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NCI Awardee Skills Development Consortium

Cells of the Immune System

Andrea Schietinger
Associate Member • Immunology Program

Memorial Sloan Kettering Cancer Center

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OVERVIEW

1. The Origins of Immune Cells
2. Principles of Innate Immunity
3. Principles of Adaptive Immunity
4. Immune Cells and Responses in Tumors

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1. The Origins of Immune Cells

Immune cells derive from hematopoietic stem cells

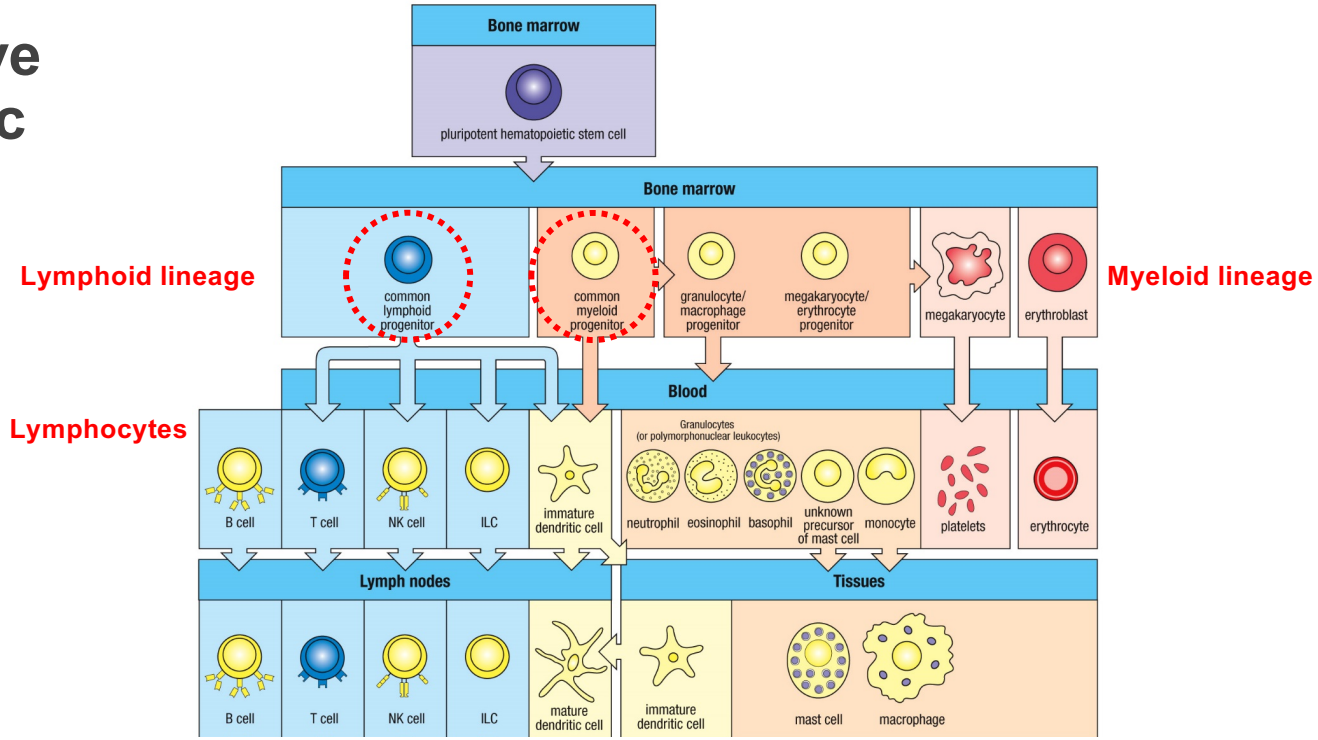
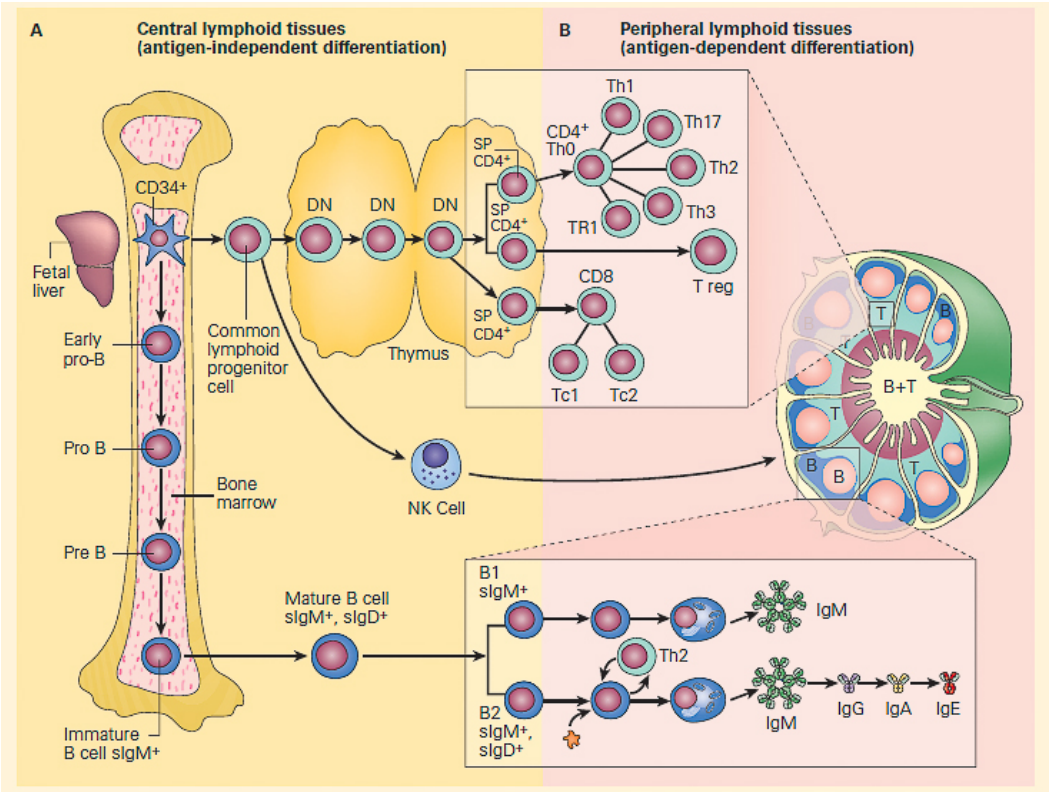


Figure 1.3 Janeway's Immunobiology, 9th ed. (© Garland Science 2017)

