

Immunology 101 for the Practicing Oncologist

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

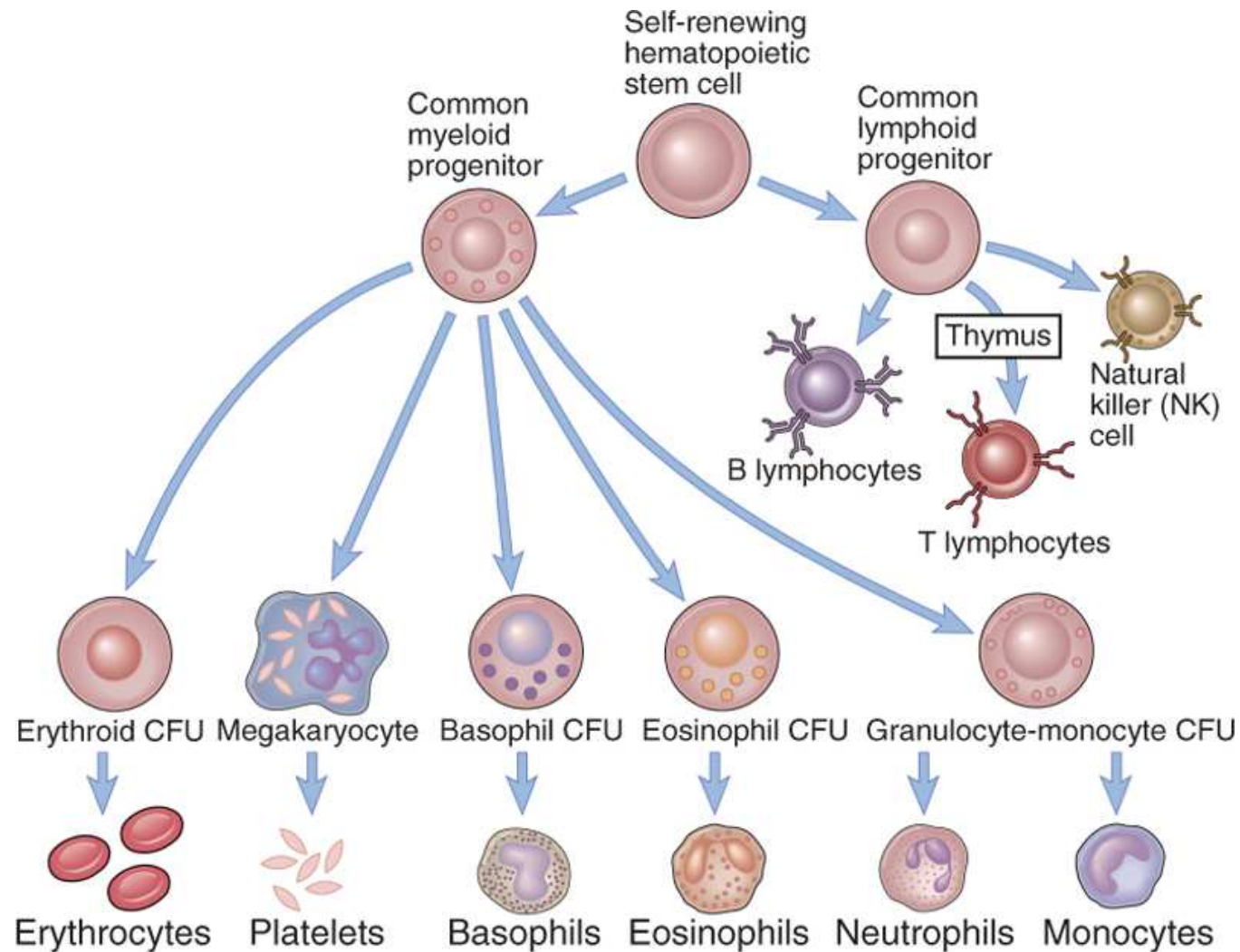
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Disclosures

Consulting Fees

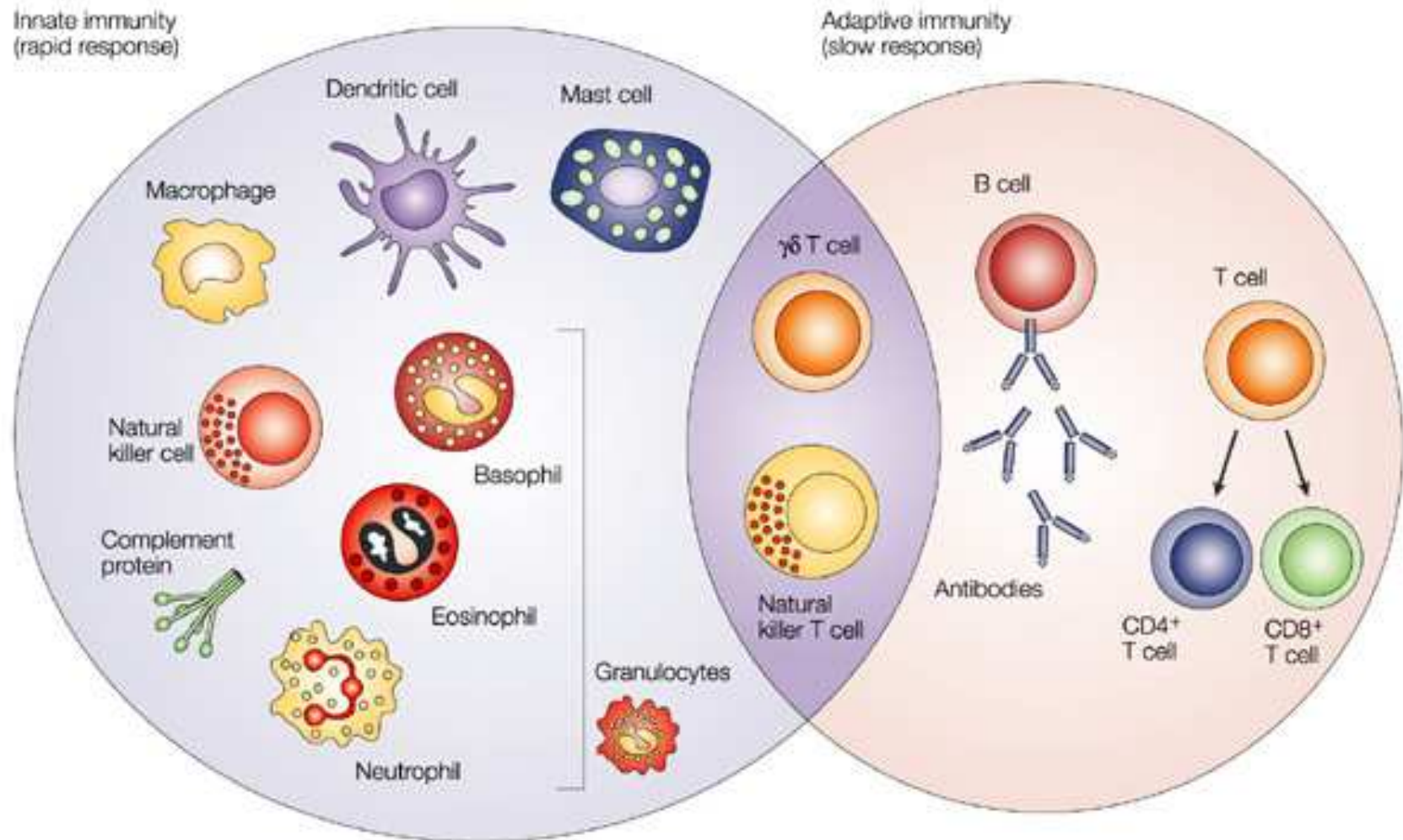
- Pharmacyclics
- Amgen

Hematopoiesis



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Innate and Adaptive Immunity



