



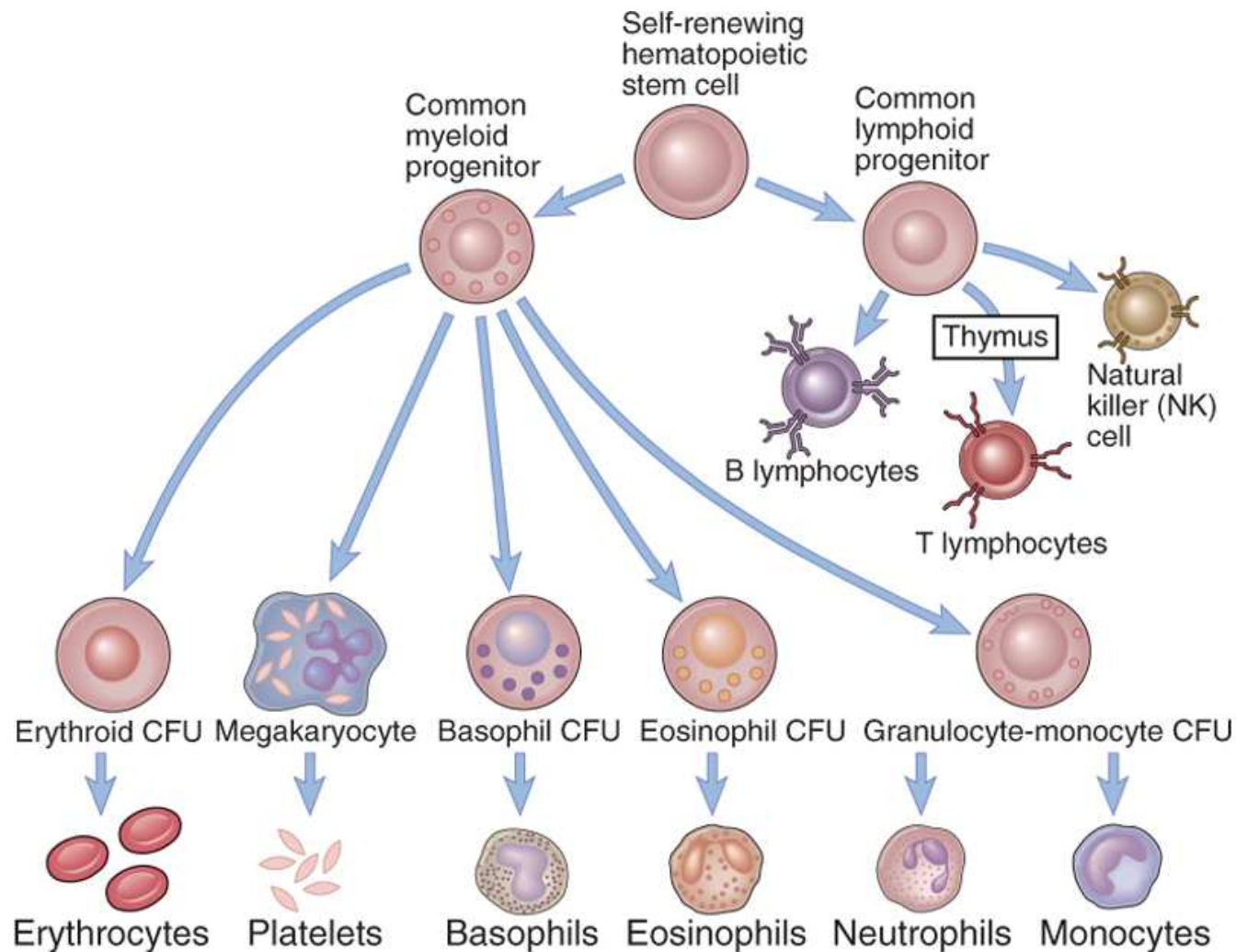
Immunology 101 for the Practicing Oncologist

**Division of Malignant
Hematology and Blood and
Marrow Transplantation**

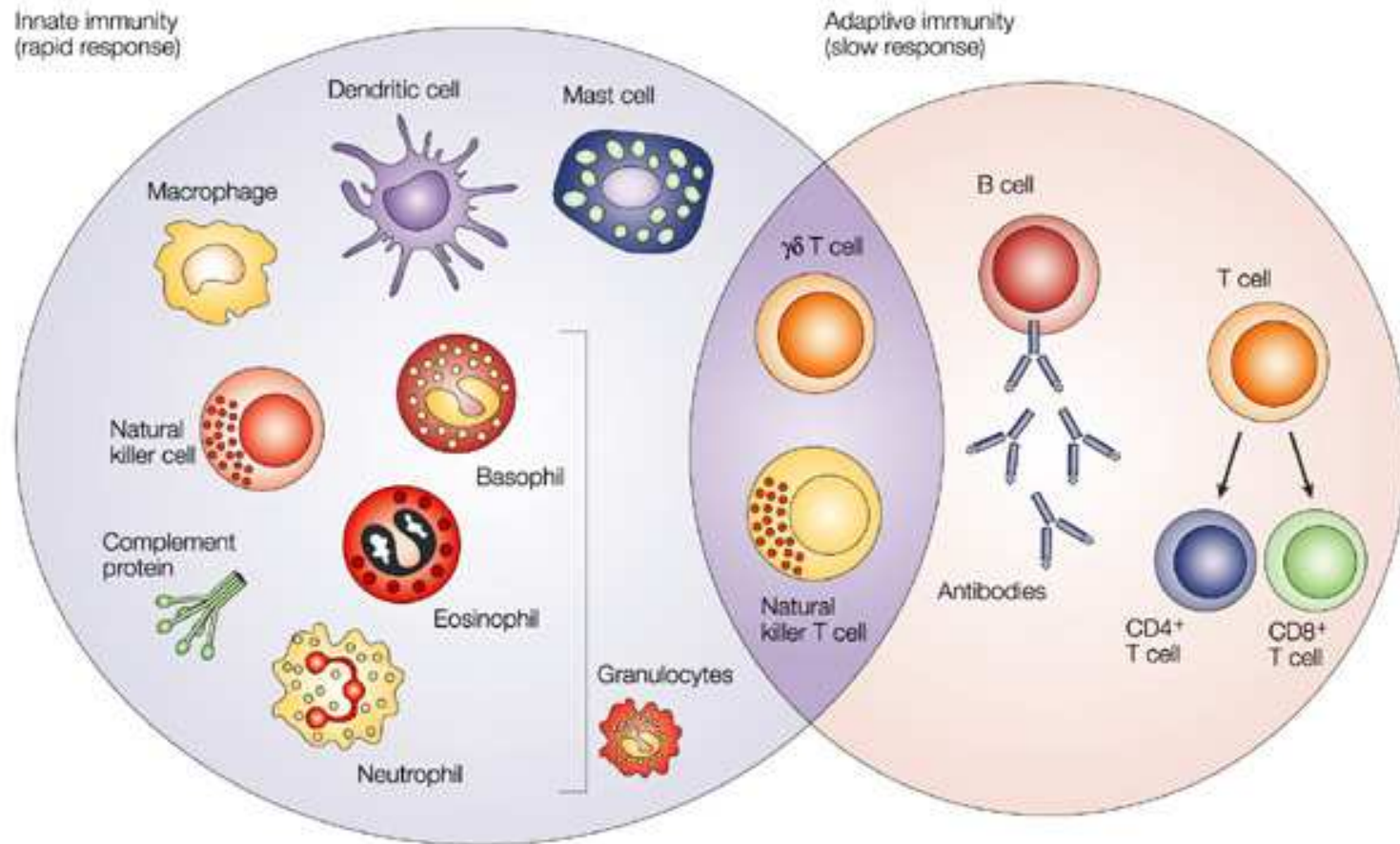
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December 14, 2013

Hematopoiesis



Innate and Adaptive Immunity



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Innate and Adaptive Immunity

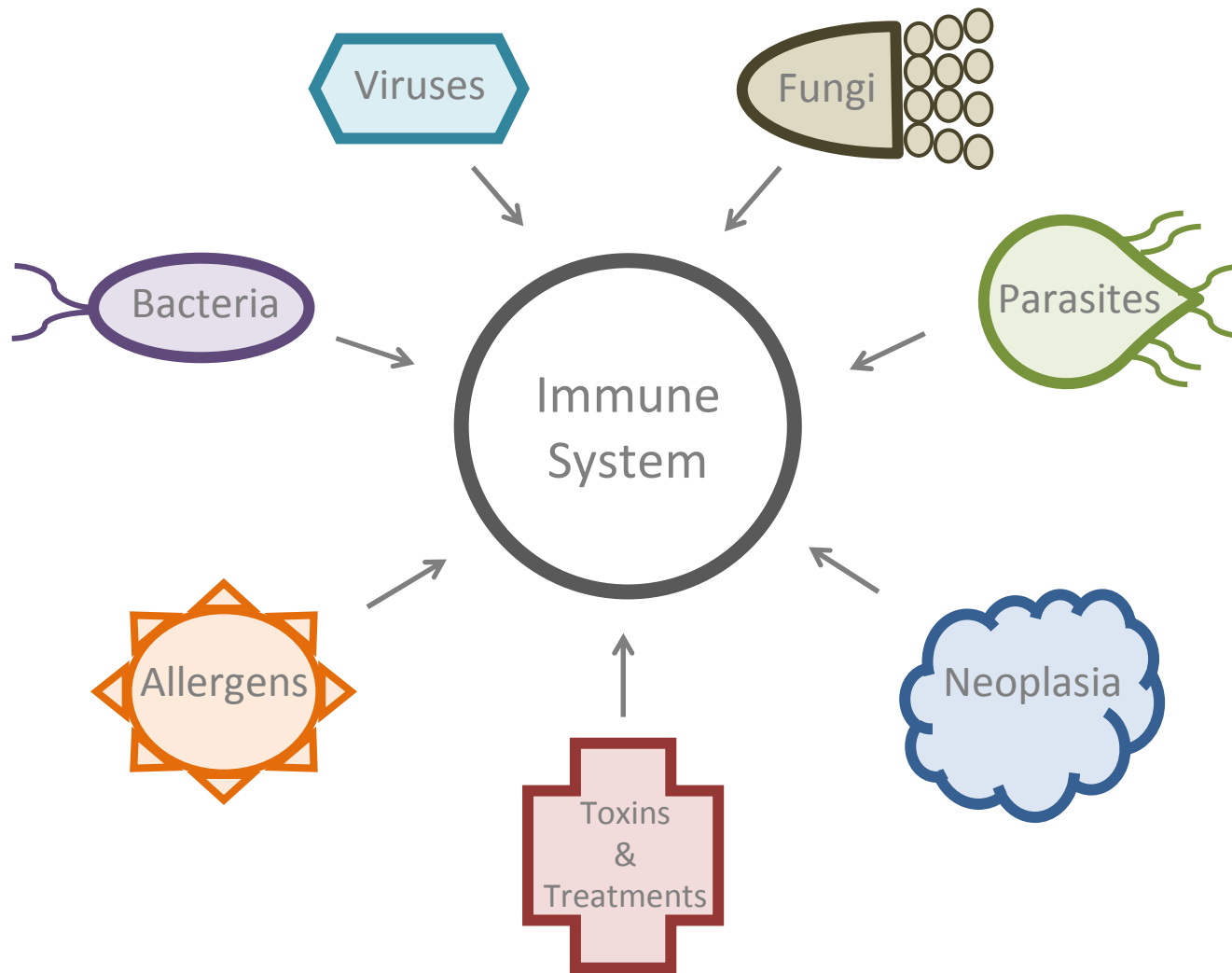
Innate Immunity

- First line of defense
- Immediate reactivity
- Not antigen-specific
- No memory