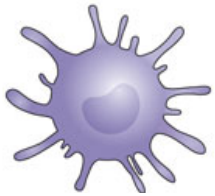
Ontogeny of the immune system



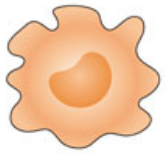
immunopaedia.org

Immune System

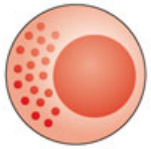
Innate immune system



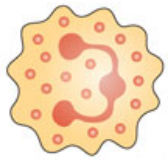
Dendritic Cell



Macrophage

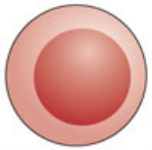


Natural Killer cell

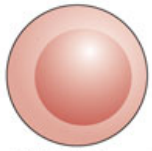


Neutrophil

Adaptive immune system



CD4 T cell
(Helper T cell)



CD8 T cell
(Cytotoxic Killer T cell)

B cell

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2. Principles of Innate Immunity

The myeloid lineage comprises most of the cells of the innate immune system

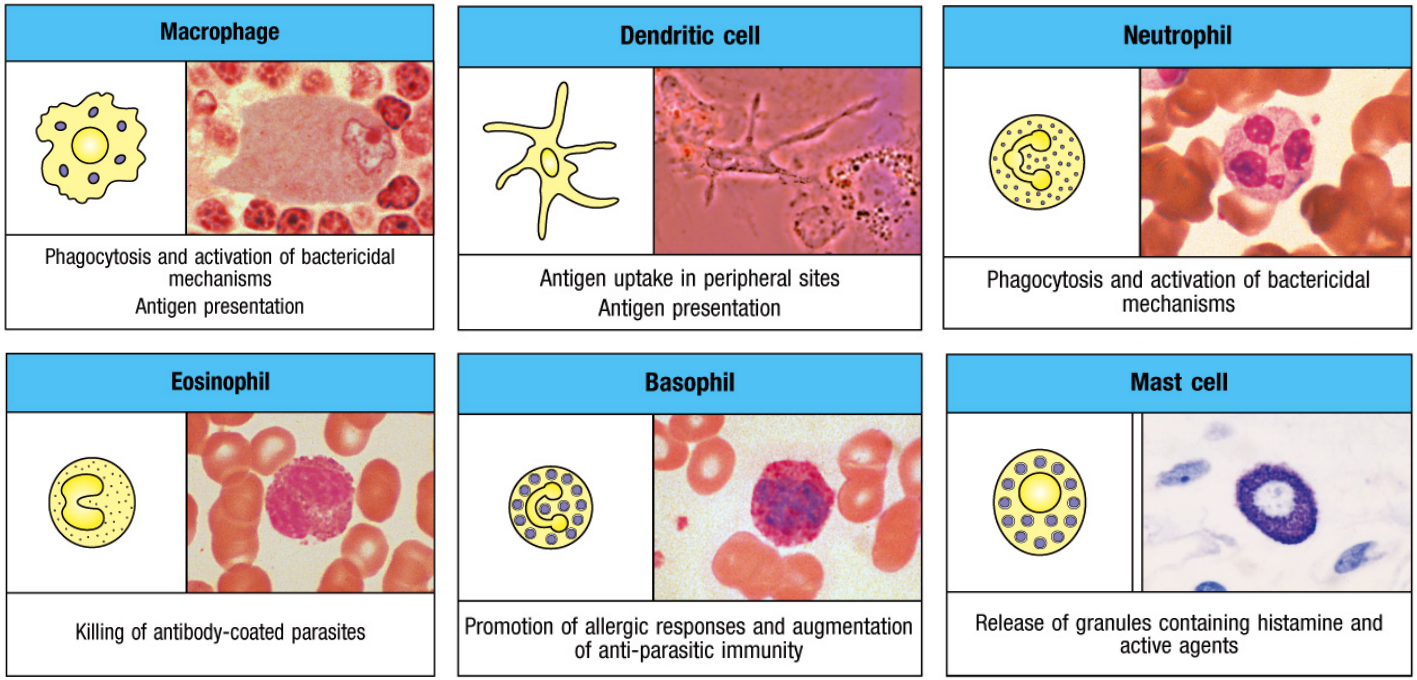


Figure 1.8 Janeway's Immunobiology, 9th ed. (© Garland Science 2017)

The innate immune response causes inflammation at sites of infection

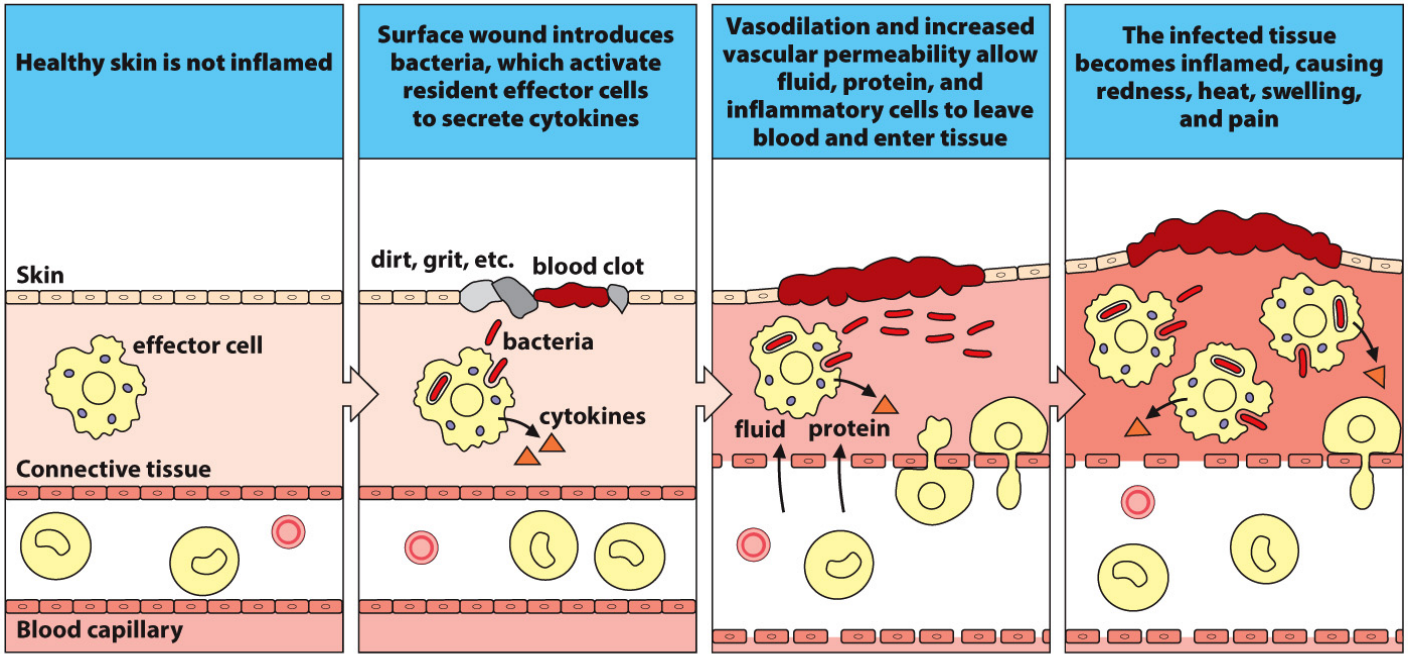


Figure 1.7 The Immune System, 4th ed. (© Garland Science 2016)