Innate and Adaptive Immunity

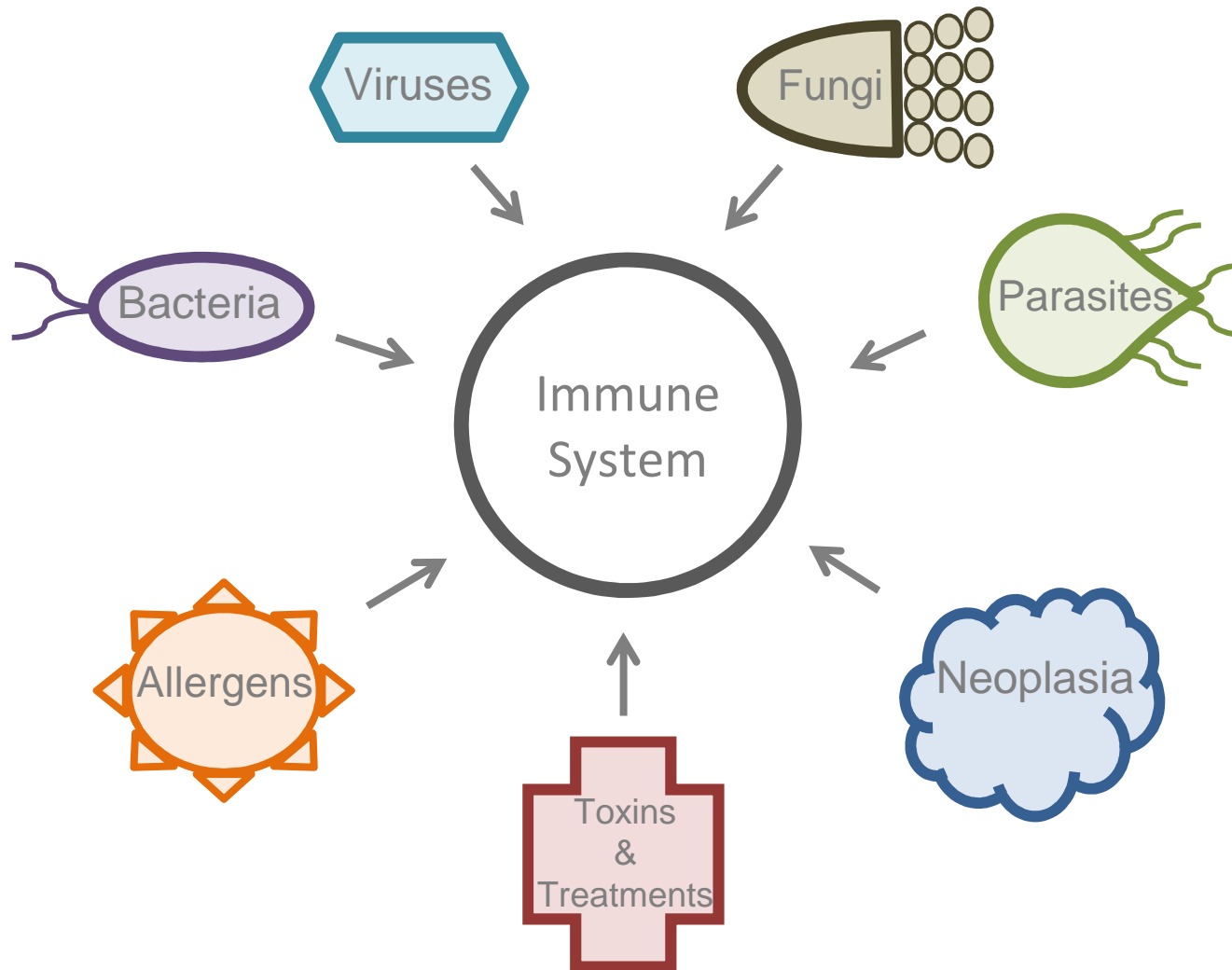
Innate Immunity

- 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



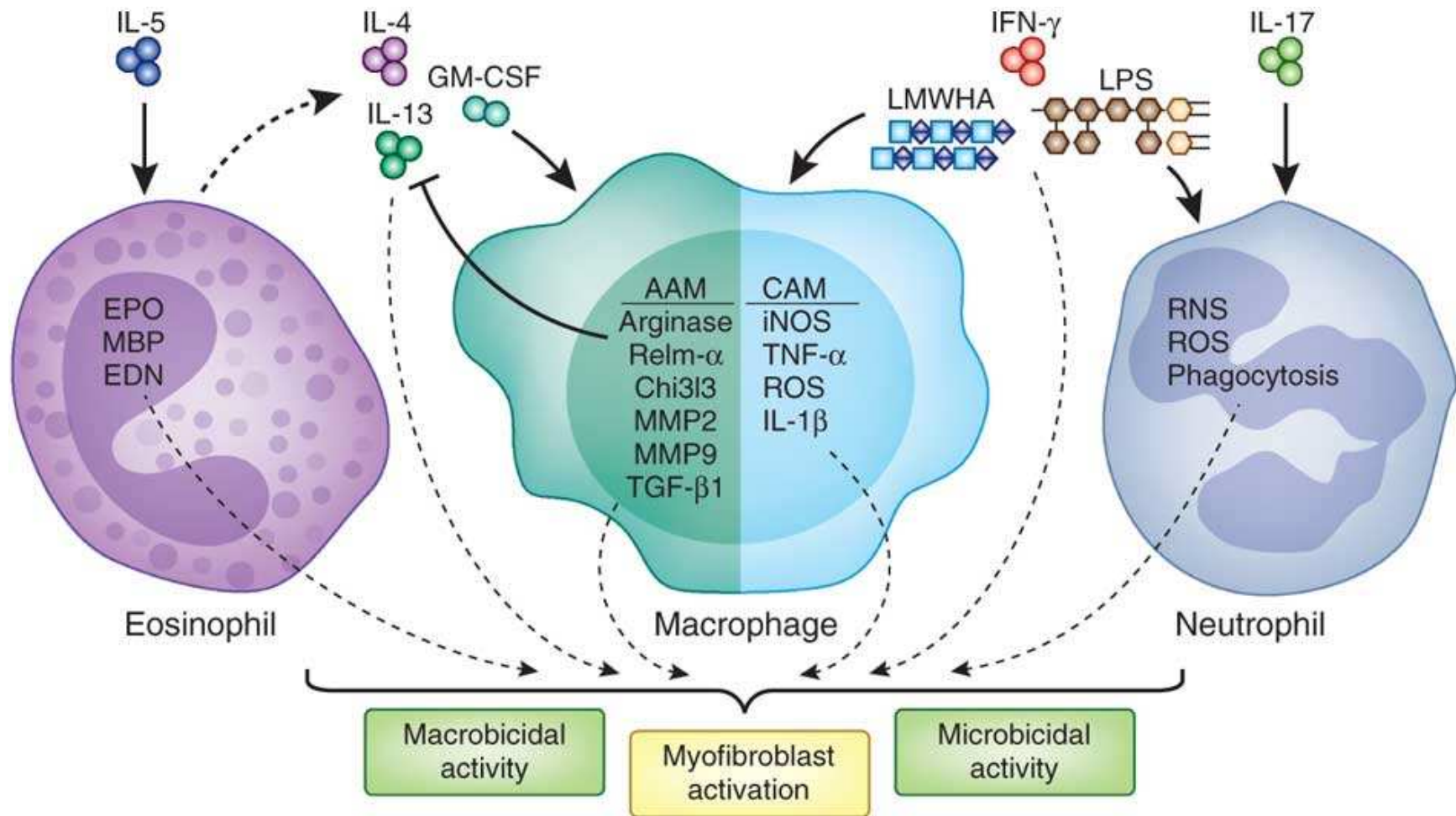
Effective Immunity Requires Balance

**Control
pathogens/malignancy**

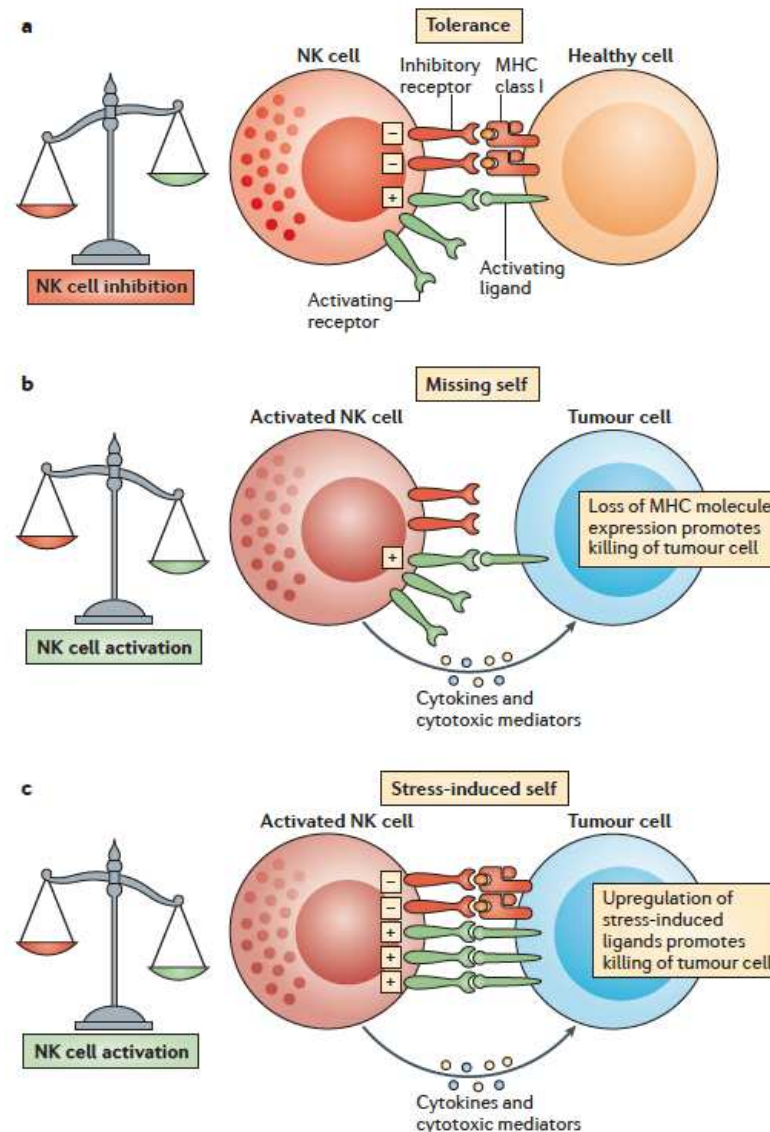
**Prevent
auto-immunity**



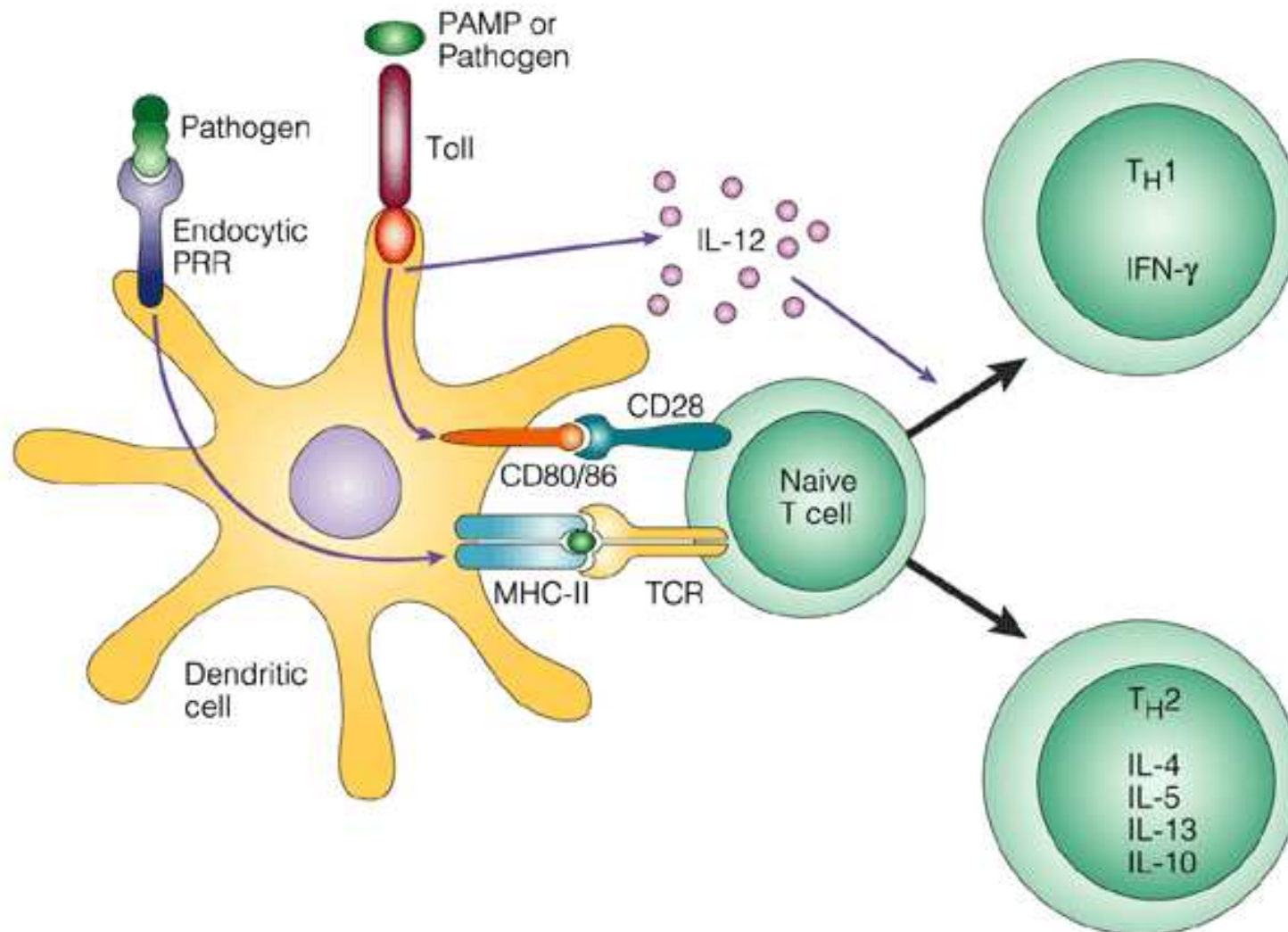
Innate Immunity



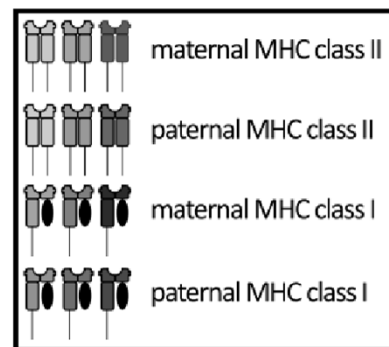