Adaptive Immunity

- Antigen-specific
- First encounter may take time to build up efficacy
- Life-long immunity possible
- Preemptive immunization (vaccination) possible

Innate and Adaptive Immunity



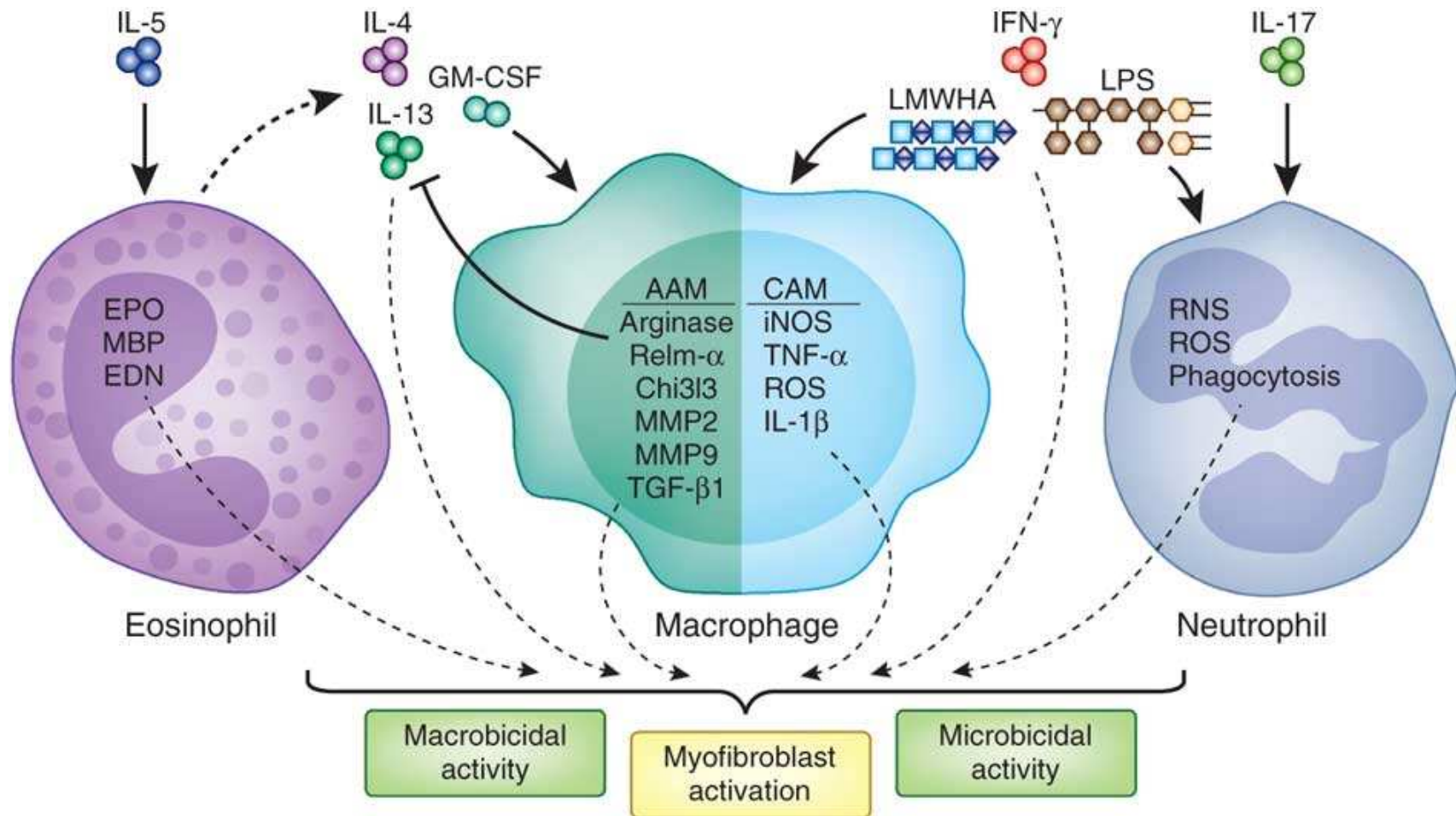
Effective Immunity Requires Balance

Control
pathogens/malignancy

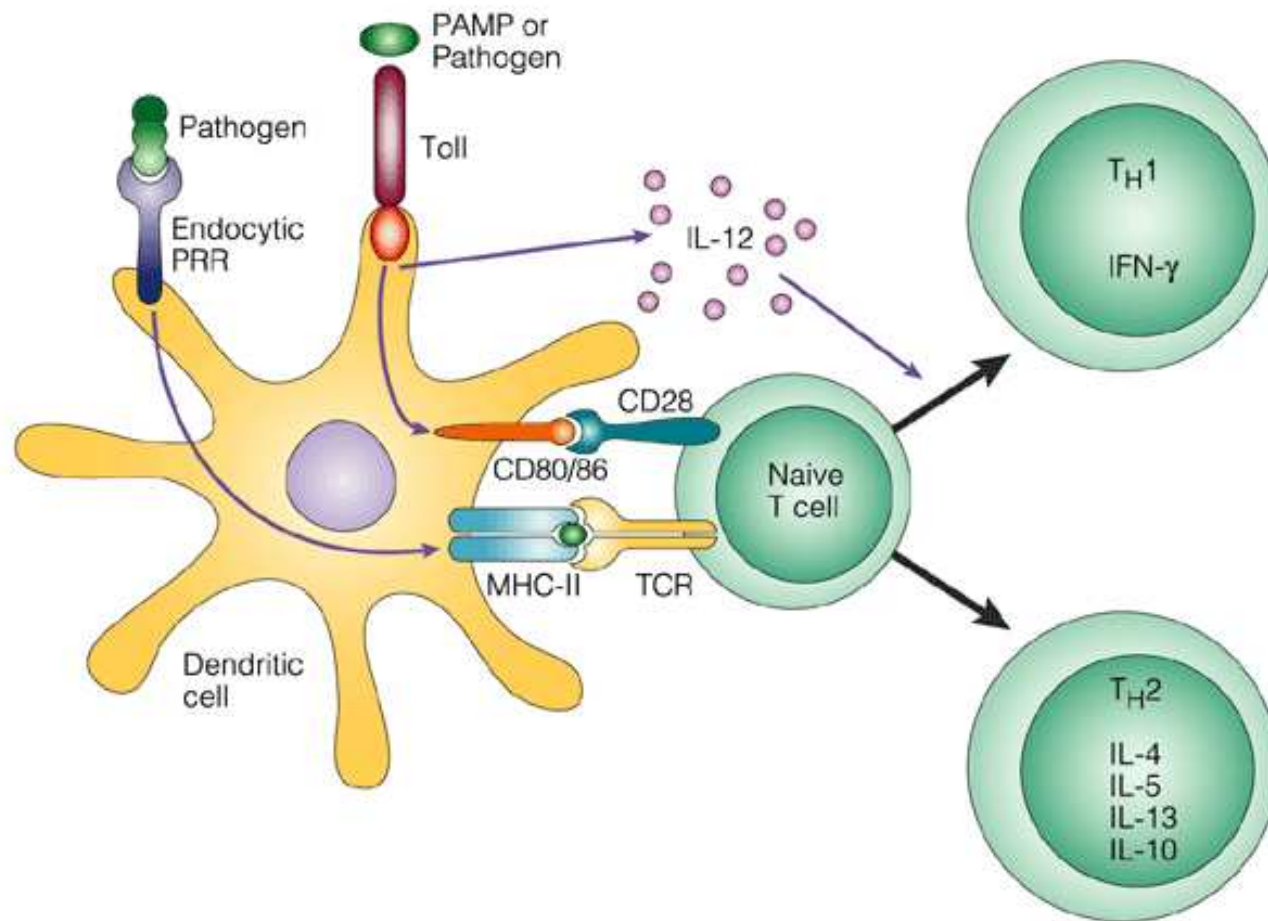
Prevent
auto-immunity



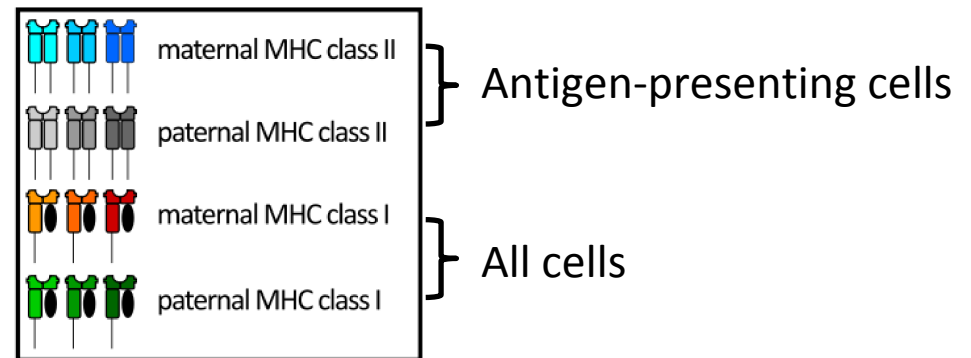
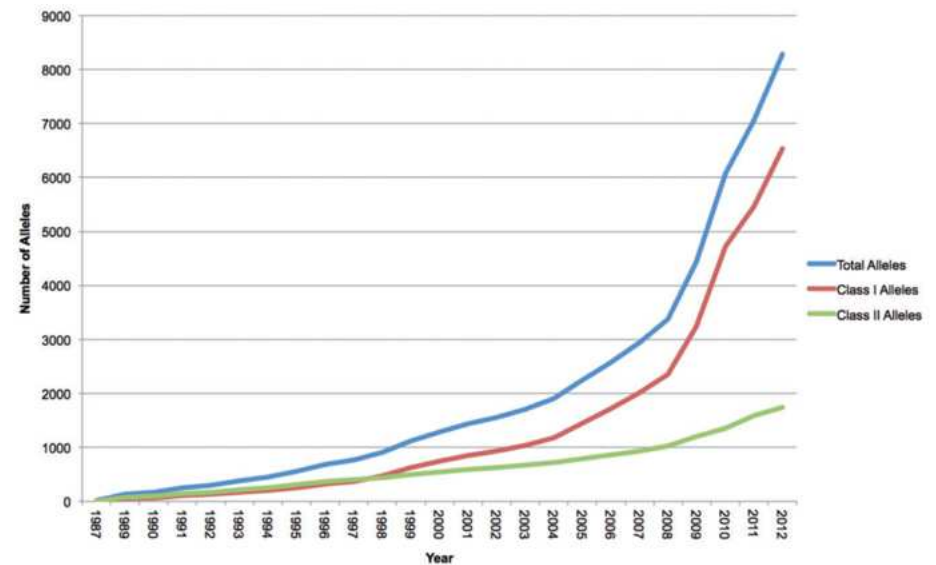
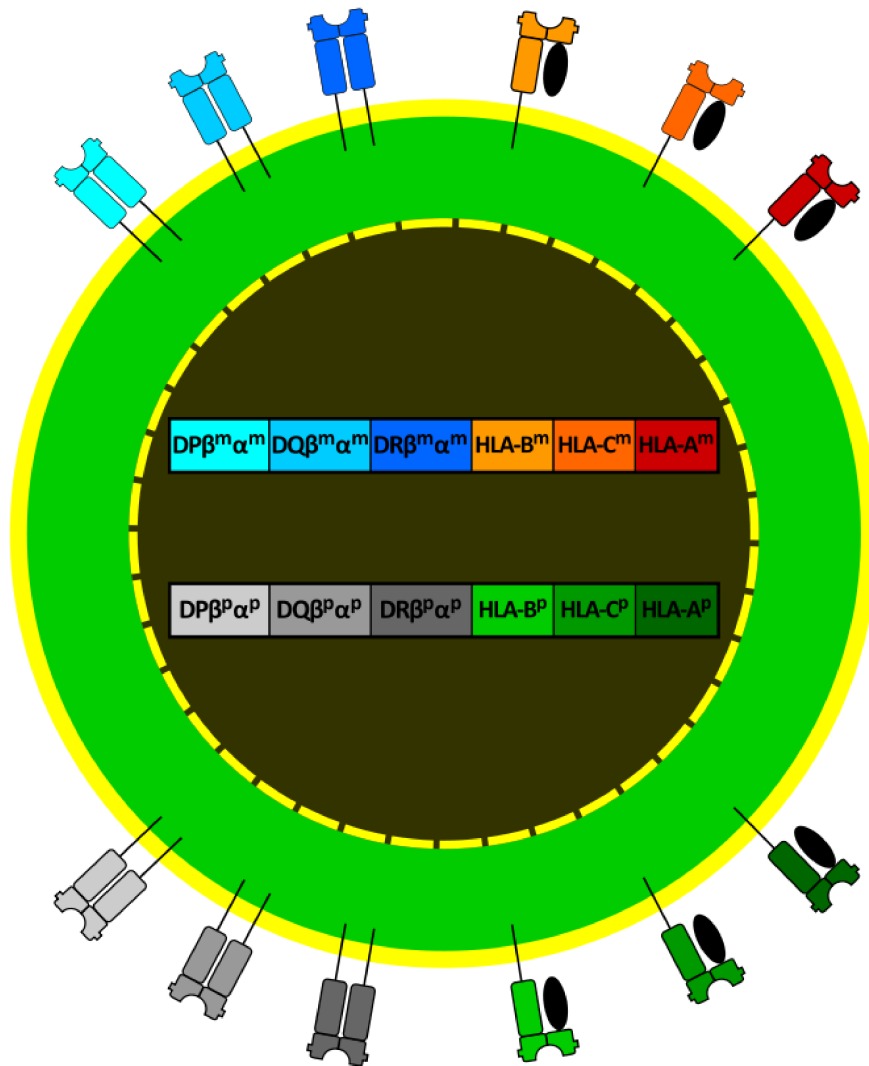
Innate Immunity