Sensor cells (e.g. macrophages) express pattern recognition receptors that provide recognition of non-self

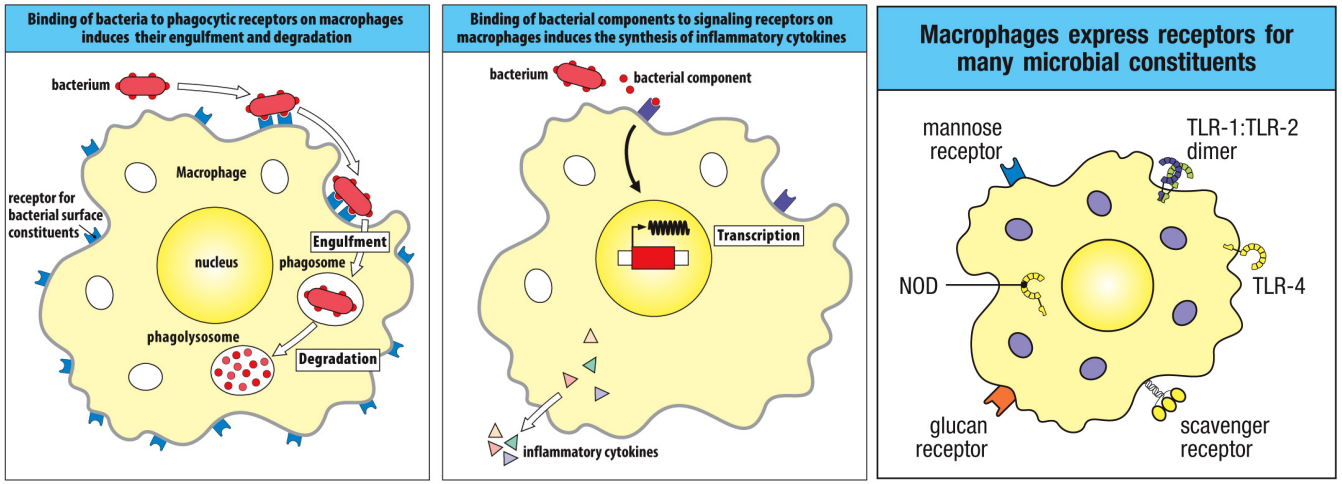
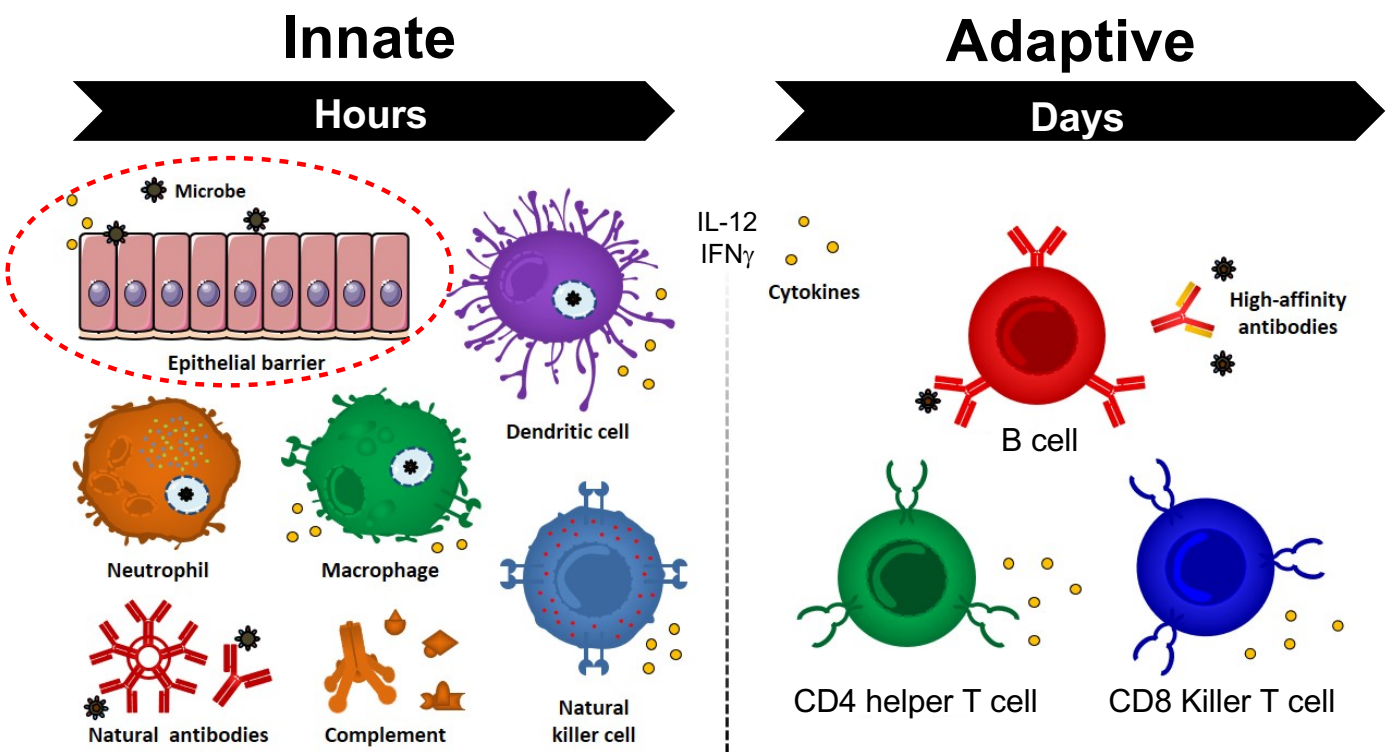


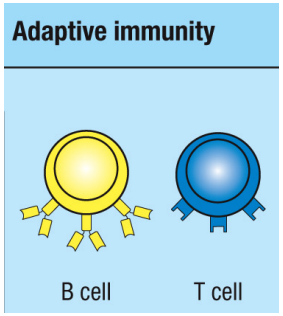
Figure 1.16 The Immune System, 4th ed. (© Garland Science 2015)

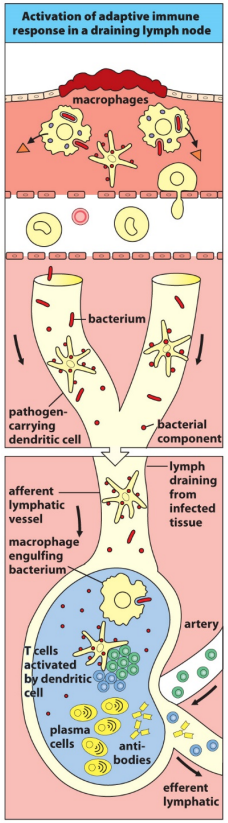
Innate vs Adaptive Immune Responses:

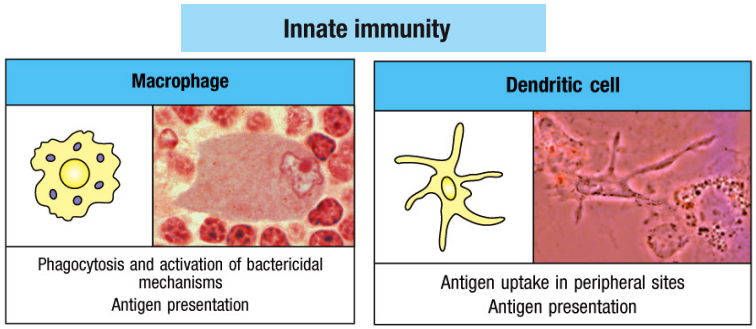
during infections



Adaptive immunity is initiated in secondary lymphoid tissues







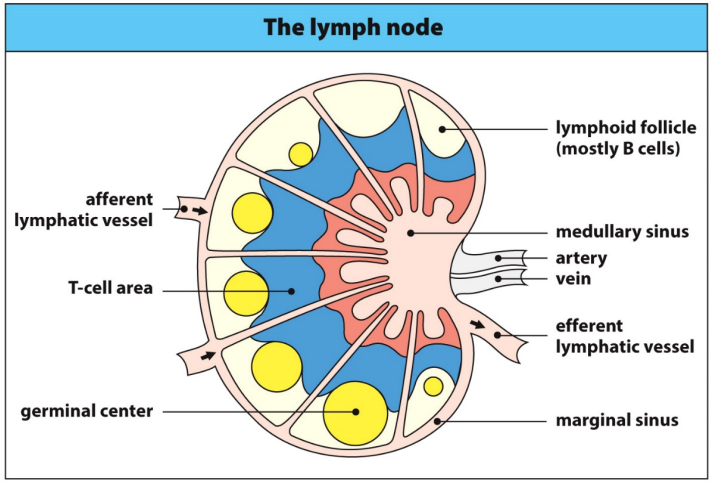


Figure 1.23 The Immune System, 4th ed. (© Garland Science 2015)

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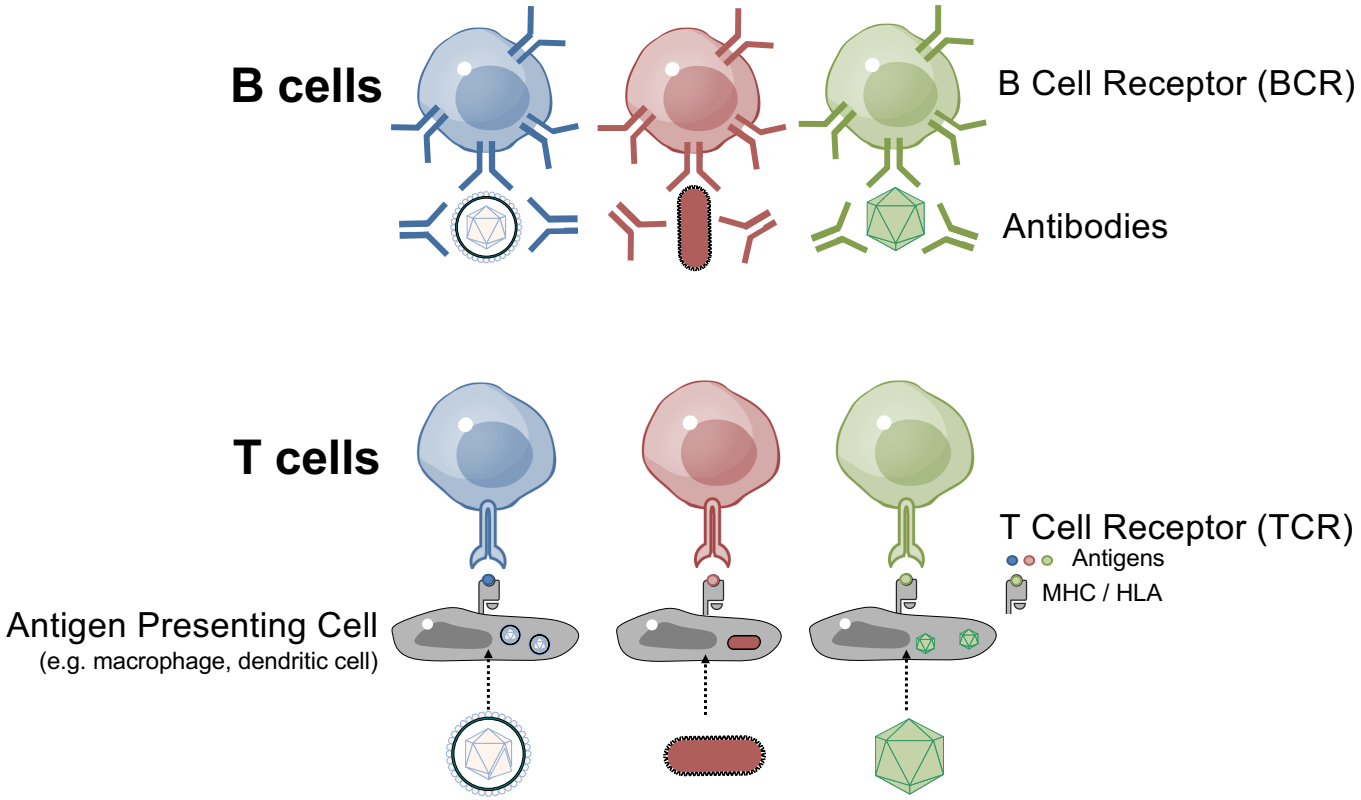
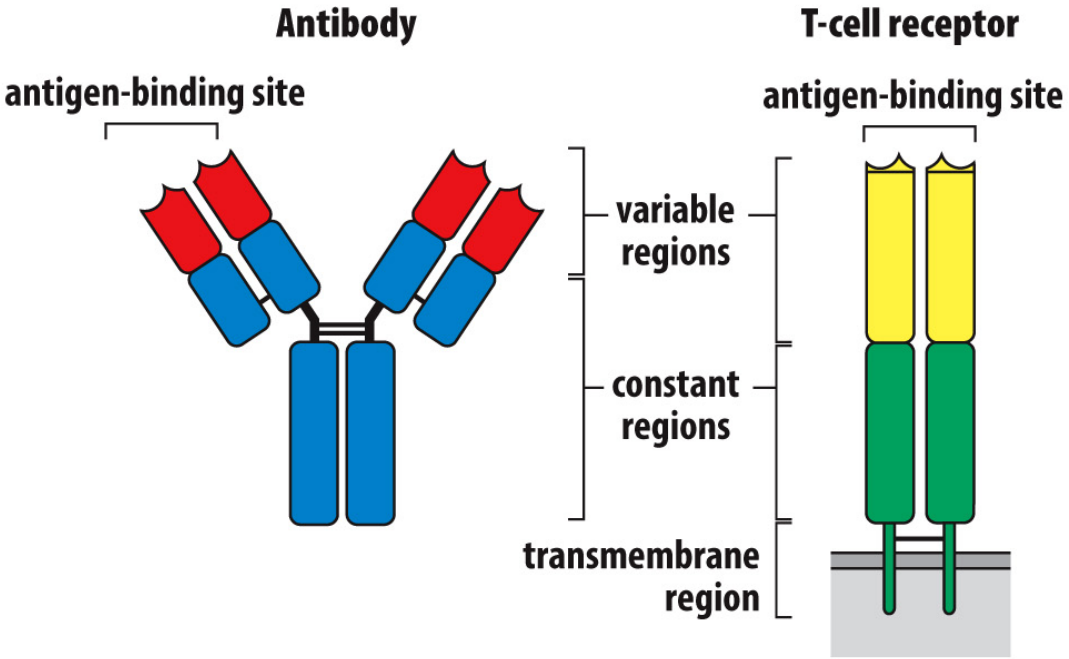
3. Principles of Adaptive Immunity