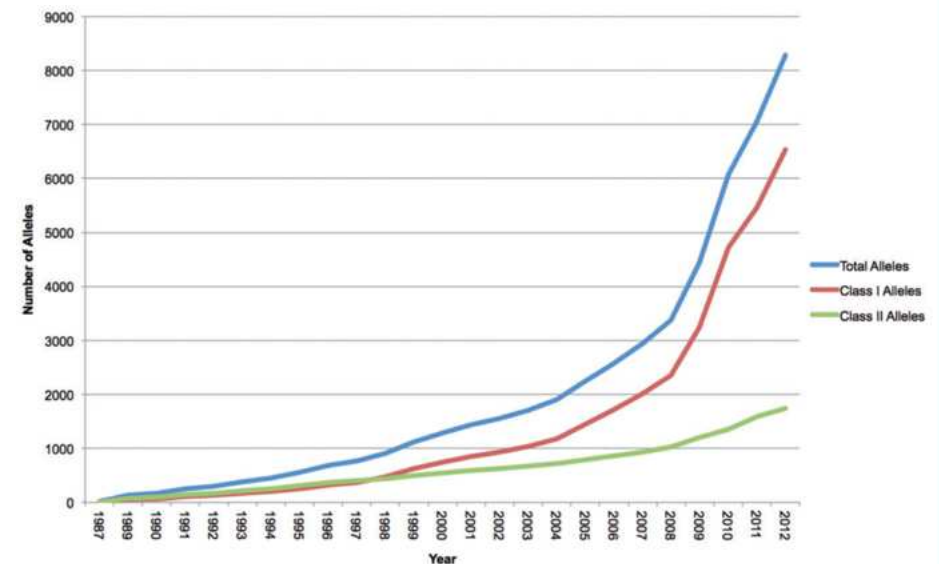
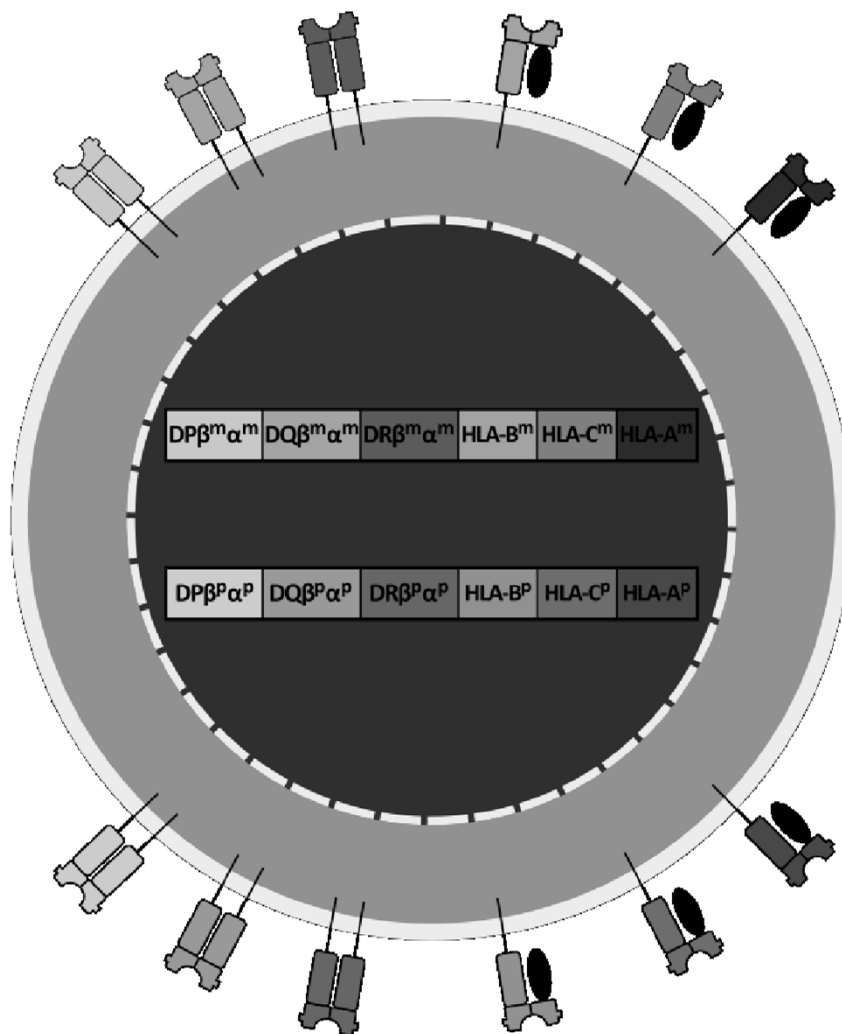
Innate Immunity — Natural Killer Cells



Antigen Presenting Cells



Major Histocompatibility Antigens (HLA)



Antigen-presenting cells

All cells

Antigen Presentation

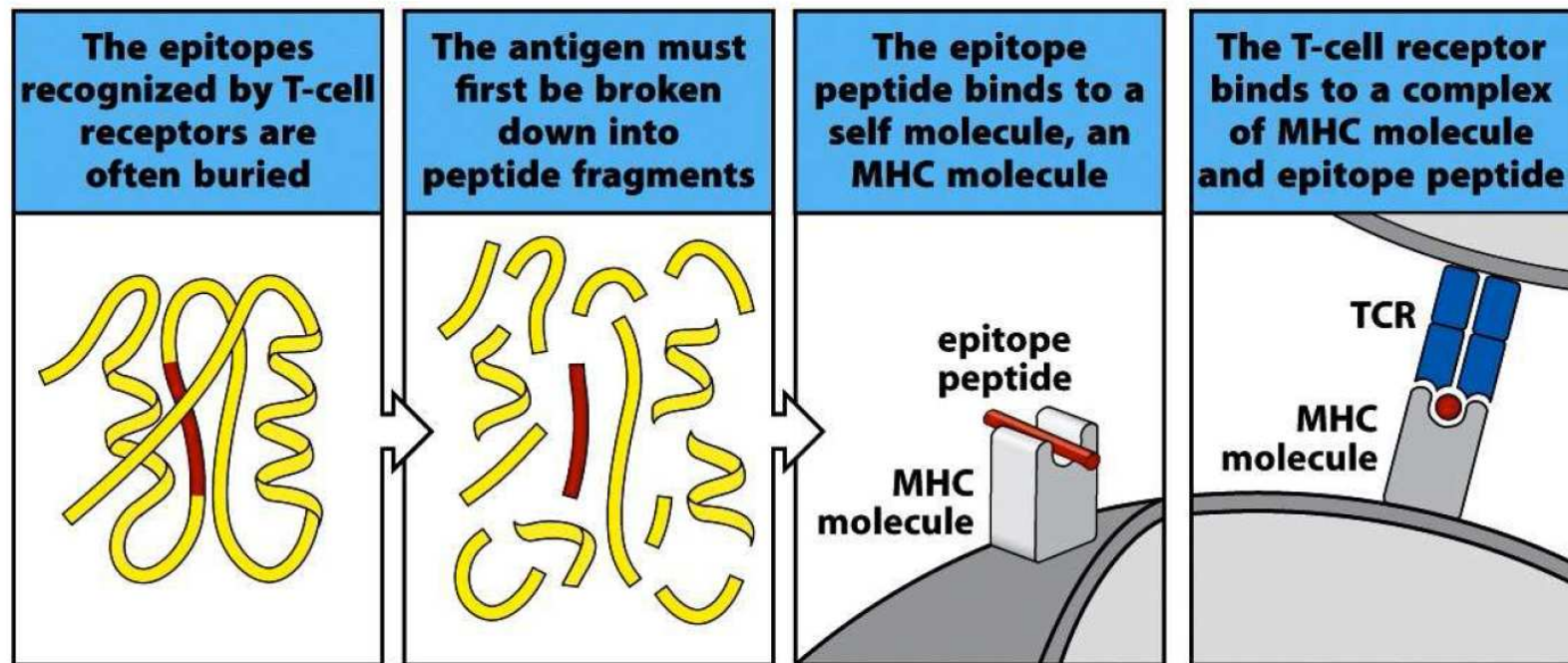
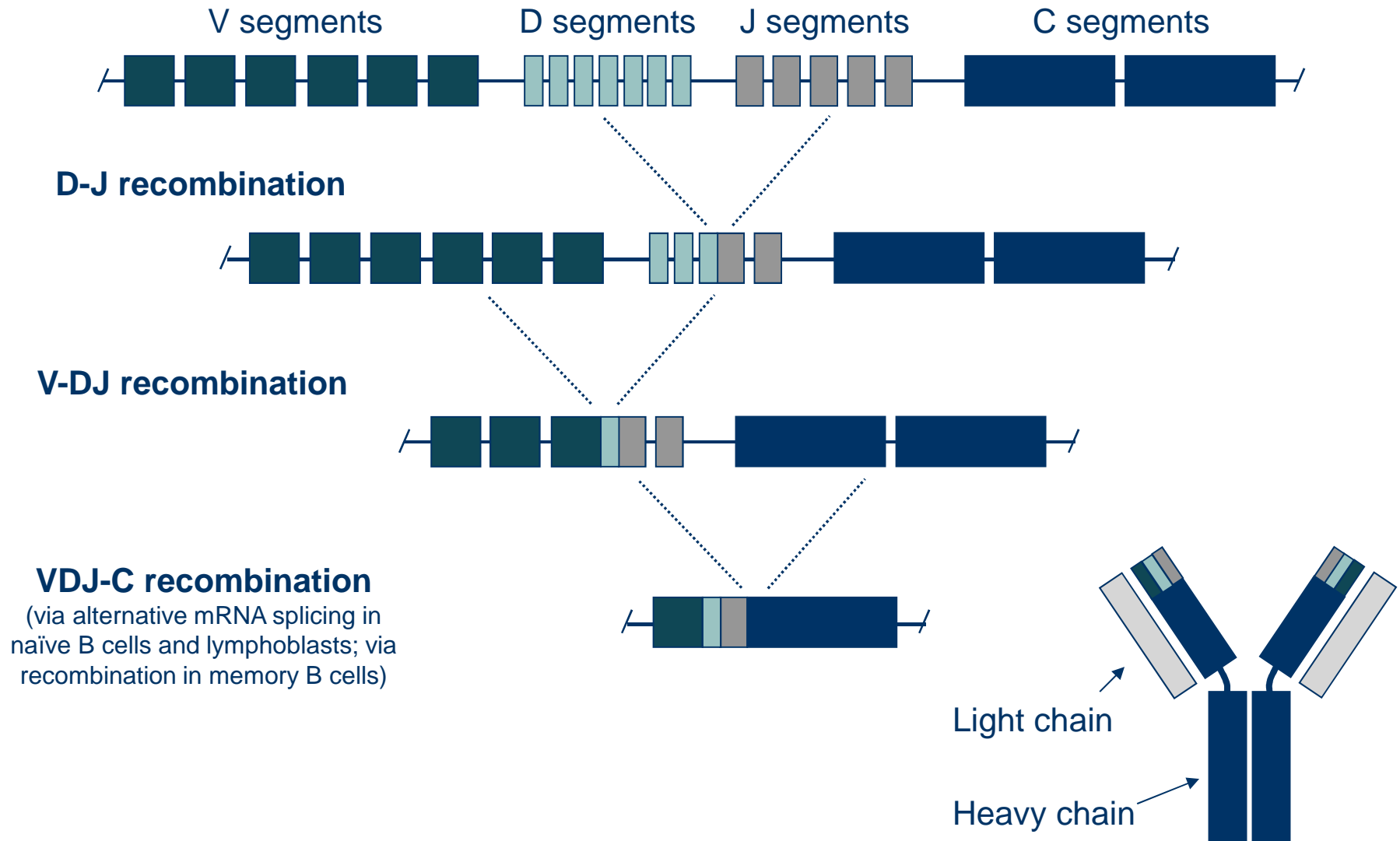


Figure 1-16 Immunobiology, 7ed. (© Garland Science 2008)