Antigen Presenting Cells



Major Histocompatibility Antigens (HLA)



Antigen Presentation

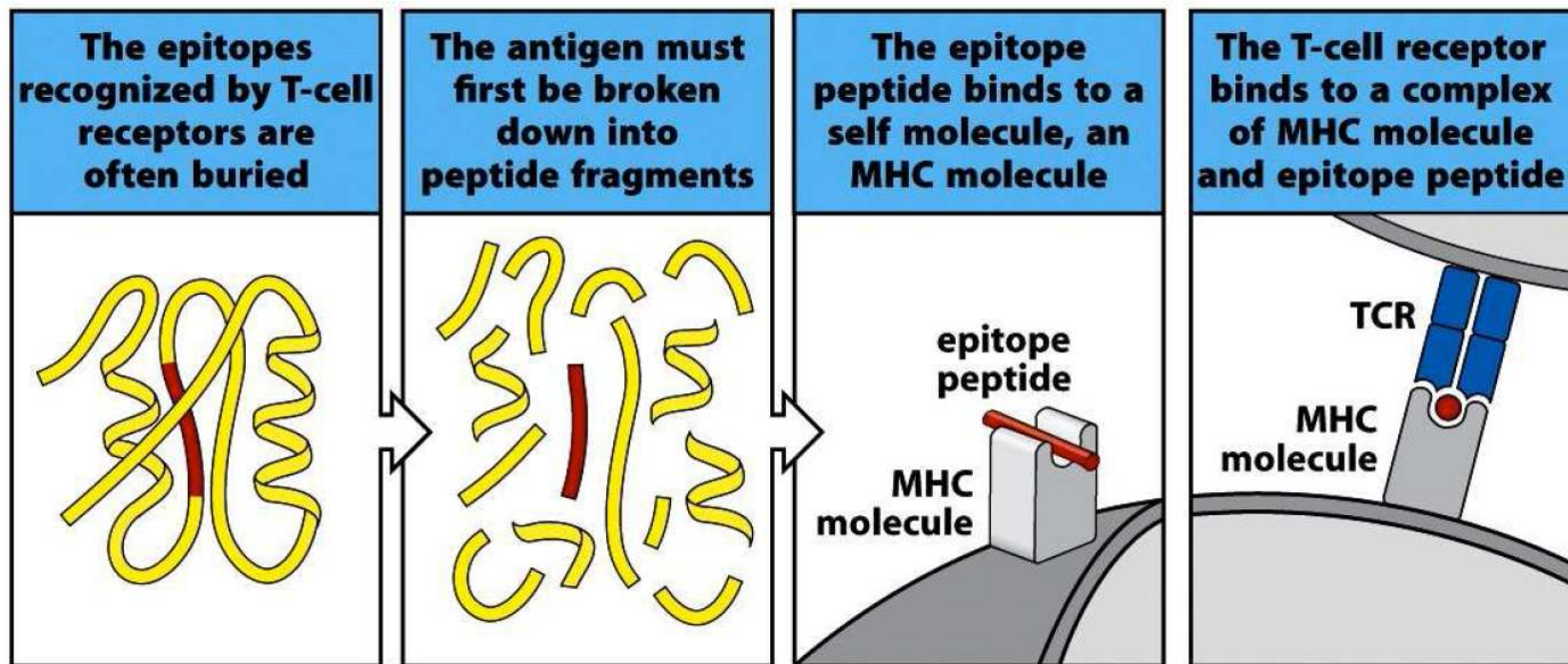
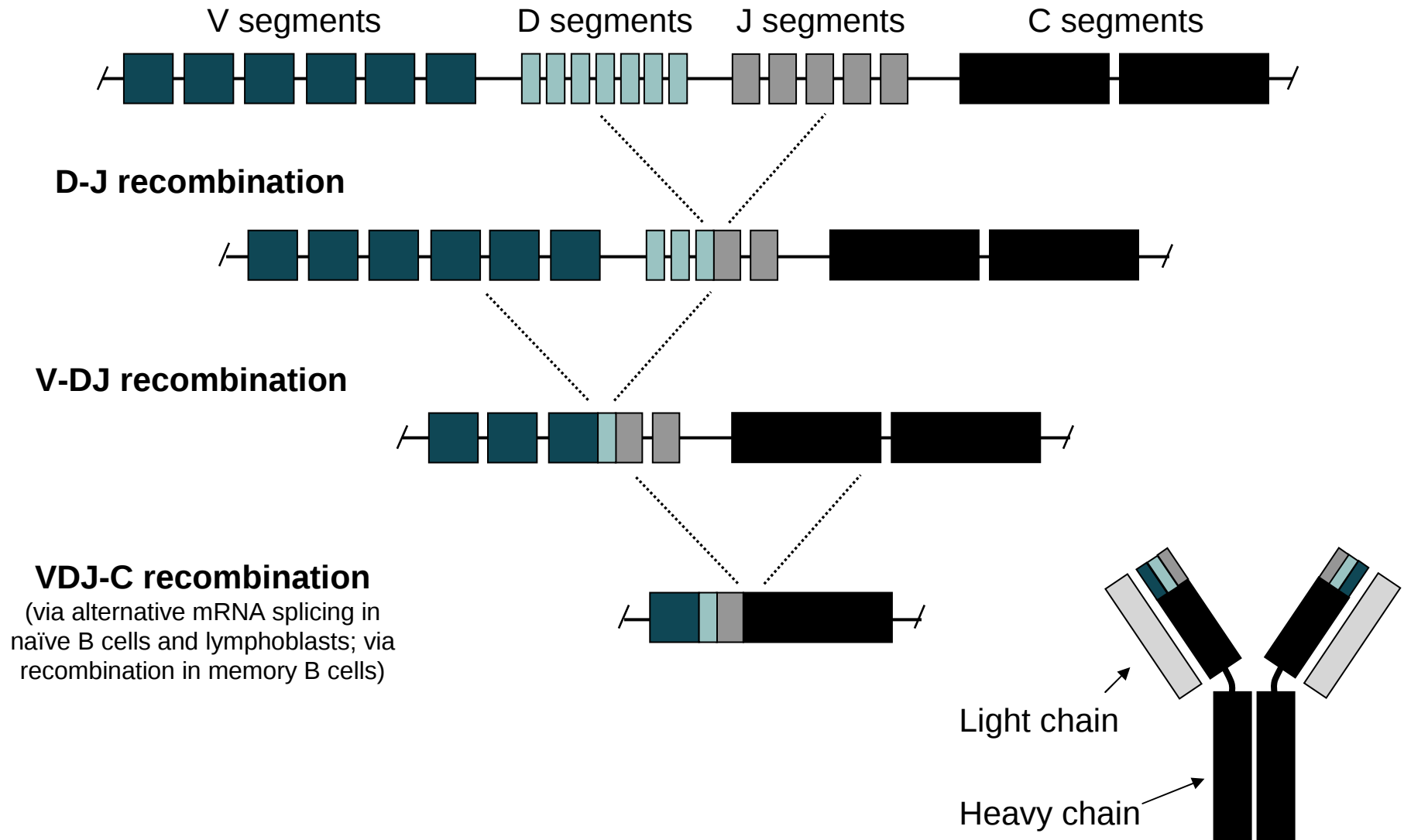


Figure 1-16 Immunobiology, 7ed. (© Garland Science 2008)