B and T cells recognize their specific antigens via B and T cell receptors, respectively

Antibodies and TCR recognize antigens by fundamentally different mechanisms



Immune receptors



Antigen recognition

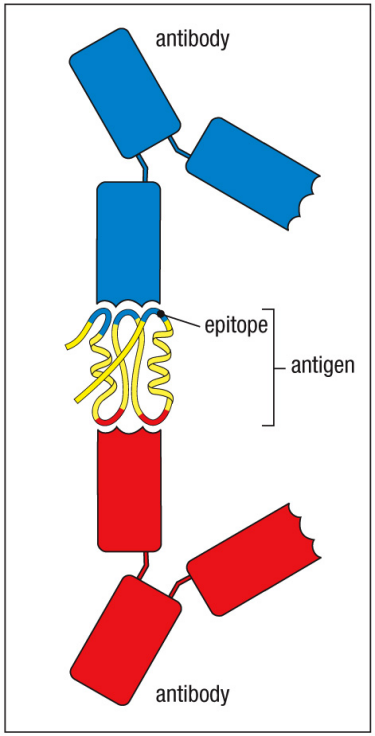
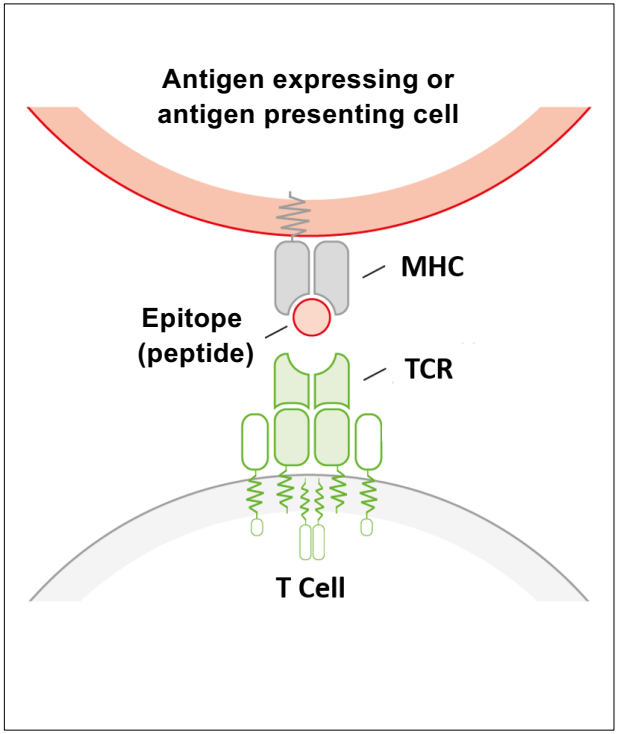


Figure 1.14 Janeway's Immunobiology, 9th ed. (© Garland Science 2017)



Immune receptor diversity

	B cells		T cells	
Element	**Immunoglobulin**		**α:β receptors**	
	H	**κ+λ**	**β**	**α**
Variable segments (V)	65	70	52	~70
Diversity segments (D)	27	0	2	0
D segments read in 3 frames	rarely	–	often	–
Joining segments (J)	6	5(κ) 4(λ)	13	61
Joints with N- and P- nucleotides	2	50% of joints	2	1
Number of V gene pairs	3.4×10^6		5.8×10^6	
Junctional diversity	$\sim 3 \times 10^7$		$\sim 2 \times 10^{11}$	
Total diversity	$\sim 10^{14}$		$\sim 10^{18}$	

Antigens have to be presented on MHC molecules on the surface of cells in order to be seen by T cells (TCR)