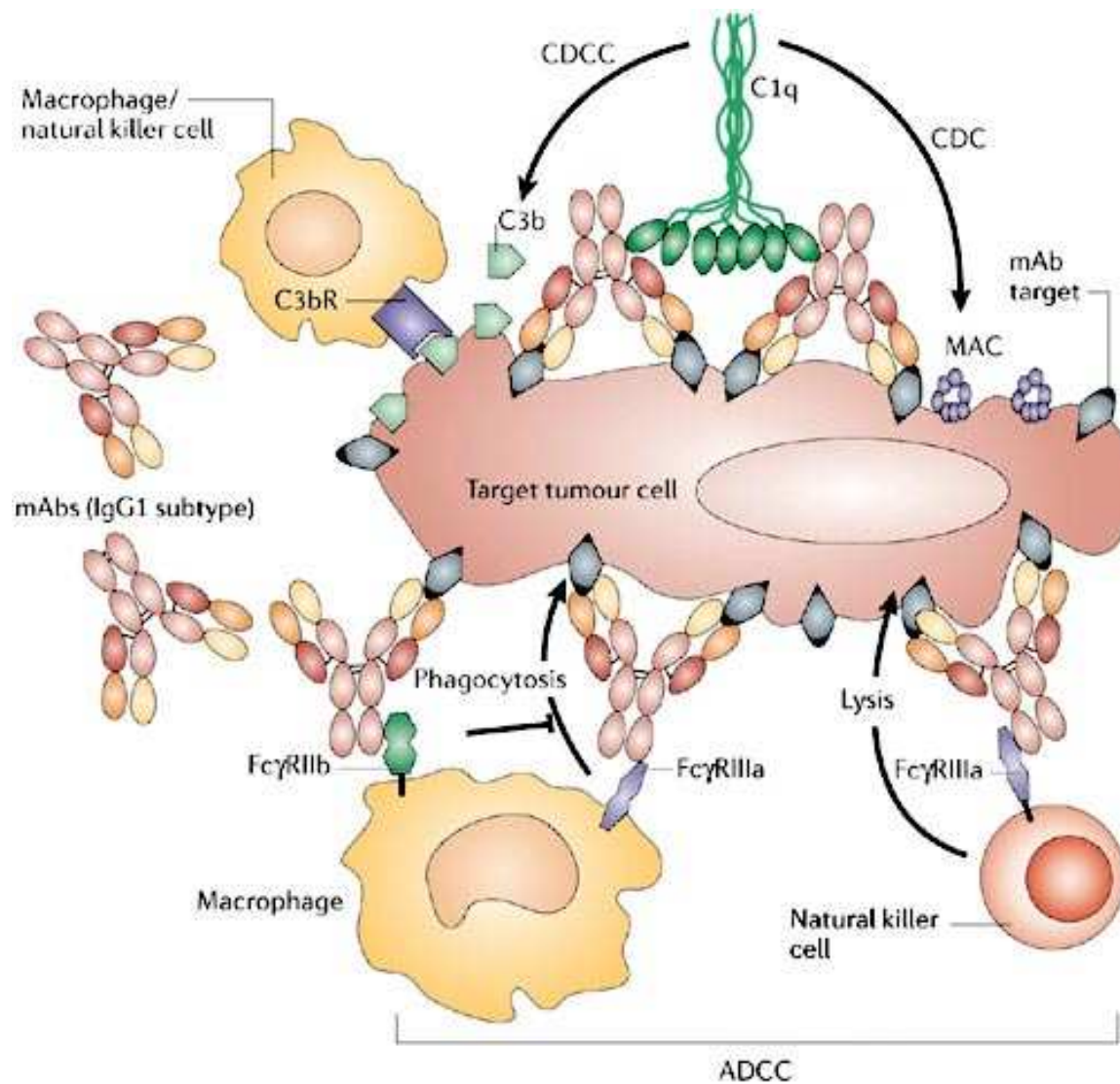
Adaptive Immunity is Epitope-Specific

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

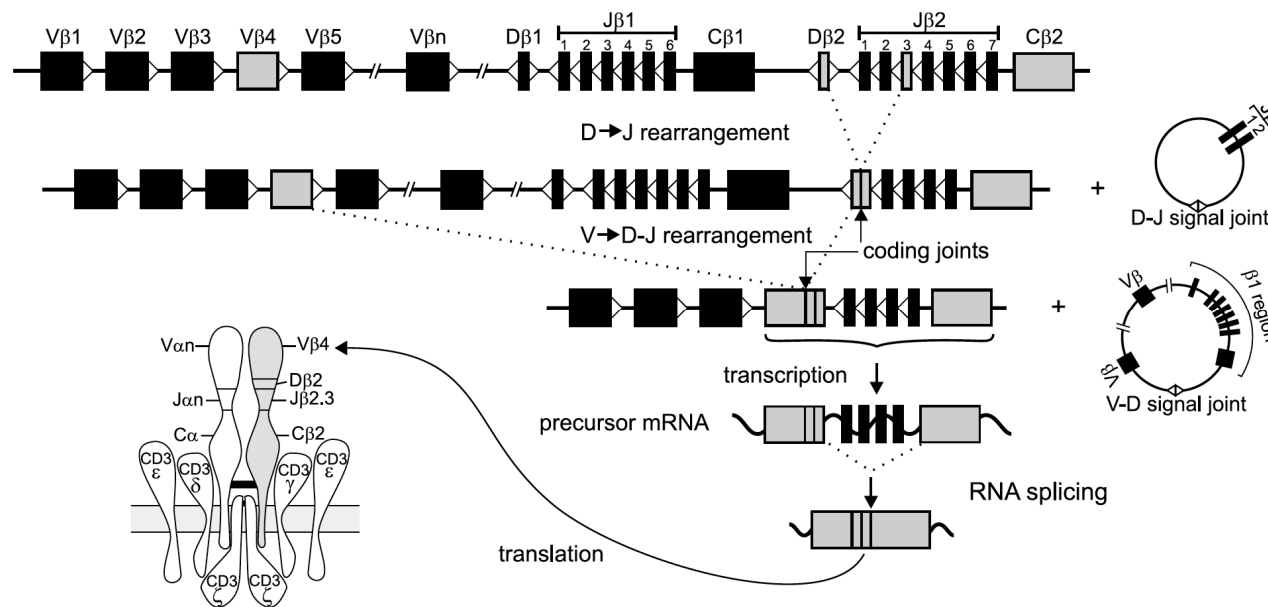
Immunoglobulin Gene Rearrangement



Immunoglobulin Mechanisms of Action

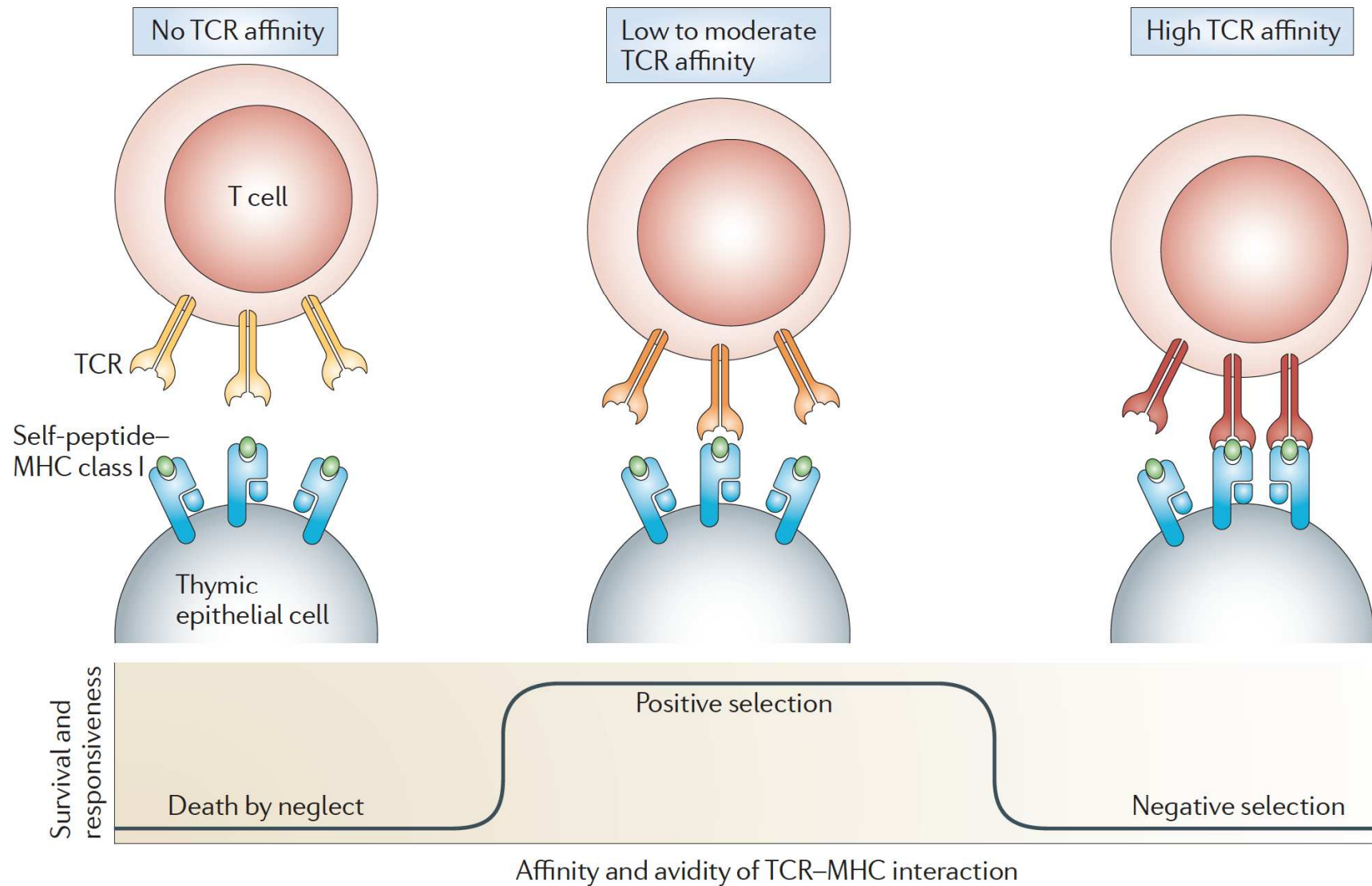


B and T Cell Repertoire Diversity

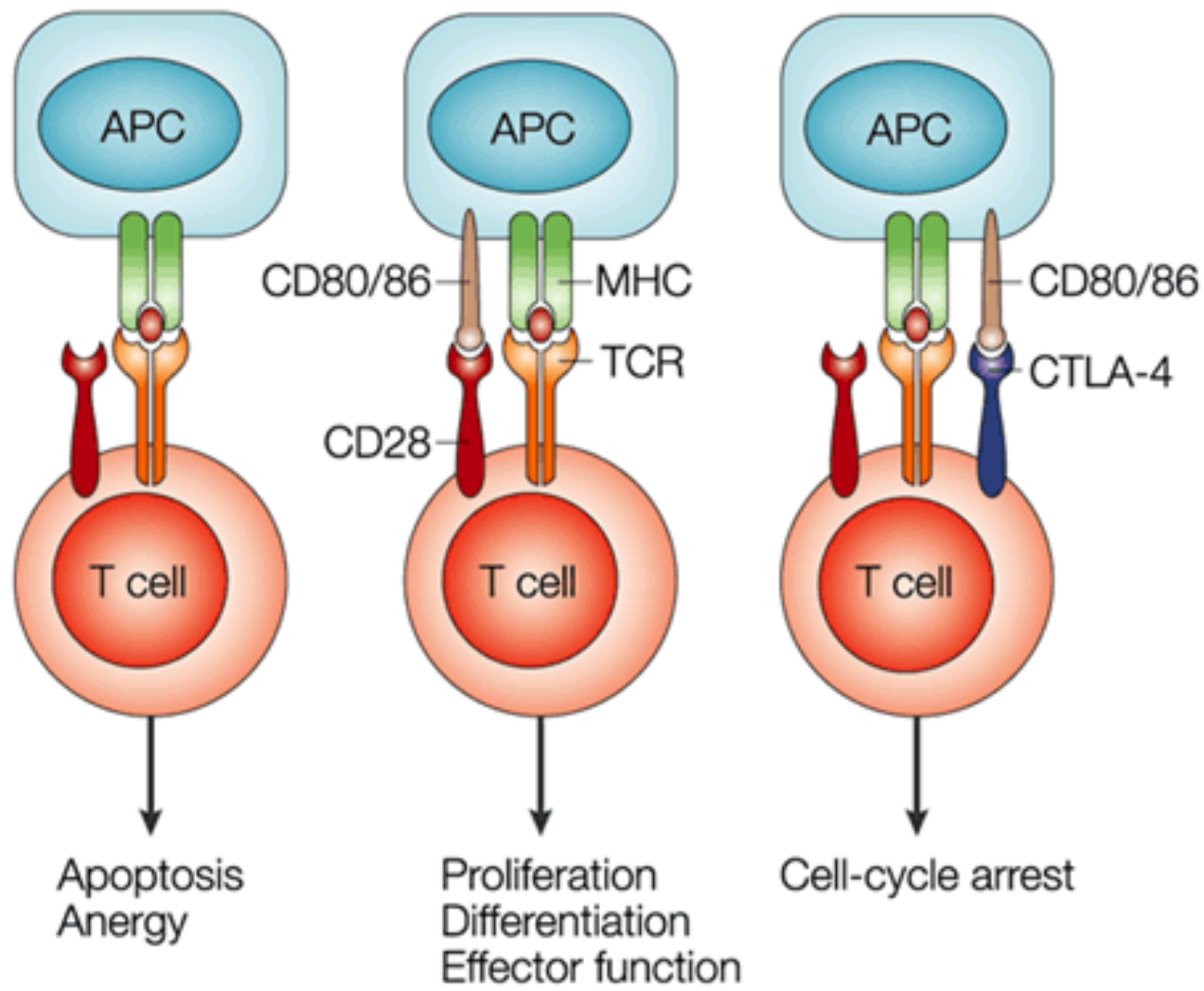


Gene segment	<i>IGH</i>	<i>IGK</i>	<i>IGL</i>	<i>TCRA</i>	<i>TCRB</i>	<i>TCRG</i>	<i>TCRD</i>
<i>V segments</i>							
Functional (family)	44 (7)	43 (7)	38 (10)	46 (32)	47 (23)	6 (4)	8
Rearrangeable (family)	66 (7) ^b	76 (7)	56 (11)	54 (32)	67 (30)	9 (4)	8
<i>D segments</i>							
Rearrangeable (family)	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