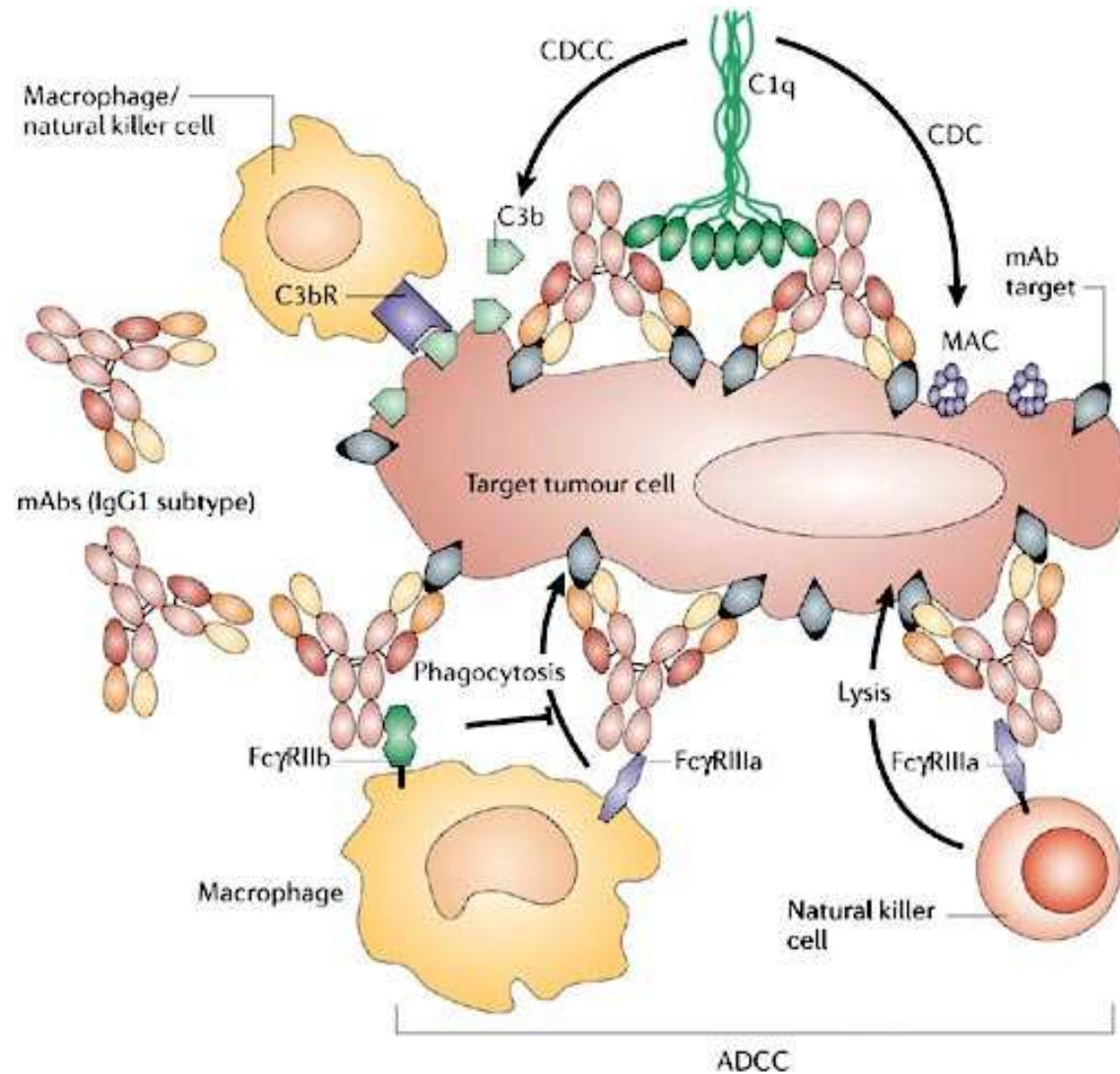
Adaptive Immunity is Epitope-Specific

With a genome possessing only ~20,000 genes, how can humans develop immunity to specific epitopes from thousands of pathogens?

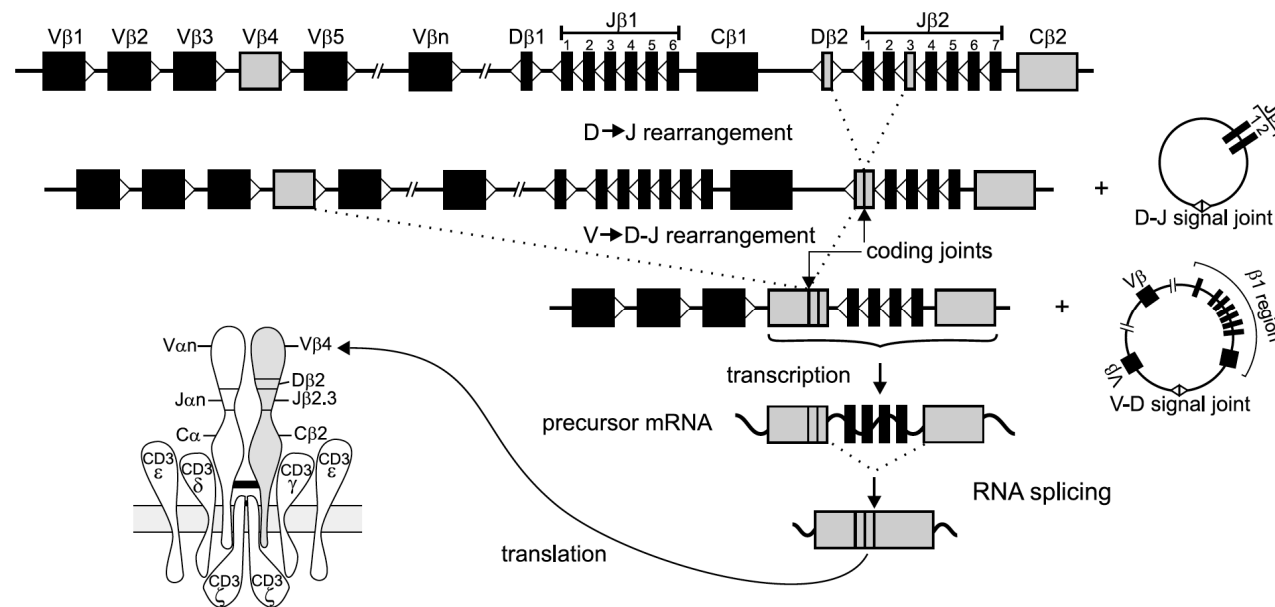
Immunoglobulin Gene Rearrangement



Immunoglobulin Mechanisms of Action

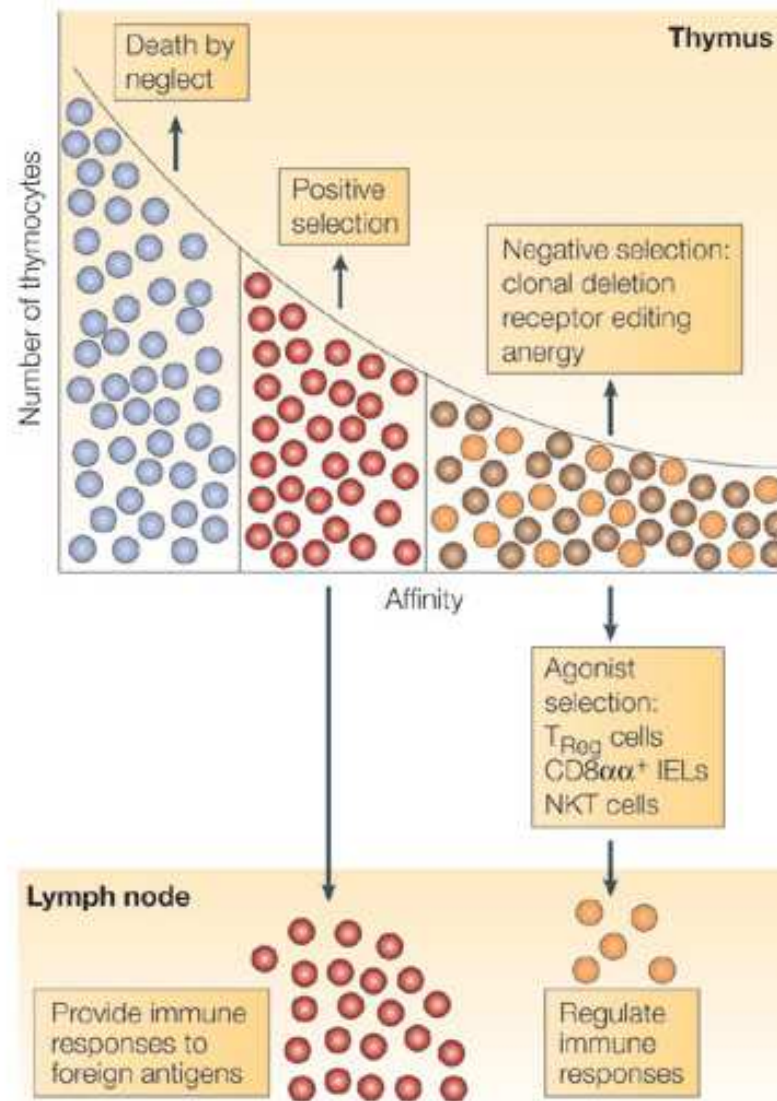


B and T Cell Repertoire Diversity

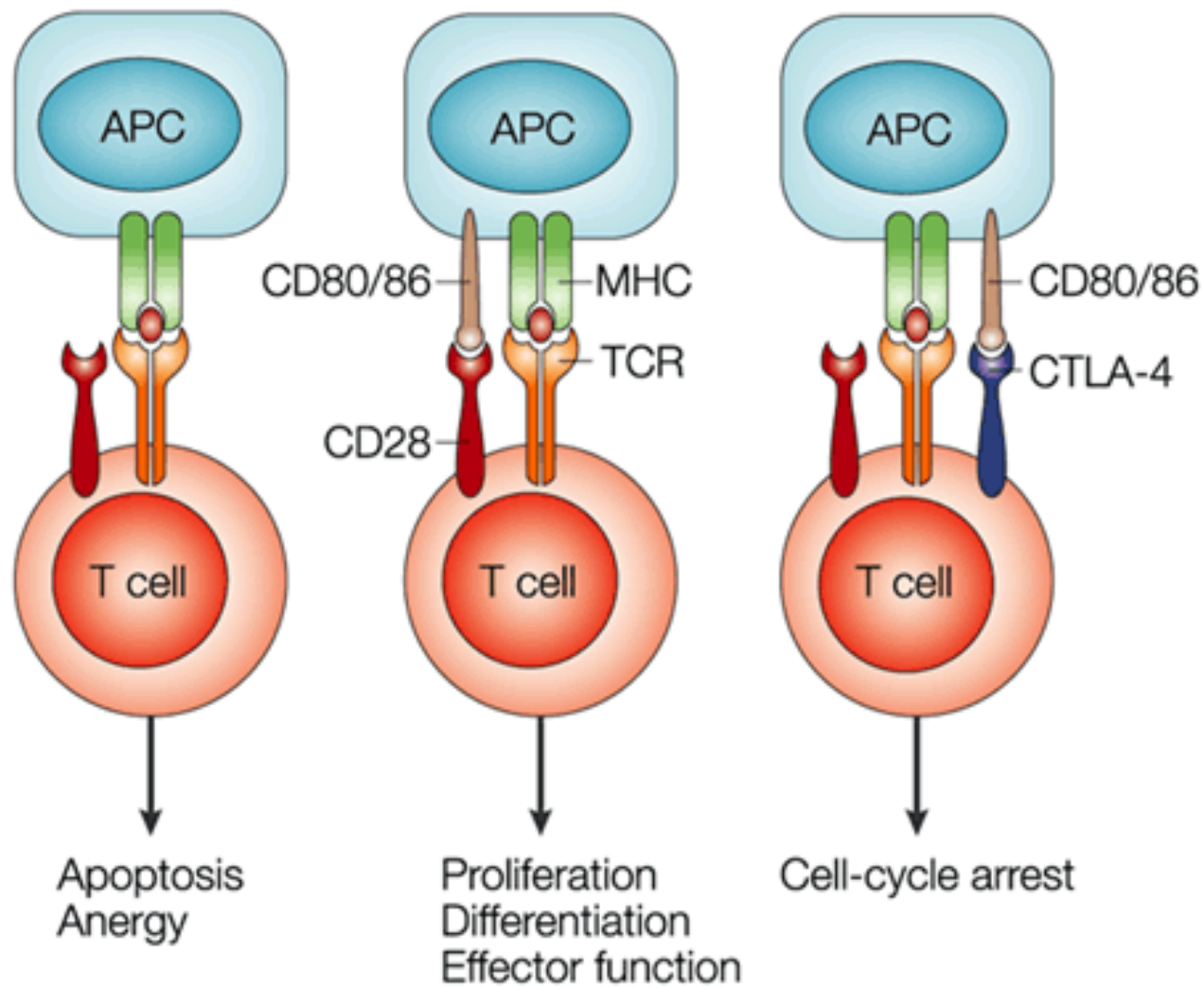


Gene segment	IGH	IGK	IGL	TCRA	TCRB	TCRG	TCRD
<i>V segments</i>							
Functional (family)	44 (7)	43 (7)	38 (10)	46 (32)	47 (23)	6 (4)	8
Rearrangeable (family)	66 (7) ^b	76 (7)	56 (11)	54 (32)	67 (30)	9 (4)	8
<i>D segments</i>							
Rearrangeable (family)	27 (7)	—	—	—	2	—	3
<i>J segments</i>							
Functional	6 ^c	5 ^d	4	53	13	5	4
Rearrangeable	6 ^c	5 ^d	5 ^e	61	13	5	4