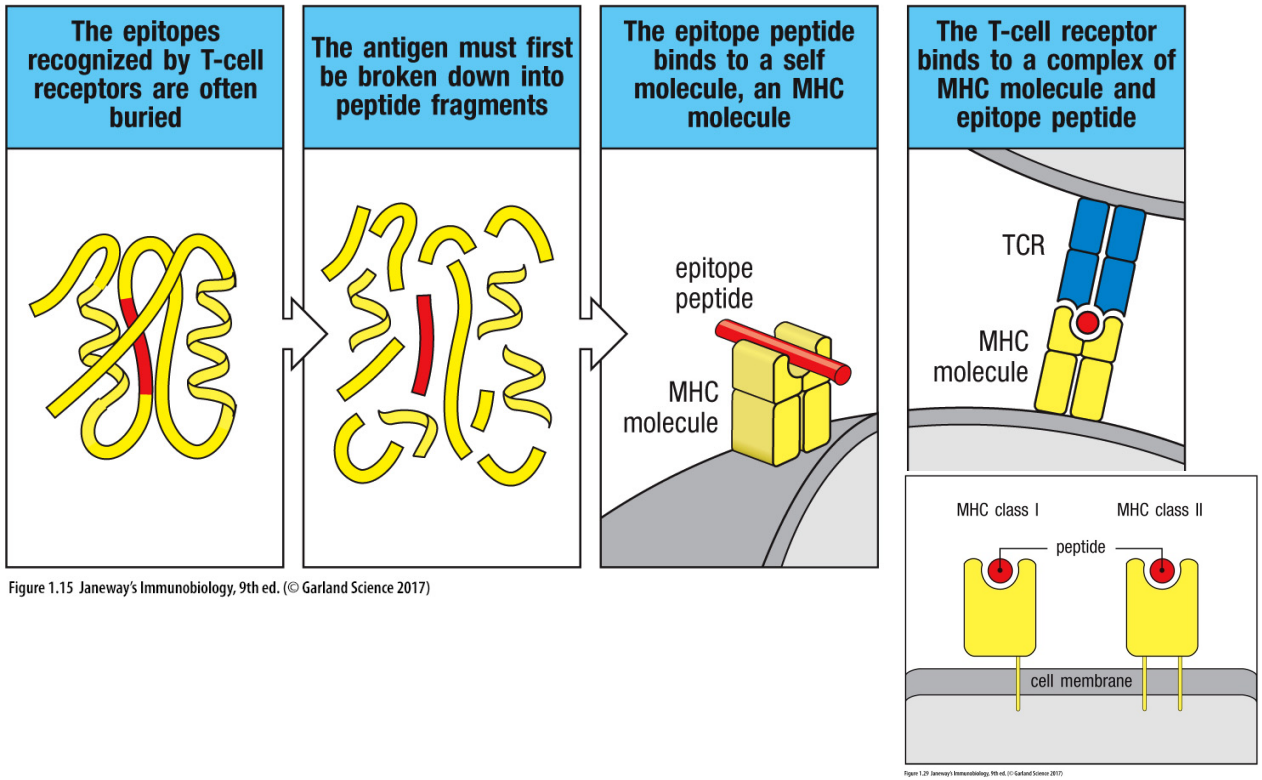


Figure 1.15 Janeway's Immunobiology, 9th ed. (© Garland Science 2017)

Figure 1.15 Janeway's Immunobiology, 9th ed. (© Garland Science 2017)

T cells recognizing their cognate antigen on MHC

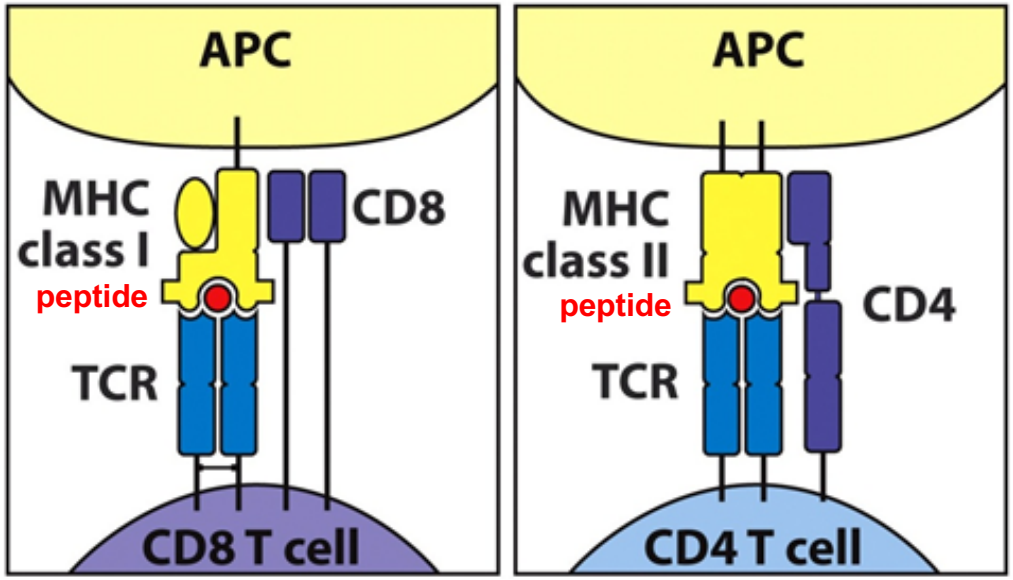


Figure 1.15 Janeway's Immunobiology, 9th ed. (© Garland Science 2017)

CD8 and CD4 T cell responses

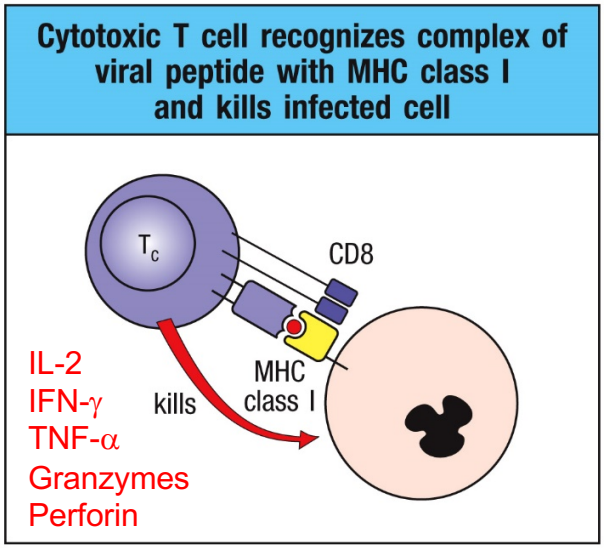


Figure 1.32 Janeway's Immunobiology, 9th ed. (© Garland Science 2017)

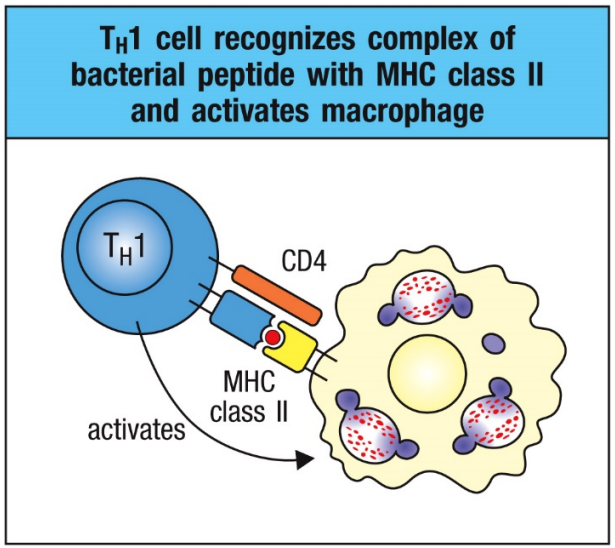


Figure 1.33 (part 1 of 2) Janeway's Immunobiology, 9th ed. (© Garland Science 2017)

