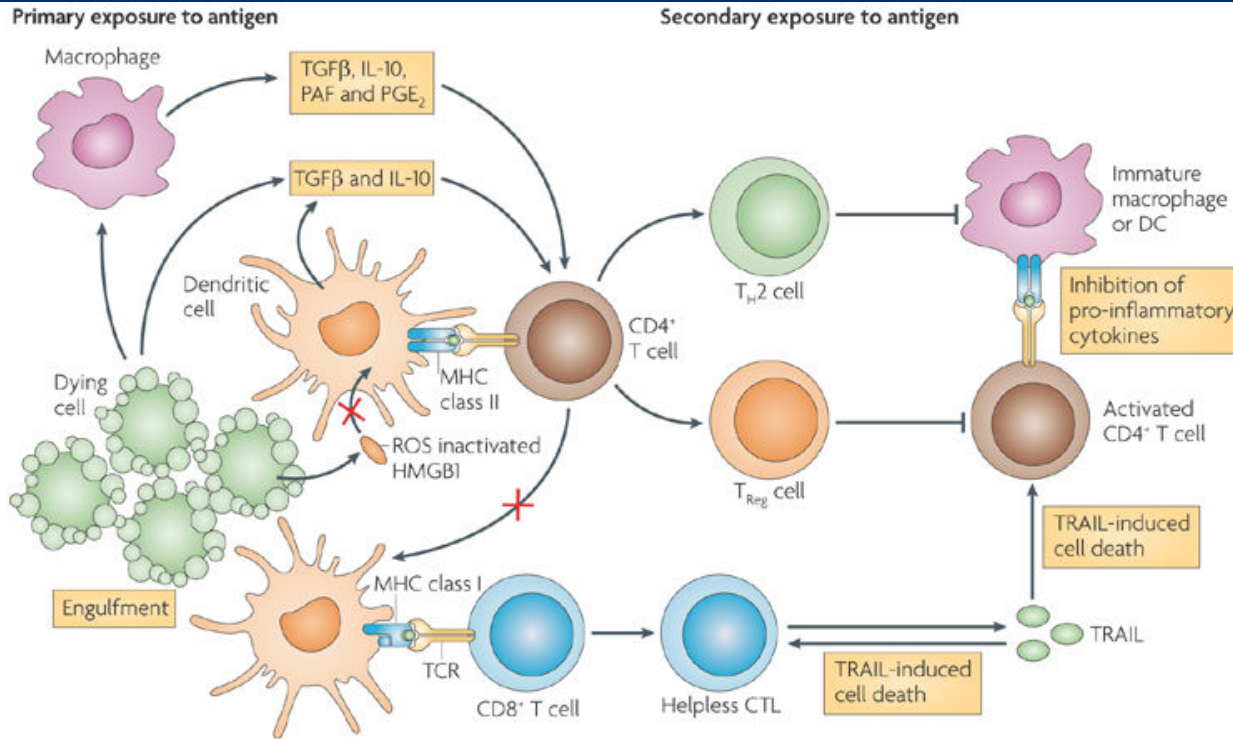




# Tregs



# Functional Deviation & Activation-induced Cell Death



# Summary

Layers of self-tolerance		
Type of tolerance	Mechanism	Site of action
Central tolerance	Deletion Editing	Thymus Bone marrow
Antigen segregation	Physical barrier to self-antigen access to lymphoid system	Peripheral organs (e.g. thyroid, pancreas)
Peripheral anergy	Cellular inactivation by weak signaling without co-stimulus	Secondary lymphoid tissue
Regulatory T cells	Suppression by cytokines, intercellular signals	Secondary lymphoid tissue and sites of inflammation
Functional deviation	Differentiation of regulatory T cells that limit inflammatory cytokine secretion	Secondary lymphoid tissue and sites of inflammation
Activation-induced cell death	Apoptosis	Secondary lymphoid tissue and sites of inflammation

Figure 15.2 Janeway's Immunobiology, 8ed. (© Garland Science 2012)



JOHNS HOPKINS

WHITING SCHOOL  
*of* ENGINEERING