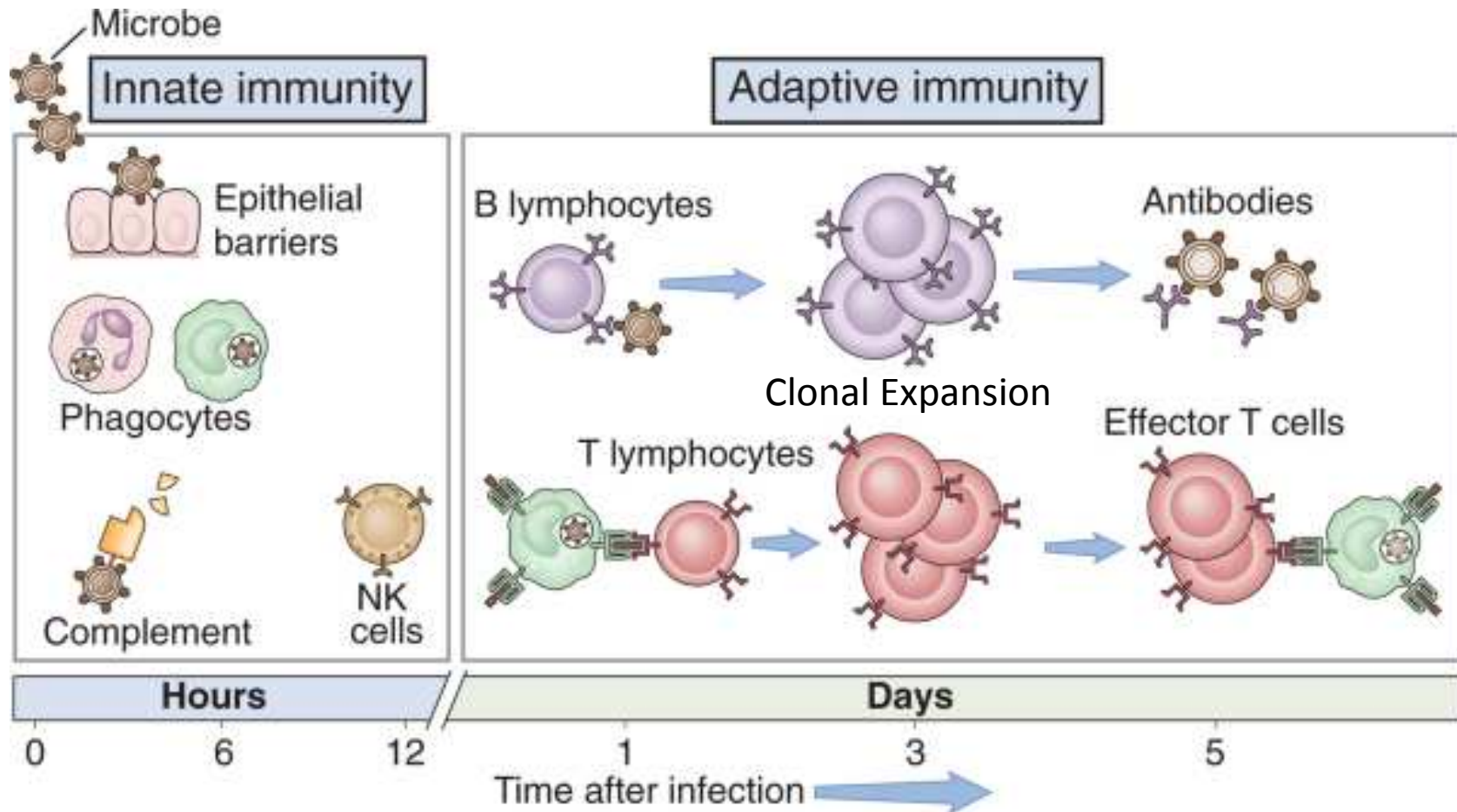
T Cell Selection



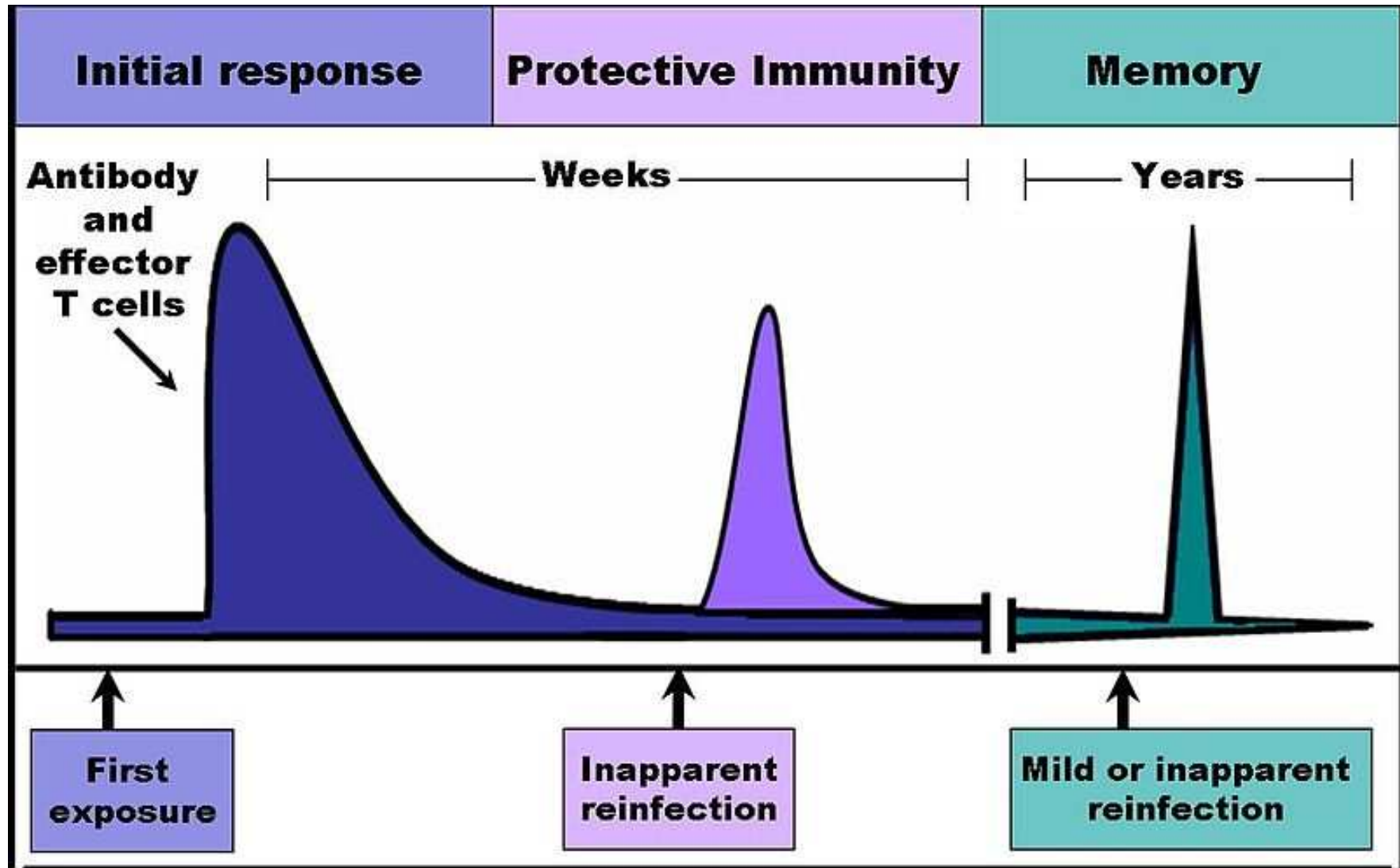
T Cell Costimulation



Innate and Adaptive Immunity Work Together

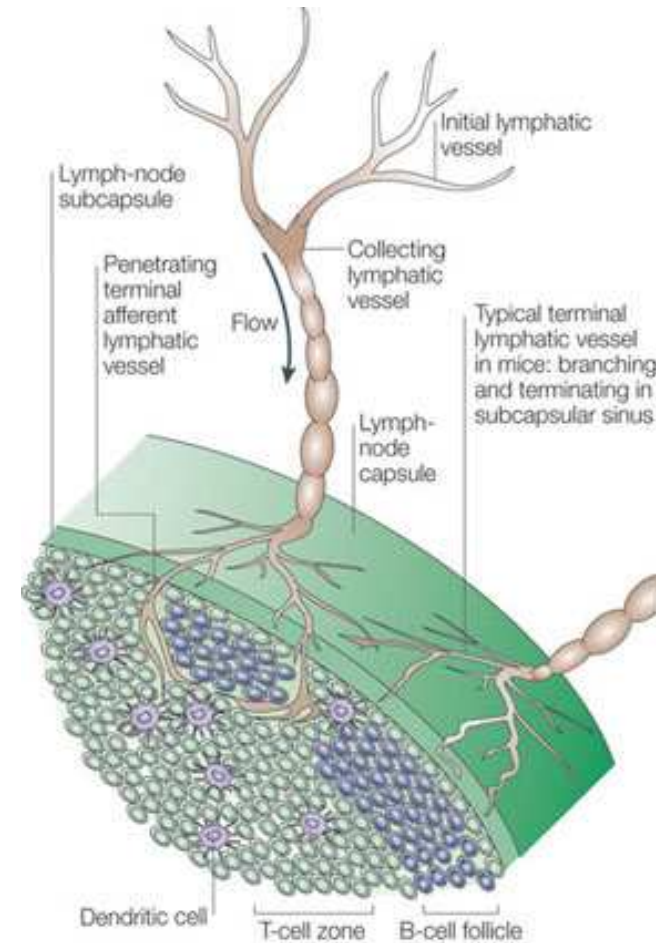
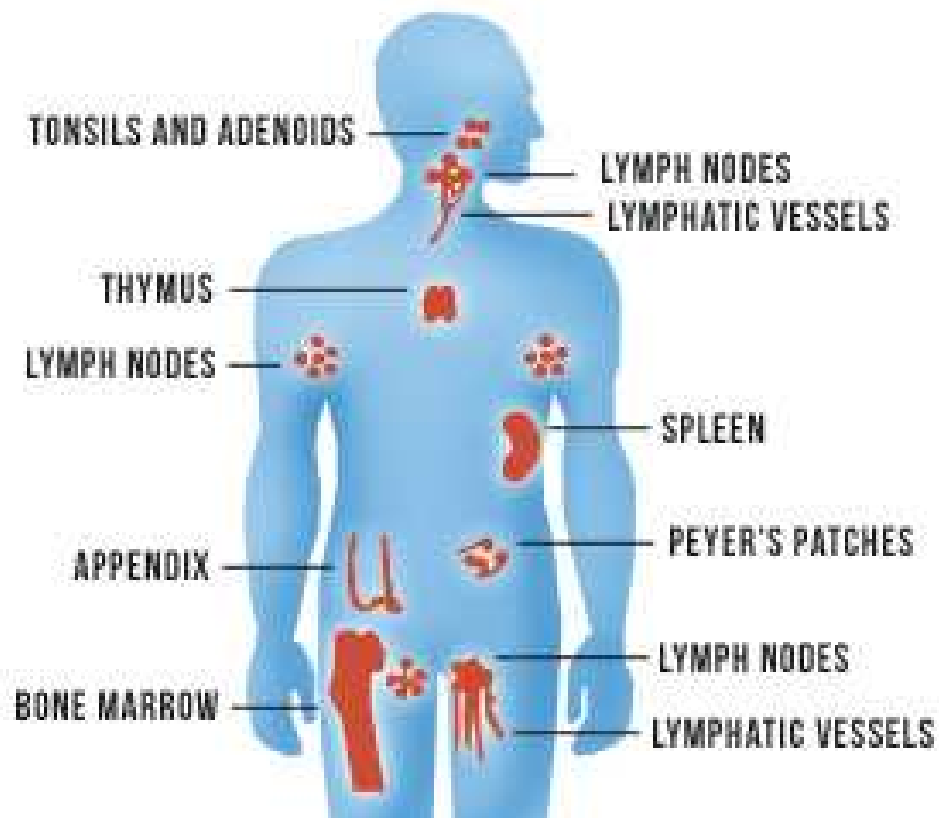