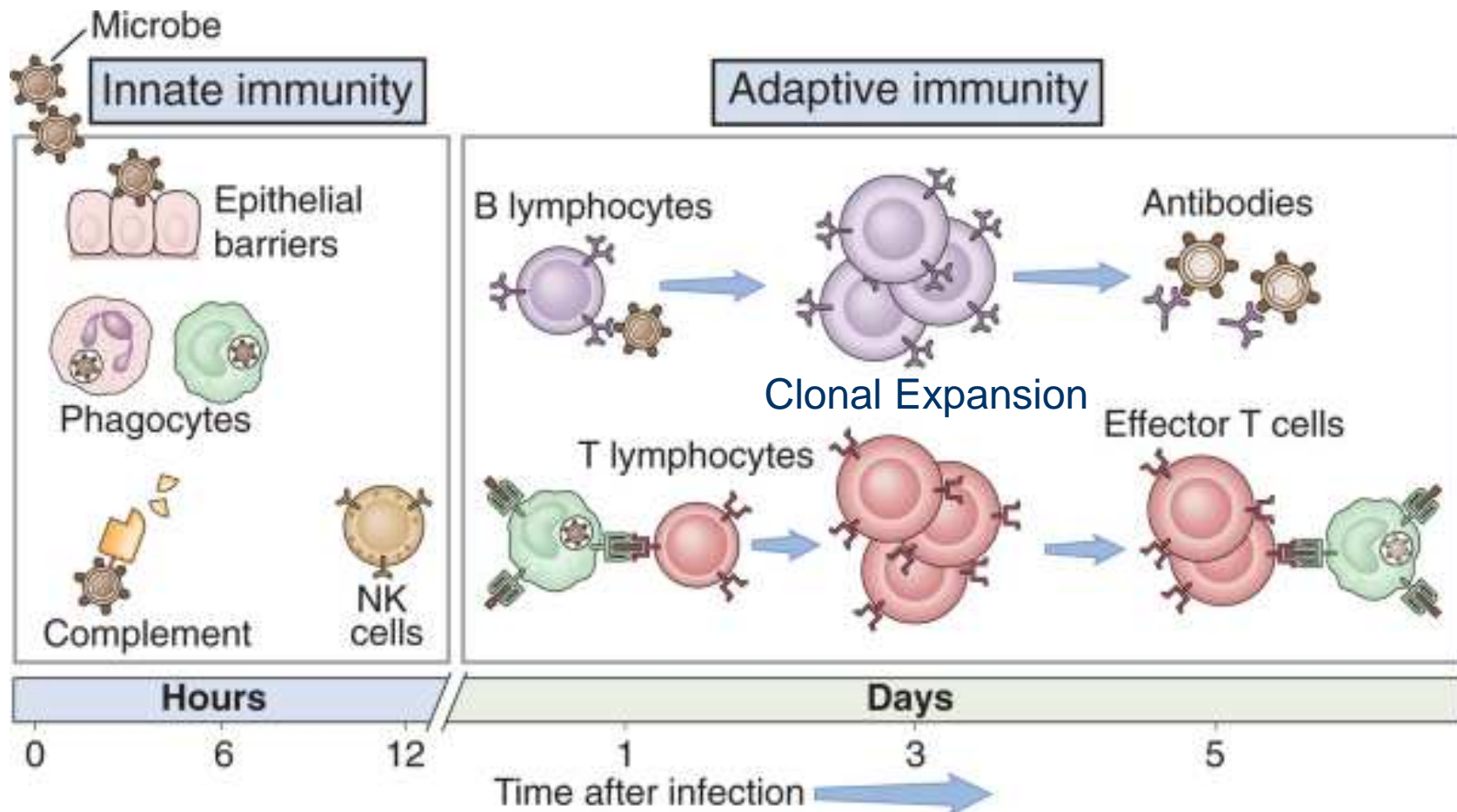
T Cell Selection



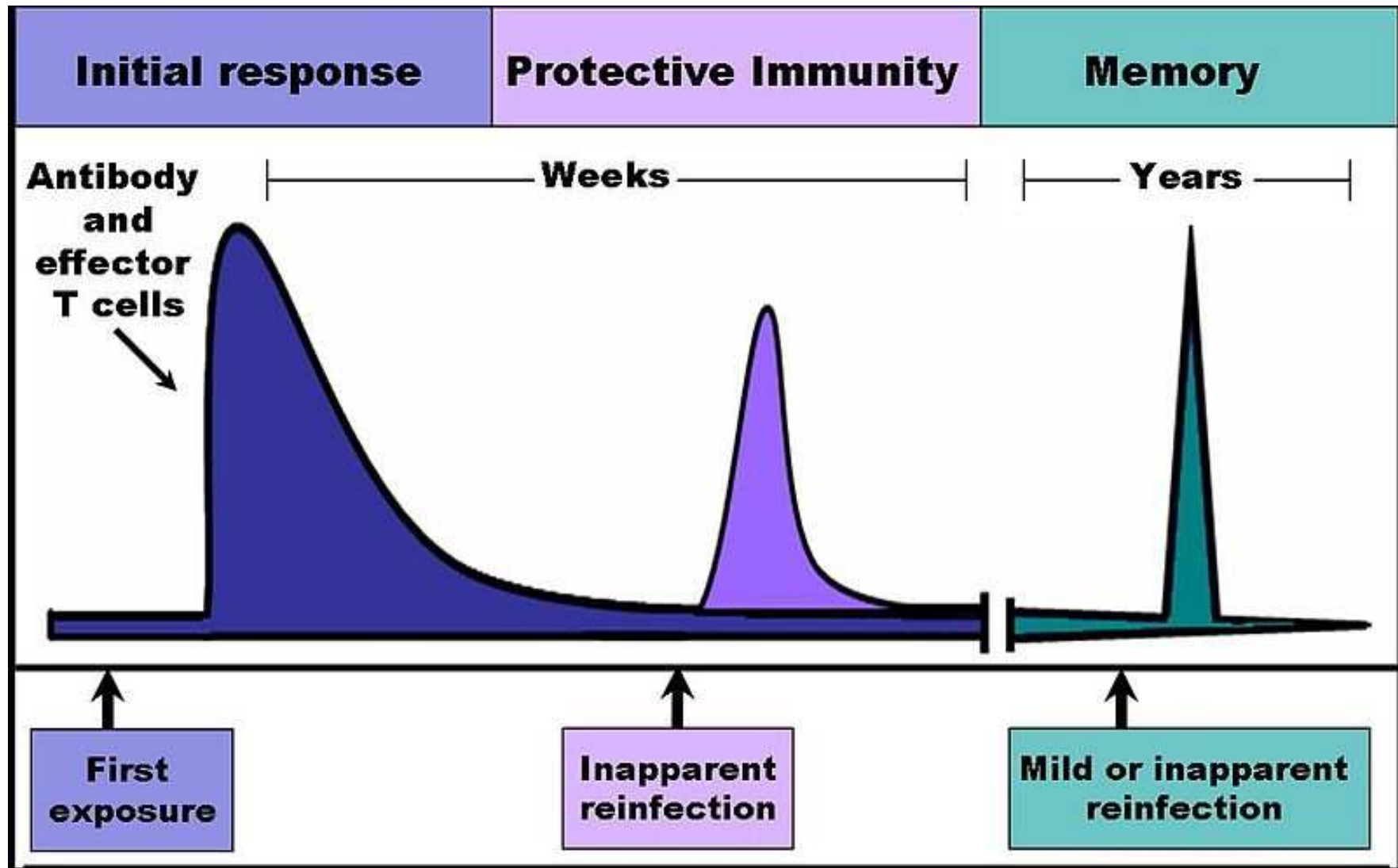
T Cell Costimulation



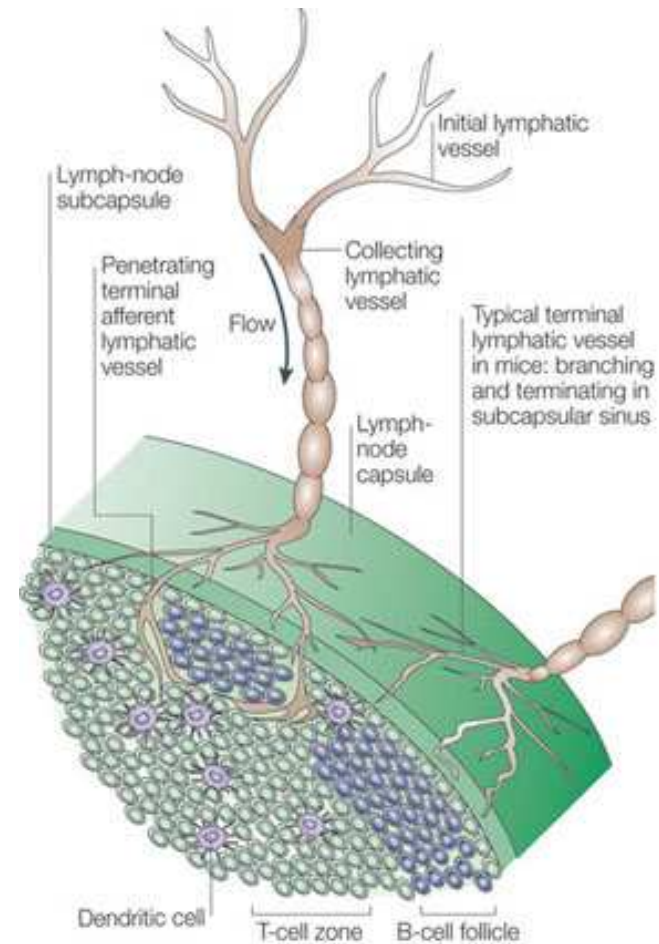
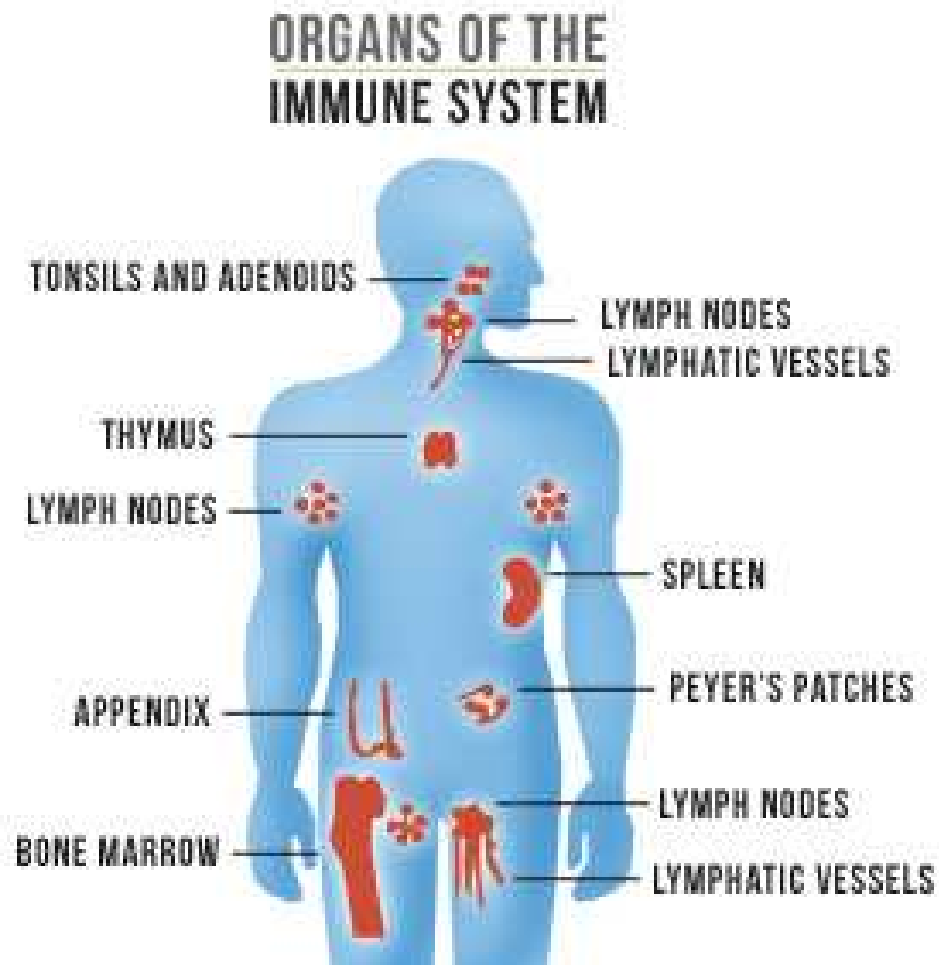
Innate and Adaptive Immunity Work Together