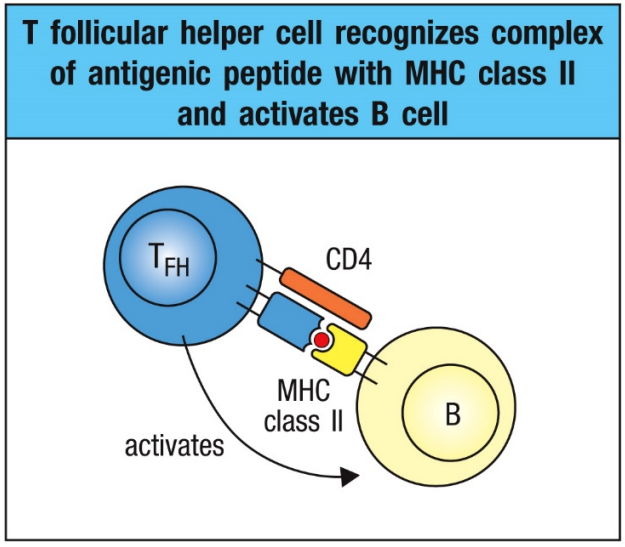


Figure 1.33 (part 2 of 2) Janeway's Immunobiology, 9th ed. (© Garland Science 2017)

CD8 T cells activated by antigen give rise to antigen-specific effector CD8 T cells that eliminate target cells

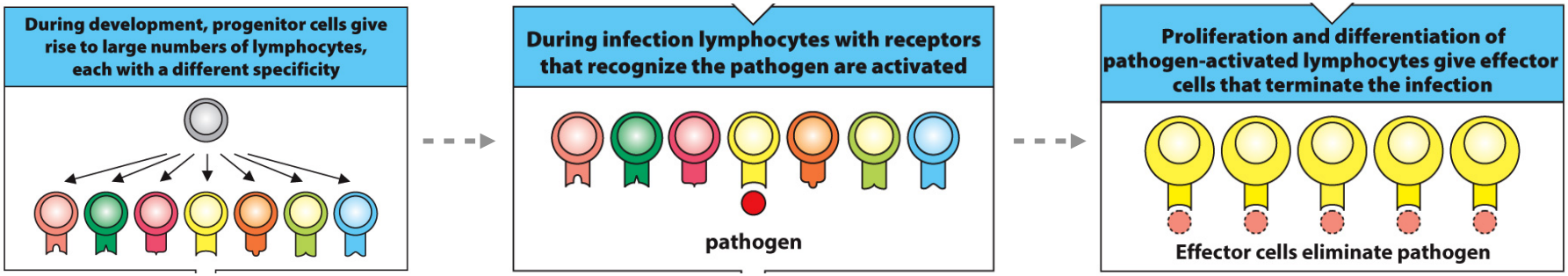
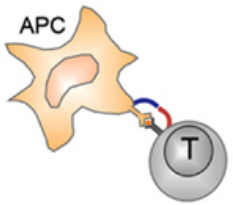


Figure 1.9 The Immune System, 4th ed. (© Garland Science 2015)

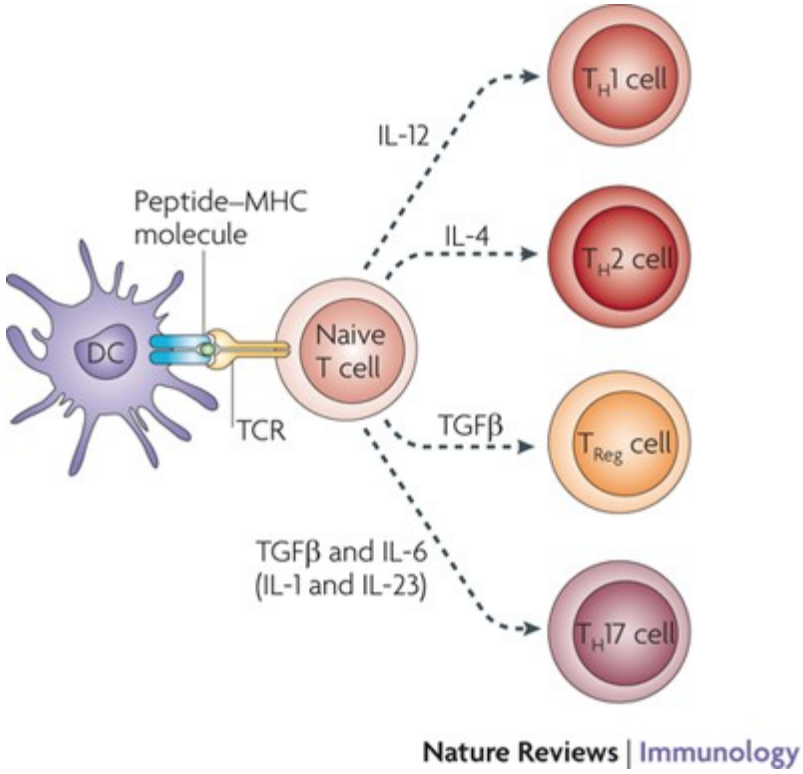
CD8 T cell activation and differentiation (e.g. during an infection)

Activation



Naïve
T cell

CD4 T cell activation and polarization into different effector T cell subsets: T helper 1 (TH1), TH2, TH17, TReg