Characteristics of Adaptive Immune Response



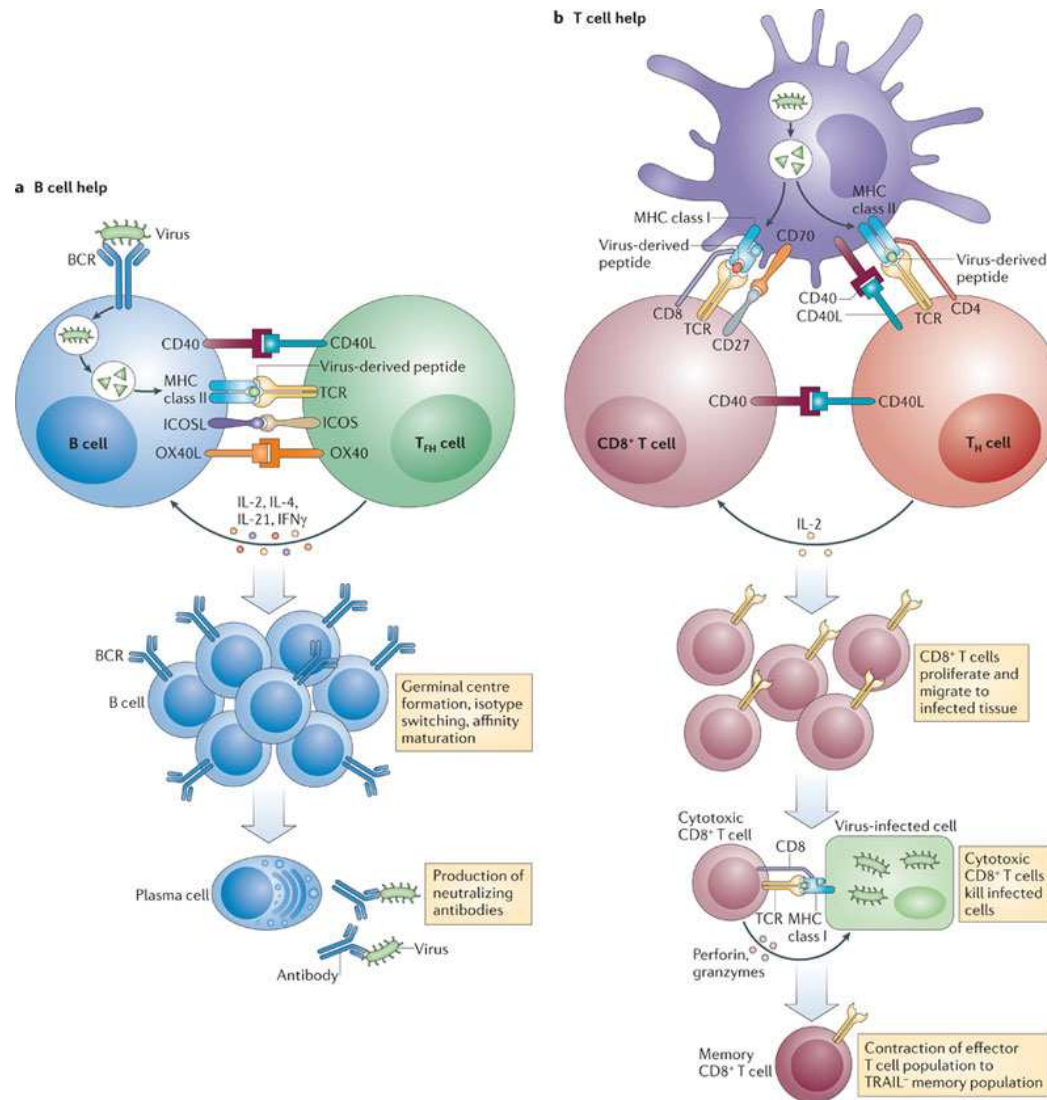
Immune Organs

ORGANS OF THE IMMUNE SYSTEM

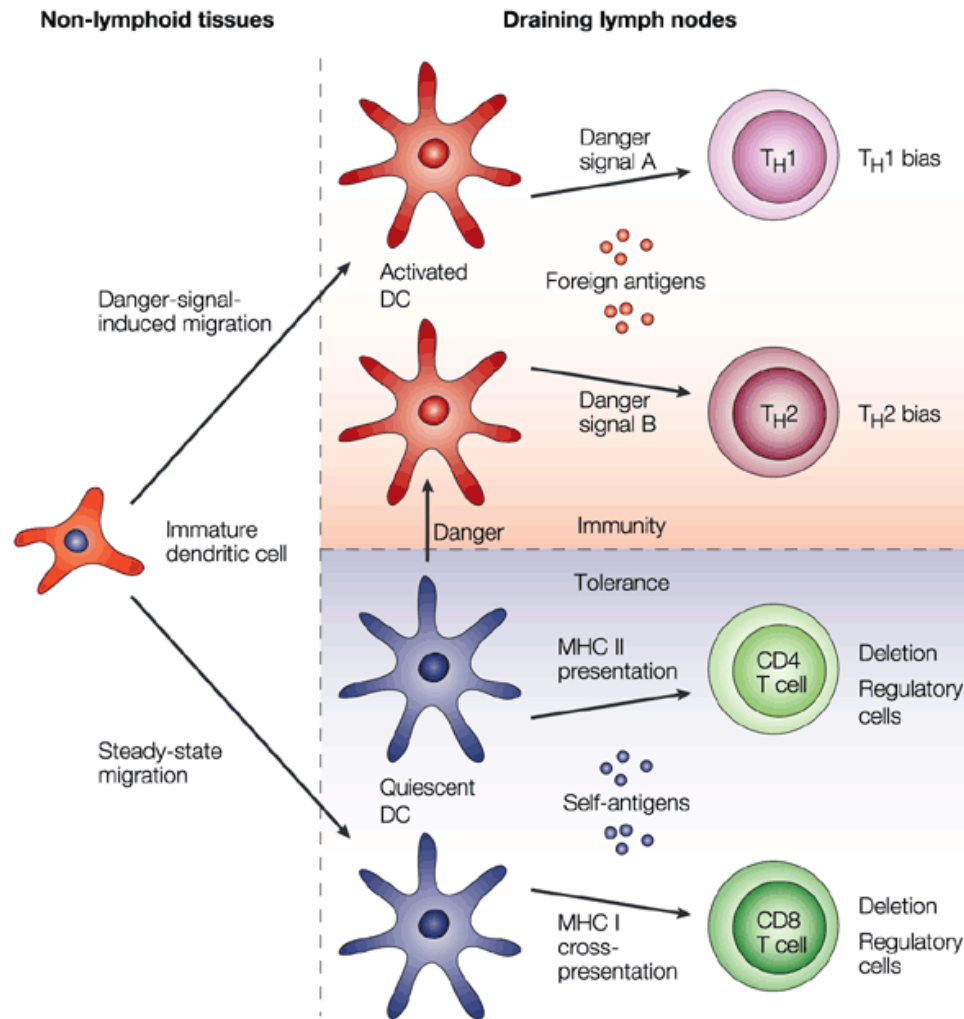


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Cytotoxic and Helper T Cells