Characteristics of Adaptive Immune Response

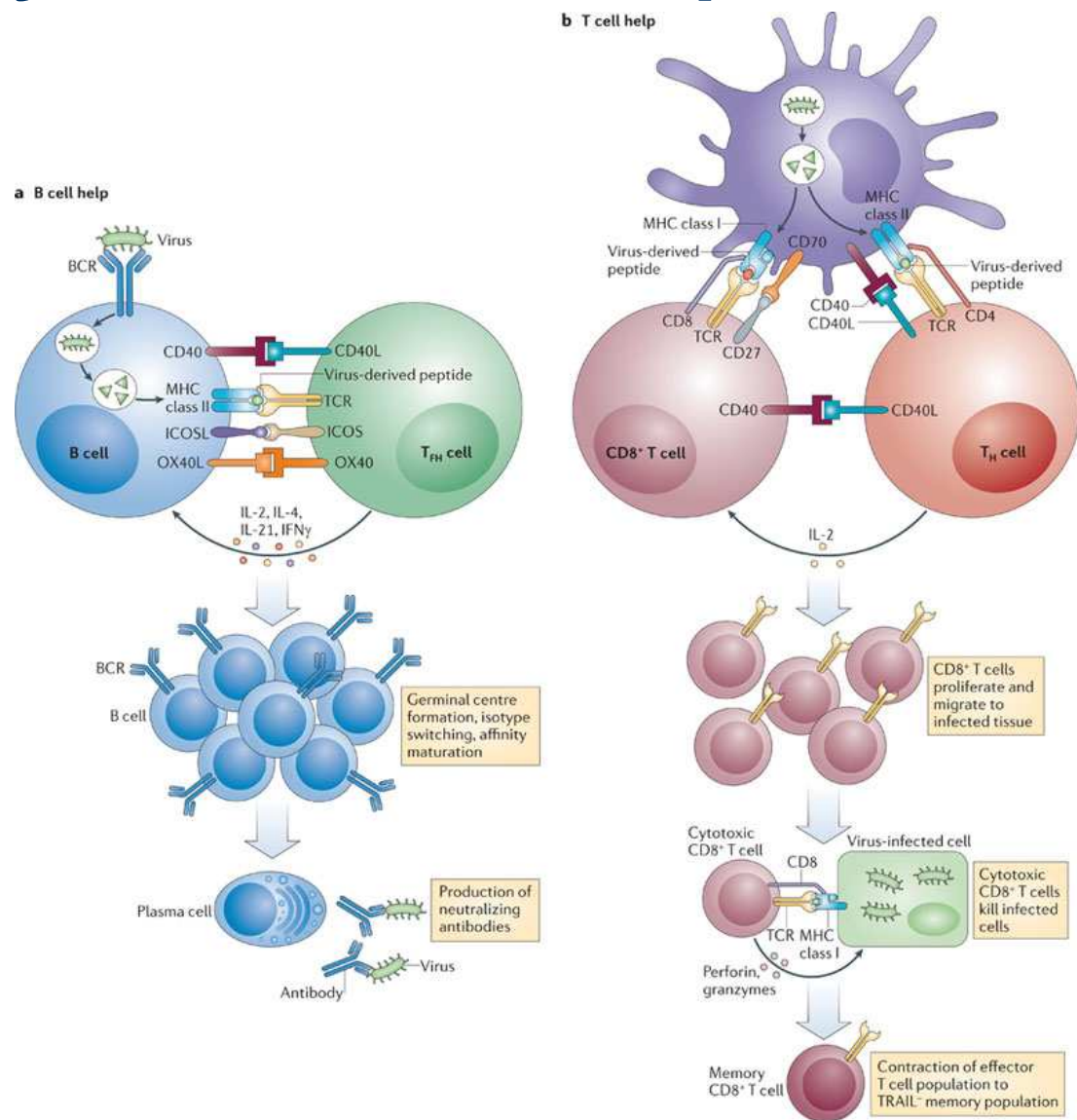


Immune Organs

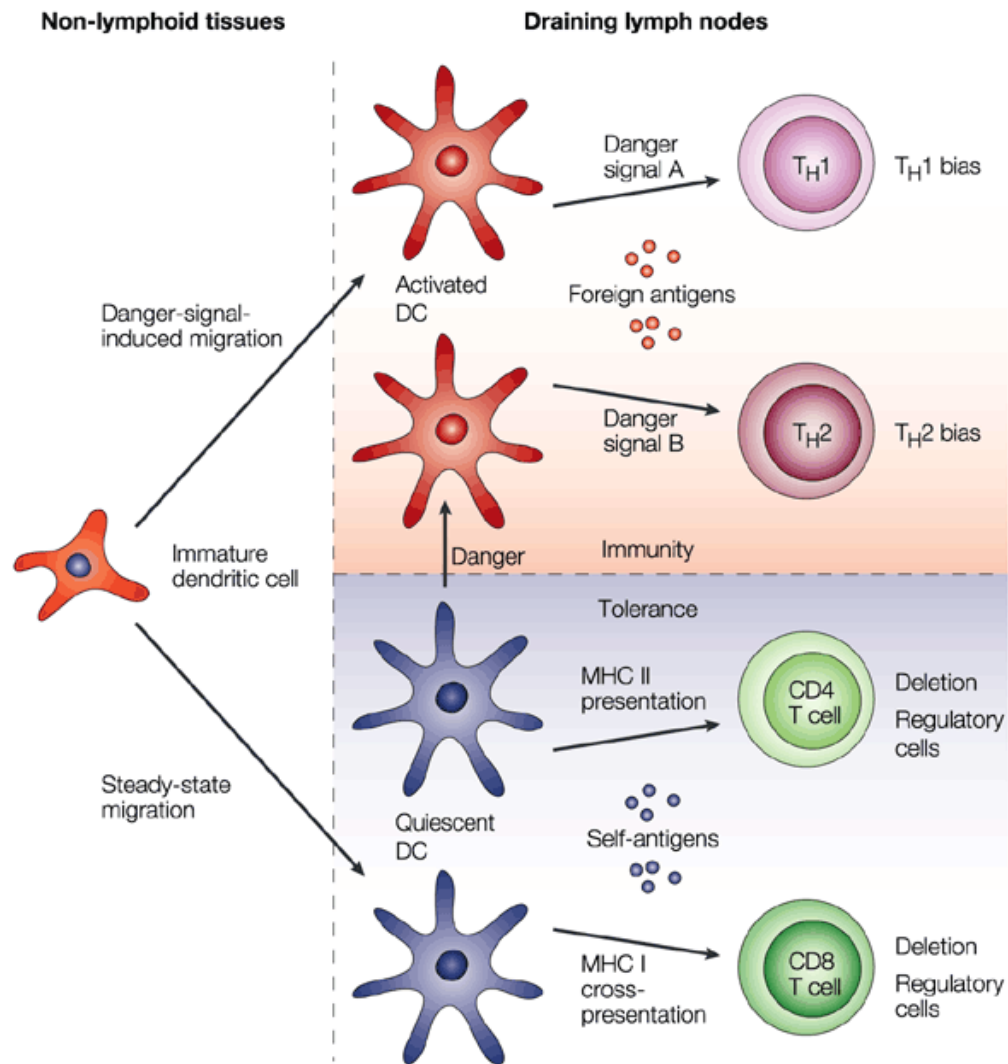


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Cytotoxic and Helper T Cells