Antiviral or antitumor immunity

Increased CD8 T cell effector function

Antiparasite immunity
Allergic responses

Suppressor T cells: Tolerance and protection from autoimmunity

Antifungal
Antibacterial immunity

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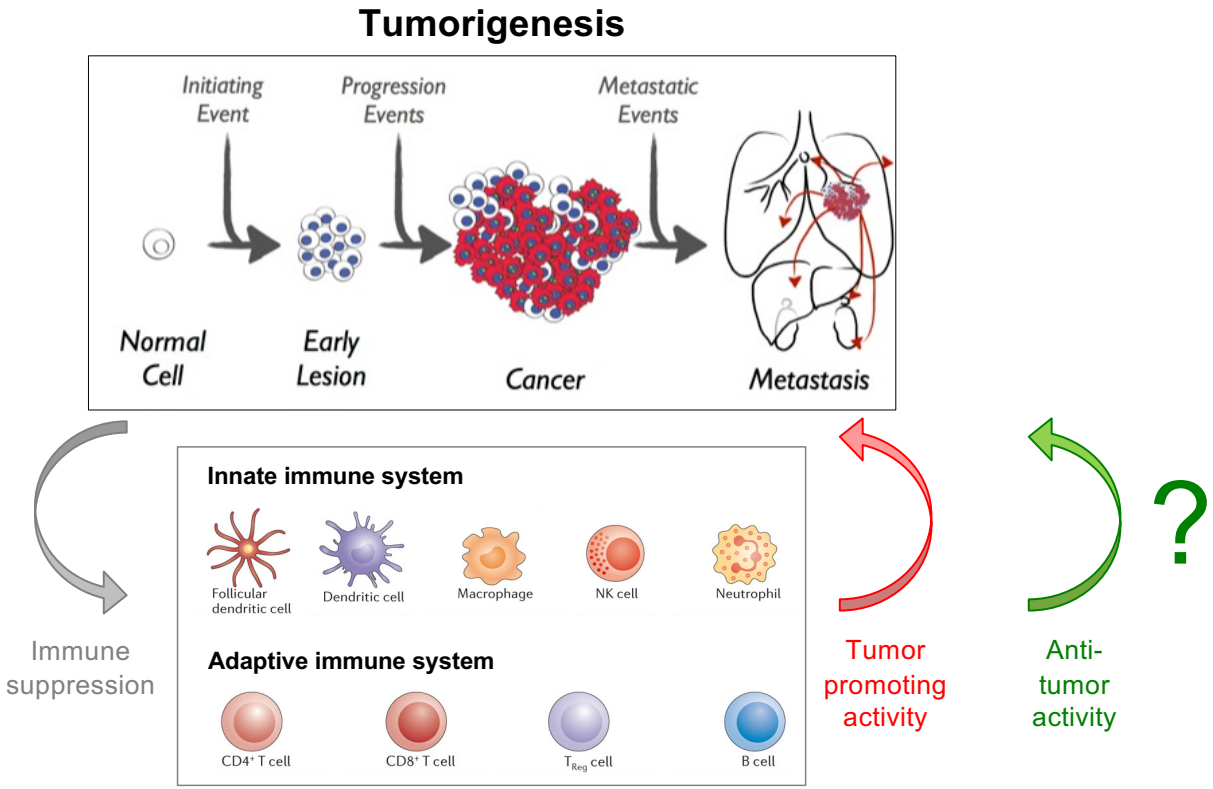
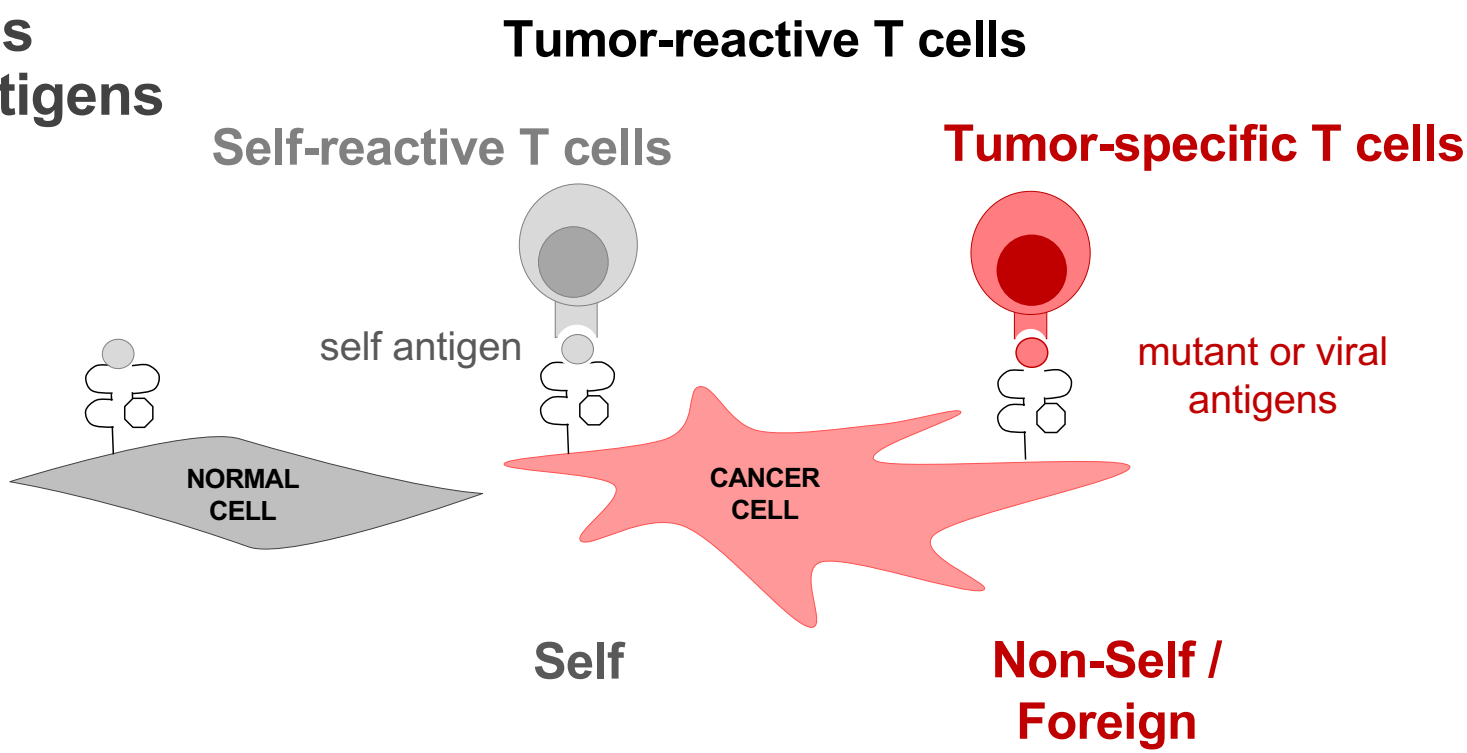
4. Immune Cells and Responses in Tumors

Anti-Tumor Immune Responses

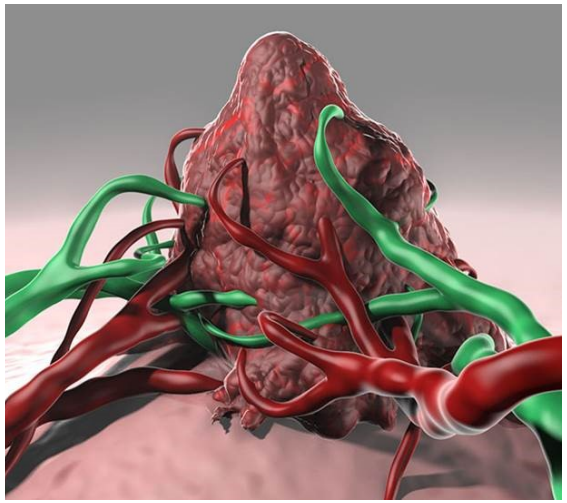


Cancer cells express antigens

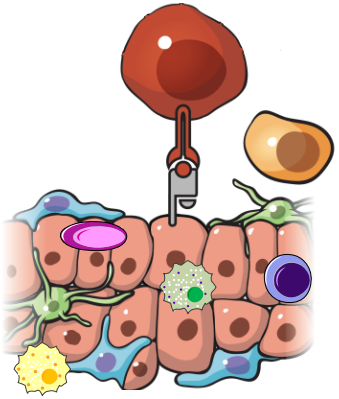


Immune suppression in tumors

Solid tumor



T cells fail to eliminate cancer cells



Immunosuppressive Microenvironment

Cellular factors
Regulatory CD4 T cells,
Suppressive Macrophages

Soluble factors
TGF-ß, IL-10

Physiological changes
Low Nutrients Levels, Low pH,
Low Oxygen