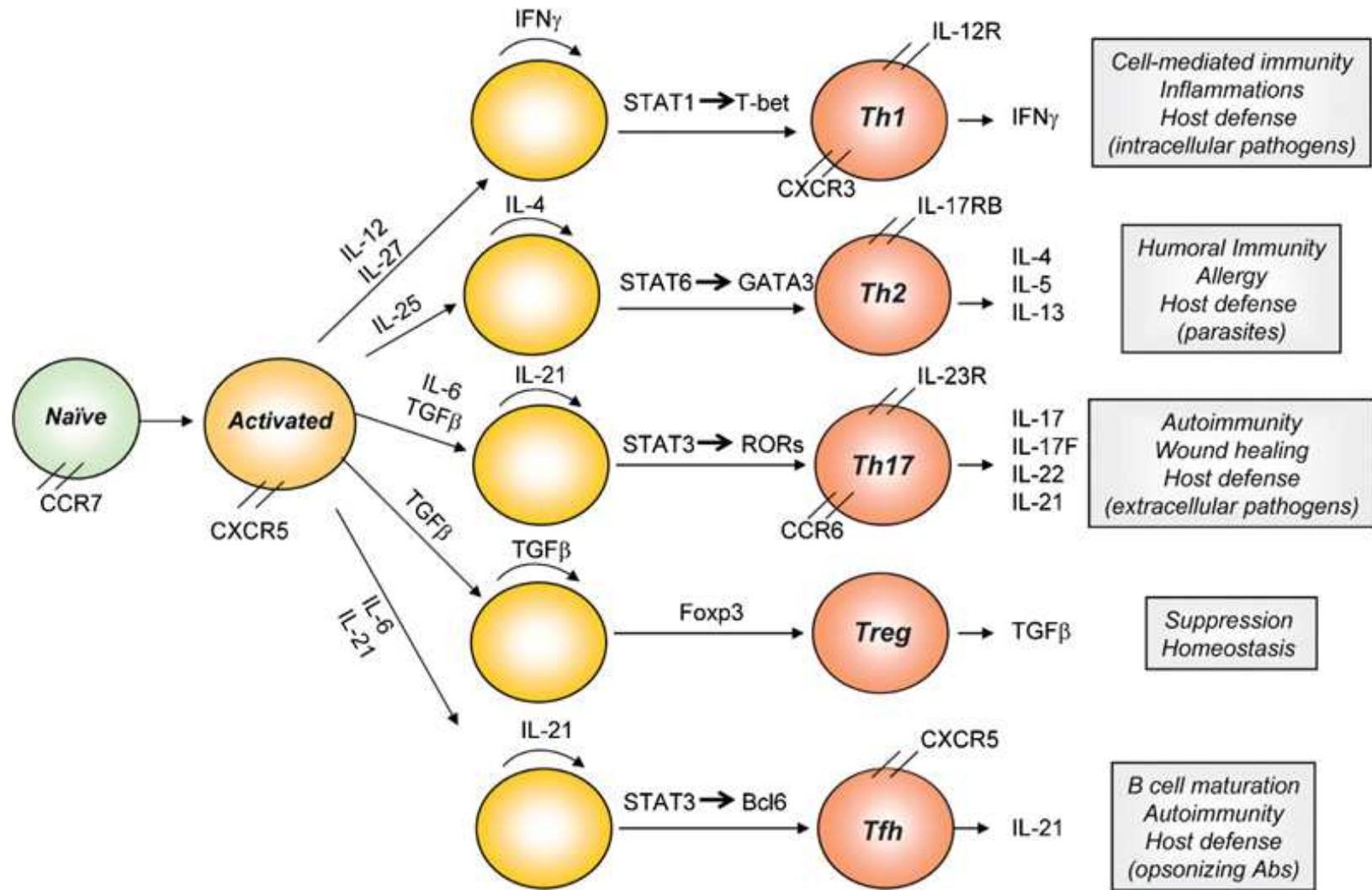


T Cell Responses are Directed by Dendritic Cells

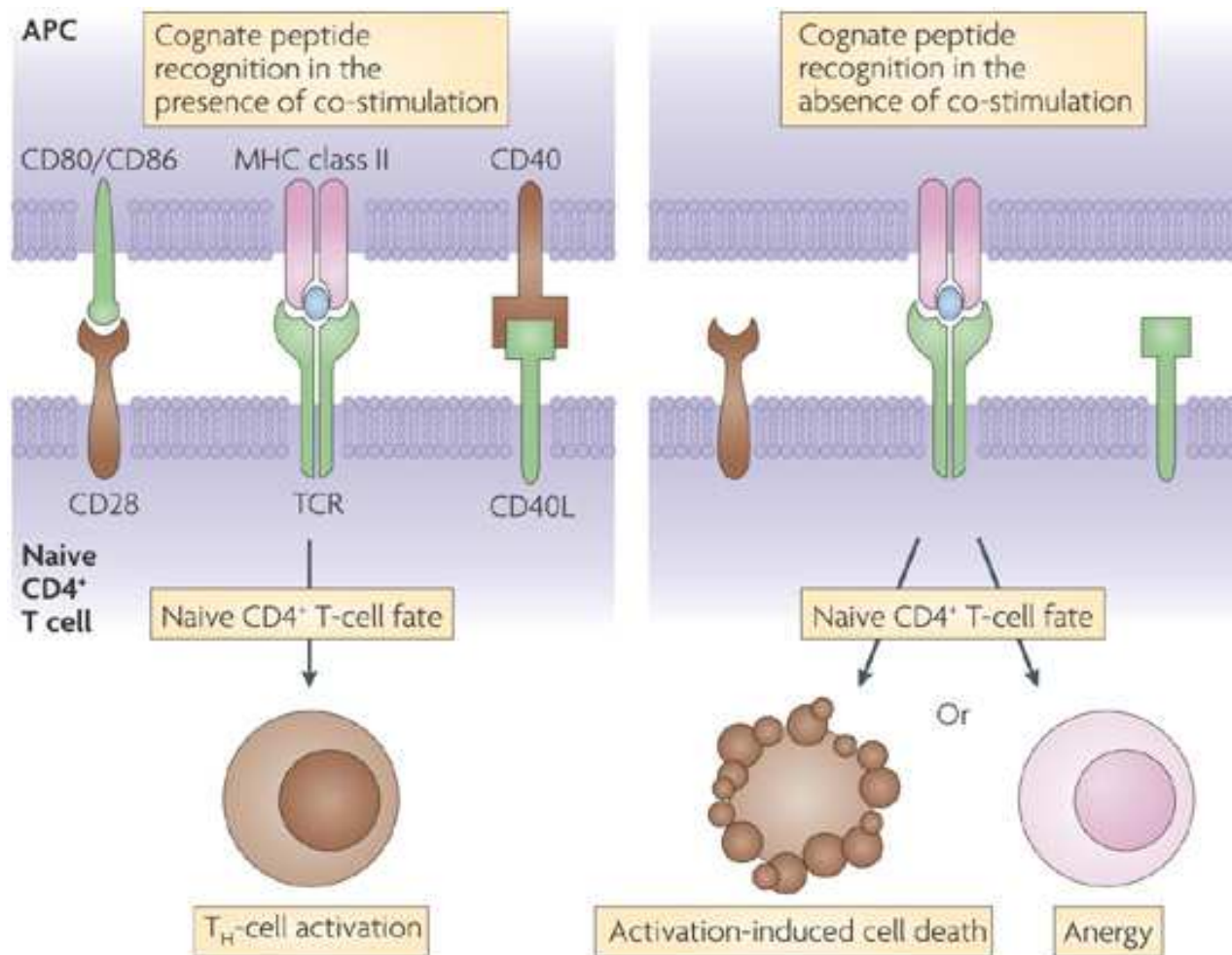


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T cell subsets: Th1, Th2, Th17, Tfh, Treg



Anergy / Peripheral Tolerance



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Regulatory T (Treg) Cells

Granzyme A or granzyme B

Perforin pore

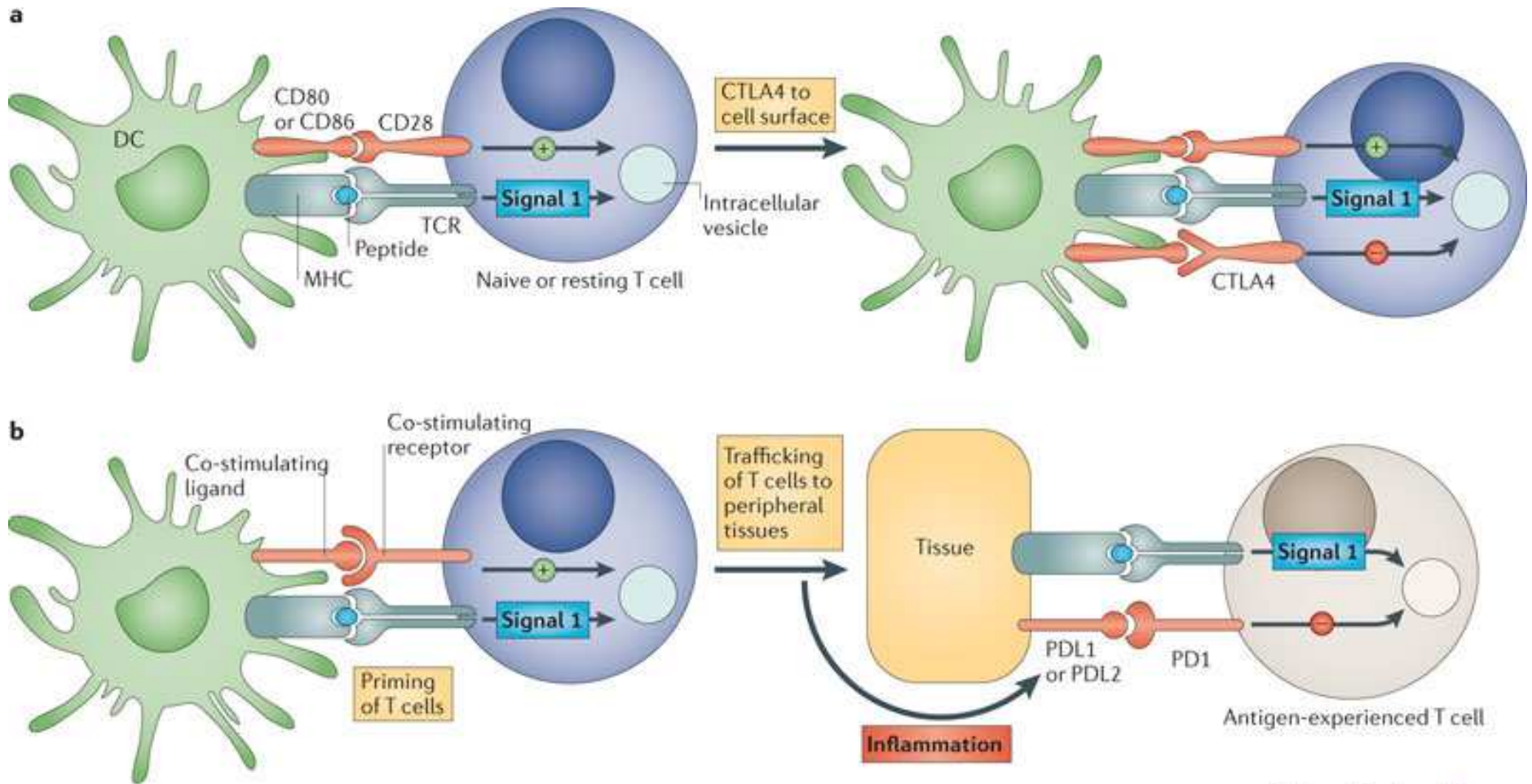
Apoptotic effector T cell

The diagram illustrates the regulation of apoptosis by CD25 and CD39/CD73. CD25 binds IL-2, and CD39/CD73 converts Adenosine. Both pathways lead to cAMP production, which inhibits apoptosis. A third pathway shows A_{2A} receptor binding to Adenosine, leading to cell death due to cytokine deprivation.

Diagram illustrating the inhibition of DC maturation and function. A DC (Dendritic Cell) is shown interacting with two T cells. The T cell on the left expresses CTLA4, which binds to CD80/CD86 on the DC. The T cell on the right expresses LAG3, which binds to MHC class II on the DC. IDO (Indoleamine 2,3-dioxygenase) is shown being secreted by the DC, which inhibits the T cell on the right. A text box at the bottom states "Inhibition of DC maturation and function".