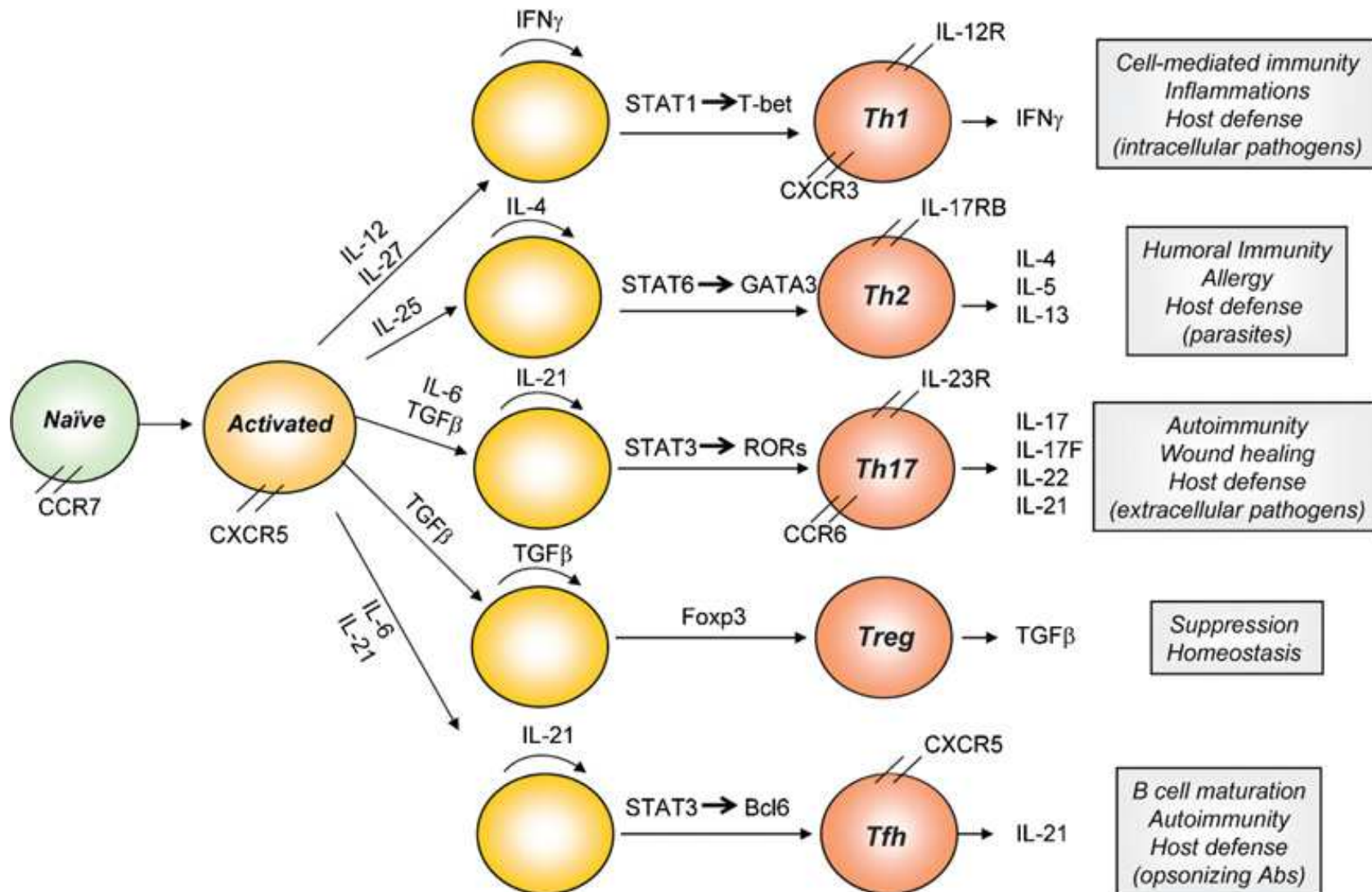


T Cell Responses are Directed by Dendritic Cells

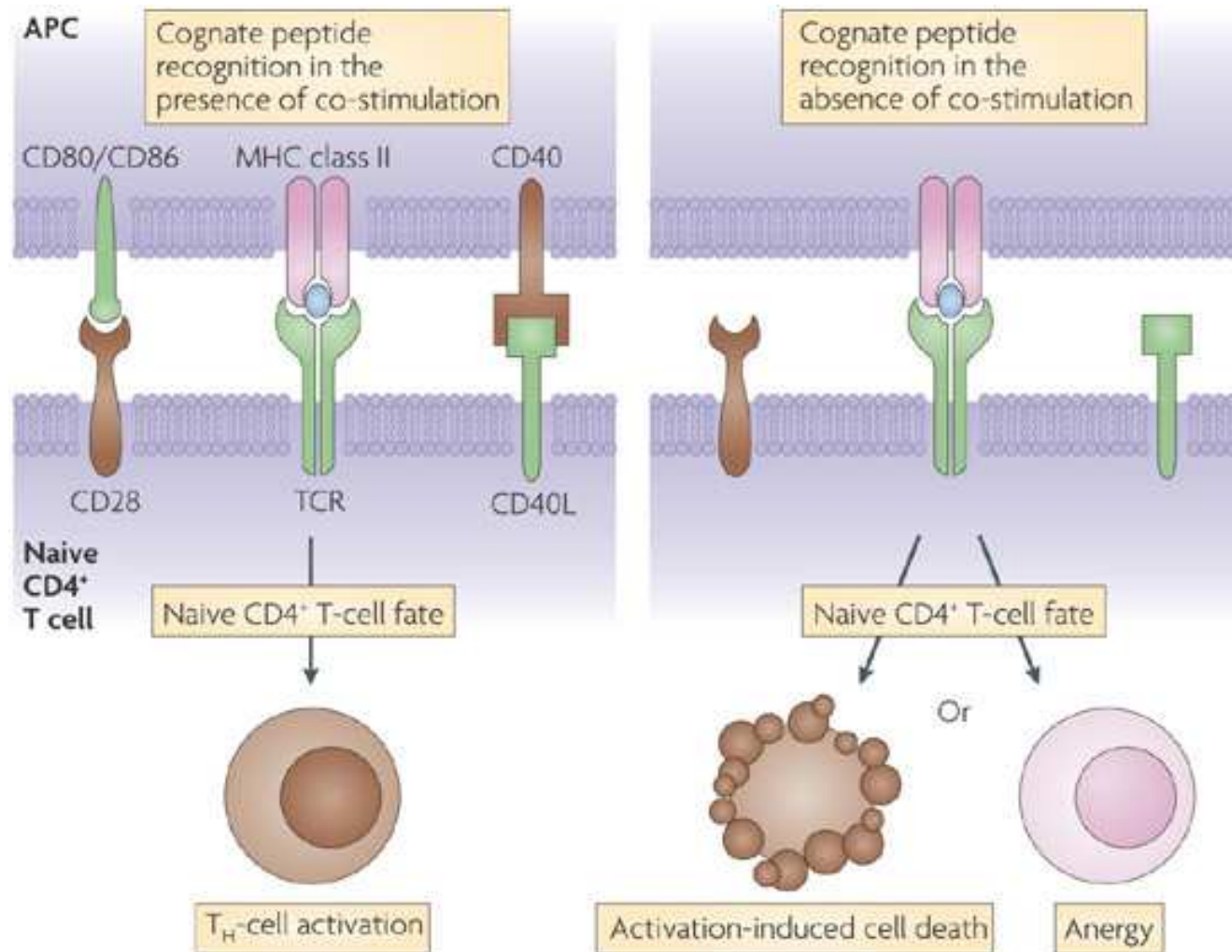


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T Cell Subsets: Th1, Th2, Th17, Tfh, Treg



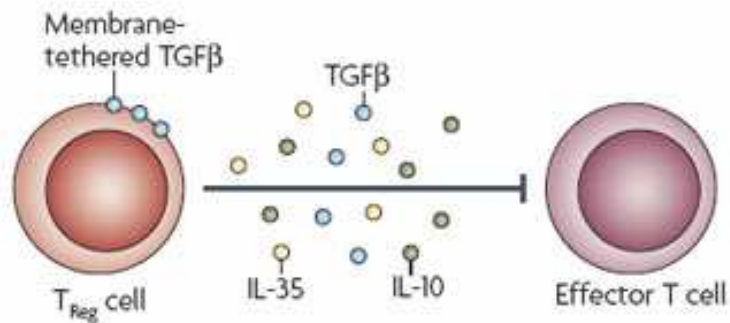
Anergy / Peripheral Tolerance



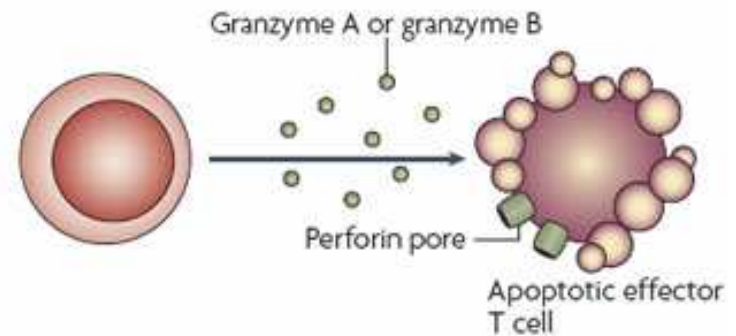
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Regulatory T (Treg) Cells

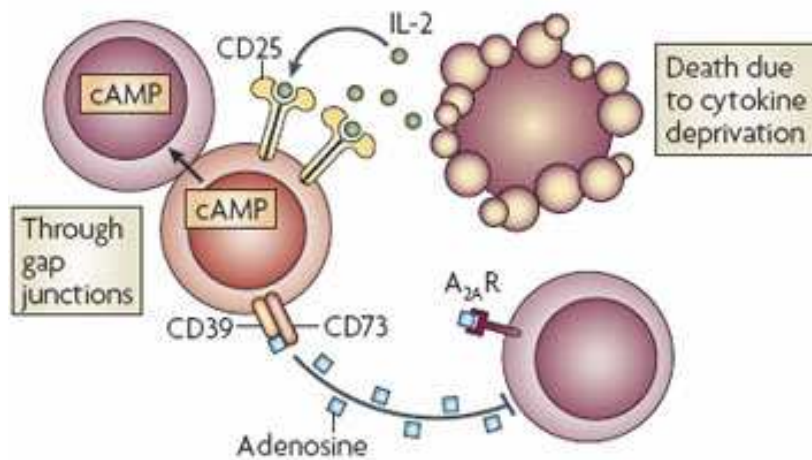
a Inhibitory cytokines



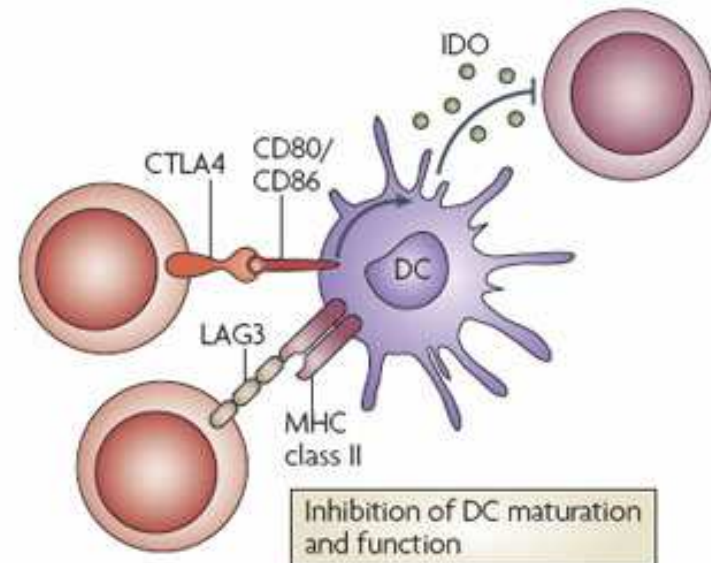
b Cytolysis



c Metabolic disruption

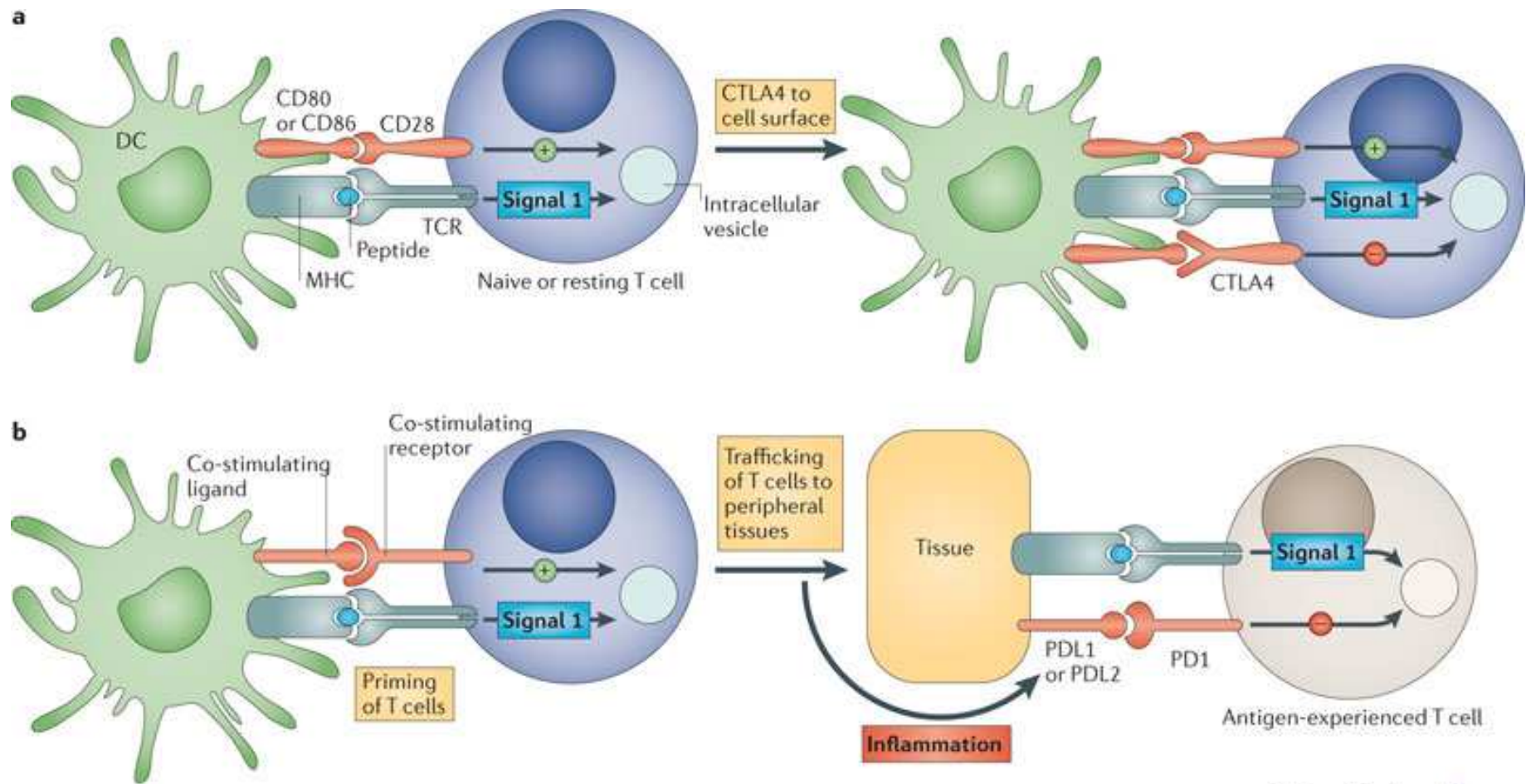


d Targeting dendritic cells



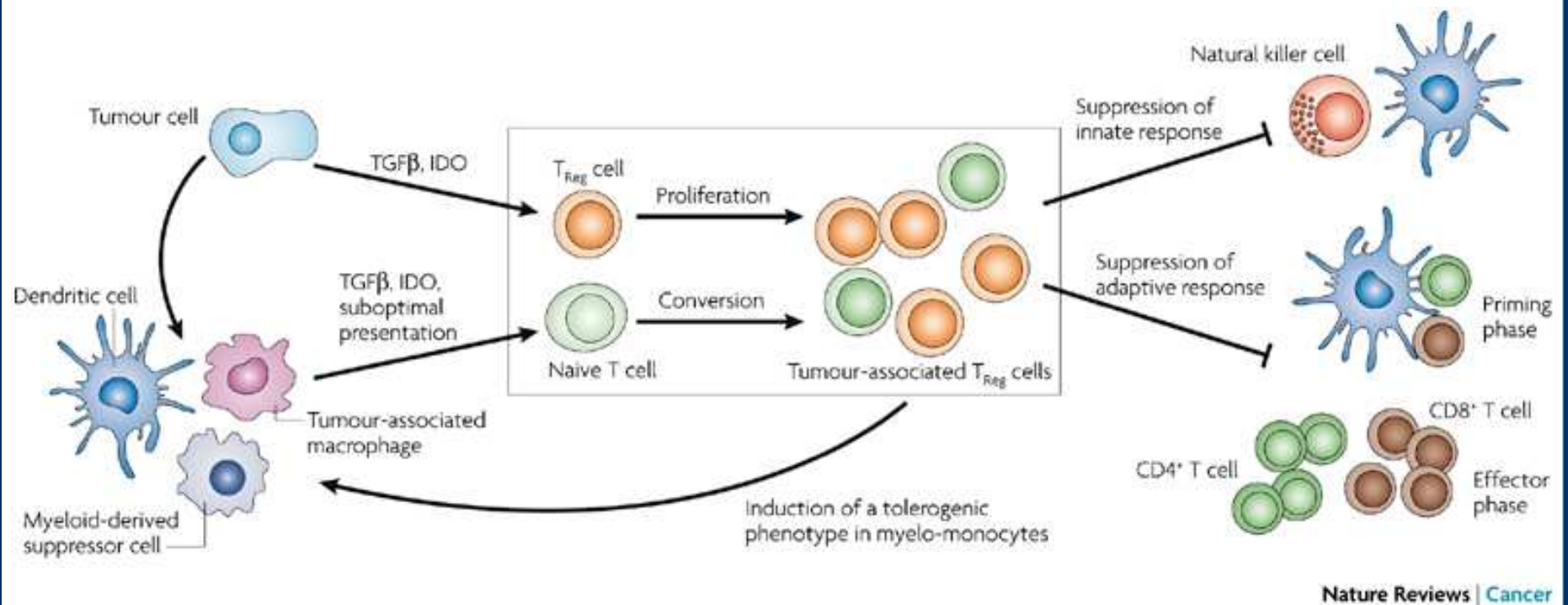
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Immune Checkpoints in Tumor Immunology

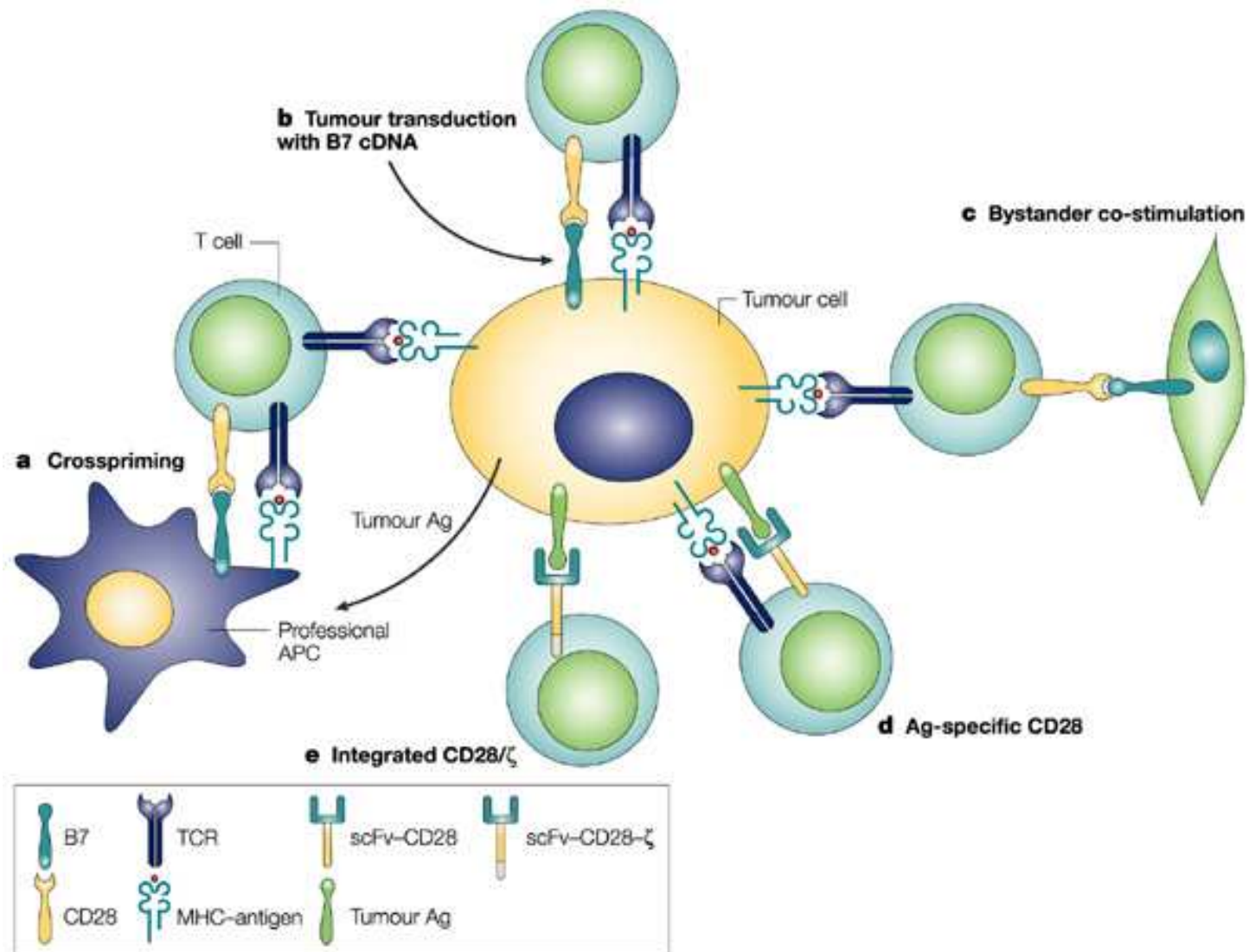


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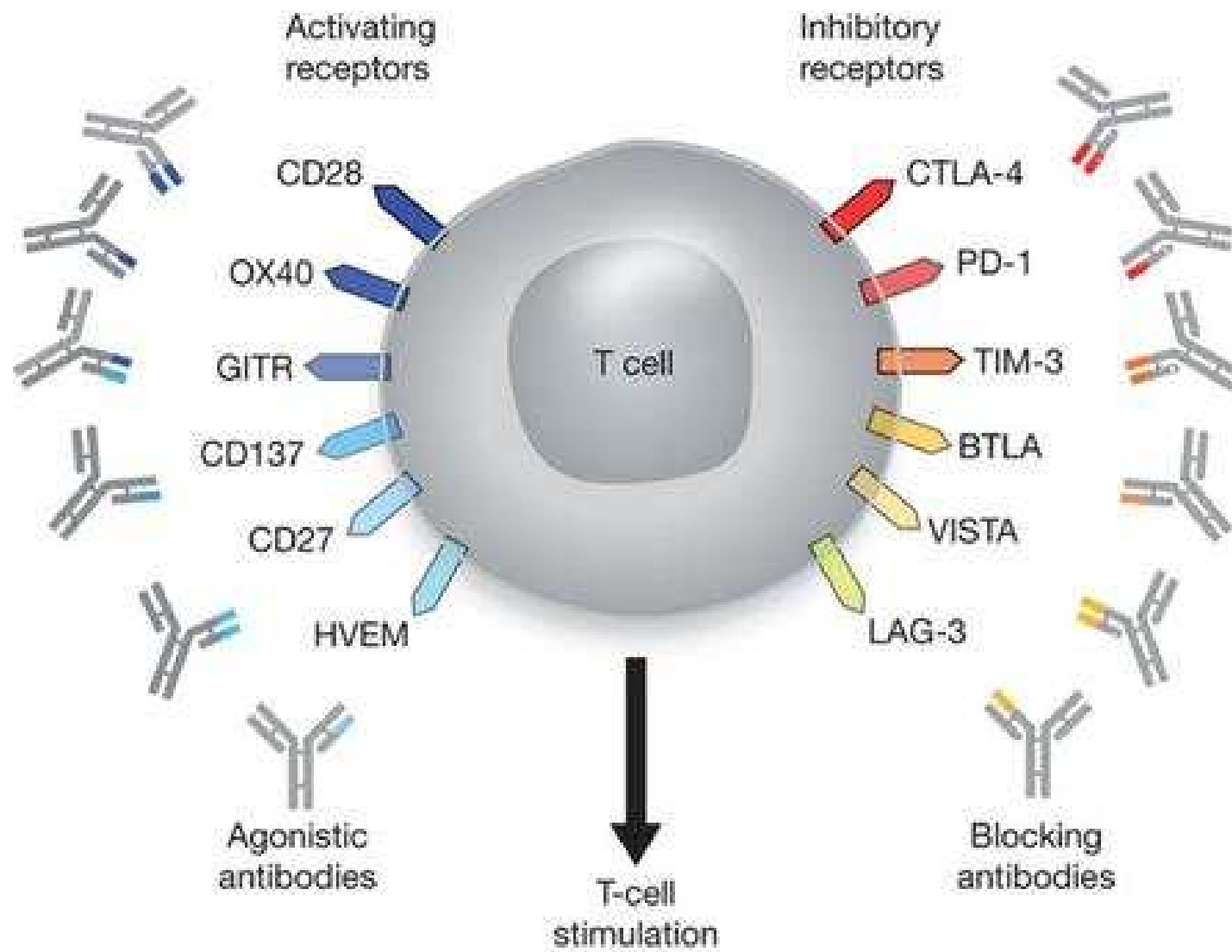
Regulatory Cells in Tumor Immunology



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

Thank you!