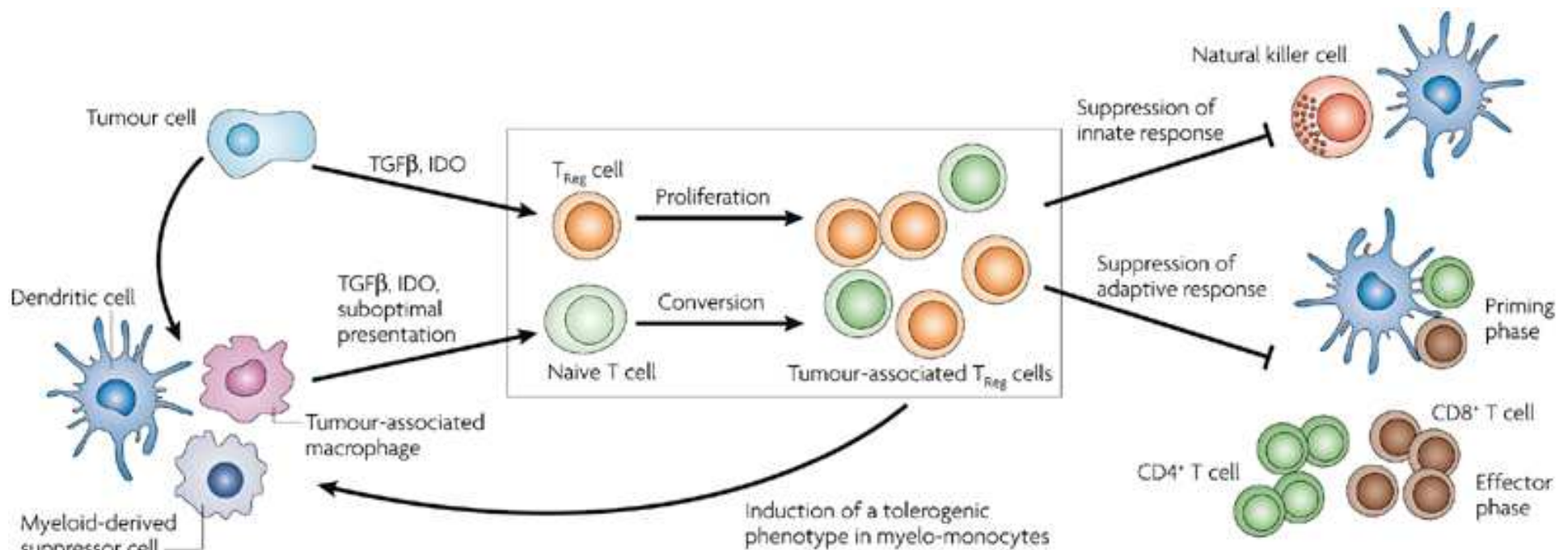
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Immune Checkpoints in Tumor Immunology



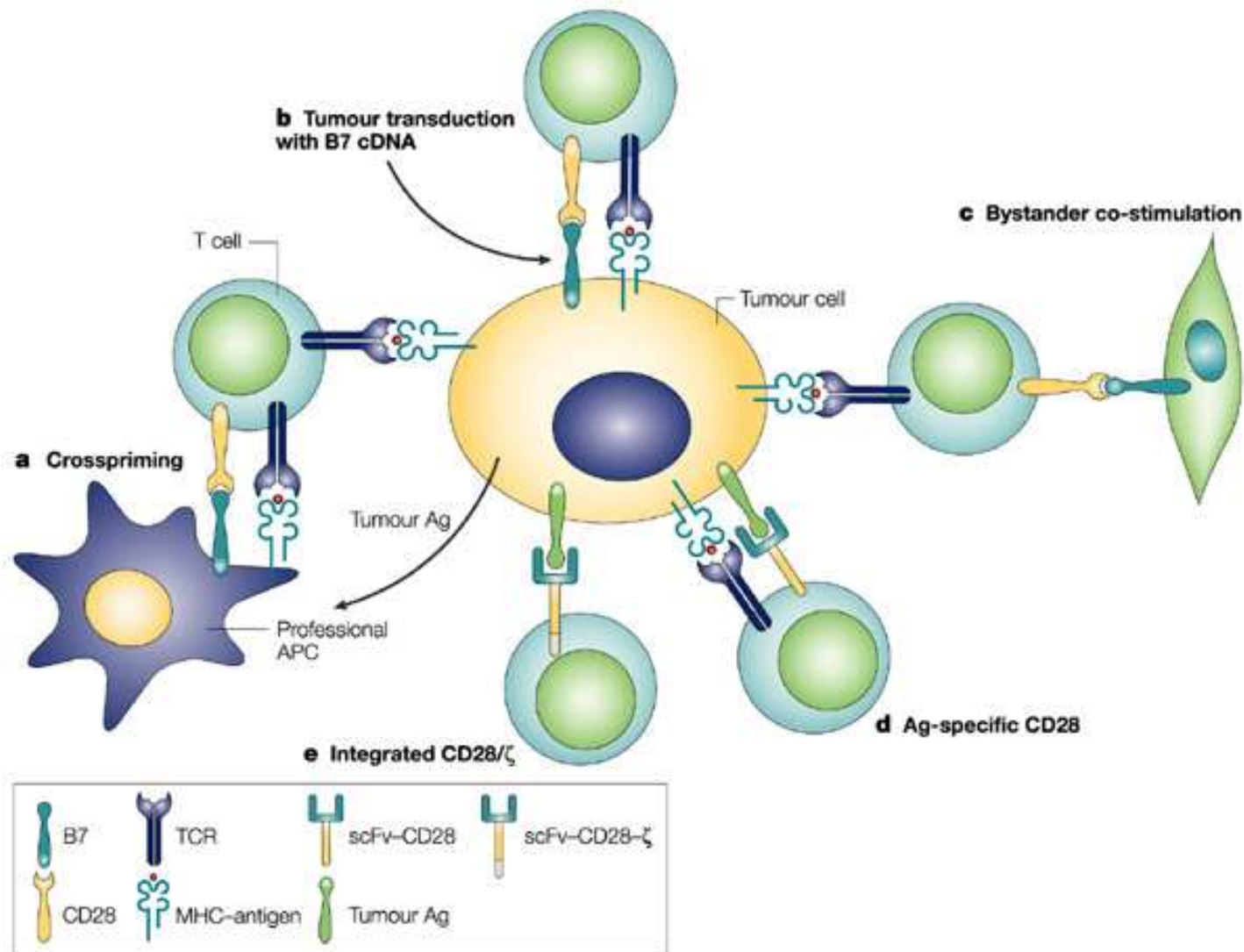
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Regulatory Cells in Tumor Immunology

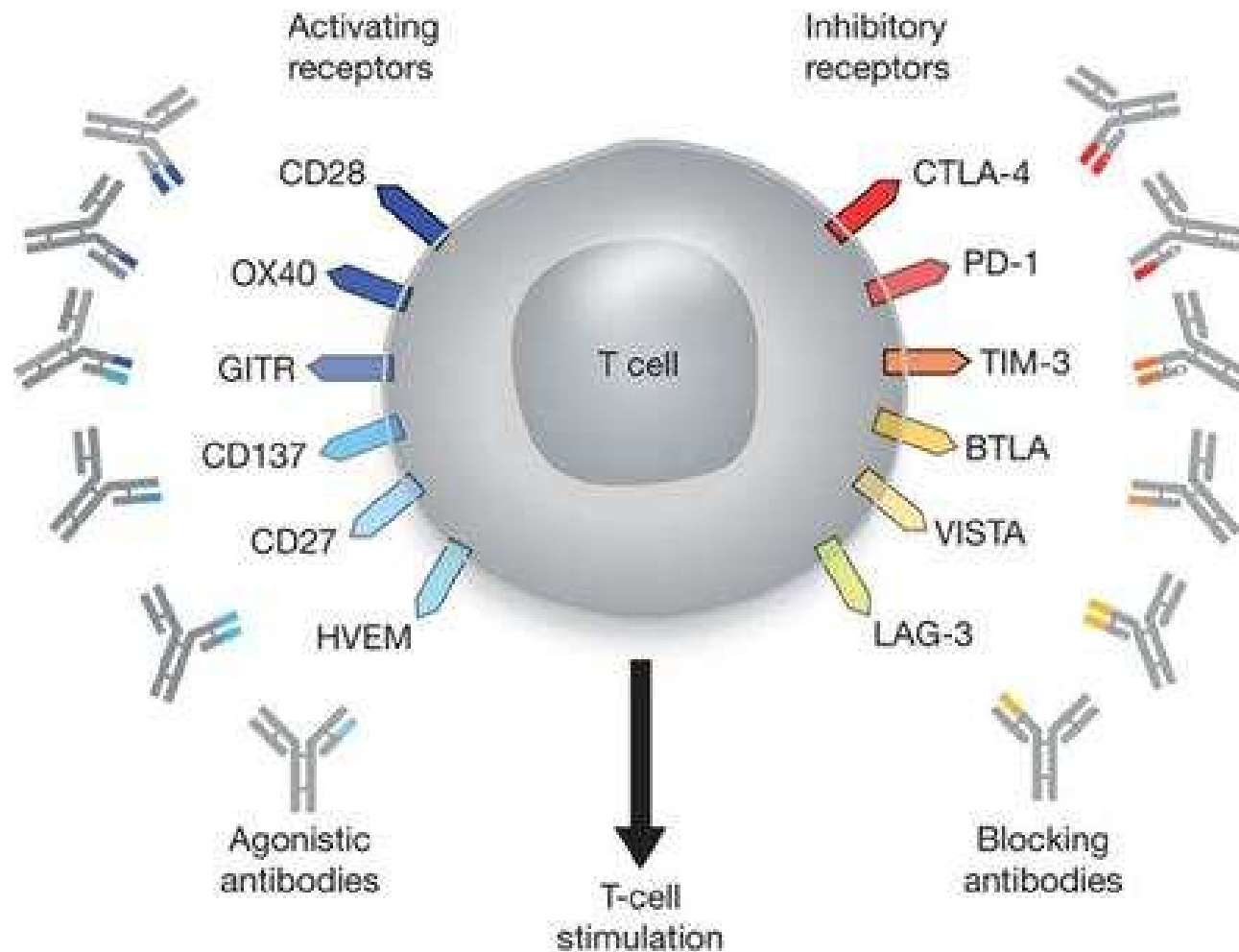


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Immunotherapy Mechanisms



Immunotherapy Mechanisms



Goals of Tumor Immunotherapy

1. Tilt the balance – break tolerance, antagonize negative regulators
2. Stimulate responses to tumor-specific or tumor-associated antigens
3. Induce lasting immunity
4. Induce a breadth of response capable of targeting multiple tumor subclones
5. Improve patient outcomes



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Question

1. The ability of the adaptive immune system to respond to an extremely diverse array of antigens requires:
 - a) Thousands of genes encoding receptors for specific pathogen epitopes
 - b) Modular rearrangement of DNA segments at immunoreceptor genes to create many gene products from single genes
 - c) Differential post-translational modification of antigen receptors
 - d) Differential use of multiple antigen receptors simultaneously
 - e) None of the above

Question

2. The major histocompatibility complex (aka, human leukocyte antigen/HLA) proteins participate in adaptive immune reactions by which mechanism:
- a) Signaling via the B cell receptor to stimulate antibody production
 - b) Causing down-regulation of checkpoint inhibitors
 - c) Secreted HLA proteins serve as chemo-attractants for T cells
 - d) Presentation of peptide fragments from proteins within the cell
 - e) None of the above

Question

3. Autoimmune T cell responses are prevented by which mechanism(s):
- a) Anergy induced by T cell receptor recognition of antigen-MHC complexes without co-stimulation
 - b) Central deletion in the spleen
 - c) Inhibition by NK cells
 - d) All of the above
 - e) None of the above

Question

4. Helper T cells are involved in which aspect(s) of immunity:
- a) Stimulation of macrophage activity
 - b) Stimulation of antibody production
 - c) Stimulation of cytotoxic T cell function
 - d) All of the above
 - e) None of the above

Question

5. Individual T cells:

- a) Are able to respond to multiple antigens via expression of multiple T cell receptors
- b) May participate in immune reactions and then undergo programmed cell death
- c) May spend part of their life functioning as cytotoxic T cells and part of their life functioning as helper T cells
- d) All of the above
- e) None of the above

Answers

1. b
2. d
3. a
4. d
5. b



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